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Review: Nutritional requirements and dietary advice targeted for pregnant and breastfeeding women

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The NHMRC commissioned Adelaide Research and Innovation to undertake this review.

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Abbreviations

Abbreviation	Meaning
AHEI-P	Alternate Healthy Eating Index for Pregnancy
BaP	Benzo(a)pyrene
BMC	Bone Mineral Content
BMI	Body Mass Index
CI	Confidence Interval
DQI-P	Diet Quality Index - Pregnancy
EPA	Eicosapentaenoic acid
FFQ	Food frequency questionnaire
GA	Gestational age
GDM	Gestational diabetes mellitus
GI	Glycaemic index
GWG	Gestational weight gain
IGT	Impaired glucose tolerance
IQR	Interquartile range
IUGR	Intrauterine growth restriction
LA	Linoleic acid
LC-PUFAs	Long-chain polyunsaturated fatty acids
LGA	Large for gestational age
MD	Mean Difference
PAH	Polycyclic aromatic hydrocarbons
PCA	Principal component factor analysis
Pns	P value not significant
PTB	Preterm birth
RCTs	Randomised controlled trials
RRR	Reduced risk regression
SD	Standard deviation
SEM	Standard error of the mean
SES	Socio-economic status
SGA	Small for gestational age
SHBG	Sex Hormone Binding Globulin
SIDs	Sudden infant death syndrome

Abbreviation	Meaning
SR	Systematic review
SSB	Sugar sweetened beverages

Review Methods

Questions
The principal question addressed in this systematic review was:
What food groups consumed by pregnant and breastfeeding women, are associated with health outcomes for the mother and/or child?
The groups included dietary patterns; fruit; vegetables; meat; dairy foods (cheese, milks and yoghurt); cereals/grains; legumes; nuts and seeds; fish; poultry; eggs; fat/oil; salt/sodium; sugars; and beverages.

Search strategy
We searched the following databases and sources:

- Cochrane Library: issue 8, 2010 (published 4 August 2010);
- Other databases and sources to 31 July 2010 (including Pubmed, EMBASE, Austhealth, Google Scholar, Google, government and agency sources, other dietary guidelines).

These sources were searched from inception, with no date restrictions applied.

We made extensive use of pearling and snowballing strategies on retrieved references.

We did not apply language or publication status restrictions.

Search terms included:

- Maternal diet, pregnancy diet, pregnancy intake, breastfeeding diet, breastfeeding intake alone and in combination with the food patterns and food groups specified above.

We used Endnote to manage the references.

Inclusion and exclusion criteria
Studies needed to:

- be applicable to an Australian population
- be food-based not nutrient-based or assessing food supplements; and
- report maternal, fetal, infant, child (or child as an adult) health outcomes.

Data extraction

We designed a data extraction sheet specifically for this project. For each included study, one person extracted descriptive information, study design, study results, potential risk of bias, and relevance of the study. At least one other person checked the data extraction.

We used the NHMRC Hierarchies of Evidence to assign a level of evidence to each study, according to its particular hierarchy. Most included studies fell into the aetiology or intervention hierarchies.

Risk of bias

We used the Cochrane risk of bias tool to criticially appraise randomised controlled trials and adapted this tool and the set of NICE critical appraisal tools to assess other study designs such as cohort (aetiology) and case control studies.

Each included study was assessed as being of low, low-moderate, moderate, moderate-high or high risk of bias.

Structure of report

For each food group, we provided:

- A table of included studies (alphabetical by first author's surname with list of outcomes included in the study);
- An evidence summary arranged chronologically by outcome (e.g. pre-pregnancy, fetal, maternal antenatal, maternal postnatal, infant, child, child as an adult) and giving a quantitative results summary for each included study;
- Evidence tables of the detailed data extraction for each study, arranged alphabetically by first author's surname); and
- References for that particular food group.

Included studies

We included a total of 170 studies, with the following breakdown by food group (there is some overlap as some studies addressed multiple food groups and multiple outcomes):

Food group	Number of included studies	Number of participants
Dietary patterns	38	198,037
Caffeine	13	42,710
Cereal	20	27,201
Dairy foods	45	91,797
Dairy foods and eggs	4	3,918
Eggs	14	17,892
Fats and oils	18	68,398
Fish	63	359,332
Fruit	28	136,026
Fruit & vegetables	10	91,247
Legumes	9	17,640
Meat	32	99,772
Nuts and seeds	9	9,581
Salt/sodium	4	6,275
Sugar	14	20,286
Vegetables	31	89,753

Excluded studies

We excluded 116 studies in the following categories:

- Narrative review 2
- No perinatal outcomes 20
- Nutrient, not food based 49
- Supplements 21
- Other 24.

Pregnancy and breastfeeding dietary patterns

Included Studies

Study	Outcomes
1. Aaltonen 2008	Birthweight, birth length, head circumference at birth, infant blood pressure at 6 months, infant heart rate at 6 months, infant weight, length and head circumference at 6 months
2. Brantsaeter 2009	Pre-eclampsia
3. Chatzi 2008	Gestational age at birth, birthweight; child persistent wheeze, atopic wheeze, atopy (all at 6.5 years)
4. Cole 2009	Child bone mass, lean mass, fat mass (all at 9 years)
5. De Batlle 2008	Asthma, wheeze, rhinitis, sneezing, itchy-watery eyes (all at 6-7 years)
6. Duarte-Salles 2010	Birthweight
7. Hattevig 1989	Eczema, asthma, other atopic/allergic manifestations; Infant weight gain; maternal return to pre-pregnancy weight within 3 months after birth; breastfeeding
8. Haugen 2008	Preterm birth
9. Haugen 2005	Fetal ductus shunting, fetal liver blood flow
10. Hill 2005	Infant colic
11. Kinnunen 2007a	Achieving recommended dietary pattern; gestational weight gain, high birthweight, low birthweight
12. Kinnunen 2007b	Postpartum weight retention
13. Knudsen 2008	SGA, birthweight
14. Koebnick 2004	Vitamin B-12 deficiency (maternal)
15. Koebnick 2001	Folate status during pregnancy
16. Lange 2010	Child recurrent wheeze, asthma, eczema, lower respiratory tract infection, atopy (all at 3 years)
17. Laraia 2007	“Pre-pregnancy BMI”
18. Mikkelsen 2008	Preterm birth
19. Moses 2009a	Women’s need for insulin, birth outcomes
20. North 2000	Child hypospadias
21. Olafsdottir 2006	Gestational weight gain
22. Radesky 2008	IGT, GDM
23. Rifas-Shiman 2009	Pre-eclampsia, GDM, IGT, blood glucose, SGA, LGA, gestational weight gain
24. Robinson 2007	Infant diet
25. Rodriguez-Bernal 2010	FGR (weight, length, head circumference at birt6h)
26. Ross 1996	Childhood leukemia

27. Shaheen 2009	Wheeze at 6 months (transient, later onset, persistent); wheezing at 3.5 years; eczema (at 2.5 and 7.5 years); IgE at 7 years; hay fever at 7.5 years, bronchial responsiveness at 8-9 years; lung function (FEV1 and FVC) at 8-9 years
28. Siega-Riz 2001	Preterm birth
29. Stuebe 2009	Gestational weight gain
30. Thompson 2010	SGA
31. Tieu 2008	Birthweight, LGA, fasting blood glucose, gestational weight gain, GDM
32. Uusitalo 2009	Gestational weight gain
33. Vujkovic 2009	Spina bifida
34. Vujkovic 2007	Cleft palate, postpartum maternal BMI
35. Wolff 1995	Birthweight
36. Xiang 2005	Breastmilk composition, infant growth
37. Zeiger 1989	Allergy (various outcomes) ; birthweight; weight and height at 4,12 and 24 months; maternal third trimester weight gain
38. Zhang 2006	GDM

Evidence Summaries

	N	Level	References
Mother			

1. In a Norwegian cohort study:
• significantly **reduced rates of pre-eclampsia** were associated with
  o a high or medium 'vegetable' pattern compared with a low 'vegetable' pattern (aOR 0.72 95% CI 0.62 to 0.85 high; aOR 0.84 95% CI 0.73 to 0.97 medium)
• significantly **increased rates of pre-eclampsia** were associated with
  o a high 'processed food' pattern compared with a low 'processed food' pattern (aOR 1.21 95% CI 1.03 to 1.41)
• no significant differences in pre-eclampsia rates were seen between
  o low and medium 'processed food' patterns (aOR 1.06 95% CI 0.91 to 1.23)
  o low and medium 'potato and fish' pattern (aOR 0.99 95% CI 0.86 to 1.15)
  o low and high 'potato and fish' pattern (aOR 1.00 95% CI 0.84 to 1.18)
  o low and medium 'cakes and sweets' pattern (aOR 1.00 95% CI 0.86 to 1.15)
  o low and high 'cakes and sweets' pattern (aOR 0.90 95% CI 0.76 to 1.06)
	23,423	II	Brantsaeter 2009

2. In a US cohort study, significantly **reduced rates of pre-eclampsia in the 2nd trimester** were associated with higher diet quality (AHEI-P) although a significant reduction was not apparent in the 1st trimester: • 1st trimester – aOR 0.96 95% CI 0.84 to 1.10 • 2nd trimester – **aOR 0.87 95% CI 0.76 to 1.00**	1777	II	Rifas-Shiman 2009
3. In a US cohort study, women who were **obese (but not overweight)** before pregnancy were significantly more likely to have a poorer quality diet (less grain, fruit and vegetables, more fat) during pregnancy compared with normal weight women: • DQI-P score 53.3 [SD 12.0] for obese women; 55.3 [SD 11.3] for normal weight women ($p < 0.05$)	2394	II	Laraia 2007
4. In a retrospective cohort study from Finland, pregnant women: • **gained more kilograms a week** with diets high in 'fast food' (1.3 kg) and 'traditional bread' (0.9 kg) (p for trend = < 0.0001 and 0.002 respectively); • **gained less weight per week** (-0.7 kg) with a diet high in 'alcohol and butter' (p for trend = 0.014); • and showed no significant differences in weight gain with 'healthy'; 'traditional meats'; 'low fat'; and 'coffee'.	3360	III-3	Uusitalo 2009
5. In a US cohort study, neither **excessive or inadequate weight gain during pregnancy** were associated with dietary quality (as assessed by AHEI-P (per 5 points): • Excessive weight gain - aOR 0.99 95% CI 0.94 to 1.04 (1st trimester) and aOR 0.99 95% CI 0.94 to 1.04 (2nd trimester)	1777	II	Rifas-Shiman 2009

• Inadequate weight gain - aOR 0.95 95% CI 0.88 to 1.02 (1st trimester) and aOR 0.99 95% CI 0.92 to 1.07 (2nd trimester) In this study, no significant associations were seen between AHEI-P scores and **gestational diabetes mellitus**: • <u>*AHEI-P score (per 5 points)*</u> aOR 0.97 95% CI 0.87 to 1.08 (1st trimester) aOR 0.98 95% CI 0.87 to 1.09) (2nd trimester)			
6. In a cohort study from Iceland, eating more in early pregnancy was not significantly associated with either at least optimal gestational weight gain or excessive gestational weight gain, but eating more in late pregnancy was associated with significant increases in **at least optimal gestational weight gain** (aOR 3.32 95% CI 1.81 to 6.09) and **excessive gestational weight gain** (aOR 2.04 95% CI 1.17 to 3.58)	495	II	Olafsdottir 2006
7. In a US cohort study, a vegetarian diet was associated with lower odds of **excessive gestational weight gain** in the first trimester (aOR 0.45 95% CI 0.27 to 0.76) but not the second trimester (aOR 0.70 95% CI 0.40 to 1.20)	1338	II	Stuebe 2009
8. In a nonrandomised intervention study from Finland, meal pattern advice and advice to consume plenty of fruits, vegetables and high fibre bread and to restrict high sugar snacks in late pregnancy was not associated with excessive gestational weight gain (aOR 1.82 95% CI 0.65 to 5.14)	132	III-2	Kinnunen 2007a
9. In a US RCT, women allocated to a dietary avoidance regimen during pregnancy compared with women with a standard diet, showed a significant reduction in third trimester weight gain (MD -1.24 kg 95% CI -1.30 to -1.18)	98	II (RCT)	Zeiger 1989
10. In a US cohort study, diagnosis of **GDM**, or a diagnosis of **either GDM or IGT**, were not associated with: • A western diet during pregnancy (red and processed meats, sugar-sweetened beverages, French fries, high-fat dairy products, desserts, butter and refined grains); p for trend across quartiles for GDM = 0.80; • A prudent diet during pregnancy (high in vegetables, fruit, legumes, fish, poultry, eggs, salad dressing, and whole grains); p for trend across quartiles for GDM = 0.35	1773	II	Radesky 2008
11. In a US cohort study, diagnosis of **GDM** was Negatively associated with: • A prudent pre-pregnancy and pregnancy (fruits, green leafy vegetables, poultry and fish): p for trend across quintiles = 0.017 (adjusted) Positively associated with: • a western pre-pregnancy and pregnancy diet (red meat, processed meat, refined grain products, sweets, desserts, French fries and pizzas); p for trend across quintiles = 0.0011 (adjusted) No longer positively associated with: • a western pre-pregnancy and pregnancy diet when adjusted for red and processed meat consumption (p for trend across quintiles = 0.697 (adjusted)	13,110	II	Zhang 2006

12. In a Cochrane systematic review of RCTs • one RCT of 63 women showed no significant differences in **diagnosis of women with gestational diabetes mellitus** between the low and high glycaemic index groups: RR 0.31 95% CI 0.01 to 7.40 • **fasting blood glucose concentrations** were significantly lower in the low glycaemic index group: MD -0.28 mmol/L 95% CI -0.53 to -0.02 (two trials, 82 women) • no significant difference was seen for **maternal weight gain during pregnancy**: MD -3.33 kg 95% CI -12.73 to 6.08 (two trials, 82 women)	82	I	Tieu 2008
13. In an Australian RCT, • fewer women with gestational diabetes mellitus in a low glycaemic index (GI) diet group **required insulin**: 9/31 women in low GI group v 19/32 women in the high GI group (p = 0.023); • and after the 19 women in the high GI group were switched to a low GI diet this became 9/31 women in low GI group v 10/32 women in the high GI group (pns)	63	II	Moses 2009a
14. In a German cohort study, compared with women with a western diet during pregnancy (high in refined grain and meat): • Women with a ovo-lacto vegetarian diet during pregnancy had significantly **lower serum B-12** concentrations during pregnancy; p < 0.001; • Women with a low meat diet during pregnancy also had significantly **lower serum B-12** concentrations during pregnancy: p = 0.05	109	II	Koebnick 2004
15. In a German cohort study, compared with women with a western diet during pregnancy (high in refined grain and meat): • Women with a ovo-lacto vegetarian diet during pregnancy had significantly higher rates of **folate deficiency** during pregnancy; aOR 0.10 95% CI 0.01 to 0.56; • But nos significant difference was seen for women with a low meat diet during pregnancy; aOR 0.52 95% CI 0.20 to 1.34	109	II	Koebnick 2001
Fetal			
16. In a UK cohort study, • **Reduced fetal ductus venous shunting** was significantly associated with an 'imprudent' diet (high intakes of crisps/chips, sugar, confectionery, white bread, soft drinks, red meat and low intakes of fruit/vegetables, rice/pasta, yoghurt and wholemeal bread) (p = 0.04); but not with a 'Western' diet (with additional high intakes of fruit and vegetables) or a 'vegetarian' diet (vegetarian foods, confectionery, snack foods). • **Increased fetal liver blood flow** was significantly associated with an 'imprudent' diet (see above) - p = 0.02; but not with a 'Western' diet (with additional high intakes of fruit and vegetables) or a 'vegetarian diet (vegetarian foods, confectionery, snack foods).	381 preg-nancies	II	Haugen 2005
Congenital Anomalies			
17. In a case control study from the Netherlands, **increased risk of cleft lip or palate or both** was associated	481	III-3	Vujkovic 2007

with a western diet (high in meat, pizza, legumes and potatoes and low in fruit) during pregnancy, but no differences were seen for a prudent diet during pregnancy • Western diet: aOR 1.7 95% CI 1.0 to 3.0 (cleft lip/palate); aOR 1.8 95% CI 1.0 to 2.9 (cleft palate only)			
18. In a case control study from the Netherlands, a reduced risk of **spina bifida** was associated with a Mediterranean diet (high intakes of vegetables, fruit, legumes, vegetable oil, cereal products, alcohol and fish; and low intake of potatoes, sugar and confectionery, sauces and condiments) in a reduced rank regression analysis: • aOR 3.5 95% CI 1.5 to 8.2 (lowest quartile v highest quartile for Mediterranean diet)	131	III-3	Vujkovic 2009
19. In a prospective cohort study, **hypospadias** in male offspring was associated with a maternal vegetarian diet during pregnancy, compared with women who consumed an omnivorous diet during pregnancy: OR 3.53 95% CI 1.56 to 7.98	7928 boys	II	North 2000
Birth Outcomes			
20. In a Danish cohort study, a Mediterranean diet (consumption of fish twice a week or more, intake of olive or canola oil, high consumption of fruits and vegetables (5 a day or more), meat (other than poultry or fish) at most twice a week, and at most 2 cups of coffee a day) was not associated with decreased preterm birth except for reduced **early preterm birth (< 35 weeks)** with the highest level of adherence to a Mediterranean diet compared with the lowest: aOR 0.28 95% CI 0.11 to 0.76 (5 v 0 criteria). • No significant differences were seen for preterm birth < 37 weeks for 5 compared with 0 criteria; or for **preterm birth < 37 weeks** when 5 criteria were compared with 1-4 criteria for a Mediterranean diet.	35,530	II	Mikkelsen 2008
21. In a Norwegian cohort study, a Mediterranean diet (2 or more serves of fish per week, 5 or more vegetable/fruit serves per day, use olive oil or canola oil for cooking and dressings, eat no more than 2 serves of meat per week and drink no more than 2 cups of coffee per day) was not associated with decreased **preterm birth** (overall, early or late) when 5 criteria were compared with one, or 5 compared with 1-4 criteria	40,817	II	Haugen 2008
22. In a cohort study from the USA, women with a less optimal compared with an optimal meal pattern during pregnancy (three meals and two or more snacks a day) demonstrated no difference in **preterm birth** rates (aOR 1.30 95% CI 0.96 to 1.76) but did show a higher rate of **premature rupture of the membranes** (aOR 1.87 95% CI 1.02 to 3.43)	2065	II	Siega-Riz 2001

23. In a Danish cohort study:
o significantly **reduced rates of SGA** (z-score below 2.5th percentile for the respective gender and GA) were associated with
    o a 'health conscious' diet compared with a 'western' diet (aOR 0.74 95% CI 0.64 to 0.86)
    o an 'intermediate' diet compared with a 'western' diet (aOR 0.68 95% CI 0.55 to 0.84)
o no significant differences in **birthweight** (g, mean [SD]) were seen between any of the dietary patterns
    o 'western' diet 3583 [525]
	44,162	II	Knudsen 2008

o 'intermediate' diet 3623 [490] o 'health conscious' diet 3616 [486], p > 0.05			
24. In a US cohort study, **SGA (< 10th percentile)** was not associated with diet quality during pregnancy in either the 1st or 2nd trimester: • AHEI-P score (per 5 points) – aOR 0.92 95% CI 0.82 to 1.02 1st trimester; aOR 1.00 95% CI 0.90 to 1.10 2nd trimester	1777	II	Rifas-Shiman 2009
25. In a Spanish cohort study, **reduced risk of fetal growth restriction** (customised; 80% below the lower limit of the CI) was associated with higher AHEI-P scores for **weight (p = 0.001 for trend across AHEI-P quintiles) but not length (p = 0.538) or head circumference (p = 0.070)**	787	II	Rodriguez-Bernal 2010
26. In a New Zealand case-control study, **reduced risk of SGA (≤ 10th percentile for sex and gestation**) was significantly associated with a 'traditional' diet (meat (lamb in particular), potatoes, carrots (and other root vegetables), peas, gravy and meat dishes such as cottage pie, apples/pears, citrus fruit, kiwifruit/feijoas, bananas, green vegetables, maize, dairy food, yoghurt and water); • OR 0.79 95% CI 0.70 to 0.89 aOR 0.86 95% CI 0.75 to 0.99 but not with a 'junk' diet (icecream, sweet biscuits, scones, cakes, sweetened cereal, crisps, pies, lollies, chocolate bars, iceblocks and milo (chocolate energy drink) or a 'fusion' diet (fruits, fried rice/noodles, boiled rice/pasta, fish/shellfish, milk and low intake for tea/coffee, sherry/wine and hard cheeses): • *Fusion* OR 1.07 95% CI 0.95 to 1.21 aOR 1.02 95% CI 0.85 to 1.21 *Junk* OR 0.97 95% CI 0.70 to 1.09 aOR 1.01 95% CI 0.88 to 1.17	1714 children (844 born SGA)	III-3	Thompson 2010
27. In a Spanish cohort study, no significant differences were seen between a high level of adherence to a Mediterranean diet by women during pregnancy and **gestational age** (p = 0.477) or **birthweight** (p = 0.906).	507	II	Chatzi 2008
28. In an Australian RCT, neither **birth centiles or ponderal index** were significantly different for women with gestational diabetes who adopted a low or high glycaemic (GI) index diet during pregnancy: • **Birth centiles** Low GI: 46.3 [SEM 5.0] v high GI: 54.3 [4.8], p = 0.25 • **Ponderal index** Low GI: 2.7 [SEM 0.05] v high GI: 2.6 [SEM 0.04], p = 0.12 Three women (over both groups) had **LGA (≥ 90th centile) babies** and two women in the low GI group had **SGA**	63	II	Moses 2009a

(≤ 10th centile) babies			
29. In a Spanish cohort study • a diet high in benzo(a)pyrene (BaP) (from processed/cured meats, nuts and fats and oils) during the first trimester was significantly associated with **lower birthweight** (mean adjusted birthweight 142.73 g lower for the fourth compared with the first quartile of dietary BaP ($p < 0.05$)); • but BaP in the third trimester was not significantly associated with **birthweight**; and total polycyclic aromatic hydrocarbon (PAH) dietary intake (from high consumption of shellfish, processed/cured meats, milk/yoghurt, bread, sweet dairy foods, alcoholic beverages and sugar and BaP) in either first or third trimesters was not significantly associated with **birthweight**	657	II	Duarte-Salles 2010
30. In a Cochrane systematic review, • there were significantly fewer **large for gestational age** infants when women adopted a low GI diet: RR 0.09, 95% CI 0.01 to 0.69 (one trial of 62 women); • No significant difference in **ponderal index**: mean difference (MD) -0.18 95% CI -0.32 to -0.04 (two trials; 82 women); • Effect for women on the LGI diet on **birthweight** were not conclusive under a random-effects model (two trials; WMD -527.64 g, 95% CI -1119.20 to 63.92)	107	I	Tieu 2008
31. In a US cohort study, **large for gestational age** was not associated with diet quality (AHEI-P) during pregnancy in either the 1st or 2nd trimester: • aOR 0.95 95% CI 0.89 to 1.02 (1st trimester) • aOR 0.99 95% CI 0.92 to 1.07 (2nd trimester)	1777	II	Rifas-Shiman 2009
32. In a nonrandomised intervention study from Finland, meal pattern advice and advice to consume plenty of fruits, vegetables and high fibre bread and to restrict high sugar snacks in late pregnancy was associated with significantly decreased rates of **high birthweight** (≥ 4000 g); $p = 0.006$) but not **low birthweight** (< 2500 g)	132	III-2	Kinnunen 2007a
33. In a Finnish RCT, compared with a control group, children of the women in the dietary advice/healthy diet group did not show significant differences for: • **Birthweight, birth length or head circumference at birth**; • Infant blood pressure, infant heart rate, infant weight, length or head circumference at six months	171	II	Aaltonen 2008
34. In a US cohort study, **birthweight** was positively associated with nutrient dense (plenty of fruit and vegetables and low fat dairy foods) and protein rich (low fat meat, processed meats and high fat dairy foods) maternal diet patterns and negatively associated with nutrient dilute (high calorie snacks and desserts) and transitional (high in fats and oils, breads and cereals, low in vitamin A and C rich vegetables, high fat meat and sugar) maternal diet patterns	549 women and their 778 children	II	Wolff 1995

Breastfeeding			
35. In a nonrandomised comparison from Sweden, **full breastfeeding rates** were not significantly different between a maternal diet group (no eggs, cow's milk or fish from birth to three months) and the no diet group: • > 3 months: 59% versus 68% • Up to 6 months: 43% versus 36%	115	III-2	Hattevig 1989
36. In a cohort study from China and Sweden, **breastmilk** of the Chinese women was less balanced (significantly richer in LA and lower in EPA and DHA) than Swedish women (who consumed higher rates of bread, potato, pasta, milk and cheese); and no differences were seen for **infant growth**	57	II	Xiang 2005
Maternal Postpartum Follow-Up			
37. In a case-control study from the Netherlands, increased **maternal postpartum BMI at 14 months** was significantly associated with a western diet (high in meat, pizza, legumes and potatoes and low in fruit) but no BMI differences were seen across the tertiles of a prudent diet (high intake of fish, garlic, nuts, and vegetables): • Western diet – p for trend 0.01 • Prudent diet – p for trend 0.75	164	III-3	Vujkovic 2007
38. In a nonrandomised comparison from Sweden, significantly more women in a diet group (no eggs, cows' milk or fish from birth to three months) returned to their **pre-pregnancy weight in three months** compared with the no diet group: 66% versus 20%, $p < 0.001$	115	III-2	Hattevig 1989
39. In a nonrandomised intervention study from Finland, meal pattern advice and advice to consume plenty of fruits, vegetables and high fibre bread and to restrict high sugar snacks after birth was associated with significantly more women **not retaining extra weight gained during gestation** (aOR 3.89 95% CI 1.16 to 13.04) at 10 months postpartum	92	III-2	Kinnunen 2007b
Childhood Asthma, Eczema and Other Allergy Outcomes			
40. In an Australian RCT, exclusively breastfed infants whose mothers consumed a low allergen diet showed significantly **greater improvement in colic symptoms** compared with mothers whose diets contained those allergenic foods: ARR 0.37 95% CI 0.18 to 0.56	107	II	Hill 2005
41. In a US RCT, women (third trimester and while breastfeeding) and their infants (when breastfeeding was supplemented or stopped) allocated to a dietary avoidance regimen compared with women and infants with a standard diet, showed: • No significant differences in **birthweight, infant weight or height at 4, 12 and 24 months;** • Lower mean **third trimester weight gain**: MD -1.24 kg 95% CI -1.30 to -1.18; • Lower rates of **any atopic disorder** at 12 months, but not at 4 or 24 months; • No significant difference in **asthma** at 4, 12 and 24 months; • Lower **food allergy** at 12 and 24 months , p = 0.007 and 0.005 respectively;	379	II	Zeiger 1989

• Cumulative reduction in **food allergy** at 4 years, with similar current prevalence; • No significant differences at 7 years for **food allergy, atopic dermatitis, allergic rhinitis, asthma, any atopic disease, lung function or aeroallergen sensitisations**			
42. In a nonrandomised comparison from Sweden, children whose mothers had a diet free from eggs, cow's milk or fish from birth to three months were significantly less likely to develop **<u>eczema</u>** up to six months compared with the no diet group, but this effect was not sustained from nine to 18 months No significant differences between the diet and no diet groups were seen for **asthma and adverse reactions** of infants to eggs, cows' milk and fish up to 18 months of age	115	III-2	Hattevig 1989
43. In a US cohort study, **recurrent wheeze, asthma, eczema, or respiratory infection in children at 3 years** was not associated with either a high maternal adherence to a Mediterranean diet (high dairy, fish, fruit, legumes, nuts, unsaturated fats, vegetables, and whole grains and low red and processed meats); or AHEI-P; or a prudent diet (fruits, tomatoes, cabbage, leafy green vegetables, poultry, fish).	1376 children	II	Lange 2010
44. In a UK cohort study, **wheeze in children at 6 months and 3.5 years, eczema at 2.5 years and 7.5 years, hay fever at 7.5 years, bronchial responsiveness and lung function at 8.9 years of age** were not generally associated with various dietary patterns such as 'health conscious', 'traditional', 'processed', 'vegetarian' or 'confectionery'. • In a subset of 4198 children, those whose mothers had a 'health conscious' diet (salad, fruit, fruit juices, rice, pasta, oat/bran based breakfast cereals, fish, pulses, cheese, nonwhite bread) were more likely to have a **positive IgE** (aOR 1.07 95% CI 1.00 to 1.14) and and those whose mothers had a 'traditional' diet (vegetables, red meat, poultry) were less likely to have a **positive IgE** (aOR 0.96 95% CI 0.91 to 1.00).	8,886 children	II	Shaheen 2009
45. In a Spanish cohort study, reductions in **persistent wheeze, atopic wheeze and atopy in children at 6.5 years of age** were associated with a high adherence to a Mediterranean diet by their mothers: • Persistent wheeze aOR 0.22 95% CI 0.08 to 0.58 • Atopic wheeze aOR 0.30 95% CI 0.10 to 0.90 • Atopy aOR 0.55 95% CI 0.31 to 0.97	483 children	II	Chatzi 2008
46. In a Mexican retrospective cohort study, **asthma, wheezing and most allergy symptoms in children at 6-7 years of age** were not associated with their mothers adhering to a Mediterranean diet (high in vegetables, legumes, fruits and nuts, cereals and fish and low in dairy products, meat, junk food and fat): • Asthma (ever in child) aOR 1.03 95% CI 0.67 to 1.56 • Wheezing (ever in child) aOR 0.74 95% CI 0.55 to 1.01 • Rhinitis (ever in child) aOR 0.64 95% CI 0.36 to 1.15	1326 children	III-2	De Batlle 2008
Other Childhood Outcomes			
47. In a cohort study from the UK, **high diet quality of infants** was positively associated with a high quality	1434	II	Robinson 2007

maternal diet: • Association between maternal prudent diet and 'infant guidelines' diet 6 months: ß 0.196 95% CI 0.135 to 0.257; p < 0.001 12 months: ß 0.282 95% CI 0.220 to 0.343; p < 0.001 • Association between maternal prudent diet and 'adult' diet 6 months: ß -0.074 95% CI -0.132 to -0.015; p < 0.05 12 months: ß -0.215 95% CI -0.270 to -0.160; p < 0.001	children		
48. In a case-control study from North America, **childhood acute myeloid leukemia (but not acute lymphoblastic leukemia) in children up to one year of age** was associated with moderate to high consumption of foods containing DNA topoisomerase II inhibitors (beans, fresh and canned vegetables, fruits, soy, coffee, wine, black and green tea and cocoa); • OR for acute myeloid leukemia (high versus low consumption): 10.2 95% CI 1.1 to 96.4) • OR for acute lymphoblastic leukemia (high versus low consumption (0.5 95% CI 0.2 to 1.4)	303 cases; 468 controls	III-3	Ross 1996
49. In a nonrandomised comparison from Sweden, **infant weight gain up to 18 months** did not differ significantly between women with a diet free from eggs, cow's milk and fish from birth to three months postpartum and women with an unrestricted diet	115	III-2	Hattevig 1989
50. In a UK cohort study, most measures of **bone mass in children at 9 years of age** were positively associated with their mothers adhering to a prudent diet (high intake of fruit, vegetables, wholemeal bread, rice, pasta, yoghurt, cheese, fish, reduced fat milk and low intake of white bread, added sugar, tinned vegetables, full fat milk and crisps) in pregnancy: • Child whole body bone area at 9 years: positive correlation with maternal prudent diet in late pregnancy: r = 0.24, p = 0.001 (adjusted for age and sex) • Bone mineral content at 9 years: positive correlation with maternal prudent diet in late pregnancy: r = 0.23, p = 0.001 (adjusted for age and sex)	198 children	II	Cole 2009

Evidence Tables

Reference	Aaltonen 2008
Dietary patterns	increased intake of unsaturated fatty acids and reduced saturated fat intake, increased vegetables, fruits, whole-grain bread and cereals, lean meat products, low-fat cheese and milk
Study type	RCT
Level of evidence	II (Intervention)
Setting	Maternal welfare clinics in Turku, Finland
Funding	Academy of Finland, Social Insurance Institute of Finland, Sigrid Juselius Foundation, Turku University Foundation, Raisio Group, Finland
Participants	171 mothers and their infants (86 randomised to diet group and 85 to control group)
Baseline comparisons	Similar in both groups (includes maternal blood pressure in third trimester, weight gain during pregnancy and duration of pregnancy)
Dietary assessment	3 day food diaries
Timing	Women recruited “early in pregnancy” and visited the clinic three times during their pregnancy and once when the infant was 6 months of age
Comparison	Dietary counselling and diet v control (part of probiotics RCT) For the intervention a dietitian counselled women to increase their intake of unsaturated fatty acids and reduce saturated fat intake; and to encourage consumption of vegetables, fruits, whole-grain bread and cereals, lean meat products, low-fat cheese and milk. Food products with favourable fat compositions (canola spreads and salad dressings) and fibre contents (fibre-enriched pasta, breakfast muesli, porridge) were provided.
Outcomes	Infant blood pressure at 6 months; infant growth (weight, length and head circumference) at 6 months; birthweight
Results	(see below)

Infant blood pressure at 6 months, mmHg (mean difference 95% CI)

	Diet group (n = 56)	Control group (n = 57)	p value
Systolic	97 (94 to 99)	98 (96 to 101)	pns
Mean	77 (75 to 79)	78 (75 to 80)	pns
Diastolic	63 (61 to 65)	64 (61 to 66)	pns

Infant heart rate at 6 months (mean difference 95% CI)

Diet group (n = 56)	Control group (n = 57)	p value
136 (132 to 140)	134 (131 to 137)	pns

Infant weight at 6 months, g (mean difference 95% CI)

Diet group (n = 73)	Control group (n = 70)	p value
8228 (8000 to 8456)	8262 (8034 to 8490)	pns

Infant length at 6 months, cm (mean difference 95% CI)

Diet group (n = 73)	Control group (n = 70)	p value
69.0 (68.5 to 69.6)	69.0 (68.5 to 69.9)	pns

Infant head circumference, cm at 6 months (mean difference 95% CI)

Diet group (n = 61)	Control group (n = 56)	p value
44.0 (43.7 to 44.4)	44.0 (43.5 to 44.5)	pns

Birthweight, g (mean difference 95% CI)

Diet group (n = 78)	Control group (n = 78)	p value

	3628 (3542 to 3713) 3600 (3483 to 3716) pns **Birth length, cm (mean difference 95% CI)** Diet group (n = 78) Control group (n = 78) p value 51.3 (51.0 to 51.7) 51.0 (50.5 to 51.5) pns **Head circumference at birth, cm (mean difference 95% CI)** Diet group (n = 78) Control group (n = 77) p value 35.1 (34.9 to 35.4) 35.1 (34.8 to 35.5) pns
Followup	6 months after birth
Confounding	NA
Risk of bias	Moderate risk of bias: No details about method of allocation concealment; Not feasible to blind this intervention; 28/171 (16.4%) lost to follow-up at 6 months – 13 in the diet group (2 miscarriages, 2 due to illness in mother, 1 due to illness in child, 4 unwilling to continue, 2 moved, 1 unknown, 1 twin pair excluded) and 15 in the control group (3 due to illness in mother, 2 due to illness in child, 8 unwilling to continue, 2 unknown). For the primary outcome of infant blood pressure at 6 months, results were available for 113/171 (66.1%) infants
Relevance	Likely to be relevant for Australian women
Other comments	NCT00167700 Total energy intake remained comparable between the groups although women in the dietary intervention group consumed significantly less butter and more margarine and vegetable oil Study probably underpowered (no sample size calculation reported)

Reference	**Brantsaeter 2009**
Dietary patterns	1) Vegetable (high positive loadings on vegetables, cooking oil, olive oil, fruits and berries, rice and chicken) 2) Processed food (high positive loadings on processed meat products, white bread, French fries, salty snacks and sugar-sweetened drinks; high negative loadings on oily fish, high fibre breakfast cereals and lean fish) 3) Potato and fish (high positive loadings on cooked potatoes, processed fish, lean fish, fish spread and shellfish and margarine) 4) Cakes and sweets (high positive loadings on cakes, waffles, pancakes, buns, ice cream, sweet biscuits, sweets and chocolate)
Study type	Prospective cohort (factor analysis)
Level of evidence	II (aetiology)
Setting	Norway, from February 2002 to 2007; part of Norwegian Mother and Child Cohort Study (MoBa)
Funding	Norwegian Ministry of Health; Norwegian Research Council; European Commission
Participants	23,423 nulliparous pregnant women; > 99% Caucasian ethnicity
Baseline comparisons	All reported baseline characteristics were adjusted – *see Confounding* [vitamin D was adjusted for in a separate analysis but this did not alter any of the associations]
Dietary assessment	FFQ
Timing	General health questionnaire at 15 weeks GA; FFQ at 17-22 weeks GA
Comparison	4 dietary patterns: *See Dietary patterns above*
Outcomes	Pre-eclampsia (defined as blood pressure > 140/90 after 20 weeks GA, combined with proteinuria >+1 dipstick on at least 2 occasions)
Results	<u>Vegetable pattern</u> **Lowest tertile v middle tertile: aOR 0.84 95% CI 0.73 to 0.97** **Lowest tertile v highest tertile: aOR 0.72 95% CI 0.62 to 0.85** <u>Processed food pattern</u> Lowest tertile v middle tertile: aOR 1.06 95% 0.91 to 1.23 **Lowest tertile v highest tertile: aOR 1.21 95% CI 1.03 to 1.41** <u>Potato and fish pattern</u> Lowest tertile v middle tertile: aOR 0.99 95% CI 0.86 to 1.15 Lowest tertile v highest tertile: aOR 1.00 95% CI 0.84 to 1.18 <u>Cakes and sweets pattern</u> Lowest tertile v middle tertile: aOR 1.00 95% CI 0.86 to 1.15 Lowest tertile v highest tertile: aOR 0.90 95% CI 0.76 to 1.06
Followup	To birth
Confounding	Adjusted for maternal prepregnancy BMI, maternal age, maternal height, length of education, smoking, hypertension prior to pregnancy, dietary supplement use, total energy intake
Risk of bias	Low-moderate: healthier women more likely to participate; possibility of residual confounding
Relevance	More fish intake than an Australian population; less ethnic diversity than Australia;
Other comments	Difficult to interpret results with some overlapping food groups between the four dietary patterns; Overall participation in MoBa was about 44%

Reference	**Chatzi 2008**
Dietary patterns	Mediterranean diet (high intake of vegetables, legumes, fruits and nuts, cereal, fish, dairy products and low intake of red meat)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women presenting antenatal care at general practices in Menorca, a Mediterranean island in Spain (mid 1997 to mid 1998)
Funding	Instituto de Salud Carlos III red de Grupos Infancia y Media Ambiente, the Fundacio "La Caixa", Instituto de Salud Carlos III, red de Centros de Investigacion en Epidemiologica y Salud Publica, EU, National Center for Environmental Health, USA, the GA2LEN project, Ministry of Education and Science, Spain, Oficina de Ciencia y Tecnologia, Generalitat Valenciana.
Participants	482 children of 507 women who had attended antenatal care in Menorca
Baseline comparisons	*See confounding below*
Timing	not clear when women did FFQ and period of pregnancy it was intended to cover
Comparison	Mediterranean diet score (0 = minimal adherence to 7 = maximal adherence): high Mediterranean diet quality (4-7) v low Mediterranean diet quality (≤ 3) [dairy assumed to be protective for pregnant women; alcohol consumption not included in the score]
Outcomes	Persistent wheeze, atopic wheeze and atopy at 6.5 years [gestational age; birthweight]
Results	***Persistent wheeze at 6.5 years*** **aOR 0.23 95% CI 0.09 to 0.60** (also adjusted for firstborn and lower respiratory tract infections at age 1) **aOR 0.22 95% CI 0.08 to 0.58** (additionally adjusted for child's adherence to a Mediterranean diet) ***Atopic wheeze at 6.5 years*** **aOR 0.34 95% CI 0.12 to 0.97** (also adjusted for birthweight and maternal atopy) **aOR 0.30 95% CI 0.10 to 0.90** (additionally adjusted for child's adherence to a Mediterranean diet) ***Atopy at 6.5 years*** **aOR 0.55 95% CI 0.32 to 0.97** (also adjusted for birthweight and maternal atopy) **aOR 0.55 95% CI 0.31 to 0.97** (additionally adjusted for child's adherence to a Mediterranean diet) High level of adherence to a Mediterranean diet and gestational age: p = 0.477 High level of adherence to a Mediterranean diet and birthweight: p = 0.906
Followup	6.5 years
Confounding	Analyses adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years and total energy intake at 6.5 years
Risk of bias	Low risk of bias: Results from 468/482 children (97%) able to be analysed (6 incomplete data and 8 implausible values);
Relevance	Diets in Menorca may differ from diets of Australian women, particularly urban women
Other comments	

Reference	**Cole 2009**
Dietary patterns	'Prudent' diet (high intake of fruit, vegetables, wholemeal bread, rice, pasta, yoghurt, cheese, fish, reduced fat milk and low intake of white bread, added sugar, tinned vegetables, full fat milk and crisps)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Princess Anne Maternity Hospital, Southampton, UK
Funding	National Osteoporosis Society, UK; North East Thames NHS R&D Directorate, Arthritis Research Campaign; The Cohen Trust; WellChild.
Participants	198 children of white women > 16 years of age with singleton pregnancies of < 17 weeks gestation. Women were recruited in 1991-2 and when their children approached 9 years of age, 461 women who still lived in Southampton were invited to participate and 251 (47%) of these women agreed to attend a clinic with their child. Exclusions: Diabetic women and those who had undergone hormonal treatment to conceive.
Baseline comparisons	Participants slightly older, less likely to have smoked at conception, better educated and had a higher late pregnancy prudent diet score than nonparticipants
Timing	FFQ for preceding 3 months in early (15 weeks gestation) and late pregnancy (32 weeks gestation)
Comparison	High score v lower score for prudent diet
Outcomes	Child's bone mass (bone mineral content (BMC)) at 9 years; lean and fat mass
Results	 ***<u>Child whole body bone area at 9 years:</u>*** **Positive correlation with maternal prudent diet in late pregnancy: r = 0.24, p = 0.001 (adjusted for age and sex)** ***<u>Child BMC at 9 years:</u>*** **Positive correlation with maternal prudent diet in late pregnancy: r = 0.23, p = 0.001 (adjusted for age and sex)** **[p = 0.02 adjusted for maternal social class, education, body build and smoking; p = 0.03 additionally adjusted for child's height, weight, sports participation, and milk intake; p = 0.04 additionally adjusted for maternal vitamin D status]** ***<u>Child areal bone mass density at 9 years:</u>*** **Positive correlation with maternal prudent diet in late pregnancy: r = 0.15, p = 0.02 (adjusted for age and sex)** *<u>Child volumetric bone density mass at 9 years:</u>* No significant relationship with maternal dietary pattern ***<u>Child lumbar spine BMC at 9 years:</u>*** **Positive correlation with maternal prudent diet in late pregnancy: r = 0.17, p = 0.02 (adjusted for age and sex)** ***<u>Child lumbar spine bone density mass at 9 years:</u>*** **Positive correlation with maternal prudent diet in late pregnancy: r = 0.18, p = 0.01 (adjusted for age and sex)** Percentage of <u>total variance in whole body bone areal bone mass density and BMC</u> explained by maternal prudent diet in late pregnancy ranged from 2% to 6%. ***<u>Child lean mass at 9 years:</u>*** **<u>For an SD increase in late pregnancy prudent diet score, lean mass rose by 656.0 g 95% CI 304.3 to 1007.7 (adjusted for age and sex) [similar results with high score in early pregnancy]</u>** *<u>Child fat mass at 9 years:</u>*

	No significant associations with prudent diet score either in early or late pregnancy
Followup	9 years
Confounding	Significant associations between diet and factors such as maternal social class; analyses adjusted for these factors only presented for BMC
Risk of bias	Moderate-high risk of bias: Poor initial response rate (47%); high attrition from 251 to 198 children (only able to trace some of the cohort); no explanation given for only including white women.
Relevance	Population and dietary patterns likely to be relevant to Australian women
Other comments	

Reference	**De Batlle 2008**
Dietary patterns	Mediterranean diet scores (women in the upper half of consumption of vegetables, legumes, fruits and nuts, cereals and fish and in the lower half of consumption of dairy products, meat, junk food and fat added 1 to their score)
Study type	Retrospective cohort study
Level of evidence	III-2 (aetiology)
Setting	Mexican schools
Funding	National Center for Enviromental Health, Center for Disease Control and Prevention, USA; Ministry of Health, Mexico; Ministry of Health, Spain, GA^2LEN Proect (EU), Ministry of Education and Science, Spain
Participants	1476 children, 6-7 years old
Baseline comparisons	Participating women were more likely to have higher education levels, less likely to smoke and less likely to have asthma
Timing	During pregnancy (not further specified)
Comparison	High versus lower Mediterranean diet scores (1^{st} tertile v 2^{nd} and 3^{rd} tertiles)
Outcomes	Asthma, allergic rhinitis
Results	*Asthma (ever in child):* aOR 1.03 95% CI 0.67 to 1.56 [n assumed to be 1326] *Wheezing (ever in child):* aOR 0.74 95% CI 0.55 to 1.01 [n assumed to be 1326] *Wheezing (currently in child):* aOR 1.02 95% CI 0.65 to 1.60 [n assumed to be 1326] *Rhinitis (ever in child):* aOR 0.64 95% CI 0.36 to 1.15 [n assumed to be 1326] *Rhinitis (currently in child):* aOR 0.87 95% CI 0.65 to 1.18 [n assumed to be 1326] ***Sneezing (currently in child):*** **aOR 0.71 95% 0.53 to 0.97 [n assumed to be 1326]** *Itchy-watery eyes (currently in child):* aOR 0.96 95% CI 0.64 to 1.45 [n assumed to be 1326] (similar results for all crude analyses)
Followup	Not stated but presumed to be 6-7 years
Confounding	Analyses were adjusted for gender of child, physical exercise of child, current tobacco smoking at home, maternal education, maternal asthma, maternal rhinitis
Risk of bias	Moderate to high risk of bias; 81% (2528/3125) parents consented to participation; 489 children were subsequently excluded because of no diet data; high risk of recall bias, as mothers were asked to recall their diet during their pregnancy from over 6 years earlier.
Relevance	Nutrition status of pregnant women in Mexico may be different to women in Australia
Other comments	This study also looked at associations between children's diet and asthma and allergy outcomes

Reference	**Duarte-Salles 2010**
Dietary patterns	Diet high in polycyclic aromatic hydrocarbons (PAH) – from high consumption of shellfish, processed/cured meats, milk/yoghurt, bread, sweet dairy foods, alcoholic beverages and sugar and benzo(a)pyrene (BaP) – from processed or cured meat, nuts and fats and oils
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Sabadell, Spain
Funding	Spanish Ministry of Health, Instituto de Salud Carlos III, Generalitat de Catalunya-CIRIT
Participants	657 women recruited in the first trimester of pregnancy (part of INMA project) from July 2004 to July 2006
Baseline comparisons	Not reported
Dietary assessment	FFQ
Timing	"during first and third trimesters"
Comparison	Amounts of dietary PAH and total PAH; and BaP
Outcomes	Birthweight
Results	**<u>Birthweight</u>** **BaP in first trimester significantly associated with lower birth weight (after adjusting for potential confounders such as cigarette smoke exposure): mean birthweight 142.73 lower for the fourth compared with the first quartile of dietary BaP ($p < 0.05$);** BaP in third trimester not significantly associated with birthweight; Total PAH in either first or third trimesters not associated with birthweight
Followup	To birth
Confounding	Not reported which confounders were used in analyses (except for cigarette smoke exposure)
Risk of bias	Unclear risk of bias: confounders and birthweight results not fully reported
Relevance	Women in this study likely to consume more cured meats than Australian women
Other comments	Smoking during pregnancy was associated with higher dietary PAH in the study population

Reference	**Hattevig 1989 (and Hattevig 1999 – 10 year follow-up)**
Food type	Eggs, cows' milk and fish
Study type	Nonrandomised concurrent comparison; groups from two different locations
Level of evidence	III-2 (intervention)
Setting	Southwestern Sweden
Funding	Swedish Medical Research Council, Konsul Th Berg Foundation, Council of Skaraborg, KSS Barnmed Foundation
Participants	115 children of pregnant women in southwestern Sweden visiting antenatal clinics from August 1984 to March 1986, with a history of previous or present atopic dermatitis, allergic rhinoconjunctivitis or asthma in the pregnant woman, her husband or their children. Families had to be non-smoking and without indoor pet animals
Baseline comparisons	Not reported
Dietary assessment	n/a
Timing	n/a
Comparison	Diet group (n = 65 infants): dietitian advised family how to achieve a diet free from eggs, cows' milk and fish from birth for 3 months (mothers were supplemented with extra calcium and multivitamins during the 3 month diet period); Non diet group (n = 50): usual care (no particular dietary information was given) Infant diet was the same for both groups – only breastmilk and/or formula based on hydrolysed casein during first 6 months, after 6 months, supplementary foods, including cows' milk products were introduced in all children. Products containing eggs and fish were not introduced until after 9 months of age. Supplemental A-D vitamins were given at 6 weeks.
Outcomes	Dermatitis (eczema), asthma (3 or more bronchial obstructions) and other atopic/allergic manifestations; Infant weight gain; Maternal return to pre-pregnancy weight within 3 months after birth; breastfeeding
Results	**<u>Maternal return to pre-pregnancy weight within 3 months after birth:</u>** **66% of mothers in the diet group compared with 20% in the non diet group; p < 0.001** **<u>Breastfeeding</u>**: Full breastfeeding > 3 months: 59% in diet group compared with 68% in non diet group, pns Full breastfeeding up to 6 months: 43% in diet group compared with 36% in non diet group, pns **<u>Infant weight gain</u>** No significant difference between infants in the diet and non diet groups (exact numbers not reported)

		Age interval (months) Diet group: n= 65; No diet group: n=50				
		0-3	**0-6**	**0-9**	**0-12**	**0-18**
Eczema	Diet	**3.1%***	**10.8%***	16.9%	23.1%	26.2%
	No diet	**22.0%***	**28.0%***	30.0%	28.0%	40.0%
Asthma / bronchial obs.	Diet	0	3.1%	4.6%	7.7%	14.0%
	No diet	0	2.0%	4.0%	8.0%	8.0%
Other	Diet	0	3.1%	9.2%	13.8%	16.9%
	No diet	0	2.0%	4.0%	10.0%	10.0%

Adverse reactions to:

Eggs	Diet	0	1.5%	1.5%	1.5%	7.7%
	No diet	2.0%	2.0%	2.0%	2.0%	6.0%
Cows' milk	Diet	0	3.1%	10.8%	10.8%	10.8%
	No diet	4.0%	6.0$	14.0%	14.0%	14.0%
Fish	Diet	0	3.1%	3.1%	3.1%	3.1%
	No Diet	0	0	0	3.1%	3.1%
Totals	Diet	0	6.0%	10.8%	10.8%	12.3%
	No Diet	6.0%	8.0%	16.0%	18.0%	18.0%

Atopic dermatitis in children at 10 years of age:
Current: 18/50 in diet group versus 14/65 in non-diet group, pns
Cumulative: 28/50 in diet group versus 30/60 in non-diet group, pns

Bronchial asthma in children at 10 years of age:
Current: 9/50 in diet group versus 11/65 in non-diet group, pns
Cumulative: 14/50 in diet group versus 14/60 in non-diet group, pns

Allergic rhinocomjunctivis in children at 10 years of age:
Current: 20/50 in diet group versus 18/65 in non-diet group, pns
Cumulative: 22/50 in diet group versus 19/60 in non-diet group, pns

Adverse reactions to food (eggs, cow's milk or fish) in children at 10 years of age:
7/50 in diet group versus 8/65 in non-diet group, pns

**** statistically significant difference between groups***

Followup	First 18 months of life; children at 10 years of age
Confounding	Not reported that any adjustments to analyses were made
Risk of bias	Moderate risk of bias; losses not clearly reported – 8/121 (6.6%) infants failed to complete study (but 237 pregnant women were recruited); imbalance in final numbers in the two study groups; groups matched on atopic but no other factors reported
Relevance	May be difficult to adhere to a strict non egg, non cows' milk and non fish diet
Other comments	Likely to be underpowered

Reference	**Haugen 2008**
Dietary patterns	Mediterranean-type diet – 5 criteria (2 or more serves of fish per week, 5 or more vegetable/fruit serves per day, use olive oil or canola oil for cooking and dressings, eat no more than 2 serves of meat per week and drink no more than 2 cups of coffee per day).
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Norway (part of the Norwegian Mother and Child Cohort Study (MoBa))
Funding	Norwegian Ministry of Health, NIH/NINDS, Norwegian Research Council/FUGE, EU FP& consortium, Metabolic Programming (EARNEST).
Participants	40,817 pregnancies of women recruited for MoBa from February 2002 to February 2005 of whom 26,563 (65%) met the following criteria: women had to be non-smoking, BMI between 19 and 32, aged between 21 and 38 years when giving birth, with a singleton birth. Exclusions: more than 3 spontaneous abortions, energy intake less than 4,200 kJ and more than 16,700 kJ.
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	at 17-24 weeks gestation
Comparison	All 5 Mediterranean diet criteria met (n = 569) v 1-4 criteria met (n = 25,397) v no criteria met (n = 159)
Outcomes	Preterm birth (after week 21 and before week 37); late preterm birth (week 35-36) and early preterm birth (< 35 weeks)
Results	**5 v 0 criteria:** *Preterm birth (< 37 weeks): (n = 728; 36 cases)* OR 0.71 95% CI 0.34 to 1.51 aOR 0.73 95% CI 0.32 to 1.68 *Early preterm birth (< 35 weeks): (n = 702; 10 cases)* OR 1.12 95% CI 0.24 to 5.33 aOR 0.93 95% CI 0.16 to 5.37 *Late preterm birth (35-36 weeks): (n = 718; 26 cases)* OR 0.62 95% CI 0.26 to 1.45 aOR 0.66 95% CI 0.25 to 1.69 **5 v 1-4 criteria:** *Preterm birth (< 37 weeks): (n = 25,966; 1174 cases)* OR 1.01 95% CI 0.68 to 1.51 aOR 1.06 95% CI 0.71 to 1.58 *Early preterm birth (< 35 weeks): (n = 25,264; 472 cases)* OR 0.77 95% CI 0.38 to 1.55 aOR 0.80 95% CI 0.40 to 1.62 *Late preterm birth (35-36 weeks): (n = 25,494; 702)* OR 1.18 95% CI 0.73 to 1.90 aOR 1.24 95% CI 0.77 to 2.0
Followup	To birth
Confounding	Analyses were adjusted for mother's BMI and height, educational level, parity and marital status
Risk of bias	Moderate: some dietary intakes were different between groups and were not controlled for (e.g. women meeting all 5 criteria had higher significantly

	higher egg consumption than the other women, and thus a higher cholesterol level); intake of nuts and cereals was not evaluated
Relevance	Moderate: low red meat consumption not typical for many Australian women
Other comments	Chosen cutoff points unbalanced – might have been better to compare all 5 criteria met v 3-4 v 1-2 v none. Preterm birth rates were lower than expected, likely due to exclusion of smokers

Reference	**Haugen 2005**
Dietary patterns	Healthy diet: Imprudent diet: high intakes of crisps/chips, sugar, confectionery, white bread, soft drinks, red meat; and low intakes of fruit/vegetables, rice/pasta, yoghurt, and wholemeal bread. Western diet: with additional high intakes of fruit and vegetables. Vegetarian: vegetarian foods, confectionery, snack foods.
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	UK
Funding	British Heart Foundation, UK Medical Research Council, Dunhill Medical Trust, Research Council of Norway
Participants	381 pregnancies in low-risk women
Baseline comparisons	Reported but not compared with relevant population
Dietary assessment	FFQ
Timing	Women recruited in early pregnancy
Comparison	Healthy; imprudent; western; 'vegetarian' diets
Outcomes	Fetal hepatic blood flow at 36 weeks gestation ('liver-sparing' leading to increased liver blood flow may be linked to increased adult cardiovascular risk)
Results	<u>**Ductus venous shunting in fetus**</u>: **Reduced with an imprudent diet (p = 0.04) (independent of maternal slimness)** No significant difference with a western diet (p = 0.45); No significant difference with a vegetarian diet (p = 0.89) <u>**Liver blood flow in fetus**</u>: **Increased with an imprudent diet (p = 0.02) (independent of maternal slimness);** No significant difference with a western diet (p = 0.83); No significant difference with a vegetarian diet (p = 0.95)
Followup	None
Confounding	"results not related to gestational age" also see comments in results
Risk of bias	Unclear; not many details reported
Relevance	Relevant population; relevance of the outcomes limited until subsequent research is undertaken
Other comments	Exploratory study

Reference	**Hill 2005**
Dietary patterns	Low allergen maternal diet: mothers excluded cow's milk, eggs, peanuts, tree nuts, wheat, soy and fish from their diet Control diet: mothers in the control group consumed the foods listed above
Study type	RCT
Level of evidence	II (intervention)
Setting	Community based infant health centres in Melbourne, Australia
Funding	Ricegrowers' Cooperative Ltd (Leeton, Australia)
Participants	107 exclusively breastfed infants presenting with colic (first six weeks of life); recruited between 2000 and 2002 – infants were well, term (> 37 weeks), singleton pregnancy, no significant obstetric complications or history of maternal substance abuse, no perinatal morbidity other than distress: Colic was defined as parent-reported infant distress exceeding 180 minutes per 24 hours on 3 days in the week before presentation; Mothers on strict vegan diets were excluded; three mothers on balanced ovo-lacto-vegetarian diets were included in the study
Baseline comparisons	NA
Dietary assessment	NA
Timing	All except three mother-child dyads commenced the intervention before infant was six weeks old (three infants were assigned at 7.4, 8.0 and 8.6 weeks respectively); intervention lasted 7 days
Comparison	Low allergen maternal diet (mothers asked to exclude all foods containing dairy products, soy, wheat, eggs, peanuts, tree nuts and fish from their diet; their diet included a rice mild drink (supplied), meats, vegetables, fruits and cereals (corn and rice) and calcium supplement) versus maternal diet (mothers received 7 days rations of a soy and cow's milk powder and were asked to consume 1 serve of peanuts, 1 serve of wheat and 1 chocolate muesli bar a day, which were supplied) Both diets avoided food preservatives, colours and additives; Adherence to the diet was monitored with diet diaries on the last 2 days of the intervention
Outcomes	Change in cry/fuss duration over 48 hours, after 7 days
Results	**Improvement of ≥ 25% in cry/fuss score (two days before intervention versus days 6 and 7)** Low allergen diet: 35/47 (74%) Control diet: 16/43 (37%) **ARR 0.37 95% CI 0.18 to 0.56, $p < 0.001$** - **This analysis restricted to women fully adhering to diets** Low allergen diet: 33/44 (75%) Control diet: 14/24 (58%) $p = 0.15$ **Cry/fuss duration ≥ 360 min per 48 hr (days 6 and 7)** Low allergen diet: 30/47 (64%) Control diet: 31/43 (72%) ARR 0.08 95% CI -0.11 to 0.27, $p = 0.402$ No significant differences seen in maternal assessments Noncompliance in the control arm was associated with a lack of early response (i.e. these women chose to eliminate some of the foods)
Followup	7 days (duration of intervention)
Confounding	NA
Risk of bias	Low risk of bias; randomisation schedule provided by statistician, third party randomisation; 90/107 infants completed the trial (47 in the low allergen group and 43 in the control group); infants of noncompleters in the control group had a higher distress score at baseline
Relevance	Relevant to Australian women and infants; low allergen diet may difficult to sustain
Other comments	

Reference	**Kinnunen 2007a**
Dietary patterns	Advice to 1) have a regular meal pattern, emphasising the importance of breakfast and at least one hot meal every day; 2) to eat at least 5 portions (400 g) per day of different kinds of vegetables, fruits and berries, 3) to consume mostly high fibre bread (≥ 5 g fibre/100 g) and 4) to restrict the intake of high-sugar snacks to ≤ 1 portion per day (e.g. 50 g sweets, one pastry, one piece of cake, two biscuits, 2 dl ice cream or a glass of soft drink) [plus advice to be physically active]
Study type	Controlled trial
Level of evidence	III-2 (nonrandomised concurrent comparison; interventions)
Setting	Six antenatal clinics in Finland (3 intervention, 3 control)
Funding	US NIH, Ministry of Education and Ministry of Social Affairs and Health, Finland
Participants	132 pregnant primiparas; recruited between August 2004 and January 2005 Exclusion criteria: under 18 years of age, type I or II diabetes mellitus (but not GDM), twin pregnancy, physical disability that prevents exercising, otherwise problematic pregnancy, substance abuse, treatment or clinical history for any psychiatric illness, inability to speak Finnish and intention to change residence within 3 months.
Baseline comparisons	Women in the intervention group were younger, less educated, more often smokers with higher pregnancy BMI than the control group
Dietary assessment	FFQ
Timing	22-24 weeks gestation, 37 weeks gestation
Comparison	Intervention (dietary and physical activity counselling) versus standard antenatal care
Outcomes	Achieving recommended dietary pattern; gestational weight gain
Results	

	Intervention (n = 48)	Control (n = 56)	p value
Total gestation weight gain (kg, SD)	14.6 [5.4]	14.3 [4.1]	0.77
Exceeding recommendations*	OR 1.82 95% CI 0.65 to 5.14	1.00	0.26
Veg, fruit, berries (portions/day) at 37 w**	3.8 [1.7] (n = 40)	3.2 [1.5] (n = 53)	
	Adj mean difference = +0.8 95% CI 0.3 to 1.4)		**0.004**
High-fibre bread (% of total bread) at 37 w**	67 [29] (n = 39)	53 [24] (n = 54)	
	Adj mean difference = +11.8 95% CI 0.6 to 23.1		**0.04**
High-sugar snacks (portions/day) at 37 w**	1.6 [1.3] (n = 40)	1.8 [1.1] (n = 55)	
	Adj mean difference =-0.3 95% CI -0.8 to 0.1)		0.16
High birthweight (≥ 4000 g)	**0**	**8**	**0.006**
Low birthweight (< 2500 g)	0	1	pns

Followup	To birth
Confounding	*Adjusted for age, pre-pregnancy BMI, education, pre-pregnancy smoking status, oedema and week of gestation in last weight measurement **adjusted for baseline intake of the outcome variable, pre-pregnancy age, BMI, education and smoking status
Risk of bias	Moderate risk of bias: 20/69 (29%) lost to followup in the intervention group and 7/63 (11%) in the control group; method of allocation to intervention or control not reported
Relevance	Likely to be reasonably relevant to Australian women
Other comments	Pilot for a larger study

Reference	**Kinnunen 2007b**
Dietary patterns	Advice to 1) have a regular meal pattern, emphasising the importance of breakfast and at least one hot meal every day; 2) to eat at least 5 portions (400 g) per day of different kinds of vegetables, fruits and berries, 3) to consume mostly high fibre bread (≥ 5 g fibre/100 g) and 4) to restrict the intake of high-sugar snacks to ≤ 1 portion per day (e.g. 50 g sweets, one pastry, one piece of cake, two biscuits, 2 dl ice cream or a glass of soft drink) [plus advice to be physically active]
Study type	Controlled trial (ISRCTN21512277)
Level of evidence	III-2 (nonrandomised concurrent comparison; interventions)
Setting	Six antenatal clinics in Finland (three intervention; three control)
Funding	US NIH, Ministry of Education and Ministry of Social Affairs and Health, Finland, Doctoral Programs in Public Health, Finland
Participants	92 postpartum primiparas; recruited between August 2004 and January 2005 Exclusion criteria: under 18 years of age, type I or II diabetes mellitus (but not GDM), twin pregnancy, physical disability that prevents exercising, otherwise problematic pregnancy, substance abuse, treatment or clinical history for any psychiatric illness, inability to speak Finnish and intention to change residence within 3 months.
Baseline comparisons	Characteristics of women in the intervention and control groups were not significantly different
Dietary assessment	FFQ
Timing	2, 5, 6 and 10 months postpartum
Comparison	Intervention (dietary and physical activity counselling from 2 to 10 months postpartum) versus standard antenatal care
Outcomes	Achieving recommended dietary pattern; gestational weight retention
Results	

	Intervention (n = 46)	**Control (n = 37)**	**aOR/MD (95% CI)**
Retained ≤ 0 kg at 10 m pp*	23 (50%)	11 (30%)	**3.89 (1.16 to 13.04)**
Weight retention, mean (kg, SD) at m pp	1.8 [4.3]	1.0 [4.4]	0.8 (-1.1 to 2.7)
Waist circumf at 10 months pp, mean (cm SD)	78.1 [10.2]	75.4 [6.2]	1.0 (0.7 to 2.7)
Veg, fruit, beries (prtions/day) at 10 m pp**	2.6 [1.4] (n = 44)	2.5 [2.1] (n = 37)	
	Adj mean difference = +0.2 95% CI -0.3 to 0.8		
High-fibre bread (% total bread) at 10 mpp**	65 [27] (n = 44)	52 [31] (n = 37)	
	Adj mean difference = + 16.1 95% CI 4.3 to 27.9		
High-sugar snacks (portions/day) at 10 mpp**	2.1 [1.2] (n = 44)	2.1 [1.4] (n = 37)	
	Adj mean difference = 0.0 95% CI -0.6 to 0.6)		

Followup	To 10 months posptpartum
Confounding	*Adjusted for age, pre-pregnancy BMI, education, gestational weight gain, weight at 2 months postpartum, duration of exclusive breastfeeding and smoking status **baseline intake of the outcome variable, age, education, smoking status, gesational weight gain and BMI at 2 months postpartum
Risk of bias	Moderate risk of bias: 5/53 (9%) lost to followup in the intervention group and 2/39 (5%) in the control group; three clinics volunteered to be intervention clinics and the other three clinics were controls
Relevance	Likely to be reasonably relevant to Australian women
Other comments	Underpowered; pilot for a larger study

Reference	**Knudsen 2008**
Dietary patterns	1) Red and processed meat, high-fat dairy; 2) Veg, fruit, poultry, fish; 3) Intermediate
Study type	Prospective cohort (factor analysis)
Level of evidence	II (aetiology)
Setting	Copenhagen, Denmark; from 1997 to 2002; part of the Danish National Birth Cohort
Funding	March of Dimes Birth Defects Foundation, Danish National Research Foundation, European Union, Pharmacy Foundation, Egmont Foundation, Augustinus Foundation, Health Foundation
Participants	44,162 adequately nourished pregnant women (who went to give birth to a live born, fullterm singleton child)
Baseline comparisons	All reported baseline characteristics were adjusted – *see Confounding*
Timing	FFQ in week 25, recording previous 4 weeks intake
Comparison	1) <u>Western Diet</u> (high intake of high-fat dairy, refined grains, processed and red meat, animal fat (butter and lard), potatoes, sweets, beer, coffee and high-energy drinks; highest energy intake (35% from fat)) 2) <u>Health Conscious Diet</u> (high intake of fruits, vegetables, fish, poultry, breakfast cereals, vegetable juice and water; avoidance of foods with a high fat content; lowest energy intake (25% from fat)) 3) <u>Intermediate</u> (high intake of low-fat dairy and fruit juice, fruits and vegetables, red meat and dairy products; 30% of energy intake from fat) Alcohol intake was low for all groups
Outcomes	Fetal growth (SGA - defined as z-score below 2.5th percentile for the respective gender and GA); birthweight
Results	<u>**SGA**</u> Western diet: OR 1.00 (reference) [n=7619] **Intermediate: OR 0.68 95% CI 0.55 to 0.84 (p=0.0004) [29,514]** **Health conscious: OR 0.74 95% CI 0.64 to 0.86) (p=0.0001) [n=7479]** <u>**Birthweight (g**) :</u>(mean, SD) Western diet: 3583 [515] Intermediate: 3623 [490] Health conscious: 3616 [486], p>0.05
Followup	To birth
Confounding	Adjusted for parity, maternal smoking, age, height, pre-pregnancy weight and father's height
Risk of bias	Low risk of bias: healthier women more likely to participate (response rate not reported but possibly about 50%); likely to be residual confounding (e.g. SES)
Relevance	Not clear how similar these patterns and their frequency would be for Australia; Only included term babies; Diet from 21-25 weeks GA may not influence fetal growth as much as dietary intake earlier in pregnancy
Other comments	Not clear which individual foods or nutrients (and relative quantities) may be particularly influencing SGA

<table>
<tr><th>Reference</th><th>Koebnick 2004</th></tr>
<tr><td>Dietary patterns</td><td><u>Vegetarian diet</u>: no meat or meat products; plant based diet (high consumption of raw vegetables (> 100 g/d), preference for wholegrain products (ratio of refined grain products/wholegrain products < 0.95))
<u>Low meat diet</u>: limited meat consumption (meat < 300 g/week and meat products < 105 g/week); plant based diet (high consumption of raw vegetables (> 100 g/d), preference for wholegrain products (ratio of refined grain products/wholegrain products < 0.95))
<u>Western diet (control group)</u>: similar to diet of average German population (mainly refined grain products (ratio of refined grain products/wholegrain products > 1.05) and > 300 g meat and 105 g meat products per week and < 100g unheated vegetables per day</td></tr>
<tr><td>Study type</td><td>Prospective cohort (3 concurrent comparisons)</td></tr>
<tr><td>Level of evidence</td><td>II (aetiology)</td></tr>
<tr><td>Setting</td><td>Erlangen, Germany</td></tr>
<tr><td>Funding</td><td>Eden Foundation, Stoll VITA Foundation, Germany</td></tr>
<tr><td>Participants</td><td>109 healthy pregnant women with less than 4 prior pregnancies at any stage of pregnancy (recruited by advertisements in health magazines and by gynaecologists from 1995 to 1997);
Participants in the vegetarian and low meat diet groups could not have changed their diet substantially for at least three years; participants in the control group were only included if they did not follow any special diet</td></tr>
<tr><td>Baseline comparisons</td><td>Vegetarians and low meat eaters had lower prepregnancy BMIs than the control group

See Confounding below</td></tr>
<tr><td>Timing</td><td>FFQ when recruited, recording usual dietary intake before pregnancy;
Information on dietary intake and blood samples were collected at 9-12 weeks, 20-22 weeks, and 36-38 weeks gestation</td></tr>
<tr><td>Comparison</td><td>Vegetarian (ovo-lacto) diet: n = 27
Low meat diet: n = 43
Western diet (control group): n = 39</td></tr>
<tr><td>Outcomes</td><td>Maternal B-12 concentrations</td></tr>
<tr><td>Results</td><td>Serum B-12 concentrations, pmol/L (medians with 25^{th} and 75^{th} percentiles)
<table>
<tr><th>Trimester</th><th>ovo-lacto vegetarian</th><th>Low meat diet</th><th>Western diet</th></tr>
<tr><td>1</td><td>179 (100-317); n=16</td><td>209 (160-293); n=29</td><td>249 (201-310); n=31</td></tr>
<tr><td>2</td><td>176 (102-271); n=25</td><td>215 (151-269); n=42</td><td>238 (190-305); n=39</td></tr>
<tr><td>3</td><td>127 (90-184); n=19</td><td>164 (125-208); n=34</td><td>169 (141-213); n=38</td></tr>
</table>
Ovo-lacto vegetarian versus western diet: p < 0.001
Low meat versus western diet: p = 0.05

<u>Low serum vitamin B-12 in at least trimester (with western diet group as reference):</u>
Ovo-lacto vegetarian diet: OR 3.9 95% CI 1.9 to 6.1
Low meat diet: OR 1.8 95% CI 1.0 to 3.9</td></tr>
<tr><td>Followup</td><td>To birth</td></tr>
<tr><td>Confounding</td><td>Adjusted for supplemental vitamin B-12,maternal age and first, second or third trimester</td></tr>
<tr><td>Risk of bias</td><td>Low-moderate risk of bias: risk of selection bias from advertising in health magazines; reasons for missing B-12 measurements not reported</td></tr>
<tr><td>Relevance</td><td>Likely to be similar to Australian women; perhaps higher use of supplements in Germany</td></tr>
<tr><td>Other comments</td><td>Other possible confounders e.g. from choosing a vegetarian lifestyle
B-12 status is a risk factor for neural tube defects</td></tr>
</table>

Reference	**Koebnick 2001**
Dietary patterns	Vegetarian diet: no meat or meat products; plant based diet (high consumption of raw vegetables (> 100 g/d), preference for wholegrain products (ratio of refined grain products/wholegrain products < 0.95)) Low meat diet: limited meat consumption (meat < 300 g/week and meat products < 105 g/week); plant based diet (high consumption of raw vegetables (> 100 g/d), preference for wholegrain products (ratio of refined grain products/wholegrain products < 0.95)) Western diet (control group): similar to diet of average German population (mainly refined grain products (ratio of refined grain products/wholegrain products > 1.05) and > 300 g meat and 105 g meat products per week and < 100g unheated vegetables per day
Study type	Prospective cohort (3 concurrent comparisons)
Level of evidence	II (aetiology)
Setting	Erlangen, Germany – same cohort as described in Koebnick 2004
Funding	Not reported
Participants	109 healthy pregnant women with less than 4 prior pregnancies at any stage of pregnancy (recruited by advertisements in health magazines and by gynaecologists from 1995 to 1997);
Baseline comparisons	Vegetarians and low meat eaters had lower prepregnancy BMIs and lower B-12 status than the control group *See Confounding below*
Timing	FFQ when recruited, recording usual dietary intake before pregnancy; Information on dietary intake and blood samples were collected at 9-12 weeks, 20-22 weeks, and 36-38 weeks gestation
Comparison	Vegetarian (ovo-lacto) diet: n = 27 Low meat diet: n = 43 Western diet (control group): n = 39
Outcomes	Maternal folate concentrations
Results	**Folate deficiency (red blood cell folate < 320 nmol/L)** Western diet: reference **Ovo lacto vegetarian diet: aOR 0.10 95% CI 0.01 to 0.56** Low meat diet: aOR 0.52 95% CI 0.20 to 1.34
Followup	To 36-38 weeks gestation
Confounding	Adjusted for age, pre-pregnancy BMI, parity, smoking habits and oral contraceptive use before pregnancy
Risk of bias	Low-moderate risk of bias: risk of selection bias from advertising in health magazines; of 249 responding women, 203 received a questionnaire; 22 were not interested in further participation and 24 were excluded from further participation (1 pregnant with twins, 9 were taking supplements, 14 lived > 200 km from the study site; 2/203 failed to complete questionnaire. 92/201 women then excluded – 10 taking supplements, 4 metabolic diseases, 68 not consuming a predominant vegetarian diet nor average western diet, 10 missing blood analyses for folate status, leaving 109 women in the study; 12/27 women in the ovo-lacto vegetarian group, 21/43 in the low meat group and 27/39 in the western diet group had a complete longitudinal assessment
Relevance	Less relevant to Australian women now that there is mandatory folate fortification in Australia
Other comments	Other possible confounders e.g. from choosing a vegetarian lifestyle?

Reference	**Lange 2010**
Dietary patterns	Mediterranean
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Women recruited obstetric offices in a large multispecialty group practice in eastern Massachusetts
Funding	NIH (Disclosure of potential conflict interest from investigators includes links with AstraZeneca, Dey, GlaxoSmithKline, Merck, Novartis)
Participants	1376 mother-infant pairs from Project Viva; women with a singleton pregnancy Exclusions: multiple gestation, inability to answer questions in English, plans to move out of the area before birth, gestational age > 22 weeks at the initial antenatal appointment
Baseline comparisons	Maternal participants in the study were more likely to be white, to have college or graduate education, higher income, low prepregnancy BMI, than the women excluded from the study
Dietary assessment	Mediterranean diet score; Alternate Healthy Eating Index modified for pregnancy (AHEI-P); principal components analysis
Timing	Women were interviewed after the initial antenatal visit, at an average of 10 weeks gestation and given questionnaires to return by mail; interview at second visit at 26-28 weeks gestation and given questionnaires to return by mail; newborn measurements were taken and a brief interview occurred within 72 hours of birth; questionnaires on infant health were administered at 6 months, 1 year and annually thereafter Mean responses to dietary assessments were averaged across the first and second trimester.
Comparison	1) Mediterranean diet score 0-9; high score best: one point if above median consumption for dairy, fish, fruit, legumes, nuts, unsaturated-to-saturated fat ratio, vegetables and whole grains, intake of red and processed meats below the median median value [alcohol was excluded from the analysis] – low (0-3) v middle (4-5) v high (6-9) score. 2) AHEI-P 90 point scale: 10 possible points for each of vegetables, fruit, ratio of white to red meat, fibre, trans fat; ratio of polyunsaturated to saturated fatty acids, folate, calcium and iron from foods – quartiles compared. 3) Patterns of correlated food groups identified through principal component analysis: a. Prudent diet: fruits, tomatoes, cabbages, leafy green vegetables, poultry, fish b. Western diet: red meat, processed meat, refined grains, snacks, sweets, desserts, French fries and pizza.
Outcomes	• Recurrent wheeze at 3 years (compared with no wheeze at all in the first 3 years of life); • Asthma (parental report of a doctor diagnosis of asthma in the child at any time up to 3 years); • Eczema (parental report of a doctor's diagnosis of eczema) up to 3 years; • Lower respiratory infection (parental report of having had bronchiolitis, pneumonia, or bronchitis/croup at any time up to 3 years) • Atopy (in a subset of 721 children at 3 years of age)
Results	**<u>Recurrent wheeze</u>:** Mediterranean diet score: OR 0.92 95% CI 0.85 to 1.00 per 1 point increase in score aOR 0.98 95% CI 0.89 to 1.08 per 1 point increase in score Mediterranean diet score (high v low): OR 0.64 95% CI 0.43 to 0.95 AHEI-P: OR 0.92 95% CI 0.77 to 1.08 per 10 points aOR 1.07 95% CI 0.87 to 1.30 per 10 points AHEI-P (highest v lowest quartile): OR 0.87 95% CI 0.55 to 1.37

	Prudent: OR 0.98 95% CI 0.82 to 1.18 aOR 1.02 95% CI 0.83 to 1.26 Western: OR 1.07 95% CI 0.91 to 1.26 aOR 0.98 95% CI 0.81 to 1.19 **Asthma:** Mediterranean diet score: OR 0.97 95% CI 0.91 to 1.03 per 1 point increase in score aOR 1.01 95% CI 0.94 to 1.09 per 1 point increase in score AHEI-P: OR 0.96 95% CI 0.84 to 1.09 per 10 points aOR 1.07 95% CI 0.92 to 1.25 per 10 points Prudent: OR 1.02 95% CI 0.89 to 1.16 aOR 1.08 95% CI 0.93 to 1.26 Western: OR 1.00 95% CI 0.87 to 1.14 aOR 0.89 95% CI 0.76 to 1.04 **Eczema:** Mediterranean diet score: OR 1.01 95% CI 0.95 to 1.06 per 1 point increase in score aOR 1.00 95% CI 0.94 to 1.06 per 1 point increase in score AHEI-P: OR 0.97 95% CI 0.87 to 1.08 per 10 points aOR 0.94 95% CI 0.82 to 1.08 per 10 points Prudent: OR 1.01 95% CI 0.90 to 1.13 aOR 0.95 95% CI 0.83 to 1.09 Western: OR 1.04 95% CI 0.93 to 1.17 aOR 1.06 95% CI 0.93 to 1.22 **Respiratory infection:** Mediterranean diet score: OR 1.03 95% CI 0.97 to 1.09 per 1 point increase in score

	aOR 1.04 95% CI 0.98 to 1.10 per 1 point increase in score AHEI-P: OR 0.95 95% CI 0.85 to 1.07 per 10 points aOR 0.96 95% CI 0.85 to 1.10 per 10 points Prudent: OR 0.96 95% CI 0.85 to 1.09 aOR 0.96 95% CI 0.84 to 1.11 Western: OR 1.09 95% CI 0.97 to 1.23 aOR 1.06 95% CI 0.93 to 1.21 **Atopy in a subset of children with IgE results (n = 721)** Mediterranean diet score: OR 1.06 95% CI 0.99 to 1.14 per 1 point increase in score aOR 1.08 95% CI 0.99 to 1.18 per 1 point increase in score AHEI-P: OR 1.16 95% CI 1.00 to 1.34 per 10 points aOR 0.96 95% CI 0.85 to 1.10 per 10 points Prudent: OR 1.24 95% CI 1.05 to 1.46 aOR 1.12 95% CI 0.93 to 1.36 Western: OR 0.90 95% CI 0.77 to 1.04 aOR 0.93 95% CI 0.79 to 1.11
Followup	3 years
Confounding	Adjusted for child's sex, maternal race, maternal education level, household income, maternal and paternal history of asthma [eczema for eczema outcome], presence of children < 12 years of age at home, maternal prepregnancy BMI, breastfeeding duration, passive smoke exposure
Risk of bias	Low risk of bias: Of the 2128 infants in Project Viva, 228 had missing maternal diet data, and an additional 524 did not have 3 year outcome data, leaving 1376 (64.7%) mother-child pairs for analysis.
Relevance	Likely to be relevant to an Australian population
Other comments	

Reference	**Laraia 2007**
Dietary patterns	Diet Quality Index for Pregnancy (DQI-P) – based on intake of grains, vegetables, fruits, folate, iron, fat and a meal pattern score
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	North Carolina, US (part of the Pregnancy, Infection and Nutrition (PIN) cohort)
Funding	National Institute of Child Health and Human Development; NIH
Participants	2394 predominantly lower to middle income women, recruited between 24 and 29 weeks gestation (1995-2000)
Baseline comparisons	Mean DQI-P score varied significantly by socio-demographic characteristics; there were higher mean DQI-scores for women who engaged in pre-pregnancy vigorous exercise and pre-pregnancy vitamin use
Dietary assessment	Modified block FFQ
Timing	Self-report at 26-28 weeks gestation covering previous 3 months (corresponding to the 2nd trimester)
Comparison	BMI categories
Outcomes	Pregravid weight status (not an outcome but there is an association)
Results	**Proportion of women meeting IOM meal pattern requirement [SD]** Underweight 70.1 [45.8] Normal weight 68.1 [46.6] Overweight 63.4 [48.3] Obese 60.0 [49.0] **Obese group significantly different from normal weight (p < 0.05) and underweight (p < 0.01)** **Average DQI-P score [SD]** Underweight 57.2 [11.7] Normal weight 55.3 [11.3] Overweight 55.2 [11.5] Obese 53.3 [12.0] **Obese group significantly different from normal weight (p < 0.05) and underweight (p < 0.01)** **Lowest v highest DQI-P tertile by BMI status (OR; 95% CIs)** OR / aOR* / aOR Obese **1.87 (1.37 to 2.55)** / **1.86 (1.32 to 2.62)** / **1.76 (1.24 to 2.49)** Overweight 1.29 (0.88 to 1.88) / 1.32 (0.88 to 1.99) / 1.31 (0.87 to 1.99) Normal weight 1.29 (0.98 to 1.72) / **1.43 (1.05 to 1.94)** / **1.38 (1.01 to 1.89)** Underweight 1.00 / 1.00 / 1.00 *adjusted for age, ethnicity, level of education, poverty, number of children, smoking during pregnancy only
Followup	26 to 31 weeks gestation
Confounding	Age, ethnicity, level of education, poverty, number of children, smoking during pregnancy, regular vitamin use prior to pregnancy, vigorous leisure activity 3 months prior to pregnancy
Risk of bias	Low risk of bias: would have been better to have used normal weight women as the reference rather than underweight women DQI-P tertile comparison
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Mikkelsen 2008**
Dietary patterns	Mediterranean diet (consumption of fish twice a week or more, intake of olive or canola oil, high consumption of fruits and vegetables (5 a day or more), meat (other than poultry or fish) at most twice a week, and at most 2 cups of coffee a day)
Study type	Prospective cohort study
Level of evidence	II
Setting	Denmark (part of the Danish National Birth Cohort (DBNC))
Funding	March of Dimes Birth Defects Foundation, Danish National Research Foundation, Danish Medical Research Foundation, Danish Health Foundation, Danish Heart Foundation, EU FP7 consortium (EARNEST), Pharmacy Foundation, Egmont Foundation, Augustinus Foundation.
Participants	35,530 pregnant women recruited from 1996 to 2002 Exclusions: women who smoked, women aged < 21 and > 38 years, BMI < 19 and > 32, a history of more than 3 abortions, twin pregnancies, chronic hypertension, women with a calculated energy intake < 4,200 kJ and > 16,700 kJ
Baseline comparisons	BMIs were significantly lower in the MD and none groups.
Dietary assessment	FFQ
Timing	FFQ mailed to all DBNC participants in 25th week of gestation
Comparison	Mediterranean diet (fulfilled all 5 criteria – see above) v partial (fulfilled 1-4 criteria) v none (none of the criteria fulfilled)
Outcomes	Preterm birth
Results	**5 v 0 CRITERIA:** **<u>Preterm birth < 37 weeks</u>** OR 0.79 95% CI 0.50 to 1.27 aOR 0.61 95% CI 0.35 to 1.05 **<u>Early preterm birth < 35 weeks</u>** OR 0.52 95% CI 0.22 to 1.22 **aOR 0.28 95% CI 0.11 to 0.76** **<u>Late preterm birth 35-36 weeks</u>** OR 0.94 95% CI 0.54 to 1.65 aOR 0.82 95% CI 0.43 to 1.57 **5 v 1-4 CRITERIA:** **<u>Preterm birth < 37 weeks</u>** OR 1.00 95% CI 0.74 to 1.33 aOR 0.92 95% CI 0.69 to 1.24 **<u>Early preterm birth < 35 weeks</u>** OR 0.63 95% CI 0.35 to 1.15 aOR 0.58 95% CI 0.32 to 1.06 **<u>Late preterm birth 35-36 weeks</u>** OR 1.20 95% CI 0.86 to 1.67 aOR 1.11 95% CI 0.80 to 1.55

Followup	To birth
Confounding	Adjusted for parity, BMI, maternal height, socioeconomic status and cohabitant status
Risk of bias	Low risk of bias; GA based mostly on ultrasound; 0.36% missing data (127/35657)
Relevance	Relevance limited by exclusion of smokers and obese women
Other comments	Partial group comprised 95.2% of all women in the study – might have been better to separate further in moderate and low fulfilment categories

Reference	**Moses 2009a**
Dietary patterns	Low versus higher glycaemic index (GI) diets (same carbohydrate intake of 175 g/day but varying foods): - Low GI (including pasta, grain breads, unprocessed breakfast cereals with a high fibre content) - High GI (advised to follow a high fibre, low sugar diet with no specific mention of glycaemic index; potatoes, whole wheat bread, specific high fibre, moderate-high GI breakfast cereals were recommended)
Study type	RCT
Level of evidence	II (intervention)
Setting	Illawarra region, NSW, Australia
Funding	Illawarra Diabetes Service and University of Sydney
Participants	63 women with gestational diabetes mellitus (GDM); aged 18 to 40 years, singleton pregnancy, no previous GDM, non-smoker, seen for first dietary visit between 28 to 32 weeks gestation (recruited between October 2007 to September 2008). Exclusions: any condition or medication that could affect glucose levels, unwillingness to follow the prescribed diet.
Baseline comparisons	NA
Dietary assessment	NA
Timing	Dietary changes starting from 28 weeks to 32 weeks gestation
Comparison	Low (31 women) v high GI diet (32 women)
Outcomes	Need for insulin (fasting glucose ≥ 5.5 mmol/L and/or 1-hour postprandial glucose was ≥ 8.0 mmol/L); birthweight (adjusted for sex, gestational age, maternal age, parity, height, and prepregnancy weight); ponderal index
Results	 **<u>Need for insulin</u>** **9/31 women in low GI group v 19/32 women in the high GI group (p = 0.023)** **<u>Need for insulin after the 19 high GI women were switched to a low GI diet</u>** 9/31 women in low GI group v 10/32 women in the high GI group (pns) **Maternal weight gain from baseline to birth; induction of labour, mode of birth, or gestational age at birth** were not significantly different between groups (data not reported in paper) **Birth centile** Low GI: 46.3 [SEM 5.0] v high GI: 54.3 [4.8], p = 0.25 **Ponderal index** Low GI: 2.7 [SEM 0.05] v high GI: 2.6 [SEM 0.04], p = 0.12 **LGA (≥ 90th centile)** 3 women (over both groups) **SGA (≤ 10th centile)** 2 women in the low GI group
Followup	To birth
Confounding	NA
Risk of bias	Moderate risk of bias: Computer generated random number list, allocation method not reported; study dietitians not blinded, no missing data reported.
Relevance	Relevant to Australian women
Other comments	Energy intake and GI were similar between groups after intervention

Reference	**North 2000**
Dietary patterns	Vegetarian diet
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Bristol, UK (part of ALSPAC and the WHO initiated European Longitudinal Study of Pregnancy and Childhood)
Funding	MRC, Wellcome Trust, Department of Health, Department of the Environment, MAFF, Nutricia, Nestle and other companies, BBC
Participants	7928 boys born to women between April 1991 and December 1992; with 51 cases of hypospadias (= 64 per 10,000 male births)
Baseline comparisons	Mothers who had influenza during pregnancy; and mothers who took codeine in the first trimester in pregnancy had high rates of hypospadias in their male offspring
Dietary assessment	Whether currently vegetarian (i.e. during pregnancy) or had previously been so
Timing	Questionnaires at 8, 18 and 32 weeks gestation (this assessed current dietary behaviour); and at various ages of the child
Comparison	Vegetarian diet (5.1% of women) versus omnivorous diet
Outcomes	Hypospadias
Results	**2.2% of women who were vegetarian during pregnancy gave birth to a boy with hypospadias, compared with 0.06% of omnivorous women; OR 3.53 95% CI 1.56 to 7.98** This did not differ greatly between vegetarian women who did and did not take iron supplements - in contrast to omnivorous women* Vegetarian women (taking or not taking iron supplements): **OR of hypospadias 4.99 95% CI 2.10 to 11.88**, using omnivorous women who did not take iron supplements as reference. Of the 163 mothers who reported only buying organic fruit and vegetables, none had a son with hypospadias (but only one case would have been expected). Incidence of hypospadias in children of women with a vegetarian diet prior to pregnancy (but not during pregnancy) was no significantly different from those women who had never been vegetarian.
Followup	To diagnosis of hypospadias
Confounding	Analyses were not adjusted
Risk of bias	Medium risk of bias: analyses were not adjusted for potentially important confounders
Relevance	Likely to be reasonably relevant to Australian women
Other comments	Authors hypothesise a possible link between phytoestrogens and hypospadias; could be pesticides, foods such as soy Omnivorous women who took iron supplements had increased risk of hypospadias in their male offspring*

Reference	**Olafsdottir 2006**
Dietary patterns	Eating more (in either early or late pregnancy)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Iceland
Funding	Icelandic Research Council, University of Iceland Research Fund
Participants	495 randomly selected healthy pregnant women attending a routine first antenatal visit
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	At 11-15 weeks gestation; and 34-37 weeks gestation (to reflect food intake for the last 3 months)
Comparison	Eating more versus not eating more than usual (in either early or late pregnancy)
Outcomes	Gestational weight gain (optimal weight gain defined as 12.1 to 18.0 kg for women with normal pre-pregnancy weight; and 7.1 to 12.0 kg for overweight women)
Results	20% of the 301 women with BMI < 25 at first visit had excessive gestational weight gain; 55% of the 194 women with BMI ≥ 25 at first visit had excessive gestational weight gain **Eating more in early pregnancy** At least optimal weight gain: aOR 1.00 95% 0.55 to 1.84 Excessive weight gain: aOR 1.60 95% CI 0.91 to 2.79 **Eating more in late pregnancy** At least optimal weight gain: **aOR 3.32 95% 1.81 to 6.09** Excessive weight gain: **aOR 2.04 95% CI 1.17 to 3.58**
Followup	To birth
Confounding	Adjusted for maternal age, gestational length and smoking
Risk of bias	Low to moderate risk of bias: of the 549 women enrolled, 495 (90%) completed the study; 54 women were excluded (17 miscarriage/stillbirths, 5 sets of twins or triplets, 17 preterm births, 15 missing data); 89 women did not complete FFQ at the second timepoint and so only 406 women could be included for measures relating to late pregnancy; limited number of confounders used in adjusted analyses
Relevance	Likely to be reasonably relevant to Australian women
Other comments	

Reference	**Radesky 2008**
Food type	Prudent pattern (high in vegetables, fruit, legumes, fish, poultry, eggs, salad dressing, and whole grains); Western pattern (red and processed meats, sugar-sweetened beverages, French fries, high-fat dairy products, desserts, butter and refined grains)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Boston, MA, USA
Funding	NIH, March of Dimes Birth Defects Foundation, Harvard Medical School Division of Nutrition, Harvard Pilgrim Health Care Foundation
Participants	1773 women with singleton pregnancies enrolled in Project Viva (initial antenatal visit before 22 weeks gestation, able to complete study forms in English, did not plan to move out of the study area before birth
Baseline comparisons	Included women had lower pregnancy BMIs than excluded women, were less likely to be African-American or Hispanic, to have low SES *See confounding below*
Dietary assessment	FFQ
Timing	FFQ completed at first antenatal visit at a mean 11.8 weeks GA (range 5-25.6 weeks) - to assess diet during first trimester
Comparison	Western pattern; prudent pattern (quartiles)
Outcomes	Glucose tolerance testing at 26-28 weeks gestation – GDM; impaired glucose tolerance (IGT) Normal glucose tolerance defined as: < 140 mg/dL 1 hour after a 50 g glucose load (non-fasting oral glucose challenge test); IGTdefined as ≥ 140 mg/dL on non-fasting oral glucose challenge test but 0 or 1 abnormal result for a fasting glucose tolerance test (100g oral glucose load where normal = < 95 mg/dL at baseline, < 180 mg/dL at 1 h, < 155 mg/dL at 2 h and < 140 mg/dL at 3 h; GDM defined as ≥ 140 mg/dL on non-fasting oral glucose challenge test with 2 or more abnormal GTT results (For the 39 women with incomplete glucose testing data, medical records were used to assign them to normal glucose tolerance (n = 7), IGT (n = 10), or GDM (n = 22).
Results	**GDM (increasing quartiles of Western pattern):** Q1: aOR 1 (reference) Q2: aOR 1.14 95% CI 0.56 to 2.29 Q3: aOR 1.63 95% CI 0.84 to 3.19 Q4: aOR 0.87 95% CI 0.41 to 1.83 *P for trend = 0.80* **GDM (increasing quartiles of Prudent pattern):** Q1: aOR 1 (reference) Q2: aOR 0.56 95% CI 0.26 to 1.21 Q3: aOR 1.06 95% CI 0.55 to 2.05 Q4: aOR 1.13 95% CI 0.59 to 2.16 *P for trend = 0.35* **Combined GDM/IGT**: similar null results (exact numbers not reported in paper)
Followup	To birth
Confounding	Adjusted for maternal age, pre-pregnancy BMI, ethnicity, family history of diabetes, history of GDM in a prior pregnancy, smoking in index pregnancy; Used energy partition models and nutrient density substitution models to study the simultaneous effects of different macronutrients on GDM and IGT risk; Other studies have not adjusted for different types of fats (which may have opposing effects on risk of GDM)

Risk of bias	Low risk of bias: Of 2128 women who gave birth to a live infant, 24 were excluded for missing or incomplete glucose tolerance testing records; 18 with a history of previous type 1 or 2 DM or PCOS with glucose intolerance, 342 missing or implausible first trimester diet information; 11 completion of FFQ after 26 weeks GA (i.e. after glucose tolerance screening) or on an unknown date; leaving 1773 (83.3%) available for analysis
Relevance	Likely to be relevant to Australian women
Other comments	Paper concludes that “nutritional status entering pregnancy, as reflected by pre-pregnancy BMI, is probably more important than pregnancy diet in development of GDM”

Reference	**Rifas-Shiman 2009**
Dietary patterns	Dietary quality (AHEI-P)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Large multispecialty urban/suburban group practice in eastern Massachusetts, USA
Funding	NIH, Harvard Medical School, Harvard Pilgrim Health Care Foundation
Participants	1,777 women (part of Project Viva) Exclusions: multiple gestations, inability to answer questions in English, plans to move out of the area before birth, GA > 22 completed weeks at initial antenatal visit
Baseline comparisons	Compared with the overall cohort, participants in this subset had higher educational status but were similar in household income, marital status, nausea status age and BMI
Dietary assessment	FFQ
Timing	FFQ assessing diet during early pregnancy; and at 26-28 weeks gestation assessing diet during the preceding 3 months
Comparison	AHEI-P scores: 90 point scale, each of the following components contributing 10 possible points: vegetables, fruit, ratio of white (poultry or fish) to red meat, fibre, trans fat, ratio of polyunsaturated to saturated fatty acids, and folate, calcium and iron from foods [excluded the nuts and soy component and the alcohol component – tofu and soybeans were included in the vegetable component]
Outcomes	Pre-eclampsia, glucose tolerance, pregnancy weight gain, SGA (< 10th percentile), LGA (> 90th percentile)
Results	**n = 1,777 for 1st trimester; 1,666 for 2nd trimester** **LGA (compared with average for GA)** *AHEI-P score (per 5 points)* aOR 0.95 95% CI 0.89 to 1.02 (1st trimester) aOR 0.99 95% CI 0.92 to 1.07 (2nd trimester) **SGA (compared with average for GA)** *AHEI-P score (per 5 points)* aOR 0.92 95% CI 0.82 to 1.02) (1st trimester) aOR 1.00 95% CI 0.90 to 1.10) (2nd trimester) **Excessive pregnancy weight gain (compared with adequate weight gain) [IOM definitions]** *AHEI-P score (per 5 points)* aOR 0.99 95% CI 0.94 to 1.04) (1st trimester) aOR 0.99 95% CI 0.94 to 1.04) (2nd trimester) **Inadequate pregnancy weight gain (compared with adequate weight gain) [IOM definitions]** *AHEI-P score (per 5 points)* aOR 0.95 95% CI 0.88 to 1.02) (1st trimester) aOR 0.99 95% CI 0.92 to 1.07) (2nd trimester) **Pre-eclampsia (compared with normal)** *AHEI-P score (per 5 points)* aOR 0.96 95% CI 0.84 to 1.10) (1st trimester) **aOR 0.87 95% CI 0.76 to 1.00) (2nd trimester)**

	<u>**Gestational diabetes (compared with normal glucose status)**</u> *<u>AHEI-P score (per 5 points)</u>* aOR 0.97 95% CI 0.87 to 1.08 (1st trimester) aOR 0.98 95% CI 0.87 to 1.09) (2nd trimester) <u>**Impaired glucose tolerance (compared with normal glucose status)**</u> *<u>AHEI-P score (per 5 points)</u>* aOR 1.00 95% CI 0.93 to 1.08 (1st trimester) aOR 0.96 95% CI 0.89 to 1.03) (2nd trimester) <u>**Blood glucose (mg/dL) regression estimate**</u> *<u>AHEI-P score (per 5 points)</u>* **-0.64 95% CI -1.25 to -0.02 (1st trimester)** **-0.83 95% CI -1.46 to -0.20 (2nd trimester)**
Followup	To birth
Confounding	Adjusted for maternal age, BMI, parity,education, and ethnicity
Risk of bias	Low risk of bias: Results for 1,777 of 2,670 (84%) women enrolled able to be included in the primary analysis
Relevance	Likely to be relevant for Australian women
Other comments	

Reference	**Robinson 2007**
Dietary patterns	Prudent diet (high intakes of fruit, vegetables, wholemeal bread, rice and pasta and low intakes of white bread, added sugar, and tinned vegetables)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Southampton
Funding	Medical Research Council, University of Southampton, British Heart Foundation and the Food Standards Agency
Participants	1434 infants born to women in the Southampton Women's Survey between 1999 and 2003
Baseline comparisons	Various maternal characteristics used in the regression analysis (see confounding below)
Dietary assessment	FFQ
Timing	Pre-pregnancy
Comparison	Prudent v less prudent maternal diet
Outcomes	Infant diet at 6 and 12 months ('infant guidelines' diet = higher consumption of fruits, vegetables and home-prepared foods; 'adult' diet = high consumption of chips, savoury snacks and biscuits)
Results	**Association between maternal prudent diet and 'infant guidelines' diet** **6 months: ß 0.196 95% CI 0.135 to 0.257; $p < 0.001$** **12 months: ß 0.282 95% CI 0.220 to 0.343; $p < 0.001$** **Association between maternal prudent diet and 'adult' diet** **6 months: ß -0.074 95% CI -0.132 to -0.015; $p < 0.05$** **12 months: ß -0.215 95% CI -0.270 to -0.160; $p < 0.001$**
Followup	To 12 months
Confounding	Adjusted for maternal education, age, BMI, smoking status, time spent watching television, age of introducing solid foods to infant, birth order
Risk of bias	Low-moderate risk of bias: results available for 1434/1973 (73%) infants at both 6 and 12 months of age (no further details given)
Relevance	Likely to be relevant to Australian women
Other comments	'Infant guidelines' diet also significantly associated with maternal education, time spent watching television, and birth order; 'Adult' diet also significantly associated with maternal education, maternal age, BMI, smoking status, age of introduction of solid foods, and birth order

Reference	**Rodriguez-Bernal 2010**
Dietary patterns	Alternate Healthy Eating Index for Pregnancy (AHEI-P) – consisting of 10 components of ideal intakes (5 serves of vegetables/day, 4 serves of fruit/day, 1 serve of nuts and soy/day, ≥ 4:1 ratio of white meat (fish and poultry) to red meat, 15 g/day cereal fibre, trans fat ≤ 0.5% of energy), ≥ 1 ratio of polyunsaturated to saturated fat, folate (≥ 600 g/day (sic)), iron (≥ 27 mg/day) and calcium (≥ 1000 mg/day) intakes from foods. Maximum possible score was 100, (10 x 10) with 1 point subtracted for each 10% decrease in intake.
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Valencia, Spain (part of the INMA cohort)
Funding	Instituto de Salud Carlos III, FISFEDER, Conselleria de Sanitat Generalit Valenciana
Participants	787 women (with a singleton live birth between May 2004 and February 2006)
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	10-13 weeks GA (to reflect diet in first trimester)
Comparison	Quintiles
Outcomes	Customised fetal growth restriction (weight, length and head circumference); taking into account parental (maternal preconception weight, height and parity and paternal height) and newborn variables (sex and gestational age). Fetal growth restriction was 80% below the lower limit of the CI.
Results	**FGR in weight** AHEI-P (range) n OR (95% CI) Q1 (35-47) 149 1.00 Q2 (48-51) 154 0.55 (0.28 to 1.08) **Q3 (52-55) 140 0.35 (0.16 to 0.76)** **Q4 (56-60) 166 0.51 (0.26 to 0.99)** **Q5 (61-75) 173 0.24 (0.10 to 0.55)** ***P for trend = 0.001*** **FGR in length** AHEI-P (range) n OR (95% CI) Q1 (35-47) 149 1.00 Q2 (48-51) 154 1.28 (0.60 to 2.73) Q3 (52-55) 140 0.62 (0.25 to 1.54) Q4 (56-60) 166 1.15 (0.54 to 2.46) Q5 (61-75) 173 0.78 (0.34 to 1.80) ***P for trend = 0.538*** **FGR in head circumference** AHEI-P (range) n OR (95% CI) Q1 (35-47) 149 1.00 **Q2 (48-51) 154 0.46 (0.21 to 0.99)** Q3 (52-55) 140 0.49 (0.22 to 1.08) Q4 (56-60) 166 0.60 (0.29 to 1.23) **Q5 (61-75) 173 0.40 (0.17 to 0.90)** ***P for trend = 0.070***
Followup	To birth
Confounding	FGR in weight: adjusted for smoking status, weight gain during first trimester, folic acid supplement use

	FGR in length: adjusted for smoking status, weight gain during first trimester, and maternal height FGR in head circumference: smoking status, caffeine intake during first trimester, parity, maternal height, and weight gain during first trimester.
Risk of bias	Moderate risk of bias: 54% participation rate; dichotomous outcomes adjusted for fewer factors than in the regression analysis (not extracted here) e.g. education level
Relevance	Likely to be relevant for Australian women
Other comments	Differs from Rifas-Shiman 2009 (Project Viva) by retaining nuts and soy category in AHEI-P and in adjusting for folic, calcium and iron supplement use (but only in some analyses)

Reference	**Ross 1996**
Dietary patterns	Foods containing DNA topoisomerase II inhibitors: beans, fresh vegetables, canned vegetables, fruits, soy, coffee, wine, black tea, green tea, cocoa
Study type	Case control study (Children's Cancer Group studies E09, E14, E15)
Level of evidence	III-3 (aetiology)
Setting	United States and Canada
Funding	University of Minnesota Children's Cancer Research Fund, NIH, NCI
Participants	303 cases diagnosed at one year or less; 468 matched controls
Baseline comparisons	See confounding below
Dietary assessment	FFQ
Timing	During pregnancy
Comparison	Low (score < 15: 28% of women) versus medium (score 15-19; 40% of women) versus high exposure (20+; 32% of women); Score = combined total for each food (0 = never; 1 = 1/month; 2 = 1-3/month; 3 = 1-3/week; 4 = 4-6/week; 5 = daily
Outcomes	Childhood leukemia: acute lymphoblastic leukemia (ALL); acute myeloid leukemia (AML)
Results	<u>**Overall leukemia**</u> **Cases** / **OR** Low 21 1.0 Medium 38 2.1 (0.9 to 5.0) High 23 1.1 (0.5 to 2.3) <u>**ALL**</u> 17 1.0 Low 26 1.3 (0.4 to 4.2) Medium 10 0.5 (0.2 to 1.4) High <u>**AML**</u> Low 4 1.0 Medium 12 **9.8 (1.1 to 84.8)** High 10 **10.2 (1.1 to 96.4)**
Followup	n/a
Confounding	Adjusted for maternal education
Risk of bias	Moderate risk of bias: results available for approx 83% of eligible cases (missing cases due to parental refusal, loss to follow-up and other unspecified reasons); Canadian mothers were subsequently excluded; adjustment made only for one variable (maternal education); mothers needed to recall exposures of up to 10 years ago
Relevance	Likely to be relevant to Australian women
Other comments	Childhood leukemias are rare – 32 cases per million livebirths in USA per year; 80% show a genetic abnormality (involving the MLL gene) which is thought to occur in utero; and these are predominantly AML

Reference	**Shaheen 2009**
Dietary patterns	5 dietary patterns *(see Comparisons below)*
Study type	Prospective cohort study: from ALSPAC
Level of evidence	II (aetiology)
Setting	Avon, UK (part of ALSPAC)
Funding	UK MRC, Wellcome Trust, University of Bristol, Asthma UK
Participants	14,062 children
Baseline comparisons	*See Confounding below*
Timing	Women completed FFQ at 32 weeks gestation
Comparisons	• 'Health conscious' salad, fruit, fruit juices, rice, pasta, oat/bran based breakfast cereals, fish, pulses, cheese, non-white bread; • 'Traditional' vegetables, red meat, poultry; • 'Processed' meat pies, sausages, burgers, fried foods, pizza, chips, crisps, white bread, eggs, baked beans; • 'Vegetarian' meat substitutes, pulses, nuts, herbal tea; • 'Confectionery' chocolate, sweets, biscuits, cakes, puddings.
Outcomes	Eczema, wheezing, asthma, hayfever, atopy, pulmonary function
Results	

	OR (95% CI)	aOR (95% CI)
Transient infant wheeze at 6 months (n = 8886)		
Health conscious	**0.88 (0.83** to 0.94)	0.98 (0.90 to 1.06)
Traditional	0.94 (0.88 to 1.10)	0.95 (0.89 to 1.02)
Processed	1.12 (1.05 to 1.20)	0.99 (0.91 to 1.08)
Confectionery	1.02 (0.96 to 1.09)	1.03 (0.95 to 1.10)
Vegetarian	1.00 (0.94 to 1.07)	1.00 (0.94 to 1.06)
Later onset wheeze at 6 months (n = 8886)		
Health conscious	0.94 (0.87 to 1.02)	0.93 (0.84 to 1.03)
Traditional	1.00 (0.93 to 1.09)	1.00 (0.92 to 1.09)
Processed	**1.10 (1.01 to 1.20)**	1.03 (0.93 to 1.13)
Confectionery	1.00 (0.93 to 1.08)	0.96 (0.87 to 1.06)
Vegetarian	0.94 (0.87 to 1.02)	**0.92 (0.85 to 1.00)**
Persistent wheeze at 6 months (n = 8886)		
Health conscious	**0.78 (0.70 to 0.87)**	1.00 (0.86 to 1.16)
Traditional	0.95 (0.85 to 1.06)	0.96 (0.86 to 1.08)
Processed	**1.27 (1.15 to 1.40)**	1.00 (0.88 to 1.13)
Confectionery	1.02 (0.91 to 1.14)	1.02 (0.90 to 1.16)
Vegetarian	1.07 (0.98 to 1.17)	1.06 (0.96 to 1.16
Eczema at 2.5 years (n = 9516)		
Health conscious	**1.12 (1.07 to 1.17)**	1.06 (0.99 to 1.12)
Traditional	0.99 (0.95 to 1.04)	1.00 (0.95 to 1.05)
Processed	0.95 (0.90 to 1.00)	0.97 (0.91 to 1.03)
Confectionery	1.02 (0.97 to 1.07)	1.03 (0.97 to 1.08)

Vegetarian	0.98 (0.94 to 1.03)	0.99 (0.94 to 1.04)
Eczema at 7.5 years (n = 7693)		
Health conscious	**1.12 (1.05 to 1.19)**	1.04 (0.95 to 1.13)
Traditional	0.99 (0.93 to 1.06)	0.99 (0.92 to 1.05)
Processed	0.95 (0.89 to 1.02)	0.96 (0.88 to 1.05)
Confectionery	1.04 (0.97 to 1.10)	1.03 (0.95 to 1.11)
Vegetarian	1.02 (0.96 to 1.08)	1.01 (0.95 to 1.08)
Wheezing at 3.5 years (n = 8886)		
Health conscious	**0.90 (0.84 to 0.96)**	0.96 (0.88 to 1.05)
Traditional	0.99 (0.93 to 1.06)	1.00 (0.93 to 1.07)
Processed	**1.14 (1.07 to 1.22)**	1.02 (0.94 to 1.10)
Confectionery	1.00 (0.94 to 1.07)	0.98 (0.91 to 1.06)
Vegetarian	0.99 (0.93 to 1.05	0.97 (0.91 to 1.04)
IgE at 7 years (n = 4819) *GM ratio*		
Health conscious	**1.07 (1.02 to 1.13)**	**1.07 (1.00 to 1.14)**
Traditional	0.98 (0.93 to 1.02)	**0.96 (0.91 to 1.00)**
Processed	1.01 (0.96 to 1.06)	0.97 (0.91 to 1.04)
Confectionery	1.00 (0.96 to 1.05)	1.00 (0.94 to 1.06)
Vegetarian	**1.05 (1.01 to 1.10)**	**1.07 (1.02 to 1.12)**
Hay fever at 7.5 years (n = 7674)		
Health conscious	1.06 (0.98 to 1.15)	1.00 (0.91 to 1.11)
Traditional	1.06 (0.98 to 1.15)	1.04 (0.96 to 1.13)
Processed	**0.91 (0.82 to 1.00)**	0.93 (0.83 to 1.04)
Confectionery	1.02 (0.94 to 1.10)	1.01 (0.92 to 1.11)
Vegetarian	0.96 (0.89 to 1.05)	0.97 (0.89 to 1.06)
Bronchial responsiveness at 8-9 years *GM ratio*		
Health conscious	0.99 (0.94 to 1.05)	1.01 (0.94 to 1.08)
Traditional	1.01 (0.96 to 1.07)	1.02 (0.97 to 1.08)
Processed	1.01 (0.95 to 1.07)	1.03 (0.96 to 1.10)
Confectionery	0.96 (0.91 to 1.01)	0.96 (0.90 to 1.02)
Vegetarian	*1.02 (0.97 to 1.08)*	*1.03 (0.98 to 1.08)*
Lung function (FEV1) at 8-9 years: n = 6192 (unadjusted and adjusted difference (SDs) and 95% CIs)		
Health conscious	**0.03 (0.01 to 0.06)**	0.02 (-0.01 to 0.06)
Traditional	0.02 (-0.01 to 0.05)	0.02 (-0.01 to 0.05)

	Processed **-0.03 (-0.06 to -0.00)** -0.02 (-0.06 to 0.01) Confectionery -0.01 (-0.03 to 0.02) -0.01 (-0.04 to 0.02) Vegetarian 0.01 (-0.02 to 0.03) 0.01 (-0.01 to 0.04) **Lung function (FVC) at 8-9 years: n = 6285 (unadjusted and adjusted difference (SDs) and 95% CIs)** Health conscious 0.01 (-0.01 to 0.04) 0.01 (-0.03 to 0.04) Traditional 0.02 (-0.01 to 0.04) 0.02 (-0.01 to 0.04) Processed **-0.05 (-0.07 to -0.02)** **-0.04 (-0.07 to -0.01)** Confectionery -0.01 (-0.03 to 0.02) -0.00 (-0.03 to 0.03) Vegetarian 0.02 (-0.01 to 0.04) 0.02 (-0.01 to 0.05)
Followup	Up to 8-9 years
Confounding	Maternal factors during pregnancy (energy intake, smoking, infections, antibiotics and paracetamol); other maternal factors (educational level, housing tenure, financial difficulties, pre-pregnancy BMI, ethnicity, age, parity, history of asthma, eczema, rhinoconjunctivitis, migraine); sex of child, gestational age, breast fed in first 6 months, day care at 8 months, multiple pregnancy, pets in infancy, damp/condensation/mould, child exposed to environmental tobacco smoke at weekends, season of birth, season of FFQ completion, birth weight, head circumference, birth length. Also number of younger siblings and child's BMI at 7 years for later childhood outcomes.
Risk of bias	Moderate risk of bias: 37% attrition at 6 months – attrition "was greatest among families of lower socioeconomic status" (no other details given). Have not controlled for child's own diet; 'over'-adjusted in other areas?
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	Siega-Riz 2001
Dietary patterns	Meal patterns in second trimester of pregnancy (reported number of meals (breakfast, lunch and dinner) and snacks consumed per day); Optimal meal pattern was defined as three meals and two or more snacks per day
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Data from Pregnancy, Infection and Nutrition (PIN) Study, USA
Funding	NICHHD, Institute of Nutrition, Wake Area Health Education Center, North Carolina, USA
Participants	2065 predominantly lower-to-middle income women between 24 and 29 weeks gestation recruited from August 1995 to December 1998; 42% African-American women
Baseline comparisons	Risk of preterm birth was slightly higher among the successfully recruited women than among those who refused *See confounding below*
Dietary assessment	FFQ
Timing	Diet assessed at 24-29 weeks GA to reflect diet during the second trimester
Comparison	Referent group: women who ate three meals and two or more snacks a day
Outcomes	Preterm birth (< 37 weeks); early preterm birth (< 34 weeks); premature rupture of the membranes
Results	(see below)

Meal Pattern	% of women	% preterm birth
3 Meals plus 2 or more snacks	**71.5**	**10.6**
3 meals plus no snacks	4	16.6
3 meals plus 1 snack	0.2	0
2 meals plus no snacks	0.5	9.0
2 meals plus 1 snack	14.5	12.4
2 meals plus 2 or more snacks	7.8	13.8
1 meal regardless of number of snacks	1.0	19.0

Preterm birth (less optimal versus optimal meal pattern)

Crude RR: 1.27 95% 0.98 to 1.63

aOR: 1.30 95% CI 0.96 to 1.76

Early preterm birth

Crude RR: 1.56 95% CI 0.92 to 2.63

aOR: 1.57 95% CI 0.88 to 2.79

Preterm Labour

Crude RR: 1.0 95% CI 0.61 to 1.65

aOR: 1.11 95% CI 0.64 to 1.89

Premature rupture of the membranes

Crude RR: 1.91 95% CI 1.09 to 3.33

aOR: 1.87 95% CI 1.02 to 3.43

Followup	To birth
Confounding	Adjusted for pregravid BMI, total energy intake, supplement use (other potential confounders discarded from model due to lack of influence); Further adjustment restricted to spontaneous preterm birth only made little difference to estimates of effect
Risk of bias	Low risk of bias: Of 4160 eligible women, 2,505 (60%) were successfully recruited into the PIN study; 2247 (90%) completed the FFQ; 2065 women had

	sufficiently complete data for analysis
Relevance	Different ethnic mix compared with Australia
Other comments	Women who consumed meals less frequently were slightly heavier prior to pregnancy, older and less compliant with taking their antenatal supplement; The total energy requirement of women consuming 3 meals plus 2 or more snacks a day was significantly higher than that of women with less than the optimal frequency of food intake

Reference	Stuebe 2009
Dietary patterns	Vegetarian diet (defined as a diet that "excludes certain animal products")
Study type	Prospective cohort study (Project Viva)
Level of evidence	II (aetiology)
Setting	8 urban and suburban obstetric offices of a multispecialty group practice in eastern Massachusetts, USA
Funding	US NIH, Harvard Medical School, Harvard Pilgrim Health Care Foundation
Participants	1338 women giving birth to a live singleton infant, < 22 weeks gestation at study entry; 379 (27%) were overweight (BMI ≥ 26); 703 (51%) experienced excessive weight gain Exclusions: not fluent in English
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Administered in first and second trimesters of pregnancy
Comparison	Vegetarian diet in first and second trimester versus not vegetarian
Outcomes	Excessive gestational weight gain (IOM 1990)
Results	**Excessive gestational weight gain: vegetarian vs no vegetarian diet:** 1st trimester: **aOR 0.45 95% CI 0.27 to 0.76** 2nd trimester: aOR 0.70 95% CI 0.40 to 1.20 **1st trimester: multivariate logistic regression model:** **aOR 0.48 95% CI 0.48 to 0.81** **-1.65 kg 95% CI -2.79 to -0.51**
Followup	To birth
Confounding	Adjusted for pre-pregnancy BMI, maternal age, race/ethnicity, smoking status, gestational age at birth, nausea in first trimester in pregnancy
Risk of bias	Low risk of bias: Of 2083 eligible women, 1388 (67%) of women had data available for analysis (31 had missing information on pre-pregnancy BMI and gestational weight gain; 226 had missing covariate information and 438 had missing data on either first or second-trimester diet and mid-pregnancy physical activity); included women were less likely to be African-American or Hispanic, to be younger, multiparous and obese
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Thompson 2010**
Dietary patterns	1) Traditional (meat (lamb in particular), potatoes, carrots (and other root vegetables), peas, gravy and meat dishes such as cottage pie, apples/pears, citrus fruit, kiwifruit/feijoas, bananas, green vegetables, maize, dairy food, yoghurt and water); 2) Junk (icecream, sweet biscuits, scones, cakes, sweetened cereal, crisps, pies, lollies, chocolate bars, iceblocks and milo (chocolate energy drink); 3) Fusion (fruits, fried rice/noodles, boiled rice/pasta, fish/shellfish, milk and low intake for tea/coffee, sherry/wine and hard cheeses).
Study type	Case-control
Level of evidence	III-3 (aetiology)
Setting	New Zealand
Funding	Health Research Council of New Zealand, Foundation for the Newborn, Child Health Research Foundation
Participants	Mothers of 1714 children born between October 1995 and November 1997 (844 born SGA and 870 born appropriate for GA)
Baseline comparisons	Different dietary patterns were associated with multiple different socio-demographic characteristics
Dietary assessment	FFQ
Timing	After birth (for diet in first and last month of pregnancy)
Comparison	Fusion v junk v traditional diets
Outcomes	SGA (≤ 10th percentile for sex and gestation)
Results	<u>**SGA**</u> *Fusion* OR 1.07 95% CI 0.95 to 1.21 aOR 1.02 95% CI 0.85 to 1.21 *Junk* OR 0.97 95% CI 0.70 to 1.09 aOR 1.01 95% CI 0.88 to 1.17 *Traditional* **OR 0.79 95% CI 0.70 to 0.89** **aOR 0.86 95% CI 0.75 to 0.99**
Followup	To birth
Confounding	Adjusted for gestation, infant sex, maternal smoking in pregnancy, maternal pre-pregnancy height and weight, parity, ethnicity and maternal hypertension
Risk of bias	Low risk of bias (in addition to that inherent in a study with a case-control design such as recall bias)
Relevance	Not clear if these three patterns reflect dietary patterns of pregnant Australian women
Other comments	Presented only the results for early diet, as relationships with late diet were very similar

Reference	**Tieu 2008**
Dietary patterns	Low v high glycaemic index
Study type	SR
Level of evidence	I (intervention)
Setting	Trials from North America and Australia
Funding	Part funding from the Australian Department of Health and Ageing
Participants	3 RCTs (total of 107 women)
Baseline comparisons	NA
Dietary assessment	NA
Timing	During pregnancy
Comparison	Low versus high glycaemic diet during pregnancy
Outcomes	LGA, birthweight, ponderal index, maternal fasting glucose concentrations
Results	In one trial of 62 women, there were significantly fewer **large for gestational age** infants when women adopted a low GI diet: **RR 0.09, 95% CI 0.01 to 0.69** **Ponderal index:** mean difference (MD) -0.18 95% CI -0.32 to -0.04 (two trials; 82 women) Results for women on the LGI diet on **birthweight** were not conclusive under a random-effects model (two trials; WMD -527.64 g, 95% CI -1119.20 to 63.92); **Maternal fasting glucose concentrations:** MD -0.28 mmol/L 95% CI -0.54 to -0.02 (two trials, 82 women). **Maternal weight gain during pregnancy**: MD -3.33 kg 95% CI -12.73 to 6.08 (two trials, 82 women)
Followup	To birth
Confounding	NA
Risk of bias	Low risk of bias
Relevance	Likely to be relevant to Australian women
Other comments	One of the trials also included a standard exercise regimen for all participants

Reference	Uusitalo 2009
Dietary patterns	Seven dietary patterns: • Fast food (sweets, fast food, snacks, chocolate, fried potatoes, soft drinks, high-fat pastry, cream, fruit juices, white bread, savoury, processed meat, sausage, eggs [low loading for wholegrain bread and potatoes]) • Alcohol and butter (beer, wine and liquor, butter, salad dressing, soft drinks [low loading of soft margarine 80%, fruits, breakfast cereals, fruit juices, high-fat milk]) • Healthy (leafy vegetables, cabbage, fish, vegetarian dishes, legumes and mushrooms, roots, berries, salad dressing, breakfast cereals, poultry, fruits, nuts and seeds, rice and pasta, eggs, low-fat cheese, low-fat sour milk, meat dishes, cream, processed vegetables) • Traditional bread (low-fat pastry, whole grain bread, high-fat pastry, tea, high-fat cheese, sugar and jam, berry juices, potatoes, breakfast cereals, butter, processed meat, savoury, nuts and seeds, meat dishes, high-fat sour milk, berries) • Traditional meat (meat, meat dishes, sausage, potatoes, processed meat, soft margarine 80%, organ meat, processed vegetables [low loading for nuts and seeds, breakfast cereals]) • Low fat (spread (butter-vegetable oil 40-60%; soft margarine 40-60%), low-fat cheese, low-fat milk, processed meat, wholegrain bread, low-fat sour milk, light soft drinks [low loading for high-fat milk, high-fat sour milk, soft margarine 80%) • Coffee (coffee, milk in coffee, high-fat milk, low-fat pastry, sausage [low loading of tea])
Study type	Retrospective cohort study
Level of evidence	III-3 (aetiology)
Setting	Oulu and Tampere, Finland (Finnish Birth Registry); part of the Finnish Type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study
Funding	Academy of Finland, Finnish Diabetes Association, Finnish Diabetes Research Foundation, Finnish Pediatric Research Foundation, Juho Vainio Foundation, Yrjo Jahnsson Foundation, Alma and K. A. Snellman Foundation, European Foundation for the Study of Diabetes, Special Public Grants for medical research at participating university hospitals, Juvenile Diabetes Research Foundation International, Novo Nordisk Foundation, EU Biomed 2.
Participants	3360 women giving birth in 1997-2002 whose baby carried human leucocyte antigen-conferred susceptibility to type 1 diabetes
Baseline comparisons	Not reported (only overall baseline characteristics)
Dietary assessment	FFQ
Timing	FFQ after birth; reflecting diet during the 8th month of pregnancy
Comparison	Seven dietary patterns: *See Dietary patterns above*
Outcomes	Maternal weight gain
Results	

Mean maternal weight gain rate (kg/week) [SE]

Dietary pattern	1st quartile (lowest)	2nd quartile	3rd quartile	4th quartile highest	P for trend
Healthy	0.427 [0.005]	0.435 [0.005]	0.431 [0.005]	0.416 [0.005]	0.059
- adjusted*	0.431 [0.010]	0.441 [0.010]	0.435 [0.010]	0.423 [0.010]	0.109
Fast food	**0.401 [0.005]**	**0.442 [0.005]**	**0.436 [0.005]**	**0.450 [0.005]**	**< 0.0001**
- **adjusted***	**0.412 [0.010]**	**0.429 [0.010]**	**0.439 [0.010]**	**0.455 [0.010]**	**< 0.0001**
Traditional meat	**0.432 [0.005]**	0.433 [0.005]	0.431 [0.005]	0.431 [0.005]	**0.022**
- adjusted*	0.431 [0.010]	0.434 [0.010]	0.440 [0.010]	0.426 [0.010]	0.262
Traditional bread	**0.407 [0.005]**	**0.434 [0.005]**	**0.429 [0.005]**	**0.438 [0.005]**	**0.0002**
- **adjusted***	**0.414 [0.010]**	**0.438 [0.010]**	**0.433 [0.009]**	**0.444 [0.010]**	**0.0002**
Low fat	0.434 [0.005]	0.419 [0.005]	0.433 [0.005]	0.423 [0.005]	0.123
- adjusted*	0.435 [0.009]	0.425 [0.010]	0.438 [0.010]	0.435 [0.010]	0.252
Coffee	**0.429 [0.005]**	**0.436 [0.005]**	**0.429 [0.005]**	**0.415 [0.005]**	**0.046**
- adjusted*	0.428 [0.010]	0.437 [0.010]	0.436 [0.010]	0.429 [0.009]	0.443
Alcohol and butter	**0.443 [0.005]**	**0.436 [0.005]**	**0.423 [0.005]**	**0.407 [0.005]**	**< 0.0001**
- **adjusted***	**0.443 [0.010]**	**0.438 [0.010]**	**0.431 [0.010]**	**0.421 [0.010]**	**0.014**

	‘Fast food’ – pregnant women in highest quartile gained 1.3 kg more weight on average during pregnancy than the lowest quartile; Respective figures for ‘traditional bread’ and ‘alcohol and butter’ were +0.9 kg and –0.7 kg
Followup	39th gestational week (range 24-44 weeks): mean follow-up time (from first antenatal visit) was 29.2 weeks SD 3.0.
Confounding	*maternal weight gain analysis was adjusted for maternal age, initial BMI, parity, vocational education, smoking, place of residence, birthweight of baby, gestational week of the first weight measurement
Risk of bias	Low risk of bias: 71% (3783/5362) DIPP study mothers took part in this study; data available for 3360/3783 (89%) of these women (53 women had incomplete FFQ, 98 twin or triplet pregnancies, 272 women with incomplete weight gain information)
Relevance	Likely to be reasonably relevant to Australian women
Other comments	

Reference	**Vujkovic 2009**
Dietary patterns	Mediterranean diet (high intakes of vegetables, fruit, legumes, vegetable oil, cereal products, alcohol and fish; and low intakes of potatoes, sugar and confectionery, sauces and condiments)
Study type	Case-control
Level of evidence	III-3 (Aetiology)
Setting	8 clinics in the Netherlands, 1999-2001 (part of a case-control study of 77 mothers of children with spina bifida and 151 control mothers)
Funding	Netherlands Organization for Scientific Research
Participants	50 mothers of children with spina bifida and 81 control mothers (specifically Dutch Caucasian mothers and children with nonsyndromic meningo(myelo)cele) Exclusion criteria were: pregnant or breastfeeding at the time of the current study, consanguinity, a familial relationship between the case and control families, maternal diabetes mellitus, changed diet compared to periconception period (4 weeks before to 8 weeks after conception, severe nausea and/or vomiting starting after the first week of pregnancy resulting in a changed or decreased food intake, mothers whose nutritional intake data and/or biomarkers were incomplete.
Baseline comparisons	Case mothers had a slightly higher BMI, lower education, and used less folic acid supplements and alcohol at the time of the study (and case mothers also used less alcohol in the periconceptional period).
Timing	FFQ at 14 months after the birth of the index child, covering intake in the previous three months
Comparison	Weak versus strong use of a Mediterranean diet (lowest v higher quartiles)
Outcomes	Risk of spina bifida
Results	**<u>Spina bifida (Principal component factor analysis (PCA))</u>** Lowest v higher quartiles: 18 v 32 children with spina bifida compared with 14 v 67 in control group: **crude OR 2.7 95% CI 1.2 to 6.1**; adjusted OR 2.3 95% CI 0.9 to 5.6 Reduced rank regression (RRR) Lowest v higher quartiles: 20 v 30 children with spina bifida compared with 13 v 68 in control group: **crude OR 3.5 95% 1.5 to 7.9; adjusted OR 3.5 95% CI 1.5 to 8.2)**
Followup	NA (case control study)
Confounding	Mediterranean diet was associated with a higher maternal age at birth of the index child, higher education and more alcohol consumption (at time of the study and in the periconceptional period). Adjustments for confounders including maternal BMI, age at the index pregnancy and periconceptional folic acid supplementation did not significantly differ from unadjusted analyses for dietary pattern assessed by reduced rank regression but for PCA, the adjusted analysis was no longer statistically significant *(see Results above).* Analyses were not adjusted for level of education because “there was a strong association between education and use of the Mediterranean diet”.
Risk of bias	Moderate risk of bias: Recall bias – women may not have been able to accurately recall whether their current diet was similar to their diet in the periconception period; Losses - 18/77 case mothers and 38/151 control mothers were excluded due to excessive vomiting and/or a reported change in nutritional intake in the periconception period compared with time of the study; a further 4 case mothers and 4 control mothers were excluded because information on excessive vomiting in the periconception period and/or change in nutritional pattern was lacking; 5 case mothers and 28 control mothers were excluded because of incomplete FFQs.
Relevance	All women were Caucasian; food fortification with folate was not mandatory
Other comments	

Reference	**Vujkovic 2007**
Dietary patterns	Western diet (high in meat, pizza, legumes and potatoes and low in fruits); Prudent diet (high intakes of fish, garlic, nuts, and vegetables and higher frequency of hot meals per day)
Study type	Case-control
Level of evidence	III-3 (aetiology)
Setting	Netherlands
Funding	Royal Netherlands Academy of Arts and Sciences, Mother and Child Centre, University Medical Center, Rotterdam
Participants	481 Dutch European mothers (203 with a child with cleft lip or cleft palate and 178 controls) Exclusions: pregnant, breastfeeding, current folic acid supplement use, a different current diet than in the preconception period, hyperemesis or nausea in pregnancy.
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Assessed 14 months after the birth of the index child (to estimate preconception intake)
Comparison	Tertiles of western diet; tertiles of prudent diet
Outcomes	Cleft lip, cleft palate, [BMI at time of study]
Results	See below

Cleft lip or palate or both

	n/N Cases	n/N Controls	OR (95% CI)	aOR1 (95% CI)	aOR cleft palate only (95% CI)
Western					
T1	58/127 (28.6%)	69 (38.8%)	1.00	1.00	1.00
T2	67/127 (33.0%)	60 (33.7)	1.3 (0.8 to 2.2)	1.2 (0.7 to 2.1)	1.2 (0.8 to 2.1)
T3	78/127 (38.4%)	49 (27.5%)	**1.9 (1.2 to 3.1)**	**1.7 (1.0 to 3.0)**	**1.8 (1.0 to 2.9)**
Prudent					
T1	68/127 (33.5%)	59 (33.1%)	1.00	1.00	1.00
T2	64/127 (31.5%)	63 (35.4%)	0.9 (0.5 to 1.4)	0.8 (0.5 to 1.4)	0.7 (0.5 to 1.2)
T3	71/127 (35.0%)	56 (31.5%)	1.1 (0.7 to 1.8)	1.7 (1.0 to 3.0)	1.3 (0.6 to 1.7)

BMI at 14 months postpartum, median (5th percentile, 95th percentile)

(N = 164; 83 case mothers, 81 control mothers)

Western

T1	23.3 (18.8, 30.9)
T2	23.9 (20.1, 30.5)
T3	25.9 (20.7, 39.6)

P value for trend 0.01

Prudent

T1	24.0 (20.1, 35.9)
T2	25.0 (17.8, 37.2)
T3	23.8 (19.6, 30.2)

P value for trend 0.75

Followup	NA
Confounding	1) Western diet adjusted for maternal education, smoking, alcohol consumption, periconception folic acid intake and/or multivitamin intake

	2) Prudent diet adjusted for maternal education, periconception folic acid intake and/or multivitamin intake
Risk of bias	Low risk of bias: 381/442 (86.2%) women's data available – 22 case and 39 control mothers were excluded; inherent risk of recall bias with study design
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Wolff 1995**
Dietary patterns	Seven patterns: nutrient dense (frequent consumption of vitamin A and vitamin C rich fruits and vegetables; other fruits and vegetables and low fat dairy products such as skim milk, low fat milk and yoghurt ("most consistent with dietary recommendations"); traditional (frequent consumption of flour and corn, legumes (including nuts and seeds, high fat meats, sugar (including soft drinks)); transitional (high in fats and oils, breads and cereals, non vitamin A and C rich vegetables, high fat meats and sugar), nutrient dilute (salty snacks (chips, popcorn, pretzels), non-dairy desserts = high calorie, high in sodium and sugar); protein rich (high consumption of dairy desserts, low fat meat (fish and poultry) and processed meats); high fat dairy foods (whole milk and cheese, soups); mixed (mixed dishes, soup, processed meats)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	United States Hispanic Health and Nutrition Examination Survey
Funding	Not reported
Participants	549 Mexican American mothers and their children (n = 778); singleton pregnancies. Women pregnant at the time of the survey and women with diabetes were excluded
Baseline comparisons	*See confounding below*
Dietary assessment	Factor analysis and FFQ
Timing	Not stated
Comparison	Seven dietary patterns as described above
Outcomes	Birthweight
Results	**Regression analysis for birthweight was significant for:** (see table below)

	Regression coefficient	**SE**	**p value**
Nutrient dense pattern	**20.4**	**4.6**	**0.0001**
Nutrient dilute pattern	**-22.2**	**10.0**	**0.05**
Protein rich pattern	**36.1**	**14.1**	**0.05**
Transitional pattern	Described as being negatively correlated with birthweight (actual numbers not reported)		

Followup	To birth
Confounding	Stepwise regression conducted but not clear how this adjusted for confounders
Risk of bias	Moderate risk of bias: unclear how adjustment for potential confounders was done; amount of missing data not clear
Relevance	Mexican American diet different from that of Australian women
Other comments	

Reference	Xiang 2005
Dietary patterns	Chinese (staples of rice, steamed bun, noodles, Chinese cabbage, bean curd and pork) v Swedish dietary pattern (bread, potato, pasta, milk, sour milk and cheese) - further details in Table III of paper
Study type	Prospective (partly retrospective) cohort study and concurrent comparison
Level of evidence	II (aetiology)
Setting	Beijing, China and Stockholm, Sweden
Funding	Not reported
Participants	40 lactating women (23 Chinese women (23 infants) and 17 Swedish women (19 infants))
Baseline comparisons	Similar except for lower weight for Chinese woman
Dietary assessment	3 day dietary records
Timing	Diet assessed 3 months after birth
Comparison	Diets of Chinese and Swedish women
Outcomes	Birthweight, birth length, weight gain at 3 months, length gain at 3 months, breastmilk composition (long-chain polyunsaturated fatty acids (LC-PUFAs))
Results	**Summary**: Breastmilk of Chinese women is less balanced in regard to LC-PUFAs than Swedish women; and infant growth did not differ significantly between the two groups **Breastmilk** of Chinese women is significantly richer in linoleic acid (LA) and lower in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) than that of Swedish women **Weight gain at 3 months (g/kg/d)** Chinese infants (n = 21): 9.68 SD?0.58 Swedish infants (n= 19): 8.56 SD?0.39 **Length gain at 3 months (cm/wk)** Chinese infants (n = 16): 0.90 SD?0.05 Swedish infants (n= 19): 0.96 SD?0.03
Followup	To 3 months
Confounding	No mention of any adjustment for confounding
Risk of bias	Moderate risk of bias: no adjustment for potential confounders; not clear if the variance measure is SD
Relevance	Swedish diet closer to the diet of most Australian women
Other comments	Study underpowered to detect infant growth differences

Reference	**Zeiger 1989; Zeiger 1995**
Dietary patterns	Combined maternal and infant dietary avoidance regimen versus standard diets
Study type	RCT
Level of evidence	II (intervention)
Setting	San Diego, USA
Funding	Mead Johnson Nutritional Division, Lincoln Diagnostic Laboratories, Marion Laboratories, Pharmacia
Participants	379 infants born to allergic parents between November 1981 and July 1984; families were included in the study if at least one parent had a history of an atopic disorder and specific IgE by skin or RAST testing ; 288 families were evaluated at 4 months (103 from the dietary avoidance group and 185 from the control group)
Baseline comparisons	NA
Dietary assessment	NA
Timing	Mother: last trimester of pregnancy and while breastfeeding Infant: when breastfeeding was supplemented or stopped
Comparison	Dietary avoidance group: Mother: total avoidance of milk (dairy food), egg, and peanut products; avoidance of concentrated soy foods (e.g. tofu) and limit of 2 daily serves of wheat, using other grains to meet cereal and starch requirements Infant: casein hydrolysate formula when breastfeeding stopped or was supplemented – until 12 months; solid foods introduced to these infants at 6 months, starting with nonlegume vegetables, followed rice cereal at 7 months, meats at 8 months, noncitrus fruits and juices at 9 months, cow'smilk at 12 months and wheat, soy, corn and citrus thereafter at monthly intervals. Egg to be started at 24 months and peanut and fish at 36 months *versus* Standard diet group: pregnant and breastfeeding women were encouraged to follow standard diets; a cow's milk based whey infant formula was provided for supplementation or weaning thorugh the first year; solids foods were introduced as follows (no solids until four months when cereal was introduced, followed by vegetables, fruits and egg yolks at 6 months, meats at 8 months, and whole cow's milk and egg whites at 12 months)
Outcomes	Atopic dermatitis (three probable or four definite of pruritus, typical morphology and distribution, tendency toward chronicity or recurrence and concurrent specific IgE at the time the rash was present); Urticaria angioedema (on basis of morphology – definite when physician confirmed or unduly severe or probable when parentally reported and consistent in morphology); Allergic rhinitis (characteristic sneezing, itching and/or rhinorrhea with existing IgE and nasal eosonophilia GI disease (vomiting or diarrhoea after ingestion of an offending food on at least two occasions with concomitant food-specific IgE Food allergy (probable when food-specific IgE was associated with atopic dermatitis, urticaria induced at least twice by foods and GI allergy; a positive double-blind food challenge or a severe food reaction with co-existing food-specific IgE was considered definite food allergy Birthweight; weight and height at 4,12 and 24 months Maternal third trimester weight gain
Results	

	N	Dietary avoidance	N	Control	
Birthweight (kg)	103	3.39 [0.50]	173	3.47 [0.59]	MD -0.08 95% CI -0.21 to 0.59
Birthweight (term singletons)	99	3.42 [4.8]	159	3.52 [0.47]	MD -0.10 95% CI -0.22 to 0.02
Weight at 4 mo	99	6.64 [0.78]	159	6.71 [0.91]	MD -0.07 95% CI -0.28 to 0.14
Weight at 12 mo	95	9.50 [1.20]	151	9.62 [1.22]	MD -0.12 95% CI -0.43 to 0.19
Weight at 24 mo	93	12.44 [1.74]	142	12.57 [1.66]	MD -0.13 95% CI -0.58 to 0.32
Height at 4 mo (cm)	99	64.8 [1.9]	159	64.9 [2.3]	MD -0.10 95% CI -0.62 to 0.42
Height at 12 mo	95	76.6 [1.9]	151	76.9 [3.0]	MD -0.30 95% CI -1.01 to 0.41
Height at 24 mo	93	88.9 [3.7]	141	89.4 [3.7]	MD -0.50 95% CI -1.47 to 0.47

	Maternal third trimester weight gain (kg) 98 4.86 [0.24] 146 6.10 [0.20] **MD -1.24 95% CI -1.30 to -1.18** **Allergic rhinitis:** no significant differences between dietary avoidance and control groups at 4, 12 and 24 months of age **Atopic dermatitis**: no significant differences between dietary avoidance and control groups at 4 and 24 months of age, **significantly lower (borderline) in dietary avoidance group at 12 months (p = 0.052)** **Hives:** no significant differences between dietary avoidance and control groups at 4 and 24 months of age, **significantly lower (?) in dietary avoidance group at 12 months (from graph; no p value given)** **Skin (AD or hives):** no significant differences between dietary avoidance and control groups at 4 and 24 months of age; **significantly lower in dietary avoidance group at 12 months (p = 0.018)** **GI disorder:** no significant differences between dietary avoidance and control groups at 4, 12 and 24 months of age **Skin or GI disorder:** no significant differences between dietary avoidance and control groups at 4 and 24 months of age, **significantly lower in dietary avoidance group at 12 months (p = 0.005)** **Asthma:** no significant differences between dietary avoidance and control groups at 4, 12 and 24 months of age **Any atopic disorder:** no significant differences between dietary avoidance and control groups at 4 and 24 months of age; **significantly lower in dietary avoidance group at 12 months (p = 0.013)** **Food allergy (includes atopic dermatitis, urticaria/ angioedema, and /or GI disease with specific food IgE)** <table><tr><td></td><td>**N**</td><td>**Dietary avoidance**</td><td>**N**</td><td>**Control**</td><td>**P-value**</td></tr><tr><td>**Food allergy (12 mo):**</td><td>99</td><td></td><td>177</td><td></td><td></td></tr><tr><td>- Definite</td><td></td><td>2.0%</td><td></td><td>7.9%</td><td>0.059</td></tr><tr><td>**- Probable**</td><td></td><td>**3.0%**</td><td></td><td>**8.5%**</td><td>**0.021**</td></tr><tr><td>**- TOTAL**</td><td></td><td>**5.0%**</td><td></td><td>**16.4%**</td><td>**0.007**</td></tr><tr><td>**Food allergy (24 mo):**</td><td>97</td><td></td><td>169</td><td></td><td></td></tr><tr><td>- Definite</td><td></td><td>4.1%</td><td></td><td>8.9%</td><td>0.216</td></tr><tr><td>**- Probable**</td><td></td><td>**3.1%**</td><td></td><td>**11.2%**</td><td>**0.021**</td></tr><tr><td>**- TOTAL**</td><td></td><td>**7.2%**</td><td></td><td>**20.1%**</td><td>**0.005**</td></tr></table> Food associated with positive challenges in the control group included egg (n=8), milk (n=4), peanut (n=1) and soy (n=1). In the dietary avoidance group, peanut (n=2) and egg (n=1) caused positive food challenges. **4 year follow-up:** cumulative reduction in food allergy in infancy by maternal/infant food allergen avoidance at 4 years, but the current prevalence at 4 years was similar (about 5% in each group) and failed to affect respiratory allergy development from birth to 4 years **7 year follow-up:** No significant differences between groups for food allergy, atopic dermatitis, allergic rhinitis, asthma, any atopic disease, lung function or aeroallergen sensitisations
Followup	Seven years
Confounding	NA
Risk of bias	Moderate risk of bias: unclear method of allocation concealment; losses to follow-up – 64/167 (38%) in the dietary avoidance group and 27/212 (13%) in the control group (14 families in each group were found not to be atopic and so they were postrandomisation exclusions; in the dietary avoidance group, 48 families had difficulty adhering and left the study; in the control group there were 7 miscarriages or stillbirth and one neonatal death, five families

	moved); at 12 months, attrition rate was 4% for the dietary avoidance group and 6% for the control group and at 24 months the respective rates of attrition were 4% and 9%; 14 infants in the dietary avoidance group were exposed to potential allergens (e.g. milk); attrition at 4 years was 15% in the dietary avoidance group and 18% in the control group)
Relevance	Relevant to Australian families; dietary intervention may be difficult to sustain
Other comments	Mothers in the diet avoidance group were supplemented with calcium; Symptoms such as colic, irritability and refusal of foods were not considered atopic manifestations; In both groups about 70% of infants breastfed for at least 4 months and about 40% at 8 months; Infants in the diet avoidance group were introduced to potentially allergenic foodstuffs later than control infants; Excluded from Kramer Cochrane review

Reference	**Zhang 2006**
Food type	Prudent diet: fruits, green leafy vegetables, poultry and fish Western diet: red meat, processed meat, refined grain products, sweets, desserts, French fries and pizza
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	USA
Funding	NIH
Participants	13,110 women who were free of cardiovascular disease, cancer, type 2 diabetes and history of GDM with at least one singleton pregnancy between 1992 to 1998 (part of the Nurses' Health Study II); Exclusions: incomplete FFQ, implausible dietary intake
Baseline comparisons	*See Confounding below* Sensitivity analyses done for nulliparous women as they were over-represented (due to exclusion of women with a history of GDM)
Dietary assessment	FFQ
Timing	Dietary intake over previous year (i.e. at least some pre-pregnancy coverage)
Comparison	Quintiles of prudent and western dietary pattern scores
Outcomes	GDM
Results	see below

GDM (RR 95% CI)

	Q1	**Q2**	**Q3**	**Q4**	**Q5**	**P for trend**
Western pattern						
Number of cases of GDM	127	135	151	155	190	
Person-years	19,231	20,227	20,269	20,146	19,759	
aRR (age, parity)	1.00	1.16 (0.91 to 1.40)	**1.39 (1.09 to 1.76)**	**1.49 (1.18 to 1.89)**	**1.97 (1.57 to 2.48)**	**< 0.0001**
aRR (age parity, BMI)	1.00	1.11 (0.87 to 1.42)	**1.28 (1.01 to 1.62)**	**1.34 (1.06 to 1.70)**	**1.68 (1.33 to 2.11)**	**< 0.0001**
aRR (see below)	1.00	1.09 (0.85 to 1.41)	1.22 (0.94 to 1.59)	1.25 (0.94 to 1.65)	**1.63 (1.20 to 2.21)**	**0.0011**
Additional adjustment for red meat and processed meat						
	1.00	*0.92 (0.71 to 1.19)*	*0.92 (0.69 to 1.22)*	*0.86 (0.62 to 1.18)*	*1.03 (0.72 to 1.48)*	*0.697*
Prudent pattern						
Number of cases of GDM	177	151	138	163	129	
Person-years	19,901	20,066	20,000	20,572	19,093	
aRR (age, parity)	**1.41 (1.12 to 1.77)**	1.18 (0.94 to 1.50)	1.07 (0.84 to 1.36)	1.21 (0.96 to 1.53)	1.00	**0.010**
aRR (age parity, BMI)	**1.37 (1.09 to 1.72)**	1.19 (0.94 to 1.51)	1.07 (0.84 to 1.36)	1.20 (0.95 to 1.51)	**1.00**	**0.017**

NOTE: no data in paper for the third adjusted prudent pattern analysis, have assumed ***p for trend is 0.018***

Followup	variable
Confounding	Analyses were adjusted for parity, age, BMI, smoking status, race/ethnicity, family history of diabetes, physical activity, alcohol consumption, and total energy intake
Risk of bias	Low risk of bias
Relevance	Likely to be relevant to Australian women
Other comments	Based on assumption that a woman's diet remains similar over time

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Caffeine

Included Studies

Study	Outcomes
1. Adeney 2007	GDM
2. Bakker 2010	Fetal growth, SGA, preterm birth, low birthweight, birthweight
3. Brekke 2009	Beta cell autoimmunity
4. Chen 2009	GDM
5. Giordano 2008	Child hypospadias and cryptorchidism
6. Greenwood 2010	Miscarriage/stillbirth
7. Haggarty 2009	Deprivation
8. Knox 1972	Anencephalus
9. Lagiou 2006	Maternal pregnancy oestradiol, unconjugated oestriol, sex hormone binding globulin (SHBG), progesterone, prolactin
10. Leviton 2002 SR	Maternal outcomes, spontaneous abortion, fetal death, congenital anomalies, preterm birth, low birthweight, SGA, perinatal death, infant growth, SIDS
11. Peck 2010 SR	Spontaneous abortion, fetal death, preterm birth, congenital anomalies, SGA, LBW
12. Pollack 2010	Pregnancy loss
13. Robinson 2009	Maternal blood glucose, insulin and insulin sensitivity index

Evidence Summaries

	N	Level	References
Maternal Outcomes			
1. In a US cohort study, consumption of sugar-sweetened cola beverages was associated with an increased risk of **gestational diabetes mellitus**, although this was not the case for diet cola beverages: • aOR for GDM with sugar-sweetened cola beverages: 1.22 (1.01 to 1.47); p_{trend} = 0.04 • aOR for GDM with diet cola beverages: 0.90 (0.78 to 1.03) p_{trend} = 0.07	13,475	II	Chen 2009
2. In a Canadian crossover RCT, women with gestational diabetes mellitus who consumed a caffeine capsule (equivalent to 1- 2 cups of coffee) had a significantly lower **insulin sensitivity index**: 3.96 [1.02] caffeine versus 4.81 [1.05] placebo, p = 0.01	27 (8)	II	Robinson 2009
3. In a US cohort study, moderate caffeine consumption prior to and during pregnancy (up to one cup a day) was significantly associated with reduced risk of **gestational diabetes mellitus**: aRR 0.48 95% CI 0.28 to 0.82 particularly for caffeine consumption prior to pregnancy (but not for high consumption (more than one cup a day))	1744	II	Adeney 2007
4. In a Scottish cohort study, high intakes of tea and coffee were significantly associated with higher levels of **deprivation** ($p < 0.001$)	1277	II	Haggarty 2009
5. In a US cohort study, caffeine intake during pregnancy was not associated with the following **possible breast cancer precursors** (maternal pregnancy oestradiol, unconjugated oestriol, sex hormone binding globulin (SHBG), progesterone, and prolactin)	277	II	Lagiou 2006
6. In a systematic review, one cohort study reported that women who consumed more than five cups of coffee a day during pregnancy had increased rates of **heart failure and anaemia** (unadjusted analyses)	1 study (9921 women)	I	Leviton 2002
Congenital Anomalies			
7. In a UK case control study, coffee, cocoa and drinking chocolate were negatively associated with cases of **anencephalus**; and tea was positively associated with cases of **anencephalus**	Not reported	III-3	Knox 1972
8. In a Sicilian case control study, no associations were seen between caffeine consumption during pregnancy and **hypospadias and/or cryptorchidism**	90 cases; 202 controls	III-3	Giordano 2008
9. In the eight studies (including over 33,500 women) in the systematic review addressing this question, caffeine/coffee consumption prior to, or during, pregnancy was not generally associated with risk of **congenital anomalies**	8 studies	I	Leviton 2002
10. In the eleven studies (including over 33,000 women) in the systematic review addressing	11 studies	I	Peck 2010

this question, caffeine/coffee consumption prior to, or during, pregnancy was not associated with risk of **congenital anomalies** in five studies. In other studies, intake of tea showed some association with reduced risk of **Down syndrome and spina bifida** and caffeine overall or coffee showed associations with increased risk of **oral clefts, cryptorchidism and spina bifida**			
Pregnancy Loss/Spontaneous Abortion/Fetal Death			
11. In a UK cohort study, high caffeine intake (300 mg/day or more) in the first trimester was significantly associated with **miscarriage or stillbirth** (aOR 5.1 95% CI 1.6 to 16.4)	2643	II	Greenwood 2010
12. In a systematic review, all but three of the 13 relevant cohort and case-control studies reported that high to very high caffeine intake in the preconception period and/or the first trimester of pregnancy was **significantly associated with spontaneous abortion or fetal death;** • In the largest study (Bech 2005; 88,842 pregnancies) HR for spontaneous abortion < 20 weeks gestation was 1.5 95% CI 1.0 to 2.2 for women consuming ≥ 8 cups of coffee a day during pregnancy compared with non-coffee drinkers; the corresponding HR for stillbirth at 20-27 weeks gestation was 2.3 95% CI 1.3 to 3.9	13 studies	I	Peck 2010
13. In a US cohort study of women planning a pregnancy, pre-pregnancy caffeine consumption was associated with a marginally lower risk of **pregnancy loss**: aRR 0.98 95% CI 0.96 to 0.99	66	II	Pollack 2010
14. Of the 16 studies in the systematic review addressing this question, only four reported significantly higher rates of spontaneous abortion with high caffeine/coffee consumption prior to, or during, pregnancy	16 studies	I	Leviton 2002
Preterm Birth, SGA, Low Birthweight			
15. In a Dutch cohort study, caffeine consumption during pregnancy was inversely associated with **low birthweight** and **small for gestational age**, but no association was seen for **preterm birth**: • Low birthweight: aOR 2.58 95% CI 1.26 to 5.30 (≥ 6 cups/day versus < 2) • Small for gestational age: aOR 1.38 95% CI 1.08 to 1.76 (2 to 3.9 cups/day versus < 2) • Preterm birth: aOR 1.35 95% 0.58 to 3.15 (≥ 6 cups/day versus < 2)	7346	II	Bakker 2010
16. Only one of the 14 relevant studies in this systematic review reported that maternal caffeine consumption prior to or during pregnancy was associated with an increased risk of **preterm birth**; approximately half the studies addressing **SGA/IUGR and LBW** reported positive associations	14 studies (preterm birth); 10 studies (SGA);	I	Leviton 2002

	9 studies (LBW)		
17. Review concludes that "Larger studies considering total caffeine exposure consistently reported no increased risk of delivery **before 37 weeks** of gestation"; approximately half the studies addressing **SGA/IUGR and LBW** reported positive associations with caffeine exposure	11 studies (preterm birth); 15 studies (SGA/LBW)	I	Peck 2010
Child Outcomes			
18. In a Swedish cohort study less than daily caffeine consumption during pregnancy was associated with a reduced risk of beta cell autoimmunity, but this association disappeared after adjustment	5724	II	Brekke 2009

Evidence Tables

Reference	**Adeney 2007**
CAFFEINE	Coffee
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Seattle and Tacoma, WA, USA (part of the OMEGA study); December 1996 and September 2002
Funding	NIH
Participants	1744 non-diabetic pregnant women
Baseline comparisons	*See confounding below*
Dietary assessment	Structured interview
Timing	At 13 weeks gestation
Comparison	None versus moderate (0.5 to 7 cups of caffeinated coffee a week) versus high (more than 7 cups of caffeinated coffee a week)
Outcomes	GDM
Results	**GDM (aRR): weekly caffeinated coffee consumption** | | **n/N** | **aRR** | **P value for trend** | None | 36/600 | 1.00 | Moderate | 24/798 | **0.48 95% CI 0.28 to 0.82** | High | 15/346 | 0.66 95% CI 0.35 to 1.25 | 0.22 **GDM (aRR): timing of caffeinated coffee consumption** | | **n/N** | **aRR** Never | 36/589 | 1.00 Before pregnancy only | 16/567 | **0.45 95% CI 0.25 to 0.83** Before and during pregnancy | 23/576 | 0.64 95% CI 0.37 to 1.10
Followup	To GDM diagnosis
Confounding	Adjusted for maternal age, smoking during pregnancy, alcohol use before pregnancy, maternal race, pre-pregnancy BMI, chronic hypertension
Risk of bias	Low risk of bias: Of the 2381 women approached, results from 1744 (73.2%) women were available for analysis: 381 refused to participate, 120 women were lost to follow-up and exclusions were spontaneous (n = 34) or induced (n = 15) abortion, fetal death prior to 28 weeks gestation (n = 5), prior insulin-dependent (n = 18) or type 2 (n = 7) diabetes, missing or incomplete data (n = 57)
Relevance	Probably relevant to Australian women
Other comments	

Results — GDM (aRR): weekly caffeinated coffee consumption

	n/N	aRR	P value for trend
None	36/600	1.00	
Moderate	24/798	**0.48 95% CI 0.28 to 0.82**	
High	15/346	0.66 95% CI 0.35 to 1.25	0.22

Results — GDM (aRR): timing of caffeinated coffee consumption

	n/N	aRR
Never	36/589	1.00
Before pregnancy only	16/567	**0.45 95% CI 0.25 to 0.83**
Before and during pregnancy	23/576	0.64 95% CI 0.37 to 1.10

Reference	**Bakker 2010**
CAFFEINE	Coffee and tea (unit = 90 mg caffeine, based on 1 cup of caffeinated coffee)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Rotterdam, Netherlands (2001-2005)
Funding	Erasmus Medical Center Rotterdam, Erasmus University Rotterdam, Netherlands Organization for Health Research and Development
Participants	7346 pregnant women of all ethnicities (part of Generation R study)
Baseline comparisons	Compared with women consuming no or < 2 units of caffeine a day, women consuming more caffeine tended to be older and taller and to have more previous births and be more frequently Dutch or European, less frequently smokers and more frequently alcohol consumers, with higher total dietary energy intakes.
Dietary assessment	Postal questionnaires
Timing	In the first, second and third trimester (91%, 80% and 77% response rate respectively)
Comparison	< 2, 2-3.9, 4-5.9 and ≥ 6 units/day
Outcomes	Fetal growth characteristics in each trimester, small for gestational age (defined as gestational age-adjusted birthweight below 5th percentile in the study cohort) low birthweight (< 2500 g), preterm birth (< 37 weeks)
Results	 **Head circumference in 2nd, 3rd trimester and birth:** Not consistently associated with maternal caffeine intake **Estimated fetal weight in 2nd and 3rd trimester:** Not consistently associated with maternal caffeine intake **All length measures**: **Inversely associated with caffeine intake ($p < 0.05$)** **Fetal crown-rump length in 1st trimester:** ≥ 6 caffeine units/day v no caffeine during pregnancy **MD -4.54 mm 95% CI -8.89 to -0.09** **Fetal femur length in 3rd trimester:** ≥ 6 caffeine units/day v no caffeine during pregnancy **MD -0.55 mm 95% CI -1.09 to -0.02** **Fetal head circumference growth:** No consistent association with maternal caffeine intake on regression analysis **Fetal weight growth:** **Impaired growth with maternal caffeine intake** **Fetal length growth**: **Impaired growth with maternal caffeine intake** **Birthweight:** ≥ 6 caffeine units/day v no caffeine during pregnancy **MD -100.27 g 95% CI -197.05 to -3.49** **Low birthweight:** < 2 caffeine units/day = reference (n = 205/4329)

	2-3.9 caffeine units/day aOR 1.08 (95% CI 0.84 to 1.40) (n = 96/2211) 4-5.9 caffeine units/day aOR 1.19 95% CI 0.73 to 1.95 (n = 19/439) ≥ 6 caffeine units/day **aOR 2.58 95% CI 1.26 to 5.30** (n = 9/104) **Small for gestational age:** < 2 caffeine units/day = reference (n = 204/4329) 2-3.9 caffeine units/day **aOR 1.38 (95% CI 1.08 to 1.76)** (n = 119/2211) 4-5.9 caffeine units/day aOR 1.50 95% CI 0.96 to 2.36 (n = 24/439) ≥ 6 caffeine units/day **aOR 1.87 95% CI 0.84 to 4.15** (n = 7/104) **Preterm birth:** < 2 caffeine units/day = reference (n = 193/4329) 2-3.9 caffeine units/day aOR 0.92 95% CI 0.72 to 1.18) (n = 116/2211) 4-5.9 caffeine units/day aOR 1.12 95% CI 0.71 to 1.73 (n = 21/439) ≥ 6 caffeine units/day aOR 1.35 95% CI 0.58 to 3.15 (n = 7/104)
Followup	To birth
Confounding	Adjusted for gestational age at visit, maternal age, educational level, ethnicity, parity, smoking habits, alcohol consumption, height, BMI at intake, nutritional intake (total energy, total carbohydrate, total fat and total protein), folic acid supplement use, maternal pregnancy complications (pregnancy-induced hypertension, pre-eclampsia and gestational diabetes) and fetal sex.
Risk of bias	Moderate: Only a minority of women were in the lowest (= none) and highest consumption groups (238, 5.8% and 111, 2.9% respectively in the third trimester, for example). This means that outcomes such as low birthweight are based on low numbers. Missing data: 8880 pregnant women enrolled; 1284 (14.5%) excluded due to no information about coffee or tea consumption, further exclusions for 80 twin births, 23 induced abortions, 68 fetal deaths, 28 losses to follow-up, 48 missing birthweights and 3 gestational age < 25 weeks, leaving outcomes for 7346 women for analysis; Fetal ultrasounds only done when last menstrual period was reliably known and only 5324/7346 (73%) of women's birth outcomes available for analysis.
Relevance	Probably relevant to Australian women, though caffeine intake patterns may be different
Other comments	More detailed results available from supplementary online files; No apparent dose response e.g. for SGA

Reference	**Brekke 2009**
Food type	Caffeine
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	5 year follow up of babies born in Southeast Sweden between 1 October 1997 and 1 October 1999 and invited to be in the South east Sweden (ABIS) study.
Funding	JDRF-Wallenberg Foundations, Swedish Medical Research Council, Swedish Child Diabetes Foundation, Swedish Diabetes Association, Swedish Dairy Association R & D, Majblomman Foundation and the Novo Nordisk Foundation.
Participants	5 year follow up of 5724 children who completed 2 of the 3 possible blood samplings (study cohort), 36% of the total 16004 children participating in ABIS (the primary cohort).
Dietary assessment	FFQ performed after birth, but used to recall diet during pregnancy, Food groups classified according to daily, 3-5 times/week, 1-2 times/wk or <1 time/wk.
Baseline comparisons	*See confounding below*
Timing	After birth women recalled their diet in pregnancy, covering the whole pregnancy.
Comparison	Frequency of consumption of foods in pregnancy amongst the group of infants with beta-cell autoimmunity vs infants without beta-cell autoimmunity.
Outcomes	Beta-cell autoimmunity in the child up to 5 years defined as being positive for two or more autoantibodies (GADA, IA-2A, IAA) at any of the three follow up time points or being diagnosed with diabetes during the 5 year follow up period.

Results

Summary: less than daily consumption of coffee was associated with a reduced risk of beta-cell autoimmunity;

191/5724 (3.3%) children were classified as having beta-cell autoimmunity

Beta-cell autoimmunity in the child up to 5 years

Coffee intake	**Unadjusted OR**	**Adjusted OR (95% CI)**
Never	**0.63 (0.42-0.94**)	0.67 (0.41-1.10)
Seldom (<1 time/month)	1.17 (0.74-1.8)	1.56 (0.92-2.65)
Sometimes (>1 time/month)	0.59 (0.34-1.01)	0.72 (0.38-1.36)
Often (2-6 times/month)	**0.64(0.52-0.96)**	0.73 (0.44-1.20)
Daily (ref)	1.00	1.00

Followup	1, 2.5 and 5 years
Confounding	Analyses adjusted for maternal education, weight increase from birth to 2.5yr, breastfeeding duration and introduction of cow's milk protein. Authors comment that 'adjusting for additional possible confounders like type 1 diabetes in first degree relative, maternal age, delivery mode, smoking during pregnancy, use of vitamin D containing multivitamin supplement in pregnancy and time for introduction of gluten did not change the results.'
Risk of bias	Moderate risk of bias (recall, ascertainment): Study cohort differed significantly from the primary cohort. Mothers of women in the study cohort were generally higher on measures of SES (age, education, country of birth, marital status). There was no adjustment for the child's dietary intake during the follow up period.
Relevance	Diets in Sweden may differ from diets of Australian women, particularly in relation to access to seafood.
Other comments	Some funding from Swedish Dairy Association.

Reference	**Chen 2009**

Food groups	Caffeine: sugar-sweetened cola beverages (SSB); diet cola beverages
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	US (Nurses' Health Study)
Funding	NIH
Participants	13,475 women who reported at least one singleton pregnancy between 1992 and 2001 Exclusions: history of diabetes, cancer, cardiovascular disease or GDM on 1989 or 1991 questionnaires
Baseline comparisons	*See confounding below*
Dietary assessments	FFQ
Timing	Consumption of cola SSBs before pregnancy
Comparison	0.3 serves of SSBs a month versus 1-4 a week versus ≥ 5 a week versus 1 a day
Outcomes	GDM
Results	

GDM (RR 95% CI)
□SSB consumption

	0-3 serves/month	**1-4 serves/week**	**≥5 servers/week**	**1 serve/day**	**P for trend**
Sugar-sweetened cola					
Cases/person-years	544/332,516	168/113,899	148/98,214		
Model 1	1.00	1.12 (0.94 to 1.33)	**1.39 (1.16 to 1.67)**	**1.39 (1.16 to 1.67)**	< 0
Model 2	0	1.07 (0.90 to 1.28)	**1.26 (1.04 to 1.51)**	**1.25 (1.04 to 1.51)**	0.02
Model 3	1.00	1.11 (0.93 to 1.32)	**1.29 (1.07 to 1.56)**	**1.29 (1.07 to 1.55)**	0.007
Model 4	1.00	1.08 (0.90 to 1.28)	**1.22 (1.01 to 1.47)**	**1.22 (1.01 to 1.47)**	0.04
Diet Cola					
Cases/person-years	356/472,125	322/42,326	182/30,178		
Model 1	1.00	0.92 (0.75 to1.13)	1.03 (0.88 to 1.20)	1.04 (0.92 to 1.17)	0.53
Model 2	1.00	0.97 (0.79 to 1.19)	1.07 (0.91 to 1.25)	1.06 (0.94 to 1.20)	0.34
Model 3	1.00	0.87 (0.71 to 1.07)	0.86 (0.73 to 1.00)	0.90 (0.79 to 1.02)	0.10
Model 4	1.00	0.90 (0.72 to 1.12)	0.86 (0.72 to 1.02)	0.90 (0.78 to 1.03)	0.07

Length of followup	10 years
Confounding	Model 1: adjusted for age and parity Model 2: adjusted for age and parity; plus race/ethnicity; smoking status, family history of diabetes in a first degree relative, alcohol intake, physical activity Model 3: adjusted for age and parity, race/ethnicity; smoking status, family history of diabetes in a first degree relative, alcohol intake, physical activity; plus BMI Model 4: adjusted for age and parity, race/ethnicity; smoking status, family history of diabetes in a first degree relative, alcohol intake, physical activity; BMI, plus Western dietary pattern
Risk of bias	Low-moderate risk of bias: typically 90% followup rate; analyses did not control for other caffeine use
Relevance	Likely to be relevant to Australian women
Other comments	Caramel colouring in cola drinks is rich in advanced glycation end products, but positive association was not seen for diet cola (see Caffeine food group) – may be that consuming cola SSBs is a lifestyle marker;

Reference	**Giordano 2008**

Food type	Caffeine: coffee
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Sicily, Italy
Funding	Sicilian Congenital Malformation Registry
Participants	90 cases: 43 cases of hypospadias and 48 cases of cryptorchidism (both in one infant) 202 controls: randomly selected controls born in the same year and the same region Births between 1998 to 2003
Baseline comparisons	Low birthweight, low maternal education, mother's history of gynaecological disease and father's history of urogenital diseases differed significantly between cases and controls *See confounding below*
Dietary assessment	Interview on maternal diet and food frequencies
Timing	FFQ
Comparison	Consumption of coffee versus no coffee consumption
Outcomes	Hypospadias and cryptorchidism
Results	(see table below)
Followup	n/a
Confounding	Results for coffee were not presented as adjusted analyses
Risk of bias	Moderate risk of bias: Participation rate of parents and data collection rate of cases was lower than that of controls (76% versus 91%);
Relevance	Likely to be reasonably relevant for Australian women, although hypospadias rates very high and unlikely that most Australian women will have such high pesticide exposure
Other comments	Ragusa region in Sicily is a region of intensive agriculture (involving high rates of pesticide and other chemical use) with high rates of hypospadias and cryptorchidism

Results:

	Cases	**Controls**	**OR**
Coffee			
Hypospadias			
No	10 (23.3%)	54 (26.7%)	1.00
Yes	33 (76.7%)	148 (73.3%)	1.20 95% CI 0.56 to 2.61
Cryptorchidism			
No	12 (25.0%)	54 (26.7%)	1.00
Yes	36 (75.0%)	148 (73.3%)	1.09 95% CI 0.53 to 2.26
Hypospadias and cryptorchidism			
No	22 (24.4%)	54 (26.7%)	1.00
Yes	68 (75.6%)	148 (73.3%)	1.13 95% CI 0.64 to 2.00

Reference	**Greenwood 2010 (CARE group)**
Food type	Caffeine (both food and drink and over the counter medications)

Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Two UK maternity units recruited women from September 2003 to June 2006
Funding	Food Standards Agency, UK
Participants	2643 pregnant women (between 8 and 12 weeks gestation) aged 18-45 years with singleton pregnancies Exclusions: women with prior chronic disease, psychiatric disease, HIV or hepatitis B
Dietary assessment	Validated tool to assess caffeine intake at different stages of pregnancy (4 weeks before pregnancy, weeks 1-4, weeks 5-12, weeks 13-28, weeks 28-36 or end of pregnancy)
Baseline comparisons	*See confounding below*
Timing	*See Dietary assessment*
Comparison	< 100 versus 100-199 versus 200-299 versus 300+ mg caffeine per day
Outcomes	Miscarriage (spontaneous pregnancy loss between 12 and 24 weeks), and stillbirth (birth ≥ 24 weeks with no signs of life at birth) [fetal growth was reported in CARE 2008 included in Peck 2010 SR]

Results

Miscarriage or stillbirth	Caffeine (mg/day)	n/N	aOR (95% CI)	P trend
Average caffeine intake over 1st tri□e□□□r	<100	6/□98	1	0.004
	100-199	7/656	2.2 (0.7 to 7.1)	
	200-299	3/402	1.7 (0.4 to 7.1)	
	300+	9/426	5.1 (1.6 to 16.4)	
4 weeks before pregnancy	<100	3/604	1	<0.001
	100-199	5/570	1.4 (0.3 to 6.3)	
	200-299	5/460	2.2 (0.5 to 9.4)	
	300+	12/870	3.0 (0.8 to 10.9)	
Weeks 1 – 4	<100	3/781	1	<0.001
	100-199	5/572	1.8 (0.4 to 8.2)	
	200-299	6/441	3.9 (0.9 to 16.7)	
	300+	11/706	4.7 (1.2 to 18.7)	
Weeks 5 – 12	<100	12/1,302	1	0.2
	100-199	3/497	0.8 (0.2 to 3.0)	
	200-299	6/325	2.5 (0.9 to 7.0)	
	300+	4/373	1.6 (0.5 to 5.5)	

Followup	To 36 weeks/end of pregnancy
Confounding	Adjusted for maternal age, parity, amount smoked (cotinine concentration), alcohol intake
Risk of bias	Moderate risk of bias: 2643 (20%) of 13071 eligible women agreed to participate; 8 women were excluded as they had terminations
Relevance	Likely to be relevant to Australian women, although tea consumption in this study probably higher than in Australia
Other comments	Median (IQR) caffeine intake over the first trimester was 132 (58-241) mg/day; tea contributed more than half of all caffeine consumption during pregnancy

Reference	**Haggarty 2009**

Dietary patterns	Caffeine: tea and coffee
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Aberdeen, Scotland
Funding	UK Food Standards Agency
Participants	1277 sequentially enrolled pregnant women attending Aberdeen Maternity Hospital for ultrasound (a further 184 women were recruited later in pregnancy). Exclusions: diabetic women, women with multiple pregnancies, women who conceived as a result of fertility treatment, or clinical data not available
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	Assessed at 19 weeks gestation
Comparison	Intake of tea and coffee by deciles of deprivation
Outcomes	Deprivation (assessed using the Scottish Index of Multiple Deprivation); Low birthweight (defined as < 2500 g or lowest decile for birthweight z score adjusted for gestational age, sex and parity) Preterm birth (< 37 weeks) Admission to neonatal unit
Results	**Deprivation** Tea and coffee: significantly higher intake with higher levels of deprivation ($p < 0.001$)
Followup	To neonatal period
Confounding	(Some?) analyses adjusted for energy intake
Risk of bias	Low to moderate risk of bias: low attrition, some lack of detail in reporting of outcomes
Relevance	Likely to be relevant to Australian women
Other comments	About 40-50% of the least deprived women reported taking folic acid supplements compared with about 20% for the most deprived women; Most birth outcome associations were reported by nutrient rather than food group; Not easy to deduce quantities of intake of foods (main graphs reported as change in intake by deprivation decile)

Reference	**Knox 1972**
Food type	Caffeine: coffee powder, cocoa, drinking chocolate, tea
Study type	Case control (cases matched to food consumption at population level for a particular period)
Level of evidence	III-3 (aetiology)
Setting	Birmingham, UK
Funding	Not reported
Cases	Stillbirths and infant deaths due to anencephalus between 1961 and 1967
Baseline comparisons	n/a
Dietary assessment	Population surveys
Timing	Each quarter
Comparison	Monthly stillbirths and infant deaths due to anencephalus matched to quarterly consumption of main food stuffs (in previous five to nine months)
Outcomes	Anencephalus
Results	**Coffee powder negatively associated with cases of anencephalus; r = -0.59 after a lag interval of six months** **Cocoa, drinking chocolate negatively associated with cases of anencephalus; r = -0.71 after a lag interval of five months** **Tea positively associated with cases of anencephalus; r = +0.49 after a lag interval of nine months**
Followup	n/a
Confounding	Analyses were not adjusted
Risk of bias	High risk of bias: links between population consumption of foods and anencephalus very distal and no control for potential confounders
Relevance	Likely to differ from a modern Australian diet
Other comments	Food consumption of total population not likely to reflect food consumption of pregnant women; and will not be able to reflect differences between diets of individual or specific groups

Reference	**Lagiou 2006**
Food type	Caffeine
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Boston, USA
Funding	NIH
Participants	277 pregnant women who were Caucasian, < 40 years old and having a parity of no more than two (recruited between March 1994 and October 1995). Exclusions: women who had taken any kind of hormonal medication during the index pregnancy, with a prior diagnosis of diabetes mellitus or thyroid disease, or if the fetus had a known major anomaly.
Dietary assessment	FFQ
Timing	Mailed to women prior to a routine antenatal visit around 27 weeks GA, to reflect women's dietary intake during the second trimester of pregnancy
Baseline comparisons	Women in the study likely to be older, better educated, primiparae, lower BMI and less likely to smoke than pregnant women in the general US population
Comparison	Coffee during pregnancy v none
Outcomes	Maternal pregnancy oestradiol, unconjugated oestriol, sex hormone binding globulin (SHBG), progesterone, prolactin – women's blood was taken at 16 and 27 completed weeks GA.
Results	**Maternal oestradiol** 16 completed weeks GA: -2.4% change 95% CI -12.0 to 8.3 27 completed weeks GA: -4.8% change 95% CI -8.9 to 0.5 **Maternal oestriol** 16 completed weeks GA: -4-6% change 95% CI -13.7 to 5.4 27 completed weeks GA: -3.0% change 95% CI -10.6 to 5.4 **Maternal SHBG** 16 completed weeks GA: -3.9% change 95% CI -10.3 to 2.9 27 completed weeks GA: -1.0% change 95% CI -7.9 to 6.5 **Maternal progesterone** 16 completed weeks GA: 5.7% change 95% CI -0.6 to 12.3 27 completed weeks GA: 3.6% change 95% CI -2.5 to 10.1 **Maternal prolactin** 16 completed weeks GA: -0.5% change 95% CI -12.7 to 13.5 27 completed weeks GA: 7.9% change 95% CI -2.4 to 19.2
Followup	27 completed weeks GA
Confounding	Adjusted for age, parity, gender of offspring, smoking and GA at blood measurement
Risk of bias	Low to moderate risk of bias: 277 of 402 (68.9%) eligible women were included – 77 refused to participate, 9 were subsequently excluded because the index pregnancy was terminated through a spontaneous or induced abortion, 2 were excluded because of twin birth and 10 were lost to follow-up after the initial meeting.
Relevance	Indirect outcomes for (risk of) breast cancer
Other comments	Study authors postulate that the associations between breast cancer risk and increased birthweight are mediated through endocrine hormones

Reference	**Leviton 2002**
Food type	Caffeine
Study type	SR (included studies: Al-Ansary 1994, Alderette 1995, Armstrong 1992, Barr 1984, Beaulac-Baillargeon 1987, Berkowitz 1982, Bolumar 1997, Borlee 1978, Brooke 1989, Caan 1989, Christianson 1989, Cnattingius 2000, Cook 1996, Curtis 1997, Dlugosz 1996, Dominguez-Rojas 1994, Fenster 1991a and b, Fenster 1997, Florack 1994, Ford 1998, Fortier 1993, Fried 1987, Furuhashi 1985, Grodstein 1993, Grosso 2001, Hansteen 1990, Hatch 1993, Infante-Rivard 1993, Joesoef 1990, Klebanoff 1999, Kline 1991, Kurrpa 1983, Kuzma 1982, Larroque 1993, Linn 1982, Little 1993, Martin 1986, Martin 1987, Mau 1974, McDonald 1992a and b, Mills 1993, Munoz 1988, Olsen 1991, Parazzini 1991, Parazzini 1994, Pastore 1995, Peacock 1991, Peacock 1995, Rondo 1996, Rosenberg 1982, Shu 1995, Srisuphan 1986, Stanton 1995, Tebbutt 1984, Tierson 1987, van den Berg 1977, Vlajinac 1997, Warburton 1980, Watkinson 1985, Weathersbee 1977, Wilcox 1988, Williams 1990, Williams 1992, Windham 1995, Wisborg 1996
Level of evidence	I (aetiology)
Setting	Varied between studies
Funding	Not reported
Participants	65 studies
Dietary assessment	Varied between studies
Timing	Varied between studies
Baseline comparisons	Varied between studies
Comparison	Varied between studies
Outcomes	Maternal outcomes, spontaneous abortion, fetal death, congenital anomalies, preterm birth, low birthweight, SGA, perinatal death, infant growth, SIDS [birthweight was included as an outcome in the review but was not included here]
Results	**Maternal Outcomes** • *Furuhashi 1985 (9921 women)* Women who consumed more than 5 cups of coffee a day during pregnancy had increased rates of heart failure and anaemia (unadjusted analyses) **Spontaneous Abortion** • *Weathersbee 1977 (489 households)* Of the 16 women (1%) consuming at least 600 mg of caffeine per day, 15 had birth complications (including eight miscarriages); this study had a number of serious flaws • *Warburton 1980* This abstract reports an association between caffeine consumption and triploid abortions, but may be a chance finding • *Watkinson 1985 (284 women)* This study did not find an association between caffeine consumption and spontaneous abortion • *Srisuphan 1986 (3135 women)* "non-significant elevation" in risk of late spontaneous abortion; OR 1.95, p = 0.07) • *Hansteen 1990* *"observation of an over-representation of "heavy" coffee drinkers among aborters has virtually no meaning"* • *Furuhashi 1985 (9921 women)* Women who consumed more than 5 cups of coffee a day had increased rates of "impending abortion" and compared with women who did not drink coffee during pregnancy, all coffee drinkers combined had a **significantly higher rate of spontaneous abortion** (unadjusted analyses) • *Hansteen 1990* Study has "virtually no meaning" • *Fenster 1991 (607 cases; 1284 controls)* For heavy caffeine consumers (300 mg or more of caffeine a day) aOR of spontaneous abortion was 1.2 95% 0.8 to 1.9 • *Kline 1991 (927 women)* The only form of spontaneous abortion associated with caffeine consumption in the month before pregnancy was for monosomy X; for caffeine

consumption during pregnancy, there was a significant association with both chromosomally normal and chromosomally aberrant spontaneous abortions

- *Parazzini 1991 (94 cases with recurrent miscarriages, 176 controls)*
  Coffee consumption was not associated with risk of recurrent abortion (OR 1.4 95% CI 0.7 to 2.6)
- *Armstrong 1992 (56,067 women)*
  OR for spontaneous abortion was **1.2 95% CI 1.0 to 1.3** for women who consumed 5-9 cups of coffee during the index pregnancy and 1.2 95% CI 0.97 to 1.5 for women who consumed 10 or more cups of coffee a day; study likely to be subject to selection bias
- *Mills 1993 (431 women)*
  aOR for spontaneous abortion among women in the highest caffeine consumption group (300 mg or more per day) was 1.2 95% CI 0.9 to 1.5 (study likely to be underpowered)
- *Al-Ansary 1994 (226 cases; 226 controls)*
  More cases consumed > 150 mg caffeine per day than did controls (**OR 1.9 95% 1.2 to 3.0**) – not adjusted for potential confounders
- *Parazzini 1994 (462 cases; 814 controls)*
  aOR 2.1 95% CI 1.7 to 2.1 for spontaneous abortion associated with any coffee consumption during pregnancy
- *Dominguez-Rojas 1994 (711 women; retrospective study)*
  24% rate of spontaneous abortion in women who drank any coffee and **71% in women who consumed more than 420 mg of caffeine a day** during the first trimester (unadjusted analyses)
- *Dlugosz 1996 (2849 women)*
  The increased risk of fetal loss associated with consumption of 3 or more cups of coffee/day was not seen with consumption of more than 300 mg of caffeine
- *Fenster 1997 (5144 women)*
  Consumption of caffeine was not associated with spontaneous abortion but **decaffeinated coffee was**
- *Klebanoff 1999 (591 cases; 2558 controls)*
  Only extremely high serum paraxanthine concentrations (a coffee metabolite) **were associated with spontaneous abortion**
- *Cnattingius 2000 (562 cases; 953 controls)*
  Women who drank the most caffeine were at **elevated risk of miscarriage**

Fetal Death

- *Weathersbee 1977 (489 households)*
  Of the 16 women (1%) consuming at least 600 mg of caffeine per day, 15 had birth complications (including five stillbirths); this study had a number of serious flaws
- *Tierson 1987 (400 women)*
  "A strong inverse association was seen between fetal death and the consumption of "some caffeine" during the pregnancy"
- *Infante-Rivard 1993 (331 cases; 993 controls)*
  aOR for fetal loss associated with caffeine intake > 321 mg per day during pregnancy were 2.6 95% CI 1.4 to 5.0; with a dose-related linear trend in which the OR was increased by a factor of 1.2 for each 100 mg of caffeine consumed per day during pregnancy (results regarded as unreliable due to selection bias and confounding)
- *Little 1993 (set of case-control studies, n's not reported)*
  AOR of antepartum stillbirth was 1.4 and 1.2 for intrapartum stillbirth (95% CIs not reported) where mothers consumed five or more cups of caffeine-containing coffee or tea a day (results regarded as unreliable due to surprising effects of adjustment (smoking and alcohol both showed protective effects))

Congenital Anomalies

- *Borlee 1978 (case control study with 202 cases and 175 controls)*
  Consumption of 8 or more cups of coffee a day in mothers of infants with congenital anomalies was nearly twice as common in case mothers as in

control mothers. No adjustment for alcohol consumption was made.

- *Linn 1982 (12,205 women)*
  After adjustment for potential confounders, coffee consumption during pregnancy was not significantly associated with congenital anomalies.
- *Rosenberg 1982 (2030 cases, 712 controls)*
  After adjustment for confounders, no significant associations were seen between maternal caffeine use (up to 400 mg/day or more) and six groups of congenital malformations (inguinal hernia, cleft lip with or without cleft palate, isolated cleft palate, cardiac defect excluding isolated heart murmur, plyloric stenosis and neural tube fusion defect).
- *Kurrpa 1983 (case control study with 806 cases and 806 controls)*
  No significant association between coffee drinking during pregnancy and risk of any malformation (aOR 1.1 95% CI 0.8 to 1.3). Malformations included CNS defects, orofacial clefts, structural skeletal defects, or cardiovascular malformations.
- *Tebbutt 1984 (39 women)*
  "No valid conclusions about the association of caffeine and pregnancy outcome can be based on the results of this study"
- *Furuhashi 1985 (9921 women)*
  Women who consumed more than 5 cups of coffee a day had an increased incidence of offspring of chromosomal anomalies or multiple congenital anomalies (but this was not shown for risk of overall congenital anomalies); analyses were unadjusted
- *Kline 1991 (927 women)*
  The only form of spontaneous abortion associated with caffeine consumption in the month before pregnancy was for monosomy X; for caffeine consumption during pregnancy, there was a significant association with both chromosomally normal and chromosomally aberrant spontaneous abortions
- *McDonald 1992 (number of women not reported)*
  Of the eight groups of congenital defects evaluated, only the cardiovascular group showed a statistically significant association with consumption of three or more cups per day (OR 1.5 95% CI 1.1 to 2.2)

<u>Preterm birth, low birthweight, SGA, IUGR</u>

- *Mau 1974 (5200 women)*
  "Frequent" consumption of coffee during the first three months of pregnancy was associated with an increased frequency of low birthweight (< 2500 g) and birthweights below the 10th percentile for gestational age, but was not significantly related to preterm birth (before day 260).
  "Frequent" consumption of tea or cola was not related to low birthweight. Study was inadequately controlled.
- *Weathersbee 1977 (489 households)*
  Of the 16 women (1%) consuming at least 600 mg of caffeine per day, 15 had birth complications (including two preterm births); this study had a number of serious flaws
- *Van den Berg 1977 (15,000 women) – Hogue 1981 reanalysis*
  Maternal consumption of 7 or more cups of coffee a day had a significantly increased risk of low birthweight babies (RR 1.2 – no CIs reported). Some adjustment for smoking but this was judged to be inadequate.
- *Berkowitz 1982*
  Consumption of four or more cups of coffee per day during pregnancy does not appear to increase the risk of preterm birth by a factor of 2.5
- *Linn 1982 (12,205 women)*
  After adjustment for potential confounders, coffee consumption during pregnancy was not significantly associated with low birthweight, or preterm birth, but aOR of 1.5 was found for premature rupture of membranes in women drinking 4 or more cups of coffee a day.
- *Kuzma 1982 (5093 women)*
  Review authors conclude that due to multiple flaws, this study cannot be used to draw any inferences about maternal caffeine consumption and intrauterine growth
- *Tebbutt 1984 (39 women)*
  "No valid conclusions about the association of caffeine and pregnancy outcome can be based on the results of this study"
- *Furuhashi 1985 (9921 women)*

	Women who consumed more than 5 cups of coffee a day had increased rates of preterm labour and SGA babies (unadjusted analyses) • *Martin 1986 (number of women not reported)* Caffeine consumption during pregnancy is not significantly related to the risk of low birthweight or preterm birth • *Beaulac-Baillargeon 1987 (number of women not reported); retrospective study* Birthweight was lowest for offspring of women who smoked 15 or more cigarettes a day and consumed 300 or more mg of caffeine a day • *Martin 1987 (number of women not reported)* Odds (adjusted) of low birthweight in term infants were higher for caffeine use during pregnancy in a dose response fashion; no significant relationship was seen between caffeine consumption and preterm birth • *Caan 1989 (131 cases; 136 controls)* Consumption of more than 300 mg of caffeine a day during pregnancy was not associated with a significantly higher risk of low birthweight compared with women who consumed no caffeine • *Fenster 1991 (1230 women – retrospective study)* Consumption of 300 mg or more of caffeine per day during the month before pregnancy was associated with a significantly increased risk of intrauterine growth restriction but not with low birthweight or preterm birth • *McDonald 1992 (40,000 women)* OR for preterm birth was 1.1 95% CI 0.9 to 1.3 for women who consumed 5-9 cups a day and 1.2 95% CI 0.9 to 1.8 for women who consumed 10 cups a day or more during the pregnancy; OR for SGA (bottom 5% for gestational age) was 1.3 95% 1.1 to 1.7 and 1.4 95% CI 0.97 to 2.0, respectively; OR for low birthweight was 1.4 95% CI 1.0 to 2.0 for women who consumed 10 cups of coffee or more during the pregnancy • *Williams 1992 (307 women)* Compared with women who consumed no coffee, those who consumed three cups of coffee a day during pregnancy had OR for premature rupture of membranes **2.4 95% CI 1.5 to 4.0**, but the risk did not increase with increasing number of cups of coffee consumed per day (analyses not adjusted for smoking) • *Mills 1993 (431 women)* aOR for IUGR (<10^{th} percentile birthweight for gestational age) among women in the highest caffeine consumption group (300 mg or more a day) was 1.1 95% CI 0.9 to 1.4 (study likely to be underpowered) • *Fortier 1993 (7025 women) – retrospective study* Caffeine consumption was not related to preterm birth or low birthweight; compared with women who consumed less than 10 mg of caffeine a day, those who consumed 11-150 mg caffeine per day had **aOR of IUGR of 1.3 95% CI 1.0 to 1.6**; **aOR 1.4 95% CI 1.1 to 1.9** for 151-300 mg a day and **aOR 1.6 95% CI 1.1 to 2.3** for more than 300 mg a day • *Pastore 1995 (408 cases; 490 controls)* “The lack of a dose response relation in both trimesters reduces the likelihood that observed increases and decreases in risk reflect a causal association between caffeinated beverages and preterm delivery” • *Peacock 1995 (1513 women)* Women who consumed ≥ 2801 mg/week of caffeine did not have a higher rate of prematurity than women who consumed less or no caffeine during pregnancy • *Rondo 1996 (356 controls; number of controls not reported)* Women who consumed 3 or more cups of coffee a day were **twice as likely** as women who did not consume coffee to have a term birth in the lowest birthweight decile (study likely to be inadequately adjusted for confounders) • *Wisborg 1996 (4260 women)* 4.0% of women who consumed less than 400 mg/day of caffeine had a preterm birth, compared with 4.7% among women who consumed more caffeine • *Grosso 2001 (2714 women)* No association with caffeine seen on fetal growth

	Perinatal Deaths • *Tebbutt 1984 (39 women)* "No valid conclusions about the association of caffeine and pregnancy outcome can be based on the results of this study" **SIDS** • *Ford 1998 (number of women not reported)* Consumption of more than 400 mg of caffeine during the third trimester was associated with an increased risk of cot death months after birth (did not control for smoking) **Infant Growth** • *Barr 1984 (1529 women)* Caffeine consumption during pregnancy was not related to infant length, weight or head circumference at 8 months of age (adjusted analyses) • *Fried 1987 (number of women not stated)* Caffeine consumption during pregnancy was not significantly related to infant growth at 12 or 24 months of age
Followup	Varied between studies
Confounding	Varied between studies
Risk of bias	Low-moderate risk bias: some study outcomes are incompletely reported; Confounding (especially smoking) and failure to adjust for lack of coffee 'aversion' increased the risk of bias in many of the included studies; Also see comments above in *Results section*
Relevance	Likely to be relevant to Australian women
Other comments	The Martin 1985 study demonstrated that women with high caffeine consumption are distinctly different from other pregnant women, underlying the importance of controlled for the confounding effects of smoking. Pregnancy signal postulate – continued caffeine consumption during pregnancy may be a marker of suboptimal placental hormonal synthesis, which may lead to pregnancy loss

Reference	**Peck 2010**
Food group	**CAFFEINE:** Beverages (coffee, tea, soft drinks), chocolate and some medications
Study type	Systematic review Includes: Balat 2003, Bech 2005, Bech 2006, Bech 2007 (RCT), Bille 2007, Bracken 2003, Browne 2007, CARE Study Group 2008 (=Boylan 2008), Chiaffarino 2006, Clausson 2002, Collier 2009, Diego 2007, George 2006, Gianelli 2003, Grosso 2001, Grosso 2006, Haugen 2008, Infante-Rivard 2007, Johansen 2009, Karypidis 2006, Khoury 2004, Klebanoff 2002, Klonoff-Cohen 2002, Maconochie 2007, Matijasevich 2006, Mikkelsen 2008, Miller 2009, Mongraw-Chaffin 2008, Natsume 2000, Orskou 2003, Parazzini 2005, Rasch 2003, Santos 2005, Sata 2005, Savitz 2008, Schmidt 2009, Signorello 2001, Slickers 2008, Tolstrup 2003, Torfs 2000, Tough 2003, Tsubouchi 2006, Vik 2003, Wen 2001, Weng 2008, Wisborg 2003, Xue 2008, Zusterzeel 2000.
Level of evidence	I (Aetiology)
Setting	International (human studies of caffeine and reproductive health published between January 2000 and December 2009)
Funding	Caffeine Working Group of the North American Branch of the International Life Sciences Institute (which received funding for this project from the National Coffee Association)
Participants	48 studies
Baseline comparisons	NA
Dietary assessment	Varied between studies
Timing	Varied between studies
Comparison	Varied between studies
Outcomes	Reproductive health outcomes (spontaneous abortion, fetal death, preterm birth, congenital malformations, fetal growth restriction)
Results	**Spontaneous Abortion** ***Summary from paper: "current evidence remains insufficient to permit conclusions regarding the potential role of caffeine in spontaneous abortion"*** • *Wen 2001 (584 women)*: ≥ 100 mg/day caffeine during the first trimester at elevated risk **100-299 mg/day RR 2.0 95% CI 1.0 to 4.1; ≥ 300 mg/day RR 2.5 95% CI 1.0 to 6.4** (compared with < 20 mg/day), partially controlled for smoking. • *Klonoff-Cohen 2002 (62 women)*: In IVF pregnancies, miscarriage with > 50 mg/day caffeine during the week of the initial clinic visits OR 6.2 95% CI 0.9 to 40.8, (not controlled for smoking). • *Khoury 2004 (191 women)*: In women with type 1 diabetes pregnant or planning a pregnancy, spontaneous abortions ≤ 20 weeks with first trimester consumption of **1-2 cups of caffeinated beverages/day OR 3.8 95% CI 0.8 to 16.9** and for **≥ 3 cups per day** OR **5.5 95% CI 1.2 to 22.0** compared with no caffeine intake, (did not account for different amounts of caffeine in different beverages). • *Bech 2005 (88,482 pregnancies)*: Heavy coffee drinkers (≥ 8 cups/day) **HR 1.5 95% 1.0 to 2.2** for spontaneous abortion < 20 weeks gestation (compared with non-coffee drinkers). • *Weng 2008 (1063 women):* Caffeine intake ≥ 200 mg/day **HR 2.2 95% CI 1.3 to 3.7** for miscarriage compared with no caffeine intake, (result likely to be affected by confounding) • *Savitz 2008 (2407 women)* Among women interviewed after miscarriage, current caffeine consumption of ≥ 144.3 mg/day OR was **1.9 95% CI 1.1 to 3.5** for spontaneous abortion compared with women not consuming caffeine. In contrast, OR was 1.1 95% CI 0.6 to 1.8 among women interviewed before their loss (indicating possible recall bias) • *Tolstrup 2003 (1381 pregnancies)* aOR **1.7 95% CI 1.0 to 3.0** for miscarriage (defined in this study as < 28 weeks gestation) for women consuming > 900 mg caffeine per day from coffee or tea (after adjustment for maternal age, marital status, cigarette smoking, and alcohol intake. At lower consumption levels (similar to other studies e.g. 300 mg/day) no association was seen between caffeine intake and miscarriage.

- *Giannelli 2003 (160 cases; 314 controls)*
  Women consuming > 300 mg/day during pregnancy (compared with < 151 mg/day): OR **1.9 95% CI 1.0 to 3.6 for 301-500 mg/day and OR 2.2 95% CI 1.1 to 4.4 for ≥ 500 mg/day.**
- *Rasch 2003 (303 cases; 1168 controls)*
  Women consuming ≥ 375 mg/day (compared with ≤ 199 mg/day): **OR 2.2 95% CI 1.5 to 3.2** (result may be affected by confounding and missing data)
- *Maconochie 2007 (603 cases; 6116 controls)*
  aOR 1.0 95% CI 0.7 to 1.5 for miscarriage with 301-500 mg/day; and 1.1 95% CI 0.8 to 1.7 for > 500 mg/day, compared with no caffeine consumption (includes adjustment for nausea severity), potential for differential recall between cases and controls
- *George 2006 (108 cases, 583 controls)*
  OR for repeated miscarriage 1.8 95% CI 0.8 to 3.9 for ≥ 300 mg/day; significant for non-smoker subgroup and nonsignificant for smoker subgroup (interaction test not significant)

Fetal Death:
- *Wisborg 2003 (18,478 pregnancies)*
  OR 2.2 95% CI 1.0 to 4.7 of stillbirth for women drinking ≥ 8 cups of coffee at 16 weeks gestation compared with women not drinking coffee; pregnancy 'signal' not considered
- *Bech 2005 (88,482 pregnancies)*
  Women consuming ≥ 8 cups of coffee/day **HR 2.3 95% CI 1.3 to 3.9 for stillbirth at 20-27 weeks gestation**, HR 1.3 95% CI at 0.7 to 2.4 after 27 weeks gestation (not stated, but assumed to be compared with non-coffee drinkers);
  Women consuming ≥ 4 cups of coffee/day **HR 2.3 95% 1.2 to 4.3 for stillbirth due to placental dysfunction**, but associations were not apparent for unexplained intrauterine deaths, umbilical cord complications, congenital malformations, other conditions such as infection and maternal disease, or intrapartum deaths.
- *Matijasevich 2006 (382 cases, 792 controls)*
  OR 2.3 95% CI 1.2 to 4.4 of fetal death with mean caffeine (from mate (herbal tea) and coffee) consumption of ≥ 300 mg/day, likely exposure misclassification as soft drink, chocolate and black tea not considered.

Preterm Birth
Summary from paper: "Larger studies considering total caffeine exposure consistently reported no increased risk fo delivery before 37 weeks of gestation"
- *Clausson 2002 (873 women)*
  No significant difference seen for gestational age for groups of 0-99, 100-299, 300-499 or ≥ 500 mg caffeine/day across entire pregnancy
- *Klebanoff 2002 (2515 women)*
  Data for caffeine metabolites in serum do not support an association between third trimester paraxanthine concentrations and pregnancy duration or preterm birth
- *Klonoff-Cohen 2002 (39 women)*:
  Maternal caffeine intake > 50 mg/day during the week of the first fertility clinic visit was associated with a 3.5 week decrease (95% CI -6.7 to -0.3) in gestational age compared with women reporting 0-2 mg/day [results for intake during pregnancy were not reported]
- *Bracken 2003 (2291 women)*
  No associations between caffeine use (≥ 150 mg/day v < 150 mg/day) and preterm birth were seen (self-reported caffeine use and urinary caffeine concentrations)
- *Tough 2003 (323 women – case-control)*
  Crude OR **1.4 95% CI 1.0 to 1.9** between coffee consumption (< 1 cup/day versus ≥ 1 cup/day) but this association lost its significance on multivariate analysis
- *Khoury 2004 (191 women with diabetic pregnancies)*

No association seen for serves of caffeine drinks (coffee, tea and soft drinks all equally weighted) and preterm birth

- *Santos 2005 (5189 women – retrospective)*
  No significant relationship seen between caffeine consumption (mate) and preterm birth
- *Chiaffarino 2006 (520 cases, 1966 controls)*
  Reduced risk for women who consumed two or more servings of coffee a day compared with nonconsumers (**OR 0.5 95%CI 0.3 to 0.8**); but did not reach statistical significance for preterm birth of an appropriate for gestational age infant (OR 0.8 95% CI 0.6 to 1.1)
- *Bech 2007 (RCT of 1197 heavy coffee drinkers in last half of pregnancy)*
  No significant relationship seen between caffeine consumption and preterm birth
- *Mikkelsen 2008 (35530 women)*
  Coffee intake ≤ 2 cups per day was associated with lower odds of early preterm birth (aOR 0.7 95% CI 0.6 to 0.9), with no association with later preterm birth (aOR 0.9 95% CI 0.8 to 1.1) compared with > 2 cups per day.
- *Haugen 2008 (26,563 women)*
  Consuming ≤ 2 cups of coffee a day was not associated with reduced odds of giving birth before 35 weeks (OR 1.11 95% CI 0.83 to 1.49) or during the 35th and 36th weeks (OR 1.15 95% CI 0.90 to 1.46)

Congenital Malformations

- *Natsume 2000 (306 cases and matched controls)*
  Due to high risk of bias review authors conclude that this study "does not make a meaningful contribution"
- *Khoury 2004 (191 pregnant women with type 1 diabetes)*
  Any consumption of caffeine during the first trimester (none versus one or more cups of coffee, tea or soft drinks) was not associated with major malformations (crude OR 2.0 95% CI 0.4 to 11.2)
- *Torfs 2000 (997 cases; 1007 controls)*
  A protective association between heavy coffee intake (≥ 4 cups a day compared to < 4 cups a day) and Down syndrome was observed among non-smokers (**OR 0.5 95% CI 0.3 to 0.8**) but not smokers (OR 1.6 95% CI 0.8 to 3.4) (non-smoking heavy caffeine users more likely to miscarry?)
- *Bille 2007 (134 cases; 828 controls)*
  No associations with coffee intake for all oral clefts combined or by subtype; mothers of babies with isolated cleft palate had **2.5 95% CI 1.1 to 5.6** greater odds of consuming 5 or more cups of tea a day compared with mothers of controls. Weekly cola intake exceeding one litre was marginally associated with cleft lip with or without cleft palate (OR 1.5 95% CI 0.9 to 2.4)
- *Browne 2007 (4196 cases; 3957 controls)*
  No positive associations between pre-pregnancy caffeine intake and cardiovascular malformations
- *Mongraw-Chaffin 2008 (84 cases; 252 controls)*
  Significant association between cryptorchidism and caffeine intake equivalent to three cups of coffee a day (**aOR 1.4 95% CI 1.1 to 1.9)**
- *Slickers 2008 (75 cases; 868 controls)*
  No associations with 'non-negligible' caffeine intake in the year preceding pregnancy and renal agenesis or renal hypoplasia were seen (aOR 1.01 95% CI 0.58 to 1.75)
- *Miller 2009 (464 cases; 4940 controls)*
  Significant associations were seen between risk of anorectal atresia in offspring and caffeine intake: **OR 1.4 95% CI 1.0 to 1.9** for 10 to 99 mg; **OR 1.3 95% CI 1.0 to 1.8** for 100 to 299 mg; **OR 1.5 95% CI 1.0 to 2.2** for ≥ 300 mg – compared with < 10 mg (analyses not adjusted e.g. for smoking)
- *Johansen 2009 (573 cases; 763 controls)*
  No associations seen for total caffeine intake (coffee, tea and soft drink) and risk of cleft lip with or without cleft palate (aOR 1.2 95% CI 0.7 to 2.0 for ≥ 500 mg compared with 0 to 100 mg; or cleft palate only (aOR 1.1 95% CI 0.5 to 2.2): coffee intake was associated with cleft lip with or without cleft palate (**aOR 1.6 95% CI 1.1 to 2.4** for ≥ 3 cups a day), but not cleft palate only. In contrast tea appeared to be protective.
- *Schmidt 2009 (758 cases; 4143 controls)*
  Associations with spina bifida were seen for any consumption of caffeine in the year prior to pregnancy (≥ 10 mg/day: **OR 1.4 95% CI 1.1 to 1.9**) any caffeinated coffee (≥ 1 cup/month: **OR 1.3 95% CI 1.0 to 1.6**) and any caffeinated soft drink (> 0 per day; **OR 1.2 95% CI 1.0 to 1.6**). Any

	consumption of caffeinated tea was found to be protective for spina bifida (**OR 0.7 95% CI 0.6 to 0.9**) Associations with **encephalocele** were seen for coffee (only 1 cup/day and not higher) and tea; no associations with anencephaly were observed • *Collier 2009 (2344 cases; 5711 controls)* Modestly elevated risk for most orofacial cleft outcomes for total caffeine intake in the year prior to pregnancy (coffee, tea, soft drink, and chocolate) but no dose response effect seen **<u>Fetal Growth Restriction</u>** • *Grosso 2001 (2714 women)* No association seen between IUGR and caffeine intake during the first or seventh month of pregnancy • *Clausson 2002 (873 women)* No differences seen in Z-scores across categories of caffeine intake • *Klebanoff 2002 (number of women not reported)* Risk of SGA increased with rising third trimester serum paraxanthine concentrations but only among smokers
Followup	Varied between studies
Confounding	Varied between studies; see comments above in *Results section*
Risk of bias	Low to moderate risk of bias: Confounding (especially smoking) and failure to adjust for lack of coffee 'aversion' increased the risk of bias in many of the included studies; Also see comments above in *Results section*
Relevance	Results from most studies relevant to Australian women
Other comments	Pregnancy signal – see comments for Leviton 2002

Reference	**Pollack 2010**
Food group	Caffeine
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	USA
Funding	Great Lakes Protection Fund, Agency for Toxic Substances and Disease Registry, Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development
Participants	79 women discontinuing contraception and planning to become pregnant in the next 6 months; 68 (86%) of women became pregnant, with 54 (79%) women having live births and 14 (21%) experiencing pregnancy losses
Baseline comparisons	*See confounding below*
Dietary assessment	Daily diaries
Timing	Through 12 menstrual cycles (or until pregnancy)
Comparison	Amount of caffeine intake as daily cups (actual amounts not reported but only 24% of women consumed more than three caffeinated beverages daily; equating to > 300 mg caffeine)
Outcomes	Pregnancy loss
Results	(see table below)
Followup	Until pregnancy confirmed or up to 12 menstrual cycles
Confounding	Adjusted for age and average alcohol and cigarette consumption per standardised 28-day cycle (and prior spontaneous pregnancy loss for gravid women)
Risk of bias	Moderate risk of bias: 113/244 women (43%) agreed to participate, 79 women completed the study; women who conceived earlier had lower caffeine exposure
Relevance	Likely to be of relevance to Australian women
Other comments	Study likely to be underpowered

Results:

	n	**Risk of pregnancy loss**	**Hazard of pregnancy loss**
All women	66	**aRR 0.98 95% CI 0.96 to 0.99**	**aHR 0.97 95% CI 0.95 to 1.00**
Nulligravid	13	aRR 0.98 95% CI 0.95 to 1.01	aHR 0.98 95% CI 0.94 to 1.02
Gravid	53	**aRR 0.96 95% CI 0.94 to 0.99**	**aHR 0.96 95% CI 0.92 to 1.00**

Reference	**Robinson 2009**
Food group	Caffeine
Study type	RCT (crossover)
Level of evidence	II (intervention)
Setting	Canada
Funding	Canadian Foundation for Women's Health
Participants	27 pregnant women recruited as part of routine screening for gestational diabetes mellitus at 24 to 28 weeks gestation (19 negative screens and 8 with an initial positive screen) Exclusions: pre-pregnancy BMI > 30, smokers, taking medications that could interfere with glucose uptake or metabolism, known medical or obstetrical complications
Baseline comparisons	n/a
Dietary assessment	n/a
Timing	28 to 29 weeks gestation; and 29 to 30 weeks gestation (crossover)
Comparison	Caffeine capsule (3 mg/kg; equivalent to 1-2 cups coffee) versus placebo capsule
Outcomes	Maternal blood glucose, insulin and insulin sensitivity index
Results	

	Pregnant women (controls): n = 19			**Women with GDM: n = 8**		
Mean [SEM]	**Placebo**	**Caffeine**	**p**	**Placebo**	**Caffeine**	**p**
Glucose (mmol/L/2h)	381 [28]	392 [23]	ns	**518 [35]**	**616 [42]**	**0.001**
Insulin (pmol/L/2h)	39236 [4653]	42632 [4675]	ns	53661 [9141]	67207 [12538]	0.07
Insulin Sensitivity Index	8.65 [0.74]	8.24 [0.90]	ns	**4.81 [1.05]**	**3.96 [1.02]**	**0.01**

Followup	To 30 weeks gestation
Confounding	n/a
Risk of bias	Unclear risk of bias: process of allocation concealment not described, trial described as "double blind"
Relevance	Likely to be relevant to Australian women
Other comments	Small sample size

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Cereal

Included Studies

Study	Outcomes
1. Chatzi 2008	Child persistent wheeze, atopic wheeze, atopy (all at 6.5 years)
2. George 2005	"Breastfeeding"
3. Godfrey 1996	Placental weight, birthweight
4. Herrick 2003	Cortisol concentrations in offspring at 30 years of age
5. Jensen 2004	Childhood acute lymphoblastic leukemia
6. Knox 1972	Anencephalus
7. Kwan 2009	Childhood acute lymphoblastic leukemia
8. Lamb 2008	Islet autoimmunity
9. Laraia 2007	"Pre-pregnancy BMI"
10. Latva-Pukkila 2009	Nausea and vomiting during pregnancy
11. Mitchell 2004	SGA
12. Nwaru 2010	Allergic sensitisation in offspring by 5 years
13. Petridou 2005	Childhood acute lymphoblastic leukemia
14. Petridou 1998a	Cerebral palsy at 8 years
15. Petridou 1998b	Birthweight
16. Radesky 2008	IGT, GDM
17. Stuebe 2009	GWG
18. Venter 2009	Food hypersensitivity (FHS) in infants up to three years of age
19. Willers 2007	Asthma, respiratory and atopic symptoms at 5 y
20. Zhang 2006	GDM

Evidence Summaries

	N	Level	References
Maternal Outcomes/Associations			
1. In a US cohort study, women who were **obese before pregnancy** were significantly less likely to meet recommendations for cereal intake compared with overweight women: • Adherence for normal or overweight women was 41.2% [SD 22.7] and 42.8% [SD 24.4] respectively compared with 40.4% [SD 23.6] for obese women ($p < 0.05$)	2394	II	Laraia 2007
2. In a US cohort study, maternal consumption of whole grains during pregnancy was not associated with **excessive gestational weight gain**: aOR 1.06 95% CI 0.95 to 1.19	1338	II	Stuebe 2009
3. In a US cohort study, incidences of **impaired glucose tolerance or gestational diabetes mellitus** were not associated with maternal intake of whole grains during pregnancy: • IGT (per serve of whole grains): aOR 1.05 95% CI 0.92 to 1.19 • GDM (per serve of whole grains): aOR 0.90 95% CI 0.73 to 1.13	1773	II	Radesky 2008
4. In a US cohort study, a reduced risk of **gestational diabetes mellitus** was seen in women consuming high amounts of cereal fibre during or before pregnancy – aOR 0.76 95% CI 0.59 to 0.99 for > 7.2 g/day versus < 3.5 g/day; and aOR 0.77 95% CI 0.64 to 0.91 for each 5 g/day increment	13,110	II	Zhang 2006
5. In a Finnish cohort study, **nausea and vomiting** during pregnancy was not associated with consumption of grain products during pregnancy	256	II	Latva-Pukkila 2009
Congenital Anomalies			
6. In a case-control study from the UK, maternal consumption of total cereals was positively associated with cases of **anencephalus**: r = +0.56 after a lag interval of five months	Not reported	III-3	Knox 1972
Birth Outcomes			
7. In a New Zealand case-control study, a reduced **small-for-gestational age** was associated with maternal cereal intake in the pre-conception period ($p = 0.04$) but this did not hold for cereal intake in the last month of pregnancy	844 cases, 870 controls	III-3	Mitchell 2004
8. In a retrospective cohort study from Greece, there was a small but insignificant increase in **birthweight** (31 g [SE37], $p = 0.40$) for each daily consumption of cereals and starchy roots,	368	III-2	Petridou 1998b
9. In a cohort study, no significant associations were seen in **placental weight and birthweight** (both $p = 0.2$) and maternal intake of cereal in late pregnancy	538	II	Godfrey 1996
Breastfeeding			
10. In a US cohort study, • **lactating women** consumed significantly more wholegrain bread and significantly less white bread during pregnancy and in the postpartum period than non-lactating women ($p < 0.05$);	149	II	George 2005

• nonlactating women significantly reduced their consumption of sugared cereals in the postpartum period compared with pregnancy ($p < 0.05$)			
Allergy Outcomes			
11. In a Spanish cohort study, no significant associations were seen between **wheeze and atopy in children at 6.5 years of age** and maternal cereal intake during pregnancy	482 children	II	Chatzi 2008
12. In a Finnish cohort study, no significant associations were seen between **allergic sensitisation** in children by 5 years of age and maternal cereal intake during pregnancy	931 children	II	Nwaru 2010
13. In a UK cohort study, associations between **food hypersensitivity** in children up to three years of age and maternal intake of wheat during pregnancy could not be determined due to small numbers	696 children	II	Venter 2009
14. In a Scottish cohort study, there were no consistent linear associations with **respiratory and atopic outcomes in 5 year old children** and maternal intake of wholegrain cereals during pregnancy	1212 children	II	Willers 2007
Other Childhood Outcomes			
15. In a US cohort study, development of **islet autoimmunity** (a precursor of type 1 diabetes) in children up to 15 years was not associated with maternal intake of cereals during pregnancy • Gluten-containing foods: aHR (for one standard deviation change in reported consumption) 0.89 95% CI 0.50 to 1.58 (127 mean monthly servings) • Non-gluten cereal grains: aHR (for one standard deviation change in reported consumption) 0.98 95% CI 0.64 to 1.51 (12 mean monthly servings)	642 children	II	Lamb 2008
16. In a Greek case-control study, there was a borderline association between **reduced risk of cerebral palsy** in children and maternal intake of cereals during pregnancy: Regression analysis for each unit of consumption of cereal 3 times per week: • aOR 0.83 95% CI 0.72 to 0.96 • aOR 0.85 95% CI 0.72 to 1.00 (additionally adjusted for all food groups)	109 children (cases)	III-3	Petridou 1998a
17. In a US case-control study, there was no association between **childhood acute lymphoblastic leukemia** and maternal consumption of grain products during pregnancy: aOR 0.86 95% CI 0.37 to 1.98	138 cases, 138 controls	III-3	Jensen 2004
18. In a US case-control study, maternal consumption of grain products in pregnancy was not associated with **childhood acute lymphoblastic leukemia** (aOR 1.20 95% CI 0.70 to 2.05: median consumption 2.6 (25^{th} 75^{th} percentiles 2.0, 3.3) serves per day) whereas maternal consumption of fibre cereals was significantly associated with a higher risk (aOR 1.12 95% CI 1.07 to 1.26)	866 total	III-3	Kwan 2009

19. In a Greek case-control, there was no association between **childhood acute lymphoblastic leukemia** and cereal/starchy root intake (median Q1; 52 g/day: median Q5 164 g/day); p for trend = 0.13	138 cases; 138 controls	III-3	Petridou 2005
Outcomes For Offspring As Adults			
20. In a Scottish cohort study, there was no association between **cortisol concentrations in adult offspring at 30 year followup** and maternal bread consumption during pregnancy	251 men and women	II	Herrick 2003

Evidence Table

Reference	**Chatzi 2008**
Food type	Cereal
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women presenting antenatal care at general practices in Menorca, a Mediterranean island in Spain (mid 1997 to mid 1998)
Funding	Instituto de Salud Carlos III red de Grupos Infancia y Media Ambiente, the Fundacio “La Caixa” , Instituto de Salud Carlos III, red de Centros de Investigacion en Epidemiologica y Salud Publica, EU, National Center for Environmental Health, USA, the GA^{2}LEN project, Ministry of Education and Science, Spain, Oficina de Ciencia y Tecnologia, Generalitat Valenciana.
Participants	482 children of 507 women who had attended antenatal care in Menorca
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	not clear when women did FFQ and period of pregnancy it was intended to cover
Comparison	≤ 11.5 v > 11.5 serves of cereal per week
Outcomes	Persistent wheeze, atopic wheeze and atopy at 6.5 years
Results	***Persistent wheeze at 6.5 years*** Low 21 (15.22%) v high 16 (11.27%); pns (also adjusted for firstborn and lower respiratory tract infections at age 1) ***Atopic wheeze at 6.5 years*** Low 14 (8.14%) v high 6 (3.51%); pns (also adjusted for birthweight and maternal atopy) ***Atopy at 6.5 years*** Low 34 (17.00%) v high 36 (17.06%) pns (also adjusted for birthweight and maternal atopy)
Followup	6.5 years
Confounding	Analyses adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years and total energy intake at 6.5 years
Risk of bias	Low risk of bias: Results from 468/482 children (97%) able to be analysed (4 incomplete data and 8 implausible values);
Relevance	Diets in Menorca may differ from diets of Australian women, particularly urban women
Other comments	

Reference	**George 2005**
Food type	Cereal (breads and sugared cereals)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Texas, US
Funding	Not reported
Participants	149 Medicaid-qualified women (30% white, 24% African American, 46% Hispanic) – recruited from a larger study on postpartum weight retention Inclusion criteria: 18 years or older; non-Hispanic white, African American or Hispanic ethnicity; birth of a health term infant, fluency and literacy in English; absence of pregnancy-related abnormalities and disease conditions.
Baseline comparisons	Significant differences between lactating and non-lactating women – higher parity, BMI and lower education levels in non-lactating women.
Dietary assessment	Semiquantitative FFQ to cover pregnancy and first six months postpartum
Timing	FFQ administered at 6 weeks and 6 months postpartum
Comparison	Number of serves of cereals
Outcomes	Breastfeeding (exclusive or partial at 6 months postpartum)
Results	**Lactating women consumed significantly more wholegrain bread and significantly less white bread during pregnancy and in the postpartum period than non-lactating women ($p < 0.05$)** **Nonlactating women significantly reduced their consumption of sugared cereals in the postpartum period compared with pregnancy ($p < 0.05$)**
Followup	6 months postpartum
Confounding	No adjustment for potential confounding
Risk of bias	Moderate-to-high risk of bias; no attempt to control for confounding despite significant baseline differences between lactating and non-lactating women.
Relevance	Possibly relevant to low-income women in Australia
Other comments	Minimal reporting of results

Reference	**Godfrey 1996**
Food type	Cereal protein
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Southampton, UK
Funding	Dunhill Trust and Medical Research Council
Participants	538 women who gave birth to a singleton term infant
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered in early and late pregnancy, to reflect diet in the previous three months
Comparison	mean daily intake of cereal protein 33.7 g IQR 27.2, 40.2 in late pregnancy
Outcomes	Birthweight, placental weight
Results	**Placental weight** No significant association seen between cereal protein intake in late pregnancy and placental weight ($p = 0.2$) **Birthweight** No significant association seen between cereal protein intake in late pregnancy and birthweight ($p = 0.2$)
Followup	To birth
Confounding	Adjusted for baby's sex and gender and duration of gestation; and nutrient intakes
Risk of bias	Low risk of bias: of 636 women recruited, 596 (94%) agreed to participate; 39 gave birth before 37 weeks, 3 were not visited in late pregnancy and placental weight was not recorded for 16, leaving 538 term pregnancies with complete birth and nutrition data (85% of the 636 women recruited)
Relevance	Likely to be relevant for Australian women
Other comments	

Reference	**Herrick 2003**
Food groups	Cereal (bread)
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Motherwell, Scotland
Funding	Dunhill Medical Trust, NIH
Participants	251 men and women whose mothers' food intakes had been recorded during pregnancy during 1967 to 1968. These women had been advised to eat 0.45 kg of red meat a day and to avoid carbohydrate-rich foods during pregnancy
Baseline comparisons	*See confounding below*
Dietary assessment	Mothers asked about consumption of 10 foods
Timing	Early pregnancy (≤ 20 weeks); late pregnancy (> 20 weeks)
Comparison	Slices of bread per day (mean consumption in late pregnancy = 0.8 SD? 1.1)
Outcomes	Cortisol concentrations in offspring aged 30 years
Results	**Cortisol (change per unit change in maternal bread consumption during pregnancy)** No significant association
Length of followup	30 years
Confounding	Analyses adjusted for offspring's gender, social class at birth, BMI, alcohol consumption, and activity level
Risk of bias	Moderate risk of bias: For the 1432 records from 1967-8 recorded liveborn, singleton births with complete names, birth measurements and ≥ 1 diet record. 965 offspring were alive and living locally; and after attrition or declining to participate, 251 (17.5%) were available for analysis.
Relevance	Very high intake of meat and very low carbohydrate intake limits the relevance to current dietary intakes of Australian women
Other comments	Authors state that "in the setting of advice to follow a pregnancy diet high in protein and low in carbohydrate, an unbalanced pattern of higher meat/fish and lower green vegetable consumption in late pregnancy leads to elevated cortisol concentrations in the offspring"

Reference	**Jensen 2004**
Food type	Cereal: grain products
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study)
Funding	PHS
Participants	138 matched cases and controls: Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, parental occupation and smoking during pregnancy – no evidence of confounding was seen for these variables. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of grain products
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Childhood acute lymphoblastic leukemia** Grain products: aOR 0.86 95% CI 0.37 to 1.98: mean consumption 2.68 [SD 1.10] serves per day
Followup	n/a
Confounding	Analyses were adjusted for variables previously shown to be significantly associated with ALL in the overall study – income, prior fetal loss, child's exposure to other children under age five, and maternal exposure to indoor insecticides during pregnancy; along with portion size and energy consumption
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 1999, 83% consented to participate; 69% of the eligible controls agreed to participate. Of the 161 matched pairs, seven pairs were excluded as the respondent was not the biological mother, 16 pairs were excluded due to questionable dietary questionnaire data, leaving 138 matched pairs (86%); some recall bias likely
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	

Reference	**Knox 1972**
Food type	Cereal
Study type	Case control (cases matched to food consumption at population level for a particular period) – numbers not reported
Level of evidence	III-3 (aetiology)
Setting	Birmingham, UK
Funding	Not reported
Cases	Stillbirths and infant deaths due to anencephalus between 1961 and 1967
Baseline comparisons	n/a
Dietary assessment	Population surveys
Timing	Each quarter
Comparison	Monthly stillbirths and infant deaths due to anencephalus matched to quarterly consumption of main food stuffs (in previous five to nine months)
Outcomes	Anencephalus
Results	**Large white loaves positively associated with cases of anencephalus: r = +0.60 after a lag interval of six months** **Total cereals positively associated with cases of anencephalus: r = +0.56 after a lag interval of five months**
Followup	n/a
Confounding	Analyses were not adjusted
Risk of bias	High risk of bias: links between population consumption of foods and anencephalus very distal and no control for potential confounders
Relevance	Likely to differ from a modern Australian diet
Other comments	Food consumption of total population not likely to reflect food consumption of pregnant women; and will not be able to reflect differences between diets of individual or specific groups

Reference	**Kwan 2009**
Food type	Cereals: rice, pasta, pizza, cereal (such as raisin bran, granola or shredded wheat, cornflakes, Cheerios, oatmeal, oat bran, grits), bagels, muffins, hamburger buns, biscuits, bread, corn bread, corn tortillas, flour tortillas
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study – phase 1 and 2 (phase 1 reported in Jensen 2004)
Funding	PHS; Paul O'Gorman Foundation for Children with Leukemia
Participants	866 individuals - 282 matched cases and controls (205 pairs and 77 trios): Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth (in phase 1 (1995-99) only due to concerns about overmatching on potential environmental exposures linked to leukemia risk) Data collected from August 1995 to November 2002
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, and smoking during pregnancy. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of cereals
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Childhood acute lymphoblastic leukemia** **Grain products:** aOR 1.20 95% CI 0.70 to 2.05: median consumption 2.6 (25^{th} 75^{th} percentiles 2.0, 3.3) serves per day **Fibre cereals:** **aOR 1.12 95% CI 1.07 to 1.26** (number of serves not reported) **Fibre from grains**: aOR 0.99 95% CI 0.60 to 1.63 median consumption 5.79 (25^{th} 75^{th} percentiles 3.84, 8.58) serves per day
Followup	n/a
Confounding	Analyses were adjusted for total energy intake, household income, indoor insecticide exposure during pregnancy; and proportion of foods reported as large or extra-large portion size Also adjusted for child's diet, with little effect seen on results
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 2002, 86% consented to participate; 56% of the eligible controls agreed to participate. 190 participants excluded: leukemia diagnosis was not ALL (n = 127); no dietary data (n = 4); a case or a control respondent was not the biological mother (n = 14), questionable dietary questionnaire data (n = 45), leaving 282 matched sets (86%).
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	Regular use of any dietary supplement was not associated with risk of ALL; Authors did not comment on the positive association with fibre cereals

Reference	**Lamb 2008**
Dietary patterns	Cereals: Gluten-containing foods (brownies, cookies, cakes, cereals, oats, other grains, bread, muffins, hamburgers, hot dogs, meat sandwiches, pancakes, pasta, pie, pizza, pastries, beer, bran and wheat germ); non-gluten containing cereals (rice and corn)
Study type	Part of a longitudinal prospective birth cohort study
Level of evidence	II (aetiology)
Setting	Denver, Colorado, US (part of the Diabetes Autoimmunity Study in the Young (the DAISY))
Funding	National Institutes of Health, Diabetes Endocrine Research Center
Participants	642 newborns at increased risk for type 1 diabetes (based on HLA genotype and family history), enrolled in the study from 1993 to 2004; 27 cases defined as testing positive for islet autoantibodies at two consecutive blood draws and still positive (diabetic) at last follow-up
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	From 1997 to 2004, mothers of infants enrolled in DAISY completed FFQ soon after birth, reflecting diet in the last trimester of pregnancy (but could submit FFQ before child reached one year of age)
Comparison	Monthly servings of gluten-containing foods and non-gluten cereal grains
Outcomes	Islet autoimmunity in children (a precursor of type 1 diabetes) at 9 months, 15 months, 2 years and annually thereafter up to the age of 15
Results	**Gluten-containing foods:** aHR (for one standard deviation change in reported consumption) 0.89 95% CI 0.50 to 1.58 (127 mean monthly servings) **Non-gluten cereal grains:** aHR (for one standard deviation change in reported consumption) 0.98 95% CI 0.64 to 1.51 (12 mean monthly servings)
Followup	Up to 15 years
Confounding	Size for gestational age, ethnicity, maternal education, household income, exposure to type 1 diabetes or GDM in utero, gender of child, maternal age at birth, total calories of maternal diet
Risk of bias	Moderate risk of bias: subset of DAISY only (later enrolments); and women were not reminded to submit FFQ, leading to possible selection bias; of the 661 FFQs returned, 5 were excluded because incomplete, and 14 for implausible dietary intakes, leaving 642 FFQs for analysis; child's diet not controlled for
Relevance	Likely to be relevant to some Australian women, although women in this study may have been at higher risk of diabetes
Other comments	

Reference	**Laraia 2007**
Dietary patterns	% of cereal serving recommendation
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	North Carolina, US (part of the Pregnancy, Infection and Nutrition (PIN) cohort)
Funding	National Institute of Child Health and Human Development; NIH
Participants	2394 predominantly lower to middle income women, recruited between 24 and 29 weeks gestation (1995-2000)
Baseline comparisons	Mean DQI-P score varied significantly by socio-demographic characteristics; there were higher mean DQI-scores for women who engaged in pre-pregnancy vigorous exercise and pre-pregnancy vitamin use
Dietary assessment	Modified block FFQ
Timing	Self-report at 26-28 weeks gestation covering previous 3 months (corresponding to the 2nd trimester)
Comparison	BMI categories
Outcomes	Pregravid weight status (not an outcome but there is an association)
Results	**Average % of cereal serving recommendation [SD]** Underweight 43.5 [22.8] Normal weight 41.2 [22.7] Overweight 42.8 [24.4] Obese 40.4 [23.6] **P value for trend < 0.05** *adjusted for age, ethnicity, level of education, poverty, number of children, smoking during pregnancy only
Followup	26 to 31 weeks gestation
Confounding	Age, ethnicity, level of education, poverty, number of children, smoking during pregnancy, regular vitamin use prior to pregnancy, vigorous leisure activity 3 months prior to pregnancy
Risk of bias	Low risk of bias: better to have used normal weight women as the reference rather than underweight women DQI-P tertile comparison
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Latva-Pukkila 2009**
Dietary patterns	Grain products
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Turku, Finland (cohort from Piirainen 2006)
Funding	Social Insurance Institution of Finland, the Sigrid Juselius Foundation and the Academy of Finland
Participants	256 pregnant women
Baseline comparisons	Women with NVP were older and tended to be primiparous compared to those without
Dietary assessment	3 day food diaries
Timing	Three times during pregnancy (mean 14, 24 and 34 weeks gestation)
Comparison	With nausea and vomiting in pregnancy (NVP) versus no NVP; 134 (72%) women reporting experiencing nausea; with 40 (30%) vomiting (9 (4.8%) more than once a day) during the first trimester
Outcomes	Influence of nausea and vomiting in pregnancy on dietary intake; Severity of NVP assessed as having no nausea and vomiting, only nausea, vomiting once a day or vomiting more than once a day, with the primary outcome being presence or absence of nausea
Results	(see table below)
Followup	To 34 weeks gestation
Confounding	Not reported if any of the analyses were adjusted
Risk of bias	Moderate risk of bias: not clear if analyses were adjusted for potential confounders
Relevance	Likely to be relevant to Australian women
Other comments	

	With NVP (n = 134)	**Without NVP (n = 53)**	**p**
Grain products (g), median (IQR) daily	211 (157 to 256)	202 (169 to 252)	0.952

Reference	**Mitchell 2004**
Dietary patterns	Cereal (carbohydrate rich food such as rice, noodles, pasta, bread, breakfast cereals – and potatoes)
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Waitemata Health or Auckland Healthcare regions, New Zealand
Funding	Health Research Council of New Zealand, Foundation for the Newborn, Child Health Research Foundation
Participants	Mothers of 1138 children born between October 1995 and November 1997 (844 born SGA and 870 born appropriate for GA); only term infants (> 37 weeks); Exclusions: preterm births (< 37 weeks), multiple births and those with congenital anomalies
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered after birth (to cover the periconception period and the last month of pregnancy)
Comparison	0-1. 5 v > 1. 5-2.25 v > 2.25-2.75 v > 2.75-3.5 v > 3.5 serves of cereal per day
Outcomes	SGA (≤ 10th centile for GA and gender)
Results	see below

SGA (cereal consumption at time of concepion

	SGA	**AGA**	**aOR (95%)**	**p value for trend**
0-1.5	154/538 (28.6%)	127/598 (21.2%)	1.31 (0.88 to 1.97)	
>1.5-2.25	114/538 (21.2%)	109/598 (18.2%)	1.22 (0.80 to 1.86)	
>2.25-2.75	105/538 (19.5%)	147/598 (24.6%)	0.81 (0.54 to 1.23)	
>2.75-3.5	70/538 (13.0%)	108/598 (18.1%)	0.77 (0.49 to 1.21)	
>3.5	96/538 (17.8%)	107/598 (17.9%)	1	**0.04**

SGA (cereal in last month of pregnancy)

0-1.5	123/539 (22.8%)	101/598 (16.9%)	1.52 (0.99 to 2.33)	
>1.5-2.25	96/539 (17.8%)	100/598 (16.7%)	1.36 (0.87 to 2.13)	
>2.25-2.75	114/539 (21.2%)	125/598 (20.9%)	1.08 (0.71 to 1.65)	
>2.75-3.5	118/539 (21.9%)	170/598 (28.4%)	1.00 (0.67 to 1.51)	
>3.5	89/539 (16.5%)	102/598 (17.1%)		0.17

Followup	NA
Confounding	Adjusted for socio-economic status, ethnicity, maternal height, maternal weight before pregnancy, maternal hypertension and maternal smoking; but folate supplementation was not controlled for (periconception folate was significantly associated with reduced SGA risk).
Risk of bias	Low-moderate risk of bias: Of the 2182 eligible infants, parents of 1714 (78.6%) completed the FFQ; 1138 (67%) of women completed the FFQ; missing items in completed FFQ treated as woman not consuming any cereal.
Relevance	Likely to be relevant to Australian women
Other comments	Only term infants included; Not clear if potatoes are also included in the vegetable category

Reference	**Nwaru 2010**
Food type	Cereal (rye, wheat, oats, barley, rice, pasta, macaroni, starches and other grains)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Tampere, Finland
Funding	Academy of Finland, Finnish Pediatric Research Foundation, the Juho Vainio Foundation, the Yrjo Jahnsson Foundation, Turku, Oulu and Tampere University Hospitals, JDRF, Novo Nordisk Foundation, EU Biomed 2 Program
Participants	931 mother-infant pairs (children with human leukocyte antigen-conferred susceptibility to type 1 diabetes) participating in the Finnish type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study between September 1996 and October 1997
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ given to women after birth, for return at the three month visit (FFQ intended to cover maternal diet during pregnancy and lactation)
Comparison	Amount of cereal intake
Outcomes	Allergic sensitisation in offspring by 5 years: food allergens (egg, cow's milk, fish, wheat); inhalant allergens (house dust mite, cat, timothy grass, birch)
Results	**Total cereals** ***Food allergens*** / ***Inhalant allergens*** OR 0.87 95% CI 0.50 to 1.52 / OR 1.00 95% CI 0.61 to 1.64 aOR 1.26 95% CI 0.66 to 2.43 / aOR 0.94 95% CI 0.53 to 1.66 **Wheat** ***Food allergens*** / ***Inhalant allergens*** OR 0.98 95% CI 0.65 to 1.49 / OR 1.12 95% CI 0.78 to 1.62 aOR 1.20 95% CI 0.75 to 1.93 / aOR 1.16 95% CI 0.77 to 1.74
Followup	To 5 years
Confounding	Adjusted for energy intake, place of birth, season of birth, sex of the child, number of siblings, gestational age at birth, parental asthma, parental allergic rhinitis, maternal age at birth, maternal smoking during pregnancy, maternal education
Risk of bias	Low risk of bias: data available for 931/1175 (79.2%) children recruited – 108 did not participate in survey, a further 49 did not have IgE measurements, a further 87 had no FFQ or an incomplete FFQ
Relevance	Likely to be relevant to Australian women; some differences in individual types of vegetables between Finland and Australia
Other comments	28% of women took vitamin D supplements, 73% took iron supplements; HLA genotype not likely to have any impact on the development of allergic diseases.

Reference	**Petridou 2005**
Food type	Cereals and starchy roots
Study type	Case-control study
Level of evidence	III-3
Setting	Greece
Funding	The Childhood Hematology-Oncology Group: Athens University Medical School, Aristotle University of Thessaloniki, University Hospital of Heraklion
Participants	Cases: 131 children with acute lymphoblastic leukemia, aged 12 to 59 months, gender and age matched to Controls: 131 children hospitalised for minor conditions between 1999 and 2003
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During index pregnancy
Comparison	Quintiles of cereal/starchy root intake – median Q1; 52 g/day: median Q5 164 g/day
Outcomes	Acute lymphoblastic leukemia (ALL)
Results	**Acute lymphoblastic leukemia (ALL)** **Median g/day — Cases — Controls — p for trend** Q1: 52 — 21 — 33 Q2: 74 — 27 — 25 Q3: 95 — 27 — 24 Q4: 113 — 27 — 26 Q5: 164 — 29 — 23 — 0.13 Logistic regression: one quintile more of cereals/starchy roots: aOR 1.23 95% CI 0.94 to 1.60
Followup	NA
Confounding	Total energy intake (but not mutually among food groups); matching variables; maternal age at birth; birthweight; maternal smoking during pregnancy; maternal years of schooling, maternal occupation
Risk of bias	Moderate: moderate risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy some time previously; Cases: 171 children with ALL were identified; 21 had missing data, consent was not given in 9 cases and 10 were unable to be matched, leaving 131 (77%) of cases available
Relevance	Diets of Greek women may differ from current diets of Australian women
Other comments	

Acute lymphoblastic leukemia (ALL)

	Median g/day	Cases	Controls	p for trend
Q1:	52	21	33	
Q2:	74	27	25	
Q3:	95	27	24	
Q4:	113	27	26	
Q5:	164	29	23	0.13

Reference	**Petridou 1998a**
Food type	Cereals and starchy roots (mostly bread – white bread, brown bread, traditional bread, pasta, various breakfast cereals, trahana, cheese pie (0.5), meat pie (0.5), vegetable pie (0.5), pizza (0.5), pastitsio (0.5), potatoes).
Study type	Case-control study
Level of evidence	III-3
Setting	Greater Athens area, Greece
Funding	Greek Ministry of Health and Welfare, and Foundation for Research in Childhood 'S. Doxiadis'
Participants	Cases: 109 children with cerebral palsy (CP), born between 1984 and 1988 (estimated to be two-thirds of the children with CP born during this period) Controls (1): 155 neighbouring children of similar sex and age (± 12 months) Controls (2): 99 healthy siblings of similar sex and age (± 12 months) of the first neurological patient seen by the attending physician after a visit by the CP patient
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During pregnancy
Comparison	≤ 1 versus 2 versus > 2 serves of cereals and starchy roots per day; regression analysis: risk of cerebral palsy with change in consumption by one unit (= consumption of cereals and starchy roots 3 times per week)
Outcomes	Cerebral palsy
Results	≤ 1 serve of cereals and starchy roots per day: 11/91 (12.1%) cases v 38/246 (15.4%) controls 2 serves of cereals and starchy roots per day: 59/91 (64.8%) cases v 89/246 (36.2%) controls > 2 serves of cereals and starchy roots per day: 21/91 (23.1%) cases v 119/246 (48.4%) controls Regression analysis for each unit of consumption of cereal 3 times per week: **aOR 0.83 95% CI 0.72 to 0.96** **aOR 0.85 95% CI 0.72 to 1.00 (additionally adjusted for all food groups)**
Followup	8 years
Confounding	Age and sex of child, maternal age at birth, maternal age at menarche, maternal chronic disease, previous spontaneous abortions, persistent vomiting during index pregnancy, multiple pregnancy, number of obstetric visits; timing of membrane rupture in index birth, use of general anaesthesia in the index birth, mode of birth, abnormal placenta, infant head circumference at birth, congenital malformation, place of index birth, use of supplementary iron during index pregnancy, physical exercise during index pregnancy, painless childbirth classes. The following were not included in the model: - Smoking or consumption of coffee or alcohol during pregnancy (stated to be "unrelated to CP and had no confounding influence"); - Gestational age, birthweight and maternal weight gain (stated to be "strong predictors of CP, but were not included in the model, since they are probably intermediate stages in a possible link between diet and CP (mediators) rather than genuine confounders"
Risk of bias	Moderate-high: High risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy 8 years previously; Cases: 109 children with CP were identified; for 6 children either collaboration with their guardian or a diagnosis of CP was not confirmed; and reliable maternal dietary intakes were not available for 12 women, leaving 91 cases available for analysis. Controls: 278 mother-child pairs were approached; 16 refused to participate; matching controls were not available in 8 instances, and reliable maternal dietary intakes were not available for 8 women, leaving 246 controls available for analysis.
Relevance	Diets of Greek women in 1998 may differ from current diets of Australian women
Other comments	

Reference	**Petridou 1998b**
Food type	Cereals and starchy roots (white bread, brown bread, traditional bread, pasta, various breakfast cereals, trahana, cheese pie (0.5), meat pie (0.5), vegetable pie (0.5), pizza (0.5), pastitsio (0.5), potatoes).
Study type	Retrospective cohort study
Level of evidence	III-2
Setting	Two cities (Athens and Larissa) in Greece
Funding	Not reported
Participants	368 nondiabetic women giving birth to healthy singleton babies from March to October 1995
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Immediately after birth
Comparison	≤ 2 versus 3 versus 4 versus > 4 serves of cereals and starchy roots per day; ≤ 2 serves per day: 69/268 (18.8%) 3 serves per day: 123/268 (33.4%) 4 serves per day: 106/268 (28.8%) >4 serves per day: 70/268 (19.0%) Regression analysis: mean change in birthweight (g) for each unit change in consumption (= consumption of cereals and starchy roots once daily)
Outcomes	Birthweight
Results	**Birthweight** **Regression analysis for each unit of consumption of cereals and starchy roots (once daily):** 31 g [SE37], p = 0.40 18 g [SE38], p = 0.63 without controlling for total energy intake
Followup	To birth
Confounding	Gender of child, birth order, maternal age, maternal education, maternal height, history of miscarriages, history of abortions, bleeding, smoking during pregnancy, coffee drinking, alcohol drinking, maternal weight gain, total energy intake, folic acid supplements
Risk of bias	Low-moderate risk of bias: of the 400 eligible women, 368 (92%) were available for analysis – 32 were unwilling or unable to participate; women would have been aware of the birthweight of their baby before completing the FFQ
Relevance	Diets of Greek women in 1995 may differ from current diets of Australian women
Other comments	

Reference	**Radesky 2008**
Food type	Cereal (whole grains)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Boston, MA, USA
Funding	NIH, March of Dimes Birth Defects Foundation, Harvard Medical School Division of Nutrition, Harvard Pilgrim Health Care Foundation
Participants	1773 women with singleton pregnancies enrolled in Project Viva (initial antenatal visit before 22 weeks gestation, able to complete study forms in English, did not plan to move out of the study area before birth
Baseline comparisons	Included women had lower pregnancy BMIs than excluded women, were less likely to be African-American or Hispanic, to have low SES *See confounding below*
Dietary assessment	FFQ
Timing	FFQ completed at first antenatal visit at a mean 11.8 weeks GA (range 5-25.6 weeks) - to assess diet during first trimester
Comparison	Serves of whole grains
Outcomes	Glucose tolerance testing at 26-28 weeks gestation – GDM; impaired glucose tolerance (IGT) Normal glucose tolerance defined as: < 140 mg/dL 1 hour after a 50 g glucose load (non-fasting oral glucose challenge test); IGT defined as ≥ 140 mg/dL on non-fasting oral glucose challenge test but 0 or 1 abnormal result for a fasting glucose tolerance test (100g oral glucose load where normal = < 95 mg/dL at baseline, < 180 mg/dL at 1 h, < 155 mg/dL at 2 h and < 140 mg/dL at 3 h; GDM defined as ≥ 140 mg/dL on non-fasting oral glucose challenge test with 2 or more abnormal GTT results (For the 39 women with incomplete glucose testing data, medical records were used to assign them to normal glucose tolerance (n = 7), IGT (n = 10), or GDM (n = 22).
Results	**Impaired glucose tolerance (per serve of whole grains):** aOR 1.05 95% CI 0.92 to 1.19 **GDM (per serve of whole grains):** aOR 0.90 95% CI 0.73 to 1.13
Followup	To birth
Confounding	Adjusted for maternal age, pre-pregnancy BMI, ethnicity, family history of diabetes, history of GDM in a prior pregnancy, smoking in index pregnancy; Used energy partition models and nutrient density substitution models to study the simultaneous effects of different macronutrients on GDM and IGT risk; Other studies have not adjusted for different types of fats (which may have opposing effects on risk of GDM)
Risk of bias	Low risk of bias: Of 2128 women who gave birth to a live infant, 24 were excluded for missing or incomplete glucose tolerance testing records; 18 with a history of previous type 1 or 2 DM or PCOS with glucose intolerance, 342 missing or implausible first trimester diet information; 11 completion of FFQ after 26 weeks GA (i.e. after glucose tolerance screening) or on an unknown date; leaving 1773 (83.3%) available for analysis
Relevance	Likely to be relevant to Australian women
Other comments	Paper concludes that “nutritional status entering pregnancy, as reflected by pre-pregnancy BMI, is probably more important than pregnancy diet in development of GDM”

Reference	**Stuebe 2009**
Dietary patterns	Cereals: whole grains
Study type	Prospective cohort study (Project Viva)
Level of evidence	II (aetiology)
Setting	8 urban and suburban obstetric offices of a multispecialty group practice in eastern Massachusetts, USA
Funding	US NIH, Harvard Medical School, Harvard Pilgrim Health Care Foundation
Participants	1338 women giving birth to a live singleton infant, < 22 weeks gestation at study entry; 379 (27%) were overweight (BMI ≥ 26); 703 (51%) experienced excessive weight gain Exclusions: not fluent in English
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Administered in first and second trimesters of pregnancy
Comparison	Whole grains (serves per day)
Outcomes	Excessive gestational weight gain (IOM 1990)
Results	**Excessive gestational weight gain: whole grains**
Followup	To birth
Confounding	Adjusted for pre-pregnancy BMI, maternal age, race/ethnicity, smoking status, gestational age at birth, nausea in first trimester in pregnancy
Risk of bias	Low risk of bias: Of 2083 eligible women, 1388 (67%) of women had data available for analysis (31 had missing information on pre-pregnancy BMI and gestational weight gain; 226 had missing covariate information and 438 had missing data on either first or second-trimester diet and mid-pregnancy physical activity); included women were less likely to be African-American or Hispanic, to be younger, multiparous and obese
Relevance	Likely to be relevant to Australian women
Other comments	

Results: **Excessive gestational weight gain: whole grains**

	Serves per day, median		aOR (95% CI)
	Inadequate/adequate GWG	**excessive GWG**	
Whole grains	1.25 [SD1.03]	1.27 [SD1.04]	1.06 (0.95 to 1.19)

Reference	**Venter 2009**
Food groups	Cereal: wheat
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Portsmouth, UK
Funding	Food Standards Agency
Participants	696 pregnant women at 12 weeks gestation (with estimated birth date between 1 September 2001 and 31 August 2002)
Baseline comparisons	Pregnant women with a maternal history of atopic disease were more likely to smoke
Dietary assessment	FFQ
Timing	FFQ at 36 weeks gestation
Comparison	No (< 1% of women) versus moderate (8%) versus frequent (92%) versus uncertain (< 1%) consumption of wheat during pregnancy
Outcomes	Food hypersensitivity (FHS) in infants up to three years of age
Results	**Infant FHS at one year:** 4/933 infants showed FHS to milk in the first year (4 where mothers reported frequent consumption of milk during pregnancy) **Infant FHS at three years:** 4/933 infants showed FHS to milk in the first three years (4 where mothers reported frequent consumption of milk during pregnancy) “Statistical inferences could not be measured due to the small numbers”
Length of followup	Up to three years
Confounding	Analyses do not appear to have been adjusted
Risk of bias	Moderate-high risk of bias: Data were obtained from 91% (n = 969) of the birth cohort; at 1 year follow-up data were available for 77.6% (752/969) and for 65.2% (632/969) at 3 years; analyses probably not adjusted for confounders
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Willers 2007**
Food type	Cereals (whole grain products)
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Antenatal clinics at Aberdeen Maternity Hospital, Aberdeen, Scotland
Funding	Asthma UK, GA^2LEN European Network of Excellence on Global Allergy and Asthma
Participants	1212 children (singleton births) whose mothers were recruited between October 1997 and April 1999 at a median gestational age of 12 weeks
Baseline comparisons	Women were representative of the local obstetric population *See confounding below*
Dietary assessment	FFQ
Timing	FFQ mailed at 32 weeks gestation to cover dietary intake over the previous 2-3 months
Comparison	Tertiles:
Outcomes	Wheeze, asthma, allergic rhinitis, atopic eczema, hay fever at 5 years
Results	**Whole grain products** – no consistent linear associations with respiratory and atopic outcomes in 5 year old children (exact numbers not reported in the paper).
Followup	5 years
Confounding	Adjusted for maternal age, paternal social class, maternal education, maternal smoking during pregnancy, smoking in the child's home at 5 years, energy intake, maternal asthma, maternal atopy, child's birthweight, child's sex, presence of older siblings, and breastfeeding
Risk of bias	Low risk of bias: Initial study population of 1924 children dropped to 1212 participants with complete data (63.0%) (questionnaire, at least one of the outcome time points).
Relevance	Likely to be reasonably relevant to Australian women
Other comments	Inclusion of maternal supplement use during pregnancy did not materially change the results

Reference	**Zhang 2006**
Food type	Cereal fibre
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	USA (Nurses' Health Study II)
Funding	NIH
Participants	13,110 women who reported having at least one singleton pregnancy lasting ≥ 6 months, between 1992 and 1998 Exclusions: implausible total energy intake (< 500 kcal/day or > 3,500 kcal/day); multiple gestation; history of diabetes, cancer, cardiovascular disease, or GDM on the 1989 or 1991 questionnaire.
Baseline comparisons	*See results*
Dietary assessment	FFQ
Timing	FFQs administered in 1991 or 1995 to reflect dietary intake over the past year
Comparison	Quintiles of cereal fibre intake (lowest quintile = reference)
Outcomes	Self-reported diagnosis of gestational diabetes mellitus (GDM)
Results	

GDM (adjusted for age, parity, BMI)

g/day	Cases/person-years	RR (95% CI)	p-value for trend
Q1 (<3.5)	179/18,701	1.00	
Q2 (3.6 to 4.5)	185/19,996	1.03 (0.83 to 1.28)	
Q3 (4.6 to 5.6)	136/20,229	**0.80 (0.64 to 1.00)**	
Q4 (5.7 to 7.2)	140/20,048	0.87 (0.69 to 1.08)	
Q5 (>7.2)	118/20,688	**0.69 (0.54 to 0.87)**	**<0.001**
Each 5 g/day increment		**0.72 (0.06 to 0.87)**	

GDM (adjusted for age, parity, BMI, race/ethnicity, smoking, family history of diabetes, alcohol intake, physical activity, total energy, protein intake, saturated fat, and polyunsaturated, monounsaturated and trans fatty acids)

g/day	Cases/person-years	RR (95% CI)	p-value for trend
Q1 (<3.5)	179/18,701	1.00	
Q2 (3.6 to 4.5)	185/19,996	1.03 (0.83 to 1.29)	
Q3 (4.6 to 5.6)	136/20,229	0.82 (0.65 to 1.03)	
Q4 (5.7 to 7.2)	140/20,048	0.89 (0.70 to 1.13)	
Q5 (>7.2)	118/20,688	**0.76 (0.59 to 0.99)**	**0.02**
Each 5 g/day increment		**0.76 (0.64 to 0.91)**	

GDM (adjusted for age, parity, BMI physical activity, race/ethnicity, smoking, family history of diabetes, alcohol intake, total energy, protein intake, saturated fat, and polyunsaturated, monounsaturated and trans fatty acids, and vegetable and fruit fibre)

g/day	Cases/person-years	RR (95% CI)	p-value for trend
Q1 (<3.5)	179/18,701	1.00	
Q2 (3.6 to 4.5)	185/19,996	1.04 (0.84 to 1.30)	

	Q3 (4.6 to 5.6)	136/20,229	0.83 (0.65 to 1.04)	
	Q4 (5.7 to 7.2)	140/18,826	0.89 (0.71 to 1.15)	
	Q5 (>7.2)	126/19,280	**0.76 (0.59 to 0.98)**	**0.02**
	Each 5 g/day increment		**0.77 (0.64 to 0.91)**	
Followup	Variable			
Confounding	*See results*			
Risk of bias	Low risk of bias: actual attrition figures for this substudy not reported but overall attrition reported to be 10%			
Relevance	Likely to be relevant to Australian women			
Other comments	Dietary assessment periods will differ in relation to timing of pregnancies – need to assume a woman's diet will remain similar over time and whether or she is pregnant or planning to become pregnant. This assumption may not apply to alcohol intake, for example			

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Dairy Foods

Included studies

Study	Outcomes
1. Bunin 2005	Childhood brain tumours
2. Campbell-Brown 1983	Preterm birth, birthweight, birth length, head circumference at birth, gestational weight gain
3. Chan 2006	Birthweight
4. Chang 2003	Fetal femur length
5. Chatzi 2008	Child persistent wheeze, atopic wheeze, atopy (all at 6.5 years)
6. Duvekot 2002	Pre-eclampsia
7. Elwood 1981	Gestational age, preterm birth, birthweight, SGA, birth length, head circumference at birth, milk consumption, weight, height, head circumference and skin fold of children at 5 years of age
8. Evans 1981	Colic
9. George 2005	Breastfeeding
10. Giordano 2010	Child hypospadias
11. Giordano 2008	Child hypospadias and cryptorchidism
12. Godfrey 1996	Birthweight, placental weight
13. Haggarty 2009	Deprivation
14. Herrick 2003	Cortisol concentrations in offspring at 30 years of age
15. Jakobbson 1983	Colic
16. Javaid 2005	Maternal bone mass during pregnancy
17. Jensen 2004	Childhood acute lymphoblastic leukemia
18. Jones 2000	Bone mass at 8 years
19. Knox 1972	Anencephalus
20. Kwan 2009	Childhood acute lymphoblastic leukemia
21. Lagiou 2006	Maternal sex hormone binding globulin (SHBG), progesterone
22. Lamb 2008	Islet autoimmunity
23. Latva-Pukkila 2009	Nausea and vomiting in pregnancy
24. Lovegrove 1994/1996	Clinically diagnosed atopic eczema in the infants at 18 months
25. Maconochie 2007	Miscarriage
26. Mannion 2006	Infant birth weight, crown-heel length and head circumference
27. Marcoux 1991	Pre-eclampsia, gestational hypertension
28. Mitchell 2004	SGA

29. Miyake 2006	Postpartum depression
30. Moore 2004	Birthweight, ponderal index
31. Nwaru 2010	Allergic sensitisation in offspring by 5 years
32. Oken 2007	Pre-eclampsia, gestational hypertension
33. Olafsdottir 2006	GWG
34. Olsen 2007	GWG, SGA, LGA, birthweight, birth length, head circumference, abdominal circumference, and placental weight
35. Petridou 2005	Childhood acute lymphoblastic leukemia
36. Petridou 1998	Cerebral palsy at 8 years
37. Richardson 1995	Pre-eclampsia
38. Saito 2010	Suspected atopic eczema
39. Sausenthaler 2007	Allergic sensitisation, eczema at 2 years of age
40. Stuebe 2009	GWG
41. Tennekoon 1996	Breastfeeding, resumption of regular menstruation and ovulation
42. Venter 2009	Infant food hypersensitivity up to three years
43. Willers 2007	Asthma
44. Willers 2008	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable ‘asthma symptoms’ in the last 12 months (measured longitudinally from 1 to 8 years age)
45. Yin 2010	Bone mass at 16 years

Evidence Summary

	N	Level	References
Maternal Outcomes/Associations			
1. In a case-control study from the Netherlands, drinking 5 or more units of milk a day during pregnancy was associated with a **reduced risk of pre-eclampsia**; OR 0.1 95% CI 0.03 to 0.38	163	III-3	Duvekot 2002
2. In a Canadian case-control study, while there was no clear relationship between dietary intake of calcium during pregnancy, a high dietary intake of calcium was associated with a **reduced risk of gestational hypertension** (p = 0.02)	928	III-3	Marcoux 1991
3. In a cohort study from the USA, increased consumption of milk during pregnancy was associated with **a borderline increased risk of pre-eclampsia** (aOR 1.25 95% CI 1.00 to 1.57) but not for gestational hypertension (aOR 0.93 95% CI 0.76 to 1.12)	1718	II	Oken 2007
4. In a cohort study from the USA, both low (< 1 glass a day) and high (≥ 3 glasses a day) of milk during pregnancy were associated with **an increased risk of pre-eclampsia**	9291	II	Richardson 1995
5. In a UK cohort study, pre-pregnancy milk intake of more than 1 pint of milk a day was associated with significantly **less maternal bone resorption** at 11 and 34 weeks gestation	307	II	Javaid 2005
6. In a Scottish quasi-RCT, no significant differences were seen between women supplemented with milk or cheese compared with women with a normal (unsupplemented) diet during pregnancy for **gestational weight gain**: MD 44.0 g/week 95% CI -8.55 to 96.55	180	III-3	Campbell-Brown 1983
7. In a cohort study from Iceland, increased milk consumption in late pregnancy was associated with **increased gestational weight gain**: • At least optimal weight gain: aOR 3.10 95% CI 1.57 to 6.13 (700 g/day versus 500 g/day) • Excessive weight gain: aOR 1.82 95% CI 1.08 to 3.06 (200 g/day more)	495	II	Olafsdottir 2006
8. In a Danish cohort study, increased milk consumption during pregnancy was associated with **gestational weight gain**: p < 0.001 for eight categories spanning zero to > 6 glasses of milk a day (adjusted analyses)	50,117	II	Olsen 2007
9. In a US cohort study, maternal dairy food consumption during pregnancy was significantly associated with **excessive gestational weight gain**: aOR 1.08 95% CI 1.00 to 1.17 (3 compared with 2.9 serves a day)	1338	II	Stuebe 2009
10. In a Scottish cohort study, intake of milk and cream during pregnancy was positively associated with **deprivation**, intake of cheese was negatively associated with **deprivation** and no significant associations were seen for intake of icecream or yoghurt	1277	II	Haggarty 2009
11. In a US cohort study, dairy food intake during pregnancy was not associated with the following **possible breast cancer precursors** (maternal sex hormone binding globulin (SHBG) and progesterone)	277	II	Lagiou 2006

12. In a UK case-control study, there was a borderline association between at least daily maternal intake of dairy foods during pregnancy and preventing **miscarriage**: aOR 0.75 95% CI 0.56 to 1.01	603 cases; 6116 controls	III-3	Maconochie 2007
13. In a Finnish cohort study, **nausea and vomiting** during pregnancy was not associated with consumption of either milk products or cheese during pregnancy	256	II	Latva-Pukkila 2009
Fetal Outcomes			
14. In a US retrospective cohort study of pregnant adolescent women, **fetal femur length** between 20 to 34 weeks gestation was significantly higher for women with a high antenatal dairy food consumption (≥ 3 serves per day) – p = 0.001 compared with lower dairy food intake groups	350	III-2	Chang 2003
Congenital Anomalies			
15. In a UK case-control study, cases of **anencephalus** were negatively associated with maternal intake of cheese during pregnancy, and positively associated with maternal intake of icecream during pregnancy • Cheese: r = -0.55 after a lag interval of eight months • Icecream: r = +0.60 after a lag interval of five months	NS	III-3	Knox 1972
16. In a Sicilian case-control study, no significant associations were seen between cases of **hypospadias** and maternal intake of milk or yoghurt	80 cases; 80 controls	III-3	Giordano 2010
17. In a Sicilian case-control study, no significant associations were seen between cases of **hypospadias and/or cryptorchidism** and maternal intake of milk or yoghurt	90 cases; 202 controls	III-3	Giordano 2008
Birth Outcomes			
18. In a Scottish quasi-RCT, no significant differences were seen between women supplemented with milk or cheese compared with women with a normal (unsupplemented) diet during pregnancy for: • **Preterm birth**: RR 0.88 95% CI 0.33 to 2.34 • **Birthweight**: MD 37 g 95% -75.10 to 149.10 • **Birth length**: MD 0.30 cm 95% CI -0.24 to 0.84 • **Head circumference at birth**: MD 0.20 cm 95% CI -0.18 to 0.58	180	III-3	Campbell-Brown 1983
19. In a Welsh RCT, no significant differences were seen between women eligible for free milk tokens (during pregnancy and postnatally) compared with women in a control group for: • **Preterm birth**: RR 0.87 95% CI 0.36 to 2.13 • **SGA** : RR 0.88 95% CI 0.52 to 1.50 • **Gestational age (weeks):** MD -0.10 95% CI -0.27 to 0.07 • **Birthweight (g):** MD 53.00 95% CI -5.70 to 111.70	951 children	II	Elwood 1981

• **Birth length (cm)**: MD 0.10 95% CI -0.15 to 0.35 • **Birth head circumference (cm)**: MD 0.0 95% CI -0.16 to 0.16			
20. In a New Zealand case-control study, no significant differences in **SGA** were seen for amounts of daily serves of dairy foods: • Time of conception: p value for trend = 0.21 • Last month of pregnancy: p value for trend = 0.38	1138 children	III-3	Mitchell 2004
21. In a Danish cohort study, there was a decreased rate of **SGA** and an increased rate of **LGA** with increasing milk intake e.g.: • aOR for **SGA** for > 0-1 glasses per day compared with no milk: 0.67 95% CI 0.54 to 0.85 • aOR for **SGA** for > 6 glasses per day compared with no milk: 0.51 95% CI 0.39 to 0.65 • aOR for **LGA** for > 0-1 glasses per day compared with no milk: 1.37 95% CI 1.01 to 1.84 • aOR for **LGA** for > 6 glasses per day compared with no milk: 1.59 95% CI 1.16 to 2.16 • In this study, **birthweight** (adjusted p value for trend = 0.001), **abdominal circumference, placental weight, birth length, and head circumference** (adjusted for gestational age at birth) were all significantly increased as dairy food intake in pregnancy increased.	50,117	II	Olsen 2007
22. In a UK cohort study, • **decreased placental weight** was associated with low dairy protein intake in late pregnancy (p = 0.02); attributed to dairy protein as no significant association seen with meat protein; • No significant association seen between **birthweight** and dairy protein intake in late pregnancy (p = 0.2)	538	II	Godfrey 1996
23. In a Canadian case-control study, **birthweight** (but not birth length or head circumference) was associated with maternal milk intake during pregnancy • each 250 mL increase in daily milk intake was associated with an increase in birth weight of 41.2 g (95% CI 13-75 g)	279	III-3	Mannion 2006
24. A cohort study from Australia found an association between **birthweight and ponderal index** and intake of dairy protein during pregnancy: • Each isoenergetic 1% increase in dairy protein consumption was associated with a 25 g increase in birthweight (p = 0.02) an 0.12 kg/m3 increase in ponderal index (p = 0.05)	557	II	Moore 2004
25. In a US RCT, adolescent women randomised to four serves of dairy foods a day during pregnancy gave birth to babies with significantly **higher birthweights** compared with adolescent women who consumed their usual diet during pregnancy	48	II	Chang 2006

Breastfeeding and Maternal Postpartum Followup			
26. In a US cohort study, **breastfeeding and non-breastfeeding** women consumed similar amounts of dairy products up to six months postpartum	149	II	George 2005
27. In a RCT from Sri Lanka, powdered milk supplementation in postpartum breastfeeding women did not affect the contraceptive benefit of lactation and lengthened the **duration of nearly full breastfeeding** (e.g. higher number of total breastfeeds at 48 weeks compared with women in the control group, $p < 0.05$)	60	II	Tennekoon 1996
28. In a Japanese cohort study, there was no significant association seen between **postpartum depression** and maternal intake of dairy foods during pregnancy	865	II	Miyake 2006
Childhood Asthma, Eczema and Allergy Symptoms			
29. In a Scottish cohort study, no significant association was seen between **asthma in children at 5 years** of age and maternal dairy food intake	1212 children	II	Willers 2007
30. In one German cohort study of children aged 2 years, there were no significant differences in high compared with low maternal consumption of dairy foods in late pregnancy, specifically: • **Eczema**: aOR for milk 1.04 95% CI 0.80 to 1.34 • **Allergen sensitisation**: aOR for milk 0.93 95% CI 0.67 to 1.28	2,641 children	II	Sausenthaler 2007
31. In a UK RCT, the RR for **eczema** in first 18 months was 0.73 95% 0.32 to 1.64 in the maternal milk-free group compared with the control group, in 26 children of atopic mothers	26 children	II	Lovegrove 1994/1996
32. In a Japanese cohort study, no association was seen between dairy food intake during pregnancy and **suspected atopic eczema in infants at 3-4 months** of age; p value for trend (adjusted) = 0.13	771 children	II	Saito 2010
33. In a cohort study from Spain, no significant associations were seen in adjusted analyses between dairy food intake during pregnancy and **persistent wheeze, atopic wheeze and atopy in children at 6.5 years**	482 children	II	Chatzi 2008
34. In a cohort study from Finland, no significant associations were seen between dairy food intake in pregnancy and **allergic sensitisation of children by 5 years** of age: • Food allergens aOR 0.88 95% CI 0.57 to 1.35 • Inhalant allergens aOR 0.76 95% CI 0.54 to 1.06	931 children	II	Nwaru 2010
35. In a cohort study from the Netherlands, no significant associations were seen between dairy food intake in pregnancy and **asthma symptoms in children from 1 to 8 years** of age: aOR 0.92 95% CI 0.74 to 1.15	2832 children	II	Willers 2008
36. In a cohort study from the UK, it was not clear if maternal milk consumption during pregnancy was associated with **infant food hypersensitivity at one or three years of age**	696	II	Venter 2009
37. In a crossover RCT from New Zealand, no significant differences in rates of **colic** were seen in	20 infants	II	Evans 1981

breastfed infants whether or not their mothers consumed cows milk			
38. In a crossover RCT from Sweden, 9 out of 16 infants showed signs of **colic** after their mothers had ingested cows milk	16 infants	II	Jakobbson 1983
Child Growth and Development Outcomes			
39. In a Welsh RCT, no significant differences were seen between women eligible for free milk tokens (during pregnancy and postnatally) compared with women in a control group for **infant growth at 5 years (weight, height, head circumference and skin fold)**	951 children	II	Elwood 1981
40. In one Australian cohort study, **bone mineral density of children at 8 years** was not associated with maternal dairy food intake during pregnancy: • Total body bone mineral density – p = 0.38 for adjusted regression of portions per week	173 children	II	Jones 2000
41. In an Australian cohort study (follow-up of Jones 2000) **bone mass in 16 year-old adolescents** was not associated with maternal dairy food intake during pregnancy: • Total body bone mineral density (pns) for adjusted regression of portions per week	216 children	II	Yin 2010
Other Childhood Outcomes			
42. In a Greek case-control study, **cerebral palsy in children at 8 years** was not associated with maternal dairy food intake during pregnancy: • Regression analysis for each unit of consumption of dairy foods once per day: aOR 1.12 95% CI 0.66 to 1.88 (additionally adjusted for all food groups)	109 children	III-3	Petridou 1998
43. In a US case-control study, **childhood acute lymphoblastic leukemia** was not associated with maternal dairy food intake during pregnancy: • aOR 1.16 95% CI 0.78 to 1.72; mean consumption of dairy products 2.17 [SD 1.33] serves per day	138 cases; 138 controls	III-3	Jensen 2004
44. In a US case-control study (phase 1 reported in Jensen 2004), **childhood acute lymphoblastic <u>leukemia</u>** was not associated with maternal dairy food intake during pregnancy: • aOR 1.06 95% CI 0.83 to 1.35: median consumption 2.1 (25^{th} 75^{th} percentiles 1.3, 3.0) serves per day	866 (282 cases)	III-3	Kwan 2009
45. In a Greek case-control study, **childhood acute lymphoblastic leukemia** was not associated with maternal dairy food intake: • logistic regression: one quintile more of milk/dairy products: aOR 0.82 95% CI 0.66 to 1.02	131 cases; 131 controls	III-3	Petridou 2005
46. In a case-control study from North America: • maternal intake of dairy foods in the year before pregnancy was not associated with **childhood brain tumours (medulloblastoma/PNET)**: aOR 1.1 95% CI 0.6 to 1.9; • maternal intake of hard cheese in the year before pregnancy was not associated with **childhood brain tumours (medulloblastoma/PNET)**: aOR 1.3 95% CI 0.8 to 2.0	315 cases; 315 controls	III-3	Bunin 2005

47. In a cohort study from the US, **islet autoimmunity in children up to 15 years of age** was not associated with maternal dairy food intake during pregnancy: aHR 1.18 95% CI 0.75 to 1.87	642 children	II	Lamb 2008
Outcomes For Child As An Adult			
48. In a Scottish cohort study, no significant associations were seen between **cortisol concentrations in offspring at 30 years of age** and maternal consumption of cheese or millk during pregnancy	251	II	Herrick 2003

Evidence Tables

Reference	**Bunin 2005**
Food type	Dairy foods: dairy foods in total; hard cheese
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	United States and Canada
Funding	National Cancer Institute, USA
Participants	315 cases diagnosed with medulloblastoma/PNET tumours from 0 to 5 years, between 1991 to 1997 (without a previous or recurrent cancer) 315 controls (random digit dialling, matched on area code, race and data of birth)
Baseline comparisons	See confounding below
Dietary assessment	FFQ
Timing	To reflect diet in the year before pregnancy; and the second trimester of pregnancy
Comparison	Dairy foods < 2/day to ≥ 4/day: Hard cheese < 1 serve/week ≥ 5 serves/week; data on portion size were not collected
Outcomes	Childhood brain tumours (medulloblastoma/primitive neuroectodermal (PNET) tumours)
Results	**Medulloblastoma/PNET** (see table below)

	Periconception		Midpregnancy	
	N	**aOR* (95% CI)**	**N**	**aOR* (95% CI)**
Dairy foods				
<2/day	180	1.0	122	1.0
2-<3/day	170	1.3 (0.8 to 2.1)	119	1.8 (1.0 to 3.2)
3-<4/day	120	1.2 (0.7 to 2.0)	151	1.8 (1.0 to 3.2)
≥4/day	160	0.9 (0.5 to 1.5)	238	1.1 (0.63 to 1.9)
P_{trend}		48		0.63
Hard cheese				
<1 serve/week	209	1.00	190	1.00
2-4/week	272	1.1 (0.7 to 1.7)	280	1.3 (0.8 to 2.0)
≥5/week	149	1.2 (0.7 to 2.0)	160	1.4 (0.96 to 2.4)
P_{trend}		0.57		0.19

Followup	n/a
Confounding	*adjusted for income level, mother's race, age of child at interview, date of interview, gained weight because of nausea/vomiting, number cigarettes per day, total calories
Risk of bias	Low-moderate risk of bias: 315/558 (57%) potentially eligible cases able to be included (missing cases mostly due to lack of consent from physician or parents); control resonse rates were 67% for random digit dialling and 73% for questionnaire
Relevance	Likely to be reasonably similar to Australian women
Other comments	Medulloblastomas and PNETs account for about 20% of brain tumours in children; Supplement use was also assessed in this study

Reference	**Campbell-Brown 1983**
Food type	Dairy foods (milk or cheese)
Study type	Quasi-RCT (allocation by alternation)
Level of evidence	III-1 (intervention)
Setting	Aberdeen, Scotland
Funding	Not reported
Participants	180 primiparous women at high risk of giving birth to a low birthweight baby (because of low maternal height, weight or weight-for-height at 20 weeks, or weight gain between 20 and 30 weeks)
Baseline comparisons	NA
Dietary assessment	NA
Timing	Intervention from 29 weeks gestation
Comparison	0.5 pint of flavoured milk drink or 1 pint fresh milk, or 75 g cheddar cheese (with additional supplement of 300 kcal energy and 15-20 g protein) from 29 weeks GA v normal (unsupplemented diet)
Outcomes	Preterm birth, birthweight, birth length, head circumference at birth, gestational weight gain
Results	**Preterm birth**: Milk/cheese + supplement v normal diet: RR 0.88 95% CI 0.33 to 2.34 **Birthweight**: Milk/cheese + supplement v normal diet: mean difference 37 g 95% CI -75.10 to 149.10 **Birth length** Milk/cheese + supplement v normal diet: mean difference 0.30 cm 95% CI -0.24 to 0.84 **Head circumference at birth**: Milk/cheese + supplement v normal diet: mean difference 0.20 cm 95% CI -0.18 to 0.58 **Gestational weight gain**: Milk/cheese + supplement v normal diet: mean difference 44.0 g/week 95% CI -8.55 to 96.55
Followup	To birth
Confounding	NA
Risk of bias	Moderate-high risk of bias: inadequate allocation concealment
Relevance	Study restricted to women at high risk of low birthweight
Other comments	Data extracted from Kramer 2003 (Cochrane Review); not a 'pure' comparison of dairy since women in the intervention group also received a protein/energy supplement

Reference	**Chan 2006**
Food type	Dairy foods (milk, yoghurt or cheese)
Study type	RCT (control and dairy foods arms only)
Level of evidence	II (intervention)
Setting	University of Utah, Salt Lake City, Utah, USA
Funding	National Dairy Council, USA
Participants	48 pregnant adolescent women 15-17 years of age, enrolled before 20 weeks gestation Exclusions: women with hypertension, diabetes, renal or liver diseases, and those who used alcohol, tobacco or medications that would affect calcium metabolism during the pregnancy
Baseline comparisons	NA
Dietary assessment	NA
Timing	Intervention from 20 weeks gestation
Comparison	Counselled to consume at least four serves of dairy products (more than 1200 mg Ca) daily (25 women) versus usual diet (23 women)
Outcomes	Birthweight, birth length, head circumference at birth
Results	**Birthweight**: **Dairy foods group: 3517 [SD 273] g** **Usual diet group: 3277 [SD 165] g; p < 0.001** **Birth length, head circumference at birth, blood pressure at birth** No significant difference between the two groups
Followup	To birth
Confounding	NA
Risk of bias	Moderate risk of bias: allocation concealment by sealed envelopes; moderate losses to follow-ip
Relevance	Study restricted to adolescent women
Other comments	Three arm RCT – calcium fortified orange juice arm not included here

<table>
<tr><td>Reference</td><td>Chang 2003</td></tr>
<tr><td>Food type</td><td>Dairy foods</td></tr>
<tr><td>Study type</td><td>Retrospective cohort study</td></tr>
<tr><td>Level of evidence</td><td>III-2 (aetiology)</td></tr>
<tr><td>Setting</td><td>Adolescents who had received prenatal care between 1990 and 2000 at an inner-city maternity clinic affiliated with Johns Hopkins Hospital, Baltimore, USA</td></tr>
<tr><td>Funding</td><td>Supported by National Institutes of Health grant HD035191</td></tr>
<tr><td>Participants</td><td>350 pregnant African-American adolescents (of a possible 1120 women identified as giving birth during this time frame)</td></tr>
<tr><td>Dietary assessment</td><td>24-h dietary recall and a food-frequency questionnaire collected by a registered dietitian
Dietary dairy food intake was estimated on the basis of the number of servings of dairy products.
The registered dietitian initially rated each adolescent’s calcium intake as “adequate” (4 servings/d), “fair” (2–3 servings/d), or “poor” (0–1 serving/d) on the basis of the 24-h dietary recall by using the number of dairy products consumed daily. Each serving size of dairy products contributed ~300 mg Ca. The food frequency questionnaire was then administered to determine how representative the recall data were of the adolescents’ usual intake, and 2 intermediate categories (“fair plus” and “poor plus”) were then added if the data from the food-frequency questionnaire were slightly higher than those determined from the 24-h dietary recall. Dairy food intake was classified into 1 of the 5 categories for each adolescent. The high dairy food intake group was defined as those adolescents with an “adequate” or “fair plus” intake, the medium dairy food intake group as those with a “fair” intake, and the low dairy food intake group as those with a “poor plus” or “poor” intake</td></tr>
<tr><td>Baseline comparisons</td><td>See confounding below</td></tr>
<tr><td>Timing</td><td>Dairy intake at entry into prenatal care and relationship to femur length assessed at ultrasound between 20 and 34 weeks</td></tr>
<tr><td>Comparison</td><td>Dietary and other predictors of fetal femur length</td></tr>
<tr><td>Outcomes</td><td>Fetal femur length (between 20 and 34 weeks gestation)</td></tr>
<tr><td>Results</td><td>Summary: Amongst pregnant adolescents, high (≥ 3 servings/d) maternal dairy food intake at entry into prenatal care was associated with significantly greater fetal femur length between 20-34 weeks.

Generalised multiple linear regression of dairy intake on fetal femur length, adjusting for maternal age, height, BMI, gestational age and fetal BPD.

<table>
<tr><th></th><th>β</th><th>SE</th><th>95% CI</th><th>P value</th></tr>
<tr><td>Dairy intake</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Medium</td><td>0.041</td><td>±0.024</td><td>(-0.006, 0.089)</td><td>0.089</td></tr>
<tr><td>High</td><td>0.077</td><td>±0.024</td><td>(0.030, 0.125)</td><td>0.001</td></tr>
<tr><td>Maternal age (y)</td><td>-0.002</td><td>± 0.009</td><td>(-0.020, 0.015)</td><td>0.783</td></tr>
<tr><td>Maternal height (cm)</td><td>0.0044</td><td>±0.0014</td><td>(0.0017, 0.0072)</td><td>0.002</td></tr>
<tr><td>Prepregnancy BMI (kg/m2)</td><td>0.005</td><td>±0.002</td><td>(0.001, 0.009)</td><td>0.018</td></tr>
<tr><td>Gestational age (wk)</td><td>0.141</td><td>±0.011</td><td>(0.119, 0.162)</td><td>0.001</td></tr>
<tr><td>Fetal biparietal diameter (cm)</td><td>0.373</td><td>±0.039</td><td>(0.297, 0.449)</td><td>0.001</td></tr>
</table>

Women in the high dairy food intake group had significantly higher protein (P = 0.001), vitamin A (P = 0.001), and iron (P = 0.002) intakes than did those in the lower intake groups. Similar trends were also evident for total energy and vitamin C intakes, although these results were not significant (P = 0.096 and 0.061, respectively).

When the effect of each nutrient intake on fetal femur length was examined controlling for gestational age, maternal age, maternal height, prepregnancy BMI, and fetal biparietal diameter, no significant relations of fetal femur length with intakes of protein, vitamin A, iron, energy, and vitamin C were evident, suggesting a solely dairy food effect.</td></tr>
</table>

Followup	Nil (retrospective cohort)
Confounding	Factors considered included: maternal age, height, weight, prepregnancy BMI, birth weight, duration of pregnancy, and Apgar score, cesarean delivery, preterm birth and intakes of other nutrients, including energy, protein, vitamin A, iron, and vitamin C. In final model, figures were adjusted for: gestational age, maternal age, maternal height, prepregnancy BMI, and fetal biparietal diameter.
Risk of bias	Low-moderate risk of bias: possible selection bias - 770 women were excluded for a variety of reasons (ultrasounds not performed in the timeframe, history of smoking and other drug use, stillbirth, no dietary data, other missing variables), but there appeared to be no significant differences in demographic, dairy food intake distribution, and birth outcomes between this subset and the excluded women
Relevance	The study group represents a low dairy food intake population, as the majority of women in the study consumed < 2 serves of dairy foods/day. Fetal femur lengths in this population were similar to that reported in a UK study, suggesting that they are broadly comparable to a white adult population
Other comments	

Reference	**Chatzi 2008**
Food type	Dairy foods
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women presenting antenatal care at general practices in Menorca, a Mediterranean island in Spain (mid 1997 to mid 1998)
Funding	Instituto de Salud Carlos III red de Grupos Infancia y Media Ambiente, the Fundacio "La Caixa" , Instituto de Salud Carlos III, red de Centros de Investigacion en Epidemiologica y Salud Publica, EU, National Center for Environmental Health, USA, the GA2LEN project, Ministry of Education and Science, Spain, Oficina de Ciencia y Tecnologia, Generalitat Valenciana.
Participants	482 children of 507 women who had attended antenatal care in Menorca
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	not clear when women did FFQ and period of pregnancy it was intended to cover
Comparison	≤ 23 v > 23 serves of dairy per week
Outcomes	Persistent wheeze, atopic wheeze and atopy at 6.5 years
Results	***Persistent wheeze at 6.5 years*** Low 18 (14.06%) v high 19 (12.50%); pns (also adjusted for firstborn and lower respiratory tract infections at age 1) ***Atopic wheeze at 6.5 years*** Low 12 (6.90%) v high 8(4.73%); pns (also adjusted for birthweight and maternal atopy) ***Atopy at 6.5 years*** Low 34 (16.83%) v high 36 (17.22%) pns (also adjusted for birthweight and maternal atopy)
Followup	6.5 years
Confounding	Analyses adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years and total energy intake at 6.5 years
Risk of bias	Low risk of bias: results from 468/482 children (97%) able to be analysed (4 incomplete data and 8 implausible values);
Relevance	Diets in Menorca may differ from diets of Australian women, particularly urban women
Other comments	

Reference	**Duvekot 2002**
Food type	Dairy foods (milk intake)
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	Pregnant women with pre-eclampsia and matched controls in the Netherlands, 1991-1996
Funding	Not stated
Participants	163 primiparous women with a singleton pregnancy who developed pre-eclampsia and primiparous, singleton controls (n=??) matched on maternal age and delivery date. Women with multiple pregnancy, chronic hypertension, renal disease and other chronic conditions in pregnancy were excluded.
Dietary assessment	Unclear, states a standard questionnaire was completed containing questions about milk consumption, use of calcium supplements in pregnancy and other health information
Baseline comparisons	Cases and controls were matched on maternal age and date of birth*. See also confounding below.*
Timing	Retrospective assessment of milk intake but unclear about which time period in pregnancy milk intake was assessed
Comparison	Milk intake (units per day) in women who developed pre-eclampsia vs controls
Outcomes	Development of pre-eclampsia
Results	**Summary: higher milk consumption (≥ 5 units per day, predominantly skim milk) appears to be protective against pre-eclampsia.** Mean milk consumption was lower amongst women who developed pre-eclampsia (2.4 +/- 0.1 units per day) compared with controls (3.0 +/- 0.1 units per day); p <0.01. Drinking 5 or more units per day of milk was associated with a reduced risk of pre-eclampsia (OR 0.1, 95% CI 0.03-0.38). After adjusting for family history of hypertension, BMI and smoking, consumption of ≥5 units of milk per day was associated with a reduced risk of pre-eclampsia compared with consumption of <5 units per day (adj OR 0.21, 95% CI 0.09 – 0.47). There was no difference in the consumption of calcium tablets amongst women with pre-eclampsia (4.9%) and controls (4%). Women with severe pre-eclampsia had a significantly reduced milk intake compared with controls (2.4 +/- 1.3 vs 3.0 +/- 0.1 units per day), p<0.01. No significant difference between intake amongst women with severe pre-eclampsia or eclampsia compared with pre-eclampsia (i.e. no dose response relationship)
Followup	Nil – retrospective assessment post birth
Confounding	Adjustment for family history of hypertension, BMI and smoking
Risk of bias	High risk of bias: recall bias (retrospective recall after the development of pre-eclampsia); Possible ascertainment bias as details of the questionnaire on milk intake are unclear and unclear how intake was categorised into 'units per day'; no consideration or adjustment for other dietary factors
Relevance	The Netherlands is considered to have high milk consumption across the population, which may be similar to Australia. Main source of milk is low fat milk in this population. Unclear what a 'unit of milk' was in this study and how this translates to serving sizes
Other comments	

Reference	**Elwood 1981**
Food type	Dairy foods (milk)
Study type	RCT
Level of evidence	II (intervention)
Setting	Wales (1972)
Funding	Not reported
Participants	1251 pregnant Welsh women recruited soon after first antenatal visit (data available for 951 children)
Baseline comparisons	More smokers in control group
Dietary assessment	Amount of milk consumed (via questionnaire)
Timing	Antenatal and postnatal
Comparison	Free tokens worth 0.5 pint from mid-pregnancy until child was 5 years of age v no intervention
Outcomes	Gestational age, preterm birth, birthweight, SGA, birth length, head circumference at birth, milk consumption, weight, height, head circumference and skin fold of children at 5 years of age
Results	**SGA** (extracted from Kramer Cochrane review (Kramer 2003)): RR 0.88 95% CI 0.52 to 1.50 **Preterm birth** (extracted from Kramer Cochrane review (Kramer 2003)): RR 0.87 95% CI 0.36 to 2.13 **Gestational age (weeks):** (extracted from Kramer Cochrane review (Kramer 2003)): MD -0.10 95% CI -0.27 to 0.07 **Birthweight (g):** (extracted from Kramer Cochrane review (Kramer 2003)): MD 53.00 95% CI -5.70 to 111.70 **Birth length (cm)** (extracted from Kramer Cochrane review (Kramer 2003)): MD 0.10 95% CI -0.15 to 0.35 **Birth head circumference (cm)** (extracted from Kramer Cochrane review (Kramer 2003)): MD 0.0 95% CI -0.16 to 0.16 Children in the milk token group **consumed slightly more milk at 4.5 years** (about 71 ml per day) than the control group **Children's growth at 5 years of age** was not significantly different between the intervention and control groups (weight, height, head circumference and skin fold)
Followup	5 years
Confounding	*See risk of bias below*
Risk of bias	Moderate risk of bias: unclear method of allocation (envelopes); not blinded; 24% loss to followup (with more losses in the control group); no adjustment for more smokers in the control group
Relevance	Use of tokens for milk may not be very feasible in Australia (this study was done in a period when most milk was delivered to the home)
Other comments	Intervention was entitlement to milk rather than milk (only 40% on average of entitlement taken up); Child outcomes after birth result from milk entitlement for both mothers and children (i.e. not a pure maternal intervention)

Reference	Evans 1981
Dietary patterns	Intervention period: 12 days. All mothers were instructed to keep on a cow's milk-free diet for the duration of the trial. Each day, each mother was given a 600 ml drink to be drunk by noon. On 6 of the days, the drink contained 300 ml of cow's milk and 300 ml of soya milk plus pure vanilla flavouring. On the other 6 days the drink contained 600 ml soya milk plus vanilla flavouring. The two drinks were formulated to be indistinguishable. The trial days were grouped into blocks of 2 days, randomly assigned, so that each mother received three 2-day blocks on which cow's milk was given and three 2-day blocks on which soya milk was given. An independent assessor checked at the end of each study; no mother was able to distinguish control blocks from study blocks.
Study type	Randomised cross-over trial
Level of evidence	II (intervention)
Setting	Department of Paediatrics and Surgery, Christchurch Clinical School of Medicine, Christchurch Hospital, Christchurch, New Zealand.
Funding	Canterbury Medical Research Foundation
Participants	20 exclusively breast-fed infants presenting with persistent colic; 12 girls and 8 boys. The diagnosis of colic was confirmed by a paediatrician, and the criterion was: a history of persistent crying for no apparent reason, which may have been accompanied by other symptoms including going red in the face and drawing the legs up to the stomach. 18 of the 20 were born at 39 weeks' gestation or later.
Baseline comparisons	Baseline characteristics of participants not reported.
Dietary assessment	Mothers self-reported their dietary patterns.
Timing	The children were aged 3-18 weeks (mean of 7 weeks), with median onset of colic of 3 weeks.
Comparison	See Dietary patterns section
Outcomes	Rates of colic versus: (1) maternal diet and maternal antigen responses in breast milk; (2) milk/non-milk days and maternal allergy; (3) days on which various foods were eaten by mother; (4) number of types of foods consumed by mother.
Results	(1)Rate of colic versus maternal diet and maternal antigen responses in breast milk

	All study days		**Second days only***	
	Antigen present	Antigen absent	Antigen present	Antigen absent
No cow's milk	61% (40/65)	71% (30/42)	59% (19/32)	57% (12/21)
Cow's milk	69% (46/67)	74% (31/42)	61% (20/33)	67% (14/21)

*This second day only analysis was carried out to exclude carry over effects.

(2) Rate of colic versus milk/non-milk days and maternal allergy;

	All study days		**Second days only***	
	Antigen present	Antigen absent	Antigen present	Antigen absent
No cow's milk	63% (38/60)	64% (38/59)	57% (17/30)	62% (18/29)
Cow's milk	77% (46/80)	63% (38/60)	73% (22/30)	57% (17/30)

(3) Rate of colic versus days on which various foods were eaten by mother;

Food eaten	**Yes**	**No**	**p**
Meat	67.5%(125/185)	63.6% (35/55)	> 0.05
Vegetables	67.6% (138/204)	61.1% (22/36)	> 0.05
Fish	68.1% (30/44)	66.3% (130/196)	> 0.05
Eggs	67.1% (72/106)	65.6% (88/134)	> 0.05

	Nuts 67.3% (33/49) 66.4% (127/191) > 0.05 Fruit 68.1% (150/220) 50.0% (10/20) < 0.05 Chocolate 80.4% (34/42) 63.6% (126/198) < 0.05 (4) Rate of colic versus number of types of foods consumed by mother. **Number of "types" of foods consumed by mother** 0 / 1 / 2 / 3+ / **Total** % Colic days: 28.6% (2/7days) / 60.4% (29/48) / 63.9% (55/86) / 74.7% (55/86) / 240 days* *There were 20 women and 12 days of intervention (240 days total). X^2 (trend) = 5.75; p < 0.05.
Followup	12 days duration of intervention
Confounding	No evidence.
Risk of bias	Moderate risk of bias. The methods of randomisation and randomisation concealment were not reported. The trial was reported as being double-blind. The outcomes were determined based on mother's diaries of timing and duration of colic and other symptoms and diet, and is therefore subject to bias. Two mothers did not provided specimens of breast-milk, and it was not reported why they did not.
Relevance	Limited relevance; shows increased rates of colic when chocolate and fruit were consumed, and a trend towards colic when more food types are consumed in one day.
Other comments	

Reference	**George 2005**
Food type	Dairy foods (milk and cheese)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Texas, US
Funding	Not reported
Participants	149 Medicaid-qualified women (30% white, 24% African American, 46% Hispanic) – recruited from a larger study on postpartum weight retention Inclusion criteria: 18 years or older; non-Hispanic white, African American or Hispanic ethnicity; birth of a health term infant, fluency and literacy in English; absence of pregnancy-related abnormalities and disease conditions.
Baseline comparisons	Significant differences between lactating and non-lactating women – higher parity, BMI and lower education levels in non-lactating women.
Dietary assessment	Semiquantitative FFQ to cover pregnancy and first six months postpartum
Timing	FFQ administered at 6 weeks and 6 months postpartum
Comparison	Number of serves of dairy products
Outcomes	Breastfeeding (exclusive or partial at 6 months postpartum)
Results	Lactating women and non-lactating women consumed similar amounts of dairy products in the postpartum period ($p > 0.05$)
Followup	6 months postpartum
Confounding	No adjustment for potential confounding
Risk of bias	Moderate-to-high risk of bias; no attempt to control for confounding despite significant baseline differences between lactating and non-lactating women.
Relevance	Possibly relevant to low-income women in Australia
Other comments	Minimal reporting of results

Reference	**Giordano 2010**
Food type	Dairy foods
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Rome, Italy
Funding	Not reported
Participants	80 cases of hypospadias requiring surgical treatment in children aged 0 to 24 months (mean age 57.62 weeks) 80 controls: healthy males without any congenital defect, aged 0 to 24 months (mean age 36.52 weeks); Births between September 2005 and May 2007
Baseline comparisons	*See confounding below*
Dietary assessment	Interview on 'typical' maternal diet habits in relation to the index pregnancy and food frequencies
Timing	FFQ administered on recruitment for mothers of cases and during vaccination visits for mothers of controls
Comparison	Rare versus frequent consumption of milk and dairy products
Outcomes	Hypospadias
Results	**Milk and dairy products** (see results table below)
Followup	n/a
Confounding	Adjusted for mother's BMI at conception and education of the father; Gestational age, birthweight and SGA were not included among the covariates in the regression models, as they may share a common aetiology with hypospadias
Risk of bias	Moderate risk of bias: Participation rate of parents of cases was higher than that of controls (85% versus 70%); very few potential confounders used in adjusted analyses
Relevance	Likely to be reasonably relevant for Australian women
Other comments	Likely to be underpowered

Results — Milk and dairy products:

Milk and dairy products	Cases	Controls	OR	aOR
Rare	61 (73.3%)	67 (83.8%)	1.00	1.00
Frequent	19 (23.8%)	13 (16.3%)	1.61 95% CI 0.73 to 3.52	1.73 95% CI 0.77 to 3.90

Reference	**Giordano 2008**
Food type	Dairy foods (milk, yoghurt)
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Sicily, Italy
Funding	Sicilian Congenital Malformation Registry
Participants	90 cases: 43 cases of hypospadias and 48 cases of cryptorchidism (both in one infant) 202 controls: randomly selected controls born in the same year and the same region Births between 1998 to 2003
Baseline comparisons	Low birthweight, low maternal education, mother's history of gynaecological disease and father's history of urogenital diseases differed significantly between cases and controls *See confounding below*
Dietary assessment	Interview on maternal diet and food frequencies
Timing	FFQ
Comparison	Consumption of dairy products once a week or less/more than once a week
Outcomes	Hypospadias and cryptorchidism
Results	**Milk and yoghurt** **Hypospadias** **Cases** / **Controls** / **OR** ≤ 1/week: 14 (32.6%) / 60 (29.7%) / 1.00 > 1/week: 29 (67.4%) / 142 (70.3%) / 0.88 95% CI 0.43 to 1.77 **Cryptorchidism** ≤ 1/week: 13 (27.1%) / 60 (29.7%) / 1.00 > 1/week: 35 (72.9%) / 142 (70.3%) / 1.14 95% CI 0.56 to 2.30 **Hypospadias and cryptorchidism** ≤ 1/week: 26 (28.9%) / 60 (29.7%) / 1.00 > 1/week: 64 (71.1%) / 142 (70.3%) / 1.04 95% CI 0.60 to 1.80
Followup	n/a
Confounding	Results for this food group were not presented as adjusted analyses
Risk of bias	Moderate risk of bias: Participation rate of parents and data collection rate of cases was lower than that of controls (76% versus 91%); no adjusted results presented for this food group
Relevance	Likely to be reasonably relevant for Australian women, although hypospadias rates very high and unlikely that most Australian women will have such high pesticide exposure
Other comments	Ragusa region in Sicily is a region of intensive agriculture (involving high rates of pesticide and other chemical use) with high rates of hypospadias and cryptorchidism

Reference	**Godfrey 1996**
Food type	Dairy foods
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Southampton, UK
Funding	Dunhill Trust and Medical Research Council
Participants	538 women who gave birth to a singleton term infant
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered in early and late pregnancy, to reflect diet in the previous three months
Comparison	≤ 18.5 v 18.5 to 26.5 v > 26.5 g/day dairy protein; mean daily intake 22.3 g IQR 16.4, 28.9 late pregnancy
Outcomes	Birthweight, placental weight
Results	<u>**Placental weight**</u> **Low protein intake in late pregnancy associated with decreased placental weight (p = 0.02); attributed to dairy protein as no significant association seen with meat protein;** **Placental weight fell by 1.4 g (95% CI 0.4 g to 2.4 g); p = 0.005 for each g decrease in dairy protein intake in late pregnancy** <u>**Birthweight**</u> No significant association seen between dairy protein intake in late pregnancy and birthweight (p = 0.2)
Followup	To birth
Confounding	Adjusted for baby's sex and gender and duration of gestation; and nutrient intakes
Risk of bias	Low risk of bias: of 636 women recruited, 596 (94%) agreed to participate; 39 gave birth before 37 weeks, 3 were not visited in late pregnancy and placental weight was not recorded for 16, leaving 538 term pregnancies with complete birth and nutrition data (85% of the 636 women recruited)
Relevance	Likely to be relevant for Australian women
Other comments	

Reference	**Haggarty 2009**
Dietary patterns	Dairy foods (milk and cream; cheese; yoghurt; icecream)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Aberdeen, Scotland
Funding	UK Food Standards Agency
Participants	1277 sequentially enrolled pregnant women attending Aberdeen Maternity Hospital for ultrasound (a further 184 women were recruited later in pregnancy). Exclusions: diabetic women, women with multiple pregnancies, women who conceived as a result of fertility treatment, or clinical data not available
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	Assessed at 19 weeks gestation
Comparison	Intake of milk and cream; cheese; yoghurt; icecream milk and cream; cheese; yoghurt; icecream by deciles of deprivation
Outcomes	Deprivation (assessed using the Scottish Index of Multiple Deprivation); Low birthweight (defined as < 2500 g or lowest decile for birthweight z score adjusted for gestational age, sex and parity) Preterm birth (< 37 weeks) Admission to neonatal unit
Results	 **<u>Deprivation</u>** Milk and cream: significantly higher intake with higher levels of deprivation ($p < 0.01$) Cheese: significantly lower intake with higher levels of deprivation ($p < 0.05$) Yoghurt: no significant association with deprivation Icecream: no significant association with deprivation
Followup	To neonatal period
Confounding	(Some?) analyses adjusted for energy intake
Risk of bias	Low to moderate risk of bias: low attrition, some lack of detail in reporting of outcomes
Relevance	Likely to be relevant to Australian women
Other comments	About 40-50% of the least deprived women reported taking folic acid supplements compared with about 20% for the most deprived women; Most birth outcome associations were reported by nutrient rather than food group; Not easy to deduce quantities of intake of foods (main graphs reported as change in intake by deprivation decile)

Reference	**Herrick 2003**
Food groups	Dairy foods (cheese, milk)
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Motherwell, Scotland
Funding	Dunhill Medical Trust, NIH
Participants	251 men and women whose mothers' food intakes had been recorded during pregnancy during 1967 to 1968. These women had been advised to eat 0.45 kg of red meat a day and to avoid carbohydrate-rich foods during pregnancy
Baseline comparisons	*See confounding below*
Dietary assessment	Mothers asked about consumption of 10 foods
Timing	Early pregnancy (≤ 20 weeks); late pregnancy (> 20 weeks)
Comparison	Cheese (ounces per week); Milk (pints/day)
Outcomes	Cortisol concentrations in offspring aged 30 years
Results	Cortisol (change per unit change in maternal cheese consumption during pregnancy) No significant association Cortisol (change per unit change in maternal milk consumption during pregnancy) No significant association, but trend to lower plasma cortisol with high maternal milk consumption in late pregnancy ($p = 0.06$)
Length of followup	30 years
Confounding	Analyses adjusted for offspring's gender, social class at birth, BMI, alcohol consumption, and activity level
Risk of bias	Moderate risk of bias: For the 1432 records from 1967-8 recorded liveborn, singleton births with complete names, birth measurements and ≥ 1 diet record. 965 offspring were alive and living locally; and after attrition or declining to participate, 251 (17.5%) were available for analysis.
Relevance	Very high intake of meat and very low carbohydrate intake limits the relevance to current dietary intakes of Australian women
Other comments	Authors state that "in the setting of advice to follow a pregnancy diet high in protein and low in carbohydrate, an unbalanced pattern of higher meat/fish and lower green vegetable consumption in late pregnancy leads to elevated cortisol concentrations in the offspring"

Reference	Jakobbson 1983
Dietary patterns	This study was conducted in two stages: <u>Stage 1:</u> a) All mothers (66 in total) - 1 week free of cow's milk b) "then the mothers reintroduced cow's milk in their diets" (duration not reported) It was reported that "this challenge was done twice", although "this challenge" was not defined. <u>Stage 2:</u> Active capsules: 200 mg of cow's milk whey proteins Placebo capsules: 200 mg of potato starch All 16 women who participated in the challenge received both types of capsules. Capsules were taken on day 1 and day 3. Women were "randomised" as to which of these days they received active and which they received placebo capsules. On day 6, the 16 mothers were asked to drink ½ to 1 glass of milk, three times daily. The infant's behaviour during the study (e.g. time and duration of crying, vomiting, abnormal stools, disturbed sleep) was recorded on a "standardised protocol". The mothers maintained a strict cow's milk free diet during the study.
Study type	Randomised cross-over trial
Level of evidence	II (intervention)
Setting	Department of Paediatrics, University of Lund, Malmo General Hospital, Malmo, Sweden.
Funding	Albert Pahlson Foundation, Alfred Osterlund Foundation, the Swedish Baby Food Industry Fund for Nutritional Research, and the Swedish Nutrition Foundation.
Participants	This study was conducted in two stages: Stage 1: 66 breast-fed infants with infantile colic, but otherwise healthy. The colic was confirmed by a paediatrician. Stage 2: 23 of the infants with relapse of colic after the mothers drank cow's milk in the first stage.
Baseline comparisons	Baseline characteristics of participants not reported.
Dietary assessment	NA
Timing	The "double blind challenge" was done at a mean age of 8.9 weeks in the 16 patients (16/23).
Comparison	See Dietary patterns section
Outcomes	The infant's behaviour (e.g. time and duration of crying, vomiting, abnormal stools, disturbed sleep) in relation to the mother's diet was recorded on a "standardised protocol". Who recorded this information and the exact timing of the reporting was not reported.
Results	Stage 1 results: When the colic disappeared on elimination of cow's milk and reappeared on the mother's milk challenges, the mothers were asked to participate in a double-blind crossover trial. Stage 2 results: 16 mothers underwent the challenge: -5 infants had no symptoms after either the placebo, whey capsules, or milk drinking challenge. -1 infant had no reaction after intake of either placebo or whey capsules but did react after the milk drinking challenge. -9 infants reacted with colic after their mothers ingested the capsules containing cow's milk whey protein and after the milk drinking challenge but did not react after placebo capsules.

	- 1 had colic on placebo capsules, no colic on whey protein capsules, but had cold after milk drinking challenge.
Follow-up	Unclear
Confounding	Unclear
Risk of bias	High risk of bias. The method of randomisation was not reported. There were 7 (out of 23 total) post-randomisation drop-out/exclusions (1 due to allergy, 4 refused to participate, 2 mothers had inadequate breast milk). Thus, 16 mothers/infants participated in the challenge, except that 6 "had to be taken out of the study", all due to lack of symptoms of colic.
Relevance	Poor design and reporting limits the relvance of the study findings.
Other comments	

Reference	**Javaid 2005**
Food type	Dairy foods (milk)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women living in Southampton, United Kingdom who became pregnancy during oct 1999 to January 2002, recruited through GP clinics. These women were a subset of the Southampton Women's Study (n=12,500 women not pregnant at enrolment)
Funding	Medical Research Council, UK
Participants	307 pregnant women assessed pre-pregnancy and in early and late pregnancy
Dietary assessment	Unclear – women were interviewed in person and asked about sociodemographic characteristics, lifestyle, milk intake, previous obstetric history, and recalled birthweight. During pregnancy, women were also asked about lifestyle characteristics, smoking habit, alcohol consumption, and the level of physical activity were obtained
Baseline comparisons	*See confounding below*
Timing	Diet and lifestyle assessed pre-pregnancy as well as weeks 11 and 34 of pregnancy. Maternal bone resorption measured during these times in pregnancy
Comparison	Predictors of the decline in calcaneal bone measurements in pregnancy, as assessed by ultrasound
Outcomes	Change (decline) in maternal bone resorption in pregnancy
Results	**Summary: pre-pregnancy milk intake of more than 1 pint milk/day was protective against loss of maternal bone mass in pregnancy.** During pregnancy, there was a significant (*P* < 0.001) decline in calcaneal SOS and BUA. Maternal milk intake during pregnancy was not associated with change in calcaneal quantitative ultrasound. However, those mothers drinking more than 1 pint milk/d before pregnancy tended to preserve calcaneal SOS during pregnancy (+0.32 SD, *P* < 0.01) **Multiple linear regression of change in SOS and BUA (quantitative ultrasound measures)** The changes in both SOS and BUA were influenced by season at the time of the early pregnancy visit. Change in calcaneal SOS during pregnancy was also independently predicted by parity and milk intake (>1 pint/d) before pregnancy. Maternal adiposity (MUAC) also predicted changed in BUA.

	Determinant	β	95% CI	p value
Change in SOS				
	Parity (per child)	0.1	0.05 to 0.2	0.001
	Milk intake (>1 pint)	0.3	0.07 to 0.6	0.01
	Season* (summer)	0.2	-0.01 to 0.4	0.07
Change in BUA	Season (summer)	0.2	0.05 to 0.5	0.02
	MUAC (cm)	0.8	0.2 to 1.3	0.007

SOS = calcaneal speed of sound
BUA = calcaneal broadband ultrasound attenuation
MUAC = mid upper arm circumference
*season at the time of the early pregnancy visit

Followup	Pre-pregnancy until birth
Confounding	Change in SOS and BUA measurements during pregnancy were found to be associated with changes in heel width; hence, both SOS and BUA were adjusted for mean heel width during early and late pregnancy where appropriate. Other confounders considered included: maternal age, parity,

	educational level, maternal body size (height, weight, adiposity), maternal birthweight, physical activity, maternal occupational status, maternal smoking, and maternal use of nutritional supplements
Risk of bias	Low-moderate risk of bias: possible ascertainment bias as unclear how information from questionnaire was categorised into milk intake. Also other sources of dietary calcium were not collected, nor was total energy intake
Relevance	30% of women reported consuming less than ¼ pint milk/d either before or during pregnancy, unclear if this is similar to dietary dairy consumption in Australia. Given the time frame, we could assume that the majority of milk intake in the cohort is skim milk, however this is not explicitly stated by the authors. As data on other dietary sources of calcium or vitamin D were not collected the authors stated that they are unable to estimate an adequate calcium intake needed to maintain maternal bone mass during pregnancy
Other comments	

Reference	**Jensen 2004**
Food type	Dairy products
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study)
Funding	PHS
Participants	138 matched cases and controls: Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, parental occupation and smoking during pregnancy – no evidence of confounding was seen for these variables. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of dairy products
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Childhood acute lymphoblastic leukemia** aOR 1.16 95% CI 0.78 to 1.72; mean consumption of dairy products 2.17 [SD 1.33] serves per day Analysis restricted to 66 pairs where mother did not use vitamin supplements: aOR 1.68 95% CI 0.92 to 3.07 (p = 0.09; trend to significance)
Followup	n/a
Confounding	Analyses were adjusted for variables previously shown to be significantly associated with ALL in the overall study – income, prior fetal loss, child's exposure to other children under age five, and maternal exposure to indoor insecticides during pregnancy; along with portion size and energy consumption
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 1999, 83% consented to participate; 69% of the eligible controls agreed to participate. Of the 161 matched pairs, seven pairs were excluded as the respondent was not the biological mother, 16 pairs were excluded due to questionable dietary questionnaire data, leaving 138 matched pairs (86%); some recall bias likely
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	

Reference	**Jones 2000 (see also Yin 2010)**
Food type	Dairy foods (milk)
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Southern Tasmania, Australia
Funding	NHMRC, Tasmanian Government, Royal Hobart Hospital Acute Care Program
Participants	173 mothers; and their infants born in 1988 (part of a larger infant health study of babies at high risk of SIDS) Exclusions: multiple pregnancies
Baseline comparisons	Mothers with no tertiary education more likely to have been excluded due to missing data
Dietary assessment	FFQ
Timing	Dietary intake during third trimester of pregnancy
Comparison	Linear regression of density (ml per kJ)
Outcomes	Bone mass (bone mineral density (BMD) and bone mineral content*) in 8 year old children
Results	 **BMD at 8 years;** **Total body (g/cm^2)** r^2 0% 0.000 (p = 0.76) adjusted r^2 23% 0.001 (p = 0.38) **Femoral neck (g/cm^2)** r^2 2% 0.003 (p = 0.12) **adjusted r^2 35% 0.004 (p = 0.03)** **Lumbar spine (g/cm^2)** r^2 1% 0.002 (p = 0.35) adjusted r^2 32% 0.002 (p = 0.35)
Followup	8 years
Confounding	Analyses were adjusted for method of dietary assessment, maternal education, parental unemployment, sex, weight at age 8 years, height at age 8 years, weekend sunlight exposure in winter at age 8 years, smoking during pregnancy, sports participation, ever breast-fed and current calcium intake.
Risk of bias	Moderate-high: 330 (215 males, 115 females) representing a 60% response rate from those available in 1996; 47% of the original 1988 cohort, This dropped to 173 (dietary information missing or unreliable for 115 mothers, 32 multiple births, 10 participants had missing data for confounders) representing 52% of participants from 1996 and 25% of those in the original cohort. 72% of the 173 participants were male. Gender imbalance suggests potential selection bias (due to original selection of infants at high risk of SIDS)
Relevance	Infants at high risk of SIDS represent a selected group (more males, preterm births, teenage mothers, smoking during pregnancy)
Other comments	*Bone mineral content not reported – stated to be similar to bone mineral density results

Reference	**Knox 1972**
Food type	Dairy foods (cheese)
Study type	Case control (cases matched to food consumption at population level for a particular period) – numbers not reported
Level of evidence	III-3 (aetiology)
Setting	Birmingham, UK
Funding	Not reported
Cases	Stillbirths and infant deaths due to anencephalus between 1961 and 1967
Baseline comparisons	n/a
Dietary assessment	Population surveys
Timing	Each quarter
Comparison	Monthly stillbirths and infant deaths due to anencephalus matched to quarterly consumption of main food stuffs (in previous five to nine months)
Outcomes	Anencephalus
Results	**Cheese negatively associated with cases of anencephalus: r = -0.55 after a lag interval of eight months** **Icecream positively associated with cases of anencephalus: r = +0.60 after a lag interval of five months** (icecream also included in fats and oils)
Followup	n/a
Confounding	Analyses were not adjusted
Risk of bias	High risk of bias: links between population consumption of foods and anencephalus very distal and no control for potential confounders
Relevance	Likely to differ from a modern Australian diet
Other comments	Food consumption of total population not likely to reflect food consumption of pregnant women; and will not be able to reflect differences between diets of individual or specific groups

Reference	**Kwan 2009**
Food type	Dairy foods (cheese, milk, yoghurt)
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study – phase 1 and 2 (phase 1 reported in Jensen 2004)
Funding	PHS; Paul O'Gorman Foundation for Children with Leukemia
Participants	866 individuals - 282 matched cases and controls (205 pairs and 77 trios): Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth (in phase 1 (1995-99) only due to concerns about overmatching on potential environmental exposures linked to leukemia risk) Data collected from August 1995 to November 2002
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, and smoking during pregnancy. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of dairy foods
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Childhood acute lymphoblastic leukemia** aOR 1.06 95% CI 0.83 to 1.35: median consumption 2.1 (25^{th} 75^{th} percentiles 1.3, 3.0) serves of dairy foods per day
Followup	n/a
Confounding	Analyses were adjusted for total energy intake, household income, indoor insecticide exposure during pregnancy; and proportion of foods reported as large or extra-large portion size Also adjusted for child's diet, with little effect seen on results
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 2002, 86% consented to participate; 56% of the eligible controls agreed to participate. 190 participants excluded: leukemia diagnosis was not ALL (n = 127); no dietary data (n = 4); a case or a control respondent was not the biological mother (n = 14), questionable dietary questionnaire data (n = 45), leaving 282 matched sets (86%).
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	Regular use of any dietary supplement was not associated with risk of ALL; Authors did not report on meat overall (was grouped with overall protein) or some specific meats such as liver

Reference	**Lagiou 2006**
Food type	Dairy foods
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Boston, USA
Funding	NIH
Participants	277 pregnant women who were Caucasian, < 40 years old and having a parity of no more than two (recruited between March 1994 and October 1995). Exclusions: women who had taken any kind of hormonal medication during the index pregnancy, with a prior diagnosis of diabetes mellitus or thyroid disease, or if the fetus had a known major anomaly.
Dietary assessment	FFQ
Timing	Mailed to women prior to a routine antenatal visit around 27 weeks GA, to reflect women's dietary intake during the second trimester of pregnancy
Baseline comparisons	Women in the study likely to be older, better educated, primiparae, lower BMI and less likely to smoke than pregnant women in the general US population
Comparison	Frequency of dairy food consumption (mean 102.8 times per month; increment 51.7)
Outcomes	Maternal sex hormone binding globulin (SHBG), progesterone – women's blood was taken at 16 and 27 completed weeks GA.
Results	**Maternal SHBG** 16 completed weeks GA: -3.1% change 95% CI -6.6 to 0.6 27 completed weeks GA: -3.3% change 95% CI -6.9 to 0.3 **Maternal progesterone** 16 completed weeks GA: -2.9% change 95% CI -6.0 to 0.4 27 completed weeks GA: -2.2% change 95% CI -5.4 to 1.1
Followup	27 completed weeks GA
Confounding	Adjusted for age, parity, gender of offspring, smoking and GA at blood measurement
Risk of bias	Low to moderate risk of bias: 277 of 402 (68.9%) eligible women were included – 77 refused to participate, 9 were subsequently excluded because the index pregnancy was terminated through a spontaneous or induced abortion, 2 were excluded because of twin birth and 10 were lost to follow-up after the initial meeting.
Relevance	Indirect outcomes for (risk of) breast cancer
Other comments	Study authors postulate that the associations between breast cancer risk and increased birthweight are mediated through endocrine hormones

Reference	**Lamb 2008**
Dietary patterns	Dairy foods: cow's milk products (cream cheese, other cheese, chowders and cream soups, yoghurt, sherbet, sour cream, icecream, cream skim, low-fat or whole milk)
Study type	Part of a longitudinal prospective birth cohort study
Level of evidence	II (aetiology)
Setting	Denver, Colorado, US (part of the Diabetes Autoimmunity Study in the Young (the DAISY))
Funding	National Institutes of Health, Diabetes Endocrine Research Center
Participants	642 newborns at increased risk for type 1 diabetes (based on HLA genotype and family history), enrolled in the study from 1993 to 2004; 27 cases defined as testing positive for islet autoantibodies at two consecutive blood draws and still positive (diabetic) at last follow-up
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	From 1997 to 2004, mothers of infants enrolled in DAISY completed FFQ soon after birth, reflecting diet in the last trimester of pregnancy (but could submit FFQ before child reached one year of age)
Comparison	Monthly servings of cow's milk products
Outcomes	Islet autoimmunity in children (a precursor of type 1 diabetes) at 9 months, 15 months, 2 years and annually thereafter up to the age of 15
Results	**Islet autoimmunity:** aHR (for one standard deviation change in reported consumption of cow's milk products) 1.18 95% CI 0.75 to 1.87 (95.63 mean monthly servings)
Followup	Up to 15 years
Confounding	Size for gestational age, ethnicity, maternal education, household income, exposure to type 1 diabetes or GDM in utero, gender of child, maternal age at birth, total calories of maternal diet
Risk of bias	Moderate risk of bias: subset of DAISY only (later enrolments); and women were not reminded to submit FFQ, leading to possible selection bias; of the 661 FFQs returned, 5 were excluded because incomplete, and 14 for implausible dietary intakes, leaving 642 FFQs for analysis; child's diet not controlled for
Relevance	Likely to be relevant to some Australian women, although women in this study may have been at higher risk of diabetes
Other comments	

Reference	**Latva-Pukkila 2009**
Dietary patterns	Dairy foods: milk, cheese
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Turku, Finland (cohort from Piirainen 2006)
Funding	Social Insurance Institution of Finland, the Sigrid Juselius Foundation and the Academy of Finland
Participants	256 pregnant women
Baseline comparisons	Women with NVP were older and tended to be primiparous compared to those without
Dietary assessment	3 day food diaries
Timing	Three times during pregnancy (mean 14, 24 and 34 weeks gestation)
Comparison	With nausea and vomiting in pregnancy (NVP) versus no NVP; 134 (72%) women reporting experiencing nausea; with 40 (30%) vomiting (9 (4.8%) more than once a day) during the first trimester
Outcomes	Influence of nausea and vomiting in pregnancy on dietary intake; Severity of NVP assessed as having no nausea and vomiting, only nausea, vomiting once a day or vomiting more than once a day, with the primary outcome being presence or absence of nausea
Results	(see below)

	With NVP (n = 134)	**Without NVP (n = 53)**	**p**
Milk products (g), median (IQR) daily	500 (302 to 677)	475 (306 to 787)	0.651
Cheese (g), median (IQR) daily	43 (33 to 66)	56 (31 to 87)	0.139

Followup	To 34 weeks gestation
Confounding	Not reported if any of the analyses were adjusted
Risk of bias	Moderate risk of bias: not clear if analyses were adjusted for potential confounders
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Lovegrove 1994, Lovegrove 1996**
Food type	Dairy foods (dairy food restriction)
Study type	RCT
Level of evidence	II
Setting	Pregnant women attending the antenatal clinic at St Luke's Hospital, Surrey at 30 weeks with atopy and without atopy. Conducted between May 1988 and Nov 1989
Funding	Cow & Gate, Trowbridge, Wilts' (support and provision of Peptijunior)
Participants	38 women at 30 weeks gestation identified as atopic or non-atopic according to an allergy and environmental questionnaire which had previously been validated. Women were classed as atopic if they had an allergy themselves or their partner had an allergy. Atopic women were randomly assigned to the intervention (atopic/restricted diet) or an unrestricted diet, non-atopic women served as an additional control group who followed an unrestricted diet
Dietary assessment	Women allocated to the intervention group were instructed to totally avoid all milk and dairy products from approximately 36 weeks gestation and during breastfeeding. As a milk alternative, they were given a hypoallergenic, complete infant formula, (whey hydrolysate) Peptijunior (Cow & Gate) to consume as required, and their infants were offered this if breastfeeding was supplemented or stopped. Women were also given a 1000 mg calcium supplement. Women were given information on recipes, product sources and food lists and contacted by the investigator to help with compliance. Women were asked to complete a 7 day weighed food inventory to quantify any milk protein inadvertently consumed and to record times of non-compliance. Women in the control group were encouraged to follow standard diets (all women in the control group consumed a minimum of 500 ml cows milk a day). All women were encouraged to practice exclusive breastfeeding for as long as possible, preferable for 6 months. Feeding of solids before 3 months, and provision of cows milk at < 6 months were discouraged
Baseline comparisons	Groups were similar with regard to maternal age, parity, initial allergy incidence and initial period of symptoms. However, 50% of the infants of mothers on the atopic diet (restricted diet) were male, compared with 71% of atopic mothers on an unrestricted diet and 46% of non-atopic mothers
Timing	Children followed up at 6, 12 and 18 months
Comparison	Maternal milk-free diet versus control
Outcomes	Clinically diagnosed atopic eczema in the infants at each time point (clinician blinded to treatment allocation). The mean duration of breast-feeding in the atopic-diet group was slightly longer (12 months), than the other two groups both 9 months, but difference not statistically significant)
Results	**Summary: There was a trend towards a beneficial effect of a maternal milk-free diet during late pregnancy and lactation on the allergy incidence in at-risk infants (infants of atopic mothers).** Women on the atopic diet had a significantly higher ($p<0.01$) polyunsaturated: saturated fat ratio compared with the other two groups. In the 26 children of atopic mothers, RR for eczema in first 18 months was 0.73 95% 0.32 to 1.64 in the maternal milk-free group compared with the control group. Children of atopic mothers who followed an unrestricted diet were more likely to have eczema than non-atopic mothers at the 12 and 18 months follow ups ($p<0.008$ and $p<0.02$, respectively). (Expected result) After excluding 3 infants (all with allergies) of atopic mothers on the atopic diet (restricted) who were fed cows milk formula, there was a significant

	difference between total allergy incidence at 18 months, between atopic mothers on the atopic diet compared with atopic mothers on the unrestricted diet, with a reduced incidence in the atopic diet group ($p < 0.04$). Allergy incidence at 18 months Atopic – unrestricted diet 7/14 (50%) Atopic - restricted diet 4/12 (30%) Non-atopic: 2/13 (15%) The mean duration of breast-feeding in the atopic-diet group was longer (12 (SD 3) months) although not significantly different from the other two groups (9 (SD 4) months and 9 (SD 3) months for the atopic and non-atopic groups respectively). The time of introduction of cows' milk formula, cows' milk and yoghurt was significantly later for the women in atopic diet group compared with the non-atopic group *($P < 0.05$).* The introduction of the other foods was not significantly different between the three groups. In women on the atopic diet, serum antibody levels were reduced (β -Lg-IgG and α-cas-IgG), significantly for β-Lg-IgG, after a period of 7 weeks dietary compliance, and continued to fall if the mother remained on the restricted diet. In the breast milk samples, the atopic diet prevented the appearance of cows' milk protein β -LG antigens. However, the atopic diet did not influence the levels of cows' milk protein specific IgA antibody levels after the first 5 days post-partum. The specific antibody levels against β -LG and α -cas in the three groups showed a significant variation with time. The whey-hydrolysate infant formula, Peptijunior, was used and well tolerated by 37% of the women in the intervention group and the same proportion of infants. None of the infants who routinely ingested Peptijunior had developed allergies by 18 months
Followup	From 30 weeks gestation until 18 months postpartum
Confounding	No adjustment reported
Risk of bias	High risk of bias: More males in the atopic control group, which was not accounted for in the analyses. Males may be more likely to have atopy. Also, analyses were not intention to treat, they excluded 3 infants in the atopic diet group who were given cows milk formula postpartum and who were diagnosed with allergies. 45% participation rate, 6/44 (14%) women dropped out. Atopy figures are different in each publication.
Relevance	Just over a third of participant s in the atopic diet group consumed a milk-free infant formula as an alternative to cows' milk. Unclear if this would be tolerated in Australian women, who might be more likely to consume other dairy-free products i.e. soy or rice milk.
Other comments	

Reference	**Maconochie 2007**
Food groups	Dairy foods
Study type	Case-control study (postal survey sampled from the electoral roll – National Women's Health Study)
Level of evidence	III-3 (aetiology)
Setting	UK general population
Funding	National Lottery Community Fund, Miscarriage Association
Participants	Cases: 603 women aged 18 to 55 years whose most recent pregnancy had ended in first trimester miscarriage (< 13 weeks gestation); Controls: 6116 women aged 18 to 55 years whose most recent pregnancy had progressed beyond 12 weeks
Baseline Comparisons	BMI < 18.5 was significantly associated with odds of miscarriage *Also see Confounding below*
Dietary Assessment	questionnaire
Timing	Diet in the three months prior to conception and the first 12 weeks of pregnancy
Comparison	Daily or most days
Outcomes	First trimester miscarriage
Results	**Dairy products daily or most days** (see table below)
Length of followup	n/a
Confounding	Adjusted for year of conception, maternal age, previous miscarriage and previous live birth; and further adjusted for nausea in the first 12 weeks of pregnancy
Risk of bias	Low risk of bias: 88% of eligible women responding to stage 1 agreed to participate in the second stage of the study; and 71% responded to the stage 2 questionnaire. 1071/7790 records (7508 women) were excluded (mostly due to index pregnancy being conceived prior to 1980), leaving 6719 records (86%) available for analysis
Relevance	L ikely to be relevant to Australian women
Other comments	Women who suffered from nausea in the first 12 weeks of pregnancy were almost 70% less likely to miscarry

Dairy products daily or most days

	Cases	*Controls*	*aOR (95% CI)*	*aOR further adjusted for nausea*
No	58 (10%)	5783 (95%)	1.00	1.00
Yes	528 (90%)	175 (3%)	0.75 (0.56 to 1.01)	**0.67 (0.49 to 0.91)**

Reference	**Mannion 2006**
Food type	Dairy foods
Study type	Case-control (aetiology)
Level of evidence	III-3 (aetiology)
Setting	Antenatal classes in 3 hospitals in Calgary, Alberta May 1997-June 1999
Funding	Dairy farmers of Canada and FRSQ (Fonds de recherché en Sante du Quebec)
Participants	279 (72 restrictors and 207 non-restrictors) healthy pregnant women (singleton pregnancy) who were well educated, mainly non-smoking, within 75% of recommended pregravid weight range. Please see note in other comments section.
Baseline comparisons	*See confounding below*
Dietary Assessment	24 hour recall via telephone with nutritional interviewer repeated 3 or 4 times Note: said “day-to-day variability removed” to estimate nutritional inadequacies compared with dietary reference intakes - not sure how they did this or what it involved (p. 2, last paragraph, second sentence)
Timing	During pregnancy (exact times not given)
Comparison	Analysed data with 2 models; 1=milk intake, 2=nutrient (cups of milk, vitamin D, calcium, riboflavin, protein) 1=milk intake: Non-restriction vs restrictions on milk consumption (restriction =≤250 mL per day) 2=nutrient: separate analyses for intake of vitamin D, calcium, riboflavin and protein
Outcomes	Infant birth weight, crown-heel length and head circumference
Results	Every 250 mL increase in daily milk intake associated with a significant increase in birth weight of 41.2 g (95% CI 13 to 75g). Milk intake not significantly related to infant length or head circumference. Every 1 µg increase in vitamin D intake associated with an increase in infant birth weight of 11 g (95% CI 1.2 to 20.7g). Vitamin D not significantly related to infant length or head circumference. No association with protein, riboflavin or calcium.
Follow-up	Birth
Confounding	Maternal education, height, gestational weight gain, body mass index, gestational age at delivery Smoking not included as very few in sample smoked
Risk of bias	Moderate risk of bias (see other comments)
Relevance	Similar to Australia
Other comments	Small sample size. Of 2091 screened 307 (14.7%) indicated they restricted milk consumption and only 72 of them agreed to participate (24% agreed to participate) Lower use of vitamin/mineral supplements reported by milk restrictors (p 3 in results) More milk restrictors had protein intakes below estimated average requirement (p 3 in results) Restrictors had significantly lower Vitamin D intake (table 2) *Note: not sure exactly how many included in actual analysis - reported included 216 non-restrictors, then in table 2 only 207 non-restrictors, then in table 3 have a total of 279 participants (so if 72 restrictors still included only 197 non-restrictors) and no mention of why others excluded from various stages of analysis*

Reference	**Marcoux 1991**
Food type	Dairy foods (calcium intake from dairy and from supplements)
Study type	Case-control
Level of evidence	III-3
Setting	Primiparous women who delivered in Quebec City or Montreal, Quebec, Canada, between April 1984 and December 1986.
Funding	National Health and Research Development Program of Health and Welfare Canada and the Fonds de la Recherche en Sante du Quebec.
Participants	928 primiparae in total (mainly Caucasian) including 172 women with preeclampsia, 251 women with gestational hypertension, and 505 controls. (all women had no history of high blood pressure before pregnancy and no sign of hypertension during the first 20 weeks of pregnancy)
Dietary assessment	FFQ administered within a few days of birth
Baseline comparisons	Maternal age did not differ among the three groups. The mean level of education and the proportion of smokers were lower among cases than among controls. Cases also had higher baseline blood pressure, a higher BMI and reported being less physically active during leisure time than controls
Timing	Calcium intake in the first 20 weeks of pregnancy
Comparison	Calcium intake was categorized into quartiles on the basis of its distribution among controls. Risk of PE and gestational hypertension then calculated according to quartile of intake
Outcomes	Preeclampsia and gestational hypertension according the quartile of intake of dietary calcium
Results	**Summary: no clear relationship between dietary intake of calcium and risk of PE, but a high dietary calcium intake in the first 20 weeks of pregnancy appears to be associated with a reduced risk of gestational hypertension.** Average calcium intake from dairy products among preeclamptics was lower but not statistically different from that among controls *(p* = 0.22), whereas, for gestational hypertension, the average intake was lower and this was statistically significant *(p* = 0.01). In logistic regression, dietary calcium intake from dairy products showed no consistent relation with preeclampsia (p value for trend not significant, p=0.49). However, for gestational hypertension there was a statistically significant decrease in adjusted odds ratios as dietary calcium intake increased (test for trend, *p* = 0.02) (see table below). In all groups, women who took supplements commenced them on average at 11 weeks gestation. No statistically significant different in the odds of PE or gestational hypertension between those who took calcium supplements and those who didn't.

Table 2. Odds ratios for preeclampsia and gestational hypertension according to quartile* of average daily calcium intake from dairy products and supplements in the first 20 weeks of pregnancy, Quebec, Canada, 1984-1986

	Preeclampsia			Gestational hypertension			
	No.	Odds ratio	95% confidence interval	No.	Odds ratio	95% confidence interval	No. of controls
Calcium intake from dairy products (mg/day)†							
Quartile 1 (lowest)ǂ	42	1.00		82	1.00		126
Quartile 2	55	1.34	(0.83-2.17)	65	0.81	(0.53-1.23)	126
Quartile 3	40	100	(0.60-1.67)	54	0.66	(0.42-1.03)	127
Quartile 4 (highest)	35	0.89	(0.53-1.52)	50	0.60	0.38-0.95)	126
Chi-trend		0.70			2.42		
p value		0.49			0.02		

Calcium supplementation

No ŧ	77	1.00		104	1.00		194
Yes	95	0.77	(0.54-1.09)	147	0.88	(0.65-1.20)	311

* Limits of quartiles 1 – 4 (mg/day) are: >1,089, 1,089-1,576, 1,577-1,958, and > 1,958.
† odds ratios are adjusted by polychotomous logistic regression for body mass index and energy expenditure in leisure-time physical activity
ŧ Reference category

Calcium provided by supplementation accounted only for a small proportion of the average total calcium ingested daily in the first 20 weeks of pregnancy. The odds ratios according to *total calcium intake* were very similar to those estimated for dietary calcium only.

Total calcium intake (diet and supplements)

<u>Adjusted ORs for preeclampsia</u>
Quartile 1: 1.00
Quartile 2: 1.36 (95% CI 0.84-2.20)
Quartile 3: 1.07 (95% CI 0.64-1.77)
Quartile 4: 0.85 (95% CI 0.49-1.46)

<u>Adjusted ORs for gestational hypertension</u>
Quartile 1: 1.00
Quartile 2: 0.83 (95% CI 0.54-1.26)
Quartile 3: 0.67 (95% CI 0.43-1.05)
Quartile 4: 0.57 (95% CI 0.36-0.90)

Followup	Nil
Confounding	ORs adjusted for body mass index and energy expenditure in leisure-time physical activity. The models also considered the impact of age, education level, number of cigarettes smoked daily at the onset of pregnancy, and maximal diastolic blood pressure in the first 20 weeks of pregnancy (however adjustment for these did not change the results)
Risk of bias	Low-moderate risk of bias: adjustment for energy intake was not possible however they adjusted for two factors (BMI and physical activity) known to be associated with energy intake; 96% response rate (controls and cases)
Relevance	Undertaken in a population with a high dietary calcium intake, which may be similar to Australia [Average dietary calcium intake in this study (1575 mg) was higher than the Canadian RDA for pregnant women]. Due to the time frame it was conducted in, the majority of intake from dairy in this study was likely to be from skim milk, which would be similar to Australia.
Other comments	

Reference	**Mitchell 2004**
Dietary patterns	Dairy foods (milk, cheese and yoghurt)
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Waitemata Health or Auckland Healthcare regions, New Zealand
Funding	Health Research Council of New Zealand, Foundation for the Newborn, Child Health Research Foundation
Participants	Mothers of 1138 children born between October 1995 and November 1997 (844 born SGA and 870 born appropriate for GA); only term infants (> 37 weeks); Exclusions: preterm births (< 37 weeks), multiple births and those with congenital anomalies
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered after birth (to cover the periconception period and the last month of pregnancy)
Comparison	0-1.25 v > 1.25-2.0 v > 2.0-3.0 v > 3.0-4.0 v > 4 serves of dairy per day
Outcomes	SGA (≤ 10th centile for GA and gender)
Results	**<u>SGA</u>** (Dairy consumption at time of conception) SGA / AGA / aOR (95% CI) / p value for trend 0-1.25: 108/533 (20.3%) / 92/597 (15.4%) / 1.13 (0.75 to 1.72) > 1.25-2.0: 115/533 (21.6%) / 121/597 (20.3%) / 1.09 (0.73 to 1.62) > 2.0-3.0: 114/533 (21.4%) / 152/597 (25.5%) / 0.81 (0.55 to 1.19) > 3.0-4.0: 70/533 (13.1%) / 103/597 (17.3%) / 0.74 (0.48 to 1.14) > 4: 117/533 (22.0%) / 125/597 (20.9%) / 1 / 0.21 **<u>SGA</u>** (Dairy consumption in last month of pregnancy) SGA / AGA / aOR (95% CI) / p value for trend 0-1.25: 77/536 (14.4%) / 64/596 (10.7%) / 1.21 (0.78 to 1.87) > 1.25-2.0: 81/536 (15.1%) / 85/596 (14.3%) / 1.08 (0.72 to 1.63) > 2.0-3.0: 130/536 (24.3%) / 144/596 (22.7%) / 0.98 (0.69 to 1.40) > 3.0-4.0: 158/536 (29.5%) / 124/596 (20.8%) / 0.76 (0.52 to 1.19) > 4: 102/536 (19.0%) / 175/596 (29.3%) / 1 / 0.38
Followup	NA
Confounding	Adjusted for socio-economic status, ethnicity, maternal height, maternal weight before pregnancy, maternal hypertension and maternal smoking; but folate supplementation was not controlled for (periconception folate was significantly associated with reduced SGA risk).
Risk of bias	Low-moderate risk of bias: Of the 2182 eligible infants, parents of 1714 (78.6%) completed the FFQ; 1138 (67%) of women completed the FFQ; missing items in completed FFQ treated as woman not consuming any dairy.
Relevance	Likely to be relevant to Australian women
Other comments	Only term infants included

Reference	**Miyake 2006**
Food groups	Dairy foods
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Women who became pregnant in November 2001-March 2003 Neyagawa City, Osaka Prefecture and several surrounding municipalities (Osaka Maternal and Child Health Study, Japan)
Funding	Grant-in-Aid for Scientific Research (Government grant)
Participants	865 pregnant Japanese women
Baseline comparisons	*See Confounding below*
Dietary Assessment	Dietary history questionnaire-self administered
Timing	Diet survey for previous month at baseline (period of baseline not stated), EPDS at 2-9 months post partum
Comparison	Daily intake of dairy foods Note: other dietary intakes analysed: meat, fish, eggs, total fat, saturated fatty acids, cholesterol, LA, ALA and AA
Outcomes	Postpartum depression (EPDS with postpartum depression when score ≥ 9)
Results	No significant association between dairy food intake and postpartum depression on adjusted analysis
Length of follow up	2-9 months postpartum
Confounding	Age, gestation, parity, smoking, family structure, occupation, family income, education, changes in diet in previous month, season when baseline data collected, BMI, time of delivery, medical problems in pregnancy, baby's sex, baby's birthweight
Risk of bias	Low risk of bias: data for 865/1002 (86.5%) women available for analysis
Relevance	Australian diets very different to Japanese - much less seafood intake in Australia and more white fish rather than fatty fish
Other comments	Originally 1002 women enrolled only 865 completed (note: depressed persons less likely to participate), low rate of enrolment into study (17.2% of those eligible in Neyagawa)

Reference	**Moore 2004**
Food groups	Dairy foods
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Adelaide, South Australia
Funding	Faculty of Health Sciences, The University of Adelaide; Channel 7 Children's Research Foundation of South Australia, Dairy Research and Development Corporation
Participants	557 pregnant women aged 18 to 41 years; Caucasian, in the first 16 weeks of a singleton pregnancy (without treatment for infertility), not diabetic, fluent in English; giving birth between October 1998 and April 2000
Baseline comparisons	*See Confounding below*
Dietary Assessment	FFQ
Timing	Women were interviewed before 16 weeks gestation and between 30 and 34 weeks
Comparison	Amount of dairy protein consumed
Outcomes	Birthweight, ponderal index
Results	**Each isoenergetic 1% increase in dairy protein consumption was associated with a 25 g increase in birthweight (p = 0.02) an 0.12 kg/m3 increase in ponderal index (p = 0.05)**
Length of follow up	To birth
Confounding	Maternal height, prepregnancy weight, primiparity, alcohol consumption and use of marijuana or cocaine, energy intake
Risk of bias	Low risk of bias: 65% of women invited agreed to participate (women declining were slightly younger); 557 of these 605 (92%) women completed the study (most common reason for withdrawal was miscarriage or termination of pregnancy); sensitivity analysis showed similar results for complete and incomplete data;
Relevance	Study conducted in Australia
Other comments	

Reference	**Nwaru 2010**
Food type	Dairy foods (milks, cheese, yoghurt, sour milk, curd, creams and icecreams)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Tampere, Finland
Funding	Academy of Finland, Finnish Pediatric Research Foundation, the Juho Vainio Foundation, the Yrjo Jahnsson Foundation, Turku, Oulu and Tampere University Hospitals, JDRF, Novo Nordisk Foundation, EU Biomed 2 Program
Participants	931 mother-infant pairs (children with human leukocyte antigen-conferred susceptibility to type 1 diabetes) participating in the Finnish type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study between September 1996 and October 1997
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ given to women after birth, for return at the three month visit (FFQ intended to cover maternal diet during pregnancy and lactation)
Comparison	Amount of dairy intake
Outcomes	Allergic sensitisation in offspring by 5 years: food allergens (egg, cow's milk, fish, wheat); inhalant allergens (house dust mite, cat, timothy grass, birch)
Results	**<u>Total milk and milk products</u>** ***Food allergens*** — OR 0.81 95% CI 0.56 to 1.19; aOR 0.88 95% CI 0.57 to 1.35 ***Inhalant allergens*** — OR 0.76 95% CI 0.54 to 1.06; aOR 0.76 95% CI 0.54 to 1.06 - **<u>Milk</u>** ***Food allergens*** — OR 0.92 95% CI 0.75 to 1.14; aOR 0.95 95% CI 0.76 to 1.20 ***Inhalant allergens*** — OR 0.87 95% CI 0.73 to 1.04; aOR 0.91 95% CI 0.75 to 1.12 - **<u>Fermented milk products (yoghurt, sour milk and curd)</u>** ***Food allergens*** — OR 0.97 95% CI 0.83 to 1.15; aOR 1.00 95% CI 0.83 to 1.21 ***Inhalant allergens*** — OR 1.10 95% CI 0.94 to 1.28; aOR 1.04 95% CI 0.88 to 1.23 - **<u>Cheese</u>** ***Food allergens*** — OR 0.96 95% CI 0.78 to 1.18; aOR 0.96 95% CI 0.77 to 1.19 ***Inhalant allergens*** — OR 1.09 95% CI 0.91 to 1.31; aOR 1.05 95% CI 0.86 to 1.29
Followup	To 5 years
Confounding	Adjusted for energy intake, place of birth, season of birth, sex of the child, number of siblings, gestational age at birth, parental asthma, parental allergic rhinitis, maternal age at birth, maternal smoking during pregnancy, maternal education
Risk of bias	Low risk of bias: data available for 931/1175 (79.2%) children recruited – 108 did not participate in survey, a further 49 did not have IgE measurements, a further 87 had no FFQ or an incomplete FFQ
Relevance	Likely to be relevant to Australian women
Other comments	28% of women took vitamin D supplements, 73% took iron supplements; HLA genotype not likely to have any impact on the development of allergic diseases.

Reference	**Oken 2007**
Food type	Dairy foods (milk)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Obstetric offices in Massachusetts, USA
Funding	NIH, Robert H. Ebert Fellowship, March of Dimes Birth Defects Foundation,
Participants	1718 women in Project Viva recruited from 1999 to 2002
Baseline comparisons	Study participants more likely to be white, and to be college graduates than non-participants *See confounding below*
Dietary assessment	FFQ
Timing	FFQ at study enrolment (median 10.4 weeks gestation) to cover diet since last menstrual period
Comparison	Number of serves of milk/day
Outcomes	Pre-eclampsia, gestational hypertension
Results	**Pre-eclampsia** **aOR 1.25 95% CI 1.00 to 1.57** (1.3 [SD 1.4] serves of milk/day for women with pre-eclampsia v 1.2 [1.0] for women with normal blood pressure) **Gestational hypertension** aOR 0.93 95% CI 0.76 to 1.12 (1.1 [SD 1.0] serves of milk/day for women with gestational hypertension v 1.2 [1.0] for women with normal blood pressure)
Followup	To birth
Confounding	Energy adjusted and also adjusted for maternal age, prepregnancy BMI, first trimester systolic blood pressure, ethnicity, education, parity
Risk of bias	Low risk of bias: Of the 2128 live births, 410 were excluded (45 women with unavailable medical records, 339 incomplete dietary questionnaire, 24 women with pre-existing chronic hypertension who did not develop pre-eclampsia, 2 women with missing covariate information) leaving 1718 participants (81%) available for analysis
Relevance	Likely to be relevant to Australian women
Other comments	92% of women took supplements (multivitamins) in the first trimester of pregnancy; Mean calcium intake in the study population was high (> 900 mg/day) and intakes of vitamins D, E, C and folate were also relatively high

Reference	**Olafsdottir 2006**
Dietary patterns	Dairy foods: drinking more milk in late pregnancy
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Iceland
Funding	Icelandic Research Council, University of Iceland Research Fund
Participants	495 randomly selected healthy pregnant women attending a routine first antenatal visit
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	At 11-15 weeks gestation; and 34-37 weeks gestation (to reflect food intake for the last 3 months)
Comparison	Drinking more milk versus not drinking more milk than usual (in early pregnancy)
Outcomes	Gestational weight gain (optimal weight gain defined as 12.1 to 18.0 kg for women with normal pre-pregnancy weight; and 7.1 to 12.0 kg for overweight women)
Results	20% of the 301 women with BMI < 25 at first visit had excessive gestational weight gain; 55% of the 194 women with BMI ≥ 25 at first visit had excessive gestational weight gain **Drinking more milk in early pregnancy** At least optimal weight gain: **aOR 3.10 95% 1.57 to 6.13** Excessive weight gain: **aOR 1.82 95% CI 1.08 to 3.06** Women who consumed more milk had an intake of about 700 g/day (compared with 500 g/day for other women); women with excessive gestational weight gain drank about 200 g/day more (compared with only 100 g/day for other women who increased their milk intake)
Followup	To birth
Confounding	Adjusted for maternal age, gestational length and smoking
Risk of bias	Low to moderate risk of bias: of the 549 women enrolled, 495 (90%) completed the study; 54 women were excluded (17 miscarriage/stillbirths, 5 sets of twins or triplets, 17 preterm births, 15 missing data); 89 women did not complete FFQ at the second timepoint and so only 406 women could be included for measures relating to late pregnancy; limited number of confounders used in adjusted analyses
Relevance	Likely to be reasonably relevant to Australian women
Other comments	

Reference	Olsen 2007
Food type	Dairy foods (milk intake)
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Women participating in the Danish National Birth Cohort, 1996-2002
Funding	The March of Dimes Birth Defects Foundation, Danish National Research Foundation, Pharmacy Foundation, Egmont Foundation, Augustinus Foundation, the Health Foundation, the European Union (QLK1-2000-00083), The Danish Medical Research Foundation, and the Heart Foundation
Participants	50,117 mother-infant pairs (singleton and term births only). [Original cohort was 70187, women with abnormally low or high energy intakes were also excluded]
Dietary assessment	FFQ: milk consumption was recorded in 8 questions in the FFQ; 2 of these referred to consumption of yoghurt, in portions per day (including the percentage of fat) and 6 to the consumption of milk (whole milk, 1.5% milk, 0.5% milk, skim milk, churn buttermilk, and chocolate milk), in glasses/d. Milk and yogurt variables were aggregated to obtain frequency measures; according to a Nordic standard, one glass of milk estimated to be 200 mL and one portion of yoghurt to be 150 mL.
Baseline comparisons	*See confounding below*
Timing	Mid pregnancy (~25 weeks) dietary assessment, referring to intake in the previous 4 weeks
Comparison	Amount of milk intake
Outcomes	Birthweight, birth length, head circumference, abdominal circumference, and placental weight
Results	**Summary: increasing maternal milk intake during mid-pregnancy was associated with a reduced risk of SGA, an increased risk of LGA, and an increased mean birth weight, abdominal circumference, placental weight, birth length, and head circumference adjusted for gestational age at birth.** **Gestational weight gain was significantly associated with increased milk consumption** **Birthweight** Increasing birthweight increment was seen with increasing intake of milk (adjusted p value for trend <0.001), culminating in a ~100 g difference in birthweight between those who consumed > 5 glasses compared with no milk (see table 2 below). Birthweight showed no association with fat from dairy products, but was associated with protein from dairy. Birthweight was consistent across quintiles of non-dairy protein, suggesting the association between BW and dairy protein is unlikely to reflect a general protein effect.

Table 2

Unadjusted and adjusted differences in mean birth weight increment according to frequency of milk consumption in the Danish National Birth Cohort (n = 50 117)[1]

Milk intake (glasses/d)	Difference in birth weight, unadjusted	95% CI	p[2]	Difference in birth weight, adjusted[3]	95% CI	p[2]
	g			*g*		
0 (*n*=709)	Referent	–	–	Referent	–	–
>0-1 (*n*=6503)	44.8	(7.0, 82.6)	0.020	48.2	(15.5, 80.9)	0.004
>1-2 (*n*=7943)	66.2	(28.8, 103.7)	0.001	57.2	(24.7,89.6)	0.001
>2-3 (*n*=12721)	79.0	(42.1, 115.8)	<0.001	66.3	(34.3, 98.3)	<0.001
>3-4 (*n*=9181)	89.7	(52.5, 127.0)	<0.001	78.5	(46.0, 110.9)	<0.001
>4-5 (*n*=5550)	103.0	(64.8, 141.1)	<0.001	91.0	(57.8, 124.1)	<0.001
>5-6 (*n*=3789)	105.2	(66.1, 144.3)	<0.001	100.5	(66.4, 134.6)	<0.001
>6 (*n*=3721)	105.2	(66.2, 144.5)	<0.001	107.8	(73.5, 142.5)	<0.001

P for trend[4]	<0.001	<0.001

[1] The group of women who consumed zero glasses of milk was used as reference for each pairwise comparison.
[2] Student's *t* test
[3] Adjusted for gestational age; infant's sex; mother's parity, are, height, prepregnant BMI, gestational-weight gain, smoking status, and total energy intake; father's height; and family's socioeconomic status.
[4] Student's *t* test for regression coefficient (continuous variable).

SGA and LGA

Increasing milk intake was associated with a decreased risk of SGA and an increased risk of LGA. Compared with women who reported never consuming milk, women consuming >6 glasses/d had a 49% (95% CI: 35%, 61%) lower adjusted odds of having an SGA infant. Adjusting for confounders did not change this association.

The odds of having a large-for-gestational age (LGA) infant increased with increasing milk intake ($P < 0.001$), and this association was stronger after adjustment for confounding. Compared with women who reported no milk consumption, women who reported consuming >6 glasses of milk/d had a 59% (95% CI: 16%, 116%) higher odds of having an LGA infant

Table 3
Unadjusted and adjusted odds ratio for the risk of small-for-gestational (SGA) birth according to frequency of milk intake in the Danish National Birth Cohort (*n*= 50 117)[1]

Milk intake (glasses/d)	No. of cases *n* (%)	Unadjusted odds ratios (95% CI)	Adjusted odds ratios (95% CI)[2]
SGA 10th percentile			
0(*n*=709)	104 (14.7)	1.00	1.00
>0-1 (*n*=6503)	700 (10.7)	0.70 (0.56; 0.88)	0.67 (0.54; 0.85)
>1-2 (*n*=7944)	766 (9.6)	0.62 (0.50; 0.77)	0.62 (0.49; 0.78)
>2-3 (*n*=12721)	1204 (9.5)	0.61 (0.49; 0.76)	0.62 (0.49; 0.77)
>3-4 (*n*=9181)	832 (9.1)	0.58 (0.47; 0.72)	0.59 (0.47; 0.74)
>4-5 (*n*=5551)	469 (8.5)	0.54 (0.43; 0.68)	0.53 (0.42; 0.67)
>5-6 (*n*=3789)	313 (8.3)	0.52 (0.41; 0.67)	0.51 (0.40; 0.65)
>6 (*n*=3721)	324 (8.7)	0.56 (0.44; 0.70)	0.51 (0.39; 0.65)
P for trend[3]		<0.001	<0.001
LGA, 90th percentile			
0 (*n*=709)	53 (7.5)	1.00	1.00
>0-1 (*n*= 6503)	592 (9.1)	1.24 (0.93; 1.66)	1.37 (1.01; 1.84
>1-2 (*n*=7944)	670 (8.4)	1.14 (0.85; 1.52)	1.24 (0.92; 1.68)
>2-3 (*n*=12721)	1234 (9.7)	1.33 (1.00; 1.77)	1.42 (1.06; 1.91)
>3-4 (*n*=9181)	939 (10.2)	1.41 (1.06; 1.88)	1.54 (1.15; 2.07)
>4-5 (*n*=5551)	573 (10.3)	1.42 (1.06; 1.91)	1.54 (1.14; 2.08)
>5-6 (*n*=3789)	390 (10.3)	1.42 (1.05; 1.91)	1.4 (1.13; 2.10)
>6 (*n*=3721)	392 (10.5)	1.46 (1.08; 1.96)	1.59 (1.16; 2.16)
P for trend[3]		<0.001	<0.001

[1] The group of women who consumed zero glasses of milk was used as reference for each pairwise comparison.
[2] Adjusted for mother's parity, age, height, prepregnant BMI, gestational weight gain, smoking status, and

<table>
<tr><td></td><td>total energy intake; Father’s height; and family’s socioeconomic status.
[3] Chi-square test for regression coefficient (continuous variable).

Other anthropometric measures
Mean abdominal circumference, placental weight, head circumference, and birth length all showed increases across the whole range of milk intake (P for trend<0.001). After adjustment for confounding, the total increments were 0.52 cm (0.35– 0.69 cm), 26.4 g (15.1–37.7 g), 0.13 cm (0.04–0.25 cm), and 0.31 cm (0.15– 0.46 cm) for the 4 measures, respectively

Gestational weight gain (g/wk)
Milk consumption (glasses/day (median))
<table>
<tr><th></th><th>0 (0)</th><th>> 0 to 1 (0.5)</th><th>> 1 to 2 (1.4)</th><th>>2 to 3 (2.7)</th><th>>3 to 4 (3.4)</th><th>> 4 to 5 (4.7)</th><th>> 5 to 6 (5.4)</th><th>> 6 (7.2)</th><th></th></tr>
<tr><td>N</td><td>709</td><td>6503</td><td>7943</td><td>12721</td><td>9181</td><td>5550</td><td>3789</td><td>3721</td><td></td></tr>
<tr><td>GWG (g/week)</td><td>431 [263]</td><td>455 [231]</td><td>467 [222]</td><td>463 [291]</td><td>473 [218]</td><td>480 [225]</td><td>476 [232]</td><td>484 [235]</td><td>p <0.0001</td></tr>
</table></td></tr>
<tr><td>Followup</td><td>During pregnancy until birth</td></tr>
<tr><td>Confounding</td><td>Findings were adjusted for mother’s parity, age, height, prepregnant BMI, gestational weight gain, smoking status, and total energy intake; father’s height; and family’s socioeconomic status, infant sex</td></tr>
<tr><td>Risk of bias</td><td>Low risk of bias: Large population based cohort. Prospective ascertainment of outcomes</td></tr>
<tr><td>Relevance</td><td>Mean reported consumption of milk was 3.1 (SD 2.0) glasses/d, therefore this could be classed as a high dairy population, which may be similar to Australia (however perhaps higher intake of dairy products such as buttermilk).

Hard to make recommendations in relation to LGA – as even 0-1 glasses/day was associated with an increased risk (borderline significance), although 1-2 glasses/d was not significant.</td></tr>
<tr><td>Other comments</td><td>Milk intake includes skim and full fat milk, as well as buttermilk and yoghurt</td></tr>
</table>

Reference	**Petridou 2005**
Food type	Milk and dairy products
Study type	Case-control study
Level of evidence	III-3
Setting	Greece
Funding	The Childhood Hematology-Oncology Group: Athens University Medical School, Aristotle University of Thessaloniki, University Hospital of Heraklion
Participants	Cases: 131 children with acute lymphoblastic leukemia, aged 12 to 59 months, gender and age matched to Controls: 131 children hospitalised for minor conditions between 1999 and 2003
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During index pregnancy
Comparison	Quintiles of milk/dairy products – median Q1; 39 g/day: median Q5 127 g/day
Outcomes	Acute lymphoblastic leukemia (ALL)
Results	<table><tr><th></th><th>Median g/day</th><th>Cases</th><th>Controls</th><th>p for trend</th></tr><tr><td>Q1:</td><td>39</td><td>31</td><td>21</td><td></td></tr><tr><td>Q2:</td><td>60</td><td>24</td><td>27</td><td></td></tr><tr><td>Q3:</td><td>76</td><td>25</td><td>25</td><td></td></tr><tr><td>Q4:</td><td>93</td><td>20</td><td>35</td><td></td></tr><tr><td>Q5:</td><td>127</td><td>31</td><td>23</td><td>0.49</td></tr></table> Logistic regression: one quintile more of milk/dairy products: aOR 0.82 95% CI 0.66 to 1.02
Followup	NA
Confounding	Adjusted for: total energy intake (but not mutually among food groups); matching variables; maternal age at birth; birthweight; maternal smoking during pregnancy; maternal years of schooling, maternal occupation
Risk of bias	Moderate: moderate risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy some time previously; Cases: 171 children with ALL were identified; 21 had missing data, consent was not given in 9 cases and 10 were unable to be matched, leaving 131 (77%) of cases available
Relevance	Diets of Greek women may differ from current diets of Australian women
Other comments	

Reference	**Petridou 1998a**
Food type	Dairy foods: feta cheese, kaseri cheese, other cheese, whole milk, skimmed milk, full-fat yoghurt, reduced-fat yoghurt, milk pudding, rice milk pudding, ice-cream, cheese pie (0.5), pizza (0.5).
Study type	Case-control study
Level of evidence	III-3
Setting	Greater Athens area, Greece
Funding	Greek Ministry of Health and Welfare, and Foundation for Research in Childhood 'S. Doxiadis'
Participants	Cases: 109 children with cerebral palsy (CP), born between 1984 and 1988 (estimated to be two-thirds of the children with CP born during this period) Controls (1): 155 neighbouring children of similar sex and age (± 12 months) Controls (2): 99 healthy siblings of similar sex and age (± 12 months) of the first neurological patient seen by the attending physician after a visit by the CP patient
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During pregnancy
Comparison	≤ 1 versus 2 versus > 2 serves of dairy foods per day; regression analysis: risk of cerebral palsy with change in consumption by one unit (= consumption of dairy once per day)
Outcomes	Cerebral palsy
Results	≤ 1 serve of dairy foods per day: 8/91 (8.8%) cases v 13/246 (5.3%) controls 2 serves of dairy foods per day: 25/91 (27.5%) cases v 68/246 (27.6%) controls > 2 serves of dairy foods per day: 58/91 (63.7%) cases v 165/246 (67.1%) Regression analysis for each unit of consumption of dairy foods once per week: aOR 1.12 95% CI 0.75 to 1.69 aOR 1.12 95% CI 0.66 to 1.88 (additionally adjusted for all food groups)
Followup	8 years
Confounding	Age and sex of child, maternal age at birth, maternal age at menarche, maternal chronic disease, previous spontaneous abortions, persistent vomiting during index pregnancy, multiple pregnancy, number of obstetric visits; timing of membrane rupture in index birth, use of general anaesthesia in the index birth, mode of birth, abnormal placenta, infant head circumference at birth, congenital malformation, place of index birth, use of supplementary iron during index pregnancy, physical exercise during index pregnancy, painless childbirth classes. The following were not included in the model: - Smoking or consumption of coffee or alcohol during pregnancy (stated to be "unrelated to CP and had no confounding influence"); - Gestational age, birthweight and maternal weight gain (stated to be "strong predictors of CP, but were not included in the model, since they are probably intermediate stages in a possible link between diet and CP (mediators) rather than genuine confounders"
Risk of bias	Moderate-high: High risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy 8 years previously; Cases: 109 children with CP were identified; for 6 children either collaboration with their guardian or a diagnosis of CP was not confirmed; and reliable maternal dietary intakes were not available for 12 women, leaving 91 cases available for analysis. Controls: 278 mother-child pairs were approached; 16 refused to participate; matching controls were not available in 8 instances, and reliable maternal dietary intakes were not available for 8 women, leaving 246 controls available for analysis.
Relevance	Diets of Greek women in 1998 may differ from current diets of Australian women
Other comments	

<table>
<tr><td>Reference</td><td>Richardson 1995</td></tr>
<tr><td>Food type</td><td>Milk intake (and milk + supplements)</td></tr>
<tr><td>Study type</td><td>Prospective cohort study</td></tr>
<tr><td>Level of evidence</td><td>II (aetiology)</td></tr>
<tr><td>Setting</td><td>Pregnant women in the Child Health and Development Study population, California, Berkeley, 1959-1966</td></tr>
<tr><td>Funding</td><td>College of Veterinary Medicine, Texas A&M University, College Station, TX</td></tr>
<tr><td>Participants</td><td>9,291 pregnant women (7,104 white women and 2,187 black women) (original cohort was 12,606) who met the following criteria:
delivered a single live or stillborn infant at a gestational age of > 140 days
not diagnosed with pre-existing hypertension
had provided information on milk intake and the presence or absence of
preeclampsia in the immediately preceding pregnancy
had completed an in-depth interview about health history and sociodemographic information</td></tr>
<tr><td>Dietary assessment</td><td>Unclear – most likely a FFQ, states info was obtained from a ‘detailed questionnaire’.</td></tr>
<tr><td>Baseline comparisons</td><td>See confounding</td></tr>
<tr><td>Timing</td><td>Unclear of timing of detailed interview, but looks like it was spread across each trimester (i.e. some women interview in first, some in second and some in third trimester).</td></tr>
<tr><td>Comparison</td><td>Pre-eclampsia incidence based on no. of glasses of milk consumed per day stratified by use of calcium supplements, ethnicity and parity.

Reference category – 2 glasses of milk per day</td></tr>
<tr><td>Outcomes</td><td>Pre-eclampsia</td></tr>
<tr><td>Results</td><td>Summary: both low (<1 glass of milk/day) and high (≥3 glasses per day) dairy food intake (whole milk) was associated with pre-eclampsia.

75% of women took supplements containing some amount of calcium, however most (98.5 percent) of the supplements taken contained 200-250 mg of elemental calcium, which would contribute less than the amount of calcium in one glass of milk to a woman's daily calcium intake.

Found a U-shaped distribution in relation to levels of milk intake, with and without supplement intake, however women who drank two glasses of milk per day had the lowest risk.

Results: total cohort, risk of pre-eclampsia
<table>
<tr><td></td><td>Adjusted RR (95% CI)</td></tr>
<tr><td>< 1 glass/d</td><td>1.86 (1.21-2.85)</td></tr>
<tr><td>1 glass/d</td><td>1.21 (0.74-1.98)</td></tr>
<tr><td>2 glasses/d</td><td>1.00 (ref)</td></tr>
<tr><td>3 glasses/d</td><td>2.01 (1.20-3.38)</td></tr>
<tr><td>≥ 4 glasses/d</td><td>1.82 (1.09-3.04).</td></tr>
</table>
The U shaped pattern was observed for black and white women, however, among white women, one glass per day is not associated with increased risk as it appears to be for black women.

When subgrouped based on use of supplements, the same relationship was seen for women who took supplements. Amongst women who did not take supplements (25% of sample) three glasses of milk per day appeared protective (adj RR 0.26 CI 0.03-2.24), and there was a lower risk of PE associated with <1 glass per day (adj RR 1.55 CI 0.60-4.01), than amongst women who took supplements.

When the analyses were restricted to women having their first pregnancies (e.g. excluding previous PE and previous abortion) and to women interview</td></tr>
</table>

	in the first and second trimester only (e.g. before the onset of PE) the results were essentially unchanged.
Followup	During pregnancy until birth
Confounding	Confounders considered in the analysis included PE risk factors such as: preeclampsia in the previous pregnancy; prepregnancy body mass index; number of previous pregnancies; abortion, which was defined as fetal death with gestation of less than 20 weeks; therapeutic or induced abortion (including missed abortions); excess weight gain, which was defined as weight gain of more than 30 pounds during pregnancy; as well as ethnicity, use of supplements, smoking status, educational level, marital status, year of interview, trimester of interview, or number of abortions.
Risk of bias	Low-moderate risk of bias: No adjustment for other dietary factors, including energy intake.
Relevance	This study was undertaken in the early 1960s when whole milk was the predominant form of milk being drunk by women in the US – which is likely to be different to contemporary Australian women. The biological plausibility for the association between high milk intake and pre-eclampsia is unclear, it may be confounded by other dietary factors which were not accounted for, such as fat (given the majority of dairy intake was whole milk not skim).
Other comments	

Reference	**Saito 2010**
Food type	Dairy foods (also meat, eggs, fish)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Neyagawa City, Japan
Funding	Ministry of Education, Culture, Sports, Science and Technology and Health and Labour Sciences, Ministry of Health, Labour and Welfare, Japan
Participants	771 mother-child pairs recruited from November 2001 to March 2003 at any stage of pregnancy – mean GA 18 weeks (part of the Osaka Maternal and Child Health Study)
Baseline comparisons	*See confounding below*
Dietary assessment	Diet history questionnaire (DHQ)
Timing	DHQ to assess dietary habits during the preceding month
Comparison	Quartiles of dairy food consumption
Outcomes	Suspected atopic eczema
Results	**Suspected atopic eczema** (see table below) p value for trend (unadjusted): 0.33 p value for trend (adjusted): 0.13
Followup	3-4 months
Confounding	Adjusted for maternal age, gestation at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, mite allergen level from maternal bedclothes, vacuuming living room, mould in kitchen, changes in maternal diet in previous month, season when baseline data collected, baby's older siblings, baby's sex, baby's birthweight, breastfeeding and bathing or showering infant
Risk of bias	Low risk of bias: Of 1002 eligible women, a final sample of 771 (77%) was available for analysis
Relevance	Fish intake in Japan likely to be higher than in Australia
Other comments	

Suspected atopic eczema

	n/N	*OR (95% CI)*	*aOR (95% CI)*
Q1 (52.7 g/day)	13/192	1.00	1.00
Q2 (126.0 g/day)	16/193	1.24 (0.58 to 2.71)	1.39 (0.62 to 3.20)
Q3 (191.0 g/day)	18/193	1.42 (0.68 to 3.04)	1.63 (0.73 to 3.72)
Q4 (288.3 g/day)	18/193	1.42 (0.68 to 3.04	1.84 (0.82 to 4.27)

p value for trend (unadjusted): 0.33
p value for trend (adjusted): 0.13

Reference	**Sausenthaler 2007**
Food groups	Dairy foods (also fish, eggs, nuts and seeds, fats and oils, vegetables, fruit)
Study type	Prospective cohort study: from the LISA birth cohort
Level of evidence	II (aetiology)
Setting	4 German cities (Munich, Leipzig, Wesel, Bad Honnef)
Funding	Federal Ministry for Education, Science, Research and Technology, Germany
Participants	3097 newborns recruited
Baseline comparisons	*See Confounding below*
Dietary assessment	FFQ
Timing	Maternal diet during the last 4 weeks of pregnancy (obtained shortly after birth, median 3 days)
Variable	Low intake group as reference group compared with high intake group: • Milk high intake = "more than sometimes" • Yoghurt high intake = "more than sometimes" • Cheese high intake = ≥ 4 times/week • Cream high intake = 3-4 times/week
Outcomes	Allergic sensitisation, eczema at 2 yrs
Results	(see table below)
Length of followup	2 years
Confounding	Crude and adjusted results reported (adjusted for study area, sex, maternal age, maternal smoking, level of parental education, exclusive breastfeeding ≥ 4 months, parental history of atopic diseases, season of birth and all dietary variables
Risk of bias	Low risk of bias: Two year data available for 2641/3097 children (85%): 433 lost to follow-up, 9 excluded due to chronic disease, 14 missing maternal FFQ
Relevance	Likely to be reasonably similar to dietary intakes of Australian women in Australia
Other comments	

Results:

	Doctor-diagnosed eczema	***any allergen sensitisation***	***food allergens***	***inhalant allergens***
DAIRY FOODS		***Adjusted OR (95% CI)***		
Milk	1.04 (0.80, 1.34)	0.93 (0.67, 1.28)	0.95 (0.66, 1.37)	0.95 (0.58, 1.57)
Yoghurt	0.99 (0.78, 1.27)	0.81 (0.59, 1.10)	0.89 (0.62, 1.27)	0.69 (0.43, 1.12)
Cheese	0.87 (0.68, 1.13)	0.99 (0.72, 1.36)	0.97 (0.68, 1.39)	0.93 (0.57,1.53)
Cream	1.02 (0.78, 1.34)	1.20 (0.86, 1.67)	1.26 (0.87, 1.83)	1.26 (0.76, 2.08)

Reference	**Stuebe 2009**
Dietary patterns	Dairy foods
Study type	Prospective cohort study (Project Viva)
Level of evidence	II (aetiology)
Setting	8 urban and suburban obstetric offices of a multispecialty group practice in eastern Massachusetts, USA
Funding	US NIH, Harvard Medical School, Harvard Pilgrim Health Care Foundation
Participants	1338 women giving birth to a live singleton infant, < 22 weeks gestation at study entry; 379 (27%) were overweight (BMI ≥ 26); 703 (51%) experienced excessive weight gain Exclusions: not fluent in English
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Administered in first and second trimesters of pregnancy
Comparison	Total dairy food consumption - serves per day
Outcomes	Excessive gestational weight gain (IOM 1990)
Results	see below
Followup	To birth
Confounding	Adjusted for pre-pregnancy BMI, maternal age, race/ethnicity, smoking status, gestational age at birth, nausea in first trimester in pregnancy
Risk of bias	Low risk of bias: Of 2083 eligible women, 1388 (67%) of women had data available for analysis (31 had missing information on pre-pregnancy BMI and gestational weight gain; 226 had missing covariate information and 438 had missing data on either first or second-trimester diet and mid-pregnancy physical activity); included women were less likely to be African-American or Hispanic, to be younger, multiparous and obese
Relevance	Likely to be relevant to Australian women
Other comments	

Results:

Excessive gestation weight gain: dairy food consumption

	Serves per day, mean		aOR (95% CI)
	Inadequate/adequate GWG	**Excessive GWG**	
Total dairy food	2.90 [SD1.52]	3.04 [SD1.49]	**1.08 (1.00 to 1.17)**
Low fat dairy food	1.49 [SD1.31]	1.59 [1.34]	1.08 (0.98 to 1.18)
Whole milk	1.41 [SD1.01]	1.46 [0.97]	1.06 (0.94 to 1.20)

Dairy food, per serving per day: multivariate logistic regression model:
aOR 1.09 95% CI 1.01 to 1.19
0.23 kg 95% CI 0.05 to 0.41

Reference	**Tennekoon 1996**
Food type	Dairy foods (powdered skim milk)
Study type	RCT
Level of evidence	II
Setting	Women recruited from postpartum wards of the De Soysa Hospital for Women, Sri Lanka
Funding	Unclear, no information
Participants	60 'normal, healthy lactating (exclusively breastfeeding) women matched for parity and BMI, and with previous experience of lactational amenorrhea.' Women were aged between 20-35, breastfeeding a second or third baby, had a BMI between 18-27, and had uncomplicated pregnancies. Women who were planning to use hormonal contraceptives or who had introduced other feeds to the infant by 4 weeks postpartum were excluded. All women were not in paid employment for the duration of the study
Dietary assessment	Supplemented women were given ~50g powdered skim milk/d (49.8% carbohydrates, 37.6% protein, 0.8% fatm 7.8% mineral salts, and 3.8% moisture). 100g provided 1523 kjm 600 microgram vitamin A and 10 micrograms of vitamin D. States that 24 hr home dietary records were obtained at 4 weekly intervals to determine if supplemented women consumed skim milk in addition to their normal diet. But no attempt to calculated energy intake was made because accurate information could not be obtained about the quantities of food consumed.
Baseline comparisons	No significant differences between groups in terms of maternal age, BMI, infant birth weight, frequency of breast feeds (day and night) or prolactin values. *See also confounding*
Timing	Women commenced the study at 4 weeks postpartum and continued supplementation until they had two to three regular menstrual periods
Comparison	Time to resumption of regular menstruation and ovulation in supplemented and control groups. Women were also categorised according to whether they had resumed regular menstruation and ovulation before 24 wks postpartum and after 24 weeks postpartum
Outcomes	Resumption of regular menstruation and ovulation. Urinary pregnanediol glucuronide concentration ≥ 0.1 mmol/mol creatinine during the luteal phase was considered to be evidence of ovulation
Results	No significant difference between groups in the number of women with regular menstruation before and after 24 weeks, and the number of women with first regular bleeds that were ovulatory either before or after 24 weeks (Table 2 below)

Table 2
Characteristics of the first menstrual bleed in 20 matched pairs of lactating women in which the supplemented group received skim milk

	Supplemented group	Control group
	n *(%)*	
Regular menstruation before 24 wk postpartum	17 (57)	15 (50)
Regular menstruation after 24 wk postpartum	13 (43)	15 (50)
Ovulatory first menstrual bleed	17 (57)	12 (40)
Ovulatory first menstrual bleed before 24 wk postpartum	9 (30)	5 (17)
Ovulatory first menstrual bleed after 24 wk postpartum	8 (27)	7 (23)
Not ovulated before completing the study	0	5 (17)

The number of women giving other (e.g. formula) feeds at each follow up was significantly lower in the supplemented group compared with control at 8 (p<0.02), 12 (p<0.01), 16 (P<0.05) and 20 weeks postpartum (p<0.02).

	Women in the supplemented group introduced other feeds ~5 weeks later than the control group (p<0.05). Supplemented women had a higher number of total breast feeds at 48 wk postpartum (p<0.05), high number of total breastfeeds when expressed as a percentage of all feeds at 12 wks (P<0.01), 24 (P<0.02) and 32 weeks (P<0.05) postpartum, and a lower number of other feeds at 12 (p<0.01) and 24 (P<0.02) postpartum, compared with control women. When the data was categorised according to resumption of regular menstruation or ovulation, the total number of breast feeds as a percentage of all feeds was higher in the supplemented group at -3, -2, -1, 0, 1, and 2 months of menstruation (p values range from <0.05 to <0.01), and at -1 and 1 month of ovulation (both p <0.05). **Conclusion: maternal nutritional supplementation does not appear to affect the contraceptive benefit of lactation when the frequency of breastfeeding is not compromised, but apparently lengthens the duration of nearly full breast-feeding**
Followup	4 weeks postpartum until women had two to three regular menstrual periods (typically up to one year postpartum)
Confounding	No adjustment for total energy intake; multiple linear regression used to examine the effects of previous experience of lactational amenorrhoea, frequency of breastfeeds per 24 hour at enrolment, time postpartum of introduction of solid foods and maternal BMI at enrolment; women were matched for parity and previous experience of lactational amenorrhea; duration of breastfeeding episode was not considered in the models as for almost all women this was 5-10 months
Risk of bias	High risk of bias: No blinding of either participants or investigators; not able to assess allocation concealment as no information on randomisation; no adjustment for any other dietary components including energy intake
Relevance	Intake of milk products postpartum is likely to be different to Australian women's intake, as in the control group it was stated that 'consumption of milk in the control group was rare and none of them consumed skim milk'
Other comments	Breast milk volume was not measured so hard to say whether the longer duration of breastfeeding was associated with improved maternal diet.

Reference	**Venter 2009**
Food groups	Dairy foods: milk
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Portsmouth, UK
Funding	Food Standards Agency
Participants	696 pregnant women at 12 weeks gestation (with estimated birth date between 1 September 2001 and 31 August 2002)
Baseline comparisons	Pregnant women with a maternal history of atopic disease were more likely to smoke
Dietary assessment	FFQ
Timing	FFQ at 36 weeks gestation
Comparison	No (< 1% of women) versus moderate (10%) versus frequent (89%) versus uncertain (1%) consumption of milk during pregnancy
Outcomes	Food hypersensitivity (FHS) in infants up to three years of age
Results	**Infant FHS at one year:** 22/914 infants showed FHS to milk in the first year (1 where mothers never consumed milk during pregnancy, 0 where mothers reported moderate consumption of milk during pregnancy, 18 where mothers reported frequent consumption of milk during pregnancy and 3 where mother's milk consumption during pregnancy was uncertain) **Infant FHS at three years:** 25/911 infants showed FHS to milk in the first three years (1 where mothers never consumed milk during pregnancy, 2 where mothers reported moderate consumption of milk during pregnancy, 20 where mothers reported frequent consumption of milk during pregnancy and 2 where mother's milk consumption during pregnancy was uncertain) "Statistical inferences could not be measured due to the small numbers"
Length of followup	Up to three years
Confounding	Analyses do not appear to have been adjusted
Risk of bias	Moderate-high risk of bias: Data were obtained from 91% (n = 969) of the birth cohort; at 1 year follow-up data were available for 77.6% (752/969) and for 65.2% (632/969) at 3 years; analyses probably not adjusted for confounders
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Willers 2007**
Food type	Dairy foods (fat from dairy products)
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Antenatal clinics at Aberdeen Maternity Hospital, Aberdeen, Scotland
Funding	Asthma UK, GA²LEN European Network of Excellence on Global Allergy and Asthma
Participants	1212 children (singleton births) whose mothers were recruited between October 1997 and April 1999 at a median gestational age of 12 weeks
Baseline comparisons	Women were representative of the local obstetric population *See confounding below*
Dietary assessment	FFQ
Timing	FFQ mailed at 32 weeks gestation to cover dietary intake over the previous 2-3 months
Comparison	Tertiles:
Outcomes	Wheeze, asthma, allergic rhinitis, atopic eczema, hay fever at 5 years
Results	**Fat from dairy products** – no consistent linear associations with respiratory and atopic outcomes in 5 year old children (exact numbers not reported in the paper) ***Ever had asthma – no significant association with dairy intake (exact numbers not reported)***
Followup	5 years
Confounding	Adjusted for maternal age, paternal social class, maternal education, maternal smoking during pregnancy, smoking in the child's home at 5 years, energy intake, maternal asthma, maternal atopy, child's birthweight, child's sex, presence of older siblings, and breastfeeding
Risk of bias	Low risk of bias: Initial study population of 1924 children dropped to 1212 participants with complete data (63.0%) (questionnaire, at least one of the outcome time points).
Relevance	Likely to be reasonably relevant to Australian women
Other comments	Inclusion of maternal supplement use during pregnancy did not materially change the results

Reference	**Willers 2008**
Food type	Dairy foods (milk and milk products)
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Netherlands
Funding	Netherlands Organization for Health Research and Development, Netherlands Organization for Scientific Research; Netherlands Asthma Fund; Netherlands Ministry of Spatial Planning, Housing, and the Environment; Netherlands Ministry of Health, Welfare and Sport, GlaxoSmithKline
Participants	2,832 children (part of the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered at antenatal recruitment (mean gestational ages not reported) to cover dietary intake over the previous month
Comparison	Daily (once per day or more) consumption of milk or milk products v 1-4 times a week or fewer
Outcomes	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable 'asthma symptoms' in the last 12 months (measured longitudinally from 1 to 8 years age)
Results	**Wheeze from 1 to 8 years age (n = 2788)** OR 0.84 95% CI 0.68 to 1.03 aOR 0.88 95% CI 0.71 to 1.19 **Dyspnoea from 1 to 8 years age (n = 2788)** OR 0.90 95% CI 0.71 to 1.16 aOR 0.92 95% CI 0.72 to 1.19 **Steroid use from 1 to 8 years age (n = 2788)** OR 0.99 95% CI 0.72 to 1.36 aOR 1.03 95% CI 0.74 to 1.43 **Asthma symptoms (composite of previous three outcomes) from 1 to 8 years age (n = 2788)** OR 0.89 95% CI 0.72 to 1.10 aOR 0.92 95% CI 0.74 to 1.15
Followup	8 years
Confounding	The child's dietary data on fruit, vegetables, fish, eggs, full cream milk, butter and peanut butter consumption at 2 years of age were used to check for potential confounding by the child's diet. Results were adjusted for by sex, maternal education, parental allergy, maternal smoking during pregnancy, smoking in the home at 8 years of age, breastfeeding, presence of older siblings, birthweight, maternal overweight 1 year after pregnancy, maternal supplement use during pregnancy, region and study arm (intervention or natural history arm).
Risk of bias	Moderate risk of bias: Initial study population of 4,146 mothers dropped to 2,832 participants with complete data (68.3%) (pregnancy questionnaire, at least one of the outcome time points and all confounders). Participants with complete data were more likely to have a high education level, to have daily dairy food and fruit intake during pregnancy and to have breastfed and less likely to have maternal asthma or maternal atopy, smoked during pregnancy, be from a south western region compared with participants who did not have complete data.
Relevance	Dietary intakes likely to be different from Australian e.g. low fish consumption in study participants
Other comments	Not clear when women assessed their diet during pregnancy; 83% of pregnant women used supplements (50% used folic acid/iron)

Reference	**Yin 2010 (see also Jones 2000)**
Food type	Dairy foods (milk)
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Southern Tasmania, Australia
Funding	NHMRC, Tasmanian Government, Royal Hobart Hospital Acute Care Program
Participants	216 adolescents born in 1988 (part of a larger infant health study of babies at high risk of SIDS) Exclusions: multiple pregnancies
Baseline comparisons	Children with unemployed fathers more likely to have been excluded due to missing data
Dietary assessment	FFQ
Timing	Dietary intake during third trimester of pregnancy
Comparison	Linear regression of density (portions per kJ)
Outcomes	Bone mass (bone mineral density (BMD) and bone mineral content*) in 16 year old adolescents
Results	**BMD at 16 years;** **Total body (g/cm^2)** r^2 -0.002; ß +0.14 (pns) adjusted r^2 0.326; ß +0.17 (pns) **Femoral neck (g/cm^2)** r^2 0.000 ß +0.25 (pns) adjusted r^2 0.353; ß +0.28 (pns) **Lumbar spine (g/cm^2)** r^2 0.010; ß +0.40 (pns) **adjusted r^2 0.213; ß +0.41 ($p < 0.05$)**
Followup	16 years
Confounding	Analyses were adjusted for sex, weight at age 16 years, sunlight exposure in winter at age 16 years, smoking during pregnancy, sports participation, ever breast-fed, current calcium intake, Tanner stage, maternal age at the time of childbirth and "other factors" [these other factors were not listed in the paper]
Risk of bias	Moderate-high: 415 children were followed from birth to age 16, dropped to 216 (dietary information missing or unreliable for 138 mothers, 47 multiple births, 14 participants had missing data for confounders) representing 52% of participants followed from birth to age 16. 70% of the 216 participants were male. Gender imbalance suggests potential selection bias (due to original selection of infants at high risk of SIDS)
Relevance	Infants at high risk of SIDS represent a selected group (more males, preterm births, teenage mothers, smoking during pregnancy)
Other comments	*Bone mineral content results not reported; Study flow figures differ between 2000 and 2010 reports (e.g. numbers of multiple births)

References

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Dairy foods and eggs

Included Studies

Study	Outcomes
1. Cant 1986	eczema
2. Falth-Magnusson 1987a and b, 1992	maternal weight gain, low birthweight, preterm birth, eczema, allergic rhinoconjunctivitis, asthma
3. Lilja 1988, 1989, 1991	cord blood IgE; eczema; asthma
4. Pogoda 2009	childhood brain tumours

Evidence summaries

	N	Level	References
Maternal Outcomes			
1. In a Swedish RCT, women in the dietary restriction group (no cow's milk or egg in late pregnancy) had a mean 19.3% **increase in weight during the pregnancy** compared with 22.3% in the non-diet group ($p < 0.005$)	212 women	II	Falth-Magnusson 1987a, b, 1992
Birth Outcomes			
2. In a Swedish RCT, no significant differences in **low birthweight or preterm birth** were seen for women in the dietary restriction group (no cow's milk or egg in late pregnancy) compared with women in the non-diet group	212 women	II	Falth-Magnusson 1987a, b, 1992
Childhood Outcomes			
3. In an UK RCT plus a nonrandomised study, there were no significant differences in **eczema scores in infants up to 12 weeks of age** whether their mothers consumed a diet excluding dairy foods and eggs, or not	19 (and 18)	II (and III-2)	Cant 1986
4. In a Swedish RCT, no significant differences in numbers of children with **asthma or eczema** were seen for women in the dietary restriction group (no cow's milk or egg in late pregnancy) compared with women in the non-diet group	212 women	II	Falth-Magnusson 1987a, b, 1992
5. In a Swedish RCT, no significant differences in numbers of children with **asthma or eczema** were seen for women in the dietary restriction groups (no or reduced cow's milk or egg in late pregnancy) compared with women in the non-diet groups	165	II	Lilja 1988, 1989, 1991
6. In an international multicentre case control study, maternal consumption of dairy foods and eggs during pregnancy was associated with **increased risk of childhood brain tumours**, **particularly PNET**	1281 cases; 2223 controls	III-3	Pogoda 2009

Evidence Tables

Reference	**Cant 1986**
Food type	Dairy foods (cow's milk) and egg
Study type	RCT (crossover trial) [plus non-randomised crossover trial designed to see if the soy substitute might have provoked symptoms in the RCT]
Level of evidence	II [plus III-2] (intervention)
Setting	London, UK
Funding	South West Thames Regional Health Authority, UK and Wyeth Laboratories
Participants	Mother of 37 breastfed infants wih eczema, aged 6 weeks to 6 months: RCT – 19 mothers nonRCT – 18 took part in in open exclusion of 11 foods followed by a double blind challenge in mothers whose infants seemed to respond
Baseline comparisons	Not reported
Dietary assessment	NA
Timing	2 or 4 week crossovers
Comparison	Maternal exclusion of cow milk, egg, chocolate, wheat, nuts, fish, beef, chicken, citrus fruits, colourings, and preservatives, with use of soya-based milk substitute for 4 weeks *versus* Same dietary exclusions for same duration (4 weeks) but substitute contained cow milk and egg
Outcomes	eczema
Results	**RCT (n = 17):** nonsignificant reduction in eczema activity score – mean 10.8 in exclusion period; 12.2 in control period nonsignificant reduction in eczema area score – mean 8.6 in exclusion period; 9.4 in control period **nonRCT (n = 18):** In 2 children the eczema activity score decreased by > 20% when their mothers took the exclusion diet and then increased but > 20% when their mothers returned to a normal diet; In 2 children the eczema activity scores remained unchanged when their mothers took the exclusion diet but then deteriorated when the mothers took a normal diet
Followup	12 weeks
Confounding	NA (for RCT)
Risk of bias	Moderate risk of bias (RCT): method of allocation concealment not reported, two women excluded due to poor adherence to diet; no data reported on adherence for the other 17 women
Relevance	A diet excluding milk and eggs and other foods likely to be difficult for many Australian women to adhere to during pregnancy
Other comments	

Reference	**Falth-Magnusson 1987 (1987a, 1987b, 1992)**
Food type	Dairy foods (cow's milk) and egg
Study type	RCT
Level of evidence	II (intervention)
Setting	Linkoping area, Sweden
Funding	Tore Nilson Fund for Medical Research and Medical Research Fund of the County of Ostergotland
Participants	212 women from families with at least one allergic family member (213 children) recruited from 1983
Baseline comparisons	Family allergy scores similar between groups at baseline; children's exposure to smoke was significantly less in the diet group than the non-diet group
Dietary assessment	NA
Timing	Intervention period: 28 weeks to birth
Comparison	Cow's milk and egg elimination from 28 weeks gestation to birth (and partially during early lactation) (n = 104 randomised) v usual diet (typically 0.5 L milk/day and 3-5 eggs/week) n = 108 randomised; (elimination group also had extra calcium and casein hydrolysate)
Outcomes	Cord blood IgE, maternal weight gain, low birthweight, preterm birth, eczema, allergic rhinoconjunctivitis, asthma
Results	**Maternal weight gain during pregnancy (mean %)** Diet group (n=79): mean gain of 19.3% v 22.3% in the non-diet group (n=85) (**P < 0.005)** **Low birthweight and preterm birth** No significant differences between groups – 3 babies born before 36 weeks and all < 2500 g (all in the diet group) **Cord blood IgE** No sig. differences between groups (but babies of atopic mothers had higher IgG levels than babies of non-atopic mothers regardless of diet) **Positive skin prick tests for egg and milk in infants at 6 and 18 months**: pns **Eczema** (up to five years?); 29 in the diet group and 24 in the non-diet group (pns) **Asthma in first 18 months**: 3/76 in diet group and 1/95 in the non-diet group (pns) **Allergic rhinoconjunctivitis** (up to five years?); 13 in the diet group and 14 in the non-diet group (pns) **Bronchial obstruction** (up to five years?); 29 in the diet group and 25 in the non-diet group (pns) **Intolerance to any food item** (up to five years?): 16/84 in the diet group and 20/114 non-diet (pns) **Allergic disease** (up to five years?) – probable or definite; 35 in the diet group and 37 in the non-diet group (pns)
Followup	Children at five years of age
Confounding	Not controlled for infant's diet (some food avoidance was suggested)
Risk of bias	Medium risk of bias: method of randomisation described only as "randomly allocated"; blinding of intervention not feasible; 10 post-randomisation exclusions (7 in non-diet group and 3 in diet group); 22 women in the elimination diet group interrupted their diet but completed the study; five year results available for 195/213 (92%) children (leaving 84 in the diet group and 114 in the non-diet group)
Relevance	A diet excluding milk and eggs likely to be difficult for many Australian women to adhere to during pregnancy
Other comments	

Reference	**Lilja 1988 (1989, 1991) – some data also extracted from the Kramer Cochrane review (Kramer 2006)**
Food type	Dairy foods (cow's milk); and egg
Study type	RCT
Level of evidence	II (intervention)
Setting	Antenatal clinics in Stockholm-Uppsala and Linkoping, Sweden
Funding	Swedish Medical Research Council, Riksforbundet mot Allergi, Mjolkdroppen, Konsul Th.C.Berghs Foundation, King Gustaf V 80th Birthday Fund, Bristol Myers
Participants	165 pregnant women with atopic respiratory disease with an allergy to pollen and/or animal dander (giving birth to 170 infants; 5 sets of twins)
Baseline comparisons	The almost double number of women (n = 57) allocated to the high dairy and egg diet is not explained
Dietary assessment	n/a
Timing	Allergens ingested during third trimester of pregnancy
Comparison	Four diets: 1) 'normal'; about 0.5 L cows' milk daily and three hens' eggs weekly (n = 39) 2) 'free'; no milk or eggs during the last three months of pregnancy (n = 37) 3) 'reduced'; no apparent intake, but diet not completely free of milk and eggs (n = 32) 4) 'high'; about one L milk daily and one egg daily (n = 57)
Outcomes	Cord blood IgE; eczema; asthma;
Results	**Cord blood IgE** No significant differences between the four different maternal diet groups **Eczema in first 12-18 months** No significant differences **Asthma in first 18 months** 1 case in restricted diet, 1 in unrestricted diet groups
Followup	To 18 months
Confounding	n/a
Risk of bias	Moderate risk of bias: 18/183 (10%) postrandomisation exclusions at birth because of contamination of cord blood by maternal blood; allocation described only as "randomly assigned"; no explanation given for imbalance on size of groups
Relevance	Both the 'free/reduced' diet and the 'high' diet not likely to be representative of diets of Australian women
Other comments	

Reference	**Pogoda 2009**
Food type	Eggs and dairy foods (including cheese)
Study type	Case-control study Separate centre reports: Preston-Martin 1996 (Los Angeles); Lubin 2000 (Israel); Cordier 1994 (France); McCredie 1994 (Australia)
Level of evidence	III-3 (aetiology)
Setting	International (seven countries – USA, Israel, Italy, Spain, Australia, France and Canada (International Collaborative Study of Childhood Brain Tumors)
Funding	NIH, California Department of Health, Southern California Environmental Health Sciences Center, National Cancer Institutes, Cancer Surveillance System of Western Washington, Fred Hutchinson Cancer Research Center, Fondo de Investigaciones Sanitarias of Spain, Conselleria de Sanitat i Consum of Valencian Autonomous Community for the Childhood Cancer Registry of the Province of Valencia, Spanish Society of Paediatric Oncology with the National Childhood Cancer Registry, ISCIII-RTIC, Villavecchia Foundation and Scientific Foundation of the AECC
Participants	Cases: 1281 Controls: 2223 Years of diagnosis varied between centres, ranging from 1976 to 1992 (with most diagnosed between 1982 and 1992) Controls were frequency matched to cases in US centres and in France; otherwise they were individually matched (by region of residence, age, sex, and geographic area (except for Sydney and Los Angeles))
Baseline comparisons	*See confounding below*
Dietary assessment	Standardised study questionnaire using detailed dietary recall methods and abstract food models to gauge portion size
Timing	Diet during the past year and during the index pregnancy
Comparison	Quartiles
Outcomes	Childhood brain tumours
Results	see below

Results

All tumours (n = 1203 cases)

	Controls	Cases	aOR 95% CI
Eggs/dairy foods			
Q1	554 (26%)	280 (24%)	1.0
Q2	556 (26%)	274 (24%)	1.0 (0.8 to 1.3)
Q3	533 (25%)	296 (26%)	1.1 (0.8 to 1.5)
Q4	**525 (24%)**	**301 (26%)**	**1.2 (1.0 to 1.5)**

P for trend = 0.04

Astroglials (n = 621 cases)

	Controls	Cases	aOR 95% CI
Eggs/dairy foods			
Q1	554 (26%)	142 (24%)	1.0
Q2	556 (26%)	139 (24%)	1.0 (0.7 to 1.4)
Q3	533 (25%)	151 (26%)	1.2 (0.9 to 1.5)
Q4	**525 (24%)**	**154 (26%)**	**1.3 (1.0 to 1.7)**

P for trend = 0.01

Primitive neural ectodermal tumours (PNETs) (n = 257 cases)

	Controls	Cases	aOR 95% CI
Eggs/dairy foods			
Q1	554 (26%)	49 (20%)	1.0
Q2	**556 (26%)**	**55 (23%)**	**1.3 (1.0 to 1.6)**
Q3	**533 (25%)**	**70 (29%)**	**1.6 (1.0 to 2.7)**
Q4	**525 (24%)**	**68 (28%)**	**1.6 (1.0 to 2.4)**

P for trend = 0.049

	Tumour Subtypes **Astrocytomas** <table><tr><td></td><td>**Pilocytic (142 cases)**</td><td>**Anaplastic (96 cases)**</td><td>**Other (199 cases)**</td></tr><tr><td>**Eggs/dairy foods**</td><td>**2.1 (1.0 to 4.1)**</td><td>1.1 (0.8 to 1.5)</td><td>**1.4 (1.0 to 1.8)**</td></tr><tr><td>**P for trend**</td><td>**0.02**</td><td>0.11</td><td>**0.001**</td></tr></table> **Other types** <table><tr><td></td><td>**Malignant gliomas (122 cases)**</td><td>**Medulloblastomas (193 cases)**</td><td>**PNET (64 cases)**</td><td>**Ependymomas (104 cases)**</td></tr><tr><td>**Eggs/dairy foods**</td><td>1.0 (0.4 to 2.3)</td><td>**1.4 (1.0 to 1.9)**</td><td>2.0 (0.6 to 6.1)</td><td>0.8 (0.4 to 1.6)</td></tr><tr><td>**P for trend**</td><td>0.83</td><td>0.14 (?)</td><td>0.06</td><td>0.66</td></tr></table>
Followup	n/a
Confounding	Analyses adjusted for age and sex of child, study centre and each food group; Adjustment for total intake of foods had little effect on estimates
Risk of bias	Low-moderate risk of bias: 75% of eligible cases and 71% of eligible controls participated (based on centres for which these data were available); some lack of standardisation in dietary assessments between study centres; potentially high risk of recall bias for women whose pregnancies may have been at least 10 years previously.
Relevance	Likely to be relevant to Australian women
Other comments	

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Pogoda JM, Preston-Martin S, Howe G, Lubin F, Mueller BA, Holly EA, Filippini G, Peris-Bonet R, McCredie MR, Cordier S and Choi W. "An international case-control study of maternal diet during pregnancy and childhood brain tumor risk: a histology-specific analysis by food group." ***Ann Epidemiol*** 2009: **19**(3): 148-60.

Eggs

Included Studies

Study	Outcomes
1. Cant 1985	Eczema in infants up to 6 months
2. George 2005	“Breastfeeding”
3. Giordano 2008	Cryptorchidism and hypospadias
4. Haggarty 2009	Deprivation
5. Herrick 2003	Cortisol concentrations in offspring aged 30 years
6. Jensen 2004	Childhood acute lymphoblastic leukemia
7. Lagiou 2006	Maternal pregnancy oestradiol, unconjugated oestriol, sex hormone binding globulin (SHBG), progesterone, prolactin
8. Maconochie 2007	Miscarriage
9. Miyake 2006	Postpartum depression
10. Nwaru 2010	Allergic sensitisation in offspring by 5 years
11. Saito 2010	Suspected atopic eczema in infants at 3-4 months
12. Sausenthaler 2007	Allergic sensitisation, eczema at 2 yrs
13. Vance 2004	Infant atopy up to 18 months
14. Willers 2008	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable ‘asthma symptoms’ in the last 12 months (measured longitudinally from 1 to 8 years age)

Evidence Summaries

	N	Level	References
Maternal Outcomes			
1. In a Scottish cohort study, no significant differences were seen between maternal intake of eggs during pregnancy and deciles of **deprivation**	1277	II	Haggarty 2009
2. In a US cohort study, maternal intake of eggs during pregnancy was associated with a reduction in **progesterone** at 16 completed weeks GA: -4.4% change 95% CI -8.1 to -0.6 but not at 27 completed weeks GA: -3.1% change 95% CI -6.8 to 0.8	277	II	Lagiou 2006
3. In a UK case-control study, no significant associations were seen between maternal intake of eggs during pregnancy and **miscarriage**: aOR 1.04 95% CI 0.87 to 1.24	603 cases; 6116 controls	III-3	Maconochie 2007
Congenital Anomalies			
4. In a Sicilian case-control study, no significant associations were seen between cases of **hypospadias and/or cryptorchidism** and maternal intake of eggs	90 cases; 202 controls	III-3	Giordano 2008
Postnatal Outcomes			
5. In a US cohort study, **lactating** and nonlactating women consumed similar amounts of eggs	149	II	George 2005
6. In a Japanese cohort study, **postpartum depression** was not significantly associated with egg intake during pregnancy	865	II	Miyake 2006
Childhood – Asthma, Eczema and Other Allergy Outcomes			
7. In a subset of cohort study from the UK, there was no significant association between ovalbumin concentrations in breastmilk and **eczema in infant offspring at 15 weeks of age**	19	II	Cant 1985
8. In a cohort study from Japan, there was no significant association between maternal egg consumption during pregnancy and **suspected atopic eczema in infants at 3-4 months of age**: adjusted p for trend = 0.74	771 infants	II	Saito 2010
9. In a German cohort study, there was no significant association between maternal egg consumption during pregnancy and: • **eczema in infants at 2 years of age**: aOR 0.81 95% CI 0.62 to 1.06; • **allergen sensitisation at 2 years of age:** aOR 0.91 95% CI 0.56 to 1.28	3097 infants	II	Sausenthaler 2007
10. In a RCT from the UK, there were no significant differences between an egg avoidance or a normal diet during pregnancy for **infant atopy at 18 months of age** (p = 0.869)	136 infants	II	Vance 2004

11. In a cohort study from the Netherlands no significant associations were seen between amount of egg consumption during pregnancy and the following **allergy outcomes in infants from 1 to 8 years of age**: • Wheeze: aOR 0.96 95% CI 0.84 to 1.12 • Dyspnoea: aOR 1.12 95% CI 0.80 to 1.25 • Steroid use: aOR 1.01 95% CI 0.80 to 1.28 • Asthma symptoms (composite of above): aOR 1.03 95% 0.88 to 1.20	2832 children	II	Willers 2008
12. In a Finnish cohort study, there were no significant associations between egg consumption during pregnancy and **allergic sensitisation in infants by 5 years of age** for: • Food allergens aOR 0.75% 95% CI 0.50 to 1.13 • Inhalant allergens aOR 0.91 95% CI 0.64 to 1.29	931 children	II	Nwaru 2010
Other Childhood Outcomes			
13. In a US case-control study, **childhood acute lymphoblastic leukemia** was not associated with maternal egg intake during pregnancy: • aOR 0.99 95% CI 0.83 to 1.18: mean consumption 3.99 [SD 1.67] serves per day	138 cases; 138 controls	III-3	Jensen 2004
14. In a cohort study from Scotland, there was no significant association between egg consumption during pregnancy and **cortisol concentrations in offspring at 30 years of age**	251 offspring	II	Herrick 2003

Evidence Tables

Reference	**Cant 1985**
Food type	Eggs
Study type	Prospective cohort study with concurrent comparison groups
Level of evidence	II (aetiology)
Setting	UK
Funding	AFRC/MRC
Participants	19 exclusively breastfed infants less than 6 months old (most were 3 to 4 months old) – with eczema and without eczema
Baseline comparisons	Differences in infant eczema diagnosis part of study design
Dietary assessment	Detection of ovalbumin in breastmilk
Timing	Mean 15 weeks postpartum
Comparison	Ovalbumin present or absent in breastmilk; ovalbumin concentrations
Outcomes	Eczema in infant
Results	8/11 infants (72%) with eczema and a positive skin test reaction to egg had mothers with **breastmilk containing ovalbumin**; compared with 6/8 (75%) infants with normal skin and a negative skin test reaction to egg (pns) **Mean ovalbumin concentrations in breastmilk** : Infants with eczema (n = 11): 1.6 µg/L Infants without eczema (n = 8): 2.4 µg/L, pns
Followup	13-17 weeks postpartum
Confounding	No adjustment for potential confounding
Risk of bias	Moderate risk of bias; of 105 mother-infant pairs, 22 were found to have consumed complementary formula milk and were therefore excluded from the study; only 19/83 mothers given egg challenge test (not reported these women were selected)
Relevance	Possibly relevant to women in Australia
Other comments	

Reference	**George 2005**
Food type	Eggs
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Texas, US
Funding	Not reported
Participants	149 Medicaid-qualified women (30% white, 24% African American, 46% Hispanic) – recruited from a larger study on postpartum weight retention Inclusion criteria: 18 years or older; non-Hispanic white, African American or Hispanic ethnicity; birth of a health term infant, fluency and literacy in English; absence of pregnancy-related abnormalities and disease conditions.
Baseline comparisons	Significant differences between lactating and non-lactating women – higher parity, BMI and lower education levels in non-lactating women.
Dietary assessment	Semiquantitative FFQ to cover pregnancy and first six months postpartum
Timing	FFQ administered at 6 weeks and 6 months postpartum
Comparison	Proportion of consumption of eggs
Outcomes	Breastfeeding (exclusive or partial at 6 months postpartum)
Results	Lactating women and nonlactating women consumed similar amount of eggs ($p > 0.05$) For both groups there was a significant decrease in egg consumption between pregnancy and the postpartum period ($p < 0.05$)
Followup	6 months postpartum
Confounding	No adjustment for potential confounding
Risk of bias	Moderate-to-high risk of bias; no attempt to control for confounding despite significant baseline differences between lactating and non-lactating women.
Relevance	Possibly relevant to low-income women in Australia
Other comments	Minimal reporting of results

Reference	**Giordano 2008**
Food type	Eggs
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Sicily, Italy
Funding	Sicilian Congenital Malformation Registry
Participants	90 cases: 43 cases of hypospadias and 48 cases of cryptorchidism (both in one infant) 202 controls: randomly selected controls born in the same year and the same region Births between 1998 to 2003
Baseline comparisons	Low birthweight, low maternal education, mother's history of gynaecological disease and father's history of urogenital diseases differed significantly between cases and controls *See confounding below*
Dietary assessment	Interview on maternal diet and food frequencies
Timing	FFQ
Comparison	Consumption of eggs once a week or less/more than once a week
Outcomes	Hypospadias and cryptorchidism
Results	**Eggs** **<u>Hypospadias</u>** **cases** **controls** **OR** **≤ 1/week** 17 (39.5%%) 67 (33.2%) 1.00 **>1/week** 26 (60.5%) 135 (66.8%) 0.76 95% CI 0.39 to 1.50 **<u>Cryptorchidism</u>** **cases** **controls** **OR** **≤ 1/week** 10 (20.8%) 67 (33.2%) 1.00 **>1/week** 38 (79.2%) 135 (66.8%) 1.89 95% CI 0.89 to 4.02 **<u>Hypospadias and cryptorchidism</u>** **cases** **controls** **OR** **≤ 1/week** 27 (30.0%) 67 (33.2%) 1.00 **>1/week** 63 (70.0%) 135 (66.8%) 1.16 95% CI 0.68 to 1.98
Followup	n/a
Confounding	Results for this food group were not presented as adjusted analyses
Risk of bias	Moderate risk of bias: Participation rate of parents and data collection rate of cases was lower than that of controls (76% versus 91%); no adjusted results presented for this food group
Relevance	Likely to be reasonably relevant for Australian women, although hypospadias rates very high and unlikely that most Australian women will have such high pesticide exposure
Other comments	Ragusa region in Sicily is a region of intensive agriculture (involving high rates of pesticide and other chemical use) with high rates of hypospadias and cryptorchidism

Reference	**Haggarty 2009**
Dietary patterns	Eggs
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Aberdeen, Scotland
Funding	UK Food Standards Agency
Participants	1277 sequentially enrolled pregnant women attending Aberdeen Maternity Hospital for ultrasound (a further 184 women were recruited later in pregnancy). Exclusions: diabetic women, women with multiple pregnancies, women who conceived as a result of fertility treatment, or clinical data not available
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	Assessed at 19 weeks gestation
Comparison	Intake of eggs by deciles of deprivation
Outcomes	Deprivation (assessed using the Scottish Index of Multiple Deprivation)
Results	**Deprivation** Eggs: no significant differences seen between intake of eggs and deciles of deprivation
Followup	To neonatal period
Confounding	(Some?) analyses adjusted for energy intake
Risk of bias	Low to moderate risk of bias: low attrition, some lack of detail in reporting of outcomes
Relevance	Likely to be relevant to Australian women
Other comments	About 40-50% of the least deprived women reported taking folic acid supplements compared with about 20% for the most deprived women; Most birth outcome associations were reported by nutrient rather than food group; Not easy to deduce quantities of intake of foods (main graphs reported as change in intake by deprivation decile)

Reference	**Herrick 2003**
Food groups	Eggs
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Motherwell, Scotland
Funding	Dunhill Medical Trust, NIH
Participants	251 men and women) whose mothers' food intakes had been recorded during pregnancy during 1967 to 1968. These women had been advised to eat 0.45 kg of red meat a day and to avoid carbohydrate-rich foods during pregnancy
Baseline comparisons	*See confounding below*
Dietary assessment	Mothers asked about consumption of 10 foods
Timing	Early pregnancy (≤ 20 weeks); late pregnancy (> 20 weeks)
Comparison	Number of eggs per week
Outcomes	Cortisol concentrations in offspring aged 30 years
Results	Cortisol (change per unit change in maternal egg consumption during pregnancy) No significant association
Length of followup	30 years
Confounding	Analyses adjusted for offspring's gender, social class at birth, BMI, alcohol consumption, and activity level
Risk of bias	Moderate risk of bias: For the 1432 records from 1967-8 recorded liveborn, singleton births with complete names, birth measurements and ≥ 1 diet record. 965 offspring were alive and living locally; and after attrition or declining to participate, 251 (17.5%) were available for analysis.
Relevance	Very high intake of meat and very low carbohydrate intake limits the relevance to current dietary intakes of Australian women
Other comments	Authors state that "in the setting of advice to follow a pregnancy diet high in protein and low in carbohydrate, an unbalanced pattern of higher meat/fish and lower green vegetable consumption in late pregnancy leads to elevated cortisol concentrations in the offspring"

Reference	**Jensen 2004**
Food type	Eggs
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study)
Funding	PHS
Participants	138 matched cases and controls: Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, parental occupation and smoking during pregnancy – no evidence of confounding was seen for these variables. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of eggs
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Eggs**: aOR 0.99 95% CI 0.83 to 1.18: mean consumption 3.99 [SD 1.67] serves per day*
Followup	n/a
Confounding	Analyses were adjusted for variables previously shown to be significantly associated with ALL in the overall study – income, prior fetal loss, child's exposure to other children under age five, and maternal exposure to indoor insecticides during pregnancy; along with portion size and energy consumption
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 1999, 83% consented to participate; 69% of the eligible controls agreed to participate. Of the 161 matched pairs, seven pairs were excluded as the respondent was not the biological mother, 16 pairs were excluded due to questionable dietary questionnaire data, leaving 138 matched pairs (86%); some recall bias likely
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	*Some consumption levels seem high – possibly per week rather than per day?

Reference	**Lagiou 2006**
Food type	Eggs
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Boston, USA
Funding	NIH
Participants	277 pregnant women who were Caucasian, < 40 years old and having a parity of no more than two (recruited between March 1994 and October 1995). Exclusions: women who had taken any kind of hormonal medication during the index pregnancy, with a prior diagnosis of diabetes mellitus or thyroid disease, or if the fetus had a known major anomaly.
Dietary assessment	FFQ
Timing	Mailed to women prior to a routine antenatal visit around 27 weeks GA, to reflect women's dietary intake during the second trimester of pregnancy
Baseline comparisons	Women in the study likely to be older, better educated, primiparae, lower BMI and less likely to smoke than pregnant women in the general US population
Comparison	Frequency of egg consumption (mean 6.5 times per month; increment 7.4)
Outcomes	Maternal progesterone – women's blood was taken at 16 and 27 completed weeks GA.
Results	**Maternal progesterone** **16 completed weeks GA: -4.4% change 95% CI -8.1 to -0.6** 27 completed weeks GA: -3.1% change 95% CI -6.8 to 0.8
Followup	27 completed weeks GA
Confounding	Adjusted for age, parity, gender of offspring, smoking and GA at blood measurement
Risk of bias	Low to moderate risk of bias: 277 of 402 (68.9%) eligible women were included – 77 refused to participate, 9 were subsequently excluded because the index pregnancy was terminated through a spontaneous or induced abortion, 2 were excluded because of twin birth and 10 were lost to follow-up after the initial meeting.
Relevance	Indirect outcomes for (risk of) breast cancer
Other comments	Study authors postulate that the associations between breast cancer risk and increased birthweight are mediated through endocrine hormones

Reference	**Maconochie 2007**
Food groups	Eggs
Study type	Case-control study (postal survey sampled from the electoral roll – National Women's Health Study)
Level of evidence	III-3 (aetiology)
Setting	UK general population
Funding	National Lottery Community Fund, Miscarriage Association
Participants	Cases: 603 women aged 18 to 55 years whose most recent pregnancy had ended in first trimester miscarriage (< 13 weeks gestation); Controls: 6116 women aged 18 to 55 years whose most recent pregnancy had progressed beyond 12 weeks
Baseline comparisons	BMI < 18.5 was significantly associated with odds of miscarriage *Also see Confounding below*
Dietary Assessment	questionnaire
Timing	Diet in the three months prior to conception and the first 12 weeks of pregnancy
Comparison	At least twice weekly
Outcomes	First trimester miscarriage
Results	see below
Length of followup	n/a
Confounding	Adjusted for year of conception, maternal age, previous miscarriage and previous live birth; and further adjusted for nausea in the first 12 weeks of pregnancy
Risk of bias	Low risk of bias: 88% of eligible women responding to stage 1 agreed to participate in the second stage of the study; and 71% responded to the stage 2 questionnaire. 1071/7790 records (7508 women) were excluded (mostly due to index pregnancy being conceived prior to 1980), leaving 6719 records (86%) available for analysis
Relevance	Likely to be relevant to Australian women
Other comments	Women who suffered from nausea in the first 12 weeks of pregnancy were almost 70% less likely to miscarry

Results:

Eggs twice weekly or more

	Cases	*Controls*	*aOR (95% CI)*	*aOR further adjusted for nausea*
No	323 (58%)	2888 (50%)	1.00	1.00
Yes	238 (42%)	2871 (50%)	1.04 (0.87 to 1.24)	1.02 (0.85 to 1.24)

Reference	**Miyake 2006**
Food groups	Eggs
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Women who became pregnant in November 2001-March 2003 Neyagawa City, Osaka Prefecture and several surrounding municipalities (Osaka Maternal and Child Health Study, Japan)
Funding	Grant-in-Aid for Scientific Research (Government grant)
Participants	865 pregnant Japanese women
Baseline comparisons	*See Confounding below*
Dietary Assessment	Dietary history questionnaire-self administered
Timing	Diet survey for previous month at baseline (period of baseline not stated), EPDS at 2-9 months post partum
Comparison	Daily intake of eggs Note: other dietary intakes analysed: meat, fish, dairy products, total fat, saturated fatty acids, cholesterol, LA, ALA and AA
Outcomes	Postpartum depression (EPDS with postpartum depression when score ≥ 9)
Results	No significant association between egg intake and postpartum depression on adjusted analysis
Length of follow up	2-9 months postpartum
Confounding	Adjusted for: age, gestation, parity, smoking, family structure, occupation, family income, education, changes in diet in previous month, season when baseline data collected, BMI, time of delivery, medical problems in pregnancy, baby's sex, baby's birthweight
Risk of bias	Low risk of bias: data for 865/1002 (86.5%) women available for analysis
Relevance	Australian diets very different to Japanese - much less seafood intake in Australia and more white fish rather than fatty fish
Other comments	Originally 1002 women enrolled only 865 completed (note: depressed persons less likely to participate), low rate of enrolment into study (17.2% of those eligible in Neyagawa)

Reference	**Nwaru 2010**
Food type	Eggs
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Tampere, Finland
Funding	Academy of Finland, Finnish Pediatric Research Foundation, the Juho Vainio Foundation, the Yrjo Jahnsson Foundation, Turku, Oulu and Tampere University Hospitals, JDRF, Novo Nordisk Foundation, EU Biomed 2 Program
Participants	931 mother-infant pairs (children with human leukocyte antigen-conferred susceptibility to type 1 diabetes) participating in the Finnish type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study between September 1996 and October 1997
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ given to women after birth, for return at the three month visit (FFQ intended to cover maternal diet during pregnancy and lactation)
Comparison	Amount of egg consumption
Outcomes	Allergic sensitisation in offspring by 5 years: food allergens (egg, cow's milk, fish, wheat); inhalant allergens (house dust mite, cat, timothy grass, birch)
Results	**Egg** ***Food allergens*** / ***Inhalant allergens*** OR 0.80 95% CI 0.55 to 1.16 / OR 0.92 95% CI 0.66 to 1.27 aOR 0.75 95% CI 0.50 to 1.13 / aOR 0.91 95% CI 0.64 to 1.29
Followup	To 5 years
Confounding	Adjusted for energy intake, place of birth, season of birth, sex of the child, number of siblings, gestational age at birth, parental asthma, parental allergic rhinitis, maternal age at birth, maternal smoking during pregnancy, maternal education
Risk of bias	Low risk of bias: data available for 931/1175 (79.2%) children recruited – 108 did not participate in survey, a further 49 did not have IgE measurements, a further 87 had no FFQ or an incomplete FFQ
Relevance	Likely to be relevant to Australian women; some differences in individual types of vegetables between Finland and Australia
Other comments	28% of women took vitamin D supplements, 73% took iron supplements; HLA genotype not likely to have any impact on the development of allergic diseases.

Reference	**Saito 2010**
Food type	Eggs
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Neyagawa City, Japan
Funding	Ministry of Education, Culture, Sports, Science and Technology and Health and Labour Sciences, Ministry of Health, Labour and Welfare, Japan
Participants	771 mother-child pairs recruited from November 2001 to March 2003 at any stage of pregnancy – mean GA 18 weeks (part of the Osaka Maternal and Child Health Study)
Baseline comparisons	*See confounding below*
Dietary assessment	Diet history questionnaire (DHQ)
Timing	DHQ to assess dietary habits during the preceding month
Comparison	Quartiles of egg consumption
Outcomes	Suspected atopic eczema
Results	**Suspected atopic eczema** *n/N* — *OR (95% CI)* — *aOR (95% CI)* Q1 (9.7 g/day) 17/192 1.00 1.00 Q2 (22.9 g/day) 15/193 0.87 (0.42 to 1.79) 0.87 (0.40 to 1.89) Q3 (40.7 g/day) 19/193 1.12 (0.57 to 2.25) 1.37 (0.66 to 2.86) Q4 (61.3 g/day) 14/193 0.81 (0.38 to 1.68) 0.73 (0.33 to 1.61) p value for trend (unadjusted): 0.76 p value for trend (adjusted): 0.74
Followup	3-4 months
Confounding	Adjusted for maternal age, gestation at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, mite allergen level from maternal bedclothes, vacuuming living room, mould in kitchen, changes in maternal diet in previous month, season when baseline data collected, baby's older siblings, baby's sex, baby's birthweight, breastfeeding and bathing or showering infant
Risk of bias	Low risk of bias: Of 1002 eligible women, a final sample of 771 (77%) was available for analysis
Relevance	Fish intake in Japan likely to be higher than in Australia
Other comments	

Results table:

	n/N	*OR (95% CI)*	*aOR (95% CI)*
Q1 (9.7 g/day)	17/192	1.00	1.00
Q2 (22.9 g/day)	15/193	0.87 (0.42 to 1.79)	0.87 (0.40 to 1.89)
Q3 (40.7 g/day)	19/193	1.12 (0.57 to 2.25)	1.37 (0.66 to 2.86)
Q4 (61.3 g/day)	14/193	0.81 (0.38 to 1.68)	0.73 (0.33 to 1.61)

<table>
<tr><td>Reference</td><td>Sausenthaler 2007</td></tr>
<tr><td>Food groups</td><td>Eggs</td></tr>
<tr><td>Study type</td><td>Prospective cohort study: from the LISA birth cohort</td></tr>
<tr><td>Level of evidence</td><td>II (aetiology)</td></tr>
<tr><td>Setting</td><td>4 German cities (Munich, Leipzig, Wesel, Bad Honnef)</td></tr>
<tr><td>Funding</td><td>Federal Ministry for Education, Science, Research and Technology, Germany</td></tr>
<tr><td>Participants</td><td>3097 newborns recruited</td></tr>
<tr><td>Baseline comparisons</td><td>See Confounding below</td></tr>
<tr><td>Dietary assessment</td><td>FFQ</td></tr>
<tr><td>Timing</td><td>Maternal diet during the last 4 weeks of pregnancy (obtained shortly after birth, median 3 days)</td></tr>
<tr><td>Comparison</td><td>Low intake group as reference group compared with high intake of eggs (= 1-2 times a week)</td></tr>
<tr><td>Outcomes</td><td>Allergic sensitisation, eczema at 2 yrs</td></tr>
<tr><td>Results</td><td>
<table>
<tr><td></td><td>Doctor-diagnosed eczema</td><td>any allergen sensitisation</td><td>food allergens</td><td>inhalant allergens</td></tr>
<tr><td></td><td colspan="4">Adjusted OR (95% CI)</td></tr>
<tr><td>Eggs</td><td>0.81 (0.62, 1.06)</td><td>0.91 (0.56, 1.28)</td><td>0.93 (0.63, 1.38)</td><td>0.90 (0.53, 1.53)</td></tr>
</table>
</td></tr>
<tr><td>Length of followup</td><td>2 years</td></tr>
<tr><td>Confounding</td><td>Crude and adjusted results reported (adjusted for study area, sex, maternal age, maternal smoking, level of parental education, exclusive breastfeeding ≥ 4 months, parental history of atopic diseases, season of birth and all dietary variables</td></tr>
<tr><td>Risk of bias</td><td>Low risk of bias: Two year data available for 2641/3097 children (85%): 433 lost to follow-up, 9 excluded due to chronic disease, 14 missing maternal FFQ</td></tr>
<tr><td>Relevance</td><td>Likely to be reasonably similar to dietary intakes of Australian women in Australia</td></tr>
<tr><td>Other comments</td><td></td></tr>
</table>

Reference	**Vance 2004**
Food groups	Eggs
Study type	RCT
Level of evidence	II (intervention)
Setting	Southampton, UK
Funding	Food Standards Agency
Participants	229 women with a personal or partner history of allergy (and 231 infants – 2 sets of twins); Exclusions: pregnancy complications, birds in the home, were egg allergic, had ongoing dietary restrictions
Baseline comparisons	Not reported
Dietary assessment	FFQ and food diaries
Timing	FFQ detailing egg intake over the month prior to recruitment; food dairy kept during the week prior to recruitment to assess general nutrition adequacy (repeated at 24 and 32 weeks gestation); 7 day food diary for preceding week also repeated at 24 and 32 weeks gestation
Comparison	Egg avoidance from second trimester of pregnancy (17 to 20 weeks gestation) until end of lactation (n = 115) versus unmodified health diet (n = 114)
Outcomes	Infant atopy at 6, 12 and 18 months of age – in a subgroup of 136 infants with IgG measurements at birth
Results	**Allergic phenotype in infant (egg avoidance v normal diet group)** 6 months: p = 0.794 12 months: p = 0.457 18 months: p = 0.126 **Atopy in infant (egg avoidance v normal diet group)** 6 months: p = 0.938 12 months: p = 0.582 18 months: p = 0.869
Length of followup	18 months
Confounding	n/a
Risk of bias	Unclear-moderate risk of bias: no details reported on method of allocation concealment, assessment of allergy outcomes was blinded; reason for IgG measurements in only 136/231 (58.9%) of infants not reported
Relevance	Likely to be reasonably similar to dietary intakes of Australian women in Australia
Other comments	

Reference	**Willers 2008**
Food type	Eggs
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Netherlands
Funding	Netherlands Organization for Health Research and Development, Netherlands Organization for Scientific Research; Netherlands Asthma Fund; Netherlands Ministry of Spatial Planning, Housing, and the Environment; Netherlands Ministry of Health, Welfare and Sport, GlaxoSmithKline
Participants	2,832 children (part of the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered at antenatal recruitment (mean gestational ages not reported) to cover dietary intake over the previous month
Comparison	Daily (once per day or more) v 1-4 times a week or fewer
Outcomes	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable 'asthma symptoms' in the last 12 months (measured longitudinally from 1 to 8 years age)
Results	**Wheeze from 1 to 8 years age (n = 2818)** OR 0.97 95% CI 0.84 to 1.12 aOR 0.96 95% CI 0.84 to 1.12 **Dyspnoea from 1 to 8 years age (n = 2818)** OR 1.10 95% CI 0.92 to 1.31 aOR 1.12 95% CI 0.94 to 1.34 **Steroid use from 1 to 8 years age (n = 2818)** OR 0.99 95% CI 0.79 to 1.25 aOR 1.01 95% CI 0.80 to 1.28 **Asthma symptoms (composite of previous three outcomes) from 1 to 8 years age (n = 2818)** OR 1.02 95% CI 0.87 to 1.19 aOR 1.03 95% CI 0.88 to 1.20
Followup	8 years
Confounding	The child's dietary data on fruit, vegetables, fish, eggs, full cream milk, butter and peanut butter consumption at 2 years of age were used to check for potential confounding by the child's diet. Results were adjusted by sex, maternal education, parental allergy, maternal smoking during pregnancy, smoking in the home at 8 years of age, breastfeeding, presence of older siblings, birthweight, maternal overweight 1 year after pregnancy, maternal supplement use during pregnancy, region and study arm (intervention or natural history arm).
Risk of bias	Moderate risk of bias: Initial study population of 4,146 mothers dropped to 2,832 participants with complete data (68.3%) (pregnancy questionnaire, at least one of the outcome time points and all confounders). Participants with complete data were more likely to have a high education level, to have daily dairy and fruit intake during pregnancy and to have breastfed and less likely to have maternal asthma or maternal atopy, smoked during pregnancy, be from a south western region compared with participants who did not have complete data.
Relevance	Dietary intakes likely to be different from Australian e.g. low fish consumption in study participants
Other comments	Not clear when women assessed their diet during pregnancy; 83% of pregnant women used supplements (50% used folic acid/iron)

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Fats and Oils

Included Studies

Study	Outcomes
1. Calvani 2006	Allergy; food sensitisation
2. Fard 2004 (RCT)	Maternal fat intake at childbirth and during lactation; birthweight and height; weight and height at one year, infant cholesterol
3. George 2005	“Breastfeeding”
4. Giordano 2008	Hypospadias and cryptorchidism
5. Gonzalez-Clemente 2007	GDM
6. Haggarty 2009	Deprivation, preterm birth
7. Haugen 2008	Preterm birth
8. Khoury 2005	Preterm birth
9. Knox 1972	Anencephalus
10. Mellies 1978; 1979 (RCT)	Cholesterol and phytosterol in maternal plasma, breast milk and infant plasma
11. Mikkelsen 2008	Preterm birth
12. Nwaru 2010	Allergic sensitisation by 5 years
13. Petridou 2005	Childhood acute lymphoblastic leukemia
14. Petridou 1998	Cerebral palsy at 8 years
15. Sausenthaler 2007	Allergic sensitisation, eczema at 2 years of age
16. Signorello 1998	Hyperemesis gravidarum
17. Stuebe 2009	GWG
18. Willers 2007	Allergy symptoms

Evidence Summaries

	N	Level	References
Maternal Outcomes			
1. In a Scottish cohort study, total maternal fat consumption during pregnancy did not differ significantly between deciles of **deprivation** on regression analysis	1277	II	Haggarty 2009
2. In a Norwegian RCT, women in the "cholesterol-lowering" diet group gained **less weight in mid-late pregnancy** than women keeping to their usual diets (MD 0.6 kg 95% CI 0.05 to 1.1)	290	II (RCT)	Khoury 2005
3. In a US cohort study, maternal consumption of fried foods (mean serve/day of 0.11) was associated with **excessive gestational weight gain**: aOR 4.24 95% CI 1.04 to 17.18 per serving per day: multivariate logistic regression model	1338	II	Stuebe 2009
4. In a cross-sectional study from Spain, cholesterol intake at time of diagnosis was associated with a significantly increased risk of **GDM**, but this association was not apparent for monounsaturated, polyunsaturated or saturated fats: • aOR 1.88 95% CI 1.09 to 3.23 of GDM for each 50 mg/1000 kcal increase of cholesterol intake	335	IV	Gonzalez-Clemente 2007
5. In a US case-control study, **hyperemesis gravidarum** was associated with a maternal diet in the year before pregnancy which was high in total fat (> 72 g/dayZ; aOR 2.9 95% CI 1.4 to 6.0 per 25 g/day increase) and saturated fat (> 28 g/day; aOR 5.4 95% CI 2.0 to 14.8 per 15 g/day increase)	44 cases; 87 controls	III-3	Signorello 1998
Birth Outcomes			
6. In a Scottish cohort study, increased rates of **preterm birth** were significantly associated with maternal diets during pregnancy which were rich in fat: aOR 1.51 95% CI 1.10 to 2.01	1277	II	Haggarty 2009
7. In a cohort study from Norway, no association was seen between **preterm birth** and maternal intake of olive or canola oil: aOR 1.00 95% CI 0.86 to 1.16 (≥ 5 versus < 5 times a day)	25,256	II	Haugen 2008
8. In a Danish cohort study, no association was seen between **preterm birth** and maternal intake of olive or canola oil: aOR 0.93 95% CI 0.84 to 1.04 (use versus no use of oil)	35,350	II	Mikkelsen 2008
9. In a Norwegian RCT, a "cholesterol-lowering" diet during pregnancy, compared with usual diet, significantly reduced the risk of **preterm birth**: RR 0.10 95% CI 0.01 to 0.77	290	II (RCT)	Khoury 2005
10. In a RCT from Iran, no evidence of effect of a fat modified diet for women during pregnancy and lactation was seen on **birthweight, length at birth, weight or height of infant at one year**	180	II (RCT)	Fard 2004
Congenital Anomalies			

11. In an Italian case-control study: • **hypospadias or cryptorchidism** was not associated with maternal consumption of dressings with animal fat during pregnancy; • **cryptorchidism (but not hypospadias)** was associated with frequent maternal consumption of fried foods during pregnancy (aOR 1.94 95% CI 1.00 to 3.75 – often versus rarely or never)	90 cases; 202 controls	III-3	Giordano 2008
12. In a Scottish case-control study, maternal intake of icecream during pregnancy was positively associated with cases of **anencephalus**: r = +0.60 after a lag interval of five months	Not reported	III-3	Knox 1972
Breastfeeding			
13. In a US cohort study, no significant differences were seen between **lactating** and nonlactating women on their postpartum consumption of foods with added fats (potato and corn chips; butter; margarine; and French fries, hash browns)	149	II	George 2005
Asthma and Allergy Outcomes			
14. In a retrospective cohort study from Italy, **food or inhalant sensitisations in children (median age of 5)** were not associated with maternal intake of either butter or margarine during pregnancy (≤ 1 serve/month versus ≥ 2-3 serves/week)	988 children	III-2	Calvani 2006
15. In a Finnish cohort study, no significant associations were seen between **food or inhalant allergen sensitisation in infants up to 5 years of age** and dietary fats overall or butter and butter spreads, margarine or low fat spreads, and oils	931 children	II	Nwaru 2009
16. In a German cohort study, • increased rates of **eczema** were associated with the following high maternal intakes during pregnancy: margarine (aOR 1.49 95% CI 1.08 to 2.04; ≥ 4 times a week) and vegetable oils (aOR 1.48 95% CI 1.14 to 1.91; 3-4 times a week) but not with butter (aOR 1.08 95% 0.79 to 1.46) or deep frying vegetable fat (aOR 1.10 95% CI 0.87 to 1.41) • **allergen sensitisation** was not associated with maternal fat and oil intake during pregnancy except for inhalant allergen sensitisation and deep frying vegetable fat (aOR 1.61 95% CI 1.02 to 2.54; ≥ 2-3 times/month)	3097 children	II	Sausenthaler 2007
17. In a Scottish cohort study, **respiratory and atopic outcomes in children up to 5 years of age** were not associated with maternal intake of either butter or margarine/low fat spread during pregnancy	1212 children	II	Willers 2007
Other Childhood Outcomes			
18. In a RCT from Iran, **infant lipid profiles at one year of age were improved** (significantly less total cholesterol, triglyceride and significantly more LDL-cholesterol) for children of women on a fat-modified (reduced) diet during pregnancy and lactation	180	II (RCT)	Fard 2004

19. In a US RCT, there was no evidence of an effect on **infant cholesterol concentrations two months after birth** for a low cholesterol diet compared with a high cholesterol diet	14	II (RCT)	Mellies 1978/9
20. In a Greek case-control study, no association was seen between **acute lymphoblastic leukemia in children up to five years of age** and maternal intake of butter or margarine (p for trend = 0.07; highest tertile median 21 g/day)	131 cases and 131 controls	III-3	Petridou 2005
21. In a Greek case-control study, **cerebral palsy in children up to eight years of age** was not associated with maternal consumption of fats and oils during pregnancy; regression analysis for each unit (once a week) aOR 1.08 95% CI 0.84 to 1.40	138 cases; 138 controls	III-3	Petridou 1998

Evidence Tables

Reference	**Calvani 2006**
Food type	Butter; margarine
Study type	Retrospective cohort study
Level of evidence	III-2 (aetiology)
Setting	Rome, Italy
Funding	Not reported
Participants	988 offspring of allergic (n = 295) and non-allergic (n = 693) mothers; recruited from outpatient allergy clinics between September 2001 and March 2002; with a median age of 5 years (range of 17 years); part of the APAL study 744/988 children were affected by atopic diseases (asthma, rhinitis, eczema) and the remaining 244 were attending due to respiratory, gastrointestinal symptoms, or skin disease; Exclusions: immunodeficiency, connective tissue disease, or chronic respiratory tract disease other than asthma
Baseline comparisons	*See Confounding below*
Dietary assessment	Questionnaire
Timing	At recruitment, women were asked to recall their intake of fish, butter and margarine during pregnancy
Comparison	≤ 1 serve/month (reference) v 1 serve/week v ≥ 2-3 serves/week
Outcomes	Allergic sensitisations
Results	See below

Results

Butter

Food sensitisation (positive skin prick test mainly for raw cow's milk and egg-white)

	n/N (%)	OR (95% CI)	aOR (95% CI)*	p-value for trend
Allergic mothers				
≤ 1 serve/month	19/156 (12.2%)	1	1	0.80
1 serve/week	6/72 (8.3)	0.65 (0.25 to 1.71)	0.49 (0.16 to 1.43)	
≥2-3 serves/week	6/49 (12.2%)	1.00 (0.37 to 2.67)	0.84 (0.26 to 2.71)	

*adjusted for age, occupation and eczema

	n/N (%)	OR (95% CI)	aOR (95% CI)*	p-value for trend
Non-allergic mothers				
≤ 1 serve/month	29/373 (7.8)	1	1	0.46
1 serve/week	11/168 (6.5%)	0.83 (0.40 to 1.70)	0.91 (0.37 to 2.25)	
≥2-3 serves/week	5/86 (5.8%)	0.73 (0.27 to 1.95)	0.92 (0.27 to 3.13)	

*adjusted for age, gestation age, maternal occupation, oculorhinitis and eczema

Inhalant sensitation (positive skin prick test for a range of allergens)

	n/N	OR (95% CI)	aOR (95% CI)*	p-value for trend
Allergic mothers				
≤ 1 serve/month	76/156 (48.7%)	1	1	0.77
1 serve/week	25/72 (34.7%	**0.55 (0.31 to 0.99)**	**0.27 (0.10 to 0.73)**	
≥2-3 serves/week	28/49 (57.1%)	1.40 (0.73 to 2.68)	1.59 (0.51 to 4.97)	

*adjusted for age, allergy clinics, maternal age, preterm labour, occupation, asthma, oculorhinitis and eczema

	n/N	OR (95% CI)	aOR (95% CI)*	p-value for trend
Non-allergic mothers				
≤ 1 serve/month	150/373 (40.2%)	1	1	0.15
1 serve/week	88/168 (52.4%)	**1.6□(1.13 to 2.35)**	**1.73 (1.00 to 2.99)**	
≥2-3 serves/week	37/86 (43%)	1.12 (0.69 to 1.80)	0.81 (0.38 to 1.70)	

*adjusted for age, gender, number of older siblings, allergy clinics, maternal age, number of pregnancies, maternal occupation, paternal atopy, □asthma, oculorhinitis

Margarine
Food sensitisation (positive skin prick test mainly for raw cow's milk and egg-white)

	n/N (%)	OR (95% CI)	aOR (95% CI)*	p-value for trend
Allergic mothers				
≤ 1 serve/month	24/214 (11.2%)	1	1	□0.67
1 serve/week	2/34 (5.9%)	0.49 (0.11 to 2.19)	0.26 (0.02 to 2.54)	
≥2-3 serves/week	4/22 (18.2%)	1.75 (0.54 to 5.63)	2.24 (0.59 to 8.49)	

*adjusted for age, occupation and eczema

	n/N (%)	OR (95% CI)	aOR (95% CI)*	p-value for trend
Non-allergic mothers				
≤ 1 serve/month	39/528 (7.4%)	1		□0.45
1 serve/week	□3/43 (7.0%)	0.94 (0.27 to 3.17)	1.63 (0.38 to 6.87)	
≥2-3 serves/week	2/47 (4.3%)	0.55 (0.13 to 2.38)	0.51 (0.06 to 4.32)	

*adjusted for age, gestation age, maternal occupation, oculorhinitis and□eczema

Inhalant sensitisation (positive skin prick test for a range of allergens)

	n/N	OR (95% CI)	aOR (95% CI)*	p-value for trend
Allergic mothers				
≤ 1 serve/month	100/214 (46.7%)	1	1	0.85
1 serve/week	13/34 (38.2%)	0.70 (0.33 to 1.48)	0.39 (0.10 to 1.48)	
≥2-3 serves/ week	12/22 (54.5%)	1.36 (0.56 to 3.30)	3.02 (0.52 to 17.2)	

*adjusted for age, allergy clinics, maternal age, preterm labour, occupation, asthma, oculorhinitis and eczema

	n/N	OR (95% CI)	aOR (95% CI)*	p-value for trend
Non-allergic mothers				
≤ 1 serve/month	229/5□8 (43.4%)	1	1	0.54
1 serve/week	25/43□(58.1%)	1.81 (0.96 to 3.40)	1.28 (0.53 to 3.07)	
≥2-3 serves/ week	20/47 (42.6%)	0.69 (0.52 to 1.76)	0.52 (0.19 to 1.43)	

*adjusted for age, gender, number of older siblings, allergy clinics, maternal age, number of pregnancies, maternal occupation,□paternal atopy, asthma, oculorhinitis

Followup	NA
Confounding	Analyses only adjusted for a limited number of factors; different factors were used for the analyses of allergic and non-allergic mothers; and for food and inhalant sensitisations.
Risk of bias	Moderate risk of bias: recall bias likely for women remembering diet during a pregnancy up to 17 years earlier; data for maternal atopy available for 988 of the 1044 consecutively recruited children (94.6%); children attending allergy clinics likely to be different for a general population of children.
Relevance	Diets of pregnant Italian women may differ from those of Australian women e.g. lower levels of maternal margarine and butter consumption in this study
Other comments	Clinical significance of skin prick tests?; Wide age range (1 to 18?) makes interpretation of allergic sensitisations difficult

Reference	**Fard 2004**

Dietary patterns	*See comparison below*
Study type	RCT
Level of evidence	II (intervention)
Setting	Isfahan Cardiovascular Research Center, Iran
Funding	Not reported
Participants	180 pregnant women, aged 18-35 years, at 4 month's gestation with atherogenic diets (total fat ≥ 30% or saturated fat intake ≥ 10% of daily energy intake or whose daily cholesterol intake was > 300 mg) Exclusions: diabetic women, history of heart disease, hypothyroidism, hyperthyroidism, severe obesity (≥ 40) or having twins
Baseline comparisons	n/a
Assessment	n/a
Timing	Intervention during pregnancy and lactation (up to one year of birth)
Comparison	Fat modified diet (saturated fatty acid < 10%; monosaturated fatty acids 10-15%; polyunsaturated fat up to 10%; cholesterol < 300 mg/day) and dietary advice during pregnancy versus dietary advice alone
Outcomes	Maternal fat intake, serum lipids of infants at birth; and one year of age
Results	See below

Fat intake of women at childbirth (mean, SD)	**Intervention (n = 90)**	**Control (n = 90)**	**P**
Total fat (% energy)	**27.5 [2.4]**	**28.5 [2.2]**	**0.004**
Saturated fatty acid (% energy)	**5.7 [3.6]**	**14.7 [6.1]**	**0.000**
Monounsaturated fatty acid (% energy)	**13.6 [4.1]**	**6.9 [3.2]**	**0.000**
Polyunsaturated fatty acid (% energy)	**9.2 [3.6]**	**5.3 [3.9]**	**0.000**
Cholesterol (mg)	261 [112]	289 [149]	0.15
Fat intake of women during lactation (mean, SD)			
Total fat (% energy)	27.3 [5.8]	25.8 [10.4]	pns
Saturated fatty acid (% energy)	**5.8 [3.4]**	**14.8 [7.6]**	**0.000**
Monounsaturated fatty acid (% energy)	**12.6 [4.7]**	**7.1 [4.4]**	**0.000**
Polyunsaturated fatty acid (% energy)	**8.9 [3.1]**	**3.9 1.6]**	**0.000**
Cholesterol (mg)	272 [143]	279 [151]	pns
Placental lipid profile (mg/dl (mean, SD))			
Total cholesterol	**70.3 [15.9]**	**81.4 [17.2]**	**0.009**
Triglyceride	**85.3 [16.7]**	**97.5 [18.2]**	**0.00**
LDL-cholesterol	**27.8 [15.2]**	**34.8 [17.1]**	**0.04**
HDL-cholesterol	25.8 [4.3]	27 [5.7]	0.35
Non-HDL-cholesterol	**44.5 [7.2]**	**54.5 [8.1]**	**0.02**
Infant lipid profile (at one year) (mg/dl, (mean, SD))			
Total cholesterol	**145.7 [51.4]**	**161.4 [56.2]**	**0.03**
Triglyceride	**90.1 [13.8]**	**98.3 [33.1]**	**0.02**
LDL-cholesterol	**85.6 [20.4]**	**92.3 [19.6]**	**0.05**
HDL-cholesterol	32.1 [8.7]	32.6 [8.5]	0.43
Non-HDL-cholesterol	**113.6 [30.2]**	**128.8 [34.7]**	**0.04**
Birthweight (kg)	3.5 [2.7]	3.6 [3.2]	pns
Height at birth (cm)	50.4 [10.8]	51.2 [12.2]	pns

	Weight at one year (kg)	11.4 [3.5]	12.1 [4.8]	pns
	Height at one year (cm)	77.3 [18.7]	80.9 [20.1]	pns
Followup	Until children reached one year of age			
Confounding	n/a			
Risk of bias	Unclear risk of bias: randomisation method described only as “divided into two groups randomly”			
Relevance	Likely to be reasonably relevant, though Iranian diet may differ from that of Australian women			
Other comments				

Reference	**George 2005**
Food type	Foods with added fats: potato and corn chips; butter; margarine; French fries, hash browns
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Texas, US
Funding	Not reported
Participants	149 Medicaid-qualified women (30% white, 24% African American, 46% Hispanic) – recruited from a larger study on postpartum weight retention Inclusion criteria: 18 years or older; non-Hispanic white, African American or Hispanic ethnicity; birth of a healthy term infant, fluency and literacy in English; absence of pregnancy-related abnormalities and disease conditions.
Baseline comparisons	Significant differences between lactating and non-lactating women – higher parity, BMI and lower education levels in non-lactating women.
Dietary assessment	Semiquantitative FFQ to cover pregnancy and first six months postpartum
Timing	FFQ administered at 6 weeks and 6 months postpartum
Comparison	Proportion of consumption of different types of foods with added fats
Outcomes	Breastfeeding (exclusive or partial at 6 months postpartum)
Results	No significant differences seen between lactating and lactating women on their postpartum consumption of potato and corn chips; butter; margarine; French fries, hash browns
Followup	6 months postpartum
Confounding	No adjustment for potential confounding
Risk of bias	Moderate-to-high risk of bias; no attempt to control for confounding despite significant baseline differences between lactating and non-lactating women.
Relevance	Possibly relevant to low-income women in Australia
Other comments	Minimal reporting of results

Reference	**Giordano 2008**
Food type	Fats and oils: dressings with animal fat (lard, butter etc), fried foods
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Sicily, Italy
Funding	Sicilian Congenital Malformation Registry
Participants	90 cases: 43 cases of hypospadias and 48 cases of cryptorchidism (both in one infant) 202 controls: randomly selected controls born in the same year and the same region Births between 1998 to 2003
Baseline comparisons	Low birthweight, low maternal education, mother's history of gynaecological disease and father's history of urogenital diseases differed significantly between cases and controls *See confounding below*
Dietary assessment	Interview on maternal diet and food frequencies
Timing	FFQ
Comparison	Consumption of dressings with animal fat once a week or less vs more than once a week; Consumption of fried foods never or rarely vs often
Outcomes	Hypospadias and cryptorchidism
Results	***<u>Dressings with animal fat</u>*** **<u>Hypospadias</u>** **Cases** / **Controls** / **OR** **No**: 40 (93.0%) / 178 (88.1%) / 1.00 **Yes**: 3 (7.0%) / 24 (11.9%) / 0.56 95% CI 0.16 to 1.94 **<u>Cryptorchidism</u>** **No**: 44 (91.7%) / 178 (88.1%) / 1.00 **Yes**: 4 (8.3%) / 24 (11.9%) / 0.67 95% CI 0.22 to 2.04 **<u>Hypospadias and cryptorchidism</u>** **No**: 83 (92.2%) / 178 (88.1%) / 1.00 **Yes**: 7 (7.8%) / 24 (11.9%) / 0.63 95% CI 0.26 to 1.51 ***<u>Fried food: adjusted analysis*</u>*** **aOR** **Hypospadias** **Often**: 0.78 95% CI 0.35 to 1.74 **Cryptorchidism** **Often**: **1.94 95% CI 1.00 to 3.75** **Hypospadias and cryptorchidism** **Often**: 1.27 95% CI 95% CI 0.73 to 2.20
Followup	n/a
Confounding	*Fried food was were additionally adjusted for mother's age, parity, education, gynaecological diseases; paternal urogenital diseases, and use of pesticides; birthweight

Risk of bias	Moderate risk of bias: Participation rate of parents and data collection rate of cases was lower than that of controls (76% versus 91%)
Relevance	Likely to be reasonably relevant for Australian women, although hypospadias rates very high and unlikely that most Australian women will have such high pesticide exposure
Other comments	Ragusa region in Sicily is a region of intensive agriculture (involving high rates of pesticide and other chemical use) with high rates of hypospadias and cryptorchidism

Reference	**Gonzalez-Clemente 2007**
Dietary patterns	Total fat, saturated fat, monounsaturated fat, polyunsaturated fat; cholesterol
Study type	Cross-sectional study
Level of evidence	IV (aetiology)
Setting	Barcelona, Spain
Funding	Institut Universitari Parc Tauli; Instituto de Salud Carlos III, Ministerio de Sanidad y Consumo, Spain
Participants	335 pregnant women, consecutively referred for gestational diabetes mellitus screening (93 between 14 to 18 weeks gestation and the remainder between 18 and 28 weeks gestation) Exclusions: pregnant women known to have diabetes mellitus or a disease affecting glucose metabolism
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	Assessed at screening for gestational diabetes mellitus, to reflect dietary intake in the previous year
Comparison	Intake of saturated, polyunsaturated and monounsaturated fat; and cholesterol
Outcomes	GDM
Results	| | **GDM** | **no GDM** | **p** | | **Saturated fat (% total kcal)** | 11.2 [SEM 0.1] | 11.2 [SEM 0.2] | 0.99 | | **Polyunsaturated fat (% total kcal)** | 5.7 [SEM 0.1] | 5.7 [SEM 0.2] | 0.84 | | **Monounsaturated fat (% total kcal)** | 20.0 [SEM 0.2] | 20.1 [SEM 0.5] | 0.89 | | **Cholesterol (mg/100 kcal)** | **134.5 [SEM 1.6]** | **145.3 [SEM 4.5]** | **0.03** | **<u>Cholesterol intake (multiple logistic regression analysis)*</u>** **aOR 1.88 95% CI 1.09 to 3.23 of GDM for each 50 mg/1000 kcal increase of cholesterol intake**
Followup	To 28 weeks gestation
Confounding	*adjusted for age, BMI before pregnancy, family history of type 2 diabetes, previous GDM, protein intake, carbohydrate intake, fat intake, saturated, polyunsaturated and monounsaturated fat intake, fibre intake and trans unsaturated fat intake
Risk of bias	Low risk of bias: women were consecutively recruited
Relevance	Of some relevance to Australian women, although diet composition of Spanish women likely to have some differences
Other comments	A high cholesterol intake was the only dietary factor associated with a diagnosis of GDM in this group of pregnant women on a Mediterranean diet (rich in monosaturated fat)

Reference	**Haggarty 2009**
Dietary patterns	Total fat, saturated fat, monounsaturated fat, polyunsaturated fat; fried potatoes
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Aberdeen, Scotland
Funding	UK Food Standards Agency
Participants	1277 sequentially enrolled pregnant women attending Aberdeen Maternity Hospital for ultrasound (a further 184 women were recruited later in pregnancy). Exclusions: diabetic women, women with multiple pregnancies, women who conceived as a result of fertility treatment, or clinical dat not available
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	Assessed at 19 weeks gestation
Comparison	Deciles of deprivation
Outcomes	Deprivation (assessed using the Scottish Index of Multiple Deprivation); Low birthweight (defined as < 2500 g or lowest decile for birthweight z score adjusted for gestational age, sex and parity) Preterm birth (< 37 weeks) Admission to neonatal unit
Results	**Deprivation** Pattern for dietary fat was complicated, with total fat, saturated, monounsaturated, and polyunsaturated fat following a biphasic relationship with “deprivation decile” i.e. higher for both low and high deprivation compared with the mid ranges of deprivation Total fat consumption did not differ significantly between deciles of deprivation on regression analysis Fried potatoes: significantly higher intake with higher levels of deprivation ($p < 0.001$) **Preterm birth:** aOR for diets rich in fat: **1.51 95% CI 1.10 to 2.01**
Followup	To neonatal period
Confounding	(Some?) analyses adjusted for energy intake
Risk of bias	Low to moderate risk of bias: low attrition, some lack of detail in reporting of outcomes
Relevance	Likely to be relevant to Australian women
Other comments	About 40-50% of the least deprived women reported taking folic acid supplements compared with about 20% for the most deprived women; Most birth outcome associations were reported by nutrient rather than food group; Not easy to deduce quantities of intake of foods (main graphs reported as change in intake by deprivation decile)

Reference	**Haugen 2008**
Dietary patterns	Olive/canola oil as part of Mediterranean-type diet (2 or more serves of fish per week)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Norway (part of the Norwegian Mother and Child Cohort Study (MoBa))
Funding	Norwegian Ministry of Health, NIH/NINDS, Norwegian Research Council/FUGE, EU FP& consortium, Metabolic Programming (EARNEST).
Participants	40,817 pregnancies of women recruited for MoBa from February 2002 to February 2005 of whom 26,563 (65%) met the following criteria: women had to be non-smoking, BMI between 19 and 32, aged between 21 and 38 years when giving birth, with a singleton birth. Exclusions: more than 3 spontaneous abortions, energy intake less than 4,200 kJ and more than 16,700 kJ.
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	at 17-24 weeks gestation
Comparison	Olive/canola oil ≥ 5 times per day v < 5 times a day
Outcomes	Preterm birth (after week 21 and before week 37); late preterm birth (week 35-36) and early preterm birth (< 35 weeks)
Results	***Preterm birth (< 37 weeks): (n = 25,966; 1174 cases)*** OR 0.92 95% CI 0.80 to 1.06 aOR 1.00 95% CI 0.86 to 1.16 ***Early preterm birth (< 35 weeks): (n = 25,256; 474 cases)*** OR 0.93 95% CI 0.74 to 1.16 aOR 1.02 95% CI 0.81 to 1.28 ***Late preterm birth (35-36 weeks): (n = 25,492; 710 cases)*** OR 0.91 95% CI 0.76 to 1.10 aOR 0.98 95% CI 0.82 to 1.19
Followup	To birth
Confounding	Analyses were adjusted for remaining Mediterranean diet criteria, mother's BMI and height, educational level, parity and marital status
Risk of bias	Moderate risk of bias: some dietary intakes were different between groups and were not controlled for
Relevance	Moderate: low red meat consumption not typical for many Australian women
Other comments	Preterm birth rates were lower than expected, likely due to exclusion of smokers

Reference	**Khoury 2007**
Food type	“Cholesterol-lowering” diet (promoting fish, low-fat meats and dairy products, oils, wholegrains, fruits, vegetables and legumes)
Study type	RCT – CARDIPP (Cardiovascular Risk Reduction Diet in Pregnancy) study
Level of evidence	II (intervention)
Setting	Oslo, Norway
Funding	Norwegian Council on Cardiovascular Disease
Participants	290 nonsmoking white women with singleton pregnancies, aged between 21 and 38 years, with no previous pregnancy-related complications (who were not vegetarian or following a Mediterranean-type diet)
Baseline comparisons	n/a
Dietary assessment	n/a
Timing	Diet commencing from 17 to 20 weeks gestation
Comparison	“Cholesterol-lowering” diet (141 women randomised) versus usual diet (149 women randomised)
Outcomes	Gestational weight gain; maternal cholesterol concentrations; neonatal lipid profiles; preterm birth < 37 weeks
Results	***Gestational weight gain (week 17-20 to week 30):*** Diet group: mean 5.4 kg [SD 2.3] Control group: mean 6.0 kg [SD 2.2] **MD 0.6 kg 95% CI 0.05 to 1.1** ***Total maternal cholesterol at week 36 (mg/dL)*** Diet group (n=127): mean 257 [SD 45.9] Control group (n=132): mean 259 [SD 43.8] pns ***Total neonatal cholesterol (mg/dL)*** Diet group (n=125): mean 113 [SD 25] Control group (n=134): mean 107 [SD 23] pns ***Preterm birth*** **Diet group: 1/141 vs Control group: 11/149: RR 0.10 95% CI 0.01 to 0.77**
Followup	To birth
Confounding	n/a
Risk of bias	Low-moderate risk of bias; method of allocation concealment not reported; 21/290 (7%) losses to follow-up (results also presented with all 290 women included)
Relevance	Likely to be reasonably similar to Australian women
Other comments	

Reference	**Knox 1972**
Food type	Fats and oils (icecream)
Study type	Case control (cases matched to food consumption at population level for a particular period)
Level of evidence	III-3 (aetiology)
Setting	Birmingham, UK
Funding	Not reported
Cases	Stillbirths and infant deaths due to anencephalus between 1961 and 1967
Baseline comparisons	n/a
Dietary assessment	Population surveys
Timing	Each quarter
Comparison	Monthly stillbirths and infant deaths due to anencephalus matched to quarterly consumption of main food stuffs (in previous five to nine months)
Outcomes	Anencephalus
Results	**Icecream positively associated with cases of anencephalus: r = +0.60 after a lag interval of five months** (icecream also included in dairy foods)
Followup	n/a
Confounding	Analyses were not adjusted
Risk of bias	High risk of bias: links between population consumption of foods and anencephalus very distal and no control for potential confounders
Relevance	Likely to differ from a modern Australian diet
Other comments	Food consumption of total population not likely to reflect food consumption of pregnant women; and will not be able to reflect differences between diets of individual or specific groups

Reference	**Mellies 1978; 1979**
Dietary patterns	*See comparisons below*
Study type	RCT (cross-over)
Level of evidence	II (intervention)
Setting	Cincinnati, USA
Funding	General Clinical Research Center, Mead Johnson Company, Ross Laboratories
Participants	14 lactating mothers and their healthy term infants Exclusions: women with thyroid, hepatic, renal or diabetic disorders
Baseline comparisons	n/a
Dietary assessment	n/a
Timing	Women were randomised 30 days after birth; After 4 weeks on either diet, mothers crossed over to the other diet for a second 4 week period
Comparison	Diet containing 190 mg cholesterol and 1200 mg phytosterol per day and a polyunsaturated/saturated fat ratio of 1.8 Versus High cholesterol diet (520 mg cholesterol and 50 mg phytosterol per day and a polyunsaturated/saturated fat ratio of 0.12
Outcomes	Cholesterol and phytosterol in maternal plasma, breast milk and infant plasma
Results	No significant correlations were observed between maternal plasma and milk cholesterol levels, or between maternal milk and infant plasma cholesterol levels
Followup	2 months after birth
Confounding	n/a
Risk of bias	Unclear risk of bias: details about randomisation and losses to follow-up not full reported
Relevance	Low cholesterol diet may be difficult to adhere to
Other comments	

Reference	**Mikkelsen 2008**
Dietary patterns	Mediterranean diet (consumption of fish twice a week or more, **intake of olive or canola oil**, high consumption of fruits and vegetables (5 a day or more), meat (other than poultry or fish) at most twice a week, and at most 2 cups of coffee a day)
Study type	Prospective cohort study
Level of evidence	II
Setting	Denmark (part of the Danish National Birth Cohort (DBNC))
Funding	March of Dimes Birth Defects Foundation, Danish National Research Foundation, Danish Medical Research Foundation, Danish Health Foundation, Danish Heart Foundation, EU FP7 consortium (EARNEST), Pharmacy Foundation, Egmont Foundation, Augustinus Foundation.
Participants	35,530 pregnant women recruited from 1996 to 2002 Exclusions: women who smoked, women aged < 21 and > 38 years, BMI < 19 and > 32, a history of more than 3 abortions, twin pregnancies, chronic hypertension, women with a calculated energy intake < 4,200 kJ and > 16,700 kJ
Baseline comparisons	BMIs were significantly lower in the MD and no use of oil groups.
Dietary assessment	FFQ
Timing	FFQ mailed to all DBNC participants in 25th week of gestation
Comparison	Assumed to be use of olive oil or canola oil v no use
Outcomes	Preterm birth
Results	**Preterm birth < 37 weeks** OR 0.95 95% CI 0.86 to 1.06 aOR 0.93 95% CI 0.84 to 1.04 **Early preterm birth < 35 weeks** OR 1.03 95% CI 0.87 to 1.22 aOR 1.02 95% CI 0.86 to 1.23 **Late preterm birth 35-36 weeks** OR 0.91 95% CI 0.80 to 1.04 aOR 0.89 95% CI 0.78 to 1.02
Followup	To birth
Confounding	Adjusted for parity, BMI, maternal height, socioeconomic status and cohabitant status
Risk of bias	Low risk of bias; GA based mostly on ultrasound; 0.36% missing data (127/35657)
Relevance	Relevance limited by exclusion of smokers and obese women
Other comments	

Reference	**Nwaru 2010**
Food type	Fats and oils: total; butter and butter spreads; margarine and low fat spreads; oils
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Tampere, Finland
Funding	Academy of Finland, Finnish Pediatric Research Foundation, the Juho Vainio Foundation, the Yrjo Jahnsson Foundation, Turku, Oulu and Tampere University Hospitals, JDRF, Novo Nordisk Foundation, EU Biomed 2 Program
Participants	931 mother-infant pairs (children with human leukocyte antigen-conferred susceptibility to type 1 diabetes) participating in the Finnish type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study between September 1996 and October 1997
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ given to women after birth, for return at the three month visit (FFQ intended to cover maternal diet during pregnancy and lactation)
Comparison	Amount and type of fat intake
Outcomes	Allergic sensitisation in offspring by 5 years: food allergens (egg, cow's milk, fish, wheat); inhalant allergens (house dust mite, cat, timothy grass, birch)
Results	**Dietary fats** ***Food allergens*** / ***Inhalant allergens*** OR 0.79 95% CI 0.49 to 1.29 / OR 0.91 95% CI 0.60 to 1.41 aOR 0.86 95% CI 0.50 to 1.48 / aOR 1.07 95% CI 0.66 to 1.73 - **Butter and butter spreads** ***Food allergens*** / ***Inhalant allergens*** OR 1.05 95% CI 0.81 to 1.35 / OR 1.15 95% CI 0.92 to 1.43 aOR 1.08 95% CI 0.81 to 1.43 / aOR 1.20 95% CI 0.94 to 1.54 - **Margarine and low fat spreads** ***Food allergens*** / ***Inhalant allergens*** OR 0.96 95% CI 0.78 to 1.17 / OR 0.93 95% CI 0.79 to 1.10 aOR 0.95 95% CI 0.76 to 1.20 / aOR 0.96 95% CI 0.79 to 1.17 - **Oils** ***Food allergens*** / ***Inhalant allergens*** OR 0.86 95% CI 0.55 to 1.36 / OR 1.19 95% CI 0.75 to 1.67 aOR 0.83 95% CI 0.51 to 1.36 / aOR 0.97 95% CI 0.62 to 1.49
Followup	To 5 years
Confounding	Adjusted for energy intake, place of birth, season of birth, sex of the child, number of siblings, gestational age at birth, parental asthma, parental allergic rhinitis, maternal age at birth, maternal smoking during pregnancy, maternal education
Risk of bias	Low risk of bias: data available for 931/1175 (79.2%) children recruited – 108 did not participate in survey, a further 49 did not have IgE measurements, a further 87 had no FFQ or an incomplete FFQ
Relevance	Likely to be relevant to Australian women
Other comments	28% of women took vitamin D supplements, 73% took iron supplements; HLA genotype not likely to have any impact on the development of allergic diseases.

Reference	**Petridou 2005**

Food type	Butter/margarine
Study type	Case-control study
Level of evidence	III-3
Setting	Greece
Funding	The Childhood Hematology-Oncology Group: Athens University Medical School, Aristotle University of Thessaloniki, University Hospital of Heraklion
Participants	Cases: 131 children with acute lymphoblastic leukemia, aged 12 to 59 months, gender and age matched to Controls: 131 children hospitalised for minor conditions between 1999 and 2003
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During index pregnancy
Comparison	Tertiles of butter/margarine – median Q1; 0 g/day: median Q3 21 g/day
Outcomes	Acute lymphoblastic leukemia (ALL)
Results	**Acute lymphoblastic leukemia (ALL)** **Median g/day / Cases / Controls / p for trend** Q1: 0 / 42 / 51 Q2: 6 / 45 / 50 Q3: 21 / 44 / 30 / 0.07 Logistic regression: one tertile more of butter/margarine: aOR 1.41 95% CI 0.97 to 2.06
Followup	NA
Confounding	Total energy intake (but not mutually among food groups); matching variables; maternal age at birth; birthweight; maternal smoking during pregnancy; maternal years of schooling, maternal occupation
Risk of bias	Moderate: moderate risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy some time previously; Cases: 171 children with ALL were identified; 21 had missing data, consent was not given in 9 cases and 10 were unable to be matched, leaving 131 (77%) of cases available
Relevance	Diets of Greek women may differ from current diets of Australian women
Other comments	

Reference	**Petridou 1998**
Food type	Fats and oils: butter on bread, butter for cooking, margarine on bread, margarine for cooking, seed oils, olive oils, olives.
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Greater Athens area, Greece
Funding	Greek Ministry of Health and Welfare, and Foundation for Research in Childhood 'S. Doxiadis'
Participants	Cases: 109 children with cerebral palsy (CP), born between 1984 and 1988 (estimated to be two-thirds of the children with CP born during this period) Controls (1): 155 neighbouring children of similar sex and age (± 12 months) Controls (2): 99 healthy siblings of similar sex and age (± 12 months) of the first neurological patient seen by the attending physician after a visit by the CP patient
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During pregnancy
Comparison	≤ 8 versus 9 v 10 v > 10 serves of fats and oils per week; regression analysis: risk of cerebral palsy with change in consumption by one unit (= consumption of fats and oils once per week)
Outcomes	Cerebral palsy
Results	≤ 8 serves of fats and oils per week: 10/91 (11.0%) cases v 32/246 (13.0%) controls 9 serves of fats and oils per week: 25/91 (27.4%) cases v 67/246 (27.2%) controls 10 serves of fats and oils per week: 23/91 (25.3%) cases v 64/246 (26.0%) controls > 10 serves of fats and oils per week: 33/91 (36.3%) cases v 83/246 (33.8%) Regression analysis for each unit of consumption of fats and oils (once per week): aOR 1.09 95% CI 0.85 to 1.39 aOR 1.08 95% CI 0.84 to 1.40 (additionally adjusted for all food groups)
Followup	8 years
Confounding	Age and sex of child, maternal age at birth, maternal age at menarche, maternal chronic disease, previous spontaneous abortions, persistent vomiting during index pregnancy, multiple pregnancy, number of obstetric visits; timing of membrane rupture in index birth, use of general anaesthesia in the index birth, mode of birth, abnormal placenta, infant head circumference at birth, congenital malformation, place of index birth, use of supplementary iron during index pregnancy, physical exercise during index pregnancy, painless childbirth classes. The following were not included in the model: - Smoking or consumption of coffee or alcohol during pregnancy (stated to be "unrelated to CP and had no confounding influence"); - Gestational age, birthweight and maternal weight gain (stated to be "strong predictors of CP, but were not included in the model, since they are probably intermediate stages in a possible link between diet and CP (mediators) rather than genuine confounders"
Risk of bias	Moderate-high: High risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy 8 years previously; Cases: 109 children with CP were identified; for 6 children either collaboration with their guardian or a diagnosis of CP was not confirmed; and reliable maternal dietary intakes were not available for 12 women, leaving 91 cases available for analysis. Controls: 278 mother-child pairs were approached; 16 refused to participate; matching controls were not available in 8 instances, and reliable maternal dietary intakes were not available for 8 women, leaving 246 controls available for analysis.
Relevance	Diets of Greek women in 1998 may differ from current diets of Australian women
Other comments	

Reference	**Sausenthaler 2007**

Food groups	Fats and oils
Study type	Prospective cohort study: from the LISA birth cohort
Level of evidence	II (aetiology)
Setting	4 German cities (Munich, Leipzig, Wesel, Bad Honnef)
Funding	Federal Ministry for Education, Science, Research and Technology, Germany
Participants	3097 newborns recruited
Baseline comparisons	*See Confounding below*
Dietary assessment	FFQ
Timing	Maternal diet during the last 4 weeks of pregnancy (obtained shortly after birth, median 3 days)
Variable	Low intake group as reference group compared with high intake group: • Butter high intake = 3-4 times/week • Margarine high intake = ≥ 4 times/week • Vegetable oils high intake = 3-4 times/week • Deep frying vegetable fat high intake = ≥ 2-3 times/month
Outcomes	Allergic sensitisation, eczema at 2 yrs
Results	

	Doctor-diagnosed eczema	Any allergen sensitisation	Food allergens	Inhalant allergens
Fats and oils		Adjusted OR (95% CI)		
Butter	1.08 (0.79, 1.46)	0.97 (0.66, 1.42)	0.93 (0.60, 1.43)	0.86 (0.48, 1.53)
Margarine	**1.49 (1.08, 2.04)**	0.85 (0.56, 1.27)	0.80 (0.50, 1.27)	0.93 (0.50, 1.73)
Vegetable oils	**1.48 (1.14, 1.91)**	0.88 (0.63, 1.25)	0.91 (0.61, 1.34)	0.89 (0.53, 1.51)
Deep frying veg. fat	1.10 (0.87, 1.41)	1.25 (0.92, 1.70)	1.12 (0.79, 1.58)	**1.61 (1.02, 2.54)**

Length of followup	2 years
Confounding	Crude and adjusted results reported (adjusted for study area, sex, maternal age, maternal smoking, level of parental education, exclusive breastfeeding ≥ 4 months, parental history of atopic diseases, season of birth and all dietary variables
Risk of bias	Low risk of bias: Two year data available for 2641/3097 children (85%): 433 lost to follow-up, 9 excluded due to chronic disease, 14 missing maternal FFQ
Relevance	Likely to be reasonably similar to dietary intakes of Australian women in Australia
Other comments	

Reference	**Signorello 1998**
Food groups	Fats
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Boston, MA, USA
Funding	Milton Fund, Harvard Medical School, Boston, MA
Participants	Cases: 44 women previously hospitalised for severe hyperemesis gravidarum with a singleton birth between January 1, 1993 and Decemeber 31, 1995 Controls: 87 women at the same hospital with a singleton birth during the same period who experienced less than 20 hours of nausea and fewer than thre episodes of vomiting over the duration of their pregnancies
Baseline comparisons	Controls had higher education levels and were more likely to be employed
Dietary assessment	FFQ
Timing	To reflect average diet in the year before pregnancy
Variable	Total fat and saturated fat intake
Outcomes	Severe hyperemesis gravidarum
Results	

	Cases	*Controls*	*(a)OR (95% CI)*
Total fat intake (g/day)			
<53	6	28	1.0
53-72	11	30	1.7 (0.6 to 5.2)
>72	27	29	**4.3 (1.6 to 12.1)**
Total fat intake (per 25 g increase)			**aOR 2.9 (1.4 to 6.0)**
Saturated fat intake (g/day)			
<18	6	29	1.0
18-28	17	31	2.7 (0.9 to 7.6)
>28	21	27	**3.8 (1.3 to 10.7)**
Total saturated fat intake (per 15g increase) (Equivalent to 70 g cheddar cheese)			**aOR 5.4 (2.0 to 14.8)**

Length of followup	NA
Confounding	Adjusted for age, year of infant's birth, total energy intake, vitamin C intake, education, employment status
Risk of bias	Low risk of bias: Cases: 44/70 (63%) of women approached participated; controls: 87/131 (66%) of women approached participated; 40 cases and 80 controls were appropriately matched
Relevance	Likely to be reasonably similar to dietary intakes of Australian women in Australia
Other comments	Also assessed other food groups; these data were presented as nutrient intakes only (only fat intake showed a significant relationship with hyperemesis gravidarum); there was not a significant association with total energy intake

Reference	**Stuebe 2009**

Dietary patterns	Fats and oils: Fried foods
Study type	Prospective cohort study (Project Viva)
Level of evidence	II (aetiology)
Setting	8 urban and suburban obstetric offices of a multispecialty group practice in eastern Massachusetts, USA
Funding	US NIH, Harvard Medical School, Harvard Pilgrim Health Care Foundation
Participants	1338 women giving birth to a live singleton infant, < 22 weeks gestation at study entry; 379 (27%) were overweight (BMI ≥ 26); 703 (51%) experienced excessive weight gain Exclusions: not fluent in English
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Administered in first and second trimesters of pregnancy
Comparison	Fried foods: serves per day
Outcomes	Excessive gestational weight gain (IOM 1990)
Results	**Excessive gestational weight gain: fried food consumption** **Serves per day, median (0.11 IQR 0.07 to 0.14)** **Excessive GWG versus adequate/inadequate** Fried foods **aOR 3.68 95% CI 0.96 to 14.13** **Fried foods, per serving per day: multivariate logistic regression model:** **aOR GWG: 4.24 95% CI 1.04 to 17.18** **Total weight gain** 1.21 kg 95% CI -1.93 to 4.34
Followup	To birth
Confounding	Adjusted for pre-pregnancy BMI, maternal age, race/ethnicity, smoking status, gestational age at birth, nausea in first trimester in pregnancy
Risk of bias	Low risk of bias: Of 2083 eligible women, 1388 (67%) of women had data available for analysis (31 had missing information on pre-pregnancy BMI and gestational weight gain; 226 had missing covariate information and 438 had missing data on either first or second-trimester diet and mid-pregnancy physical activity); included women were less likely to be African-American or Hispanic, to be younger, multiparous and obese
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Willers 2007**
Food type	Fats and oils
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Antenatal clinics at Aberdeen Maternity Hospital, Aberdeen, Scotland
Funding	Asthma UK, GA^2LEN European Network of Excellence on Global Allergy and Asthma
Participants	1212 children (singleton births) whose mothers were recruited between October 1997 and April 1999 at a median gestational age of 12 weeks
Baseline comparisons	Women were representative of the local obstetric population *See confounding below*
Dietary assessment	FFQ
Timing	FFQ mailed at 32 weeks gestation to cover dietary intake over the previous 2-3 months
Comparison	Tertiles: Butter versus margarine/low fat spread
Outcomes	Wheeze, allergic rhinitis, atopic eczema, hay fever at 5 years
Results	**Butter or margarine/low fat spread** – no consistent linear associations with respiratory and atopic outcomes in 5 year old children (exact numbers not reported in the paper).
Followup	5 years
Confounding	Adjusted for maternal age, paternal social class, maternal education, maternal asthma (for wheeze, asthma and hay fever outcomes), maternal atopy, child's birthweight, child's sex, presence of older siblings, breastfeeding and smoking in the child's home at 5 years
Risk of bias	Low risk of bias: Initial study population of 1924 children dropped to 1212 participants with complete data (63.0%) (questionnaire, at least one of the outcome time points).
Relevance	Likely to be reasonably relevant to Australian women
Other comments	Inclusion of maternal supplement use during pregnancy did not materially change the results

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Fish

Included Studies

Study	Outcomes
1. Akre 2008	Child hypospadias
2. Browne 2006	Postnatal depression within 6 months of birth
3. Buck 2003	Birth size (weight, length, head circumference and chest circumference)
4. Bunin 2006; 2005	Childhood brain tumours
5. Calvani 2006	Allergy sensitisation (median age of child 5 y)
6. Chatzi 2008	Child persistent wheeze, atopic wheeze, atopy (all at 6.5 years)
7. Daniels 2004	Child development at 18 months
8. Gale 2008	Child cognition and behaviour
9. Giordano 2010	Child hypospadias
10. Giordano 2008	Child hypospadias and cryptorchidism
11. Golding 2009	Antenatal and postnatal depressive symptoms
12. Guldner 2007	SGA; preterm birth; gestational age, birthweight
13. Haggarty 2009	Deprivation
14. Halldorsson 2007	Birthweight, birth length, head circumference, SGA
15. Halldorsson 2008	Maternal PCB concentration, birthweight, birth length, head circumference, placental weight
16. Haugen 2008	Preterm birth
17. Hibbeln 2007	Child development up to 8 years
18. Jedrychowski 2010	Birthweight
19. Jedrychowski 2008	Child respiratory symptoms up to 2 years (cough, wheezing, difficult breathing)
20. Jensen 2004	Childhood acute lymphoblastic leukemia
21. Jones 2000	Bone mass at 8 years
22. Lamb 2008	Islet autoimmunity
23. Latva-Pukkila 2009	Nausea, vomiting
24. Lauritzen 2004-2009	Child development, cognition and growth
25. Maconochie 2007	Miscarriage
26. Mendez 2010	SGA
27. Mendez 2009	Child cognition at 4 y
28. Mikkelsen 2008	Preterm birth
29. Mitchell 2004	SGA

30. Miyake 2006	Postpartum depression
31. Miyake 2009	Infant wheeze and eczema up to 24 months
32. Nwaru 2010	Allergic sensitisation by 5 y
33. Oien 2010	Childhood asthma and eczema at 2 years
34. Oken 2008a	Child cognition at 3 years
35. Oken 2008b	Child development at 18 months; child development (motor and social/cognitive) also assessed at 6 months
36. Oken 2007	Pre-eclampsia, gestational hypertension
37. Oken 2005	Infant cognition at 6 months
38. Oken 2004	Preterm birth, low birthweight, SGA
39. Olsen 2002	Preterm birth, low birthweight, IUGR
40. Olsen 1993	Birthweight, fetal growth, length of gestation
41. Olsen 1990	Placental weight, infant size
42. Petridou 2005	Childhood acute lymphoblastic leukemia
43. Petridou 1998a	Cerebral palsy at 8 years
44. Pogoda 2009	Childhood brain tumours
45. Ramon 2009	Birthweight, birth length, SGA
46. Rogers 2004	Low birthweight, preterm birth, IUGR
47. Romieu 2007	Atopy, eczema
48. Saito 2010	Eczema at 24 months
49. Salam 2005	Asthma
50. Sausenthaler 2007	Allergic sensitisation, eczema at 2 years of age
51. Schoeman 2010	Hair mercury concentrations in women planning a pregnancy
52. Shiell 2001	Offspring blood pressure at 27-30 years
53. Sontrop 2008	Antenatal depressive symptoms
54. Strain 2008	Child development at nine and 30 months
55. Strom 2009	Postpartum depression
56. Thorsdottir 2004	Infant size (birthweight, length, ponderal index and head circumference)
57. Thurston 2007; Myers 2003	Child development at 9 years, blood pressure at 12 and 15 years
58. Venter 2009	Food hypersensitivity (FHS) in infants up to three years of age
59. Willers 2007	Eczema, atopic symptoms at 5 years
60. Willers 2008	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable 'asthma symptoms' in the last 12 months (measured longitudinally from 1 to 8 years age)
61. Williams 2001	Child stereoacuity at 3.5 years

62. Xue 2007	Preterm birth, very preterm birth
63. Yin 2010	Bone mass at 16 years

Evidence Summary

	N	LoE	Study
Pre-Pregnancy			
1. In a Canadian cohort study, women planning a pregnancy and concerned about the safety of consuming fish during pregnancy had a median hair mercury concentration of less than 0.5 μg/g	22	IV	Schoeman 2010
Maternal (Antenatal) Outcomes			
2. In a cohort study from the UK, mothers who consumed no seafood were 50% more likely to have high **levels of depressive symptoms at 32 weeks gestation** compared with those who consumed substantial amounts of seafood (aOR 1.54 95% CI 1.25 to 1.89); with only a weak association seen at 18 weeks gestation	9960	II	Golding 2009
3. In a Canadian cohort study, **antenatal depressive symptoms** were not significantly associated with maternal fish intake during pregnancy: multiple linear regression of depressive symptoms β -0.2 95% CI -0.9 to 0.4 from no fish intake to > 1 serve per week	2061	II	Sontrop 2008
4. In a cohort study from Finland, no association was seen between maternal fish consumption during pregnancy and **nausea and vomiting in pregnancy**	256	II	Latva-Pukkila 2009
5. In a cohort study from the US, maternal fish intake during pregnancy was not associated with risk of **pre-eclampsia** (aOR 0.91 95% CI 0.75 to 1.09) or gestational hypertension (aOR 1.4 95% CI 0.94 to 1.15)	1718	II	Oken 2007
6. In a Scottish cohort study, while overall intake of fish during pregnancy was not associated with **deprivation**, lower levels of oily fish intake during pregnancy were significantly associated with higher levels of **deprivation (p < 0.01)**	1277	II	Haggarty
7. In a UK case-control study, maternal consumption of fish twice weekly or more in the three months before conception and the first 12 weeks of pregnancy were significantly less likely to have a **miscarriage** (aOR 0.83 95% CI 0.69 to 1.00) which become slightly more borderline when adjusted for nausea (aOR 0.86 95% CI 0.71 to 1.03)	603 cases; 6116 controls	III-3	Maconochie 2007
Congenital Anomalies			
8. In a Scandinavian case-control study, low maternal fish consumption during pregnancy (less than once a week) was associated with an increased risk of **hypospadias**: aOR 2.7 95% CI 1.3 to 5.5	292 cases; 427 controls	III-3	Akre 2008
9. In an Italian cohort study, frequent maternal fish consumption during pregnancy was associated with an increased risk of **hypospadias**: aOR 2.73 95% CI 1.09 to 6.82	80 cases; 80	III-3	Giordano 2010

	controls		
10. In an Italian case-control study, frequent maternal fish consumption during pregnancy was associated with an increased risk of **hypospadias**: aOR 2.33 95% CI 1.03 to 5.31, but not **cryptorchidism**: aOR 1.33 95% CI 0.61 to 2.90	90 cases; 202 controls	III-3	Giordano 2008
Birth – Preterm Birth, SGA, IUGR			
11. In a Danish cohort study, there was no evidence of an overall association between fish intake during pregnancy and small for gestational age, although a significantly higher rate for **small for gestational age** was seen for the highest intake of fish category: aOR 1.24 95% CI 1.01 to 1.43) and for fatty fish aOR 1.18 95% CI 1.03 to 1.35	44,824	II	Halldorsson 2007
12. In a cohort study from Norway , the risk of **preterm birth** was significantly reduced with higher maternal fish intake during pregnancy: aOR 0.84 95% CI 0.74 to 0.95 for ≥ 2 v < 2 serves of fish per week	40,817	II	Haugen 2005
13. In a Spanish cohort study, overall fish and seafood intake during pregnancy (> 6 serves/week) was not associated with **small for gestational age** (aOR 3.89 95% CI 0.82 to 18.59), although > 1 serve of crustaceans per week (aOR 3.24 95% CI 1.34 to 7.83) and canned tuna > 1 per week (aOR 2.61 95% CI 1.12 to 6.07) showed significantly **higher SGA** rates, with the latter significant result disappearing when adjusted for persistent organic pollutants	657	II	Mendez 2010
14. In a Danish cohort study, **preterm birth** was not significantly associated with maternal fish intake during pregnancy: aOR 0.95 95% CI 0.84 to 1.08; ≥ 2 v < 2 serves of fish per week	35,530	II	Mikkelsen 2008
15. In a New Zealand case-control study, the risk of **small for gestational age** was increased when mothers consumed no fish at the time of conception compared with > 1 serve per week: aOR 1.69 95% CI 1.07 to 2.69	1138	III-3	Mitchell 2004
16. In a US cohort study, no differences were seen for risk of **preterm birth** or **small for gestational age** and maternal fish intake during pregnancy (only reported as p-value not significant).	1797	II	Oken 2004
17. In a Danish cohort study, the risk of: • **preterm birth** was significantly higher when no maternal fish consumption was compared with daily fish consumption during pregnancy: aOR 2.69 95% CI 1.49 to 4.84; • no significant differences between no, and daily, fish consumption were seen for **IUGR**: aOR 1.01 95% CI 0.45 to 2.26	8729	II	Olsen 2002
18. In a Spanish cohort study, fish intake of ≥ 2 serves per week compared with less than one serve a month was associated with significantly less risk of **small for gestational age** for	554	II	Ramon 2009

canned tuna (p = 0.01 for weight) but this was not the case for oily fish or lean fish			
19. In a UK cohort study • no differences were detected in the risk of **preterm birth** when the lowest and highest fish intake in pregnancy categories were compared : aOR 0.76 95% CI 0.52 to 1.13 for no fish intake compared with a mean of 4.4 serves a week; • there was a higher risk of **IUGR** with no fish intake in pregnancy compared with a mean of 4.4 serves a week: aOR 1.37 95% CI 1.02 to 1.84)	10,040	II	Rogers 2004
20. In a US cohort study, while the risk of **any preterm** birth did not differ significantly between high mercury levels in mothers' hair (in turn significantly related to high fish intake) aOR 1.55 95% CI 0.79 to 2.90, **very preterm birth** (< 35 weeks) was significantly associated with high maternal mercury levels aOR 3.0 95% CI 1.3 to 6.7	1226	II	Xue 2007
21. In a US cohort study, maternal lifetime fish consumption was not associated with any measures of **birth size** (weight, length, head circumference and chest circumference) of their infants	2716	II	Buck 2003
22. In a Danish cohort study, maternal fish consumption during pregnancy was not significantly associated with **gestational age or birth length** but there was a significant positive association for **placental weight and head circumference at birth**. There was no an overall association between maternal fish intake during pregnancy and **birthweight** although in non-smokers, **birthweight** did show a positive association with increased maternal fish consumption	11,980	II	Olsen 1990
23. In a cohort study from France • maternal consumption of fish (not including shellfish) before pregnancy was significantly associated with **reduced risk of small for gestational age babies and low birthweight** babies, but not preterm birth; with a significant increase in length of gestation shown with multiple linear regression (p = 0.03) • maternal consumption of shellfish before pregnancy did not show these associations in adjusted analyses, instead indicating an **increased risk of small for gestational age babies** with consumption ≥ 2 serves of shellfish a week	2398	II	Guldner 2007
Birth Outcomes – Birthweight and Other Measures of Size At Birth			
24. In a Danish cohort study, **maternal PCB concentrations** were significantly with higher fish intake during pregnancy and in turn, higher maternal PCB was correlated with lower **birthweight** (p = 0.03) and lower **placental weight** (p = 0.004) but not significantly so with **birth length** (p = 0.08) or **head circumference at birth** (p = 0.2)	100	II	Halldorsson 2008
25. In a Danish cohort study, higher fish intake was not significantly correlated with **birthweight** (p = 0.09), but there was a significant correlation with lower **birth length** (p =	44,824	II	Halldorsson 2007

0.04) and reduced **head circumference at birth** (p = 0.005). For lean fish, there were no significant associations and for fatty fish, high intake was significantly associated with higher birthweight (p = 0.04) and with reduced head circumference (p = 0.003) with no significant association seen for birth length (p = 012).			
26. In a cohort study from Poland and the US, low fish intake (< 91 g/week) during pregnancy and high antenatal fine particulate matter concentrations (> 46.3 μg/m^3) were significantly associated with lower **birthweight**: regression coefficient: -133.26 g birthweight (p = 0.052)	481	II	Jedrychowski 2010
27. In a retrospective cohort study from the Faroe Islands, higher maternal fish intake during pregnancy was associated with increased **birthweight** (p = 0.02) and increased **birth length** (p = 0.002) for variability of means between groups, with placental weight and gestational age not showing significant associations	1012	III-2	Olsen 1993
28. In a Spanish cohort study, maternal fish intake of ≥ 2 serves per week compared with less than one serve a month during pregnancy was associated with significantly higher **birthweight** for canned tuna (p = 0.03) but not for lean or oily fish, and there were no significant associations for **birth length** with any type of fish	554	II	Ramon 2009
29. In a cohort study from Iceland, maternal fish intake during pregnancy of > 6 serves compared with < 4 serves per month was significantly associated with increased **birth length** (p = 0.007) and **head circumference at birth** (p = 0.005), but this did not apply for birthweight and ponderal index	491	II	Thorsdottir 2004
30. In a cohort study from France, maternal intake of either fish or shellfish before pregnancy was not associated with **birthweight** (p = 0.8 and 1.0 respectively for multiple linear regression)	2398	II	Guldner 2007
Childhood – Asthma, Eczema And Other Allergy Outcomes			
31. In a case-control study from Spain, increased intake of fish sticks during pregnancy was associated with increased **childhood asthma** (p = 0.01), but this was not seen with oily fish consumption	891	III-3	Salam 2005
32. In a cohort study from Norway, no association was seen between maternal consumption of fish once a week or more during pregnancy and **childhood asthma at two years**; OR 0.99 95% CI 0.72 to 1.37	3086	III-2	Oien 2010
33. In a Japanese cohort study, fish intake during pregnancy was not associated with **childhood eczema at 3-4 months**	771	II	Saito 2010
34. In a cohort study from Norway, no association was seen between maternal consumption of fish once a week or more during pregnancy and **childhood eczema at two years**; OR 1.02 95% CI 0.82 to 1.26	3086	III-2	Oien 2010

35. In a Japanese cohort study, fish intake during pregnancy was not associated with **childhood eczema, or infant wheeze at 16-24 months**	763	II	Miyake 2009
36. In a cohort study from Poland, fish intake during pregnancy did not significantly modify the effect of fine particulate matter on **coughing in infants up to 2 years of age** (aIRR 1.36 95% CI 0.79 to 1.43); but significant reductions in **wheezing and difficult breathing in** infants up to 2 years of age were seen (aIRR 0.80 95% CI 0.72 to 0.89 and 0.81 95% CI 0.72 to 0.91 respectively)	465 infants	II	Jedrychowski 2008
37. In a Spanish cohort study, each unit increase of fish intake during pregnancy was associated with a reduction in **childhood eczema at 1 year of age**: p = 0.036; and for **atopic wheeze at 6 years** (aOR 0.55 95% CI 0.31 to 0.96), but not for **IgE at 4 years**, or **allergen sensitisation at 6 years of age**	458	II	Romieu 2007
38. In a German cohort study, high fish intake in pregnancy was associated with a reduction risk of **childhood eczema at 2 years of age** (aOR 0.75 95% CI 0.57 to 0.98), but no significant effect was seen for **allergen sensitisation** at 2 years of age	3097	II	Sausenthaler 2007
39. In a Scottish cohort study, high fish intake during pregnancy (≥ once per week) was associated with a reduction in **childhood eczema at 5 years of age** (aOR 0.57 95% CI 0.35 to 0.92; A significant reduction in **hay fever** at 5 years of age was also seen	1212	II	Willers 2007
40. In a cohort study from the Netherlands, no associations were found between fish intake in pregnancy and **asthma symptoms (e.g. wheeze) in children aged from 1 to 8 years**	2832	II	Willers 2008
41. In an Italian cohort study, **reduced food allergen sensitisation** in infants (median age 5 years) was significantly associated with one serve or more of fish per week in their mothers during pregnancy in non-allergenic mothers (p for trend = 0.002, adjusted) but not for allergenic mothers (p for trend = 0.72, adjusted); • No effect was seen on inhalant allergen sensitisation	988	III-2	Calvani 2006
42. In a Spanish cohort study, high fish intake during pregnancy was associated with a reduction in **persistent wheeze in children at 6.5 years** of age: aOR 0.34 95% CI 0.13 to 0.84	487	II	Chatzi 2008
Childhood – Child Development Outcomes			
43. In a UK cohort study, high fish intake during pregnancy was associated with significantly increased **vocabulary comprehension** (p = 0.03), **social activity** (p = 0.002), and **language** (p = 0.004) at 18 months but no significant association was seen with the **social** component of the assessment	10,092 children	II	Daniels 2004
44. In a UK cohort study, increased fish intake during pregnancy was associated with a significant increase in **IQ** (p = 0.0389) but no significant associations were seen for **child**	8801 children	II	Hibbeln 2007

behaviour or child development at 8 years			
45. In a Spanish cohort study, some measures (but not all) of **child cognition at 4 years** were significantly higher with higher fish intake during pregnancy	482 children	II	Mendez 2009
46. In a US cohort study, higher fish intake during pregnancy was associated with significantly increased **infant cognition at six months** (adjusted change in visual recognition memory score 4.0 95% CI 1.3 to 6.7 for effect per weekly fish serving)	135 mother-infant pairs	II	Oken 2005
47. In a US cohort study, higher fish intake during pregnancy was associated with better **child cognitive test performance at 3 years of age**	480 children	II	Oken 2008a
48. In a US cohort study, higher fish intake during pregnancy was associated with increased **general child development at 18 months** (aOR 1.29 95% CI 1.20 to 1.38)	25,446 children	II	Oken 2008b
49. In a UK cohort study, higher fish intake pregnancy (three or more times a week) was not significantly associated with: • **child behaviour score** (aOR for high total difficulties score 0.23 95% CI 0.04 to 1.24 compared with mothers who never ate fish); or • **overall IQ** (although children of mothers who ate fish had a **verbal IQ** (adjusted) that was 7.55 points higher (95% CI 0.75 to 14.4) than children of mothers who did not eat fish	217	II	Gale 2008
50. In a UK cohort study, higher fish intake during pregnancy was significantly associated with increased **stereoacuity in children at 3.5 years of age** (p = 0.046)	641	II	Williams 2001
51. In a Danish non-randomised study, there were no significant differences seen between a low and high fish maternal intake group during lactation for **problem solving at nine months; and linguistic development at one and two years; head circumference, weight, length/height, ponderal index or BMI from birth to 7 years of age; and blood pressure at 2.5 years in their children**	110	III-3	Lauritzen 2005a and b; Ulbak 2004; Asserhoj 2009
52. In a cohort study from the Seychelles, maternal hair mercury concentrations (reflecting antenatal fish intake) were not associated with **mental development index scores** of the infant at nine months or 30 months of age, or with **psychomotor development index scores** at 9 months of age; however there was a significant association with **lower psychomotor development index** scores at 30 months of age	229	II	Strain 2008
53. In a cohort study from the Seychelles, maternal hair mercury concentrations (reflecting antenatal fish intake) were not generally associated with **child development at 9 years, or blood pressure of offspring at 12 and 15 years**	779 mothers and children	II	Thurston 2007; Myers 2003
Maternal Outcomes – Postnatal			

54. In a New Zealand case-control study, **depression in the postnatal period** was not associated with maternal fish consumption during pregnancy: p > 0.29 (adjusted)	80	III-3	Browne 2006
55. In a Japanese cohort study, depression in the postnatal period was not associated with maternal fish consumption during pregnancy: p > 0.37 for trend (adjusted)	865	II	Miyake 2006
56. In a cohort study from the UK, a weak association was seen between no maternal seafood intake during pregnancy and **depressive symptoms at 8 months postnatal** compared with those who consumed substantial amounts of seafood; with no significant association seen at 2 months postnatal	9960	II	Golding 2009
57. In a Danish study, fish intake during pregnancy was not associated with **depression in the postnatal period requiring admission** (p= 0.5 for trend from 0-3 g/day to > 30 g/day) but, intake of 0-3 g/day was associated with **depression in the postnatal period requiring a prescription** compared with > 30 g/day (aOR 1.46 95% CI 1.12 to 1.9), with p for a trend across categories of fish intake	54,502	II	Strom 2009
Childhood and Adult Outcomes – Other			
58. In an international multi-centre case-control study, maternal fresh fish consumption during pregnancy was associated with a reduced risk of **childhood brain tumours** (aOR 0.7 95% CI 0.6 to 0.9)	1281 cases; 2223 controls	III-3	Pogoda 2009
59. In a North American case-control study, maternal intake of smoked fish or lox in the year before pregnancy was not associated with risk of **childhood brain tumours (medulloblastoma/PNET)**; aOR 1.3 95% CI 0.6 to 2.6	315 cases; 315 controls	III-3	Bunin 2006; 2005
60. In a Greek case-control study, **cerebral palsy in children at 8 years** was not associated with maternal fish intake during pregnancy: • Regression analysis for each unit of consumption of fish once per week: aOR 0.63 95% CI 0.37 to 1.08 (additionally adjusted for all food groups)	109 children (cases)	III-3	Petridou 1998
61. In a Greek case-control study, maternal fish and seafood intake during pregnancy was associated with a significant decrease in the risk of **childhood acute lymphoblastic leukemia**: aOR 0.72 95% CI 0.59 to 0.89 for each quintile more of fish/seafood	131 cases; 131 controls	III-3	Petridou 2005
62. In a US case-control study, **childhood acute lymphoblastic leukemia** was not generally associated with maternal intake of fish during pregnancy	138 cases; 138 controls	III-3	Jensen 2004
63. In a US cohort study, no significant association was seen between maternal fish intake	642	II	Lamb

during pregnancy and **islet autoimmunity in children up to 15 years of age**: aHR (for one standard deviation change in reported consumption) 0.90 95% CI 0.54 to 1.51 (5.10 mean monthly servings)	children		
64. In one Australian cohort study, **bone mineral density of children at 8 years** was not associated with maternal fish intake during pregnancy: Total body bone mineral density – p = 0.153 for adjusted regression of portions per week	173 children	II	Jones 2000
65. In an Australian cohort study (follow-up of Jones 2000) **bone mass in 16 year-old adolescents** was not associated with maternal vegetable intake during pregnancy: Total body bone mineral density r^2 0.323; ß +14.9 (pns) for adjusted regression of portions per week	216 children	II	Yin 2010
66. In a cohort study from Scotland, **diastolic (but not systolic) blood pressure** was significantly increased in offspring aged 27 to 30 years with increased fish consumption in pregnancy; regression coefficient for amount of maternal fish consumption; ß 1.00 95% CI 0.18 to 1.82, p = 0.02	626 adult off-spring	II	Shiell 2001

Evidence Tables

Reference	**Akre 2008**
Food type	Fish
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Sweden and Denmark from 2000 to 2005
Funding	European Chemical Industry Council
Participants	292 cases 427 controls
Baseline comparisons	*See confounding below*
Dietary assessment	Questionnaire
Timing	Questionnaire completed by mother when son was 2 months old in Sweden and when 6 months old in Denmark
Comparison	None, less than once, once or twice, more than twice a week consumption of fish during pregnancy
Outcomes	Hypospadias
Results	<u>**Hypospadias**</u> **Weekly fish consumption** None aOR 1.4 95% CI 0.84 to 2.2 **< once aOR 2.7 95% CI 1.3 to 5.5** Once or twice 1 More than twice aOR 0.88 95% CI 0.31 to 2.5 **P value for trend = 0.02**
Followup	n/a
Confounding	Analyses adjusted for maternal age, maternal pre-pregnancy BMI, maternal education, contraceptive use at conception, proteinuria, maternal nausea in the index pregnancy, passive maternal exposure to tobacco smoke during index pregnancy, fish consumption; weight for gestational age, gestational age at birth; neonatal jaundice
Risk of bias	Low risk of bias: response rate was 88% for cases and 81% for controls; ascertainment of cases of hypospadias likely to be high.
Relevance	Likely to be reasonably similar for the relatively small number of Australian women who do not consume fish during pregnancy
Other comments	Different recruitment methods were used in Sweden and Denmark

Reference	**Browne 2006**
Food type	Fish
Study type	Case- control study (aetiology)
Level of evidence	III-3 (aetiology)
Setting	South Island, New Zealand
Funding	Foundation for Research, Science and Technology, New Zealand.
Participants	First-time mothers who had previously taken part in studies conducted by Victoria University and the Uni of Otago, NZ, and were within 6 months of having given birth. Caseness determined on study entry. Cases: n=41 (on or over cut off on one or both screening instruments ≥ 10 on BDI-II, &/or ≥ 9 EPDSl; those meeting CIDI criteria for Dx depression 'diagnosis group', n=21, those that did not 'screened high' group, n = 20) Controls: n=39 (<10 on BDI-II or <9 on EPDS – preference to those at lower end of continuum)
Baseline comparisons	Household income significantly different: ***Cases (n = 41)*** ***Controls (n =39)*** Income <$70K: 21 (51%); 7 (18%) Currently breastfeeding: 19 (46%); 32 (82%)
Dietary Assessment Method	Food frequency questionnaire
Timing	Data collected during participation in other studies (not clear which period FFQ covered): fish consumption, alcohol intake, tobacco smoking, and dietary supplement use during pregnancy, plus demographic data (ethnicity, household income). All asked additional questions re postnatal changes in alcohol, tobacco, fish consumption, anti-depressant medication and dietary supplements – within six months of birth.
Comparison	Prenatal fish consumption: none versus any
Outcomes	Postnatal depression within 6 months of birth
Results	Fish intake - any: Cases: 33/41 (80%) [diagnosis 19/21 (90%), screened high 14/20 (70%)] Controls: 32/39 (82%) **Prenatal fish consumption: not predictive of postnatal depression p > 0.29 (adjusted)** **Postnatal omega-3 status not associated with depression: p > 0.25 (adjusted)** Fish consumption and omega-3 status: prenatal fish consumption predicts omega-3 status after birth
Follow-up	Up to 6 months postpartum
Confounding	Analyses adjusted for household income and current breastfeeding status
Risk of bias	Moderate: poor response rate (421 invitations sent, 244 replies, 80 participated 80/244 = 33%), possibility of selection bias with those with postnatal depression less likely to respond.
Relevance	Diets in New Zealand will be similar to Australian diets
Other comments	Fish included: canned tuna, salmon, sardines, mackerel, eel, fish battered, fried, steamed, baked, grilled or raw, shellfish, or other seafood.

Reference	**Buck 2003**
Food type	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	New York State Angler Cohort Study (NYSACS) 1986-1991 with residents from Lake Ontario and its tributaries
Funding	Great Lakes Protection Fund, Agency for Toxic Substances and Disease Registry
Participants	2,716 infants born as most recent singleton births in NYSACS (70% of infants) Excluded infants with birth defects from most analyses (n=469), and excluded infants with missing data from various analyses.
Baseline comparisons	*See confounding below*
Dietary Assessment	Lifetime fish consumption-self administered questionnaire (referred to number of years consuming fish from Lake Ontario)
Timing	Unclear
Comparison	Duration of fish consumption in years-none, 1-2, 3-7, ≥8 (number of years between 1955 and birth of infant)
Outcomes	Birth size (weight, length, head circumference and chest circumference)
Results	

Duration fish consumption in years β (95% CI)	**1-2**	**3-7**	**≥8**
Including infants with birth defects	6.37 (-46.75, 59.49)	-20.46 (-75.93, 35.02)	-37.62 (-94.25, 19.02)
Weight	0.06 (-.23, 0.36)	0.03 (-0.27, 0.33)	0.06 (-0.25, 0.36)
Length	-0.04 (-0.22, 0.14)	-0.05 (-0.24, 0.14)	-0.18 (-0.38, 0.01)
Head circumference	-0.23 (-0.54, 0.08)	-0.24 (-0.57, 0.09)	-0.29 (-0.65, 0.06)
Chest circumference			
Including infants without birth defects			
Weight	13.49 (-41.42, 68.41)	-14.45 (-72.7, 43.8)	-37.03 (-96.66, 22.6)
Length	0.09 (-0.21, 0.39)	0.12 (-0.2, 0.44)	0.06 (-0.27, 0.38)
Head circumference	0.04 (-0.15, 0.22)	-0.03 (-0.23, 0.16)	-0.15 (-0.35, 0.05)
Chest circumference	-0.16 (-0.48, 0.16)	-0.29 (-0.64, 0.06)	-0.49 (-0.87, -0.11)

Duration fish consumption in years (%)	**0**	**1-2**	**3-7**	**≥8**
Gestational age (weeks)				
<37	4	1	4	4
37-41	88	90	87	89
≥42	8	9	9	7

Follow-up	Birth
Confounding	Gestation, infant sex, infant birth defects, parity, placental infarction, uterine bleeding, average number of cigarettes smoked daily during pregnancy, maternal and infant race
Risk of bias	Low
Relevance	Consumption of fish only from the "most polluted Great Lake and its tributaries" (p3, 2nd par in Data collection) - not relevant to Australia
Other comments	Original study had 4226 infants. Original NYSACS looked at fish consumption in licensed anglers from Lake Ontario and had a low follow up rate (49% for females and 39% for males). Post hoc power-able to detect 61g reduction in birth weight with 80% power and 5% alpha

Reference	**Bunin 2006 (and Bunin 2005)**
Food type	Smoked fish or lox
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	United States and Canada
Funding	National Cancer Institute, USA
Participants	315 cases diagnosed with medulloblastoma/PNET tumours from 0 to 5 years, between 1991 to 1997 (without a previous or recurrent cancer) 315 controls (random digit dialling, matched on area code, race and data of birth)
Baseline comparisons	See confounding below
Dietary assessment	FFQ
Timing	To reflect diet in the year before pregnancy; and the second trimester of pregnancy
Comparison	<1 serve month to >1 serve/week; data on portion size were not collected
Outcomes	Childhood brain tumours (medulloblastoma/primitive neuroectodermal (PNET) tumours)
Results	see below
Followup	n/a
Confounding	*adjusted for income level, mother's race, age of child at interview, date of interview, nausea/vomiting, number cigarettes per day, total calories **adjusted for mother's race, age of child at interview, income, number of cigarettes per day, maternal weight gain (yes/no)
Risk of bias	Low-moderate risk of bias: 315/558 (57%) potentially eligible cases able to be included (missing cases mostly due to lack of consent from physician or parents); control resonse rates were 67% for random digit dialling and 73% for questionnaire
Relevance	Likely to be reasonably similar
Other comments	Medulloblastomas and PNETs account for about 20% of brain tumours in children; Supplement use was also assessed in this study

Results:

Medulloblastoma/PNET

	Periconception		**Midpregnancy**	
	N	**aOR* (95% CI)**	**N**	**aOR* (95% CI)**
<1 serve/month	584	1.00	584	1.00
≥1/month	47	1.3 (0.7 to 2.6)	46	1.3 (0.6 to 2.6)
P_{trend}		0.42		0.47

Reference	**Calvani 2006**
Food type	Fish
Study type	Retrospective cohort study
Level of evidence	III-2 (aetiology)
Setting	Rome, Italy
Funding	Not reported
Participants	988 offspring of allergic (n = 295) and non-allergic (n = 693) mothers; recruited from outpatient allergy clinics between September 2001 and March 2002; with a median age of 5 years (range of 17 years); part of the APAL study 744/988 children were affected by atopic diseases (asthma, rhinitis, eczema) and the remaining 244 were attending due to respiratory, gastrointestinal symptoms, or skin disease; Exclusions: immunodeficiency, connective tissue disease, or chronic respiratory tract disease other than asthma
Baseline comparisons	*See Confounding below*
Dietary assessment	Questionnaire
Timing	At recruitment, women were asked to recall their intake of fish, butter and margarine during pregnancy
Comparison	≤ 1 serve/month (reference) v 1 serve/week v ≥ 2-3 serves/week
Outcomes	Allergic sensitisations
Results	see below

Food sensitisation (positive skin prick test mainly for raw cow's milk and egg-white)

	n/N (%)	OR (95% CI)	aOR (95% CI)	p-value for trend
Allergic mothers				
≤ 1 serve/month	7/62 (11.3%)	1	1	0.72
1 serve/week	16/138 (11.6%)	1.03 (0.40 to 2.64)	1.15 (0.38 to 3.47)	
≥2-3 serves/week	8/38 (9.6%)	0.83 (0.28 to 2.44)	1.13 (0.31 to 4.1)	

*adjusted for age, occupation and eczema

	n/N (%)	OR (95% CI)	aOR (95% CI)	p-value for trend
Non-allergic mothers				
≤ 1 serve/month	20/136 (14.7%)	1	1	**0.002**
1 serve/week	16/330 (4.8%)	**0.29 (0.14 to 0.58)**	**0.22 (0.08 to 0.55)**	
≥2-3 serves/week	10/197 (5.1%)	**0.31 (0.14 to 0.68)**	**0.23 (0.08 to 0.69)**	

*adjusted for age, gestational age, maternal occupation, oculorhinitis and eczema

aOR in non-allergic mothers for 1 serve/week: 0.13 95% CI 0.04 to 0.38; aOR for ≥2-3 serves/week 0.14 95% CI 0.04 to 0.47
(additionally adjusted for maternal butter and margarine intake and hyperemesis)

aOR in non-allergic mothers for milk sensitisation: 1 serve per week 0.15 95% CI 0.04 to 0.59 and ≥2-3 serves/week 0.05 95% CI 0.00 to 0.54

aOR in non-allergenic mothers for egg sensitisation: 1 serve per week 0.26 95% CI 0.09 to 0.76 and ≥2-3 serves/week 0.33 95% CI 0.10 to 1.07

Food sensitisation in whole population: p value for trend 0.008
1 serve per week: aOR* 0.34 95% CI 0.15 to 0.75
≥ 2-3 serves/week: aOR* 0.42 95% CI 0.17 to 1.02
*adjusted for age, number of older siblings, allergy clinics, maternal age, gestation age, gender, maternal education, paternal atopy,

maternal atopy

Inhalant sensitisation (positive skin prick test for a range of allergens)

	n/N	OR (95%)	aOR (95% CI)	p-value for trend
Allergic mothers				
≤ 1 serve/month	27/62 (43.5%)	1	1	0.76
1 serve/week	63/138 (50.7%)	1.33 (0.73 to 2.43)	0.89 (0.30 to 2.60)	
≥2-3 serves/week	48/83 (42.2%)	0.94 (0.48 to 1.83)	0.74 (0.23 to 2.37)	

*adjusted for age, number of older siblings, allergy clinics, maternal age, gestation age, gender, maternal education, paternal atopy, maternal atopy

Non-allergic mothers				
≤ 1 serve/month	69/136 (50.7%)	1	1	0.62
1 serve/week	137/330 (41.5%)	0.68 (0.46 to 1.02)	0.70 (0.38 to 1.30)	
≥2-3 serves/week	92/197 (46.7%)	0.85 (0.54 to 1.31)	0.55 (0.28 to 1.08)	

*adjusted for age, gender, number of older siblings, allergy clinics, maternal age, number of pregnancies, maternal occupation, paternal atopy, asthma, oculorhinitis

Inhalant sensitisation in whole population:

≥2-3 serves/week: aOR* 0.57 95% CI 0.32 to 1.03

*adjusted for age, gender, oculorhinitis, asthma, number of older siblings, allergy clinics, maternal age, number of pregnancies, maternal education, preterm labour, paternal atopy, maternal atopy: did not vary significantly with amount of butter intake

Followup	NA
Confounding	Analyses only adjusted for a limited number of factors; different factors were used for the analyses of allergic and non-allergic mothers; and for food and inhalant sensitisations (included if significant in univariate analyses).
Risk of bias	Moderate risk of bias: recall bias likely for women remembering diet during a pregnancy up to 17 years earlier; data for maternal atopy available for 988 of the 1044 consecutively recruited children (94.6%); data for maternal fish intake during pregnancy available for 946/988 (95.7%); children attending allergy clinics likely to be different for a general population of children.
Relevance	Diets of pregnant Italian women may differ from those of Australian women e.g. there were low levels of maternal margarine and butter consumption in this study
Other comments	Clinical significance of skin prick tests? Wide age range (1 to 18?) makes interpretation of allergic sensitisations difficult

Reference	**Chatzi 2008**
Food type	Fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women presenting for antenatal care at general practices in Menorca, a Mediterranean island in Spain (mid 1997 to mid 1998)
Funding	Instituto de Salud Carlos III red de Grupos Infancia y Media Ambiente, the Fundacio "La Caixa" , Instituto de Salud Carlos III, red de Centros de Investigacion en Epidemiologica y Salud Publica, EU, National Center for Environmental Health, USA, the GA2LEN project, Ministry of Education and Science, Spain, Oficina de Ciencia y Tecnologia, Generalitat Valenciana.
Participants	482 children of 507 women who had attended antenatal care in Menorca
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	not clear when women did FFQ and period of pregnancy it was intended to cover
Comparison	≤ 2.5 versus > 2.5 serves of fish per week
Outcomes	Persistent wheeze, atopic wheeze and atopy at 6.5 years
Results	***Persistent wheeze at 6.5 years*** **Low 24 (17.02%) v high 13 (9.35%); OR 0.34 95% CI 0.13 to 0.84** (also adjusted for firstborn and lower respiratory tract infections at age 1) ***Atopic wheeze at 6.5 years*** Low 13 (7.10%) v high 7 (4.38%); pns (also adjusted for birthweight and maternal atopy) ***Atopy at 6.5 years*** Low 36 (16.59%) v high 34 (17.53%) pns (also adjusted for birthweight and maternal atopy)
Followup	6.5 years
Confounding	Analyses adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years and total energy intake at 6.5 years
Risk of bias	Low risk of bias: Results from 468/482 children (97%) able to be analysed (6 incomplete data and 8 implausible values);
Relevance	Diets in Menorca may differ from diets of Australian women, particularly urban women
Other comments	

Reference	**Daniels 2004**
Food type	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	South West England, Avon Longitudinal Study of Parents and Children (ALSPAC), recruited during prenatal health visits. Eligible for ALSPAC - all children born to mothers residing in Bristol and surrounding areas between April 1991 and December 1992. An estimated 85% participated.
Funding	Medical Research Council, the Wellcome Trust, The Department of Health, The Department of the Environment, the DfEE, Nutricia and other companies
Participants	10,092 singleton-term infants – 7421 included in analysis (74%) as completed the developmental assessments within target time frame and mothers provided questionnaires throughout pregnancy and who had no missing data. Children were excluded if both developmental tests took place more than 4 months after the target test date (n = 47) or if there were missing data on maternal dental history (n = 1833), breastfeeding (n = 258), parity (n = 254), infant fish intake (n = 209), HOME score (n = 145), or alcohol use (n = 25).
Baseline comparisons	Mothers in this analysis older than other ALSPAC population (mean age, 29 vs. 27 years), more likely to have had a university degree (16% vs. 6%), and to have breastfed their child (67% vs. 55%), and less likely to have smoked during pregnancy (15% vs. 28%). *See Confounding below*
Dietary Assessment	Mother- Food frequency questionnaire-self administered. Mothers reported the frequency with which they ate white fish (cod, haddock, plaice, fish fingers etc) and oily fish (pilchards, sardines, mackerel, tuna, herring, kippers, trout, salmon, etc). Child-Not reported how.
Timing	Mother - FFQ at 32 weeks gestation Child - 6 & 15 months
Comparison	Maternal fish meals (combined oily and white): never-rarely, once per 2 weeks, 1-3 times per week, ≥4 times per week. Assumed that each fish meal averaged 4.5 ounces to estimate the median ounces of fish eaten per week; this resulted in a corresponding ordinal variable with the values 0, 2.25, 9, and 18 ounces of fish per week. Child fish meals: at least once per week at 6 months and at least once per week at 12 months =yes/no
Outcomes	Vocabulary comprehension, Social Activity, Language and Social development (adaptation of MacArthur Communicative Development Inventory at 15 months, adaptation of Denver Developmental Screening Test at 18 months-both completed by parents at home)
Results	88% ate fish during pregnancy **Adjusted mean score: mean (95% CI) and trend estimates**

Maternal fish meals β±SE *= (P)	**Never-rarely**	**1 per 2 weeks**	**1-3 per week**	**≥4 per week**
Vocabulary comprehension **0.11 ±0.05 (0.03)**	68.2 (66.3-70.5)	70.9 (69-72.9)	73 (71.3-74.8)	71.9 (70.5-73.8)
Social Activity **0.03 ±0.009 (0.002)**	16.4 (16-16.7)	17 (16.6-17.3)	17.1 (16.8-17.4)	17.2 (16.9-17.5)
Languag **0.01 ±0.004 (0.004)**	7.1 (6.9-7.3)	7.4 (7.2-7.5)	7.4 (7.3-7.5)	7.4 (7.3-7.6)
Social 0.002 ±0.004 (0.5)	8.1 (7.9-8.2)	8.1 (8-8.2)	8.2 (8.1-8.3)	8.2 (8-8.3)

*change in developmental score points per ounce increase of maternal fish intake per week

Adjusted association of maternal fish intake and LOW developmental assessment scores: OR (95% CI)

Maternal fish meals β±SE= (*P*)	**Never-rarely**	**1 per 2 weeks**	**1-3 per week**	**≥4 per week**

	Vocabulary comprehension 1 0.8 (0.6-1.1) 0.8 (0.6-1) 0.9 (0.7-1.2) 0.0003 ±0.0006 (0.9) Social Activity 1 0.8 (0.6-1.1) 0.6 (0.5-0.8) 0.7 (0.5-0.9) -**0.02 ±0.007 (0.02)** Language 1 0.8 (0.6-1.2) 0.7 (0.5-0.9) 0.7 (0.5-0.9) -**0.02 ±0.007 (0.04)** Social 1 1.2 (0.8-1.8) 1 (0.7-1.4) 1.1 (0.7-1.5) 0.002 ±0.008 (0.7) **=** change in odds of low developmental score points per ounce increase of maternal fish intake per week. Note: above associations not influenced by child fish intake, but infant fish intake was independently associated with an increase in most neurodevelopmental assessment scores
Follow-up	15 and 18 months of age
Confounding	All analyses adjusted for child sex, age at testing (weeks), breastfeeding (reported at 15 months, ever/never [duration found to be not important]), maternal dental treatment (reported at 33 months), age (years), prenatal smoking, prenatal alcohol use, birth order (1st born, non-first born), maternal education, quality of parent/home environment.
Risk of bias	Low-moderate: see attrition comments above; not adjusted for maternal IQ
Relevance	English diet similar to Australian
Other comments	Developmental assessments completed by mother at home Developmental assessment only done within 4 months of target test date for 7421/10,092 children Only 10,092 out of original 14,150 and group analysed here slightly older mothers, more likely to have had a university degree and to have breastfed infant, and less likely to have smoked whilst pregnant. Women who ate white fish more likely to have breastfed infant, women who had oily fish more likely to have higher education and have breastfed infant (compared to women who did not eat fish)

Reference	**Gale 2008**
Food type	Fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	1991-2, Midwives antenatal booking clinic at the Princess Anna Maternity Hospital, Southhampton, UK
Funding	Medical Research Council, WellChild
Participants	217 Caucasian women aged ≥ 16 years with singleton pregnancies of < 17 weeks gestation and their infants Excluded diabetics and those who undertook hormonal treatments in order to conceive. Only children with complete data for all outcomes and potential confounding factors.
Baseline comparisons	*See confounding below*
Dietary Assessment Method	Food frequency questionnaire (self administered)
Timing	15 and 32 weeks gestation for questionnaire which related to previous 3 months
Comparison	Consumption of various types of fish and shellfish in 8 categories: Never, once every 2-3 months, once a month, once a fortnight, 1-2 times per week, 3-6 times per week, once a day, more than once a day. Note for analysis of Overall Fish intake: combined 8 categories into 4 (never, <1/week, 1-2/week, ≥3 times/week) Note for analysis of Oily Fish intake: combined 8 categories into 3 (never, <1/week, >1/week) Compared intake for early and late pregnancy
Outcomes	Cognitive functioning (measured on Weschler Abbreviated Scale of Intelligence) and maladaptive behaviour (risk of hyperactivity + conduct problems + peer problems, emotional symptoms + prosocial behaviour=total difficulties) as measured on Strengths and Difficulties Questionnaire
Results	See below

Results

Adjusted overall fish intake throughout pregnancy and overall behaviour score OR (95% CI):
Compared to mothers who never ate fish, the multivariate adjusted odds ratio (95% CI) for a high total difficulties score was 0.32 (0.08-1.26) in those whose mothers ate fish once or twice a week and 0.23 (0.04-1.24)

Adjusted oily fish intake in early and late pregnancy and overall behaviour score OR (95% CI):

State of pregnancy		Early Pregnancy			Late pregnancy	
Fish consumption	Never	<1/week	≥1/week	Never	<1/week	≥1/week
Total difficulties	1	1.23 (0.41-3.66)	0.83 (0.22-3.04)	1	1.25 (0.43-3.6)	1.2 (0.32-4.49)

Adjusted oily fish intake in early and late pregnancy and Hyperactivity and Conduct problem OR (95% CI):

State of pregnancy		Early Pregnancy			Late pregnancy	
Oily Fish consumption	Never	<1/week	≥1/week	Never	<1/week	≥1/week
Hyperactivity	1	0.3 (0.12, 0.76)	0.41 (0.15, 1.12)	1	0.4 (0.16, 0.98)	0.72 (0.26, 1.98)
Conduct problems	1	0.58 (0.22, 1.53)	0.36 (0.11, 1.21)	1	0.46 (0.18, 1.17)	0.31 (0.08, 1.1)

There were no significant associations between intake of oily fish either in early pregnancy or late pregnancy and risk of peer problems, emotional symptoms or a higher total difficulties score.

Adjusted oily fish intake in early and late pregnancy and IQ score regression coefficient (95% CI):

State of pregnancy		Early Pregnancy				Late pregnancy		
Overall fish consumption	Never	<1/week	1-2/week	≥3week	Never	≤1/week	1-2/week	≥3/week
IQ	1	5.12 (-1.95, 12.2)	0.37 (-3.74, 9.88)	1.19 (-6.24, 8.61)	1	7.76 (0.38, 15.1)	6.91 (0.19, 7.65)	5.86 (-1.55, 13.3)

Oily fish consumption	Never	<1/week	≥1/week	Never	<1/week	≥1/week
IQ	1	2.52 (-1.89, 6.94)	-0.99 (-6.01, 4.02)	1	3.43 (-0.8, 7.65)	-0.29 (-5.35, 4.76)

There were no significant associations between intake of overall fish either in early pregnancy or late pregnancy and performance IQ or between early pregnancy and verbal IQ. There were no significant associations between intake of oily fish either in early pregnancy or late pregnancy and performance or verbal IQ.

After adjustments, compared to those whose mothers ate no fish, verbal IQ was increased by 7.66 points (95% CI -.1 to 15.4) in those whose mothers fish less than I per week, 7.32 points (95% CI 0.26 to 14.4) in those whose mothers ate fish once or twice a week, and 8.07 points (95% CI 0.28 to 15.9) in those whose mothers ate fish 3 or more times a week.

After adjustments, compared to those whose mothers ate no fish, those whose mothers ate fish had a verbal IQ that was 7.55 points higher (95% CI 0.75 to 14.4).

Follow-up	9 years
Confounding	Maternal social class, educational qualifications, IQ, age, smoking and alcohol use in pregnancy, duration of breastfeeding, birthweight
Risk of bias	Moderate (see other comments)
Relevance	Similar to Australian
Other comments	Unclear how many initially enrolled, 559 children in study at 9 months of age, at 9 years 461 (all those still living in area) were invited and only 226 accepted (49% of those invited) (only 217 of these included in analyses-47%) Mothers of those followed up at 9 years were older, better educated and more likely to come from non-manual occupational social class compared with mothers not followed up at 9 years (using data from 9 months follow-up). Mothers who ate fish whilst pregnant were more educated, had higher IQ's, were older and more likely to come from non-manual occupational social class compared with mothers who didn't eat fish. Consumption of oily fish related to less smoking whilst pregnant but higher prevalence of drinking whilst pregnant Mothers who ate oily fish in late pregnancy had babies with heavier birth weight and breastfed for longer

<table>
<tr><td>Reference</td><td>Giordano 2010</td></tr>
<tr><td>Food type</td><td>Fish and shellfish</td></tr>
<tr><td>Study type</td><td>Case-control study</td></tr>
<tr><td>Level of evidence</td><td>III-3 (aetiology)</td></tr>
<tr><td>Setting</td><td>Rome, Italy</td></tr>
<tr><td>Funding</td><td>Not reported</td></tr>
<tr><td>Participants</td><td>80 cases of hypospadias requiring surgical treatment in children aged 0 to 24 months (mean age 57.62 weeks)
80 controls: healthy males without any congenital defect, aged 0 to 24 months (mean age 36.52 weeks);
recruited between September 2005 and May 2007</td></tr>
<tr><td>Baseline comparisons</td><td>See confounding below</td></tr>
<tr><td>Dietary assessment</td><td>Interview on ‘typical’ maternal diet habits in relation to the index pregnancy and food frequencies</td></tr>
<tr><td>Timing</td><td>FFQ administered on recruitment for mothers of cases and during vaccination visits for mothers of controls</td></tr>
<tr><td>Comparison</td><td>Rare versus frequent consumption of fish and shellfish</td></tr>
<tr><td>Outcomes</td><td>Hypospadias</td></tr>
<tr><td>Results</td><td>
<table>
<tr><td colspan="5">Fish or shellfish</td></tr>
<tr><td></td><td>Cases</td><td>Controls</td><td>OR</td><td>aOR</td></tr>
<tr><td>Rare</td><td>58 (72.5%)</td><td>72 (90.0%)</td><td>1.00</td><td>1.00</td></tr>
<tr><td>Frequent</td><td>22 (27.5%)</td><td>8 (10.0%)</td><td>3.41 95% CI 1.42 to 8.23</td><td>2.73 95% CI 1.09 to 6.82</td></tr>
</table>
</td></tr>
<tr><td>Followup</td><td>n/a</td></tr>
<tr><td>Confounding</td><td>Adjusted for mother’s BMI at conception and education of the father;
Gestational age, birthweight and SGA were not included among the covariates in the regression models, as they may share a common aetiology with hypospadias</td></tr>
<tr><td>Risk of bias</td><td>Moderate risk of bias: Participation rate of parents of cases was higher than that of controls (85% versus 70%); very few potential confounders used in adjusted analyses</td></tr>
<tr><td>Relevance</td><td>Likely to be reasonably relevant for Australian women, although risk of pollution less likely in Australia</td></tr>
<tr><td>Other comments</td><td>Likely to be underpowered;
Authors postulate the positive finding may be due to the presence of persistent organic pollutants in fish</td></tr>
</table>

Reference	**Giordano 2008**
Food type	Fish and shellfish
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Sicily, Italy
Funding	Sicilian Congenital Malformation Registry
Participants	90 cases: 43 cases of hypospadias and 48 cases of cryptorchidism (both in one infant) 202 controls: randomly selected controls born in the same year and the same region Births between 1998 to 2003
Baseline comparisons	Low birthweight, low maternal education, mother's history of gynaecological disease and father's history of urogenital diseases differed significantly between cases and controls *See confounding below*
Dietary assessment	Interview on maternal diet and food frequencies
Timing	FFQ
Comparison	Consumption of fish once a week or less vs more than once a week; Consumption of shellfish once a week or less vs more than once a week
Outcomes	Hypospadias and cryptorchidism
Results	

Fish
Hypospadias

	Cases	**Controls**	**OR**
≤ 1/week	25 (58.1%)	140 (69.3%)	1.00
>1/week	18 (41.9%)	62 (30.7%)	1.63 95% CI 0.83 to 3.20
Cryptorchidism			
≤ 1/week	29 (60.4%)	140 (69.3%)	1.00
>1/week	19 (39.6%)	62 (30.7%)	1.48 95% CI 0.77 to 2.84
Hypospadias and cryptorchidism			
≤ 1/week	53 (58.9%)	140 (69.3%)	1.00
>1/week	37 (41.1%)	62 (30.7%)	1.58 95% CI 0.94 to 2.64
Shellfish			
Hypospadias			
≤ 1/week	40 (93.0%)	197 (97.5%)	1.00
>1/week	3 (7.0%)	5 (2.5%)	2.96 95% CI 0.68 to 12.87
Cryptorchidism			
≤ 1/week	43 (93.8%)	197 (97.5%)	1.00
>1/week	3 (6.2%)	5 (2.5%)	2.63 95% CI 0.61 to 11.40
Hypospadias and cryptorchidism			
≤ 1/week	84 (93.3%)	197 (97.5%)	1.00

	>1/week	6 (6.7%)	5 (2.5%)	2.81 95% CI 0.84 TO 9.48
	Fish: adjusted analysis*			
		aOR		
	Hypospadias			
	>1/week	**2.33 95% CI 1.03 to 5.31**		
	Cryptorchidism			
	>1/week	1.33 95% CI 0.61 to 2.90		
	Hypospadias and cryptorchidism			
	>1/week	1.75 95% CI 0.95 to 3.24		
Followup	n/a			
Confounding	*Fish were additionally adjusted for mother's age, parity, education, gynaecological diseases; paternal urogenital diseases, and use of pesticides; birthweight			
Risk of bias	Moderate risk of bias: Participation rate of parents and data collection rate of cases was lower than that of controls (76% versus 91%)			
Relevance	Likely to be reasonably relevant for Australian women, although hypospadias rates very high and unlikely that most Australian women will have such high pesticide exposure			
Other comments	Ragusa region in Sicily is a region of intensive agriculture (involving high rates of pesticide and other chemical use) with high rates of hypospadias and cryptorchidism			

Reference	**Golding 2009**
Food type	Fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	South West England, Avon Longitudinal Study of Parents and Children (ALSPAC), recruited during prenatal health visits. Eligible for ALSPAC - all children born to mothers residing in Bristol and surrounding areas between April 1991 and December 1992.
Funding	The UK Medical Research Council, the Wellcome Trust, and the University of Bristol currently provide core support for ALSPAC; a variety of sources including UK Department of the Environment and the Ministry of Agriculture, Fisheries, and Food; and supported in part by the Intramural Research Program of the NIH, NIAAA, and by a personal gift of John M. Davis.
Participants	9,960 singleton pregnancies, (from initial cohort =14,541) expected birth April 1991-December 1992
Baseline comparisons	See confounding
Dietary Assessment	Food frequency questionnaire
Timing	FFQ and Edinburgh Postnatal Depression Scale (EPDS) at 32 weeks gestation
Comparison	Seafood exposure: a) None b) Between 1 and 340 g/week (equates to <3 average portions fish per week) c) >340 g/week (equates to 3 or more average portions fish per week) Further grouped to: Omega-3 grams/week None, 0.1-0.4; 0.4-1.5; >1.5
Outcomes	High levels depressive symptoms (self report at 32 weeks gestation, using EPDS score > 12)) at 18 and 32 weeks gestation and at 2 and 8 months after birth
Results	Mothers who consumed **no seafood were 50% more likely to have high levels of depressive symptoms** compared to those who consumed substantial amounts of seafood at 32 weeks gestation **Omega-3 Intake (g/wk)** — **Adjusted OR (95% CI)** None — **1.54 (1.25–1.89)** 0.1–0.4 — **1.37 (1.13–1.66)** 0.4–1.5 — **1.20 (1.03–1.41)** >1.5 (ref category) — 1.00 *P* for trend — <0.0001
	Weak associations seen at 18 weeks gestation and 8 months postnatal but not at 2 months postnatal; Sig. interactions across the 4 time points (p = 0.0017)
Follow-up	18 and 32 weeks gestation and 2 and 8 months after birth
Confounding	Considered as potential confounding because of association with depression or with fish eating or both: maternal age (<25, 25+ years); parity, previous pregnancies; outcome of immediately preceding pregnancy (none, survivor, other); maternal education; housing tenure (owned/mortgaged, council rented, other); crowding, mothers' life events in childhood scale; chronic stress as measured by a Family Adversity Index, maternal smoking; alcohol; and maternal ethnic origin.
Risk of bias	Low-moderate risk of bias: Only 9,960 out of 14,541 women (68%) - not stated how these were selected/excluded
Relevance	Relevant, UK not dissimilar to Australia
Other comments	Not clear if low fish intake has varying associations at different times, or a less reliable estimate of intake at 32 weeks

Reference	**Guldner 2007**

Dietary patterns	Fish and shellfish: salt-water fish (including salmon); molluscs (oysters, mussels, etc.); crustaceans (crabs, shrimp etc.)
Study type	Prospective cohort study (PELAGIE)
Level of evidence	II (aetiology)
Setting	Brittany, France
Funding	Regional Council of Brittany, National Institute for Public Health Surveillance (inVS), Ministry of Labor
Participants	2398 pregnant women enrolled from April 2002 to February in the first trimester of their pregnancy
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	During first trimester of pregnancy, to reflect pre-pregnancy consumption
Comparison	‘never or less than once a month’ versus ‘every day’: 0.5, 3, 10, 20 and 30 meals of the specific foods a month
Outcomes	SGA < 10th percentile of gestational age and sex, according to French reference curves); preterm birth < 37 weeks; gestational age, birthweight; low birthweight

Results

	PTB	**LBW**	**SGA**	**aOR (95% CI)** **PTB**	**LBW**	**SGA**
Fish						
< 1/month (n=406)	4.5%	4.4%	7.1%	1.00	1.00	1.00
1-4/month (n=1266)	4.6%	3.3%	5.1%	1.06 (0.60 to 1.87)	0.59 (0.23 to 1.55)	0.72 (0.44 to 1.19)
≥2/week (n=606)	3.0%	1.8%	4.5%	0.71 (0.35 to 1.46)	0.59 (0.18 to 1.91)	0.57 (0.31 to 1.05)
P (linear trend)	1.0	**0.0008**	**0.04**	0.3	0.4	0.07

Multiple linear regression for length of gestation (weeks): β 0.018 95% CI 0.002 to 0.035; p = 0.03
Multiple linear regression for birthweight (g): β -1.556 95% CI -5.587 to 2.476; p = 0.8

	PTB	**LBW**	**SGA**	**PTB**	**LBW**	**SGA**
Shellfish						
< 1/month (n=1548)	4.6%	3.4%	4.8%	1.00	1.00	1.00
1-4/month (n=548)	3.3%	2.4%	5.7%	0.81 (0.47 to 1.39)	1.09 (0.45 to 2.62)	1.33 (0.83 to 2.11)
≥2/week (n=182)	2.8%	3.3%	7.7%	0.66 (0.26 to 1.70)	2.24 (0.70 to 7.15)	**2.14 (1.13 to 4.07)**
P (linear trend)	**0.06**	0.3	**0.05**	0.3	0.2	**0.02**

Multiple linear regression for length of gestation (weeks): β -0.018 95% CI -0.041 to 0.005; p = 0.1
Multiple regression for birthweight (g): β 1.50 95% CI -4.017 to 7.016; p = 1.0

Followup	To birth
Confounding	Analyses adjusted for maternal age, marital status, education level, parity, BMI, maternal height, smoking status, alcohol consumption, diabetes, gender of child (low birthweight was additionally adjusted for duration of gestation)
Risk of bias	Low risk of bias: 80% return of questionnaire (n = 2398 returned); birth outcomes available for 2353 (89%) of women
Relevance	High fish consumption in this population
Other comments	Average of 7.6 seafood meals a month (4.6 fish and 3.0 shellfish) equates to mean daily intake of 20.4 g/day of fish and 19.7 g/day of shellfish’; Differences in findings may be due to higher levels of contaminants in shellfish (due to their filter feeding)

Reference	**Haggarty 2009**

Dietary patterns	Fish: oily fish, other fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Aberdeen, Scotland
Funding	UK Food Standards Agency
Participants	1277 sequentially enrolled pregnant women attending Aberdeen Maternity Hospital for ultrasound (a further 184 women were recruited later in pregnancy). Exclusions: diabetic women, women with multiple pregnancies, women who conceived as a result of fertility treatment, or clinical data not available
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	Assessed at 19 weeks gestation
Comparison	Intake of fish and oily fish by deciles of deprivation
Outcomes	Deprivation (assessed using the Scottish Index of Multiple Deprivation) Low birthweight (defined as < 2500 g or lowest decile for birthweight z score adjusted for gestational age, sex and parity) Preterm birth (< 37 weeks) Admission to neonatal unit
Results	**<u>Deprivation</u>** Fish overall: no significant differences seen between intake of fish and deciles of deprivation **Oily fish: significantly lower intake with higher levels of deprivation (p < 0.01)**
Followup	To neonatal period
Confounding	(Some?) analyses adjusted for energy intake
Risk of bias	Low to moderate risk of bias: low attrition, some lack of detail in reporting of outcomes
Relevance	Likely to be relevant to Australian women
Other comments	About 40-50% of the least deprived women reported taking folic acid supplements compared with about 20% for the most deprived women; Most birth outcome associations were reported by nutrient rather than food group; Not easy to deduce quantities of intake of foods (main graphs reported as change in intake by deprivation decile)

Reference	**Halldorsson 2007**
Food type	Fish
Study type	Prospective cohort from the Danish National Birth Cohort
Level of evidence	II (aetiology)
Setting	Denmark
Funding	Nordic Academy for Advanced Study, Nordic Working Group on Fishery Research, EARNEST, March of Dimes, Danish National Research Foundation, Danish Pharmacy Foundation, Egmont Foundation, Augustinus Foundation, Health Foundation, European Union, Danish Medical Research Foundation, Heart Foundation
Participants	44,824 pregnant women (6-10 weeks gestation) attending first antenatal visit at the general practitioner between 1996 and 2002
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ on type & frequency of fish consumed
Timing	~25 weeks GA
Comparison	Total fish intake (g/d): <=5, >5-20, >20-40, >40-60, >60; Frequency of intake (meal/month): 0, 1, 2-3, adjusted OR for SGA 1.18, 95% CI: 1.03, 1.35; ≥ 4 for both fatty & lean fish
Outcomes	Birth weight, length, head circumference and small for gestational age
Results	**Total intake with birthweight:** Unadjusted: +ve association, p<0.05; lower risk of SGA for moderate intake (OR: 0.82, 95% CI: 0.72, 0.93) vs lowest intake. Adjusted: no association, p=0.09, higher risk of SGA for the highest intake (OR: 1.24, 95% CI:1.01, 1.43) **Total intake with length:** Unadjusted: no association; lower risk of SGA for moderate intake (OR: 0.86, 95% CI: 0.74, 0.99). Adjusted: -ve association p=0.04 for length **Total intake with HC:** Unadjusted: no association; adjusted: -ve association, p=0.005, no difference in risk of SGA. **Type & frequency of intake:** **Fatty fish**: inverse association between frequency of intake & birth wt, length & HC in adjusted & unadjusted (not for HC). For intake ≥ 4 meals /month compared with none, adjusted OR for SGA 1.18, 95%CI: 1.03, 1.35, p=0.04 for wt, OR 1.22, 95%CI: 1.05, 1.40, p=0.003 for length, OR: 1.10, 95% CI: 0.97, 1.25, p = 0.12 for HC. **Lean fish:** no association in adjusted analyses.
Followup	n/a
Confounding	Adjusted for total energy intake, GA, sex, parity, maternal age, maternal & paternal height, pre-pregnancy BMI, maternal smoking, family socioeconomic status (occupation)
Risk of bias	Low to moderate risk of bias: High attrition rate (44,824 out of 101,046 recruited - only 11,157 excluded (women with missing data, multiple birth (8,174) or taking fish oil supplements (2,983) so 45,065 unaccounted for)
Relevance	Relevant to Australian women
Other comments	Fish consumption was strongly associated with other characteristics (smoking, SES, parity and pre-pregnancy body mass index) of the sample that are strong predictors of fetal growth, did not include non-fish forms of seafood

Reference	**Halldorsson 2008**
Food groups	Fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Danish National Birth Cohort, Denmark 1996-2002, recruited during first antenatal visit with GP
Funding	Nordic Academy for Advanced Study, Nordic Working Group on Fishery Research, EARNEST, NewGeneris, March of Dimes, Danish National Research Foundation, Danish Pharmaceutical Foundation, Danish Medical Research Foundation, Danish Heart Association, Ministry of Health (Denmark), National Board of Health (Denmark), Sygekasserenes Helsefond, Statens Serum Institut
Participants	100 nulliparous women aged 25-35 years with normal pre-pregnancy BMI and consistent fish intake and recruited between 1998 and 2002
Baseline comparisons	*See confounding below*
Dietary Assessment	FFQ assessing fish consumption at 25 weeks gestation-self administered, 10-15 min phone interview at 12 and 30 weeks gestation
Timing	FFQ assessing fish consumption at 25 weeks gestation and frequency of fish (species not specified) intake asked at 12 and 30 weeks gestation over the phone, cord blood and 2 maternal blood samples collected at routine GP visits (8 and 25 weeks gestation)
Comparison	Average fish intake: low (0), medium (1-3) or high (≥4) meals per month of fatty fish
Outcomes	Plasma concentrations of PCBs, association between maternal PCB concentration and birth weight, height, head circumference and placental weight

Results

Spearmans r=0.54, P<0.0001) association between fatty fish intake (grams per day) and plasma PCB concentration

Adjusted association for fatty fish intake (per month) and plasma PCB concentration

	β	**95% CI**
Low	0	Referent
Medium	3	-9, 15
High	18	5, 34
P for trend (two sided)		**0.005**
R^2		0.62

Adjusted association between log transformed PCB concentration and fetal growth

	β	**95% CI**	**P value (two sided)**
Birth weight (g)	**-334**	**-628, -40**	**0.03**
Birth length (cm)	-1.2	-2.5, -1.2	0.08
Head circumference (cm)	-0.8	-19, 0.4	0.2
Placental weight (g)	**-174**	**-291, -57**	**0.004**

Length of follow up	Birth
Confounding	Fish intake vs plasma PCB - Crude and adjusted results reported (maternal age, pre-pregnancy BMI, recruitment year, plasma lipid concentration) PCB vs fetal growth- Crude and adjusted results reported (gestational age, infant sex, maternal smoking, pre-pregnancy BMI, plasma lipid concentration)
Risk of bias	Moderate risk of bias
Relevance	Australian diet likely to be slightly diff from Danish diet (average 27g fish intake per day?)
Other comments	Did not include non-fish forms of seafood, Excluded many women from analysis (only included 100 out of 101,046)

Reference	**Haugen 2008**
Dietary patterns	Fish as part of Mediterranean-type diet (2 or more serves of fish per week)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Norway (part of the Norwegian Mother and Child Cohort Study (MoBa))
Funding	Norwegian Ministry of Health, NIH/NINDS, Norwegian Research Council/FUGE, EU FP& consortium, Metabolic Programming (EARNEST).
Participants	40,817 pregnancies of women recruited for MoBa from February 2002 to February 2005 of whom 26,563 (65%) met the following criteria: women had to be non-smoking, BMI between 19 and 32, aged between 21 and 38 years when giving birth, with a singleton birth. Exclusions: more than 3 spontaneous abortions, energy intake less than 4,200 kJ and more than 16,700 kJ.
Baseline comparisons	*See confounding below*
Timing	FFQ at 17-24 weeks gestation
Comparison	Fish ≥ 2 times a week v < 2 times a week
Outcomes	Preterm birth (after week 21 and before week 37); late preterm birth (week 35-36) and early preterm birth (< 35 weeks)
Results	***Preterm birth (< 37 weeks): (n = 25,966; 1174 cases)*** **OR 0.81 95% CI 0.72 to 0.92** **aOR 0.84 95% CI 0.74 to 0.95** ***Early preterm birth (< 35 weeks): (n = 25,256; 474 cases)*** **OR 0.81 95% CI 0.67 to 0.97** aOR 0.84 95% CI 0.70 to 1.02 ***Late preterm birth (35-36 weeks): (n = 25,492; 710 cases)*** **OR 0.83 95% CI 0.71 to 0.96** **aOR 0.84 95% CI 0.72 to 0.98**
Followup	To birth
Confounding	Analyses were adjusted for remaining Mediterranean diet criteria, mother's BMI and height, educational level, parity and marital status
Risk of bias	Moderate: some dietary intakes were different between groups and were not controlled for
Relevance	Moderate: low red meat consumption not typical for many Australian women
Other comments	Preterm birth rates were lower than expected, likely due to exclusion of smokers

Reference	**Hibbeln 2007**
Food groups	Seafood (white fish, oily fish, shellfish)
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Bristol region, UK (ALSPAC)
Funding	Medical Research Council, Wellcome Trust, University of Bristol, UK government departments, "medical charities and other sources", NIH.
Participants	8801 pregnant women with an expected due date between April 1, 1991 and Dec 31, 1992
Baseline comparisons	*See Confounding below*
Dietary assessment	FFQ
Timing	FFQ assessing seafood consumption at 32 weeks' gestation
Comparisons	> 340 g seafood per week v 1-340 g seafood per week v none; three serves of seafood a week equates to about 347 g per week
Outcomes	Child: Cognition at 8 years (verbal, performance, total IQ); Behaviour at 7 years (prosocial, peer problems, hyperactivity, emotional, conduct, total); Gross motor skills (6, 18, 30, 42 months); Fine motor skills (6, 18, 30, 42 months); Social skills (6, 18, 30, 42 months); Communication skills (6, 18 months)
Results	

Child cognition at 8 years (aOR 95% CI)

	N	*None v > 340 g/wk*	*1-340 g/wk v > 340 g/wk*	*p for trend*
Verbal IQ	5047	**1.48 (1.16 to 1.90)**	1.09 (0.92 to 1.29)	**0.0041**
Performance IQ	5042	0.98 (0.76 to 1.27)	0.99 (0.84 to 1.18)	0.9015
Full scale IQ	5000	1.29 (0.99 to 1.69)	1.19 (0.99 to 1.42)	**0.0389**

Child behaviour at 7 years (aOR 95% CI)

	N	*None v > 340 g/wk*	*1-340 g/wk v > 340 g/wk*	*p for trend*
Prosocial	6582	**1.44 (1.05 to 1.97)**	1.16 (0.93 to 1.44)	**0.0249**
Hyperactivity	6575	1.13 (0.84 to 1.53	0.91 (0.73 to 1.12)	0.6293
Emotional	6582	1.09 (0.83 to 1.44)	0.96 (0.80 to 1.17)	0.6810
Conduct	6586	1.21 (0.89 to 1.64)	1.01 (0.81 to 1.25)	0.2869
Peer problems	6581	1.25 (0.96 to 1.62)	0.97 (0.80 to 1.16)	0.1753
Total score	6570	1.17 (0.86 to 1.60)	0.98 (0.79 to 1.22)	0.3832

Child development at 6 to 42 months (aOR 95% CI)

	N	*None v > 340 g/wk*	*1-340 g/wk v > 340 g/wk*	*p for trend*
Gross motor skills				
6 months	8764	1.10 (0.90 to 1.34	1.06 (0.92 to 1.21)	0.3262
18 months	8227	1.02 (0.85 to 1.22)	1.10 (0.89 to 1.13)	0.8420
30 months	7720	0.97 (0.80 to 1.18)	1.03 (0.90 to 1.17)	0.9402
42 months	7603	0.96 (0.78 to 1.18)	0.99 (0.87 to 1.13)	0.7159
Fine motor skills				
6 months	8746	1.01 (0.83 to 1.23)	1.12 (0.99 to 1.28)	0.5191
18 months	8228	**1.25 (1.04 to 1.51)**	1.09 (0.96 to 1.23)	**0.0222**
30 months	7728	1.04 (0.85 to 1.27)	1.04 (0.91 to 1.19)	0.6163
42 months	7596	**1.35 (1.09 to 1.66)**	1.14 (0.98 to 1.31)	**0.0053**
Social development				
6 months	8743	1.15 (0.95 to 1.40)	1.01 (0.89 to 1.16)	0.2173
18 months	8226	1.01 (0.83 to 1.24)	1.01 (0.88 to 1.15)	0.8937
30 months	7711	**1.24 (1.01 to 1.53)**	1.12 (0.98 to 1.29)	**0.0326**

	42 months	7592	1.21 (0.98 to 1.50)	**1.17 (1.01 to 1.35)**	**0.0377**
	Communication				
	6 months	8745	**1.30 (1.04 to 1.63)**	1.15 (0.98 to 1.35)	**0.0184**
	18 months	8237	**1.26 (1.03 to 1.53)**	1.02 (0.90 to 1.17)	**0.0485**
Length of followup	6 months to 8 years (depending on outcome – see above)				
Confounding	Analyses adjusted for maternal education, housing, crowding at home, life events, partner, maternal age, maternal smoking in pregnancy, maternal alcohol use in pregnancy, parity, breastfeeding, gender of child, ethnic origin, birthweight, preterm birth, 12 non-fish food groups				
Risk of bias	Low-moderate risk of bias: not adjusted for maternal IQ or home environment; attrition was disproportionately high in families with social disadvantage and lower seafood intake; however this may have acted to underestimate any association with child development - 8801/11,875 (74.1%) women had data available for confounding variables and had completed at least one valid response on the questionnaire. This dropped to 5,000 (42.1%) at 8 year follow-up.				
Relevance	Likely to be relevant to Australian women				
Other comments	Only 1.7% of women in the study took fish oil supplements; ALSPAC is reasonably representative of the British population which has a mean mercury consumption (0.05 µg/kg bodyweight); higher than US (0.02)				

Reference	**Jedrychowski 2010**
Dietary patterns	Fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	New York City, USA and Krakow, Poland
Funding	NIEHS, Gladys and Roland Harriman Foundation, New York
Participants	481 nonsmoking women with singleton pregnancies, 18-35 years of age, giving birth at term (> 36 weeks) between January 2001 and February 2004; eligible if attending antenatal care in 1st and 2nd trimesters and free from chronic diseases such as diabetes and hypertension
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ twice (in 2nd and 3rd trimester)
Comparison	Fish intake: never, < once per month, once a week, 1-2 times a week, 3-4 times a week, every day (assumed each meal = 150 g of fish)
Outcomes	Fine particulate matter (from personal monitoring during 2nd trimester); birthweight
Results	**BIRTHWEIGHT** **Low fish intake (< 91 g/week) and high antenatal fine particulate matter concentrations (> 46.3 μg/m^3)** **Regression coefficient: -133.26 g birthweight (p = 0.052)** **Medium fish intake (91 to 205 g/week) and high antenatal fine particulate matter concentrations (> 46.3 μg/m^3)** Regression coefficient: -93.38 g birthweight (p = 0.247) **High fish intake (> 205 g/week) and high antenatal fine particulate matter concentrations (> 46.3 μg/m^3)** Regression coefficient: -23.69 g birthweight (p = 0.811)
Followup	To birth
Confounding	Maternal age, maternal size (height, prepregnancy weight), maternal education, parity, gestational age, gender of child, season of birth
Risk of bias	Moderate risk of bias: selection bias from excluding smokers and women with conditions that may affect fetal growth
Relevance	Unclear if exposures to fine particulate matter are similar in Australia
Other comments	Neither birthweight or amount of fine particulate matter alone were significantly associated with amount of fish intake

Reference	**Jedrychowski 2008**
Dietary patterns	Fish (smoked, fried, roasted, grilled)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Krakow, Poland
Funding	NIEHS, Gladys and Roland Harriman Foundation
Participants	465 nonsmoking women aged 18-35 years who gave birth between 29 and 43 weeks gestation between January 2001 and February 2004; eligible if attending antenatal care in 1st and 2nd trimesters; with singleton pregnancies and free from chronic diseases such as diabetes and hypertension
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ twice (in 2nd and 3rd trimester)
Comparison	Fish intake: range 0 to 1050 g/week; median 150 g/week (95% CI 145 to 150)
Outcomes	Fine particulate matter (from personal monitoring during 2nd trimester); respiratory symptoms in 2 year infants
Results	**Coughing in infants up to 2 years of age** Interaction term ($PM_{2.5}$ category X fish consumption level): aIRR 1.36 95% CI 0.79 to 1.43 **Wheezing in infants up to 2 years of age** Interaction term ($PM_{2.5}$ category X fish consumption level): **aIRR 0.80 95% CI 0.72 to 0.89** **Difficult breathing in infants up to 2 years of age** Interaction term ($PM_{2.5}$ category X fish consumption level): **aIRR 0.81 95% CI 0.72 to 0.91**
Followup	Until infants reached 2 years of age
Confounding	Maternal education, maternal atopy, breastfeeding, postnatal environmental tobacco smoke, parity, gestational age, gender of child, moulds in the household
Risk of bias	Low-moderate risk of bias: not stated if any participants were lost to follow up; smokers were excluded
Relevance	Unclear if exposures to fine particulate matter are similar in Australia
Other comments	Likely to be the same population as Jedrychowski 2010

Reference	**Jensen 2004**
Food type	Fish: Oysters, fried fish, fish (broiled or baked)
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study)
Funding	PHS
Participants	138 matched cases and controls: Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, parental occupation and smoking during pregnancy – no evidence of confounding was seen for these variables. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of fish
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Oysters:** aOR 1.00 95% CI 0.52 to 1.94: mean consumption 1.11 [SD 0.44] serves per day* **Fried fish:** aOR 0.97 95% CI 0.82 to 1.30: mean consumption 1.64 [SD 1.13] serves per day **Fish (broiled or baked):** aOR 1.03 95% CI 0.71 to 1.08: mean consumption 2.11 [SD 1.40] serves per day
Followup	n/a
Confounding	Analyses were adjusted for variables previously shown to be significantly associated with ALL in the overall study – income, prior fetal loss, child's exposure to other children under age five, and maternal exposure to indoor insecticides during pregnancy; along with portion size and energy consumption
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 1999, 83% consented to participate; 69% of the eligible controls agreed to participate. Of the 161 matched pairs, seven pairs were excluded as the respondent was not the biological mother, 16 pairs were excluded due to questionable dietary questionnaire data, leaving 138 matched pairs (86%); some recall bias likely
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	*Some consumption levels seem high – possibly per week rather than per day? Fish as a group not reported (included under a protein group)

Reference	**Jones 2000 (see also Yin 2010)**
Food type	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Southern Tasmania, Australia
Funding	NHMRC, Tasmanian Government, Royal Hobart Hospital Acute Care Program
Participants	173 mothers; and their infants born in 1988 (part of a larger infant health study of babies at high risk of SIDS) Exclusions: multiple pregnancies
Baseline comparisons	Mothers with no tertiary education more likely to have been excluded due to missing data
Dietary assessment	FFQ
Timing	Dietary intake during third trimester of pregnancy
Comparison	Linear regression of density (portions per kJ)
Outcomes	Bone mass (bone mineral density (BMD) and bone mineral content*) in 8 year old children
Results	**BMD at 8 years;** **Total body (g/cm^2)** **r^2 2% 0.049 (p = 0.05)** adjusted r^2 24% 0.034 (p = 0.15) **Femoral neck (g/cm^2)** r^2 1% 0.035 (p = 0.43) adjusted r^2 33% 0.020 (p = 0.57) **Lumbar spine (g/cm^2)** r^2 0% 0.010 (p = 0.86) adjusted r^2 32% -0.010 (p = 0.75)
Followup	8 years
Confounding	Analyses were adjusted for method of dietary assessment, maternal education, parental unemployment, sex, weight at age 8 years, height at age 8 years, weekend sunlight exposure in winter at age 8 years, smoking during pregnancy, sports participation, ever breast-fed and current calcium intake.
Risk of bias	Moderate-high: 330 (215 males, 115 females) representing a 60% response rate from those available in 1996; 47% of the original 1988 cohort, This dropped to 173 (dietary information missing or unreliable for 115 mothers, 32 multiple births, 10 participants had missing data for confounders) representing 52% of participants from 1996 and 25% of those in the original cohort. 72% of the 173 participants were male. Gender imbalance suggests potential selection bias (due to original selection of infants at high risk of SIDS)
Relevance	Infants at high risk of SIDS represent a selected group (more males, preterm births, teenage mothers, smoking during pregnancy)
Other comments	*Bone mineral content not reported – stated to be similar to bone mineral density results

Reference	**Lamb 2008**
Dietary patterns	Fish: canned tuna, dark-meat fish (mackerel, salmon, sardines, bluefish, swordfish etc), other fish, and shrimp, lobster or scallops as a main dish
Study type	Part of a longitudinal prospective birth cohort study
Level of evidence	II (aetiology)
Setting	Denver, Colorado, US (part of the Diabetes Autoimmunity Study in the Young (the DAISY))
Funding	National Institutes of Health, Diabetes Endocrine Research Center
Participants	642 newborns at increased risk for type 1 diabetes (based on HLA genotype and family history), enrolled in the study from 1993 to 2004; 27 cases defined as testing positive for islet autoantibodies at two consecutive blood draws and still positive (diabetic) at last follow-up
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	From 1997 to 2004, mothers of infants enrolled in DAISY completed FFQ soon after birth, reflecting diet in the last trimester of pregnancy (but could submit FFQ before child reached one year of age)
Comparison	Monthly servings of fish
Outcomes	Islet autoimmunity in children (a precursor of type 1 diabetes) at 9 months, 15 months, 2 years and annually thereafter up to the age of 15
Results	**Fish:** aHR (for one standard deviation change in reported consumption) 0.90 95% CI 0.54 to 1.51 (5.10 mean monthly servings)
Followup	Up to 15 years
Confounding	Size for gestational age, ethnicity, maternal education, household income, exposure to type 1 diabetes or GDM in utero, gender of child, maternal age at birth, total calories of maternal diet
Risk of bias	Moderate risk of bias: subset of DAISY only (later enrolments); and women were not reminded to submit FFQ, leading to possible selection bias; of the 661 FFQs returned, 5 were excluded because incomplete, and 14 for implausible dietary intakes, leaving 642 FFQs for analysis; child's diet not controlled for
Relevance	Likely to be relevant to some Australian women, although women in this study may have been at higher risk of diabetes
Other comments	

Reference	**Latva-Pukkila 2009**
Dietary patterns	Fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Turku, Finland (cohort from Piirainen 2006)
Funding	Social Insurance Institution of Finland, the Sigrid Juselius Foundation and the Academy of Finland
Participants	256 pregnant women
Baseline comparisons	Women with NVP were older and tended to be primiparous compared to those without
Dietary assessment	3 day food diaries
Timing	Three times during pregnancy (mean 14, 24 and 34 weeks gestation)
Comparison	With nausea and vomiting in pregnancy (NVP) versus no NVP; 134 (72%) women reported experiencing nausea; with 40 (30%) vomiting (9 (4.8%) more than once a day) during the first trimester
Outcomes	Influence of nausea and vomiting in pregnancy on dietary intake; Severity of NVP assessed as having no nausea and vomiting, only nausea, vomiting once a day or vomiting more than once a day, with the primary outcome being presence or absence of nausea
Results	<table><tr><th></th><th>***With NVP (n = 134***</th><th>***Without NVP (n = 53)***</th><th>***p***</th></tr><tr><td>**Fish products (g), median (IQR) daily**</td><td>18 (0 to 40)</td><td>20 (0 to 55)</td><td>0.446</td></tr></table>
Followup	To 34 weeks gestation
Confounding	Not reported if any of the analyses were adjusted
Risk of bias	Moderate risk of bias: not clear if analyses were adjusted for potential confounders
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Lauritzen 2005a; Lauritzen 2005b; Lauritzen 2005c; Lauritzen 2004a; Ulbak 2004; Asserhoj 2009**
Dietary patterns	Fish
Study type	Non-randomised comparative study (control arm of RCT compared with a reference group)
Level of evidence	III-2 (intervention)
Setting	Denmark (women recruited from the Danish National Birth Cohort during 1999)
Funding	FOTEK (Danish Research and Development Program for Food and Technology) and BASF Aktiengesellschaft
Participants	110 pregnant women (60 with a low fish intake; < 0.4 g n-3 LCPUFA.d^{-1} and 50 with a high fish intake > 0.8 g n-3 LCPUFA.$^{d-1}$) with an uncomplicated pregnancy, normal pre-pregnancy BMI, no metabolic disorders, an intention to breastfeed for at least four months, with healthy singleton term infants with normal weight for gestation and an Apgar score > 7 at 5 minutes.
Baseline comparisons	*n/a*
Dietary assessment	Low fish intake ascertained by FFQ at 25 weeks gestation to reflect diet in previous four weeks
Timing	*See above*
Comparison	Low fish intake; below population median (without fish oil supplementation) versus high fish intake (upper quartile of the population) during first four months of maternal lactation
Outcomes	Infant problem solving ability at nine months (The Infant Planning Test); infant linguistic development at one and two years of age (Macarthur Communicative Development Inventory); overall motor function; sitting without support; children's blood pressure at 2.5 years of age
Results	**Visual acuity at 4 months** No significant differences between the low and high fish intake groups were seen for visual acuity at 4 months **Problem solving at nine months (intention score entire problem)** Low fish intake: 4.3 [SD3.6] (n = 38); High fish intake: 4.5 [SD3.3] (n = 42) ***Linguistic development at one year:*** **Starting to talk (%)** Low fish intake: 16/37 (43.2%); High fish intake: 17/42 (40.5%) **Vocabulary comprehension (no. of words)** Low fish intake: 71 [SD45] (n = 37); High fish intake: 65 [SD40] (n = 42) ***Linguistic development at two years:*** **Vocabulary production (no. of words)** Low fish intake: 297 [SD147] (n = 31); High fish intake: 312 [SD146] (n = 40) **Sitting without support** Low fish intake: 6.5 [SD0.8]; High fish intake: 6.4 [SD1.0] **Overall motor function** No significant differences between the low and high fish intake groups (numeric results not reported) ***2.5 year followup*** **Blood pressure at 2.5 years** No significant differences seen between the low (n=22) and high fish intake groups (n=25) No significant differences seen between the low and high fish intake groups for head circumference, weight, length/height, ponderal index or BMI from birth to 2.5 years of age

	<u>**Seven year follow-up**</u> **Amount of time very active was significantly higher in the high fish intake group than the low fish intake group (p = 0.039)** No significant differences between the two groups at 7 years were seen in body composition measures (such as head circumference, BMI or being overweight) or blood pressure
Followup	To seven years of age
Confounding	*n/a*
Risk of bias	Low to moderate risk of bias: 13/60 (21.7%) from the low fish intake group and 2/50 (4%) from the high fish intake group were lost to followup; at 2.5 years follow-up, 22/60 and 21/50 respectively were available for analysis; at seven years, 28/60 and 34/50 respectively; not all analyses controlled for confounders
Relevance	Likely to be relevant to Australian women
Other comments	Likely to be underpowered, particularly with losses to follow-up over time

Reference	**Maconochie 2007**
Food groups	Fish
Study type	Case-control study (postal survey sampled from the electoral roll – National Women's Health Study)
Level of evidence	III-3 (aetiology)
Setting	UK general population
Funding	National Lottery Community Fund, Miscarriage Association
Participants	Cases: 603 women aged 18 to 55 years whose most recent pregnancy had ended in first trimester miscarriage (< 13 weeks gestation); Controls: 6116 women aged 18 to 55 years whose most recent pregnancy had progressed beyond 12 weeks
Baseline Comparisons	BMI < 18.5 was significantly associated with odds of miscarriage *Also see Confounding below*
Dietary Assessment	questionnaire
Timing	Diet in the three months prior to conception and the first 12 weeks of pregnancy
Comparison	At least twice weekly
Outcomes	First trimester miscarriage
Results	**Fish twice weekly or more** (see table below)
Length of followup	n/a
Confounding	Adjusted for year of conception, maternal age, previous miscarriage and previous live birth; and further adjusted for nausea in the first 12 weeks of pregnancy
Risk of bias	Low risk of bias: 88% of eligible women responding to stage 1 agreed to participate in the second stage of the study; and 71% responded to the stage 2 questionnaire. 1071/7790 records (7508 women) were excluded (mostly due to index pregnancy being conceived prior to 1980), leaving 6719 records (86%) available for analysis
Relevance	Likely to be relevant to Australian women
Other comments	Women who suffered from nausea in the first 12 weeks of pregnancy were almost 70% less likely to miscarry

Fish twice weekly or more

	Cases	Controls	aOR (95% CI)	aOR further adjusted for nausea
No	372 (66%)	3552 (62%)	1.00	1.00
Yes	189 (34%)	2207 (38%)	**0.83 (0.69 to 1.00)**	0.86 (0.71 to 1.03)

Reference	**Mendez 2010**
Food type	Fish (fatty fish, lean fish, canned tuna, crustaceans and other shellfish)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Mediterranean coast of Spain
Funding	Spanish Ministry of Health, Instituto de Salud Carlos III, Generalitat de Catalunya-CIRIT, European Union sixth framework project EARNEST
Participants	657 women recruited in first trimester of pregnancy between July 2004 and July 2006 in a Mediterranean area with high seafood intake (Sabadell cohort of the Childhood and Environment study 'INMA')
Baseline comparisons	See confounding below
Dietary assessment	FFQ
Timing	FFQ at recruitment (to cover intake since the start of pregnancy)
Comparison	*See Results below*
Outcomes	SGA (< 10th centile of a Spanish reference population)
Results	**Maternal consumption of crustaceans (at least once per week) and canned tuna (at least once per week) but not fatty fish, lean fish or other shellfish, was consistently and significantly associated with <u>increased risk of SGA</u> (with little effect from adjusted for several persistent organic pollutants – such as PCBs, HCB and DDE)**

	Adjusted OR (95% CI)		**Additionally adjusted for contaminants**	
	SGA	**SGA adj***	**SGA**	**SGA adj***
<u>All seafood</u>				
≤ 3/week	1.00	1.00	1.00	1.00
More than 3-6/week	1.63 (0.50 to 5.27)	1.41 (0.37 to 5.41)	1.95 (0.52 to 7.31)	1.91 (0.38 to 9.58)
More than 6/week	2.41 (0.76 to 7.69)	2.77 (0.77 to 9.89)	2.91 (0.78 to 10.87)	3.89 (0.82 to 18.59)
Crustaceans > 1/week	**2.45 (1.11 to 5.41)**	**3.05 (1.34 to 6.99)**	**2.56 (1.11 to 5.89)**	**3.24 (1.34 to 7.83)**
Other Shellfish > 1/week	0.85 (0.41 to 1.80)	1.10 (0.50 to 2.43)	0.93 (0.43 to 2.00)	1.27 (0.56 to 2.89)
Fatty fish > 1/week	1.58 (0.82 to 3.04)	1.13 (0.55 to 2.34)	**2.03 (1.01 to 4.07)**	1.52 (0.70 to 3.30)
Lean fish > 1/week	0.94 (0.48 to 1.82)	0.99 (0.48 to 2.03)	0.77 (0.38 to 1.55)	0.76 (0.35 to 1.65)
Canned Tuna > 1/week	**2.80 (1.23 to 6.40)**	**2.49 (1.04 to 5.97)**	**2.61 (1.12 to 6.07)**	**2.39 (0.96 to 5.96)**

*SGA adj excludes infants whose actual birth weights exceeded the 10th percentile

Followup	To birth
Confounding	Adjusted for energy intake, child sex, maternal age, nulliparity, paternal BMI, maternal BMI, education, under-reporting and smoking during pregnancy (models for seafood subtypes also adjusted for other types) (Omitted variables for maternal intakes of meats, eggs, vegetables, fruits, legumes, dairy products, dietary fat, alcohol and coffee as associations were virtually unchanged)
Risk of bias	Low risk of bias: birth outcomes were available for 616/657 women (94%), including 596 term births; maternal characteristics and dietary data were available for 610 and 592 women respectively
Relevance	Seafood consumption higher in this study than in Australia (mean 40-80 g/day)
Other comments	Study focussed on term births as there were only 20 preterm births; Maternal seafood consumption in this study was not strongly related to sociodemographic or other parental characteristics including BMI

<table>
<tr><td>**Reference**</td><td>**Mendez 2009**</td></tr>
<tr><td>**Food groups**</td><td>Fish, octopus/squid and shellfish</td></tr>
<tr><td>**Study type**</td><td>Prospective cohort</td></tr>
<tr><td>**Level of evidence**</td><td>II (aetiology)</td></tr>
<tr><td>**Setting**</td><td>General practices in Menorca, a Mediterranean island in Spain (mid 1997 to mid 1998)</td></tr>
<tr><td>**Funding**</td><td>Instituto de Salud Carlos III red de Grupos Infancia y Media Ambiente, the Fundacio “La Caixa” , Instituto de Salud Carlos III, red de Centros de Investigacion en Epidemiologica y Salud Publica, EU, National Center for Environmental Health, USA, the GA2LEN project, Ministry of Education and Science, Spain, Oficina de Ciencia y Tecnologia, Generalitat Valenciana.</td></tr>
<tr><td>**Participants**</td><td>482 women presenting to antenatal care</td></tr>
<tr><td>**Baseline Comparisons**</td><td>Baseline difference in age – women who had fish >3 times per week older. *See Confounding below*</td></tr>
<tr><td>**Dietary Assessment**</td><td>FFQ (semi-quantitative)</td></tr>
<tr><td>**Timing**</td><td>Pregnancy: FFQ of fish intake during pregnancy interviewer administered conducted 3 months after birth</td></tr>
<tr><td>**Comparison**</td><td>Fish intake ≤1, >1 to 2, >2-3 or >3 times per week
Shellfish and squid analysed separately (low DHA): ≤0.5, >0.5 to 1, >1 times per week</td></tr>
<tr><td>**Outcomes**</td><td>Cognitive performance at 4 years (McCarthy Scales of Children’s Abilities)</td></tr>
<tr><td>**Results**</td><td>Fish consumption not related to duration of breastfeeding or any maternal characteristics
More frequent fish consumption associated with higher parity and BF ≥ 6/12 months

Adjusted multivariate association between general cognitive performance and maternal fish intake (95% CI) with ≤1 times/week as referent category
<table>
<tr><th>Maternal weekly fish intake frequency:</th><th>≤1</th><th>>1-2</th><th>>2-3</th><th>>3</th><th>P</th></tr>
<tr><td></td><td></td><td>n = 129 (33%)</td><td>n = 50 (13%)</td><td>n = 20 (5%)</td><td></td></tr>
<tr><td>Breastfed <6 months</td><td>Ref</td><td>+2.7 (-1.2, 6.5)</td><td>**+11.0 (5.0, 7.1)***</td><td>-1.2 (-9.8, 7.3)</td><td></td></tr>
<tr><td>Breastfed ≥ 6 months</td><td>Ref</td><td>-0.7 (-7.0, 5.7)</td><td>-0.7 (-8.3, 6.9)</td><td>-5.3 (-17.9, 7.3)</td><td></td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>*P<0.05</td></tr>
</table></td></tr>
<tr><td>**Length of followup**</td><td>4 years</td></tr>
<tr><td>**Confounding**</td><td>Covariates: Breast feeding duration (<6 months vs ≥6 months), maternal education, parity, child sex, birth weight, weeks of gestation, child age at test administration, current trimester grade and psychologist performing test
Variables excluded (no confounding associations between fish consumption and development): maternal age, pre-pregnancy overweight/obesity, smoking during pregnancy, social class (based on occupation), child overweight at 4 years, other aspects of maternal diet during pregnancy (supplements, meat, fruit, vegetables, alcohol, coffee) and children’s current diets (meat, fruit, vegetables)</td></tr>
<tr><td>**Risk of bias**</td><td>Low-moderate risk of bias: original cohort of 482 (95% participation). Analysed in this study 392 (81%) children born at term with no missing data, excluded 23 preterm babies (392/459; 85%), and those with missing data, low numbers in > 3 times per week group, possibility of poorer neurodevelopmental outcomes in those who did not participate; not adjusted for maternal IQ or home enviroment.</td></tr>
<tr><td>**Relevance**</td><td>Australian diet likely to differ slightly from Spanish ‘island’ diet.</td></tr>
<tr><td>**Other comments**</td><td>108 children not included</td></tr>
</table>

Reference	**Mikkelsen 2008**
Dietary patterns	Mediterranean diet (**consumption of fish twice a week or more**, intake of olive or canola oil, high consumption of fruits and vegetables (5 a day or more), meat (other than poultry or fish) at most twice a week, and at most 2 cups of coffee a day)
Study type	Prospective cohort study
Level of evidence	II
Setting	Denmark (part of the Danish National Birth Cohort (DBNC))
Funding	March of Dimes Birth Defects Foundation, Danish National Research Foundation, Danish Medical Research Foundation, Danish Health Foundation, Danish Heart Foundation, EU FP7 consortium (EARNEST), Pharmacy Foundation, Egmont Foundation, Augustinus Foundation.
Participants	35,530 pregnant women recruited from 1996 to 2002 Exclusions: women who smoked, women aged < 21 and > 38 years, BMI < 19 and > 32, a history of more than 3 abortions, twin pregnancies, chronic hypertension, women with a calculated energy intake < 4,200 kJ and > 16,700 kJ
Baseline comparisons	BMIs were significantly lower in the MD and none groups.
Dietary assessment	FFQ
Timing	FFQ mailed to all DBNC participants in 25^{th} week of gestation
Comparison	≥ 2 serves a fish per week v < 2
Outcomes	Preterm birth
Results	**<u>Preterm birth < 37 weeks</u>** OR 0.90 95% CI 0.79 to 1.02 aOR 0.95 95% CI 0.84 to 1.08 **<u>Early preterm birth < 35 weeks</u>** OR 0.91 95% CI 0.74 to 1.12 aOR 0.96 95% CI 0.78 to 1.19 **<u>Late preterm birth 35-36 weeks</u>** OR 0.89 95% CI 0.76 to 1.04 aOR 0.94 95% CI 0.81 to 1.10
Followup	To birth
Confounding	Adjusted for parity, BMI, maternal height, socioeconomic status and cohabitant status
Risk of bias	Low risk of bias; GA based mostly on ultrasound; 0.36% missing data (127/35657)
Relevance	Relevance limited by exclusion of smokers and obese women
Other comments	

Reference	**Mitchell 2004**
Dietary patterns	Fish (including shellfish)
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Waitemata Health or Auckland Healthcare regions, New Zealand
Funding	Health Research Council of New Zealand, Foundation for the Newborn, Child Health Research Foundation
Participants	Mothers of 1138 children born between October 1995 and November 1997 (844 born SGA and 870 born appropriate for GA); only term infants (> 37 weeks); Exclusions: preterm births (< 37 weeks), multiple births and those with congenital anomalies
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered after birth (to cover the periconception period and the last month of pregnancy)
Comparison	None v ≤ 1 v > 1 serves of fish per week
Outcomes	SGA (≤ 10th centile for GA and gender)
Results	**SGA** (fish consumption at time of conception) | | SGA | AGA | aOR (95% CI) | p value for trend | None | 110/529 (20.8%) | 84/592 (14.2%) | **1.69 (1.07 to 2.69)** | ≤ 1 | 312/529 (59.0%) | □8□/592 (64.5%) | 1.09 (0.75 to 1.58) | > 1 | 107/529 (20.2%) | 126/592 (21.3%) | 1 | 0.04 **SGA** (fish consumption in last month of pregnancy) None | 138/529 (26.0%) | 137/593 (23.1%) | 1.29 (0.83 to 1.99) | ≤ 1 | 284/529 (53.7%) | 344/593 (58.0%) | 1.07 (0.73 to 1.57) | □ 1 | 144/529 (27.2%) | 112/593 (18.9%) | 1 | 0.39
Followup	NA
Confounding	Adjusted for socio-economic status, ethnicity, maternal height, maternal weight before pregnancy, maternal hypertension and maternal smoking; but folate supplementation was not controlled for (periconception folate was significantly associated with reduced SGA risk).
Risk of bias	Low-moderate risk of bias: Of the 2182 eligible infants, parents of 1714 (78.6%) completed the FFQ; 1138 (67%) of women completed the FFQ; missing items in completed FFQ treated as woman not consuming any fish)
Relevance	Likely to be relevant to Australian women, although fish consumption in New Zealand low (less than one serve a week)
Other comments	Only term infants included

Reference	**Miyake 2009**
Dietary patterns	Fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
etting	Osaka, Japan
Funding	Ministry of Education, Culture, Sports, Science, and Technology and Health and Labour Sciences Research Grants, Ministry of Health, Labour and Welfare, Japan
Participants	763 mother-child pairs (part of the Osaka Maternal and Child Health Study). Pregnant women recruited between November 2001 and March 2003
Baseline comparisons	*See below*
Dietary assessment	Diet history questionnaire (DHQ)
Timing	DHQ at mean 17.7 [SD 6.7] weeks gestation to reflect dietary intake for the previous month
Comparison	Quartiles of maternal fish consumption during pregnancy (medians in g/day adjusted energy intake; Q1 23.4; Q2 38.7; Q3 51.7; Q4 73.2
Outcomes	Wheeze and eczema in infants aged 16-24 months (ISAAC definitions)
Results	**Infant wheeze at 16-24 months (n = 763)** **OR (95% CI)** / **aOR (95% CI)** Q1: 1.00 / 1.00 Q2: 0.79 (0.49 to 1.26) / 0.88 (0.49 to 1.58) Q3: 0.74 (0.46 to 1.19) / 0.68 (0.34 to 1.36) Q4: 0.76 (0.47 to 1.23) / 0.67 (0.30 to 1.48) P for trend: 0.25 / 0.28 **Infant eczema at 16-24 months (n = 763)** Q1: 1.00 / 1.00 Q2: 0.87 (0.52 to 1.44) / 1.10 (0.59 to 2.05) Q3: 1.03 (0.62 to 1.69) / 1.33 (0.65 to 2.72) Q4: 0.67 (0.39 to 1.13) / 0.73 (0.30 to 1.75) P for trend: 0.24 / 0.68
Followup	16-24 months after birth
Confounding	Adjusted for maternal age, gestation at baseline, place of residence at baseline, family income, maternal and paternal income, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, maternal intake of vitamin D and E during pregnancy, changes in maternal diet during the previous month, season when baseline data were collected, maternal smoking during pregnancy, baby's older siblings, baby's sex, baby's birthweight, household smoking, breastfeeding duration and time of birth before third follow-up survey
Risk of bias	Low risk of bias; of the 1002 women initially recruited, 763 mother-child pairs (76.3%) completed all three surveys (compared with non-participants, participants had higher incomes, higher education levels and were more likely higher intakes of fat, cholesterol, and vitamin D and E
Relevance	Fish intake in Japan likely to be higher than in Australia
Other comments	75% of infants were breastfed for 6 months or longer

Reference	**Miyake 2006**
Food groups	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Women who became pregnant in November 2001-March 2003 Neyagawa City, Osaka Prefecture and several surrounding municipalities (Osaka Maternal and Child Health Study, Japan)
Funding	Grant-in-Aid for Scientific Research (Government grant)
Participants	865 pregnant Japanese women
Baseline comparisons	*See Confounding below*
Dietary Assessment	Dietary history questionnaire-self administered [For fatty fish (eel, red-meat fish, dried fish, tuna), white fish (codfish, shellfish, octopus) and other fish (boiled fish in soy sauce, salted gut, fish eggs)]
Timing	Diet survey for previous month at baseline (period of baseline not stated), EPDS at 2-9 months post partum
Comparison	Quartile of intake of fish (grams per day): 1 (23.1), 2 (37.9), 3 (51.4) and 4 (72.9), adjusted for energy Note: other dietary intakes analysed: meat, eggs, dairy products, total fat, saturated fatty acids, cholesterol, LA, ALA and AA
Outcomes	Postpartum depression (EPDS with postpartum depression when score ≥ 9)
Results	see below
Length of follow up	2-9 months postpartum
Confounding	Age, gestation, parity, smoking, family structure, occupation, family income, education, changes in diet in previous month, season when baseline data collected, BMI, time of delivery, medical problems in pregnancy, baby's sex, baby's birthweight
Risk of bias	Low risk of bias: data for 865/1002 (86.5%) women available for analysis
Relevance	Australian diets very different to Japanese - much less seafood intake in Australia and more white fish rather than fatty fish
Other comments	Originally 1002 women enrolled only 865 completed (note: depressed persons less likely to participate), low rate of enrolment into study (17.2% of those eligible in Neyagawa)

Results:

EPDS with postpartum depression when score ≥ 9

Fish intake (g per day)	**23.1**	**37.9**	**51.4**	**72.9**
No of depression cases	32	37	24	28
Crude OR (95% CI)	1	1.19 (0.71-2)	0.72 (0.4-1.26)	0.85 (0.49-1.47)
p for trend 0.27				
Multivariate OR (95% CI)	1	1.25 (0.73-2.12)	0.74 (0.41-1.33)	0.89 (0.5-1.59)
p for trend 0.37				

Also reported OR forn-3, DHA, DPA intake, all no difference.
No significant dose-response associations between intake of fish, meat, eggs, dairy products, total fat, saturated fatty acids, cholesterol. LA, ALA and AA with risk of postpartum depression

Reference	**Nwaru 2010**
Food type	Fish and fish products
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Tampere, Finland
Funding	Academy of Finland, Finnish Pediatric Research Foundation, the Juho Vainio Foundation, the Yrjo Jahnsson Foundation, Turku, Oulu and Tampere University Hospitals, JDRF, Novo Nordisk Foundation, EU Biomed 2 Program
Participants	931 mother-infant pairs (children with human leukocyte antigen-conferred susceptibility to type 1 diabetes) participating in the Finnish type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study between September 1996 and October 1997
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ given to women after birth, for return at the three month visit (FFQ intended to cover maternal diet during pregnancy and lactation)
Comparison	Amount of fish intake
Outcomes	Allergic sensitisation in offspring by 5 years: food allergens (egg, cow's milk, fish, wheat); inhalant allergens (house dust mite, cat, timothy grass, birch)
Results	**Total fish and fish products** ***Food allergens*** / ***Inhalant allergens*** OR 0.96 95% CI 0.87 to 1.05 / OR 0.98 95% CI 0.90 to 1.07 aOR 0.98 95% CI 0.88 to 1.09 / aOR 1.00 95% CI 0.91 to 1.10 - **Fish** ***Food allergens*** / ***Inhalant allergens*** OR 0.97 95% CI 0.89 to 1.06 / OR 0.99 95% CI 0.91 to 1.07 aOR 0.99 95% CI 0.89 to 1.09 / aOR 1.02 95% CI 0.93 to 1.12
Followup	To 5 years
Confounding	Adjusted for energy intake, place of birth, season of birth, sex of the child, number of siblings, gestational age at birth, parental asthma, parental allergic rhinitis, maternal age at birth, maternal smoking during pregnancy, maternal education
Risk of bias	Low risk of bias: data available for 931/1175 (79.2%) children recruited – 108 did not participate in survey, a further 49 did not have IgE measurements, a further 87 had no FFQ or an incomplete FFQ
Relevance	Likely to be relevant to Australian women
Other comments	28% of women took vitamin D supplements, 73% took iron supplements; HLA genotype not likely to have any impact on the development of allergic diseases.

Reference	**Oien 2010**
Food type	Fish:
Study type	Retrospective* cohort study (Prevention of Allergy among Children in Trondheim (PACT) study)
Level of evidence	III-2 (aetiology)
Setting	Trondheim, Norway
Funding	Norwegian Department of Health and Social Affairs, Astra Zeneca Norway, Norwegian Medical Association, SINTEF Unimed 1999
Participants	3086 children
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Administered when child was one year of age
Comparison	Amount of fish intake; 68% of mothers reported eating fish once a week or more (and 46% took cod liver oil four or more times a week during pregnancy)
Outcomes	Childhood eczema, asthma at two years
Results	**<u>Eczema at 2 years</u>** Never or < once a week (n = 961) versus ≥ once per week (n = 2052): OR 1.02 95% CI 0.82 to 1.26 **<u>Asthma at 2 years</u>** Never or < once a week (n = 964) versus ≥ once per week (n = 2061): OR 0.99 95% CI 0.72 to 1.37
Followup	To two years
Confounding	Maternal intake during pregnancy analyses were not adjusted
Risk of bias	Moderate to high risk of bias: of the 5171 eligible children, questionnaires were completed for 3086 children (59.7%); analyses were not adjusted; mothers needed to recall their diet more than a year previously
Relevance	Likely to be relevant to Australian women
Other comments	Children were followed prospectively from one year of age to approximately two years of age; *information on exposure was assessed retrospectively when the child was one year of age; Mothers' consumption of fish and vegetables and children's consumption of fish and vegetables were highly correlated; Children's fish consumption more important than maternal consumption during pregnancy.

<table>
<tr><td>Reference</td><td>Oken 2008a</td></tr>
<tr><td>Food type</td><td>Fish</td></tr>
<tr><td>Study type</td><td>Prospective cohort</td></tr>
<tr><td>Level of evidence</td><td>II (aetiology)</td></tr>
<tr><td>Setting</td><td>Project Viva (Pre-birth cohort study), Massachusetts, USA 1999-2002</td></tr>
<tr><td>Funding</td><td>National Health Institute (Bethesda, Maryland), Harvard Medical School, Harvard Pilgrim Health Care Foundation</td></tr>
<tr><td>Participants</td><td>341 mother-infant pairs</td></tr>
<tr><td>Baseline comparisons</td><td>Comparison with 1238 excluded: similar fish intakes (1.5 vs. 1.7 servings/week) slightly older (32.6 vs 31.9 years), more likely to be white (82 vs. 65%), better educated (41 vs. 30% with a graduate degree), less likely to smoke (8 vs. 13%), had higher Peabody Picture Vocabulary Test (PPVT) scores (108.8 vs. 104.6). For included children compared breastfeeding duration longer (7.0 vs. 6.0 months).

See confounding</td></tr>
<tr><td>Dietary Assessment</td><td>Self-administered semi-quantitative food frequency questionnaire of previous 3 months-self administered
[note: included canned tuna fish, shrimp, lobster, scallops, clams, dark-meat fish (mackerel, salmon, sardines, bluefish, swordfish), other fish (cod, haddock, halibut)]</td></tr>
<tr><td>Timing</td><td>Second trimester study visit for FFQ (for previous 3 months)</td></tr>
<tr><td>Comparison</td><td>Fish intake of never, > never and ≤ 2 or > 2 times per week
(Note: also looked at red blood cell mercury, EPA and DHA at second trimester)</td></tr>
<tr><td>Outcomes</td><td>Child cognition at 3 years (PPVT-Peabody Picture Vocabulary Test and WRAVMA-Wide Range Assessment of Visual Motor Abilities)
(For fish intake and mercury levels)</td></tr>
<tr><td>Results</td><td>Higher fish intake associated with better child cognitive test performance
<table>
<tr><td>Fish intake (servings per week)</td><td>Never</td><td>≤2</td><td>>2</td></tr>
<tr><td>PPVT unadjusted</td><td>107.5</td><td>105.2</td><td>106.3</td></tr>
<tr><td>Adjusted (95% CI)</td><td>0</td><td>-2.1 (-5.1, 1.4)</td><td>1.2 (-3.5, 6)</td></tr>
<tr><td>Adjusted [erythrocyte mercury (95% CI)]</td><td>0</td><td>-1.8 (-5.4, 1.8)</td><td>2.2 (-2.6, 7)</td></tr>
<tr><td>WRAVMA total unadjusted</td><td>100.1</td><td>102.8</td><td>106.4</td></tr>
<tr><td>Adjusted (95% CI)</td><td>0</td><td>1.1 (-2.2, 4.4)</td><td>5.3 (0.9, 9.6)</td></tr>
<tr><td>Adjusted [erythrocyte mercury (95% CI)]</td><td>0</td><td>1.5 (-1.8, 4.7)</td><td>6.4 (2.0, 10.8)</td></tr>
</table>
Higher mercury levels associated with poorer cognitive performance
<table>
<tr><td>Erythrocyte mercury levels</td><td><90th percentile</td><td>Top decile</td></tr>
<tr><td>PPVT unadjusted</td><td>106.2</td><td>100.9</td></tr>
<tr><td>Adjusted (Beta, 95% CI)</td><td>Referent</td><td>-4.0 (-8.0 to 0.05)</td></tr>
<tr><td>Adjusted [fish intake (beta, 95% CI)]</td><td>Referent</td><td>-4.5 (-8.0 to -0.4)</td></tr>
<tr><td>WRAVMA total unadjusted</td><td>103.5</td><td>100.1</td></tr>
<tr><td>Adjusted (Beta 95% CI)</td><td>Referent</td><td>-3.5 (-7.2 to 0.2)</td></tr>
<tr><td>Adjusted [fish intake (beta, 95% CI)]</td><td>Referent</td><td>-4.6 (-8.3 to -0.9)</td></tr>
</table></td></tr>
<tr><td>Follow-up</td><td>3 years</td></tr>
<tr><td>Confounding</td><td>Covariates (independent predictors of child cognition): smoking, maternal age, pre-pregnancy BMI, prenatal smoking and alcohol consumption,</td></tr>
</table>

	race/ethnicity, marital status, education, birth order, child sex, fetal growth, gestation length, duration of breast feeding, primary language, age at cognitive test, maternal education and paternal education Checked co-variability of: household income, maternal Western or prudent dietary pattern, depression at 6 months postpartum, child BMI, test administrator
Risk of bias	Moderate risk of bias: Selection bias - differences between original cohort and this sample. Of 2,128 women who delivered singleton infant, 1,579 (74%) eligible for 3 year visit (had completed prenatal dietary questionnaire and had not withdrawn). 896 (42%) women-child pairs had maternal fish intake data, blood samples and cognitive test results. **341 (16%) included in study** (due to available funding to measure RBC mercury). 341 selected due to experiencing preterm or small for gestational age birth (n=45), mothers had available hair samples (n=98) and remaining 198 were selected at random. Maternal erythrocyte proxy for fetal methylmercury exposure. Home environment not assessed. Other fish contaminants not measured e.g. polychlorinated biphenyls
Relevance	Australian diet reasonably similar to American
Other comments	

Reference	**Oken 2008b**
Food type	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Danish National Birth Cohort 1997-2002, recruited during first antenatal visit with GP (6-12 weeks gestation)
Funding	Danish National Research Foundation, the Danish Pharmaceutical Association, the Danish Ministry of Health, the Danish National Board of Health, Statens Serum Institut, BIOMED, the March of Dimes Birth Defects Foundation, the Danish Heart Association, the Danish Medical Research Council, and Sygekassernes Helsefond (to the Danish National Birth Cohort); by the Early Nutrition Programming Project [(EARNEST) Project No. FOOD-CT-2005-007036]; and by grant no. HD44807 from the National Institutes of Health and a fellowship from the American Scandinavian Foundation, Inger and Jens Bruun Foundation (both to EO). In addition, the March of Dimes Birth Defects Foundation supported collaboration between the Maternal Nutrition Group at the Statens Serum Institut and Harvard Medical School.
Participants	25,446 live born singleton children born to mothers in the Danish National Birth Cohort who responded to 18 month outcome between 18.0-20.9 months and had no missing data for covariates. Total cohort enrolled 92 676 liveborn singleton = 27% of original cohort.
Baseline comparisons	*See Confounding below*
Dietary Assessment	Food frequency questionnaire for previous month diet - self administered
Timing	FFQ in mid-pregnancy (approximately 25 weeks gestation) for month preceding questionnaire completion
Comparison	Maternal fish intake (grams per week): 0, 1-340 (1-2 servings/week), > 340 (≥ 3 servings/week) Median fish intake in quintiles (grams per day): 5.9, 14.5, 22.2, 32.2, 50.8
Outcomes	Primary outcome total development at 18 months; child development (motor and social/cognitive) also assessed at 6 months. Assessment by interview with parent
Results	**Median fish intake (g/day) aOR (95% CI)**

Median fish intake (g/day) aOR (95% CI)	**5.9**	**14.5**	**22.2**	**32.2**	**50.8**
Motor Development at 6 mo	Referent	0.98 (0.92-1.05)	1.03 (0.97-1.11)	1.05 (0.98-1.12)	**1.17 (1.09-1.25)**
Social or cognitive at 6 mo	Referent	1 (0.93-1.07)	1.07 (0.99-1.15)	1.18 (0.09-1.27)	**1.33 (1.23-1.44)**
Total development at 6 mo	Referent	0.99 (0.92-1.05)	1.05 (0.99-1.13)	**1.09 (1.02-1.17)**	**1.25 (1.17-1.34)**
Motor Development at 18 mo	Referent	1 (0.93-1.07)	**1.08 (1-1.16)**	**1.11 (1.03-1.19)**	**1.24 (1.15-1.33)**
Social or cognitive at 18 mo	Referent	1 (0.94-1.08)	**1.11 (1.04-1.19)**	**1.15 (1.07-1.24)**	**1.28 (1.19-1.37)**
Total Development at 18 mo	Referent	0.99 (0.93-1.07)	**1.09 (1.01-1.17)**	**1.14 (1.06-1.22)**	**1.29 (1.20-1.38)**

Associations of fish intake with child development did not differ by breastfeeding duration.

Follow-up	6 and 18 months
Confounding	Covariates: maternal age, social status, marital status, parity, smoking and alcohol use during pregnancy, maternal and paternal education, child gestational age, child birth weight (*z* score), child sex, breastfeeding, child age at questionnaire completion, occurrence or non-occurrence of post partum depression , parental social class and learning difficulties: Also measured: pre-pregnancy BMI, history of parental school problems, child birth length and head circumference at birth and at routine GP visits at 5 and 12 months (5 & 12 months measures not included due to much missing data, however a check with provided data found no relationship difference)
Risk of bias	Moderate (attrition bias; not adjusted for maternal IQ or home environment)
Relevance	Australian diet likely to be slightly different from Danish diet (average 27g fish intake per day?). Particularly high intake of oily fish –salmon, herring & mackerel)
Other comments	Enrolled 101,042 pregnant women - women included in this study less likely to be single or smoked cigarettes during pregnancy and breastfed for longer than women not included and included children had greater gestation length and birth weight than non-included children

Reference	**Oken 2007**
Food type	Fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Obstetric offices in Massachusetts, USA
Funding	NIH, Robert H. Ebert Fellowship, March of Dimes Birth Defects Foundation,
Participants	1718 women in Project Viva recruited from 1999 to 2002
Baseline comparisons	Study participants more likely to be white, and to be college graduates than non-participants *See confounding below*
Dietary assessment	FFQ
Timing	FFQ at study enrolment (median 10.4 weeks gestation) to cover diet since last menstrual period
Comparison	Number of serves of fish per day
Outcomes	Pre-eclampsia, gestational hypertension
Results	 **<u>Pre-eclampsia</u>** aOR 0.91 95% CI 0.75 to 1.09 (per weekly serving) (0.22 [SD 0.19] serves of fish/day for women with pre-eclampsia v 0.25 [0.24] for women with normal blood pressure) **<u>Gestational hypertension</u>** aOR 1.04 95% CI 0.94 to 1.15 (per weekly serving) (0.27 [SD 0.29] serves of fish/day for women with gestational hypertension v 0.25 [0.24] for women with normal blood pressure)
Followup	To birth
Confounding	Energy adjusted and also adjusted for maternal age, prepregnancy BMI, first trimester systolic blood pressure, ethnicity, education, parity
Risk of bias	Low risk of bias: Of the 2128 live births, 410 were excluded (45 women with unavailable medical records, 339 incomplete dietary questionnaire, 24 women with pre-existing chronic hypertension who did not develop pre-eclampsia, 2 women with missing covariate information) leaving 1718 participants (81%) available for analysis
Relevance	Likely to be relevant to Australian women
Other comments	92% of women took supplements (multivitamins) in the first trimester of pregnancy; Mean calcium intake in the study population was high (> 900 mg/day) and intakes of vitamins D, E, C and folate were also relatively high

Reference	**Oken 2005**
Food type	Fish
Study type	Prospective Cohort Study
Level of evidence	II (aetiology)
Setting	Project Viva, Eastern Massachusetts April 1999-February 2003; women recruited at initial clinical obstetric appointment
Funding	National Institutes of Health, Harvard Medical School, Harvard Pilgrim Health Care Foundation
Participants	135 mother-infant pairs enrolled in Project Viva where maternal hair sample was taken and complete data for 2nd trimester diet and infant's cognitive assessment Eligible if <22 weeks gestation at recruitment with a singleton pregnancy, able to complete forms in English, no plans to move out of the study area before delivery
Baseline comparisons	*See confounding below*
Dietary Assessment Method	Semi quantitative food frequency questionnaire (self administered) related to the 2nd trimester of pregnancy Questionnaire had previously been calibrated against blood levels of LCPUFA
Timing	26-28 weeks gestation
Comparison	Participants rated intake of 1. canned tuna fish, 2. shrimp, lobster, scallops, clams, 3. dark meat fish, 4. other fish on a scale of 6 ranging from "never/less than once per month" to "1 or more servings per day" Note: actual categories not shown
Outcomes	Infant cognition (assessed via visual recognition memory) at 6 months of age
Results	

Table 2. Associations of maternal second-trimester fish consumption and maternal hair mercury at delivery with infant cognition at 6 months (VRM score): results from six linear regression models among 135 mother–infant pairs in Project Viva.

Model	Change in VRM score [% novelty preference (95% CI)]: Effect per weekly fish serving	Effect per ppm maternal hair mercury
Fish only	2.5 (–0.01 to 5.0)	—
Fish and participant characteristics[a]	2.8 (0.2 to 5.4)	—
Mercury only	—	–4.6 (–10.3 to 1.1)
Mercury and participant characteristics[a]	—	–4.0 (–10.0 to 2.0)
Fish and mercury	3.9 (1.2 to 6.5)	–8.1 (–14.1 to –2.0)
Fish, mercury, and participant characteristics[a]	4.0 (1.3 to 6.7)	–7.5 (–13.7 to –1.2)

[a]Participant characteristics adjusted for include maternal age (continuous), race/ethnicity (white vs. nonwhite), education (college graduate vs. not), marital status (married or cohabiting vs. not), and infant sex, gestational age at birth (continuous), birth weight for gestational age (continuous), breast-feeding duration (continuous), and age at cognitive testing (continuous).

Table 3. Mean cognitive (VRM) scores (% novelty preference) among offspring of mothers with high or low second-trimester fish intake and high or low hair mercury levels at delivery.

Weekly fish intake	Hair mercury: ≤ 1.2 ppm	> 1.2 ppm
> 2 servings	72 (*n* = 7)	55 (*n* = 2)
≤ 2 servings	60 (*n* = 114)	53 (*n* = 12)

Follow-up	6 months
Confounding	Maternal age, race, ethnicity, education, marital status, infant sex, gestational age at birth, birth weight for gestational age, breast-feeding duration, age at cognitive testing. Maternal hair mercury level also used as a predictor variable in the model.
Risk of bias	Moderate (very low retention rate; not adjusted for maternal IQ or home environment)
Relevance	American diet similar to Australian
Other comments	2,128 participants in Project Viva delivered a live infant, 409 of them in the time during hair sample collection, 302 were asked for a sample, 211 consented and were able to and only 135 had full data, therefore 135/2128 (6.3%) very low follow up rate (or 135/409 (33%)during hair sample collection period still low) Majority of participants breastfed infants, 79% consumed alcohol during pregnancy, 6 infants born preterm and 3 were born small for gestational age.

Reference	**Oken 2004**
Food type	Fish (canned tuna fish, shrimp, lobster, scallops, clams, dark meat fish (mackerel, salmon, sardines, bluefish, swordfish), other fish (cod, haddock, halibut)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Massachusetts, USA
Funding	NIH, Agency for Health Care Research and Quality, March of Dimes Birth Defects Foundation, Harvard Medical School, Harvard Pilgrim Health Care Foundation
Participants	1797 children of women enrolled in Project Viva from 1999 to 2002
Baseline comparisons	Women who consumed more seafood more likely to be older, not white, more educated and less likely to be experiencing their first pregnancy
Dietary assessment	FFQ
Timing	FFQ at study enrolment (to cover the period from beginning of pregnancy), at 26 to 28 weeks gestation (to cover the past three months), and just after birth (to cover the month before birth)
Comparison	No intake of fish and tertiles of fish intake
Outcomes	Birthweight, fetal growth (birthweight for gestational age), length of gestation
Results	see below

	Birthweight difference (g)	**Fetal growth (z value)**	**Length of gestation (days)**
First trimester (n = 1797)	*aMD (95%CI)*	*aMD (95%CI)*	*aMD (95%CI)*
No intake (n = 233)	70 (-18 to 158)	0.13 (-0.01 to 0.28)	-0.8 (-2.7 to 1.1)
Tertile 1 (n = 597)	48 (-21 to 117)	0.08 (-0.03 to 0.20)	0.2 (-1.3 to 1.7)
Tertile 2 (n = 568)	7 (-62 to 77)	-0.01 (-0.12 to 0.10)	-0.4 (-2.0 to 1.1)
Tertile 3 (n = 399)			
P for trend	**0.05**		
Second trimester (n = 1663)			
No intake (n= 215)	21 (-64 to 1.05)	0.09 (-0.06 to 0.24)	0.5 (-1.3 to 2.3)
Tertile 1 (n = 564)	39 (-27 to 105)	0.06 (-0.05 to 0.18)	0.1 (-1.3 to 1.4)
Tertile 2 (n = 493)	-29 (096 to 38)	-0.05 (-0.17 to 0.07)	-0.8 (-2.2 to 0.6)
Tertile 3 (n = 391)			
P for trend	0.19		

No association of seafood intake with low birthweight, SGA and preterm birth as dichotomous measures (actual numbers not reported in paper)

Followup	To birth
Confounding	Adjusted for enrolment site, infant sex, maternal age, height, intrapartum weight gain, prepregnancy BMI, ethnicity, smoking during pregnancy, education, gravidity
Risk of bias	Low-moderate risk of bias: 2109/2128 (99%) of women who gave birth to a live infant completed at least one dietary questionnaire
Relevance	Likely to be reasonably relevant for Australian women (e.g. lower seafood intakes than Scandinavian and Japanese studies)
Other comments	6 women reported taking cod liver oil or fish oil supplements (their exclusion did not change results)

Reference	**Olsen 2002**
Food type	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Routine antenatal care in Aarhus, Denmark 1992-1996
Funding	Novo Nordisk Forskningsfond, Aage-Louis Hansens Fond, Danish National Research Foundation, March of Dimes Birth Defects Foundation, Danish Health Research Foundation, Egmont Fonden
Participants	8729 pregnant women (with singleton, live born babies without detected malformations), who had not consumed fish oil supplements
Baseline comparisons	*See Confounding below*
Dietary Assessment	Fish (roe, prawn, crab and mussels) and fish oil questionnaire
Timing	Fish and fish oil intake at 16 weeks during period from when they knew of pregnancy until completion of questionnaire
Comparison	Fish intake per 28 days: 0, 0.5, 2, 4, 29 and 28 servings (1 serving =144g fish) Fish as a hot meal or in open sandwiches per month: 0, > 0-< 1, 1-3, ≥ 1 (per week)
Outcomes	Preterm birth (<259 days), low birthweight (<2500g) and intrauterine growth retardation (IUGR) below the 10th centile and birth weight expected from gestational age from the infant's birth weight, gestational age, and sex, on the basis of a Danish standard

Results

Adjusted OR (95% CI) for n=7902

All fish intake **Fish servings per 28 days**	**0**	**0.5**	**2**	**4**	**29**	**28**	**P**
Low birth weight	**3.22 (4.73-6)**	1.31 (0.82-2.1)	1.54 (0.97-2.46)	0.99 (0.6-1.63)	1.16 (0.69-1.94)	Reference	0.004
Preterm birth	**2.69 (1.49-4.84)**	1.48 (0.99-2.21)	1.44 (0.96-2.16)	0.90 (0.59-1.39)	1.31 (0.85-2.01)	Reference	0.003
IUGR	1.14 (0.67-1.98)	**1.45 (1.09-1.94)**	1.31 (0.97-1.77)	1.03 (0.76-1.40)	1.25 (0.91-1.72)	Reference	0.09

Adjusted OR (95% CI) for n=1159

Fish as a hot meal or in open sandwiches per month	**0**	**>0-<2**	**1-3**	**≥1 (per week)**	**P**
Low birth weight	**3.57 (1.14-11.14)**	1.39 (0.41-4.67)	1.25 (0.39-3.94)	Reference	0.02
Preterm birth	**3.60 (1.15-11.20)**	2.09 (0.66-6.62)	1.58 (0.52-4.83)	Reference	0.06
IUGR	1.01 (0.45-2.26)	1.26 (0.59-2.66)	1.02 (0.50-2.08)	Reference	0.08

Follow-up	Birth
Confounding	Covariates: sex of infant, smoking, alcohol consumption in pregnancy, maternal age, parity, height and pre-pregnant weight, length of education and whether mother had co-habitant
Risk of bias	Low-moderate risk of bias (due to confounding and attrition); Only n=7902 included in 1st adjusted analysis, and n=1159 in second adjusted analysis - no mention of why rest aren't included.
Relevance	Danish diet differs from Australian diet
Other comments	Smokers, primiparous women, teenagers and women with low weight, short stature and without high school education and cohabitation were more frequent in low fish exposure groups.

Reference	**Olsen 1993**
Food type	Fish
Study type	Retrospective cohort study
Level of evidence	III-2 (aetiology)
Setting	Faroe Islands
Funding	Danish Medical Research Council, Danish Health Foundation, the Hojgaard Foundation, the Vestnorden Foundation, the Danish Agency for Environmental Protection, the Director Jacob Madsens Foundation and Michaelesen Fonden
Participants	1012 women giving birth in the Faroe Islands from 1986-7
Baseline comparisons	Study participants had a longer gestation than the women who did not participate
Dietary assessment	Standard questions
Timing	Questionnaire administered after birth to assess diet during pregnancy
Comparison	Number of seafood dinners per week (0, 1, 2, 3, 4, 5, 6+)
Outcomes	Gestational age, birthweight, birth length, placental weight
Results	**Gestational age** (days): p = 0.4 for variability of means between groups **Birthweight (g): p = 0.02 for variability of means between groups** **(additionally adjusted for gestational age): p = 0.026 for variability of means between groups** **Birth length (cm) p = 0.002 for variability of means between groups** **(additionally adjusted for gestational age): p = 0.006 for variability of means between groups** **Placental weight (g)***: p = 0.10 for variability of means between groups (additionally adjusted for gestational age): p = 0.13 for variability of means between groups *n = 767
Followup	To birth
Confounding	Adjusted for maternal height, weight, parity, age, marital status, smoking
Risk of bias	Low risk of bias: study group comprised 75% of all births taking place during the study period
Relevance	Of some relevance to Australian women (more and different types of fish (e.g. whale) consumed by women in the Faroe Islands)
Other comments	The association does not appear to be a strict dose response one – positive effect plateaus at about 3 fish dinners per week

Reference	**Olsen 1990**
Food type	Fish
Study type	Prospective cohort study (Healthy Habits for Two community trial)
Level of evidence	II (aetiology)
Setting	Odense and Aalborg, Denmark
Funding	Helsefondet, Egmont Fondet, The National Board of Health, and the County of Funen
Participants	11,980 pregnant Danish women giving birth to a singleton baby; study ran from 1984 to 1987
Baseline comparisons	*See confounding below*
Dietary assessment	Questionnaire
Timing	36 weeks GA; to reflect fish consumption in the previous month
Comparison	No versus 1-2 versus 3-4 versus 5+ fish meals during the previous month
Outcomes	Placental weight, head circumference at birth, birthweight, birth length, gestational age
Results	**Non Smokers**

Fish meals past month	**N**		**Test of linearity**
		Birthweight, g (mean [SD])	
0	932	3544 [486]	**p=0.04**
1-2	3165	3570 [497]	
3-4	1858	3582 [499]	
5+	588	3590 [490]	
All	6543	3572 [490]	
		Birth length, cm (mean [SD])	
0	9298	52.52 [2.28]	p=0.7
1-2	3157	52.61 [2.38]	
3-4	1854	52.66 [2.37]	
5+	587	52.50 [2.46]	
All	6526	52.60 [2.73]	
		Head circumference, cm (mean [SD])	
0	861	35.23 [1.63]	**p=0.0007**
1-2	2862	35.42 [1.54]	
3-4	1689	35.47 [1.58]	
5+	540	35.49 [1.47]	
All	5952	35.41 [1.56]	
		Placental weight, g (mean [SD])	
0	929	548.7 [134]	**p=0.0002**
1-2	3154	559.4 [134]	
3-4	1855	560.1 [134]	
5+	585	579.5 [145]	
All	6523	559.9 [135]	
		Gestational age, days {mean [SD])	
0	933	282.0 [10.3]	P=0.1
1-2	3150	282.2 [10.4]	
3-4	1850	282.1 [10.4]	
5+	584	281.0 [10.2]	

	All	6517	282.1 [10.4]
	Multiple regression (smokers and nonsmokers)		
			Birthweight
	Smoking	**N**	**Regression coefficient, g (mean, 95% CI)**
	0	6569	15.8 (-2.3 to 33.9)
	1+	4594	-16.0 (-37.7 to 5.7)
			Birth length
	Smoking	**N**	**Regression coefficient, cm (mean, 95% CI)**
	0	6569	0.02 (-0.07 to 0.11)
	1+	4594	-0.01 (-0.12 to 0.10)
			Head circumference
	Smoking	**N**	**Regression coefficient, cm (mean, 95% CI)**
	0	6569	0.080 (0.016 to 0.144)
	1+	4594	-0.041 (-0.122 to 0.041)
			Placental weight
	Smoking	**N**	**Regression coefficient, g (mean, 95% CI)**
	0	6569	10.8 (5.1 to 16.50)
	1+	4594	-0.6 (-6.2 to 7.30)
			Gestational age
	Smoking	**N**	**Regression coefficient, days (mean, 95% CI)**
	0	6569	-0.38 (-0.82 to 0.05)
	1+	4594	-0.08 (-0.63 to 0.47)
Followup	To birth		
Confounding	Adjusted for maternal age, weight, height, intrapartum weight gain, age, parity, sex of child, maternal and paternal education, maternal employment during 1st to 16th week of gestation, certainty of gestational age assessment, cohabitation, frequency of intake of vegetables, raw vegetables, fruit, offal, poultry, cake, alcohol, smoking – and gestational age when assessing effects on size of the newborn and placental weight		
Risk of bias	Low risk of bias: 83% of all eligible women in the two areas were recruited;		
Relevance	Likely to be reasonably relevant for Australian women		
Other comments			

Reference	**Petridou 2005**
Food type	Fish and seafood
Study type	Case-control study
Level of evidence	III-3
Setting	Greece
Funding	The Childhood Hematology-Oncology Group: Athens University Medical School, Aristotle University of Thessaloniki, University Hospital of Heraklion
Participants	Cases: 131 children with acute lymphoblastic leukemia, aged 12 to 59 months, gender and age matched to Controls: 131 children hospitalised for minor conditions between 1999 and 2003
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During index pregnancy
Comparison	Quintiles of fish/seafood – median Q1; 3 g/day: median Q5 14 g/day
Outcomes	Acute lymphoblastic leukemia (ALL)
Results	see below
Followup	NA
Confounding	Total energy intake (but not mutually among food groups); matching variables; maternal age at birth; birthweight; maternal smoking during pregnancy; maternal years of schooling, maternal occupation
Risk of bias	Moderate: moderate risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy some time previously; Cases: 171 children with ALL were identified; 21 had missing data, consent was not given in 9 cases and 10 were unable to be matched, leaving 131 (77%) of cases available
Relevance	Diets of Greek women may differ from current diets of Australian women
Other comments	

Results:

	Median g/day	**Cases**	**Controls**	**P for trend**
Q1:	3	36	20	
Q2:	6	28	25	
Q3:	7	16	24	
Q4:	9	23	41	
Q5:	14	28	21	0.09

Logistic regression: one quintile more of fish/seafood: aOR 0.72 95% CI 0.59 to 0.89

Reference	**Petridou 1998a**
Food type	Fish, shellfish
Study type	Case-control study
Level of evidence	III-3
Setting	Greater Athens area, Greece
Funding	Greek Ministry of Health and Welfare, and Foundation for Research in Childhood 'S. Doxiadis'
Participants	Cases: 109 children with cerebral palsy (CP), born between 1984 and 1988 (estimated to be two-thirds of the children with CP born during this period) Controls (1): 155 neighbouring children of similar sex and age (± 12 months) Controls (2): 99 healthy siblings of similar sex and age (± 12 months) of the first neurological patient seen by the attending physician after a visit by the CP patient
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During pregnancy
Comparison	< 1 versus 1 versus > 1 serves of fish per week; regression analysis: risk of cerebral palsy with change in consumption by one unit (= consumption of fish once a week)
Outcomes	Cerebral palsy
Results	< 1 serve of fish per week: 33/91 (36.3%) cases v 80/246 (32.5%) controls 1 serve of fish per week: 42/91 (46.1%) cases v 124/246 (50.4%) controls More than 1 serve of fish per week: 16 (17.6%) cases v 42/246 (17.1%) controls *Regression analysis for each unit of consumption of fish once a week:* aOR 0.77 95% CI 0.48 to 1.24 aOR 0.63 95% CI 0.37 to 1.08 (additionally adjusted for all food groups)
Followup	8 years
Confounding	Age and sex of child, maternal age at birth, maternal age at menarche, maternal chronic disease, previous spontaneous abortions, persistent vomiting during index pregnancy, multiple pregnancy, number of obstetric visits; timing of membrane rupture in index birth, use of general anaesthesia in the index birth, mode of birth, abnormal placenta, infant head circumference at birth, congenital malformation, place of index birth, use of supplementary iron during index pregnancy, physical exercise during index pregnancy, painless childbirth classes. The following were not included in the model: - Smoking or consumption of coffee or alcohol during pregnancy (stated to be "unrelated to CP and had no confounding influence"); - Gestational age, birthweight and maternal weight gain (stated to be "strong predictors of CP, but were not included in the model, since they are probably intermediate stages in a possible link between diet and CP (mediators) rather than genuine confounders"
Risk of bias	Moderate-high: High risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy 8 years previously; Cases: 109 children with CP were identified; for 6 children either collaboration with their guardian or a diagnosis of CP was not confirmed; and reliable maternal dietary intakes were not available for 12 women, leaving 91 cases available for analysis. Controls: 278 mother-child pairs were approached; 16 refused to participate; matching controls were not available in 8 instances, and reliable maternal dietary intakes were not available for 8 women, leaving 246 controls available for analysis.
Relevance	Diets of Greek women in 1998 may differ from current diets of Australian women
Other comments	

Reference	**Pogoda 2009**
Food type	Fish (fresh)
Study type	Case-control study Separate centre reports: Preston-Martin 1996 (Los Angeles); Lubin 2000 (Israel); Cordier 1994 (France); McCredie 1994 (Australia)
Level of evidence	III-3 (aetiology)
Setting	International (seven countries – USA, Israel, Italy, Spain, Australia, France and Canada (International Collaborative Study of Childhood Brain Tumors)
Funding	NIH, California Department of Health, Southern California Environmental Health Sciences Center, National Cancer Institutes, Cancer Surveillance System of Western Washington, Fred Hutchinson Cancer Research Center, Fondo de Investigaciones Sanitarias of Spain, Conselleria de Sanitat i Consum of Valencian Autonomous Community for the Childhood Cancer Registry of the Province of Valencia, Spanish Society of Paediatric Oncology with the National Childhood Cancer Registry, ISCIII-RTIC, Villavecchia Foundation and Scientific Foundation of the AECC
Participants	Cases: 1281 Controls: 2223 Years of diagnosis varied between centres, ranging from 1976 to 1992 (with most diagnosed between 1982 and 1992) Controls were frequency matched to cases in US centres and in France; otherwise they were individually matched (by region of residence, age, sex, and geographic area (except for Sydney and Los Angeles))
Baseline comparisons	*See confounding below*
Dietary assessment	Standardised study questionnaire using detailed dietary recall methods and abstract food models to gauge portion size
Timing	Diet during the past year and during the index pregnancy
Comparison	Quartiles
Outcomes	Childhood brain tumours
Results	

All tumours (n = 1203 cases)

	Controls	Cases	aOR% CI
Fresh fish			
Q1	654 (30%)	410 (35%)	1.0
Q2	427 (20%)	242 (21%)	1.2 (0.9 to 1.6)
Q3	535 (25%)	289 (25%)	1.0 (0.9 to 1.2)
Q4	566 (26%)	237 (20%)	**0.7 (0.6 to 0.9)**
P for trend = 0.01			

Astroglials (n = 621 cases)

Fresh fish			
Q1	654 (30%)	219 (36%)	1.0
Q2	427 (20%)	115 (19%)	1.1 (0.8 to 1.4)
Q3	535 (25%)	157 (26%)	1.0 (0.9 to 1.2)
Q4	566 (26%)	112 (19%)	**0.6 (0.5 to 0.9)**
P for trend = 0.005			

TUMOUR SUBTYPES
Astrocytomas

	Pilocytic (142 cases)	Anaplastic (96 cases)	Other (199 cases)
Fresh fish	0.7 (0.4 to 1.2)	**1.6 (1.1 to 2.4)**	**0.7 (0.4 to 1.0)**
P for trend	*0.19*	***0.02***	***0.054***

	<u>Other types</u> | | **Malignant gliomas (122 cases)** | **Medulloblastomas (193 cases)** | **PNET (64 cases)** | **Ependymomas (104 cases)** | Fresh fish | **0.5 (0.3 to 0.6)** | 1.0 (0.6 to 1.7) | 0.8 (0.5 to 1.7) | 0.9 (0.5 to 1.5) *P for trend* | 0.001 | 0.71 | 0.29 | 0.24
Followup	n/a
Confounding	Analyses adjusted for age and sex of child, study centre and each food group; Adjustment for total intake of foods had little effect on estimates
Risk of bias	Low-moderate risk of bias: 75% of eligible cases and 71% of eligible controls participated (based on centres for which these data were available); some lack of standardisation in dietary assessments between study centres; potentially high risk of recall bias for women whose pregnancies may have been at least 10 years previously.
Relevance	Likely to be relevant to Australian women
Other comments	

Other types	Malignant gliomas (122 cases)	Medulloblastomas (193 cases)	PNET (64 cases)	Ependymomas (104 cases)
Fresh fish	**0.5 (0.3 to 0.6)**	1.0 (0.6 to 1.7)	0.8 (0.5 to 1.7)	0.9 (0.5 to 1.5)
P for trend	0.001	0.71	0.29	0.24

Reference	**Ramón 2009**
Food type	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	2004-2006 INMA Valencia cohort, Spain
Funding	Instituto de Salud Carlos III, Ministerio Sandidad y Consumo and Ministerio Educacion y Ciencia
Participants	554/787 singleton live born infants of mother enrolled in INMA Valencia cohort and born Hospital La Fe of Valencia May 2004-February 2006 with available cord blood samples
Baseline comparisons	*See Confounding below*
Dietary Assessment	Semi-quantitative food frequency questionnaire-interview (about fish intake, not other forms of seafood)
Timing	FFQ at 28-32 weeks gestation (covered time from last FFQ-at 10-13 weeks- till current questionnaire completion), blood sample before placenta was delivered
Comparison	Fish consumption of canned tuna, lean fish and oily fish separately: < 1 portion/mo, 1-3 portions/mo, 1 portion/wk and ≥ 2 portions/wk
Outcomes	Birth weight, birth length and SGA
Results	

Portions of fish:	**<1/month**	**1-3/month**	**1/week**	**≥2/week**	**P**
Mercury concentration	adjusted: mean (95% CI)				
Canned tuna	**7.5 (6.4, 8.7)**	**9.5 (8.4, 10.8)**	**9.6 (8.6, 10.6)**	**11.4 (10.1, 12.9)**	**<0.001**
Lean fish	**8 (7, 9.1)**	**9.4 (8.1, 10.8)**	**9.7 (8.7, 10.8)**	**11.7 (10.2, 13.3)**	**<0.01**
Oily fish	**7.3 (6.6, 8)**	**9.7 (8.4, 11.2)**	**13 (11.6, 14.6)**	**12.3 (10, 15.3)**	**<0.001**
Birthweight [adjusted β (95% CI)]					
Canned tuna	**Referent**	**10.7 (-100.6, 121.9)**	**34.5 (-69.9, 139)**	**116.4 (2.8, 230)**	**0.03**
Lean fish	Referent	15.2 (-95.7, 126)	-26.9 (-123.7, 69.8)	46.4 (-63.7, 156.6)	0.68
Oily fish	Referent	28.3 (-70.9, 127.5)	42.9 (-46.3, 132.1)	-69.9 (-202.9, 63.1)	0.94
Birth length [adjusted β (95%)]					
Canned tuna	Referent	0.26 (-0.25, 0.77)	0.26 (-0.21, 0.73)	0.27 (-0.25, 0.78)	0.38
Lean fish	Referent	0.17 (-0.33, 0.67)	0.06 (-0.37,0.50)	0.25 (-0.24, 0.75)	0.43
Oily fish	Referent	0.11 (-0.34, 0.56)	-0.16 (-0.56, 0.25)	-0.4 (-1.01, 0.21)	0.19
SGA for weight					
Canned tuna	**Referent**	**0.6 (0.2-1.4)**	**0.4 (0.2-1.1)**	**0.3 (0.1-0.8)**	**0.01**
Lean fish	Referent	1.0 (0.4-2.7)	1.2 (0.5-2.9)	0.3 (0.1-1.0)	0.18
Oily fish	Referent	0.8 (0.3-1.9)	0.7 (0.3-1.7)	4.6 (1.4-15.4)	0.27
SGA for length					
Canned tuna	Referent	0.2 (0.1-0.9)	0.3 (0.1-1.2)	0.3 (0.1-1.1)	0.18
Lean fish	Referent	0.5 (0.1-2.2)	1.0 (0.3-2.8)	0.1 (0.0-0.6)	0.07
Oily fish	Referent	1.3 (0.4-4.5)	1.0 (0.3-3.1)	1.9 (0.3-13.7)	0.76

Adjusted for energy & vegetable intake

Follow-up	Birth
Confounding	Birth weight and length analyses adjusted for gestational age and sex Other covariates: age, pregnancy weight, gestational weight gain (according to Institute of Medicine Guidelines), parity, education, employment status, socio-occupational status, country of origin, residence, season of conception, smoking at 28-32 weeks gestation, mean vegetable intake, mean energy intake, mean caffeine intake, mean alcohol intake and parental height
Risk of bias	Low
Relevance	Spanish diet may be different from Australian diet
Other comments	FFQ at 10-13 weeks gestation (not included in analyses)

Reference	**Rogers 2004**
Food type	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	South west England, ALSPAC (Avon Longitudinal Study of Parents and Children)
Funding	University of Bristol, MRC, Wellcome Trust, the Department of the Environment, MAFF, various medical charities and commercial companies
Participants	10, 040 pregnant women with live born singleton babies, expected delivery date April 1991-December 1992 and not taking fish oil supplements at any point in pregnancy
Baseline comparisons	*See Confounding below*
Dietary Assessment	Food frequency questionnaire- self administered
Timing	FFQ at 32 weeks gestation
Comparison	Mean daily fish intake (grams per day): 0, 9.7, 15.6, 33.8, 45.4, 77.4 Mean frequency of fish consumption per week (portions per week): 0.74, 2.29, 4.44
Outcomes	Low birthweight, preterm birth and intrauterine growth retardation (IUGR) - defined as birth weight for gestational age and sex below the 10th centile)
Results	**Mean Daily fish intake (grams per day) aOR (95% CI):**

	0	**9.7**	**15.6**	**33.8**	**45.4**	**77.4**	**Trend p**
Preterm birth all	0.85 (0.59-1.22)	0.95 (0.68-1.31)	1.2 (0.88-1.63)	1.1 (0.8-1.51)	0.93 (0.68-1.28)	Referent	0.684
Non-Smokers	1 (0.67-1.49)	1.03 (0.72-1.49)	1.19 (0.85-1.67)	1.13 (0.79-1.62)	0.93 (0.65-1.33)	Referent	0.649
Low birthweight all	1.08 (0.73-1.59)	1.2 (0.84-1.72)	1.33 (0.94-1.88)	1.32 (0.93-1.89)	0.96 (0.66-1.39)	Referent	0.311
Non-Smokers	1.11 (0.7-1.75)	1.25 (0.82-1.89)	1.29 (0.87-1.91)	1.27 (0.84-1.91)	0.86 (0.56-1.32)	Referent	0.186
IUGR all	1.2 (0.93-1.55)	1.06 (0.83-1.35)	1.05 (0.83-1.34)	0.93 (0.72-1.19)	0.94 (0.73-1.2)	Referent	0.083
Non-smokers	1.24 (0.91-1.69)	1.13 (0.85-1.51)	1.13 (0.85-1.49)	1.01 (0.75-1.36)	0.96 (0.73-1.28)	Referent	0.083

Mean frequency of fish consumption per week (portions per week) aOR (95% CI):

	0	**0.74**	**2.29**	**4.4**	**Linear trend P**
Preterm birth all	0.76 (0.52-1.13)	1.01 (0.74-1.38)	0.91 (0.66-1.27)	Referent	0.418
Non-Smokers	0.95 (0.61-1.46)	1.08 (0.76-1.52)	0.96 (0.66-1.37)	Referent	0.872
Low birthweight all	1.07 (0.69-1.65)	1.25 (0.86-1.8)	1.07 (0.73-1.58)	Referent	0.492
Non-Smokers	1.18 (0.71-1.97)	1.32(0.87-2)	0.98 (0.69-1.2)	Referent	0.179
IUGR all	**1.37 (1.02-1.84)**	1.17 (0.91-1.51)	1.05 (0.81-1.38)	Referent	0.017
Non-smokers	1.4 (1-1.98)	1.25 (0.93-1.67)	1.09 (0.8-1.48)	Referent	0.027

Follow-up	Birth
Confounding	Maternal age, height, weight, education, parity, smoking and drinking in pregnancy, and whether mothers living with a partner
Risk of bias	Low to moderate (attrition bias); Originally 14,150 pregnancies reaching 32 weeks gestation, 12,441 returned questionnaire, 12, 200 completed FFQ, then excluded still births, multiple births and women who took fish oil supplements leaving 11, 585 but information on confounders only for 10, 040 (71% of original cohort). The proportion of smokers, less educated mothers, primiparas, single women, short women, teenage mothers and non drinkers were all lower with higher n-3 FA intake. Low pre-pregnant weight, also non-linear relationship with fish intake.
Relevance	UK diet similar to Australian
Other comments	

Reference	**Romieu 2007**
Food type	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	All women presenting for antenatal care in Menorca, Spain from mid 1997-mid 1998
Funding	Instituto de Salud Carlos III red de Grupos Infancia y Media Ambiente and Fundacio 'La Caixa' and Instituto de Salud Carlos III red de Centros de Investigacion en Epidemiologia y Salud Publica. National Center for Environmental Health and Ministry of Education and Science, Spain.
Participants	458 mothers and their children
Baseline comparisons	*See Confounding below*
Dietary Assessment	Food frequency questionnaire - Interview
Timing	FFQ-3 months after delivery (referring to pregnancy) Same FFQ for child at 4 years
Comparison	Fish intake as portions per week: 0, 1/52 (once per 52 weeks), ¼ (once per month), 1 (once per week) and 7 (once per day) (note: fish intake score was log transformed to normalise its distribution)
Outcomes	Incidence of atopy and eczema at 1 year, IgE to any/house dust mite (HDM) at 4 years, SPT to any/HDM at 6 years, persistent and atopic wheeze at 6 years)
Results	**Adjusted OR (95% CI) per unit increase of log transformed weekly fish consumption** — **OR (95% CI)** — **P** **Eczema at 1 year** — **0.73 (0.55-0.98)** — **0.036** Specific IgE to any at 4 years — 0.93 (0.59-1.47) — 0.768 Specific IgE to HDM at 4 years — 1 (0.62-1.62) — 0.984 Specific SPT to any at 6 years — 0.74 (0.5-1.09) — 0.123 Specific SPT to HDM at 6 years — 0.68 (0.46-1.01) — 0.058 Persistent wheeze at 6 years — 0.87 (0.51-1.49) — 0.615 **Atopic wheeze at 6 years** — **0.55 (0.31-0.96)** — **0.034**
Follow-up	6. 5 years
Confounding	Variables all tested for covariability (only those significant were adjusted for): Gender, maternal age, maternal and paternal atopy, maternal and paternal asthma, maternal and paternal social class, maternal smoking during pregnancy, maternal BMI before pregnancy, gender, gestational age, birth weight, type of fish, parity, breastfeeding, ownership of pets, BMI at 6.5 years, dichlorodiphenyldichloroethylene in cord blood, child fish consumption at 4 years
Risk of bias	Low risk of bias: 507 pregnant women originally recruited, then 482 children subsequently enrolled and 462 of them completed until 6.5 years follow up.
Relevance	Spanish diet differs from Australian diet
Other comments	Excluded women (21) who reported never eating fish as likely that their disease (high prevalence of atopy and asthma) modified their fish intake. Women medically diagnosed with asthma ate significantly less fish Women who didn't breastfeed more likely to be from lower social class and have a low-birth weight baby - taken into account in regression models.

Reference	**Saito 2010**
Food type	Fish (also meat, eggs, dairy)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Neyagawa City, Japan
Funding	Ministry of Education, Culture, Sports, Science and Technology and Health and Labour Sciences, Ministry of Health, Labour and Welfare, Japan
Participants	771 mother-child pairs recruited from November 2001 to March 2003 at any stage of pregnancy – mean GA 18 weeks (part of the Osaka Maternal and Child Health Study)
Baseline comparisons	*See confounding below*
Dietary assessment	Diet history questionnaire (DHQ)
Timing	DHQ to assess dietary habits during the preceding month
Comparison	Quartiles of fish consumption
Outcomes	Suspected atopic eczema
Results	**Suspected atopic eczema** *n/N* — *OR (95% CI)* — *aOR (95% CI)* Q1 (23.0 g/day): 14/192 — 1.00 — 1.00 Q2 (37.8 g/day): 15/193 — 1.07 (0.50 to 2.31) — 0.93 (0.41 to 2.13) Q3 (51.4 g/day): 21/193 — 1.55 (0.77 to 3.21) — 1.60 (0.75 to 3.51) Q4 (73.1 g/day): 15/193 — 1.07 (0.50 to 2.31) — 1.15 (0.51 to 2.62) p value for trend (unadjusted): 0.61 p value for trend (adjusted): 0.44
Followup	3-4 months
Confounding	Adjusted for maternal age, gestation at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, mite allergen level from maternal bedclothes, vacuuming living room, mould in kitchen, changes in maternal diet in previous month, season when baseline data collected, baby's older siblings, baby's sex, baby's birthweight, breastfeeding and bathing or showering infant
Risk of bias	Low risk of bias: Of 1002 eligible women, a final sample of 771 (77%) was available for analysis
Relevance	Fish intake in Japan likely to be higher than in Australia
Other comments	

Reference	**Salam 2005**
Food type	Fish
Study type	Nested case-control study
Level of evidence	III-3 (aetiology)
Setting	Children's Health Study (CHS) in California: 4th, 7th and 10th grade students in 1993 and 4th grade students in 1995 who attending public school in 12 Southern California communities
Funding	California Air Resources Board, the National Institute of Environmental Health Services, U.S. Environmental Protection Agency, National Heart, Lung and Blood Institute and Hastings Foundation
Participants	891 CHS children with asthma diagnosis by age 5 years (n=338) + randomly selected asthma free controls matched on in utero exposure to maternal smoking Recruited Dec 1999-Dec 2001 n=279 (82.5%) cases and n=412 (72.3%) controls with parents/guardians able to be contacted and interviewed

Baseline comparisons

	Case *n* (%)	Control n (%)	OR (95% CI)
n	279	412	
Born ≥4 weeks preterm	26 (9.4)	13□ (2□3)	2.71 (1.2-6.15
In utero exposure to maternal smoking – YES	68 (24.4)	263 (18.4)	1.56 (1.14-2.14)

See confounding below

Dietary Assessment	Self completed Questionnaire on frequency of fish intake during the pregnancy, appears that this was collected retrospectively
Timing	Not clear - seems to be when child was recruited (in grade 4, 7 or 10)
Comparison	Maternal fish intake during pregnancy (for fish sticks and oily fish): never, rarely, at least monthly
Outcomes	Early transient asthma (diagnosed before 3 years old but no symptoms/medication after first grade or previous 12 months to study entry), Early persistent asthma (diagnosis before 3 years old and ≥1 asthma episode or medication use since grade 1 0r within 12 months of study entry), Late-onset asthma (diagnosed after age 3 years). Parental report of physician-diagnosed asthma.

Results

Fish intake OR (95% CI):	**Never**	**Rarely**	**≥ monthly**	**P trend**
Oily fish				
Any asthma	1	1.01 (0.54-1.89)	0.80 (0.47-1.36)	0.40
Early transient asthma	1	0.68 (0.17-2.67)	0.99 (0.34-2.87)	0.92
Early persistent asthma	1	1.07 (0.53-2.17)	**0.45 (0.23-0.91)**	**0.04**
Late-onset asthma	1	0.8 (0.26-3.09)	0.84 (0.33-2.12)	0.66
Fish Stick				
Any asthma	**1**	**1.15 (0.66-2.01)**	**2.04 (1.18-3.51)**	0.01
Early transient asthma	1	0.74 (0.24-2.27)	2.26 (0.67-7.58)	0.3
Early persistent asthma	1	1.51 (0.75-3.04)	**2.46 (1.26-4.8)**	0.01
Late-onset asthma	1	0.98 (0.34-2.89)	**3.05 (1.04-8.93)**	0.07
Oily Fish intake OR (95% CI):				
Any asthma	1	1.31 (0.65-2.67)	1.09 (0.61-1.94)	0.70
Early transient asthma	1	0.7 (0.16-3.11)	1.38 (0.42-4.61)	0.67
Early persistent asthma	1	1.55 (0.68-3.52)	0.62 (0.29-1.31)	0.35
Late-onset asthma	1	0.84 (0.19-3.71)	1.43 (0.51-3.99)	0.42
Maternal asthma- YES				

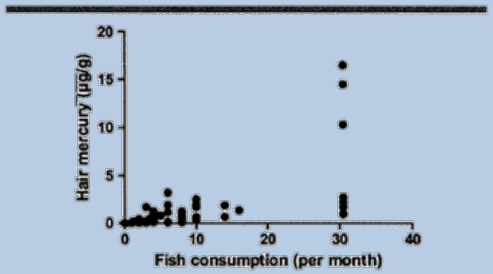
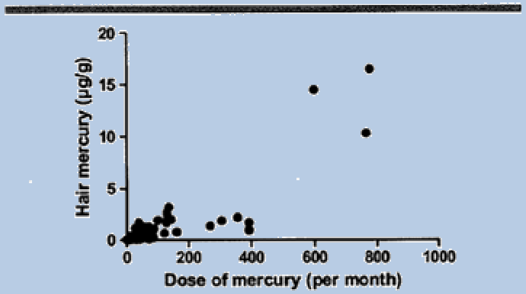
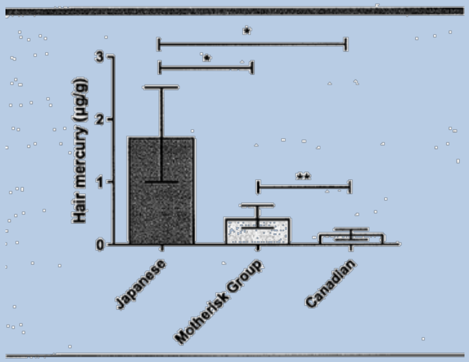
	(reference: no) Any asthma **3.97 (2.07-7.63** **1.78 (0.54-5.90)** **0.81 (0.29-2.28)** **0.006** Early transient asthma 3.89 (0.83-18.18) 1.95 (0.1-40.01) 0.98 (0.12-7.82) 0.31 Early persistent asthma **5.58 (2.52-12.33)** 2.13 (0.57-7.99) 0.63 (0.16-2.56) **0.006** Late-onset asthma **6.47 (1.92-21.81)** **8.11 (0.47-14.71)** 0.33 (0.04-2.76) **0.01** Note also looked at relationship for non-oily fish and canned fish and found no association with asthma
Follow-up	3 years-study entry (grade 4, 7 or 10)
Confounding	Adjusted for maternal asthma, race/ethnicity, maternal age, maternal education, gestational age, number of siblings, exclusive breastfeeding, number of siblings, other fish variable in table (oily fish, fish stick) Other measured variables not found to be covariates: paternal history of asthma, maternal smoking during pregnancy, second-hand tobacco exposure, yearly family income
Risk of bias	Low to moderate risk of bias: Not very detailed estimation of fish intake - debatable accuracy of measure if done years after pregnancy
Relevance	Few women reported eating fish daily *or* weekly basis, only monthly - seems less fish than Australian diet
Other comments	Fish intake categories broad.

Reference	**Sausenthaler 2007**
Food groups	Fish
Study type	Prospective cohort study: from the LISA birth cohort
Level of evidence	II (aetiology)
Setting	4 German cities (Munich, Leipzig, Wesel, Bad Honnef)
Funding	Federal Ministry for Education, Science, Research and Technology, Germany
Participants	3097 newborns recruited
Baseline comparisons	*See Confounding below*
Dietary assessment	FFQ
Timing	Maternal diet during the last 4 weeks of pregnancy (obtained shortly after birth, median 3 days)
Variable	Low intake group as reference group compared with high intake group: • High fish intake = 1-2 times/week
Outcomes	Allergic sensitisation, eczema at 2 yrs
Results	
Length of followup	2 years
Confounding	Crude and adjusted results reported (adjusted for study area, sex, maternal age, maternal smoking, level of parental education, exclusive breastfeeding ≥ 4 months, parental history of atopic diseases, season of birth and all dietary variables
Risk of bias	Low risk of bias: Two year data available for 2641/3097 children (85%): 433 lost to follow-up, 9 excluded due to chronic disease, 14 missing maternal FFQ
Relevance	Likely to be reasonably similar to dietary intakes of Australian women in Australia
Other comments	

Results:

	Doctor-diagnosed eczema	any allergen sensitisation	food allergens	inhalant allergens
	Adjusted OR (95% CI)			
Fish intake	**0.75 (0.57, 0.98)**	1.02 (0.73, 1.43)	1.01 (0.69, 1.48)	0.94 (0.56, 1.57)

Reference	**Schoeman 2010**

Food type	Fish
Study type	Cross-sectional study
Level of evidence	IV (aetiology)
Setting	Canada
Funding	Grants from the First Nation and Inuit Branch, Government of Canada and Health Canada.
Participants	1) 22 Canadian women aged 22-42 years old who called the Motherisk program whilst planning pregnancy in 2006-07 for information on the safety of consuming fish during pregnancy. Women ineligible if declined, could not be reached by telephone, not fluent in English, had not called Motherisk about Mercury in fish or had other exposures to mercury. 2) 20 Canadian (Southwestern Ontario) women aged 22-29 years old who did not consult the Motherisk program and were not concerned about fish consumption and who were acquaintances of the researcher. This group was matched to group 1 on completion of post-secondary education. Women were contacted over the phone or email between July-November 2008. 3) 23 Japanese men and women aged 21-44 years old in Toronto who frequently consumed large amounts of seafood as part of their diet. Participants approached through a group of Japanese researchers and their families in Toronto, a Japanese restaurant and a Japanese fish market (where 5 workers agreed to participate).
Baseline comparisons	*See confounding below*
Dietary Assessment Method	Food frequency questionnaire
Timing	Not stated
Comparison	Monthly fish consumption (analysed with correlation)
Outcomes	Hair mercury level in women of reproductive age (not pregnant) and some similarly aged Japanese men
Results	 **Figure 2.** Correlation between hair mercury content and number of fish servings reportedly eaten by participants (*r* = 0.73, *P* < .0001, n = 65).  **Figure 3.** Correlation between hair mercury content and estimated intake dose of mercury (*r* = 0.81, *P* < .0001, n = 65).  **Figure 1.** Median hair mercury concentrations for the 3 cohorts. (Values plotted are median ± interquartile range; medians were significantly different for the 3 cohorts when compared by a Kruskal-Wallis test followed by a Mann Whitney *U* test) (**P* < .0001; ** *P* < .001).
Follow-up	Not stated
Confounding	None stated
Risk of bias	Medium risk of bias: Participation rate not given; possibly very biased sample; significant differences between women in group 1 and group 3
Relevance	Japanese diet not similar to Australian; Canadian diet is.
Other comments	Group 2 were acquaintances of researcher as were some of group 3; Japanese would have very different diet to Canadian women in more areas than just seafood.
Reference	**Shiell 2001**

Food groups	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Motherwell, Scotland
Funding	Dunhill Medical Trust
Participants	626 (274 men and 352 women) whose mothers' food intakes had been recorded during pregnancy during 1967 to 1968. These women had been advised to eat 0.45 kg of red meat a day and to avoid carbohydrate-rich foods during pregnancy
Baseline comparisons	*See confounding below*
Dietary assessment	Mothers asked about consumption of 10 foods
Timing	Early pregnancy (≤ 20 weeks); late pregnancy (> 20 weeks)
Comparison	Maternal consumption of fish (mean consumption in late pregnancy was 1.4 [SD 0.8] serves per week
Outcomes	Systolic and diastolic blood pressure at in offspring aged 27 to 30 years
Results	**Systolic blood pressure at 27 to 30 years** Regression coefficient for amount of maternal fish consumption; ß 0.97 95% CI -0.11 to 2.05, p = 0.08 **Diastolic blood pressure at 27 to 30 years** **Regression coefficient for amount of maternal fish consumption; ß 1.00 95% CI 0.18 to 1.82, p = 0.02**
Length of followup	27 to 30 years
Confounding	Analyses adjusted for offspring's gender, BMI, alcohol consumption, and cuff size used for blood pressure
Risk of bias	Moderate risk of bias: For the 1432 records from 1967-8 recorded liveborn, singleton births with complete names, birth measurements and ≥ 1 diet record. 965 offspring were alive and living locally; and after attrition or declining to participate, 626 (43.7%) were available for analysis.
Relevance	Very high intake of meat and very low carbohydrate intake limits the relevance to current dietary intakes of Australian women
Other comments	Authors state that "low intake of green vegetables, a source of folate, accentuated the effect of high meat and fish consumption on systolic blood pressure"

Reference	**Sontrop 2008**
Food type	Fish
Study type	Prospective cohort (Perinatal Health Project)
Level of evidence	II (aetiology)
Setting	London, Ontario, Canada 2002-2005 from 10 ultrasound clinics
Funding	Canadian Institute of Health Research
Participants	2061 English speaking women experiencing normal, singleton pregnancies (GA 10-20 weeks) over the age of 16 and residing in Middlesex County. Excluded from analysis if taking antidepressants or n-3 PUFA supplements or if energy intake >± 2SD from the mean
Baseline comparisons	*See Confounding below for other*
Dietary Assessment	Food frequency questionnaire-phone interview
Timing	FFQ at 12-24 weeks gestation
Comparison	Fish consumption per week: 0, 1, >1 EPA + DHA intake in mg per day: <85, ≥85
Outcomes	Prenatal depressive symptoms (CES-D: Center for Epidemiological Studies-Depression Scale)
Results	**Multiple linear regression of depressive symptoms and confounders** **Adjusted fish consumption per week (0, 1, >1)** — **B (95% CI)**: -0.2 (-0.9 to 0.4) **Adjusted EPA + DHA intake in mg per day (<85, ≥85)** — **β (95% CI)**: 0.1 (-0.6 to 0.8) Interaction EPA+ DHA with former smoker: 0.4 (-1.5 to 2.3) Interaction EPA+ DHA with current smoker: **-2.5 (-4.6 to -0.4)*** Interaction EPA+ DHA with single/separated/divorced: **-3 (-5.5 to -0.5)*** **P* < 0.5 Adjusted for energy intake
Follow-up	NA
Confounding	Confounding = changed coefficient by ≥10%: age, marital status, education, income, occupational status, smoking status, physical activity and meeting Canada Food Guide to Healthy Living guidelines
Risk of bias	Low risk of bias
Relevance	Canadian diet similar to Australia
Other comments	Depression scale used not validated for pregnant women 3656 women eligible, 2747 enrolled, 2421 completed interview –some enrolled twice (with separate pregnancies so one pregnancy excluded) leaving 2394 - but only 2061 included in analyses and no mention of where other 333 went

Reference	**Strain 2008; Davidson 2008a; Davidson 2008b;**
Food type	Fish
Study type	Prospective cohort (Seychelles Child Development Nutrition Study)
Level of evidence	II (aetiology)
Setting	Seychelles
Funding	US National Institute of Environmental Health Sciences, NIH, Government of Seychelles
Participants	229 women at their first antenatal visit, aged over 16 years, native born Seychellois; Mean maternal mercury concentration was 5.7 ppm [SD3.7]; range 0.2 to 18.5; mean consumption was 9 fish meals per week estimated 537 g of fish per week) Exclusions: 4 infants with major congenital anomalies, 1 set of twins
Baseline comparisons	*See Confounding below*
Dietary Assessment	Maternal hair methylmercury concentrations
Timing	Measured antenatally at 28 weeks gestation; and 1 day after birth
Comparison	Mercury concentrations in mothers' hair
Outcomes	Bayley Scales of Infant Development (BSID-II); (MDI) and Psychomotor Developmental Index (PDI) at 9 and 30 months; Bender Visual Motor Gestalt Test at 66 months and 10.7 years of age
Results	At infant age of 9 months, maternal hair mercury concentrations were not associated with MDI or PDI scores At infant age of 30 months, maternal hair mercury concentrations were associated with a **significantly lower PDI score (p = 0.05)** but not a lower MDI score
Follow-up	To 30 months of age
Confounding	Adjusted for DHA and AA
Risk of bias	Low to moderate risk of bias: 300 women recruited with 229 (76.3%) analysed (reasons for losses not reported); insufficient consideration of confounders?
Relevance	Of some relevance to Australian women but fish consumption in the Seychelles is much higher as are mercury concentrations in fish
Other comments	

Reference	**Strom 2009**
Food type	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Danish National Birth Cohort 1996-2002, recruited during first antenatal visit with GP (6-10 weeks gestation)
Funding	Faroese Research Council, the Fisheries Research Fund of the Faroe Islands, the European Union 6th framework programme Integrated Research Project SEAFOODplus (FOOD-CT-2004-506359), and the European Union 6th framework programme EARNEST (FOOD-CT-2005-007036). Funding for the Danish National Birth Cohort was provided by the March of Dimes Birth Defects Foundation, the Danish Heart Association, the Danish Medical Research Council, Sygekassernes Helsefond, the Danish National Research Foundation, the Danish Pharmaceutical Association, the Ministry of Health, the National Board of Health, and Statens Serum Institut.
Participants	54,202 Danish women living in Denmark and fluent in Danish Data analysed for first singleton pregnancies (n=86453) who had not taken fish oil supplements during pregnancy and had no missing data
Baseline comparisons	*See Confounding below*
Dietary Assessment	Food frequency questionnaire - self administered
Timing	FFQ in mid-pregnancy (approximately 25 weeks gestation) for month preceding questionnaire completion Telephone interview (not diet related) at 12 & 30 weeks gestation and at 6 & 18 months after birth
Comparison	Average fish consumption (grams per day): 0-3, >3-10, >10-20, >20-30 , >30 Average intake of n-3 PUFA's derived from fish consumption (mg per day): 9.1, 14.1, 18.1, 22.2, 27, 32.7, 39.6, 48.4, 72.8
Outcomes	Hospital admission for postpartum depression (PPD), prescription for antidepressants due to postpartum depression
Results	See below

Adjusted PPD-admission and PPD-antidepressant prescription aOR (95% CI)
Average fish consumption (g/day):

	0-3	**>3-10**	**>10-20**	**>20-30**	**>30**	**P**
PPD admission	0.82 (0.42-1.64)	1.09 (0.64-1.84)	1.34 (0.84-2.15)	1.11 (0.64-1.92)	Reference	0.5
PPD prescription	**1.46 (1.12-1.9**	1.1 (0.87-1.38)	1.18 (0.95-1.45)	1.03 (0.81-1.32)	Reference	**0.04**

Average intake n-3 PUFA's (mg/day):

	PPD admission	**PPD prescription**
9.1 mg/day	0.96 (0.51-1.78)	1.24 (0.96-1.61)
14.1	1.03 (0.55-1.92)	1.17 (0.9-1.53)
18.1	0.73 (0.36-1.48)	0.99 (0.75-1.31)
22.2	1.33 (0.74-2.39)	1.29 (0.99-1.68)
27	1.21 (0.66-2.21)	1.09 (0.83-1.44)
32.7	1.65 (0.95-2.88)	1.11 (0.84-1.46)
39.9	1.3 (0.72-2.36)	1.04 (0.79-1.38)
48.4	0.79 (0.39-1.59)	0.89 (0.67-1.2)
72.8	Reference	Reference
P	0.38	0.33

Follow-up	6 and 18 months after birth
Confounding	Covariates defined a priori: age, parity, pre-pregnancy BMI, total energy intake, alcohol intake during pregnancy, smoking during pregnancy, occupation, education, homeownership, marital status, social support, history of depression.
Risk of bias	Low-moderate risk of bias: high attrition - Danish National Birth cohort covered >100,000 pregnancies with >90,000 women enrolled, but only 60% participation rate and only 35% of eligible women entered the cohort; however not biased from normal population in terms of in vitro fertilisation, preterm birth, smoking during pregnancy, small-for-gestational age, pre-pregnancy BMI and antepartum stillbirth-but could be biased for post partum depression

	outcomes. Those in low fish intake groups more likely to be <25 years old, nulliparous, single/unmarried, smokers, overweight, report poor social support but were less likely to use alcohol, be white-collar workers, have >4 years post secondary education or be homeowners.
Relevance	Danish diet differs from Australian diet
Other comments	

<table>
<tr><td>Reference</td><td>Thorsdottir 2004</td></tr>
<tr><td>Food type</td><td>Fish</td></tr>
<tr><td>Study type</td><td>Retrospective cohort</td></tr>
<tr><td>Level of evidence</td><td>II (aetiology)</td></tr>
<tr><td>Setting</td><td>Icelandic (Reykjavik) fishing community women selected randomly by computer if they fulfilled the 1-year inclusion criteria according to birth records, 1998</td></tr>
<tr><td>Funding</td><td>Nil stated in paper</td></tr>
<tr><td>Participants</td><td>491 (of 614) women aged 20-40 years who were healthy and of normal weight (BMI 19.5-25.5) before pregnancy, without a history of hypertension, diabetes, cardiovascular disease or thyroid problems. Only singleton term infants included whose mothers agreed to their maternity records viewed after the birth of their infant</td></tr>
<tr><td>Baseline comparisons</td><td>See Confounding below</td></tr>
<tr><td>Dietary Assessment</td><td>Food frequency questionnaire-self administered</td></tr>
<tr><td>Timing</td><td>Not reported (after birth - around 1 year?)</td></tr>
<tr><td>Comparison</td><td>Frequency of fish consumption as main meal (monthly): < 4, 4-6, > 6</td></tr>
<tr><td>Outcomes</td><td>Infant size (birthweight, length, ponderal index and head circumference)</td></tr>
<tr><td>Results</td><td>Only 1% never consumed any fish. Fish liver oil was used as a supplement by 44.8 percent (n = 218) of the women during pregnancy and by 38.7 percent throughout the whole pregnancy.

Adjusted mean*
Frequency of fish consumption as main meal (monthly):
<table>
<tr><th></th><th><4</th><th>4-6</th><th>>6</th><th>β</th><th>p value</th></tr>
<tr><td>Birth weight (g)</td><td>3725</td><td>3780</td><td>3810</td><td>50</td><td>0.098</td></tr>
<tr><td>Birth length (cm)</td><td>51.8</td><td>52.1</td><td>52.3</td><td>0.35</td><td>0.007</td></tr>
<tr><td>Head circumference (cm)</td><td>3□.6</td><td>36</td><td>36.1</td><td>0.24</td><td>0.005</td></tr>
<tr><td>Ponderal index</td><td>26.6</td><td>26.7</td><td>26.5</td><td>-0.43</td><td>0.340</td></tr>
</table>
*Adjusted for weight gain in pregnancy, maternal height, parity, smoking, infant’s gender, gestational length, and fish liver oil supplementation

Infants of women in the lowest quartile of fish consumption (0–20 g/day) weighed less (p =0.036), were shorter (p = 0.003), and had a smaller head circumference (p < 0.001) at birth than those of women eating more fish per day.

Adjusted mean**
Fish liver oil intake quartile group:
<table>
<tr><th></th><th>1</th><th>2</th><th>3</th><th>4</th><th>β</th><th>p value</th></tr>
<tr><td>Birth weight (g)</td><td>3805</td><td>3795</td><td>3800</td><td>3695</td><td>-8</td><td>0.184</td></tr>
<tr><td>Birth length (cm)</td><td>52.3</td><td>52.1</td><td>52.2</td><td>51.8</td><td>-0.04</td><td>0.036</td></tr>
<tr><td>Head circumference (cm)</td><td>36.1</td><td>36</td><td>35.9</td><td>35.5</td><td>-0.04</td><td>0.003</td></tr>
<tr><td>Ponderal index</td><td>26.6</td><td>26.8</td><td>26.6</td><td>26.6</td><td>0.02</td><td>0.598</td></tr>
</table>
**Adjusted for weight gain in pregnancy, ma□ernal height, parity, smoking, infant’s gender, gestational length, and fish consumption.

Results indicate that constituents of fish and fish liver oil affect birth size differently, depending on the amount consumed, and that moderate consumption should be recommended.</td></tr>
<tr><td>Follow-up</td><td>Birth</td></tr>
<tr><td>Confounding</td><td>Pre-pregnant weight, weight gain in pregnancy, maternal height, age, parity, smoking , marital status, pregnancy complications, infant’s gender, gestational length</td></tr>
</table>

Risk of bias	Low risk of bias
Relevance	Fishing community likely to have much higher fish intake (average 47 g/d) than general Australian diet and very high use of fish liver oil supplements during pregnancy (44.8%, and 38.7% throughout entire pregnancy).
Other comments	The sample population is already known as having higher than average birth size. 614 eligible and agreed to maternity records accessed but only 491 completed FFQ (80%)

Reference	**Thurston 2007; Myers 2003**
Food type	Fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Seychelles Child Development Study on the Island of Màhe.
Funding	Grant from the National Institutes of Environmental Health Sciences and the National Institute of Health and the National Centre for Research Resources
Participants	779 mother-child pairs enrolled in 1989-1990 when children were 6 months old (approximately 50% of live-births during that period). Excluded 44 mothers and children with disorders highly associated with traumatic brain injury, meningitis, epilepsy or severe neonatal illness. 18 children excluded for closed head trauma and meningitis
Baseline comparisons	*See confounding below*
Dietary Assessment Method	Food frequency questionnaire, (weighed) food record, 24 hour recall, diet history
Timing	Unclear
Comparison	Prenatal methyl mercury exposure (indicative of ocean fish consumption); this population of women consumed about 12 fish meals a week
Outcomes	Child development; blood pressure (available from routine school and kindergarten examinations-not part of original study design), height and weight
Results	***Neurodevelopment (cognition and achievement) at 9 years*** No significant differences seen ***Neurodevelopment (motor, perceptual motor and memory) at 9 years*** No significant differences seen, except for decreased performance in the grooved pegboard test for males using the nondominant hand associated with increased exposure to methyl mercury ***Neurodevelopment (attention and behaviour) at 9 years*** No significant differences seen, except for improve scores in hyperactivity index ***Blood pressure at 15 years*** No association between antenatal MeHg exposure and blood pressure in girls at either 12 or 15 years, or boys at 12 years of age; at age 15 years, diastolic BP in boys increased with increasing antenatal MeHg exposure, while systolic BP was unaffected.

Table 2
Pearson correlations between average blood pressure measurements (mmHg) at a single age and between two ages, and correlations between average BP and prenatal MeHg exposure.

	N	**Systolic BP and diastolic BP**	**Diastolic BP (2 ages)**	**Systolic BP (2 ages)**	**Diastolic BP and MeHg**	**Systolic BP and MeHg**
Both sexes						
12 years	644	0.64	–	–	–0.02	0.02
15 years	559	0.50	–	–	0.10	0.03
Across years	524	–	0.32	0.34	–	–
Boys						
12 years	313	0.59	–	–	–0.03	0.03
15 years	267	0.55	–		0.17	0.06
Across years	244	–	0.22	0.34	–	–
Girls						

	<table><tr><td>12 years</td><td>331</td><td>0.69</td><td>–</td><td>–</td><td>–0.03</td><td>0</td></tr><tr><td>15 years</td><td>292</td><td>0.55</td><td>–</td><td>–</td><td>0.04</td><td>0.04</td></tr><tr><td>Across years</td><td>280</td><td>–</td><td>0.39</td><td>0.40</td><td>–</td><td>–</td></tr></table> BP measurements are the average of duplicate readings. BP = blood pressure, MeHg = methylmercury. Column 3 of this table gives the correlations between average diastolic and average systolic BP at a single are (12 years or 15 years, as indicated in column 1). Correlations between measurements at two different ages are given in columns 4 and 5. For example, column 4 gives the correlation between diastolic BP at age 12 and diastolic BP at age 15.
Follow-up	Child cognitive development at 9 years (Myers 2003) Children's blood pressure - 7 (10 years old) and 10 (15 years old) (Thurston 2007)
Confounding	Adjusted for gender, prenatal mercury exposure, maternal hypertension during pregnancy that required medical treatment, birth weight, age at testing, BMI and height
Risk of bias	Low risk of bias: Was done double blind; 7 participants excluded due to missing covariates, one with implausible weight and one over 18 years old. 86% participation in 2001 and 80% participation in 2002; SES was missing in over 10% of the sample (pp 926) 650 children participated at 12 years, Complete data available for 644 (313 boys, 331 girls) 568 children participated at 15 years, Complete data available for 559 (267 boys, 292 girls)
Relevance	Not similar to Australia, the authors report the Màhe island has high fish consumption.
Other comments	Note: outcome not analysed in relation to dietary intake of fish or other food (only to mercury); mercury concentration in Seychelles not excessively high

Reference	**Venter 2009**
Food groups	Fish: white fish, shellfish, oily fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Portsmouth, UK
Funding	Food Standards Agency
Participants	969 pregnant women at 12 weeks gestation (with estimated birth date between 1 September 2001 and 31 August 2002)
Baseline comparisons	Pregnant women with a maternal history of atopic disease were more likely to smoke
Dietary assessment	FFQ
Timing	FFQ at 36 weeks gestation
Comparison	No versus moderate versus frequent versus uncertain consumption of fish during pregnancy **None / Moderate / Frequent / Uncertain** White fish: 11% / 84% / 5% / < 1% Shellfish: 60% / 40% / < 1% / < 1% Oily fish: 53% / 45% / 1% / < 1%
Outcomes	Food hypersensitivity (FHS) in infants up to three years of age
Results	**Infant FHS at three years:** 1/936 infants showed FHS to milk in the first three years (mother reported moderate consumption of fish during pregnancy) "Statistical inferences could not be measured due to the small numbers"
Length of followup	Up to three years
Confounding	Analyses do not appear to have been adjusted
Risk of bias	Moderate-high risk of bias: Data were obtained from 91% (n = 969) of the birth cohort; at 1 year follow-up data were available for 77.6% (752/969) and for 65.2% (632/969) at 3 years; analyses probably not adjusted for confounders
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Willers 2007**
Food type	Fish
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Antenatal clinics at Aberdeen Maternity Hospital, Aberdeen, Scotland
Funding	Asthma UK, GA^2LEN European Network of Excellence on Global Allergy and Asthma
Participants	1212 children (singleton births) whose mothers were recruited between October 1997 and April 1999 at a median gestational age of 12 weeks
Baseline comparisons	Women were representative of the local obstetric population *See confounding below*
Dietary assessment	FFQ
Timing	FFQ mailed at 32 weeks gestation to cover dietary intake over the previous 2-3 months
Comparison	Tertiles:
Outcomes	Eczema, hay fever at 5 years
Results	

Total fish consumption	*N*	*T1 (never)* *n* = 107	*T2 (< 1/week)* *n* = 255	*T1 (≥ 1/week)* *n* = 831	*P trend*
Doctor confirmed eczema	979				
OR (95% CI)		**1**	**0.77 (0.46 to 1.28)**	**0.60 (0.38 to 0.96)**	**0.016**
aOR (95% CI)		**1**	**0.79 (0.47 to 1.32)**	**0.57 (0.35 to 0.92)**	**0.008**
Current eczema medication	982				
OR (95% CI)		1	0.85 (0.45 to 1.61)	0.67 (0.38 to 1.19)	0.111
aOR (95% CI)		**1**	**0.88 (0.46 to 1.67)**	**0.58 (0.32 to 1.06)**	0.028
Ever had eczema	983				
OR (95% CI)		1	0.88 (0.53 to 1.47)	0.73 (0.47 to 1.16)	0.111
aOR (95% CI)		**1**	**0.91 (0.54 to 1.53)**	**0.68 (0.43 to 1.10)**	0.050
Total oily fish consumption		*n* = 629	*n* = 414	*n* = 161	
Doctor confirmed hay fever	990				
OR (95% CI)		1	**0.57 (0.31 to 1.08)**	**0.20 (0.05 to 0.85)**	0.006
aOR (95% CI)		1	**0.66 (0.34 to 1.28)**	**0.28 (0.06 to 1.19)**	0.043
Current hay fever medication	988				
OR (95% CI)		1	1.08 (0.53 to 2.22)	0.20 (0.03 to 1.53)	0.226
aOR (95% CI)		1	1.02 (0.48 to 2.20)	0.19 (0.02 to 1.48)	0.194
Ever had hay fever					
OR (95% CI)		1	1.11 (0.70 to 1.75)	**0.38 (0.15 to 0.98)**	0.155
aOR (95% CI)		1	1.11 (0.68 to 1.82)	**0.37 (0.14 to 0.98)**	0.159

Followup	5 years
Confounding	Adjusted for maternal age, paternal social class, maternal education, maternal smoking during pregnancy, smoking in the child's home at 5 years, energy intake, maternal asthma, maternal atopy, child's birthweight, child's sex, presence of older siblings, and breastfeeding
Risk of bias	Low risk of bias: Initial study population of 1924 children dropped to 1212 participants with complete data (63.0%) (questionnaire, at least one of the outcome time points).
Relevance	Likely to be reasonably relevant to Australian women
Other comments	Inclusion of maternal supplement use during pregnancy did not materially change the results; Only eczema and hay fever outcomes reported for fish consumption – assume that no association was found for other outcomes such as asthma?

Reference	**Willers 2008**
Food type	Fish
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Netherlands
Funding	Netherlands Organization for Health Research and Development, Netherlands Organization for Scientific Research; Netherlands Asthma Fund; Netherlands Ministry of Spatial Planning, Housing, and the Environment; Netherlands Ministry of Health, Welfare and Sport, GlaxoSmithKline
Participants	2,832 children (part of the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered at antenatal recruitment (mean gestational ages not reported) to cover dietary intake over the previous month
Comparison	Daily (once per day or more) v 1-4 times a week or fewer
Outcomes	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable 'asthma symptoms' in the last 12 months (measured longitudinally from 1 to 8 years age)
Results	**Wheeze from 1 to 8 years age (n = 2811)** OR 1.15 95% CI 0.99 to 1.35 aOR 1.10 95% CI 0.94 to 1.29 **Dyspnoea from 1 to 8 years age (n = 2811)** OR 1.11 95% CI 0.92 to 1.33 aOR 1.07 95% CI 0.89 to 1.29 **Steroid use from 1 to 8 years age (n = 2811)** OR 0.86 95% CI 0.67 to 1.12 aOR 0.85 95% CI 0.66 to 1.10 **Asthma symptoms (composite of previous three outcomes) from 1 to 8 years age (n = 2811)** OR 1.03 95% CI 0.88 to 1.23 aOR 1.01 95% CI 0.85 to 1.20
Followup	8 years
Confounding	The child's dietary data on fruit, vegetables, fish, eggs, full cream milk, butter and peanut butter consumption at 2 years of age were used to check for potential confounding by the child's diet. Results were adjusted for by sex, maternal education, parental allergy, maternal smoking during pregnancy, smoking in the home at 8 years of age, breastfeeding, presence of older siblings, birthweight, maternal overweight 1 year after pregnancy, maternal supplement use during pregnancy, region and study arm (intervention or natural history arm).
Risk of bias	Moderate risk of bias: Initial study population of 4,146 mothers dropped to 2,832 participants with complete data (68.3%) (pregnancy questionnaire, at least one of the outcome time points and all confounders). Participants with complete data were more likely to have a high education level, to have daily dairy and fruit intake during pregnancy and to have breastfed and less likely to have maternal asthma or maternal atopy, smoked during pregnancy, be from a south western region compared with participants who did not have complete data.
Relevance	Dietary intakes likely to be different from Australian e.g. low fish consumption in study participants
Other comments	Not clear when women assessed their diet during pregnancy; 83% of pregnant women used supplements (50% used folic acid/iron)

Reference	**Williams 2001**
Food type	Fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Southwest England, ALSPAC (Avon Longitudinal Study of Parents and Children) 1st April 1991- 31st December 1992
Funding	Supported by The Medical Research Council; the Wellcome Trust; The Ministry of Agriculture, Foods and Fisheries; the Departments of Health and the Environment; The South West Regional Health Authority; the National Eye Research Centre; Cow and Gate; and Milupa, all in the United Kingdom. The docosahexaenoic acid assays of maternal blood were carried out by Scotia Pharmaceuticals, Stirling, United Kingdom, at the instigation of DF Horrobin
Participants	Random subset (n=641) of full term children born in the last 6 months of ALSPAC assessed, excluded if strabismus, reduced vision, high refractive error (n=55, 9%), preterm (n=16, 2.5%) missing dietary data or non-compliance with visual assessment (n=135, 21%). 435 (68%) included in analyses. Foveal stereoacuity n=150, macular stereoacuity n=229, peripheral stereoacuity n=56
Baseline comparisons	*See Confounding below*
Dietary Assessment	Food frequency questionnaire-self administered
Timing	FFQ at 32 weeks gestation
Comparison	Maternal intake of any fish (white, oily, shellfish) during pregnancy: yes, no
Outcomes	Stereoacuity (foveal stereoacuity, macular stereoacuity, peripheral stereoacuity)
Results	

Univariate chi-square analysis

Mother ate any fish	**yes**	**no**
Foveal stereoacuity	33.9	36.4
Macular stereoacuity	52.1	54.5
Peripheral stereoacuity	14	9.1
P= 0.046		
Mother ate any white fish		
Foveal stereoacuity	36.7	29.6
Macular stereoacuity	51.2	53.5
Peripheral stereoacuity	12.1	16.9
p = 0.274		
Mother ate any shellfish		
Foveal stereoacuity	36	34.8
Macular stereoacuity	54.6	51
Peripheral stereoacuity	7.3	16.3
P = 0.582		
Mother ate any oily fish		
Foveal stereoacuity	40.1	27.5
Macular stereoacuity	48	57.5
Peripheral stereoacuity	11.9	15.6
P = 0.012		
maternal oily fish aOR (95% CI)	**No**	**yes**
	Referent	**1.57 (1-2.45)**

Follow-up	3.5 years
Confounding	For adjusted analysis: breastfeeding, child's sex, maternal education, maternal age, housing tenure, financial difficulties, maternal smoking, older siblings, paid child care, mother's paid employment since child birth, mother is vegetarian, maternal consumption of any fish/white fish/shell fish, child consumption of oily fish at 36 months
Risk of bias	Low-moderate risk of bias: not adjusted for maternal IQ, home environment
Relevance	UK diet similar to Australian
Other comments	641 children out of 14,541 women assessed - not stated how these were selected/excluded. Only 2/3rd of those randomly selected who attended were actually tested – reasons not given as to why not the other 1/3rd were not. Children who did not comply with the test were significantly more likely to live in public housing and have older siblings than those who complied with the test. Mothers who children were assessed had higher red blood cell DHA concentrations than the general population of the ALSPAC study (2.71 vs. 2.36% respectively, $p<0.0001$).

Reference	**Xue 2007**
Food type	Fish
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Pregnancy Outcomes and Community Health (POUCH) study, women enrolled from 52 prenatal clinics in Michigan between 15 and 27 weeks
Funding	The National Institute of Child Health and Human Development, the National Institute of Nursing Research, the March of Dimes Perinatal Epidemiology Research Initiative, the Agency for Toxic Substances and Disease Registry.
Participants	1226 women with a singleton pregnancy over 14 years old who spoke English and were screened for maternal serum alpha-fetoprotein levels between 15 and 22 weeks gestation. Women were not eligible if there were any known congenital or chromosomal anomalies at the time of recruitment, or diabetes mellitus.
Baseline comparisons	*See Confounding below*
Dietary Assessment	Food frequency interview
Timing	At enrolment (between 15 and 27 weeks) for the time of the pregnancy thus far
Comparison	Maternal fish consumption (no. of meals per 6 months): 0, 1-5, 6-23, ≥24
Outcomes	Fish intake and mercury level in maternal hair sample. Maternal mercury level and gestational age at birth **NOTE: outcome is not directly related to maternal fish intake**
Results	**Total maternal fish consumption (no. of meals per 6 months):** **0 (ref)** **1-5** **6-23** **≥24** Mean mercury (µg/g) 0.11 (0.1-0.13) 0.17 (0.16-0.18) **0.21 (0.2-0.23)** **0.25 (0.23-0.27)** **Adjusted association between high mercury hair levels and risk of preterm birth OR (95% CI)** <u>Term (≥ 37 weeks)</u> All preterm (< 37 weeks) 1.55 (0.79-2.9) Moderately preterm (35-36 weeks) 0.4□(0.1-1.9) **V□ry preterm (< 35 weeks)** **3.0 (1.3-6.7)**
Follow-up	Birth
Confounding	Adjusted for total fish consumption, maternal age, ethnicity, Medicaid status and community.
Risk of bias	Low risk of bias: 1,226 of enrolled women were excluded from analysis 16% loss to follow up (n=5) or no available hair sample (n=197).
Relevance	American diet similar to Australian diet
Other comments	1226 women enrolled in POUCH, fewer African American over 30 years old enrolled in the study than in the general population. Interview and questions about diet (specifically about fish) may have influenced participants' subsequent diet for the remainder of the pregnancy

Reference	**Yin 2010 (see also Jones 2000)**
Food type	Fish
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Southern Tasmania, Australia
Funding	NHMRC, Tasmanian Government, Royal Hobart Hospital Acute Care Program
Participants	216 adolescents born in 1988 (part of a larger infant health study of babies at high risk of SIDS) Exclusions: multiple pregnancies
Baseline comparisons	Children with unemployed fathers more likely to have been excluded due to missing data
Dietary assessment	FFQ
Timing	Dietary intake during third trimester of pregnancy
Comparison	Linear regression of density (portions per kJ)
Outcomes	Bone mass (bone mineral density (BMD) and bone mineral content*) in 16 year old adolescents
Results	**BMD at 16 years;** **Total body (g/cm^2)** r^2 0.010; ß +70.5 (pns) adjusted r^2 0.323; ß +14.9 (pns) **Femoral neck (g/cm^2)** r^2 0.009 ß +92.2 (pns) adjusted r^2 0.349; ß +32.7 (pns) **Lumbar spine (g/cm^2)** r^2 -0.004; ß +12.6 (pns) adjusted r^2 0.198; ß -27.0 (pns)
Followup	16 years
Confounding	Analyses were adjusted for sex, weight at age 16 years, sunlight exposure in winter at age 16 years, smoking during pregnancy, sports participation, ever breast-fed, current calcium intake, Tanner stage, maternal age at the time of childbirth and “other factors” [these other factors were not listed in the paper]
Risk of bias	Moderate to high risk of bias: 415 children were followed from birth to age 16. This dropped to 216 (dietary information missing or unreliable for 138 mothers, 47 multiple births, 14 participants had missing data for confounders) representing 52% of participants followed from birth to age 16; 70% of the 216 participants male; suggests potential selection bias (due to original selection of infants at high risk of SIDS)
Relevance	Infants at high risk of SIDS represent a selected group (more males, preterm births, teenage mothers, smoking during pregnancy)
Other comments	*Bone mineral content results not reported; Study flow figures differ between 2000 and 2010 reports (e.g. numbers of multiple births)

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Fruit

Included Studies

Study	Outcomes
1. Bunin 2005	Childhood brain tumours (medulloblastoma/PNET)
2. Bunin 1993	Childhood brain tumours (PNET)
3. Chatzi 2008	Child persistent wheeze, atopic wheeze, atopy (all at 6.5 years)
4. George 2005	“Breastfeeding”
5. Giordano 2010	Child hypospadias
6. Giordano 2008	Child hypospadias and cryptorchidism
7. Haggarty 2009	Deprivation
8. Jensen 2004	Childhood acute lymphoblastic leukemia
9. Jones 2000	Bone mass at 8 years
10. Klemmensen 2009	Pre-eclampsia
11. Knox 1972	Anencephalus
12. Kwan 2009	Childhood acute lymphoblastic leukemia
13. Lamb 2008	Islet autoimmunity
14. Laraia 2007	“Pre-pregnancy BMI”
15. Li 2009	Maternal URTI
16. Martindale 2005	Wheeze and eczema in 2nd year of child’s life
17. Mikkelsen 2006	Birthweight
18. Mitchell 2004	SGA
19. Miyake 2010	Infant wheeze and eczema up to 24 months
20. Nwaru 2010	Allergen sensitisation by 5 years
21. Petridou 2005	Acute lymphoblastic leukemia
22. Petridou 1998	Cerebral palsy at 8 years
23. Ramon 2009	Birthweight, SGA
24. Sausenthaler 2007	Allergic sensitisation, eczema at 2 years of age
25. Willers 2007	Asthma, wheeze, respiratory and atopic symptoms at 5 y
26. Willers 2008	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable ‘asthma symptoms’ in the last 12 months (measured longitudinally from 1 to 8 years age)
27. Yin 2010	Bone mass at 16 years
28. Zhang 2006	GDM

Evidence Summaries

	N	Level	References
Maternal Outcomes			
1. In a US cohort study, **women who were obese prior to their pregnancy** had a lower maternal intake of fruit during pregnancy than did overweight women ($p < 0.05$)	2394	II	Laraia 2007
2. In a Scottish cohort study, lower maternal intakes of fruit ($p < 0.001$) and fruit juice ($p < 0.05$) were associated with higher levels of **deprivation**	1277	II	Haggarty 2009
3. In a US cohort study, **fewer** women had **gestational diabetes mellitus (GDM)** as their intake of fruit fibre before or during pregnancy increased: • aRR 0.74 95% CI 0.58 to 0.95 for each 5 g/day increment of fruit fibre (about two serves of fruit a day); with benefit seen from at least 1.5 g of fruit fibre a day	13,110	II	Zhang 2006
4. In a North American retrospective cohort study, no association was seen between **upper respiratory infections** in women during the first half of pregnancy and their intake of fruit (p value for trend of 5 month risk = 0.18)	1034	III-2	Li 2006
5. In a Danish cohort study, risk of **pre-eclampsia** was not associated with maternal fruit intake during pregnancy: • aOR for 1st quintile of fruit intake 1.19 95% CI 0.99 to 1.42 and 1.15 95% CI 0.97 to 1.39 for the 5th quintile.	57,346 preg-nancies	II	Klemmensen 2009
Birth Outcomes			
6. In a Danish cohort study, **birthweight** was significantly associated with maternal intake of fruit during pregnancy: • Adjusted regression coefficient 10.4 95% CI 6.9 to 13.9 (additionally energy-adjusted); increments of about 43 g birthweight across quintiles	43,585	II	Mikkelsen 2006
7. In a Spanish cohort study • **birthweight** was not significantly associated with maternal fruit intake during pregnancy: • **SGA for weight and for length (customised < 10th percentile)** were not associated with maternal fruit intake in the first trimester ($p = 0.08$ and $p = 0.41$ for adjusted trend) and third trimester ($p = 0.44$ and $p = 0.20$) for adjusted trend across quintiles.	787 infants	II	Ramon 2009
8. In a New Zealand case-control study, maternal intake of fruit during pregnancy was not associated with **SGA term infants** (either for fruit consumption in the periconception period or the last month of pregnancy)	844 cases; 870 controls	III-3	Mitchell 2004
Congenital Anomalies			
9. In a UK case control study, apples were negatively associated with cases of **anencephalus**;	Not	III-3	Knox 1972

and canned peaches, pears, pineapple; oranges; and bananas were positively associated with cases of **anencephalus**	reporte d		
10. In a case-control study from Rome in Italy, maternal intake of fruit (including fruit juice) during pregnancy was not associated with **hypospadias** in male offspring (aOR 0.64 95% CI 0.20 to 2.07)	80 cases; 80 controls	III-3	Giordano 2010
11. In a case-control study from Sicily in Italy, maternal intake of market fruit was associated with **hypospadias (**OR 3.50 95% CI 1.03 to 11.87) **but not cryptorchidism** (OR 0.79 95% CI 0.38 to 1.64) in male offspring	90 cases; 202 controls	III-3	Giordano 2008
Breastfeeding			
12. In a US study, **lactating women** consumed significantly more fruit (5.0 v 3.1 serves per day) during pregnancy ($p < 0.016$) and the postpartum period (2.2 v 1.6 serves per day ($p < 0.05$) than non-lactating women	149	II	George 2005
Asthma, Eczema and Other Childhood Allergy Outcomes			
13. In a Japanese cohort study: • **Wheeze in children at 16-24 months** was not associated with total maternal fruit intake, apples or citrus fruits during pregnancy. • **Eczema in children at 16-24 months** was not associated with total maternal fruit intake during pregnancy except for citrus fruit where risk of eczema was decreased with increased intake: p = 0.03 for adjusted trend)	763	II	Miyake 2010
14. In a German cohort study, **allergen sensitisation or eczema in children at 2 years of age** were not generally associated with maternal intake of specific fruit in pregnancy except for: • Significantly increased allergen sensitisation with **citrus** intake 3-4 times a week or more (aOR for any sensitisation 1.82 95% CI 1.29 to 2.56); • Significantly increased allergen sensitisation with **banana** intake ≥ 4 times a week (aOR for any sensitisation 1.08 95% CI 0.75 to 1.55).	3097 children	II	Sausenthaler 2007
15. In a Finnish cohort study, fruit intake during pregnancy: • was not associated with **food allergen sensitisation in children at 5 years of age:** aOR 0.97 95% CI 0.77 to 1.23 • But was with **inhalant allergen sensitisation** aOR 1.36 95% CI 1.09 to 1.70, specifically for **citrus**: aOR 1.14 95% CI 1.05 to 1.25	931 children	II	Nwaru 2010
16. In a Scottish cohort study, a reduced risk of doctor-confirmed **asthma** in children at 5 years of age was associated with increased apple consumption during pregnancy (> 1	1212	II	Willers 2007

apple v 1 or less per week: aOR 0.47 95% CI 0.27 to 0.82 (p for trend = 0.008)			
17. In a Spanish cohort study, **persistent wheeze and atopy or atopic wheeze**) **in children at 6.5 years** were not associated with maternal fruit intake during pregnancy	482 children	II	Chatzi 2008
18. In a cohort study from the Netherlands, **wheeze, dyspnoea, steroid use or asthma symptoms** (composite of previous three) **in children longitudinally over 1 to 8 years of age** were not associated with maternal fruit intake during pregnancy (once per day or more v 1-4 times a week or fewer): • Wheeze aOR 0.89 95% CI 0.75 to 1.04 • Dyspnoea aOR 0.90 95% CI 0.74 to 1.10 • Steroid use aOR 0.89 95% CI 0.68 to 1.16 • Asthma symptoms aOR 0.91 95% CI 0.77 to 1.09	2830 children	II	Willers 2008
19. In a Scottish cohort study, maternal intake of more than one portion of fruit a day was positively associated with **eczema in children at two years of age** (aOR 1.67 95% 1.16 to 2.40) but there were no significant associations for fruit juice and **eczema**; and for fruit juice and **wheeze in children at two years of age**	1300	II	Martindale 2005
Other Childhood Outcomes			
20. In a case-control study from USA, maternal consumption of fruit during pregnancy was not associated **with childhood acute lymphoblastic leukemia;** aOR 0.71 95% CI 0.49 to 1.04	138 cases; 138 controls	III-3	Jensen 2004
21. In a case-control study for USA, maternal fruit consumption during pregnancy was associated with fewer cases of **childhood acute lymphoblastic leukemia**: • Fruit (excluding fruit juice); aOR 0.81 95% CI 0.65 to 1.00 (more than half to one serve a day) • Oranges; aOR 0.87 95% CI 0.77 to 0.99; • Cantaloupes; aOR 0.87 95% CI 0.76 to 0.98	282 cases; 641 controls	III-3	Kwan 2009
22. In a Greek case-control study, maternal fruit consumption during pregnancy (over 51 g per day) was associated with fewer cases of **childhood acute lymphoblastic leukemia**; aOR 0.72 95% CI 0.57 to 0.91 for an extra quintile of fruit under logistic regression analysis	131 cases; 131 controls	III-3	Petridou 2005
23. In a North American case control study, no significant associations between maternal consumption of specific fruits and cases of primitive **neuroectodermal brain tumours (PNET) in their children**, except for a protective effect with oranges and grapefruit (OR 0.49 95% CI 0.29 to 0.82) and canned, dried, or fozen peaches or apricots (OR 0.39 95% CI 0.22 to 0.70)	166 cases; 166 controls	III-3	Bunin 1993

24. In a North American case-control study, no significant associations between maternal consumption of fruits and cases of **medulloblastoma/primitive neuroectodermal brain tumours (PNET) in their children** were seen (p trend 0.26 for preconception consumption and p trend 0.39 for midpregnancy consumption (< 0.6 verssu > 2 serves a day)	315 cases; 315 controls	III-3	Bunin 2005
25. In a US cohort study, no significant association was seen between maternal consumption of fruit during pregnancy (mean three daily serves) and **islet immunity in children up to 15 years of age**: aHR 0.86 95% CI 0.52 to 1.42 for each SD change in consumption)	642 children	II	Lamb 2008
26. In one Australian cohort study: **Bone mineral density of children at 8 years** was not associated with maternal fruit intake during pregnancy: • Total body bone mineral density: p = 0.17 for adjusted regression of portions per week	173 children	II	Jones 2000
27. In one Greek case-control study, **cerebral palsy in children at 8 years** was not associated with maternal fruit intake during pregnancy: • Regression analysis for each unit of consumption of vegetables once per day: aOR 1.11 95% CI 0.98 to 1.27 (additionally adjusted for all food groups)	109 children	III-3	Petridou 1998a
28. In an Australian cohort study (follow-up of Jones 2000) **bone mass in 16 year-old adolescents** was not associated with maternal vegetable intake during pregnancy: • Total body bone mineral density r^2 0.333; ß +12.0 (pns) for adjusted regression of portions per week	216 children	II	Yin 2010

Evidence Tables

Reference	**Bunin 2005**
Food type	Fruit: fruit overall; fruit and fruit juice; citrus fruit and juice; fruit juice not citrus; apricots or peaches (canned, frozen or dried)
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	United States and Canada
Funding	National Cancer Institute, USA
Participants	315 cases diagnosed with medulloblastoma/PNET tumours from 0 to 5 years, between 1991 to 1997 (without a previous or recurrent cancer) 315 controls (random digit dialling, matched on area code, race and data of birth)
Baseline comparisons	See confounding below
Dietary assessment	FFQ
Timing	To reflect diet in the year before pregnancy; and the second trimester of pregnancy
Comparison	Fruit overall: < 0.6 serves/day to > 2/day; fruit and fruit juice: ≤ 1/day to > 3/day; citrus fruit and juice: ≤ 1/day to > 7/week; fruit juice (not citrus): < 1/month to ≥5/week; apricots or peaches: <1/month to ≥1/week data on portion size were not collected
Outcomes	Childhood brain tumours (medulloblastoma/primitive neuroectodermal (PNET) tumours)
Results	

Medulloblastoma/PNET

Fruit overall

		Preconception		Midpregnancy
	N	**aOR* (95% CI)**	**N**	**aOR* (95% CI)**
<0.6/day	162	1.00	138	1.00
0.6 to 1.2/day	152	1.2 (0.7 to 2.1)	141	1.3 (0.7 to 2.2)
1.2 to 2/day	151	1.1 (0.6 to 1.8)	162	1.0 (0.6 to 1.7)
>2/day	165	0.8 (0.5 to 1.4)	189	0.9 (0.5 to 1.5)
P_{trend}		0.26		0.39
Fruit and fruit juice				
≤1 serve/day	138	1.0	119	1.0
1 to 2/day	187	0.9 (0.5 to 1.5)	147	0.4 (0.4 to 1.3
2-3/day	147	0.9 (0.5 to 1.6)	160	0.6 (0.4 to 1.1)
> 3	158	0.6 (0.3 to 1.1)	204	0.6 (0.3 to 1.0)
P_{trend}		0.17		0.07
Citrus fruit and juice (svgs/wk)				
≤ 1/wk	145	1.0	141	1.0
> 1-≤3.5/wk	121	1.0 (0.6 to 1.8)	111	1.1 (0.6 to 2.0)
> 3.5-≤7wk	212	1.2 (0.7 to 1.9)	196	1.3 (0.8 to 2.0)
> 7/wk	152	0.9 (0.5 to 1.5)	182	0.8 (0.5 to 1.4)
P_{trend}		0.79		0.44
Fruit juice, not citrus				
<1/mo	261	1.0	247	1.0
≥1/mo - ≤1/wk	138	0.8 (0.6 to 1.3)	122	0.8 (0.5 to 1.3)

	2-4/wk 133 0.8 (0.5 to 1.2) 124 0.7 (0.4 to 1.2) ≥5/wk 97 **0.5 (0.3 to 0.9)** 136 **0.6 (0.3 to 0.9)** P_{trend} **0.02** **0.03** **Apricots or peaches, canned, frozen or dried** < 1/mo 415 1.0 416 1.0 1-3/mo 171 0.9 (0.6 tp 1.4) 168 0.9 (0.6 to 1.4) ≥ 1/wk 43 **0.4 (0.2 to 0.9)** 45 **0.4 (0.2 to 0.9)** P_{trend} **0.02** **0.03**
Followup	n/a
Confounding	*adjusted for income level, mother's race, age of child at interview, date of interview, gained weight because of nausea/vomiting, number cigarettes per day, total calories **adjusted for mother's race, age of child at interview, income, number of cigarettes per day, maternal weight gain (yes/no) because of pregnancy nausea/vomiting
Risk of bias	Low-moderate risk of bias: 315/558 (57%) potentially eligible cases able to be included (missing cases mostly due to lack of consent from physician or parents); control resonse rates were 67% for random digit dialling and 73% for questionnaire
Relevance	Likely to be reasonably similar
Other comments	Medulloblastomas and PNETs account for about 20% of brain tumours in children; Supplement use was also assessed in this study

Reference	**Bunin 1993**
Food type	Fruit: fruits and fruit juice; bananas; oranges and grapefruit; fresh peaches, apricots, nectarines; canned, dried or frozen peaches, apricots; cantaloupe; watermelon; mango, papaya; fruit juice
Study type	Case control study (Children's Cancer Group)
Level of evidence	III-3 (aetiology)
Setting	North America
Funding	NIH, Japan National Committee of the International Union against Cancer, Olympus Optical Company, International Agency for Research on Cancer, WHO.
Participants	166 cases (children diagnosed with primitive neuroectodermal brain tumours (PNET) before the age of six years from 1986 to 1989); 166 matched controls
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During pregnancy
Comparison	Consumption at least once per week versus less than once a week; and quartiles of consumption
Outcomes	PNET
Results	**Bananas:** OR 0.90 95% CI 0.55 to 1.48 **Oranges and grapefruit:** **OR 0.49 95% CI 0.29 to 0.82** **Fresh peaches, apricots, nectarines:** OR 0.56 95% CI 0.26 to 1.18 **Canned, dried, or frozen peaches, apricots:** **OR 0.39 95% CI 0.22 to 0.70** **Cantaloupe:** OR 1.00 95% CI 0.41 to 2.43 **Watermelon:** OR 0.89 95% CI 0.56 to 1.42 **Mango, papaya:** OR 2.25 95% CI 0.63 to 10.0 **Fruit juice:** OR 0.56 95% CI 0.26 to 1.18
Followup	n/a
Confounding	Analyses for individual food groups were not adjusted for potential confounders
Risk of bias	Moderate risk of bias: 116 cases (41%) included from 281 potentially eligible children
Relevance	Likely to be reasonably similar to diets of Australian women
Other comments	Nearly all case and control mothers took multivitamins during their pregnancies; Diet and supplemental vitamin use in child's first year of life was also recorded

Reference	**Chatzi 2008**
Food type	Fruit
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women presenting antenatal care at general practices in Menorca, a Mediterranean island in Spain (mid 1997 to mid 1998)
Funding	Instituto de Salud Carlos III red de Grupos Infancia y Media Ambiente, the Fundacio "La Caixa" , Instituto de Salud Carlos III, red de Centros de Investigacion en Epidemiologica y Salud Publica, EU, National Center for Environmental Health, USA, the GA2LEN project, Ministry of Education and Science, Spain, Oficina de Ciencia y Tecnologia, Generalitata Valenciana.
Participants	482 children of 507 women who had attended antenatal care in Menorca
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	not clear when women did FFQ and period of pregnancy it was intended to cover
Comparison	≤ 14 v > 14 serves per week
Outcomes	Persistent wheeze, atopic wheeze and atopy at 6.5 years
Results	***Persistent wheeze at 6.5 years*** Low 22 (13.58%) v high 19 (12.50%); pns (also adjusted for firstborn and lower respiratory tract infections at age 1) ***Atopic wheeze at 6.5 years*** Low 13 (6.13%) v high 7 (5.43%); pns (also adjusted for birthweight and maternal atopy) ***Atopy at 6.5 years*** Low 45 (17.65%) v high 25 (16.23%) pns (also adjusted for birthweight and maternal atopy)
Followup	6.5 years
Confounding	Analyses adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years and total energy intake at 6.5 years
Risk of bias	Results from 468/482 children (97%) able to be analysed (4 incomplete data and 8 implausible values);
Relevance	Diets in Menorca may differ from diets of Australian women, particularly urban women
Other comments	

Reference	**George 2005**
Food type	Fruit (orange and apple juice, bananas)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Texas, US
Funding	Not reported
Participants	149 Medicaid-qualified women (30% white, 24% African American, 46% Hispanic) – recruited from a larger study on postpartum weight retention Inclusion criteria: 18 years or older; non-Hispanic white, African American or Hispanic ethnicity; birth of a health term infant, fluency and literacy in English; absence of pregnancy-related abnormalities and disease conditions.
Baseline comparisons	Significant differences between lactating and non-lactating women – higher parity, BMI and lower education levels in non-lactating women.
Dietary assessment	Semiquantitative FFQ to cover pregnancy and first six months postpartum
Timing	FFQ administered at 6 weeks and 6 months postpartum
Comparison	Number of serves of fruits
Outcomes	Breastfeeding (exclusive or partial at 6 months postpartum)
Results	**Lactating women consumed significantly more fruit (5.0 v 3.1 serves per day) during pregnancy ($p < 0.016$) and the postpartum period (2.2 v 1.6 serves per day ($p < 0.05$) than non-lactating women** **There was a significant decrease overall in fruit consumption from pregnancy to the postpartum period**
Followup	6 months postpartum
Confounding	No adjustment for potential confounding
Risk of bias	Moderate-to-high risk of bias; no attempt to control for confounding despite significant baseline differences between lactating and non-lactating women.
Relevance	Possibly relevant to low-income women in Australia
Other comments	Minimal reporting of results

Reference	**Giordano 2010**
Food type	Fruit (including fruit juice)
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Rome, Italy
Funding	Not reported
Participants	80 cases of hypospadias requiring surgical treatment in children aged 0 to 24 months (mean age 57.62 weeks) 80 controls: healthy males without any congenital defect, aged 0 to 24 months (mean age 36.52 weeks); recruited between September 2005 and May 2007
Baseline comparisons	*See confounding below*
Dietary assessment	Interview on 'typical' maternal diet habits in relation to the index pregnancy and food frequencies
Timing	FFQ administered on recruitment for mothers of cases and during vaccination visits for mothers of controls
Comparison	Rare versus frequent consumption of fruit
Outcomes	Hypospadias
Results	see below
Followup	n/a
Confounding	Adjusted for mother's BMI at conception and education of the father; Gestational age, birthweight and SGA were not included among the covariates in the regression models, as they may share a common aetiology with hypospadias
Risk of bias	Moderate risk of bias: Participation rate of parents of cases was higher than that of controls (85% versus 70%); very few potential confounders used in adjusted analyses
Relevance	Likely to be reasonably relevant for Australian women
Other comments	Likely to be underpowered

Results:

Fruit (including fruit juice)

	Cases	**Controls**	**OR**	**aOR**
Rare	74 (92.5%)	72 (90.0%)	1.00	1.00
Frequent	6 (7.5%)	8 (10.0%)	0.73 95% CI 0.24 to 2.21	0.64 95% CI 0.20 to 2.07

Reference	**Giordano 2008**
Food type	Fruit: mostly market fruit
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Sicily, Italy
Funding	Sicilian Congenital Malformation Registry
Participants	90 cases: 43 cases of hypospadias and 48 cases of cryptorchidism (both in one infant) 202 controls: randomly selected controls born in the same year and the same region Births between 1998 to 2003
Baseline comparisons	Low birthweight, low maternal education, mother's history of gynaecological disease and father's history of urogenital diseases differed significantly between cases and controls *See confounding below*
Dietary assessment	Interview on maternal diet and food frequencies
Timing	FFQ
Comparison	Consumption of market fruit versus no consumption of market fruit
Outcomes	Hypospadias and cryptorchidism
Results	**Market fruit**

Market fruit	**Cases**	**Controls**	**OR**
Hypospadias			
No	3 (7.0%)	42 (20.8%)	1.00
Yes	40 (93.0%)	160 (79.2%)	**3.50 95% CI 1.03 to 11.87**
Cryptorchidism			
No	12 (25.0%)	42 (20.8%)	1.00
Yes	36 (75.0%)	160 (79.2%)	0.79 95% CI 0.38 to 1.64
Hypospadias and cryptorchidism			
No	15 (16.7%)	42 (20.8%)	1.00
Yes	75 (83.3%)	160 (79.2%)	1.31 95% CI 0.69 to 2.51

Followup	n/a
Confounding	Results for this food group were not presented as adjusted analyses *Adjusted for mother's age, parity, education, gynaecological diseases; paternal urogenital diseases, and use of pesticides; birthweight
Risk of bias	Moderate risk of bias: Participation rate of parents and data collection rate of cases was lower than that of controls (76% versus 91%); no adjusted results presented for this food group
Relevance	Likely to be reasonably relevant for Australian women, although hypospadias rates very high and unlikely that most Australian women will have such high pesticide exposure
Other comments	Ragusa region in Sicily is a region of intensive agriculture (involving high rates of pesticide and other chemical use) with high rates of hypospadias and cryptorchidism

Reference	**Haggarty 2009**
Dietary patterns	Fruit: fruit and fruit juice
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Aberdeen, Scotland
Funding	UK Food Standards Agency
Participants	1277 sequentially enrolled pregnant women attending Aberdeen Maternity Hospital for ultrasound (a further 184 women were recruited later in pregnancy). Exclusions: diabetic women, women with multiple pregnancies, women who conceived as a result of fertility treatment, or clinical data not available
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	Assessed at 19 weeks gestation
Comparison	Intake of fruit and fruit juice by deciles of deprivation
Outcomes	Deprivation (assessed using the Scottish Index of Multiple Deprivation) Low birthweight (defined as < 2500 g or lowest decile for birthweight z score adjusted for gestational age, sex and parity) Preterm birth (< 37 weeks) Admission to neonatal unit
Results	**Deprivation** **Fruit: significantly lower intake with higher levels of deprivation ($p < 0.001$)** **Fruit juice: significantly lower intake with higher levels of deprivation ($p < 0.05$)**
Followup	To neonatal period
Confounding	(Some?) analyses adjusted for energy intake
Risk of bias	Low to moderate risk of bias: low attrition, some lack of detail in reporting of outcomes
Relevance	Likely to be relevant to Australian women
Other comments	About 40-50% of the least deprived women reported taking folic acid supplements compared with about 20% for the most deprived women; Most birth outcome associations were reported by nutrient rather than food group; Not easy to deduce quantities of intake of foods (main graphs reported as change in intake by deprivation decile)

Reference	**Jensen 2004**
Food type	Fruit: peaches, apricots, oranges or grapefruit, mangoes or papayas, cantaloupe, bananas, apples/apple sauce
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study)
Funding	PHS
Participants	138 matched cases and controls: Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, parental occupation and smoking during pregnancy – no evidence of confounding was seen for these variables. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of fruit
Outcomes	Childhood acute lymphoblastic leukemia
Results	**OVERALL** aOR 0.71 95% CI 0.49 to 1.04; mean consumption of fruit 0.78 [SD 0.58] serves per day **INDIVIDUAL FRUITS** aOR 1.03 95% CI 0.86 to 1.23; mean consumption of peaches, apricots (canned, dried) 2.11 [SD 1.58] serves per day* aOR 0.98 95% CI 0.86 to 1.12; mean consumption of peaches, apricots, fresh 3.68 [SD 2.19] serves per day* aOR 0.91 95% CI 0.79 to 1.04; mean consumption of oranges or grapefruit 4.30 [SD 2.16] serves per day* aOR 0.90 95% CI 0.77 to 1.06; mean consumption of mangoes or papaya 2.20 [SD 2.03] serves per day* aOR 0.87 95% CI 0.75 to 1.02; mean consumption of cantaloupe 3.30 [SD 1.89] serves per day* aOR 0.99 95% CI 0.85 to 1.16; mean consumption of bananas 4.57 [SD 1.81] serves per day* aOR 0.99 95% CI 0.87 to 1.12; mean consumption of fruit 4.13 [SD 2.01] serves per day*
Followup	n/a
Confounding	Analyses were adjusted for variables previously shown to be significantly associated with ALL in the overall study – income, prior fetal loss, child's exposure to other children under age five, and maternal exposure to indoor insecticides during pregnancy; along with portion size and energy consumption
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 1999, 83% consented to participate; 69% of the eligible controls agreed to participate. Of the 161 matched pairs, seven pairs were excluded as the respondent was not the biological mother, 16 pairs were excluded due to questionable dietary questionnaire data, leaving 138 matched pairs (86%); some recall bias likely
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	*Some consumption levels seem high – possibly per week rather than per day?

Reference	**Jones 2000 (see also Yin 2010)**
Food type	Fruit
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Southern Tasmania, Australia
Funding	NHMRC, Tasmanian Government, Royal Hobart Hospital Acute Care Program
Participants	173 mothers; and their infants born in 1988 (part of a larger infant health study of babies at high risk of SIDS) Exclusions: multiple pregnancies
Baseline comparisons	Mothers with no tertiary education more likely to have been excluded due to missing data
Dietary assessment	FFQ
Timing	Dietary intake during third trimester of pregnancy
Comparison	Linear regression of density (portions per kJ)
Outcomes	Bone mass (bone mineral density (BMD) and bone mineral content*) in 8 year old children
Results	**BMD at 8 years;** **Total body (g/cm^2)** **r^2 3% 0.007 (p = 0.03)** adjusted r^2 24% 0.004 (p = 0.17) **Femoral neck (g/cm^2)** r^2 2% 0.009 (p = 0.09) adjusted r^2 32% 0.005 (p = 0.23) **Lumbar spine (g/cm^2)** r^2 2% 0.008 (p = 0.16) adjusted r^2 33% 0.003 (p = 0.47)
Followup	8 years
Confounding	Analyses were adjusted for method of dietary assessment, maternal education, parental unemployment, sex, weight at age 8 years, height at age 8 years, weekend sunlight exposure in winter at age 8 years, smoking during pregnancy, sports participation, ever breast-fed and current calcium intake.
Risk of bias	Moderate-high: 330 (215 males, 115 females) representing a 60% response rate from those available in 1996; 47% of the original 1988 cohort, This dropped to 173 (dietary information missing or unreliable for 115 mothers, 32 multiple births, 10 participants had missing data for confounders) representing 52% of participants from 1996 and 25% of those in the original cohort. 72% of the 173 participants were male. Gender imbalance suggests potential selection bias (due to original selection of infants at high risk of SIDS)
Relevance	Infants at high risk of SIDS represent a selected group (more males, preterm births, teenage mothers, smoking during pregnancy)
Other comments	*Bone mineral content not reported – stated to be similar to bone mineral density results

Reference	**Klemmensen 2009**

Food type	Fruit
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women participating in the Danish National Birth Cohort, e.g. became pregnant during January 1997-October 2002 and recruited through general practitioners at approximately 6-10 weeks gestation.
Funding	Danish Foundation for Hospital Research, the Copenhagen Medical Society, University of Copenhagen, March of Dimes Birth Defects Foundation, Danish National Research Foundation, Danish Medical Research Council, Danish Health Foundation, Danish Heart Foundation, Pharmacy Foundation, Egmont Foundation, Augustinus Foundation.
Participants	57346 singleton pregnancies where the mother participated in the first telephone interview and filled in the FFQ.
Dietary assessment	FFQ compared mid-pregnancy, asking about food consumption and dietary supplements in the previous month; validated in Danish women.
Baseline comparisons	*See confounding below.*
Timing	FFQ mailed to women at 25 weeks gestation, asking about intake in the previous 4 weeks.
Comparison	Quintiles of intake of fruit and fruit (minus citrus) and the risk of pre-eclampsia and severe PE.
Outcomes	Preeclampsia (all types) and severe pre-eclampsia/eclampsia/HELLP
Results	(see below)

Results:

Risk of PE and severe PE according to fruit intake**

	PE	**Severe PE**
Fruit intake	*Adjusted OR (95% CI)*	*Adjusted OR (95% CI)*
Q1	1.19 (0.99-1.42)	1.28 (0.86-1.90)
Q2	0.95 (0.79-1.14)	0.96 (0.64-1.44)
Q3	1.07 (0.89-1.28)	1.12 (0.75-1.65)
Q4	1.15 (0.97-1.36)	1.41 (1.00-2.00)
Q5 (ref)	1.0	1.0
Fruit intake (minus citrus)	*Adjusted OR (95% CI)*	*Adjusted OR (95% CI)*
Q1	1.07 (0.90-1.27)	1.02 (0.71-1.46)
Q2	1.06 (0.89-1.26)	1.06 (0.75-1.50)
Q3	0.93 (0.78-1.10)	0.82 (0.56-1.18)
Q4	1.11 (0.94-1.31)	1.09 (0.79-1.52)
Q5 (ref)	1.0	1.0

**adjusted for confounders listed below and vitamin C and E intake

Followup	In this analysis until the end of the pregnancy.
Confounding	Analyses adjusted for total energy intake using the residual method. Adjustments also made for: maternal age, pre-pregnancy BMI, smoking, height, parity, socio-economic position, ownership of residence, marital status, physical activity and for fruit analyses – dietary intake of vitamin C and E.
Risk of bias	Low risk of bias: Large population based cohort. Prospective ascertainment of outcomes.
Relevance	Only 2.6% and 9.6% of women had an intake of vitamin C and E below the recommended Danish levels, likely to be similar to Australian women.
Comments	

Reference	**Knox 1972**

Food type	Fruit: apples, canned peaches, pears, pineapple, oranges, bananas
Study type	Case control (cases matched to food consumption at population level for a particular period) – numbers not reported
Level of evidence	III-3 (aetiology)
Setting	Birmingham, UK
Funding	Not reported
Cases	Stillbirths and infant deaths due to anencephalus between 1961 and 1967
Baseline comparisons	n/a
Dietary assessment	Population surveys
Timing	Each quarter
Comparison	Monthly stillbirths and infant deaths due to anencephalus matched to quarterly consumption of main food stuffs (in previous five to nine months)
Outcomes	Anencephalus
Results	**Apples negatively associated with cases of anencephalus: r = -0.53 after a lag interval of eight months** **Canned peaches, pears, pineapple positively associated with cases of anencephalus: r = +0.60 after a lag interval of five months** **Oranges positively associated with cases of anencephalus: r = +0.56 after a lag interval of nine months** **Bananas positively associated with cases of anencephalus: r = +0.54 after a lag interval of five months**
Followup	n/a
Confounding	Analyses were not adjusted
Risk of bias	High risk of bias: links between population consumption of foods and anencephalus very distal and no control for potential confounders
Relevance	Likely to differ from a modern Australian diet
Other comments	Food consumption of total population not likely to reflect food consumption of pregnant women; and will not be able to reflect differences between diets of individual or specific groups

Reference	**Kwan 2009**
Food type	Fruit: bananas, apples, apple sauce, peaches, apricots (canned or dried), peaches, apricots (fresh), cantaloupe, mangoes or papayas, oranges or grapefruit (not including juice)
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study – phase 1 and 2 (phase 1 reported in Jensen 2004)
Funding	PHS; Paul O'Gorman Foundation for Children with Leukemia
Participants	866 individuals - 282 matched cases and controls (205 pairs and 77 trios): Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth (in phase 1 (1995-99) only due to concerns about overmatching on potential environmental exposures linked to leukemia risk) Data collected from August 1995 to November 2002
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, and smoking during pregnancy. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of fruit
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Fruit (excludes fruit juice): aOR 0.81 95% CI 0.65 to 1.00** (median daily intake 0.6 (25^{th}, 75^{th} percentile 0.3 to 1.0) **Oranges: aOR 0.87 95% CI 0.77 to 0.99** (median daily serves not reported) **Cantaloupe: aOR 0.87 95% CI 0.76 to 0.98** (median daily serves not reported)
Followup	n/a
Confounding	Analyses were adjusted for total energy intake, household income, indoor insecticide exposure during pregnancy; and proportion of foods reported as large or extra-large portion size Also adjusted for child's diet, with little effect seen on results
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 2002, 86% consented to participate; 56% of the eligible controls agreed to participate. 190 participants excluded: leukemia diagnosis was not ALL (n = 127); no dietary data (n = 4); a case or a control respondent was not the biological mother (n = 14), questionable dietary questionnaire data (n = 45), leaving 282 matched sets (86%).
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	Regular use of any dietary supplement was not associated with risk of ALL.

Reference	**Lamb 2008**
Dietary patterns	Fruits: raisins, prunes, bananas, cantaloupes, watermelon, apples, apple juice, oranges, orange juice, grapefruit, grapefruit juice, other fruit juices, strawberries, blueberries, peaches, jams and jellies, tomatoes, tomato juice and tomato sauce
Study type	Part of a longitudinal prospective birth cohort study
Level of evidence	II (aetiology)
Setting	Denver, Colorado, US (part of the Diabetes Autoimmunity Study in the Young (the DAISY))
Funding	National Institutes of Health, Diabetes Endocrine Research Center
Participants	642 newborns at increased risk for type 1 diabetes (based on HLA genotype and family history), enrolled in the study from 1993 to 2004; 27 cases defined as testing positive for islet autoantibodies at two consecutive blood draws and still positive (diabetic) at last follow-up
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	From 1997 to 2004, mothers of infants enrolled in DAISY completed FFQ soon after birth, reflecting diet in the last trimester of pregnancy (but could submit FFQ before child reached one year of age)
Comparison	Monthly servings of fruits
Outcomes	Islet autoimmunity in children (a precursor of type 1 diabetes) at 9 months, 15 months, 2 years and annually thereafter up to the age of 15
Results	**Fruits:** aHR (for one standard deviation change in reported consumption) 0.86 95% CI 0.52 to 1.42 (91.82 mean monthly servings)
Followup	Up to 15 years
Confounding	Size for gestational age, ethnicity, maternal education, household income, exposure to type 1 diabetes or GDM in utero, gender of child, maternal age at birth, total calories of maternal diet
Risk of bias	Moderate risk of bias: subset of DAISY only (later enrolments); and women were not reminded to submit FFQ, leading to possible selection bias; of the 661 FFQs returned, 5 were excluded because incomplete, and 14 for implausible dietary intakes, leaving 642 FFQs for analysis; child's diet not controlled for
Relevance	Likely to be relevant to some Australian women, although women in this study may have been at higher risk of diabetes
Other comments	

Reference	**Laraia 2007**
Dietary patterns	% of fruit serving recommendation
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	North Carolina, US (part of the Pregnancy, Infection and Nutrition (PIN) cohort)
Funding	National Institute of Child Health and Human Development; NIH
Participants	2394 predominantly lower to middle income women, recruited between 24 and 29 weeks gestation (1995-2000)
Baseline comparisons	Mean DQI-P score varied significantly by socio-demographic characteristics; there were higher mean DQI-scores for women who engaged in pre-pregnancy vigorous exercise and pre-pregnancy vitamin use
Dietary assessment	Modified block FFQ
Timing	Self-report at 26-28 weeks gestation covering previous 3 months (corresponding to the 2nd trimester)
Comparison	BMI categories
Outcomes	Pregravid weight status (not an outcome but there is an association)
Results	**Average % of fruit serving recommendation [SD]** Underweight 118.9 [10.2.3] Normal weight 107.9 [104.7] Overweight 111.9 [106.3] Obese 103.8 [95.9] **P value for trend** **<0.05** *adjusted for age, ethnicity, level of education, poverty, number of children, smoking during pregnancy only
Followup	26 to 31 weeks gestation
Confounding	Age, ethnicity, level of education, poverty, number of children, smoking during pregnancy, regular vitamin use prior to pregnancy, vigorous leisure activity 3 months prior to pregnancy
Risk of bias	Low risk of bias: better to have used normal weight women as the reference rather than underweight women DQI-P tertile comparison
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Li 2009**
Dietary patterns	Fruit
Study type	Retrospective cohort study
Level of evidence	III-2 (aetiology)
Setting	North America
Funding	National Institute of Dental and Craniofacial Research
Participants	1034 mothers who had participated in a case-control study of children with congenital craniofacial malformations
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Fruit and vegetable intake in the six months before pregnancy
Comparison	Quartiles of fruit consumption (never to four or more times a day) Serves per day, median (range) 1st quartile 1.68 (0 to 1.30) 2nd quartile 1.80 (1.31 to 2.32) 3rd quartile 3.02 (2.33 to 3.86) 4th quartile 5.09 (3.87 to 22.51)
Outcomes	Upper respiratory infection in women during the first half of pregnancy (not including asthma or allergy) [44 URTI episodes without a known start date were excluded from hazards analysis]
Results	**URTI (five month risk)** HR (95% CI) / aHR (95% CI) / p-value for trend Q1 1.00 / 1.00 Q2 1.02 (0.77 to 1.36) / 1.03 (0.77 to 1.38) Q3 0.82 (0.61 to 1.11) / 0.83 (0.61 to 1.13) Q4 0.80 (0.60 to 1.09) / 0.85 (0.60 to 1.20) / 0.18 **URTI (three month risk)** HR (95% CI) / aHR (95% CI) / p-value for trend Q1 1.00 / 1.00 Q2 0.93 (0.64 to 1.37) / 0.97 (0.66 to 1.44) Q3 0.71 (0.47 to 1.07) / 0.76 (0.49 to 1.17) Q4 0.77 (0.52 to 1.15) / 0.84 (0.53 to 1.33) / 0.27
Followup	5 months since last menstrual period
Confounding	Adjusted for age, race, energy intake, vegetable intake
Risk of bias	Low-moderate risk of bias: 1034/1163 (88.9%) women included in analysis – 88 with an incomplete FFQ, 41 with implausible energy intakes); women were interviewed at an average of 8 months after birth, but up to 36 months, so some risk of recall bias; some evidence of increased fruit and vegetable consumption once pregnancy was known (misclassification bias)
Relevance	Likely to be relevant to Australian women
Other comments	URTI during pregnancy may be associated with preterm birth and congenital abnormalities

Reference	**Martindale 2005**

Dietary patterns	Fruit
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Aberdeen, Scotland
Funding	Asthma UK
Participants	1300 singleton children born to women recruited between October 1997 and April 1999 (at a median gestational age of 12 weeks)
Baseline comparisons	Study population were slightly older, more likely to be primiparous, less likely to be current smokers, and more likely to be from nonmanual social classes than the corresponding general population
Dietary assessment	FFQ at 34 weeks gestation (also enquired about use of vitamin and mineral supplements during the previous 3 months
Timing	Timing of FFQ at 34 weeks was chosen to "avoid the dietary disruption of early pregnancy and to provide an indication of the habitual dietary intake in middle and late pregnancy"
Comparison	Not clearly stated
Outcomes	Symptoms of wheeze, doctor-diagnosed eczema
Results	**Eczema in 2nd year of life**: Fruit: more than one portion a day was positively associated with eczema in the 2nd year of life: **OR 1.72 95% CI 1.22 to 2.43** **aOR 1.67 95% CI 1.16 to 2.40** Fruit juice: no significant association **Wheeze in 2nd year of life**: Fruit juices: no significant association
Followup	6, 12 and 24 months
Confounding	Analyses adjusted for gender, maternal age, paternal social class, maternal smoking, other children in the home and antibiotic use
Risk of bias	Low-moderate risk of bias: 1924 singletons were born to the 2000 women recruited (34 twins, 42 miscarriage, stillbirth or neonatal death), 1751 (87.6%) of women completed the FFQ, with complete data sets from all three questionnaires available at 24 months for 1300 children (67.6%)
Relevance	Reasonably relevant, probably lower fruit and vegetable intake than in Australia
Other comments	Most results reported as intake of vitamin C and E, not by number of serves of fruit and vegetables

Reference	**Mikkelsen 2006**
Food type	Fruit and vegetables
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women participating in the Danish National Birth Cohort, e.g. became pregnant during January 1997-October 2002 and recruited through general practitioners.
Funding	Danish National Research Foundation, March of Dimes Birth Defects Foundation, European Union, Novonordic Foundation, ISMF, the Health Foundation, Danish National Medical Research Foundation, Danish Heart Association.
Participants	43,585 pregnant women with singleton pregnancies for whom complete dietary info and birth records were available.
Dietary assessment	FFQ compared mid-pregnancy, validated in Danish men and women. Timeframe for food consumption unclear (i.e. consumption in last week, month etc).
Baseline comparisons	*See Confounding below.*
Timing	FFQ completed at 25 weeks gestational age.
Comparison	Birth weights in quintiles of intake of fruit Subgroup analyses performed on a group of thin women (BMI <20).
Outcomes	Birthweight and z-scores (in singletons only)
Results	Mean birthweight and Z-scores were consistently lowest in the lowest quintile for fruit. In the multivariate regression models, dietary exposures were associated with birthweight (i.e. as you move up in quintile, there were small but consistent increases in birthweight). The strongest associations were for quintiles of fruit intake. **<u>Regression coefficients of the dietary exposures and birth weight</u>** **Crude (95% CI) / Adjusted (95% CI)** **Fruit: 11.5 (8.0-15.0)**** / 10.7 (7.3-14.2)****** **Fruit – Energy adjusted: 11.1 (7.5-14.6)**** / 10.4 (6.9-13.9)****** *p<0.05 **p<0.01 *** P<0.001 **** P<0.0001 Among lean women, substantially stronger associations were seen between the dietary exposures and outcomes. For fruit intake, increments of 43g of birthweight were seen across quintiles, in the lean group the bw increment was 58g.
Followup	Until child was 18 months old (but birthweight only data reported here).
Confounding	Analyses adjusted for dietary supplements, maternal smoking, maternal height, pre-pregnant weight, paternal height, parity and maternal age. Separate analyses also adjusted for energy intake.
Risk of bias	Low risk of bias. Large population based cohort. Prospective ascertainment of outcomes.
Relevance	There may be differences between the diets of Danish and Australian women.

Reference	**Mitchell 2004**
Dietary patterns	Fruit (including bananas, apples, pears, citrus fruits, stone fruits, berries, melon and avocados)
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Waitemata Health or Auckland Healthcare regions, New Zealand
Funding	Health Research Council of New Zealand, Foundation for the Newborn, Child Health Research Foundation
Participants	Mothers of 1138 children born between October 1995 and November 1997 (844 cases (SGA) and 870 controls (born appropriate for GA)); only term infants (> 37 weeks); Exclusions: preterm births (< 37 weeks), multiple births and those with congenital anomalies
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered after birth (to cover the periconception period and the last month of pregnancy)
Comparison	0-0.75 v > 0.75-1.25 v > 1.25-2.0 v > 2.0-3.0 v > 3 serves of fruit per day
Outcomes	SGA (≤ 10th centile for GA and gender)
Results	see below

SGA (Fruit consumption at time of conception)

	SGA	AGA	aOR (95% CI)	p value for trend
0-0.75	132/542 (24.4%)	104/600 (17.3%)	**1.49 (1.00 to 2.24)**	
>0.75-1.25	107/542 (19.7%)	144/600 (24.0%)	0.99 (0.67 to 1.47)	
>1.25-2.0	115/542 (21.2%)	117/600 (19.5%)	1.44 (0.96 to 2.17)	
>2.0-3.0	84/542 (15.5%)	96/600 (16.0%)	1.23 (0.80 to 1.90)	
>3	104/542 (19.2%)	139/600 (23.2%)	1	0.12

SGA (fruit consumption in last month of pregnancy)

	SGA	AGA	aOR (95% CI)	p value for trend
0-0.75	95/540 (17.6%)	62/598 (10.3%)	1.53 (0.99 to 2.35)	
>0.75-1.25	82/540 (15.2%)	83/598 (13.9%)	1.08 (0.72 to 1.63)	
>1.25-2.0	111/540 (20.5%)	136/598 (22.7%)	0.93 (0.61 to 1.40)	
>2.0-3.0	89/540 (16.5%)	123/598 (20.6%)	1.04 (0.69 to 1.57)	
>3	163/540 (30.2%)	194/598 (32.4%)	1	0.19

Followup	NA
Confounding	Adjusted for socio-economic status, ethnicity, maternal height, maternal weight before pregnancy, maternal hypertension and maternal smoking; but folate supplementation was not controlled for (periconception folate was significantly associated with reduced SGA risk).
Risk of bias	Low-moderate risk of bias: Of the 2182 eligible infants, parents of 1714 (78.6%) completed the FFQ; 1138 (67%) of women completed the FFQ; missing items in completed FFQ treated as woman not consuming any fruit
Relevance	Likely to be relevant to Australian women
Other comments	Only term infants included

Reference	**Miyake 2010**
Food type	Fruit
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women recruited antenatally from hospital obstetric clinics in Neyagawa city and surrounding municipalities, Osaka Prefecture, Japan, from November 2001 to March 2003.
Funding	Ministry of Education, Culture, Sports, Science and Technology; and Health and Labour Sciences Research Grants, Research on Allergic Disease and Immunology, Ministry of Health, Labour and Welfare, Japan.
Participants	763 mother-infant pairs follow up until 24 months postpartum.
Dietary assessment	Self-administered FFQ undertaken during pregnancy. FFQ validated amongst 92 women against weighed dietary records.
Baseline comparisons	*See confounding below* *Vitamin C supplements or multivitamin supplements were only used by 5.6% and 4.2% of participants at least once a week, therefore contribution of micronutrients from supplements was not considered in the analysis.*
Timing	FFQ undertaken at baseline recruitment relating to diet in the month prior, but varying time of diet assessment as women were recruited from between 5 and 39 weeks gestation.
Comparison	Quartile of dietary intakes and infant wheeze and eczema at 16-24 months.
Outcomes	Infantile wheeze and eczema, based on symptoms defined according to ISAAC criteria.
Results	Prevalence of wheeze and asthma at 16-24 months was 22.1% and 18.6% respectively. 75% of infants were breastfed for at least 6 months. No significant association between maternal intake of total fruit intake, apples, or citrus fruits - and wheeze. Similar for eczema with the exception of citrus fruit: **<u>Eczema</u>** (table below)
Followup	Until 24 months postpartum
Confounding	Quartile median adjusted for energy intake. Analyses adjusted for maternal age, gestation at baseline, residence, income, maternal and parental education, maternal and parental history of asthma, atopic eczema and allergic rhinitis, changes in maternal diet in the previous month, season, maternal smoking, baby's older siblings, baby's birthweight, household smoking in the same room as infant, breastfeeding duration, and age of infant at third survey.
Risk of bias	Moderate risk of bias (selection, ascertainment and attrition): - low participation rate, women participating had higher education levels - close to 25% losses to follow up at 24 month assessment - wheeze was assessed at varying ages between 16 and 24 months.
Relevance	High prevalence of wheeze and eczema (22.1% and 18.6%) in this population aged 16-24 months - ?higher than that reported in Australia. Wheeze in infancy is not a reliable predictor of asthma in older ages.
Other comments	

Eczema (Results)

	Crude OR (95% CI)	*Adjusted OR (95% CI)*
Citrus fruit		
Q1	1.00	1.00
Q2	**0.62 (0.38-1.02)**	0.61 (0.36-1.02)
Q3	**0.56 (0.33-0.92)**	**0.57 (0.33-0.98)**
Q4	**0.49 (0.29-0.82)**	**0.53 (0.30-0.93)**
P	**0.006**	**0.03**

Reference	**Nwaru 2010**
Food type	Fruit (apple, peach, plum, brune, orange, lemon, grapefruit, mandarin, canned fruits, melons, pineapple, grapes, banana, kiwi-fruit, avocado, dried fruits, berries) and fruit and berry juices
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Tampere, Finland
Funding	Academy of Finland, Finnish Pediatric Research Foundation, the Juho Vainio Foundation, the Yrjo Jahnsson Foundation, Turku, Oulu and Tampere University Hospitals, JDRF, Novo Nordisk Foundation, EU Biomed 2 Program
Participants	931 mother-infant pairs (children with human leukocyte antigen-conferred susceptibility to type 1 diabetes) participating in the Finnish type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study between September 1996 and October 1997
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ given to women after birth, for return at the three month visit (FFQ intended to cover maternal diet during pregnancy and lactation)
Comparison	Amount of fruit intake
Outcomes	Allergic sensitisation in offspring by 5 years: food allergens (egg, cow's milk, fish, wheat); inhalant allergens (house dust mite, cat, timothy grass, birch)
Results	**Total fruits** ***Food allergens***: OR 0.97 95% CI 0.78 to 1.20; aOR 0.97 95% CI 0.77 to 1.23 ***Inhalant allergens***: **OR 1.32 95% CI 1.08 to 1.62**; **aOR 1.36 95% CI 1.09 to 1.70** - **Malaceous fruits** ***Food allergens***: OR 0.95 95% CI 0.83 to 1.09; aOR 0.97 95% CI 0.84 to 1.13 ***Inhalant allergens***: OR 0.98 95% CI 0.87 to 1.11; aOR 1.00 95% CI 0.87 to 1.14 - **Citrus fruits** ***Food allergens***: OR 0.98 95% CI 0.91 to 1.06; aOR 1.00 95% CI 0.92 to 1.09 ***Inhalant allergens***: **OR 1.11 95% CI 1.03 to 1.11**; **aOR 1.14 95% CI 1.05 to 1.25** **Berries** ***Food allergens***: OR 1.05 95% CI 0.92 to 1.19; aOR 1.07 95% CI 0.92 to 1.25 ***Inhalant allergens***: OR 1.06 95% CI 0.94 to 1.19; aOR 1.12 95% CI 0.88 to 1.28 **Juices** ***Food allergens***: OR 0.98 95% CI 0.91 to 1.07; aOR 0.99 95% CI 0.90 to 1.08 ***Inhalant allergens***: OR 0.99 95% CI 0.92 to 1.06; aOR 0.98 95% CI 0.90 to 1.06
Followup	To 5 years
Confounding	Adjusted for energy intake, place of birth, season of birth, sex of the child, number of siblings, gestational age at birth, parental asthma, parental allergic rhinitis, maternal age at birth, maternal smoking during pregnancy, maternal education

Risk of bias	Low risk of bias: data available for 931/1175 (79.2%) children recruited – 108 did not participate in survey, a further 49 did not have IgE measurements, a further 87 had no FFQ or an incomplete FFQ
Relevance	Likely to be relevant to Australian women
Other comments	28% of women took vitamin D supplements, 73% took iron supplements; HLA genotype not likely to have any impact on the development of allergic diseases.

Reference	**Petridou 2005**
Food type	Fruit
Study type	Case-control study
Level of evidence	III-3
Setting	Greece
Funding	The Childhood Hematology-Oncology Group: Athens University Medical School, Aristotle University of Thessaloniki, University Hospital of Heraklion
Participants	Cases: 131 children with acute lymphoblastic leukemia, aged 12 to 59 months, gender and age matched to Controls: 131 children hospitalised for minor conditions between 1999 and 2003
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During index pregnancy
Comparison	Quintiles of fruit intake – median Q1; 51 g/day: median Q5 228 g/day
Outcomes	Acute lymphoblastic leukemia (ALL)
Results	(see below)

	Median g/day	**Cases**	**Controls**	**p for trend**
Q1	51	28	24	
Q2	84	34	18	
Q3	122	24	30	
Q4	157	23	29	
Q5	228	22	30	**0.04**

Logistic regression: one quintile more of fruit: aOR 0.72 95% CI 0.57 to 0.91

Followup	NA
Confounding	Total energy intake (but not mutually among food groups); matching variables; maternal age at birth; birthweight; maternal smoking during pregnancy; maternal years of schooling, maternal occupation
Risk of bias	Moderate: moderate risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy some time previously; Cases: 171 children with ALL were identified; 21 had missing data, consent was not given in 9 cases and 10 were unable to be matched, leaving 131 (77%) of cases available
Relevance	Diets of Greek women may differ from current diets of Australian women
Other comments	

Reference	**Petridou 1998**
Food type	Fruit: watermelon, melon, mandarins, oranges, apples, peaches, pears, grapes, apricots, cherries, strawberries, bananas, figs, pineapple, grapefruit, fresh fruit juice, dried fruits compote (0.5).
Study type	Case-control study
Level of evidence	III-3
Setting	Greater Athens area, Greece
Funding	Greek Ministry of Health and Welfare, and Foundation for Research in Childhood 'S. Doxiadis'
Participants	Cases: 109 children with cerebral palsy (CP), born between 1984 and 1988 (estimated to be two-thirds of the children with CP born during this period) Controls (1): 155 neighbouring children of similar sex and age (± 12 months) Controls (2): 99 healthy siblings of similar sex and age (± 12 months) of the first neurological patient seen by the attending physician after a visit by the CP patient
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During pregnancy
Comparison	≤ 2 versus 3-4 versus > 4 serves of fruit per day; regression analysis: risk of cerebral palsy with change in consumption by one unit (= consumption of fruit once per day)
Outcomes	Cerebral palsy
Results	≤ 2 serves of fruit per day: 12/91 (13.2%) cases v 21/246 (8.5%) controls 3-4 serves of fruit per day: 16/91 (17.6%) cases v 64/246 (26.0%) controls > 4 serves of fruit per day: 63/91 (69.2%) cases v 161/246 (65.5%) Regression analysis for each unit of consumption of fruit once per day: **aOR 1.15 95% CI 1.03 to 1.29** aOR 1.11 95% CI 0.98 to 1.27 (additionally adjusted for all food groups)
Followup	8 years
Confounding	Age and sex of child, maternal age at birth, maternal age at menarche, maternal chronic disease, previous spontaneous abortions, persistent vomiting during index pregnancy, multiple pregnancy, number of obstetric visits; timing of membrane rupture in index birth, use of general anaesthesia in the index birth, mode of birth, abnormal placenta, infant head circumference at birth, congenital malformation, place of index birth, use of supplementary iron during index pregnancy, physical exercise during index pregnancy, painless childbirth classes. The following were not included in the model: - Smoking or consumption of coffee or alcohol during pregnancy (stated to be "unrelated to CP and had no confounding influence"); - Gestational age, birthweight and maternal weight gain (stated to be "strong predictors of CP, but were not included in the model, since they are probably intermediate stages in a possible link between diet and CP (mediators) rather than genuine confounders"
Risk of bias	Moderate-high: High risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy 8 years previously; Cases: 109 children with CP were identified; for 6 children either collaboration with their guardian or a diagnosis of CP was not confirmed; and reliable maternal dietary intakes were not available for 12 women, leaving 91 cases available for analysis. Controls: 278 mother-child pairs were approached; 16 refused to participate; matching controls were not available in 8 instances, and reliable maternal dietary intakes were not available for 8 women, leaving 246 controls available for analysis.
Relevance	Diets of Greek women in 1998 may differ from current diets of Australian women
Other comments	

Reference	**Ramon 2009**

Food type	Fruit
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women attending hospital for fetal anomaly screening in Valencia, Spain between February 2004 and June 2005 (INMA-Valencia cohort)
Funding	Instituto de Salud Carlos III, Ministerio Sanidad y Consumo, Ministerio Educacion y Ciencia.
Participants	787 infants born between May 2004 and February 2006 to women at least 16 y, singleton pregnancy, antenatal visit at 10-13 weeks, no assisted conception, no chronic hypertension Mean age 30 y (range 16 to 43); 55% primiparous, 67% completed secondary education; 62% employed; 24% overweight or obese Daily intake fruit 293.0 [216.1] g/day Daily intake veg. 213.3 [121.0] g/day
Dietary assessment	FFQ to assess diet in the first trimester (administered at 10-13 weeks) and then diet since the first assessment (administered at 28-32 weeks). FFQ validated for Spanish population.
Baseline comparisons	*See Confounding below*
Timing	FFQ administered at 10-13 wks and then again at 28-32 weeks gestation.
Comparison	Quintiles of fruit intake in first and third trimester and birthweight, birth length, SGA (weight), SGA (length). First trimester fruit intake was 85.0 g/day (range 3.4 to 137.9) for quintile 1 and 622.4 g/day (range 421.5 to 2456.9) in quintile 5
Outcomes	Birthweight standardised for gender and GA; SGA (weight or length) defined as below 10th percentile based on growth reference charts standardised for both gender and GA for the Spanish population
Results	Summary: Fruit intake not associated with risk of SGA or birthweight. **<u>Adjusted OR of the dietary exposures and SGA for weight and length (crude OR not reported)</u>** (see table below) Fruit consumption had no clear pattern with birthweight.
Followup	Until birth.
Confounding	Analyses adjusted for energy intake, maternal age, maternal pre-pregnancy weight, maternal height, paternal height, weight gain, parity, smoking during pregnancy, caffeine intake, working, country of origin, infant sex, socioeconomic status.
Risk of bias	Low/moderate risk of selection bias due to 54% participation rate. (Women who worked were more likely to participate).
Relevance	More generalisable to Australian women than other studies of fruit. Undertaken in a 'horticultural area' where fruit and vegetables are widely available.

	SGA for weight (95% CI)	**SGA for length (95% CI)**
Fruit – first trimester		
Q1	1.0 (0.5-2.2)	2.6 (0.8-8.1)
Q2	0.5 (0.2-1.2)	1.2 (0.3-4.4)
Q3	1.2 (0.6-2.5)	2.0 (0.6-6.6)
Q4	0.5 (0.2-1.1)	1.9 (0.5-6.5)
Q5	1	1
P	0.08	0.41
Fruit – 3rd trimester		
Q1	0.5 (0.2-1.1)	0.3 (0.1-1.0)
Q2	0.8 (0.4-1.8)	0.9 (0.3-2.5)
Q3	0.8 (0.4-1.7)	0.5 (0.2-1.5)
Q4	0.7 (0.3-1.5)	0.8 (0.3-2.4)
Q5	1	1
p	0.44	0.20

Other comments

Reference	**Sausenthaler 2007**
Food groups	Fruits
Study type	Prospective cohort study: from the LISA birth cohort
Level of evidence	II (aetiology)
Setting	4 German cities (Munich, Leipzig, Wesel, Bad Honnef)
Funding	Federal Ministry for Education, Science, Research and Technology, Germany
Participants	2641 children at 2 years of age
Baseline comparisons	*See Confounding below*
Dietary assessment	FFQ
Timing	Maternal diet during the last 4 weeks of pregnancy (obtained shortly after birth, median 3 days)
Variable	Low intake group as reference group compared with high intake group: • Citrus high intake = 3-4 times/week • Apples high intake = ≥ 4 times/week • Exotic fruit high intake = 3-4 times/week • Bananas high intake = ≥ 4 times/week • Strawberries high intake = 1-2 times/week • Fruit juice high intake = 3-4 times/week
Outcomes	Allergic sensitisation, eczema at 2 yrs
Results	(see table below)
Length of followup	2 years
Confounding	Crude and adjusted results reported (adjusted for study area, sex, maternal age, maternal smoking, level of parental education, exclusive breastfeeding ≥ 4 months, parental history of atopic diseases, season of birth and all dietary variables
Risk of bias	Two year data available for 2641/3097 children (85%): 433 lost to follow-up, 9 excluded due to chronic disease, 14 missing maternal FFQ
Relevance	Likely to be reasonably similar to dietary intakes of Australian women in Australia
Other comments	

Results:

Fruit	***Doctor-diagnosed eczema***	***Any allergen sensitisation***	***Food allergens***	***Inhalant allergens***
	Adjusted OR (95% CI)			
Citrus	1.03 (0.78, 1.35)	**1.82 (1.29, 2.56)**	**1.73 (1.18, 2.53)**	**1.72 (1.02, 2.92)**
Apples	0.92 (0.72, 1.21)	1.07 (0.77, 1.49)	1.01 (0.70, 1.46)	0.87 (0.52, 1.47)
Exotic fruit	0.85 (0.66, 1.11)	0.77 (0.55, 1.07)	0.84 (0.58, 1.23)	0.64 (0.39, 1.07)
Bananas	1.03 (0.77, 1.38)	**1.08 (0.75, 1.55)**	**1.14 (0.75, 1.72)**	1.10 (0.63, 1.93)
Strawberries	1.02 (0.77, 1.35)	1.06 (0.75, 1.51)	0.90 (0.60, 1.34)	1.46 (0.87, 2.47)
Fruit juice	1.18 (0.90, 1.54)	1.03 (0.73, 1.46)	1.12 (0.76, 1.65)	0.78 (0.47, 1.30)

Reference	**Willers 2007**
Food type	Fruit (apples, bananas, oranges, pears, peaches, nectarines, kiwi fruit, all other fruit (grapes, strawberries, melon, plums, etc))
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Antenatal clinics at Aberdeen Maternity Hospital, Aberdeen, Scotland
Funding	Asthma UK, GA^{2}LEN European Network of Excellence on Global Allergy and Asthma
Participants	1212 children (singleton births) whose mothers were recruited between October 1997 and April 1999 at a median gestational age of 12 weeks
Baseline comparisons	Women were representative of the local obstetric population *See confounding below*
Dietary assessment	FFQ
Timing	FFQ mailed at 32 weeks gestation to cover dietary intake over the previous 2-3 months
Comparison	Tertiles: 0-1 v 1-4 v > 4 apples per week
Outcomes	Wheeze, asthma at 5 years
Results	**Total fruit, citrus/kiwi fruit or fruit juice** – no consistent linear associations with respiratory and atopic outcomes in 5 year old children (exact numbers not reported in the paper).

Maternal apple consumption

	N	T1 (0-1/week) n = 398	T2 (1-4/week) n = 427	T3 (> 4/week) n = 384	p trend
Wheeze in last 12 months	1003				
OR (95% CI)		**1**	**1.09 (0.69 to 1.67)**	**0.61 (0.37 to 1.10)**	0.066
aOR (95% CI)		1	1.08 (0.68 to 1.71)	0.67 (0.40 to 1.13)	0.156
Wheeze without cold in last 12 months	1003				
OR (95% CI)		1	1.32 (0.72 to 2.43)	0.64 (0.31 to 1.35)	0.286
aOR (95% CI)		1	1.27 (0.67 to 2.43)	0.70 (0.32 to 1.51)	0.411
Ever wheezed	999				
OR (95% CI)		**1**	**0.86 (0.60 to 1.23)**	**0.59 (0.40 to 0.88)**	**0.009**
aOR (95% CI)		**1**	**0.85 (0.58 to 1.24)**	**0.63 (0.42 to 0.95)**	**0.029**
Asthma and wheeze in last 12 months	998				
OR (95% CI)		1	1.02 (0.60 to 1.73)	0.55 (0.29 to 1.03)	0.072
aOR (95% CI)		1	1.03 (0.59 to 1.80)	0.60 (0.31 to 1.16)	0.148
Doctor confirmed asthma	998				
OR (95% CI)		**1**	**0.87 (0.56 to 1.36)**	**0.46 (0.27 to 0.78)**	**0.005**
aOR (95% CI)		**1**	**0.83 (0.52 to 1.32)**	**0.47 (0.27 to 0.82)**	**0.008**
Ever had asthma					
OR (95% CI)		**1**	**0.90 (0.58 to 1.38)**	**0.52 (0.31 to 0.86)**	**0.013**
aOR (95% CI)		**1**	**0.86 (0.54 to 1.36)**	**0.54 (0.32 to 0.92)**	**0.026**

Followup	5 years
Confounding	Adjusted for maternal age, paternal social class, maternal education, maternal smoking during pregnancy, smoking in the child's home at 5 years,

	energy intake, maternal asthma, maternal atopy, child's birthweight, child's sex, presence of older siblings, and breastfeeding
Risk of bias	Low risk of bias: Initial study population of 1924 children dropped to 1212 participants with complete data (63.0%) (questionnaire, at least one of the outcome time points).
Relevance	Likely to be reasonably relevant to Australian women
Other comments	Inclusion of maternal supplement use during pregnancy did not materially change the results

Reference	**Willers 2008**
Food type	Fruit
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Netherlands
Funding	Netherlands Organization for Health Research and Development, Netherlands Organization for Scientific Research; Netherlands Asthma Fund; Netherlands Ministry of Spatial Planning, Housing, and the Environment; Netherlands Ministry of Health, Welfare and Sport, GlaxoSmithKline
Participants	2,832 children (part of the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered at antenatal recruitment (mean gestational ages not reported) to cover dietary intake over the previous month
Comparison	Daily (once per day or more) v 1-4 times a week or fewer
Outcomes	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable 'asthma symptoms' in the last 12 months (measured longitudinally from 1 to 8 years age)
Results	**<u>Wheeze from 1 to 8 years age (n = 2828)</u>** **OR 0.82 95% CI 0.70 to 0.96** aOR 0.89 95% CI 0.75 to 1.04 **<u>Dyspnoea from 1 to 8 years age (n = 2828)</u>** OR 0.87 95% CI 0.72 to 1.06 aOR 0.90 95% CI 0.74 to 1.10 **<u>Steroid use from 1 to 8 years age (n = 2828)</u>** OR 0.84 95% CI 0.65 to 1.09 aOR 0.89 95% CI 0.68 to 1.16 **<u>Asthma symptoms (composite of previous three outcomes) from 1 to 8 years age (n = 2828)</u>** OR 0.87 95% CI 0.73 to 1.04 aOR 0.91 95% CI 0.77 to 1.09
Followup	8 years
Confounding	The child's dietary data on fruit, vegetables, fish, eggs, full cream milk, butter and peanut butter consumption at 2 years of age were used to check for potential confounding by the child's diet. Results were adjusted for by sex, maternal education, parental allergy, maternal smoking during pregnancy, smoking in the home at 8 years of age, breastfeeding, presence of older siblings, birthweight, maternal overweight 1 year after pregnancy, maternal supplement use during pregnancy, region and study arm (intervention or natural history arm).
Risk of bias	Moderate risk of bias: Initial study population of 4,146 mothers dropped to 2,832 participants with complete data (68.3%) (pregnancy questionnaire, at least one of the outcome time points and all confounders). Participants with complete data were more likely to have a high education level, to have daily dairy and fruit intake during pregnancy and to have breastfed and less likely to have maternal asthma or maternal atopy, smoked during pregnancy, be from a south western region compared with participants who did not have complete data.
Relevance	Dietary intakes likely to be different from Australian e.g. low fish consumption in study participants
Other comments	Not clear when women assessed their diet during pregnancy; 83% of pregnant women used supplements (50% used folic acid/iron)

Reference	**Yin 2010 (see also Jones 2000)**
Food type	Fruit
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Southern Tasmania, Australia
Funding	NHMRC, Tasmanian Government, Royal Hobart Hospital Acute Care Program
Participants	216 adolescents born in 1988 (part of a larger infant health study of babies at high risk of SIDS) Exclusions: multiple pregnancies
Baseline comparisons	Children with unemployed fathers more likely to have been excluded due to missing data
Dietary assessment	FFQ
Timing	Dietary intake during third trimester of pregnancy
Comparison	Linear regression of density (portions per kJ)
Outcomes	Bone mass (bone mineral density (BMD) and bone mineral content*) in 16 year old adolescents
Results	**BMD at 16 years;** **Total body (g/cm^2)** r^2 -0.006; ß +11.7 (pns) adjusted r^2 0.333; ß +12.0 (pns) **Femoral neck (g/cm^2)** r^2 -0.005 ß -2.1 (pns) adjusted r^2 0.347; ß -0.6 (pns) **Lumbar spine (g/cm^2)** r^2 -0.003; ß +5.3 (pns) adjusted r^2 0.201; ß +9.5 (pns)
Followup	16 years
Confounding	Analyses were adjusted for sex, weight at age 16 years, sunlight exposure in winter at age 16 years, smoking during pregnancy, sports participation, ever breast-fed, current calcium intake, Tanner stage, maternal age at the time of childbirth and “other factors” [these other factors were not listed in the paper]
Risk of bias	Moderate-high: 415 children were followed from birth to age 16. This dropped to 216 (dietary information missing or unreliable for 138 mothers, 47 multiple births, 14 participants had missing data for confounders) representing 52% of participants followed from birth to age 16. 70% of the 216 participants were male. Gender imbalance suggests potential selection bias (due to original selection of infants at high risk of SIDS)
Relevance	Infants at high risk of SIDS represent a selected group (more males, preterm births, teenage mothers, smoking during pregnancy)
Other comments	*Bone mineral content results not reported; Study flow figures differ between 2000 and 2010 reports (e.g. numbers of multiple births)

Reference	**Zhang 2006**
Food type	Fruit fibre
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	USA (Nurses' Health Study II)
Funding	NIH
Participants	13,110 women who reported having at least one singleton pregnancy lasting ≥ 6 months, between 1992 and 1998 Exclusions: implausible total energy intake (< 500 kcal/day or > 3,500 kcal/day); multiple gestation; history of diabetes, cancer, cardiovascular disease, or GDM on the 1989 or 1991 questionnaire.
Baseline comparisons	*See results*
Dietary assessment	FFQ
Timing	FFQs administered in 1991 or 1995 to reflect dietary intake over the past year
Comparison	Quintiles of fruit fibre intake (lowest quintile = reference)
Outcomes	Self-reported diagnosis of gestational diabetes mellitus (GDM)
Results	

GDM (adjusted for age, parity, BMI)

	g/day	Cases/person-years	RR (95% CI)	p-value for trend
Q1	(< 1.5)	200/19,749	1.00	
Q2	(1.6 to 2.3)	137/19,360	**0.73 (0.59 to 0.91)**	
Q3	(2.4 to 3.4)	160/20,343	**0.81 (0.66 to 0.99)**	
Q4	(3.5 to 4.8)	150/20,922	**0.75 (0.61 to 0.93)**	
Q5	(> 4.8)	111/19,258	**0.57 (0.45 to 0.72)**	**< 0.001**
Each 5 g/day increment			**0.63 (0.51 to 0.78)**	

GDM (adjusted for age, parity, BMI, race/ethnicity, smoking, family history of diabetes, alcohol intake, physical activity, total energy, protein intake, saturated fat, and polyunsaturated, monounsaturated and trans fatty acids)

	g/day	Cases/person-years	RR (95% CI)	p-value for trend
Q1	(< 1.5)	200/19,749	1.00	
Q2	(1.6 to 2.3)	137/19,360	**0.74 (0.60 to 0.93)**	
Q3	(2.4 to 3.4)	160/20,343	0.85 (0.69 to 1.05)	
Q4	(3.5 to 4.8)	150/20,922	0.81 (0.65 to 1.02)	
Q5	(> 4.8)	111/19,258	**0.66 (0.51 to 0.86)**	**0.01**
Each 5 g/day increment			**0.73 (0.58 to 0.93)**	

GDM (adjusted for age, parity, BMI, physical activity, race/ethnicity, smoking, family history of diabetes, alcohol intake, total energy, protein intake, saturated fat, and polyunsaturated, monounsaturated and trans fatty acids, and cereal and vegetable fibre)

	g/day	Cases/person-years	RR (95% CI)	p-value for trend
Q1	(< 1.5)	200/19,749	1.00	
Q2	(1.6 to 2.3)	137/19,360	**0.75 (0.60 to 0.94)**	
Q3	(2.4 to 3.4)	160/20,243	0.86 (0.69 to 1.07)	
Q4	(3.5 to 4.8)	150/20,922	0.82 (0.65 to 1.04)	
Q5	(> 4.8)	111/19,258	**0.67 (0.51 to 1.87)**	**0.02**
Each 5 g/day increment			**0.74 (0.58 to 0.95)**	

Followup	Variable
Confounding	*See results*
Risk of bias	Low risk of bias: actual attrition figures for this substudy not reported but overall attrition reported to be 10%
Relevance	Likely to be relevant to Australian women
Other comments	Dietary assessment periods will differ in relation to timing of pregnancies – need to assume a woman's diet will remain similar over time and whether or she is pregnant or planning to become pregnant. This assumption may not apply to alcohol intake, for example

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Fruit & Vegetables

Included Studies

Study	Outcomes
1. Fitzsimon 2007	Child asthma at 3 years
2. Haugen 2008	Preterm birth
3. Hoppu 2005	Atopy in infant at 12 months
4. Kwan 2009	Childhood acute lymphoblastic leukemia
5. Li 2009	Maternal URTI
6. Maconochie 2007	Miscarriage
7. Mikkelsen 2008	Preterm birth
8. Mikkelsen 2006	Birthweight and z-scores
9. Spector 2005	Infant acute leukemia (AML) and childhood acute lymphoblastic leukemia (ALL)
10. Stuebe 2009	GWG

Evidence Summaries

	N	Level	References
Maternal Outcomes			
1. In a North American retrospective cohort study, women with a higher fruit and vegetable intake (quartiles from never to > 4 a day) during the first half of pregnancy had fewer **upper respiratory infections** in the first three months (aHR 0.61 95% 0.39 to 0.97; p = 0.03) but this did not remain significant at five months (aHR 0.74 95% CI 0.53 to 1.05; p = 0.11)	1034	III-2	Li 2006
2. In a US cohort study, maternal fruit and vegetable consumption during pregnancy was not associated with **excessive gestational weight gain**: aOR 1.03 95% CI 0.98 to 1.07	1338	II	Stuebe 2009
3. In a case-control study from the UK, maternal daily consumption of fruit and vegetables during pregnancy was associated with reduced odds of **miscarriage**: aOR 0.49 95% CI 0.36 to 0.66)	603 cases; 6116 controls	III-3	Maconochie 2007
Birth Outcomes			
4. In a cohort study from Norway, no significant difference was seen in the rate of **preterm birth** between ≤ 5 and > 5 daily serves of fruit and vegetables during pregnancy: aOR 0.99 95% CI 0.86 to 1.15	1138	II	Haugen 2008
5. In a Danish cohort study, no significant difference was seen in the rate of **preterm birth** between ≤ 5 and > 5 daily serves of fruit and vegetables during pregnancy: aOR 1.01 95% CI 0.90 to 1.14	35,350	II	Mikkelsen 2008
6. In a Danish cohort study, there were small but significant increases in **birthweight** as maternal intake of fruit, vegetables and juice increased: adjusted regression coefficient 7.7 95% CI 4.0 to 11.3, p < 0.001; Mean birthweight and z-scores were consistently lowest in the lowest quintile for all fruit and vegetable groupings	43,585	II	Mikkelsen 2006
Childhood – Asthma, Eczema and Other Allergy Outcomes			
7. In a Finnish cohort study, there was a significantly lower risk of **atopy** (specifically atopic eczema) in infants at 12 months of age whose mothers' breastmilk was rich in vitamin C (from a diet high in fresh fruits, berries and vegetables during lactation): OR 0.30 95% CI 0.09 to 0.94	34	II	Hoppu 2005
8. In a cohort study from Ireland, there was a significantly lower risk of **asthma in infants at 3 years of age** whose mothers had a high fruit and vegetable intake during pregnancy; aOR 0.42 95% CI 0.18 to 0.99	631 infants	III-2	Fitzsimon 2007
Other Childhood Outcomes			

9. In a US case-control study, maternal consumption of 1-2 serves of fruit and vegetables per day during pregnancy was significantly associated with reduced odds of **childhood acute lymphoblastic leukemia**: aOR 0.64 95% CI 0.48 to 0.85	282 cases; 641 controls	III-3	Kwan 2009
10. In a US case-control study, maternal consumption of fruit and vegetables was not significantly associated with reduced odds of **childhood acute lymphoblastic leukemia** (p = 0.09) or **infant acute leukemia** (p = 0.18)	240 cases; 255 controls	III-3	Spector 2005

Evidence Tables

Reference	Fitzsimon 2007
Dietary patterns	Fruit (apples, pears, oranges, satsumas and mandarins, grapefruit, bananas, grapes, melon, peaches, plums and apricots, strawberries, raspberries, kiwifruit); and vegetables (carrots, spinach, broccoli, spring greensand kale, brussel sprouts, cabbage, peas, green beans and runner beans, marrow and courgettes, cauliflower, parsnips, turnips, leeks, onions, garlic, mushrooms, sweet peppers, bean sprouts, green salad and lettuce, cucumber, celery, watercress, tomatoes, sweetcorn, beetroot, coleslaw, avocado)
Study type	Retrospective cohort study
Level of evidence	III-2 (aetiology)
Setting	Galway, Ireland (part of the Life-ways Cross-Generation Cohort Study)
Funding	Not stated
Participants	631 children turning 3 in summer of 2005
Baseline comparisons	*See Results*
Dietary assessment	FFQ
Timing	FFQ "during pregnancy"
Comparison	Quartiles of fruit and vegetable consumption during pregnancy (Q1 = 2.3 (range 0-3.4); Q2 = 4.1 (3.4-5.0); Q3 = 6.0 (5.0-7.1); Q4 = 8.9 (> 7.1) serves per day)
Outcomes	Asthma at 3 years (GP-diagnosed)

Results

Summary: women with a high fruit and vegetable and fish oil intake and relatively sparing fat intake were less likely to have children who developed asthma

Asthma (OR (95% CI))

	n/N	Q1	Q2	Q3	Q4	P for trend (Q4 v Q1+2+3)
aOR (univariate)	66/631	1	0.99 (0.51 to 1.9)	0.80 (0.39 to 1.6)	0.49 (0.22 to 1.1)	0.07
aOR (+fat)	66/631	1	0.99 (0.50 to 2.0)	0.71 (0.33 to 1.5)	**0.43 (0.19 to 0.97)**	**0.04**
aOR (+oily fish fat)	64/618	1	1.1 (0.55 to 2.3)	0.81 (0.37 to 1.7)	0.53 (0.23 to 1.2)	0.09
aOR (+birthweight, sex, smoke expos, fat, oily fish)	63/610	1	1.1 (0.53 to 2.3)	0.93 (0.42 to 2.0)	0.49 (0.20 to 1.2)	0.09
aOR (+birthweight, sex, smoke expos, fat, oily fish, GMS*)	62/605	1	1.1 (0.53 to 2.3)	0.89 (0.39 to 2.0)	0.50 (0.21 to 1.2)	0.07
aOR (+birthweight, sex, smoke expos, fat, GMS*)	64/618	1	1.0 (0.49 to 2.1)	0.76 (0.34 to 1.7)	**0.42 (0.18 to 0.99)**	**0.04**

**GMS = medical card for low-income women*

Followup	n/a
Confounding	*See Results*
Risk of bias	Moderate risk of bias: Of the 1001 singleton babies born, 631 had GP follow-up data at 3 years (63.1%)
Relevance	Likely to be relevant to Australian women

Other comments	Fat consisted of pure fat products (added or spreadable fats including butter, margarine and other spreads, salad dressings and mayonnaise) but fat from foods with partial or hidden fats was not considered here Oily fish = fresh or canned e.g. mackerel, kippers, tuna, salmon, sardines, herring

Reference	**Haugen 2008**
Dietary patterns	Fruit and vegetables as part of Mediterranean-type diet
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Norway (part of the Norwegian Mother and Child Cohort Study (MoBa))
Funding	Norwegian Ministry of Health, NIH/NINDS, Norwegian Research Council/FUGE, EU FP& consortium, Metabolic Programming (EARNEST).
Participants	40,817 pregnancies of women recruited for MoBa from February 2002 to February 2005 of whom 26,563 (65%) met the following criteria: women had to be non-smoking, BMI between 19 and 32, aged between 21 and 38 years when giving birth, with a singleton birth. Exclusions: more than 3 spontaneous abortions, energy intake less than 4,200 kJ and more than 16,700 kJ.
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ at 17-24 weeks gestation
Comparison	Fish ≥ 5 times per day v < 5 times a day
Outcomes	Preterm birth (after week 21 and before week 37); late preterm birth (week 35-36) and early preterm birth (< 35 weeks)
Results	***Preterm birth (< 37 weeks): (n = 25,966; 1174 cases)*** OR 0.95 95% CI 0.82 to 1.10 aOR 0.99 95% CI 0.86 to 1.15 ***Early preterm birth (< 35 weeks): (n = 25,256; 474 cases)*** OR 0.88 95% CI 0.70 to 1.11 aOR 0.91 95% CI 0.72 to 1.16 ***Late preterm birth (35-36 weeks): (n = 25,492; 710 cases)*** OR 1.0 95% CI 0.83 to 1.20 aOR 1.05 95% CI 0.87 to 1.26
Followup	To birth
Confounding	Analyses were adjusted for remaining Mediterranean diet criteria, mother's BMI and height, educational level, parity and marital status
Risk of bias	Moderate: some dietary intakes were different between groups and were not controlled for
Relevance	Moderate: low red meat consumption not typical for many Australian women
Other comments	Preterm birth rates were lower than expected, likely due to exclusion of smokers

Reference	**Hoppu 2005**
Dietary patterns	Fruit and vegetables (specifically recommended an abundant intake of fresh fruits, berries and vegetables during breastfeeding)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Turku, Finland
Funding	Academy of Finland, Juho Vainio Foundation, Finnish Cultural Foundation
Participants	34 mothers with atopic disease (allergic rhinitis, atopic dermatitis, asthma) recruited at the end of gestation; Infants must have been exclusively or predominantly breastfed at one month
Baseline comparisons	Similar between atopic and nonatopic infants except for positive maternal skin prick test and maternal food hypersensitivity (both adjusted for in results – see below
Dietary assessment	Questionnaire and personal interview; 4 day food records
Timing	Questionnaire at 35-35 weeks gestation; 4 day food records checked at one month postnatal visit with mothers given individual dietary counselling
Comparison	Vitamin C concentrations in breastmilk
Outcomes	Breastmilk composition at one month, atopy (specifically atopic eczema) in infant at 12 months of age
Results	Atopic infants (n = 7) consumed breastmilk with a lower concentration of vitamin C (5.2 mg/day 95% CI 4.6 to 5.7) compared with nonatopic infants (n= 27); 6.2 mg/day 95% CI 5.8 to 6.6; p = 0.02; Lower risk of atopy in infant with increased vitamin C in breastmilk: **OR 0.30 95% CI 0.09 to 0.94** This effect did not change when adjusted for maternal skin prick test and food hypersensitivity As a separate ANCOVA analysis indicated that only dietary intake of vitamin C increased the vitamin C concentration in breastmilk (p = 0.048), with supplements having no apparent effect (p = 0.78), the significantly reduced risk of infant atopy at 12 months is attributed to dietary intake of vitamin C
Followup	Infant to 12 months of age
Confounding	*See results*
Risk of bias	Moderate risk of bias: Of the 65 mothers recruited, 34 (52.3%) fulfilled the breastfeeding inclusion criteria with a food record and a breastmilk sample available
Relevance	Relevant to Australian women (although a wide range of berries less available in Australia)
Other comments	Apart from recommendation to take vitamin D during wintertime, women were not encouraged or discouraged to take vitamin or mineral supplementation, but were asked to report any use of these

Reference	**Kwan 2009**
Food type	Fruit and vegetables:
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study – phase 1 and 2 (phase 1 reported in Jensen 2004)
Funding	PHS; Paul O'Gorman Foundation for Children with Leukemia
Participants	866 individuals - 282 matched cases and controls (205 pairs and 77 trios): Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth (in phase 1 (1995-99) only due to concerns about overmatching on potential environmental exposures linked to leukemia risk) Data collected from August 1995 to November 2002
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, and smoking during pregnancy. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of fruit and vegetables
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Fruit and vegetables: aOR 0.64 95% CI 0.48 to 0.85**: median consumption 1.3 (25th 75th percentiles 0.8, 2.0) serves per day **Fibre from fruits/vegetables (g): aOR 0.52 95% CI 0.31 to 0.88:** median consumption 6.18 (25th 75th percentiles 0.97, 8.76) g per day
Followup	n/a
Confounding	Analyses were adjusted for total energy intake, household income, indoor insecticide exposure during pregnancy; and proportion of foods reported as large or extra-large portion size Also adjusted for child's diet, with little effect seen on results
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 2002, 86% consented to participate; 56% of the eligible controls agreed to participate. 190 participants excluded: leukemia diagnosis was not ALL (n = 127); no dietary data (n = 4); a case or a control respondent was not the biological mother (n = 14), questionable dietary questionnaire data (n = 45), leaving 282 matched sets (86%).
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	Regular use of any dietary supplement was not associated with risk of ALL; Authors did not comment on the positive association with fibre cereals

Reference	**Li 2009**
Dietary patterns	Fruit and vegetables
Study type	Retrospective cohort study
Level of evidence	III-2 (aetiology)
Setting	North America
Funding	National Institute of Dental and Craniofacial Research
Participants	1034 mothers who had participated in a case-control study of children with congenital craniofacial malformations
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Fruit and vegetable intake in the six months before pregnancy
Comparison	Quartiles of fruit and vegetable consumption (never to four or more times a day) Serves per day, median (range) 1st quartile 1.91 (0.07 to 2.89) 2nd quartile 3.71 (2.90 to 4.62) 3rd quartile 5.59 (4.63 to 6.70) 4th quartile 8.54 (6.71 to 29.04)
Outcomes	Upper respiratory infection in women during the first half of pregnancy (not including asthma or allergy) [44 URTI episodes without a known start date were excluded from hazards analysis]
Results	**URTI (5 month risk)** HR (95% CI) / aHR (95% CI) / p-value for trend Q1 1.00 / 1.00 Q2 0.91 (0.68 to 1.21) / 0.90 (0.67 to 1.21) Q3 0.88 (0.66 to 1.18) / 0.89 (0.65 to 1.21) Q4 **0.73 (0.54 to 0.99)** / 0.74 (0.53 to 1.05) / 0.11 **URTI (three month risk)** HR (95% CI) / aHR (95% CI) / p-value for trend Q1 1.00 / 1.00 Q2 0.77 (0.52 to 1.12) / 0.76 (0.52 to 1.13) Q3 0.68 (0.46 to 1.01) / 0.68 (0.44 to 1.03) Q4 **0.62 (0.41 to 0.93)** / **0.61 (0.39 to 0.97)** / **0.03**
Followup	5 months since last menstrual period
Confounding	Adjusted for age, race, energy intake
Risk of bias	Low-moderate risk of bias: 1034/1163 (88.9%) women included in analysis – 88 with an incomplete FFQ, 41 with implausible energy intakes); women were interviewed at an average of 8 months after birth, but up to 36 months, so some risk of recall bias; some evidence of increased fruit and vegetable consumption once pregnancy was known (misclassification bias)
Relevance	Likely to be relevant to Australian women
Other comments	URTI during pregnancy may be associated with preterm birth and congenital abnormalities

URTI (5 month risk)

	HR (95% CI)	aHR (95% CI)	p-value for trend
Q1	1.00	1.00	
Q2	0.91 (0.68 to 1.21)	0.90 (0.67 to 1.21)	
Q3	0.88 (0.66 to 1.18)	0.89 (0.65 to 1.21)	
Q4	**0.73 (0.54 to 0.99)**	0.74 (0.53 to 1.05)	0.11

URTI (three month risk)

	HR (95% CI)	aHR (95% CI)	p-value for trend
Q1	1.00	1.00	
Q2	0.77 (0.52 to 1.12)	0.76 (0.52 to 1.13)	
Q3	0.68 (0.46 to 1.01)	0.68 (0.44 to 1.03)	
Q4	**0.62 (0.41 to 0.93)**	**0.61 (0.39 to 0.97)**	**0.03**

Reference	**Maconochie 2007**
Food groups	Fresh fruit and vegetables
Study type	Case-control study (postal survey sampled from the electoral roll – National Women's Health Study)
Level of evidence	III-3 (aetiology)
Setting	UK general population
Funding	National Lottery Community Fund, Miscarriage Association
Participants	Cases: 603 women aged 18 to 55 years whose most recent pregnancy had ended in first trimester miscarriage (< 13 weeks gestation); Controls: 6116 women aged 18 to 55 years whose most recent pregnancy had progressed beyond 12 weeks
Baseline Comparisons	BMI < 18.5 was significantly associated with odds of miscarriage *Also see Confounding below*
Dietary Assessment	Questionnaire
Timing	Diet in the three months prior to conception and the first 12 weeks of pregnancy
Comparison	Daily or consumption most days
Outcomes	First trimester miscarriage
Results	**Fresh fruit and vegetables daily** | | Cases | Controls | aOR (95% CI) | aOR further adjusted for nausea | No | 69 (12%) | 402 (7%) | 1.00 | 1.00 Yes | 517 (88%) | 5563 (93%) | **0.54 (0.41 to 0.72)** | **0.49 (0.36 to 0.66)**
Length of followup	n/a
Confounding	Adjusted for year of conception, maternal age, previous miscarriage and previous live birth; and further adjusted for nausea in the first 12 weeks of pregnancy
Risk of bias	Low risk of bias: 88% of eligible women responding to stage 1 agreed to participate in the second stage of the study; and 71% responded to the stage 2 questionnaire. 1071/7790 records (7508 women) were excluded (mostly due to index pregnancy being conceived prior to 1980), leaving 6719 records (86%) available for analysis
Relevance	Likely to be relevant to Australian women
Other comments	Women who suffered from nausea in the first 12 weeks of pregnancy were almost 70% less likely to miscarry

Results (Fresh fruit and vegetables daily):

	Cases	Controls	aOR (95% CI)	aOR further adjusted for nausea
No	69 (12%)	402 (7%)	1.00	1.00
Yes	517 (88%)	5563 (93%)	**0.54 (0.41 to 0.72)**	**0.49 (0.36 to 0.66)**

Reference	**Mikkelsen 2006**
Food type	Fruit and vegetables
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women participating in the Danish National Birth Cohort e.g. became pregnant during January 1997-October 2002 and recruited through general practitioners.
Funding	Danish National Research Foundation, March of Dimes Birth Defects Foundation, European Union, Novonordic Foundation, ISMF, the Health Foundation, Danish National Medical Research Foundation, Danish Heart Association.
Participants	43,585 pregnant women with singleton pregnancies for whom complete dietary info and birth records were available.
Baseline comparisons	*See Confounding below.*
Dietary assessment	FFQ compared mid-pregnancy, validated in Danish men and women. Timeframe for food consumption unclear (i.e. consumption in last week, month etc).
Timing	FFQ completed at 25 weeks gestational age.
Comparison	Birthweights in quintiles of intake of fruit and vegetable exposures, Subgroup analyses performed on a group of thin women (BMI < 20).
Outcomes	Birthweight and z-scores (in singletons only)
Results	***Mean birthweight and Z-scores were consistently lowest in the lowest quintile for all fruit and vegetable groupings.*** In the multivariate regression models, dietary exposures were associated with birth weight (i.e. as you move up in quintile, there were small but consistent increases in birthweight). **Regression coefficients of the dietary exposures and birthweight** **Crude (95% CI) / Adjusted (95% CI)** **F & V: 9.7 (6.2-13.2)**** / 8.8 (5.3-12)****** **F & V – Energy adjusted: 9.2 (5.6-16.8)**** / 8.4 (4.8-12.0)****** **F & V & J: 5.9 (2.4-9.5)*** / 8.1 (4.6-11.5)****** **F & V & J – Energy adjusted: 5.1 (1.4-8.8)** / 7.7 (4.0-11.3)****** *p<0.05 **p<0.01 *** P<0.001 **** P<0.0001 Among lean women, substantially stronger associations were seen between the dietary exposures and outcomes.
Followup	Until child was 18 months old (but birthweight only data reported here).
Confounding	Analyses adjusted for dietary supplements, maternal smoking, maternal height, pre-pregnant weight, paternal height, parity and maternal age. Separate analyses also adjusted for energy intake.
Risk of bias	Low risk of bias: Large population based cohort. Prospective ascertainment of outcomes.
Relevance	There may be differences between the diets of Danish and Australian women.
Other comments	

Reference	**Mikkelsen 2008**

Dietary patterns	Mediterranean diet (consumption of fish twice a week or more, intake of olive or canola oil, **high consumption of fruits and vegetables (5 a day or more),** meat (other than poultry or fish) at most twice a week, and at most 2 cups of coffee a day)
Study type	Prospective cohort study
Level of evidence	II
Setting	Denmark (part of the Danish National Birth Cohort (DBNC))
Funding	March of Dimes Birth Defects Foundation, Danish National Research Foundation, Danish Medical Research Foundation, Danish Health Foundation, Danish Heart Foundation, EU FP7 consortium (EARNEST), Pharmacy Foundation, Egmont Foundation, Augustinus Foundation.
Participants	35,530 pregnant women recruited from 1996 to 2002 Exclusions: women who smoked, women aged < 21 and > 38 years, BMI < 19 and > 32, a history of more than 3 abortions, twin pregnancies, chronic hypertension, women with a calculated energy intake < 4,200 kJ and > 16,700 kJ
Baseline comparisons	BMIs were significantly lower in the MD and none groups.
Dietary assessment	FFQ
Timing	FFQ mailed to all DBNC participants in 25th week of gestation
Comparison	≥ 5 fruit and vegetables/day v < 5 per day
Outcomes	Preterm birth
Results	**Preterm birth < 37 weeks** OR 1.01 95% CI 0.90 to 1.14 aOR 1.02 95% CI 0.90 to 1.14 **Early preterm birth < 35 weeks** OR 1.03 95% CI 0.85 to 1.24 aOR 1.02 95% CI 0.84 to 1.24 **Late preterm birth 35-36 weeks** OR 1.01 95% CI 0.87 to 1.16 aOR 1.01 95% CI 0.88 to 1.17
Followup	To birth
Confounding	Adjusted for parity, BMI, maternal height, socioeconomic status and cohabitant status
Risk of bias	Low risk of bias; GA based mostly on ultrasound; 0.36% missing data (127/35657)
Relevance	Relevance limited by exclusion of smokers and obese women
Other comments	

Reference	**Spector 2005**
Dietary patterns	Fruit and vegetables: VF+ = DNAt2 inhibitor containing foods (fresh and canned fruit and vegetables, canned or dried legumes, soy (either soy sauce or other soy), coffee, black tea, green tea, cocoa, red wine, and other caffeinated beverages)
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	USA (126 Children's Oncology Groups)
Funding	National Cancer Institute, USA and Children's Cancer Research Fund
Participants	240 cases diagnosed during 1996 and 2002 (149 ALL and 91 AML); 255 controls selected by random digit dialling
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Administered to reflect entirety of pregnancy
Comparison	VF+ (quartiles)
Outcomes	Infant acute leukemia (AML) and childhood acute lymphoblastic leukemia (ALL)
Results	(see table below)
Followup	NA
Confounding	Adjusted for mother's age at birth of index child, income and education, and infant's race and sex
Risk of bias	Low-moderate risk of bias: Of the 348 potential cases identified, 240 (69%) maternal interviews were successfully completed (missing data included maternal refusal (17%), physician refusal (7%), and inability to locate mother (7%); 67% response rate for controls
Relevance	Likely to be relevant to Australian women
Other comments	Fresh fruits (r = 0.66), fresh vegetables (r = 0.69) and canned vegetables (r = 0.60) were the components most highly with the VF+ index

Results:

	Controls	**ALL cases**	**ALL aOR (95% CI)**	**AML cases**	**AML aOR (95% CI)**	**Total aOR (95% CI)**
Q1	53	46	1	25	1	1
Q2	67	37	0.7 (0.4 to 1.2)	20	0.6 (0.3 to 1.2)	**0.6 (0.4 to 1.0)**
Q3	68	28	**0.5 (0.3 to 0.9)**	27	0.8 (0.4 to 1.6)	**0.6 (0.4 to 1.0)**
Q4	27	37	0.7 (0.4 to 1.2)	19	0.6 (0.3 to 1.2)	**0.6 (0.4 to 1.0)**
P trend			0.09		0.18	**0.05**

Reference	Stuebe 2009
Dietary patterns	Fruit and vegetables
Study type	Prospective cohort study (Project Viva)
Level of evidence	II (aetiology)
Setting	8 urban and suburban obstetric offices of a multispecialty group practice in eastern Massachusetts, USA
Funding	US NIH, Harvard Medical School, Harvard Pilgrim Health Care Foundation
Participants	1338 women giving birth to a live singleton infant, < 22 weeks gestation at study entry; 379 (27%) were overweight (BMI ≥ 26); 703 (51%) experienced excessive weight gain Exclusions: not fluent in English
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Administered in first and second trimesters of pregnancy
Comparison	Fruits and vegetables (serves per day)
Outcomes	Excessive gestational weight gain (IOM 1990)
Results	**Excessive gestational weight gain: fruits and vegetables** (see table below)
Followup	To birth
Confounding	Adjusted for pre-pregnancy BMI, maternal age, race/ethnicity, smoking status, gestational age at birth, nausea in first trimester in pregnancy
Risk of bias	Low risk of bias: Of 2083 eligible women, 1388 (67%) of women had data available for analysis (31 had missing information on pre-pregnancy BMI and gestational weight gain; 226 had missing covariate information and 438 had missing data on either first or second-trimester diet and mid-pregnancy physical activity); included women were less likely to be African-American or Hispanic, to be younger, multiparous and obese
Relevance	Likely to be relevant to Australian women
Other comments	

Excessive gestational weight gain: fruits and vegetables

	Serves per day, median		
	Inadequate/adequate GWG	**Excessive GWG**	**aOR (95% CI)**
Fruit & Veg	5.84 [SD2.60]	5.90 [SD2.71]	1.03 (0.98 to 1.07)

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Maconochie N, Doyle P, Prior S and Simmons R. "Risk factors for first trimester miscarriage--results from a UK-population-based case-control study." ***BJOG*** 2007: **114**(2): 170-86.

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Stuebe AM, Oken E and Gillman MW. "Associations of diet and physical activity during pregnancy with risk for excessive gestational weight gain." ***Am J Obstet Gynecol*** 2009: **201**(1): 58 e1-8.

Legumes

Included Studies

Study	Outcomes
1. Bunin 2005	Childhood brain tumours (medulloblastoma/PNET)
2. Chatzi 2008	Child persistent wheeze, atopic wheeze, atopy (all at 6.5 years)
3. Giordano 2008	Hypospadias and cryptorchidism
4. Jensen 2004	Childhood acute lymphoblastic leukemia
5. Knox 1972	Anencephalus
6. Kwan 2009	Childhood acute lymphoblastic leukemia
7. Maconochie 2007	Miscarriage
8. North 2000	Hypospadias
9. Pierik 2004	Hypospadias and cryptorchidism

Evidence Statements

	N	Level	References
Maternal Outcomes			
1. In a case-control study from the UK, maternal intake of soy products daily during pregnancy was not associated with first trimester **miscarriage**: aOR 1.06 95% CI 0.66 to 1.70	603 cases; 6116 controls	III-3	Maconochie 2007
Congenital Anomalies			
2. In a Sicilian case-control study, no significant associations were seen between cases of **hypospadias and/or cryptorchidism** and maternal intake of legumes	90 cases; 202 controls	III-3	Giordano 2008
3. In a cohort study from the UK, there were no significant associations between cases of **hypospadias** and maternal intake of soy milk or soya meat during pregnancy, but there was a significant positive association with maternal intake of pulses during pregnancy: OR 7.56 95% CI 2.25 to 25.42 (more than 4 times a week compared with never)	7928 boys (51 cases of hypo-spadias)	II	North 2000
4. In a case-control study from the Netherlands, cases of **hypospadias and cryptorchidism** were not significantly associated with maternal intake of soy protein ≥ 20 g/day compared with none (OR 1.0 95% 0.5 to 2.2 and 0.6 95% CI 0.3 to 1.3 respectively)	78 & 56 cases; 313 controls	III-3	Pierik 2004
5. In a case-control study from the UK, cases of **anencephalus** were positively associated with maternal intake of dried pulses (r = +0.65 after a lag interval of nine months)	Not reported	III-3	Knox 1972
Childhood Outcomes			
6. In a Spanish cohort study, **persistent wheeze in children at 6.5 years of age** were associated with more than 1 serve of legumes per week in mothers during pregnancy ($p < 0.05$) but this was not the case for atopic wheeze or atopy	482 children	II	Chatzi 2008
7. In a US case-control study, • a decreased risk of **childhood acute lymphoblastic leukemia** was associated with higher maternal intakes during pregnancy of beans (aOR 0.83 95% CI 0.70 to 0.99) and string beans or peas (aOR 0.84 95% CI 0.71 to 1.00); • no significant associations were seen for tofu or peanut or peanut butter consumption	138 cases; 138 controls	III-3	Jensen 2004
8. In a case-control study from the US (with some overlap with Jensen 2004), a decreased risk of **childhood acute lymphoblastic leukemia** was associated with higher maternal intakes during pregnancy of beans (aOR 0.86 95% CI 0.74 to 0.99) and legumes overall (aOR 0.75 95% CI 0.59 to 0.95)	866 (282 matched cases and controls)	III-3	Kwan 2009
9. In a North American case-control study, no significant association was seen between	315	III-3	Bunin 2005

	childhood brain tumours (medulloblastoma/PNET) and maternal consumption of either peas or lima beans (aOR 0.7 95% CI 0.4 to 1.2) or peanut butter (aOR 0.9 95% CI 0.6 to 1.5)	cases; 315 controls		

Evidence Tables

<table>
<tr><td>Reference</td><td>Bunin 2005</td></tr>
<tr><td>Food type</td><td>Legumes: peas or lima beans; peanut butter</td></tr>
<tr><td>Study type</td><td>Case-control study</td></tr>
<tr><td>Level of evidence</td><td>III-3 (aetiology)</td></tr>
<tr><td>Setting</td><td>United States and Canada</td></tr>
<tr><td>Funding</td><td>National Cancer Institute, USA</td></tr>
<tr><td>Participants</td><td>315 cases diagnosed with medulloblastoma/PNET tumours from 0 to 5 years, between 1991 to 1997 (without a previous or recurrent cancer)
315 controls (random digit dialling, matched on area code, race and data of birth)</td></tr>
<tr><td>Baseline comparisons</td><td>See confounding below</td></tr>
<tr><td>Dietary assessment</td><td>FFQ</td></tr>
<tr><td>Timing</td><td>To reflect diet in the year before pregnancy; and the second trimester of pregnancy</td></tr>
<tr><td>Comparison</td><td>Peas or lima beans: <1 serve/month to > 2/week;
Peanut butter: <1 serve/month to ≥ 2/week
data on portion size were not collected</td></tr>
<tr><td>Outcomes</td><td>Childhood brain tumours (medulloblastoma/primitive neuroectodermal (PNET) tumours)</td></tr>
<tr><td>Results</td><td>
<u>Medulloblastoma/PNET</u>
<u>Peas or lima beans</u>
<table>
<tr><td></td><td colspan="2">Periconception</td><td colspan="2">Midpregnancy</td></tr>
<tr><td></td><td>N</td><td>aOR* (95% CI)</td><td>N</td><td>aOR* (95% CI)</td></tr>
<tr><td><1 serve/month</td><td>182</td><td>1.00</td><td>184</td><td>1.00</td></tr>
<tr><td>1-3/month</td><td>148</td><td>0.7 (0.4 to 1.1)</td><td>143</td><td>0.7 (0.4 to 1.2)</td></tr>
<tr><td>1/week</td><td>175</td><td>0.6 (0.4 to 1.0)</td><td>174</td><td>0.6 (0.4 to 1.1)</td></tr>
<tr><td>>2/week</td><td>125</td><td>0.6 (0.3 to 1.1)</td><td>129</td><td>0.7 (0.4 to 1.2)</td></tr>
<tr><td>P_{trend}</td><td></td><td>0.21</td><td></td><td>0.38</td></tr>
</table>
<u>Peanut butter</u>
<table>
<tr><td><1 serve/month</td><td>202</td><td>1.00</td><td>185</td><td>1.0</td></tr>
<tr><td>1-3/month</td><td>126</td><td>1.1 (0.6 to 1.8)</td><td>106</td><td>1.2 (0.7 to 2.1)</td></tr>
<tr><td>1/week</td><td>126</td><td>1.3 (0.8 to 2.2)</td><td>136</td><td>1.0 (0.6 to 1.5)</td></tr>
<tr><td>≥2/week</td><td>173</td><td>1.0 (0.6 to 1.7)</td><td>201</td><td>0.9 (0.6 to 1.5)</td></tr>
<tr><td>P_{trend}</td><td></td><td>0.96</td><td></td><td>0.65</td></tr>
</table>
</td></tr>
<tr><td>Followup</td><td>n/a</td></tr>
<tr><td>Confounding</td><td>*adjusted for income level, mother's race, age of child at interview, date of interview, gained weight because of nausea/vomiting, number cigarettes per day, total calories
**adjusted for mother's race, age of child at interview, income, number of cigarettes per day, maternal weight gain (yes/no) because of pregnancy nausea/vomiting</td></tr>
<tr><td>Risk of bias</td><td>Low-moderate risk of bias: 315/558 (57%) potentially eligible cases able to be included (missing cases mostly due to lack of consent from physician or parents); control resonse rates were 67% for random digit dialling and 73% for questionnaire</td></tr>
<tr><td>Relevance</td><td>Likely to be reasonably similar</td></tr>
<tr><td>Other comments</td><td>Medulloblastomas and PNETs account for about 20% of brain tumours in children;
Supplement use was also assessed in this study</td></tr>
</table>

Reference	**Chatzi 2008**
Food type	Legumes
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women presenting antenatal care at general practices in Menorca, a Mediterranean island in Spain (mid 1997 to mid 1998)
Funding	Instituto de Salud Carlos III red de Grupos Infancia y Media Ambiente, the Fundacio "La Caixa" , Instituto de Salud Carlos III, red de Centros de Investigacion en Epidemiologica y Salud Publica, EU, National Center for Environmental Health, USA, the GA^2LEN project, Ministry of Education and Science, Spain, Oficina de Ciencia y Tecnologia, Generalitat Valenciana.
Participants	482 children of 507 women who had attended antenatal care in Menorca
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	not clear when women did FFQ and period of pregnancy it was intended to cover
Comparison	≤ v > 1 serves per week
Outcomes	Persistent wheeze, atopic wheeze and atopy at 6.5 years
Results	***Persistent wheeze at 6.5 years*** **Low 26 (14.69%) v high 11 (10.68%) consumption; p < 0.05** (also adjusted for firstborn and lower respiratory tract infections at age 1) ***Atopic wheeze at 6.5 years*** Low 15 (6.79%) v high 5 (4.10); pns (also adjusted for birthweight and maternal atopy) ***Atopy at 6.5 years*** Low 49 (18.35%) v high 21 (14.58%) pns (also adjusted for birthweight and maternal atopy)
Followup	6.5 years
Confounding	Analyses adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years and total energy intake at 6.5 years
Risk of bias	Low risk of bias: Results from 468/482 children (97%) able to be analysed (4 incomplete data and 8 implausible values);
Relevance	Diets in Menorca may differ from diets of Australian women, particularly urban women
Other comments	

Reference	**Giordano 2008**
Food type	Legumes
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Sicily, Italy
Funding	Sicilian Congenital Malformation Registry
Participants	90 cases: 43 cases of hypospadias and 48 cases of cryptorchidism (both in one infant) 202 controls: randomly selected controls born in the same year and the same region Births between 1998 to 2003
Baseline comparisons	Low birthweight, low maternal education, mother's history of gynaecological disease and father's history of urogenital diseases differed significantly between cases and controls *See confounding below*
Dietary assessment	Interview on maternal diet and food frequencies
Timing	FFQ
Comparison	Consumption of legumes ≤ 1 versus more than once a week
Outcomes	Hypospadias and cryptorchidism
Results	**Legumes** **<u>Hypospadias</u>** **Cases** / **Controls** / **OR** ≤1/week: 21 (48.8%) / 105 (52.0%) / 1.00 >1/week: 22* (51.2%) / 96 (48.0%) / 1.15 95% CI 0.59 to 2.21 **<u>Cryptorchidism</u>** ≤1/week: 31 (64.6%) / 105 (52.0%) / 1.00 >1/week: 17 (35.4%) / 96 (48.0%) / 0.60 95% CI 0.31 to 1.15 **<u>Hypospadias and cryptorchidism</u>** ≤1/week: 52 (57.7%) / 105 (52.0) / 1.00 >1/week: 38 (42.2%) / 96 (48.0%) / 0.80 95% CI 0.48 to 1.32 **** reported as 2 in paper***
Followup	n/a
Confounding	Results for this food group were not presented as adjusted analyses
Risk of bias	Moderate risk of bias: Participation rate of parents and data collection rate of cases was lower than that of controls (76% versus 91%); no adjusted results presented for this food group
Relevance	Likely to be reasonably relevant for Australian women, although hypospadias rates very high and unlikely that most Australian women will have such high pesticide exposure
Other comments	Ragusa region in Sicily is a region of intensive agriculture (involving high rates of pesticide and other chemical use) with high rates of hypospadias and cryptorchidism

Results detail:

Legumes – Hypospadias	Cases	Controls	OR
≤1/week	21 (48.8%)	105 (52.0%)	1.00
>1/week	22* (51.2%)	96 (48.0%)	1.15 95% CI 0.59 to 2.21
Cryptorchidism			
≤1/week	31 (64.6%)	105 (52.0%)	1.00
>1/week	17 (35.4%)	96 (48.0%)	0.60 95% CI 0.31 to 1.15
Hypospadias and cryptorchidism			
≤1/week	52 (57.7%)	105 (52.0)	1.00
>1/week	38 (42.2%)	96 (48.0%)	0.80 95% CI 0.48 to 1.32

Reference	**Jensen 2004**
Food type	Legumes: beans as a group (string beans or peas); baked beans, kidney beans, chilli beans, bean soup, tofu, bean curd, soy milk, peanuts; individual types (tofu, peanuts and peanut butter (also in nuts), string beans or peas (also in vegetables))
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study)
Funding	PHS
Participants	138 matched cases and controls: Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, parental occupation and smoking during pregnancy – no evidence of confounding was seen for these variables. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of legumes
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Beans as a group:** **aOR 0.83 95% CI 0.70 to 0.99**: mean consumption 4.14 [SD 2.07] serves per day* **String beans or peas:** **aOR 0.84 95% CI 0.71 to 1.00**: mean consumption 3.40 [SD 1.81] serves per day **Tofu:** aOR 1.00 95% CI 0.76 to 1.31: mean consumption 1.36 [SD 1.05] serves per day **Peanuts, peanut butter**: aOR 1.00 95% CI 0.86 to 1.18: mean consumption 2.99 [SD 1.89] serves per day
Followup	n/a
Confounding	Analyses were adjusted for variables previously shown to be significantly associated with ALL in the overall study – income, prior fetal loss, child's exposure to other children under age five, and maternal exposure to indoor insecticides during pregnancy; along with portion size and energy consumption
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 1999, 83% consented to participate; 69% of the eligible controls agreed to participate. Of the 161 matched pairs, seven pairs were excluded as the respondent was not the biological mother, 16 pairs were excluded due to questionable dietary questionnaire data, leaving 138 matched pairs (86%); some recall bias likely
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	*Some consumption levels seem high – possibly per week rather than per day?

Reference	**Knox 1972**
Food type	Legumes: dried pulses
Study type	Case control (cases matched to food consumption at population level for a particular period) – numbers not reported
Level of evidence	III-3 (aetiology)
Setting	Birmingham, UK
Funding	Not reported
Cases	Stillbirths and infant deaths due to anencephalus between 1961 and 1967
Baseline comparisons	n/a
Dietary assessment	Population surveys
Timing	Each quarter
Comparison	Monthly stillbirths and infant deaths due to anencephalus matched to quarterly consumption of main food stuffs (in previous five to nine months)
Outcomes	Anencephalus
Results	**Dried pulses positively associated with cases of anencephalus: r = +0.65 after a lag interval of nine months**
Followup	n/a
Confounding	Analyses were not adjusted
Risk of bias	High risk of bias: links between population consumption of foods and anencephalus very distal and no control for potential confounders
Relevance	Likely to differ from a modern Australian diet
Other comments	Food consumption of total population not likely to reflect food consumption of pregnant women; and will not be able to reflect differences between diets of individual or specific groups

Reference	**Kwan 2009**
Food type	Legumes: string beans or peas; beans (such as baked beans, kidney beans, beans in chilli, burritos or soup); tofu, bean curd, soy milk, peanuts, peanut butter
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study – phase 1 and 2 (phase 1 reported in Jensen 2004)
Funding	PHS; Paul O'Gorman Foundation for Children with Leukemia
Participants	866 individuals - 282 matched cases and controls (205 pairs and 77 trios): Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth (in phase 1 (1995-99) only due to concerns about overmatching on potential environmental exposures linked to leukemia risk) Data collected from August 1995 to November 2002
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, and smoking during pregnancy. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of beans
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Legumes:** **aOR 0.75 95% CI 0.59 to 0.95** (median daily intake 0.5 (25th, 75th percentile 0.3 to 0.8) **Beans:** **aOR 0.86 95% CI 0.74 to 0.99** (median serves not reported) **Fibre from beans (g):** aOR 0.91 95% CI 0.73 to 1.13 (median daily intake 2.08 (25th, 75th percentile 0.87 to 4.37)
Followup	n/a
Confounding	Analyses were adjusted for total energy intake, household income, indoor insecticide exposure during pregnancy; and proportion of foods reported as large or extra-large portion size Also adjusted for child's diet, with little effect seen on results
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 2002, 86% consented to participate; 56% of the eligible controls agreed to participate. 190 participants excluded: leukemia diagnosis was not ALL (n = 127); no dietary data (n = 4); a case or a control respondent was not the biological mother (n = 14), questionable dietary questionnaire data (n = 45), leaving 282 matched sets (86%).
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	Regular use of any dietary supplement was not associated with risk of ALL.

Reference	**Maconochie 2007**
Food groups	Legumes (soy products)
Study type	Case-control study (postal survey sampled from the electoral roll – National Women's Health Study)
Level of evidence	III-3 (aetiology)
Setting	UK general population
Funding	National Lottery Community Fund, Miscarriage Association
Participants	Cases: 603 women aged 18 to 55 years whose most recent pregnancy had ended in first trimester miscarriage (< 13 weeks gestation); Controls: 6116 women aged 18 to 55 years whose most recent pregnancy had progressed beyond 12 weeks
Baseline Comparisons	BMI < 18.5 was significantly associated with odds of miscarriage *Also see Confounding below*
Dietary Assessment	questionnaire
Timing	Diet in the three months prior to conception and the first 12 weeks of pregnancy
Comparison	Daily or most days
Outcomes	First trimester miscarriage
Results	**Soy products daily or most days** *Cases* / *Controls* / *aOR (95% CI)* / *aOR further adjusted for nausea* No: 566 (97%) / 5783 (97%) / 1.00 / 1.00 Yes: 20 (3%) / 175 (3%) / 0.99 (0.61 to 1.59) / 1.06 (0.66 to 1.70)
Length of followup	n/a
Confounding	Adjusted for year of conception, maternal age, previous miscarriage and previous live birth; and further adjusted for nausea in the first 12 weeks of pregnancy
Risk of bias	Low risk of bias: 88% of eligible women responding to stage 1 agreed to participate in the second stage of the study; and 71% responded to the stage 2 questionnaire. 1071/7790 records (7508 women) were excluded (mostly due to index pregnancy being conceived prior to 1980), leaving 6719 records (86%) available for analysis
Relevance	Likely to be relevant to Australian women
Other comments	Women who suffered from nausea in the first 12 weeks of pregnancy were almost 70% less likely to miscarry

Soy products daily or most days

	Cases	*Controls*	*aOR (95% CI)*	*aOR further adjusted for nausea*
No	566 (97%)	5783 (97%)	1.00	1.00
Yes	20 (3%)	175 (3%)	0.99 (0.61 to 1.59)	1.06 (0.66 to 1.70)

Reference	**North 2000**
Dietary patterns	Legumes (soy milk, pulses, soya 'meat')
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Bristol, UK (part of ALSPAC and the WHO initiated European Longitudinal Study of Pregnancy and Childhood)
Funding	MRC, Wellcome Trust, Department of Health, Department of the Environment, MAFF, Nutricia, Nestle and other companies, BBC
Participants	7928 boys born to women between April 1991 and December 1992; with 51 cases of hypospadias (= 64 per 10,000 male births)
Baseline comparisons	Mothers who had influenza during pregnancy; and mothers who took codeine in the first trimester in pregnancy had high rates of hypospadias in their male offspring
Dietary assessment	Whether currently vegetarian (i.e. during pregnancy) or had previously been so
Timing	Questionnaires at 8, 18 and 32 weeks gestation (this assessed current dietary behaviour); and at various ages of the child
Comparison	*See Results below*
Outcomes	Hypospadias
Results	<table><tr><th></th><th>Cases (%)</th><th>OR (95% CI)</th></tr><tr><td><u>Soy milk (n = 6296)</u></td><td></td><td></td></tr><tr><td>Yes (1.4%)</td><td>2 (2.2)</td><td>3.67 (0.87 to15.44)</td></tr><tr><td>No (94.9%)</td><td>38 (0.6)</td><td>Reference</td></tr><tr><td><u>Pulses (n = 6251)</u></td><td></td><td></td></tr><tr><td>Never (76.7%)</td><td>30 (0.6)</td><td>Reference</td></tr><tr><td>Once/2 weeks (14.3%)</td><td>4 (0.4)</td><td>0.72 (0.25 to 2.04</td></tr><tr><td>1-3/weel (8.0%)</td><td>4 (0.8)</td><td>1.28 (0.45 to 3.64)</td></tr><tr><td>4+/week (1.1%)</td><td>3 (4.5%)</td><td>7.56 (2.25 to 25.42)</td></tr><tr><td><u>Soya meat (n = 6189)</u></td><td></td><td></td></tr><tr><td>Never (92.3%)</td><td>36 (0.6)</td><td>Reference</td></tr><tr><td>Once/2 weeks (5.1%)</td><td>2 (0.6)</td><td>1.01 (0.24 to 4.22)</td></tr><tr><td>1+/week (2.7%)</td><td>3 (1.8)</td><td>2.95 (0.90 to 9.68)</td></tr></table>
Followup	To diagnosis of hypospadias
Confounding	Analyses were not adjusted
Risk of bias	Moderate risk of bias: analyses were not adjusted for potentially important confounders; numbers of missing cases differ by outcome (no explanations given)
Relevance	Likely to be reasonably relevant to Australian women
Other comments	Authors hypothesise a possible link between phytoestrogens and hypospadias; could be pesticides, foods such as soy Omnivorous women who took iron supplements had increased risk of hypospadias in their male offspring

Reference	**Pierik 2004**
Food type	Soy protein
Study type	Case-control study (1999-2001)
Level of evidence	III-3
Setting	Rotterdam, Netherlands
Funding	Endocrine Modulators Study Group of the European Chemical Industry Council and Nutricia Research Foundation
Participants	Cases: 78 cryptorchidism and 56 hypospadias cases (diagnosed at first child health visit) Controls: 313 controls = 443 mother-child pairs (including four boys with both abnormalities)
Baseline comparisons	*See confounding below*
Dietary assessment	Phyto-oestrogen specific food questionnaire
Timing	During index pregnancy
Comparison	≥ 20 g/day versus > 0 to 20 g/day versus 0 g/day of soy protein
Outcomes	Cryptorchidism and hypospadias
Results	**Cryptorchidism** | **Cases** | **Controls** | **OR (95% CI)** ≥20 g/day | 8 | 51 | 0.6 (0.3 to 1.3) >0 to 20 g/day | 12 | 41 | 1.1 (0.6 to 2.3) 0 g/day | 58 | 221 | 1.0 **Hypospadias** ≥20 g□day | 9 | 51 | 1.0 (0.5 to 2.2) >0 to 20 g/day | 8 | 41 | 1.1 (0.5 to 2.5) 0 g/day | 39 | 221 | 1.0
Followup	NA
Confounding	Only univariate (unadjusted) analysis presented
Risk of bias	Moderate risk of bias: Participation rate was 85% for cases and 68% for controls; analyses were unadjusted for potential confounders
Relevance	Reasonably relevant to Australian women although likely to be different ethnic mix
Other comments	

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Meat

Included Studies

Study	Outcomes
1. Akre 2008	Hypospadias
2. Bunin 2006; 2005	Childhood brain tumours (medullobastomas and PNET)
3. Bunin 1993	Childhood brain tumours (PNET)
4. Chatzi 2008	Child persistent wheeze, atopic wheeze, atopy (all at 6.5 years)
5. George 2005	"Breastfeeding"
6. Giordano 2010	Child hypospadias
7. Giordano 2008	Child hypospadias and cryptorchidism
8. Godfrey 1996	Placental weight, birthweight
9. Haugen 2008	Preterm birth
10. Jensen 2004	Childhood acute lymphoblastic leukemia
11. Jones 2000	Bone mass at 8 years
12. Knox 1972	Anencephalus
13. Kwan 2009	Childhood acute lymphoblastic leukemia
14. Lamb 2008	Islet autoimmunity up to 15 years
15. Latva-Pukkila 2009	Nausea and vomiting in pregnancy
16. Maconochie 2007	Miscarriage
17. Mikkelsen 2008	Preterm birth
18. Mitchell 2004	SGA
19. Miyake 2009	Infant wheeze and eczema up to 24 months
20. Miyake 2006	Postpartum depression
21. Peters 1994	Childhood leukemia
22. Petridou 2005	Childhood acute lymphoblastic leukemia
23. Petridou 1998	Cerebral palsy at 8 years
24. Pogoda 2009	Childhood brain tumours
25. Pogoda 2001	Childhood brain tumours (updated analysis of Preston-Martin 1996 which is part of Pogoda 2009)
26. Radesky 2008	GDM, IGT
27. Saito 2010	Suspected atopic eczema
28. Sarasua 1994	Childhood brain tumours
29. Shiell 2001	BP in offspring at 27-30 years of age

30. Stuebe 2009	GWG
31. Yin 2010	Bone mass at 16 years
32. Zhang 2006	GDM

Evidence Summaries

	N	Level	References
Maternal Outcomes			
1. In a US cohort study, maternal intake of meat during pregnancy was not associated with **impaired glucose tolerance (IGT) or gestational diabetes mellitus (GDM):** • Red meat (per weekly serving): aOR 1.01 95% 0.95 to 1.08 for IGT and aOR 1.01 95% CI 0.91 to 1.12 • Processed meat (per weekly serving): aOR 1.02 95% CI 0.94 to 1.10 for IGT and aOR 0.95 95% CI 0.85 to 1.06	1773	II	Radesky 2008
2. In a US cohort study, maternal intake of meat in the previous year was significantly associated with **GDM**: • Red meat: p for trend (adjusted) across 1 serve per week to 1 serve per day = 0.006 • Processed meat: p for trend (adjusted) across 1 serve per week to 1 serve per day = 0.049 • Bacon: p for trend (adjusted) across 1 serve per week to 1 serve per day = 0.002 • Hot dogs: p for trend (adjusted) across 1 serve per week to 1 serve per day = 0.02 • Sausages, salami, bologna: p for trend (adjusted) across 1 serve per week to 1 serve per day = < 0.0001	13,110	II	Zhang 2006
3. In a US cohort study, maternal intake of red and processed meats during pregnancy was not significantly associated with excessive **gestational weight gain**: aOR 1.00 95% CI 0.74 to 1.34	1338	II	Stuebe 2009
4. In a UK case-control study, maternal intake of red meat twice weekly or more during pregnancy was not significantly associated with **miscarriage**: aOR 1.03 95% CI 0.86 to 1.26	603 cases; 6116 controls	III-3	Maconochie 2007
5. In a Finnish cohort study, **nausea and vomiting** during pregnancy was significantly associated with reduced subsequent daily maternal intake of meat products during pregnancy (p = 0.004)	256	II	Latva-Pukkila 2009
Congenital Anomalies			
6. In a Scandinavian case-control study, less than weekly maternal meat consumption during pregnancy compared with weekly meat consumption was associated with an increased risk of **hypospadias** in baby boys: aOR 2.4 95% CI 1.1 to 4.9	292 cases; 427 controls	III-3	Akre 2008
7. In a case-control study from Rome, Italy, rare versus frequent (once a week) maternal consumption of liver or offal during pregnancy was not associated with **hypospadias**: aOR 1.69 95% CI 0.63 to 4.55	80 cases; 80 controls	III-3	Giordano 2010
8. In a case-control study from Sicily, Italy:	90 cases;	III-3	Giordano 2008

• Maternal consumption of red meat once a week or less during pregnancy compared with more than once a week was not significantly associated with **hypospadias or cryptorchidism**; OR 0.59 95% CI 0.29 to CI 1.17 • Maternal consumption of liver and other offal more than once a week during pregnancy compared less than once a week was significantly associated with **cryptorchidism** (aOR 5.21 95% CI 1.26 to 21.50) but not **hypospadias** (aOR 4.07 95% CI 0.92 to 17.99)	202 controls		
9. In a UK case-control study total maternal meat consumption, pork, and meat (and vegetable) extracts during pregnancy were negatively associated with cases of **anencephalus**, whereas maternal consumption of mutton and lamb, and corned meat during pregnancy were positively associated with cases of **anencephalus**	Not reported	III-3	Knox 1972
Birth Outcomes			
10. In a New Zealand case-control study, no significant association was seen between **SGA** and meat intake at the time of conception (p = 0.79) or in the last month of pregnancy (p = 0.66)	1138	III-3	Mitchell 2004
11. In a Norwegian cohort study, no significant association was seen between **preterm birth** and meat intake during pregnancy (≤ 2 versus > 2 serves a week): aOR 1.09 95% CI 0.93 to 1.28	26,563	II	Haugen 2008
12. In a Danish cohort study, no significant association was seen between **preterm birth** and meat intake during pregnancy (≤ 2 versus > 2 serves a week): aOR 0.92 95% CI 0.81 to 1.05	35,350	II	Mikkelsen 2008
13. In a UK cohort study, no significant association was seen between placental weight and meat intake during pregnancy, but **birthweight** fell by 3.1 g (95% CI 0.3 g to 6.0 g; p = 0.03) for each g decrease in meat protein in late pregnancy	538	II	Godfrey 1996
Breastfeeding Associations/Outcomes			
14. In a US study, **lactating** women consumed significantly less beef and more chicken than non-lactating women (14.8% v 4.1% of women, p < 0.035) and also less hamburgers and meatloaf	149	II	George 2005
Postpartum Depressive Symptoms			
15. In a Japanese cohort study, no significant association was seen between maternal meat intake during pregnancy and **postpartum depression**	865	II	Miyake 2006
Childhood – Eczema And Other Allergy Outcomes			
16. In a Japanese cohort study, maternal meat intake during pregnancy was associated with significantly increased risk of **suspected infant atopic eczema at 3-4 months**: • 63.6 versus 33.4 g/day of meat: aOR 2.41 95% CI 1.06 to 5.75 • 89.8 versus 33.4 g/day of meat: aOR 2.59 95% CI 1.15 to 6.17	771	II	Saito 2010

17. In a follow-up study of Saito 2009, no associations were seen between meat intake during pregnancy and either **infant eczema or wheeze at 16-24 months** (p for trend = 0.28 and 0.22 respectively)	763	II	Miyake 2009
18. In a Spanish cohort study, no associations were seen between meat intake in pregnancy and **persistent wheeze, atopic wheeze or atopy at 6.5 years**	482 children	II	Chatzi 2008
Other Childhood/Adult Outcomes			
19. In a US case-control study, **childhood acute lymphoblastic leukemia** was not generally associated with maternal intake of meat (cured or not cured) during pregnancy, except for a reduced risk with increased beef consumption: aOR 0.80 95% CI 0.66 to 0.99	276 children (138 pairs)	III-3	Jensen 2004
20. In a later US case-control study (which included Jensen 2004), **childhood acute lymphoblastic leukemia** was not generally associated with maternal intake of meat, except for a reduced risk with increased beef consumption: • Cured meat: aOR 0.91 95% CI 0.78 to 1.05: median consumption 0.3 (25th 75th percentiles 0.1, 0.5) serves per day • Beef: aOR 0.82 95% CI 0.69 to 0.98 (number serves per day not reported)	866 children (205 pairs and 77 trios)	III-3	Kwan 2009
21. In a Greek case-control study, maternal consumption of meat and meat products during pregnancy was significantly associated with **acute lymphoblastic leukemia** in their children: aOR 1.25 95% CI 1.09 to 1.57 for each more quintile of meat/meat products (median consumption of 61 g/day in the highest quintile)	131 cases; 131 controls	III-3	Petridou 2005
22. In a US case-control study, maternal meat intake (breakfast meats, luncheon meats, hot dogs, charcoal broiled meats) during pregnancy was not significantly associated with risk of **childhood leukemia**	232 cases; 232 controls	III-3	Peters 1994
23. In an international case-control study, risk of **childhood brain tumours** were significantly associated with increased maternal intake of cured meat (aOR 1.51 95% CI 1.1 to 2.1) but no association was seen with noncured meat (p for trend 0.19) (in a subset of 540 cases and 801 controls, increased maternal intake of nitrite from cured meats was significantly associated with childhood brain tumours)	1281 cases; 2223 controls	III-3	Pogoda 2009 (Pogoda 2001)
24. In a North American case-control study, risk of **medulloblastoma/PNET in children up to 6 years** was not associated with maternal meat consumption during pregnancy: • Cured meat aOR 0.9 95% CI 0.6 to 1.5 periconception; aOR 0.6 95% CI 0.2 to 1.9 midpregnancy : < 2 serves/week compared with > 5 serves/week (This result varied little if smoked fish was included; or whether vitamin supplements were being taken or not)	630 children (315 pairs)	III-3	Bunin 2006
25. In a North American case-control study, **PNET in children up to the age of six years** was not associated with maternal consumption of cured meats, with possible exception of	166 cases; 166 controls	III-3	Bunin 1993

bacon: • Cured meats overall; p_{trend} over quartiles = 0.77 • Bacon at least once a week versus less than once a week OR 1.71 95% CI 1.02 to 2.89			
26. In a US case-control study: • no significant associations were seen between maternal intake of ham, bacon, sausage, hot dogs, hamburgers, lunch meats and charcoal-broiled foods during pregnancy and risk of childhood **acute lymphoblastic leukemia**; **lymphomas or soft tissue sarcoma** • no significant associations were seen between maternal intake of ham, bacon, sausage, hamburgers and charcoal-broiled foods and risk of **childhood brain tumours** • maternal intake of hot dogs (any versus none) during pregnancy was associated with an increased risk of **childhood brain tumours**: aOR 2.3 95% CI 1.0 to 5.4 • maternal intake of lunch meats during pregnancy was associated with a decreased risk of **childhood brain tumours**: aOR 0.4 95% CI 0.2 to 0.8	234 cases; 206 controls	III-3	Sarasua 1994
27. In a Greek case-control study, **cerebral palsy in children at 8 years** was associated with increased maternal meat intake during pregnancy: • Regression analysis for each unit of consumption of meat once per day: aOR 1.42 95% CI 1.07 to 1.88 (additionally adjusted for all food groups)	109 cases; 246 controls	III-3	Petridou 1998
28. In a US cohort study, no significant association was seen between maternal meat intake during pregnancy and **islet autoimmunity in children up to 15 years of age**: aHR 0.91 95% CI 0.54 to 1.51	642 children	II	Lamb 2008
29. In one Australian cohort study, **bone mineral density of children at 8 years** was not associated with maternal meat intake during pregnancy: • Total body bone mineral density – p = 0.65 for adjusted regression of portions per week	173 children	II	Jones 2000
30. In an Australian cohort study (follow-up of Jones 2000) **bone mass in 16 year-old adolescents** was not associated with maternal meat intake during pregnancy: • Total body bone mineral density r^2 0.3324; ß +6.1.3 (pns) for adjusted regression of portions per week	216 children	II	Yin 2010
31. In a cohort study from Scotland, **systolic blood pressure** was significantly increased in 27 to 30 year old offspring of women with high meat intake during pregnancy (in conjunction with a low carbohydrate diet): ß 0.21 95% CI 0.04 to 0.37, p = 0.01	626 adult off-spring	II	Shiell 2001

Evidence Tables

Reference	**Akre 2008**
Food type	Meat
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Sweden and Denmark from 2000 to 2005
Funding	European Chemical Industry Council
Participants	292 cases 427 controls
Baseline comparisons	*See confounding below*
Dietary assessment	Questionnaire
Timing	Questionnaire completed by mother when son was 2 months old in Sweden and when 6 months old in Denmark
Comparison	No weekly meat consumption versus weekly meat consumption
Outcomes	Hypospadias
Results	**Hypospadias** **No weekly meat consumption versus weekly meat consumption** **aOR 2.4 95% CI 1.1 to 4.9**
Followup	n/a
Confounding	Analyses adjusted for maternal age, maternal pre-pregnancy BMI, maternal education, contraceptive use at conception, proteinuria, maternal nausea in the index pregnancy, passive maternal exposure to tobacco smoke during index pregnancy, fish consumption; weight for gestational age, gestational age at birth; neonatal jaundice
Risk of bias	Low risk of bias: response rate was 88% for cases and 81% for controls; ascertainment of cases of hypospadias likely to be high.
Relevance	Likely to be reasonably similar for the small number of Australian women who do not consume meat (or meat or fish) during pregnancy
Other comments	Different recruitment methods were used in Sweden and Denmark

Reference	**Bunin 2006 (and Bunin 2005)**
Food type	Meat
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	United States and Canada
Funding	National Cancer Institute, USA
Participants	315 cases diagnosed with medulloblastoma/PNET tumours from 0 to 5 years, between 1991 to 1997 (without a previous or recurrent cancer) 315 controls (random digit dialling, matched on area code, race and data of birth)
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	To reflect diet in the year before pregnancy; and the second trimester of pregnancy
Comparison	<1 serve month to >1 serve/week; data on portion size were not collected
Outcomes	Childhood brain tumours (medulloblastoma/primitive neuroectodermal tumours (PNET)
Results	

Medulloblastoma/PNET

	Periconception		Midpregnancy	
	N	**aOR* (95% CI)**	**N**	**aOR* (95% CI)**
Ham				
<1 serve/month	150	1.0	168	1.0
1-3/month	244	1.4 (0.9 to 2.3)	231	1.5 (0.9 to 2.4)
1/week	151	1.4 (0.8 to 2.5)	144	1.3 (0.8 to 2.2)
>1/wk	84	0.9 (0.5 to 1.8)	86	0.9 (0.5 to 1.8)
P_{trend}		0.58		0.54
Lunchmeat				
<1 serve/month	323	1.0	333	1.0
1-3/month	130	1.5 (0.9 to 2.4)	126	1.5 (0.9 to 2.5)
1/week	102	0.9 (0.5 to 1.5)	96	1.0 (0.6 to 1.8)
>1/wk	74	1.0 (0.5 to 1.8)	74	0.9 (0.6 to 1.6)
P_{trend}		0.86		0.75
Hot dogs				
<1 serve/month	245	1.0	260	1.0
1-3/month	242	1.2 (0.8 to 1.9)	230	1.2 (0.8 to 1.8)
≥1/wk	143	0.8□(0.□ to 1.4)	140	0.9 (0.6 to 1.5)
P_{trend}		0.83		0.95
Lunch sausage				
<1 serve/month	431	1.0	442	1.0
≥1/wk	199	1.1 (0.7 to 1.6)	188	1.1 (0.7 to 1.6)
P_{trend}		0.65		0.81

Pizza with pepperoni, salami or sausage

<1 serve/month	175	1.0	206	1.0
1-3/month	270	0.9 (0.6 to 1.4)	25	1.1 (0.7 to 1.7)
≥1/wk	185	1.1 (0.6 to 1.7)	174	1.2 (0.7 to 1.9)
P_{trend}		0.90		0.53
Cured meat and fish				
<2 serves/week	162	1.0	181	1.0
2 to <3.5/week	182	1.4 (0.8 to 2.2)	176	1.1 (0.7 to 1.9)
≥3.5 to ≤5/wk	134	1.1 (0.6 to 1.9)	119	1.1 (0.6 to 2.0)
>5/wk	152	1.0 (0.6 to 1.9)	154	1.0 (0.6 to 1.8)
P_{trend}		0.81		0.99
Cured meat with low vitamin C intake or absence of multivitamin use				
Top half of cured meats/no multivitamins				
No		1.0		1.0
Yes	221	1.1 (0.8 to 1.7)		0.8 (0.3 to 2.0)
Top quartile of cured meats/no multivitamins**				
No		1.0		1.0
Yes	123	0.9 (0.6 to 1.5)		0.6 (0.2 to 1.9)
Top half of cured meats/bottom half of vitamin C				
No		1.0		1.0
Yes	151	1.2 (0.8 to 1.9)		**1.5 (1.0 to 2.3)**
Top quartile of cured meats/bottom quartile of vitamin C				
No		1.0		1.0
Yes	55	1.1 (0.6 to 2.1)		1.1 (0.6 to 2.1)
Fresh meat (from Bunin 2005)*				
≤4 serves/week	111	1.0	199	1.0
4 to <7/week	234	1.0 (0.6 to 1.7)	230	0.9 (0.5 to 1.5)
7 to <10.5/week	187	0.8 (0.4 to 1.4)	180	0.8 (0.4 to 1.4)
≥10.5/week	98	0.8 (0.4 to 1.8)	101	1.1 (0.5 to 2.3)
P_{trend}		0.45		0.92
Lean hamburger (from Bunin 2005)* - also adjusted for regular hamburger				
<1 serve/month	203	1.0	202	1.0
1-3/month	133	1.2 (0.7 to 2.1)	141	1.4 (0.8 to 2.4)
1/week	143	1.0 (0.6 to 1.7)	144	1.0 (0.6 to 1.8)
≥2/week	149	0.7 (0.4 to 1.3)	143	0.9 (0.5 to 1.6)
P_{trend}		0.14		0.44
Red meat as stew (from Bunin 2005)* - also adjusted for red meat as steak and red meat as sandwich				
<1 serve/month	276	□□0	295	1.0

	≥ 1 serve/month	354	1.1 (0.8 to 1.7) 0.92	335	1.0 (0.6 to 1.6) 0.95

Followup	n/a
Confounding	*adjusted for income level, mother's race, age of child at interview, date of interview, gained weight because of nausea/vomiting, number cigarettes per day, total calories **adjusted for mother's race, age of child at interview, income, number of cigarettes per day, maternal weight gain (yes/no) because of pregnancy nausea/vomiting
Risk of bias	Low-moderate risk of bias: 315/558 (57%) potentially eligible cases able to be included (missing cases mostly due to lack of consent from physician or parents); control resonse rates were 67% for random digit dialling and 73% for questionnaire
Relevance	Likely to be reasonably similar
Other comments	Medulloblastomas and PNETs account for about 20% of brain tumours in children; Supplement use was also assessed in this study

Reference	**Bunin 1993**
Food type	Cured meats; bacon, sausage, hot dogs, ham, lunch meat
Study type	Case control study (Children's Cancer Group)
Level of evidence	III-3 (aetiology)
Setting	North America
Funding	NIH, Japan National Committee of the International Union against Cancer, Olympus Optical Company, International Agency for Research on Cancer, WHO.
Participants	166 cases (children diagnosed with primitive neuroectodermal brain tumours (PNET) before the age of six years from 1986 to 1989); 166 matched controls
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During pregnancy
Comparison	Consumption at least once per week versus less than once a week; and quartiles of consumption
Outcomes	PNET
Results	**Cured meats overall (by quartile of consumption):** 1st — OR 1.00 2nd — OR 0.83 95% CI 0.47 to 1.48 3rd — OR 0.90 95% CI 0.50 to 1.60 4th — OR 1.10 95% CI 0.60 to 2.03 P_{trend} — 0.77 ***Consumption of cured meats at least once per week versus less than once a week:*** ***OR (95% CI)*** **Bacon: — 1.71 (1.02 to 2.89)** Sausage: — 1.44 (0.81 to 2.56) Hot dogs: — 1.00 (0.59 to 1.70) Ham: — 0.77 (0.41 to 1.41) Lunch meat: — 0.92 (0.55 to 1.53)
Followup	n/a
Confounding	Analyses for individual food groups were not adjusted for potential confounders
Risk of bias	Moderate risk of bias: 116 cases (41%) included from 281 potentially eligible children
Relevance	Likely to be reasonably similar to diets of Australian women
Other comments	Nearly all case and control mothers took multivitamins during their pregnancies; Diet and supplemental vitamin use in child's first year of life was also recorded

Reference	**Chatzi 2008**
Food type	Red meat
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women presenting antenatal care at general practices in Menorca, a Mediterranean island in Spain (mid 1997 to mid 1998)
Funding	Instituto de Salud Carlos III red de Grupos Infancia y Media Ambiente, the Fundacio "La Caixa" , Instituto de Salud Carlos III, red de Centros de Investigacion en Epidemiologica y Salud Publica, EU, National Center for Environmental Health, USA, the GA^{2}LEN project, Ministry of Education and Science, Spain, Oficina de Ciencia y Tecnologia, Generalitata Valenciana.
Participants	482 children of 507 women who had attended antenatal care in Menorca
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	not clear when women did FFQ and period of pregnancy it was intended to cover
Comparison	≥ 3.5 v < 3.25 serves of red meat a week
Outcomes	Persistent wheeze, atopic wheeze and atopy at 6.5 years
Results	***Persistent wheeze at 6.5 years*** Low 17 (16.50%) v high 20 (11.30%); pns (also adjusted for firstborn and lower respiratory tract infections at age 1) ***Atopic wheeze at 6.5 years*** Low 9 (7.63%) v high 11 (4.89%); pns (also adjusted for birthweight and maternal atopy) ***Atopy at 6.5 years*** Low 23 (16.31%) v high 47 (17.41%) pns (also adjusted for birthweight and maternal atopy)
Followup	6.5 years
Confounding	Analyses adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years and total energy intake at 6.5 years
Risk of bias	Low risk of bias: Results from 468/482 children (97%) able to be analysed (4 incomplete data and 8 implausible values);
Relevance	Diets in Menorca may differ from diets of Australian women, particularly urban women
Other comments	

Reference	**George 2005**
Food type	Meat (beef, chicken)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Texas, US
Funding	Not reported
Participants	149 Medicaid-qualified women (30% white, 24% African American, 46% Hispanic) – recruited from a larger study on postpartum weight retention Inclusion criteria: 18 years or older; non-Hispanic white, African American or Hispanic ethnicity; birth of a health term infant, fluency and literacy in English; absence of pregnancy-related abnormalities and disease conditions.
Baseline comparisons	Significant differences between lactating and non-lactating women – higher parity, BMI and lower education levels in non-lactating women.
Dietary assessment	Semiquantitative FFQ to cover pregnancy and first six months postpartum
Timing	FFQ administered at 6 weeks and 6 months postpartum
Comparison	Proportion of consumption of different types of meats
Outcomes	Breastfeeding (exclusive or partial at 6 months postpartum)
Results	**Lactating women consumed significantly more chicken and less beef than non-lactating women (14.8% v 4.1% of women; $p < 0.035$)** **Lactating women consumed significantly less hamburgers and meatloaf; beef steak and roasts than nonlacatating women**
Followup	6 months postpartum
Confounding	No adjustment for potential confounding
Risk of bias	Moderate-to-high risk of bias; no attempt to control for confounding despite significant baseline differences between lactating and non-lactating women.
Relevance	Possibly relevant to low-income women in Australia
Other comments	Minimal reporting of results

Reference	**Giordano 2010**
Food type	Meat
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Rome, Italy
Funding	Not reported
Participants	80 cases of hypospadias requiring surgical treatment in children aged 0 to 24 months (mean age 57.62 weeks) 80 controls: healthy males without any congenital defect, aged 0 to 24 months (mean age 36.52 weeks); recruited between September 2005 and May 2007
Baseline comparisons	*See confounding below*
Dietary assessment	Interview on 'typical' maternal diet habits in relation to the index pregnancy and food frequencies
Timing	FFQ administered on recruitment for mothers of cases and during vaccination visits for mothers of controls
Comparison	Rare versus frequent consumption of liver or offal (once a week)
Outcomes	Hypospadias
Results	**Liver, offal** **Cases** / **Controls** / **OR** / **aOR** **Rare**: 66 (82.5%) / 72 (90.0%) / 1.00 / 1.00 **Frequent**: 14 (17.5%) / 8 (10.0%) / 1.91 95% CI 0.75 to 4.84 / 1.69 95% CI 0.63 to 4.55
Followup	n/a
Confounding	Adjusted for mother's BMI at conception and education of the father; Gestational age, birthweight and SGA were not included among the covariates in the regression models, as they may share a common aetiology with hypospadias
Risk of bias	Moderate risk of bias: Participation rate of parents of cases was higher than that of controls (85% versus 70%); very few potential confounders used in adjusted analyses
Relevance	Likely to be reasonably relevant for Australian women
Other comments	Likely to be underpowered

Reference	**Giordano 2008**
Food type	Meat: red meat (beef, pork, lamb, mutton); liver and other offal
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Sicily, Italy
Funding	Sicilian Congenital Malformation Registry
Participants	90 cases: 43 cases of hypospadias and 48 cases of cryptorchidism (both in one infant) 202 controls: randomly selected controls born in the same year and the same region Births between 1998 to 2003
Baseline comparisons	Low birthweight, low maternal education, mother's history of gynaecological disease and father's history of urogenital diseases differed significantly between cases and controls *See confounding below*
Dietary assessment	Interview on maternal diet and food frequencies
Timing	FFQ
Comparison	Consumption of red meat once a week or less vs more than once a week; Consumption of liver and other offal once a week or less vs more than once a week;
Outcomes	Hypospadias and cryptorchidism
Results	

Red meat	**Cases**	**Controls**	**OR**
Hypospadias			
≤ 1/week	8 (19.1%)	23 (11.4%)	1.00
> 1/week	34 (80.9%)	179 (88.6%)	0.55 95% CI 0.23 to 1.32
Cryptorchidism			
≤ 1/week	8 (16.7%)	23 (11.4%)	1.00
> 1/week	40 (83.3%)	179 (88.6%)	0.64 95% CI 0.27 to 1.54
Hypospadias and cryptorchidism			
≤ 1/week	16 (17.8%)	23 (11.4%)	1.00
> 1/week	73 (81.1%)	179 (88.6%)	0.59 95% CI 0.29 to 1.17
Liver and other offal			
Hypospadias			
≤ 1/week	39 (90.7%)	195 (96.5%)	1.00
> 1/week	4 (9.3%)	7 (3.5%)	2.86 95% CI 0.80 to 10.23
Cryptorchidism			
≤ 1/week	43 (89.6%)	195 (96.5%)	1.00
> 1/week	5 (10.4%)	7 (3.5%)	3.24 95% CI 0.98 to 10.69
Hypospadias and			

	cryptorchidism			
	≤ 1/week	81 (90%)	195 (96.5%)	1.00
	> 1/week	9 (10.0%)	7 (3.5%)	**3.10 95% CI 1.11 to 8.59**
	Liver and other offal: adjusted analysis*			
		aOR		
	Hypospadias			
	> 1/week	4.07 95% CI 0.92 to 17.99		
	Cryptorchidism			
	> 1/week	**5.21 95% CI 1.26 to 21.50**		
	Hypospadias and cryptorchidism			
	> 1/week	**4.38 95% CI 1.34 to 14.26**		
Followup	n/a			
Confounding	Results for red meat were not presented as adjusted analyses *Liver and other offal results were additionally adjusted for mother's age, parity, education, gynaecological diseases; paternal urogenital diseases, and use of pesticides; birthweight			
Risk of bias	Moderate risk of bias: Participation rate of parents and data collection rate of cases was lower than that of controls (76% versus 91%);			
Relevance	Likely to be reasonably relevant for Australian women, although hypospadias rates very high and unlikely that most Australian women will have such high pesticide exposure			
Other comments	Ragusa region in Sicily is a region of intensive agriculture (involving high rates of pesticide and other chemical use) with high rates of hypospadias and cryptorchidism			

Reference	**Godfrey 1996**
Food type	Meat
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Southampton, UK
Funding	Dunhill Trust and Medical Research Council
Participants	538 women who gave birth to a singleton term infant
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered in early and late pregnancy, to reflect diet in the previous three months
Comparison	≤ 23.5 v 23.5 to 34.0 v > 34.0 g/day meat protein; mean daily intake 28.3 g IQR 20.5, 37.3
Outcomes	Birthweight, placental weight
Results	**Placental weight** No significant association seen between meat protein intake in late pregnancy and placental weight (p = 0.5) **Birthweight** **Birthweight fell by 3.1 g (95% CI 0.3g to 6.0 g; p = 0.03) for each g decrease in meat protein in late pregnancy**
Followup	To birth
Confounding	Adjusted for baby's sex and gender and duration of gestation; and nutrient intakes
Risk of bias	Low risk of bias: of 636 women recruited, 596 (94%) agreed to participate; 39 gave birth before 37 weeks, 3 were not visited in late pregnancy and placental weight was not recorded for 16, leaving 538 term pregnancies with complete birth and nutrition data (85% of the 636 women recruited)
Relevance	Likely to be relevant for Australian women
Other comments	

Reference	**Haugen 2008**
Dietary patterns	Red meat as part of Mediterranean-type diet (2 or more serves of meat per week)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Norway (part of the Norwegian Mother and Child Cohort Study (MoBa))
Funding	Norwegian Ministry of Health, NIH/NINDS, Norwegian Research Council/FUGE, EU FP& consortium, Metabolic Programming (EARNEST).
Participants	26,563 (65%) of 40,817 pregnancies of women recruited for MoBa from February 2002 to February 2005 who met the following criteria: women had to be non-smoking, BMI between 19 and 32, aged between 21 and 38 years when giving birth, with a singleton birth. Exclusions: more than 3 spontaneous abortions, energy intake less than 4,200 kJ and more than 16,700 kJ.
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	at 17-24 weeks gestation
Comparison	Red meat ≤ 2 versus > 2 times a week
Outcomes	Preterm birth (after week 21 and before week 37); late preterm birth (week 35-36) and early preterm birth (< 35 weeks)
Results	***Preterm birth (< 37 weeks): (n = 25,966; 1174 cases)*** OR 1.09 95% CI 0.93 to 1.28 aOR 1.09 95% CI 0.93 to 1.28 ***Early preterm birth (< 35 weeks): (n = 25,256; 474 cases)*** OR 1.13 95% CI 0.88 to 1.44 aOR 1.14 95% CI 0.89 to 1.46 ***Late preterm birth (35-36 weeks): (n = 25,492; 710 cases)*** OR 1.06 95% CI 0.86 to 1.30 aOR 1.05 95% CI 0.86 to 1.30
Followup	To birth
Confounding	Analyses were adjusted for remaining Mediterranean diet criteria, mother's BMI and height, educational level, parity and marital status
Risk of bias	Moderate: some dietary intakes were different between groups and were not controlled for
Relevance	Moderate: low red meat consumption not typical for many Australian women
Other comments	Preterm birth rates were lower than expected, likely due to exclusion of smokers

Reference	**Jensen 2004**
Food type	Meat: cured meat (sausage or bacon, hot dogs, ham, bologna, other lunch meats); pork; hamburger (ground); beef; liver
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study)
Funding	PHS
Participants	138 matched cases and controls: Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, parental occupation and smoking during pregnancy – no evidence of confounding was seen for these variables. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of meat products
Outcomes	Childhood acute lymphoblastic leukemia
Results	<u>**Cured meat**</u>: ALL aOR 0.71 95% CI 0.44 to 1.15: mean consumption of cured meat 0.60 [SD 0.37] serves per day* Sausage or bacon aOR 0.87 95% CI 0.71 to 1.08: mean consumption 2.73 [SD 1.57] serves per day Hot dogs aOR 0.80 95% CI 0.60 to 1.07: mean consumption 1.93 [SD 1/15] serves per day Ham, bologna, etc. aOR 0.91 95% CI 0.78 to 1.07: mean consumption 3.29 [SD 2.03] serves per day Pork aOR 0.91 95% CI 0.74 to 1.11: mean consumption 2.83 [SD 1.47] serves per day Hamburger (ground) aOR 0.90 95% CI 0.75 to 1.09: mean consumption 3.96 [SD 1.78] serves per day **Beef** **aOR 0.80 95% CI 0.66 to 0.99:** mean consumption 3.85 [SD 1.63] serves per day Liver aOR0.83 95% CI 0.53 to 1.31: mean consumption 1.24 [SD 0.73] serves per day
Followup	n/a
Confounding	Analyses were adjusted for variables previously shown to be significantly associated with ALL in the overall study – income, prior fetal loss, child's exposure to other children under age five, and maternal exposure to indoor insecticides during pregnancy; along with portion size and energy consumption
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 1999, 83% consented to participate; 69% of the eligible controls agreed to participate. Of the 161 matched pairs, seven pairs were excluded as the respondent was not the biological mother, 16 pairs were excluded due to questionable dietary questionnaire data, leaving 138 matched pairs (86%); some recall bias likely
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	*Some consumption levels seem high – possibly per week rather than per day?

Reference	**Jones 2000 (see also Yin 2010)**
Food type	Meat
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Southern Tasmania, Australia
Funding	NHMRC, Tasmanian Government, Royal Hobart Hospital Acute Care Program
Participants	173 mothers; and their infants born in 1988 (part of a larger infant health study of babies at high risk of SIDS) Exclusions: multiple pregnancies
Baseline comparisons	Mothers with no tertiary education more likely to have been excluded due to missing data
Dietary assessment	FFQ
Timing	Dietary intake during third trimester of pregnancy
Comparison	Linear regression of density (portions per kJ)
Outcomes	Bone mass (bone mineral density (BMD) and bone mineral content*) in 8 year old children
Results	**BMD at 8 years;** **Total body (g/cm^2)** r^2 0% 0.003 ($p = 0.67$) adjusted r^2 23% 0.003 ($p = 0.65$) **Femoral neck (g/cm^2)** r^2 1% 0.005 ($p = 0.55$) **adjusted r^2 33% 0.005 ($p = 0.57$)** **Lumbar spine (g/cm^2)** r^2 0% -0.001 ($p = 0.54$) adjusted r^2 32% -0.003 ($p = 0.72$)
Followup	8 years
Confounding	Analyses were adjusted for method of dietary assessment, maternal education, parental unemployment, sex, weight at age 8 years, height at age 8 years, weekend sunlight exposure in winter at age 8 years, smoking during pregnancy, sports participation, ever breast-fed and current calcium intake.
Risk of bias	Moderate-high: 330 (215 males, 115 females) representing a 60% response rate from those available in 1996; 47% of the original 1988 cohort, This dropped to 173 (dietary information missing or unreliable for 115 mothers, 32 multiple births, 10 participants had missing data for confounders) representing 52% of participants from 1996 and 25% of those in the original cohort. 72% of the 173 participants were male. Gender imbalance suggests potential selection bias (due to original selection of infants at high risk of SIDS)
Relevance	Infants at high risk of SIDS represent a selected group (more males, preterm births, teenage mothers, smoking during pregnancy)
Other comments	*Bone mineral content not reported – stated to be similar to bone mineral density results

Reference	**Knox 1972**
Food type	Meat (total meat, pork, meat and vegetable extracts, mutton and lamb, corned meat)
Study type	Case control (cases matched to food consumption at population level for a particular period)
Level of evidence	III-3 (aetiology)
Setting	Birmingham, UK
Funding	Not reported
Cases	Stillbirths and infant deaths due to anencephalus between 1961 and 1967
Baseline comparisons	n/a
Dietary assessment	Population surveys
Timing	Each quarter
Comparison	Monthly stillbirths and infant deaths due to anencephalus matched to quarterly consumption of main food stuffs (in previous five to nine months)
Outcomes	Anencephalus
Results	**Total meat negatively associated with cases of anencephalus; r = -0.66 after a lag interval of five months** **Pork negatively associated with cases of anencephalus; r = -0.75 after a lag interval of five months** **Meat and vegetable extracts negatively associated with cases of anencephalus; r = -0.69 after a lag interval of five months** **Mutton and lamb positively associated with cases of anencephalus; r = +0.63 after a lag interval of five months** **Corned meat positively associated with cases of anencephalus; r = +0.55 after a lag interval of eight months**
Followup	n/a
Confounding	Analyses were not adjusted
Risk of bias	High risk of bias: links between population consumption of foods and anencephalus very distal and no control for potential confounders
Relevance	Likely to differ from a modern Australian diet
Other comments	Food consumption of total population not likely to reflect food consumption of pregnant women; and will not be able to reflect differences between diets of individual or specific groups

Reference	**Kwan 2009**
Food type	Meat: cured meat (sausage or bacon, hot dogs, ham, bologna, other lunch meats); pork; hamburger (ground); beef; liver
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study – phase 1 and 2 (phase 1 reported in Jensen 2004)
Funding	PHS; Paul O'Gorman Foundation for Children with Leukemia
Participants	866 individuals - 282 matched cases and controls (205 pairs and 77 trios): Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth (in phase 1 (1995-99) only due to concerns about overmatching on potential environmental exposures linked to leukemia risk) Data collected from August 1995 to November 2002
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, and smoking during pregnancy. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of meat
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Cured meat:** aOR 0.91 95% CI 0.78 to 1.05: median consumption 0.3 (25th 75th percentiles 0.1, 0.5) serves per day **Beef: aOR 0.82 95% CI 0.69 to 0.98**
Followup	n/a
Confounding	Analyses were adjusted for total energy intake, household income, indoor insecticide exposure during pregnancy; and proportion of foods reported as large or extra-large portion size Also adjusted for child's diet, with little effect seen on results
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 2002, 86% consented to participate; 56% of the eligible controls agreed to participate. 190 participants excluded: leukemia diagnosis was not ALL (n = 127); no dietary data (n = 4); a case or a control respondent was not the biological mother (n = 14), questionable dietary questionnaire data (n = 45), leaving 282 matched sets (86%).
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	Regular use of any dietary supplement was not associated with risk of ALL; Authors did not report on meat overall (ws grouped with overall protein) or some specific meats such as liver

Reference	**Lamb 2008**
Dietary patterns	Meat: chicken or turkey (with or without skin), bacon, hot dogs, processed meats (sausage, salami, bologna etc.), liver, beef, pork or lamb as a sandwich or mixed dish, or beef, pork or lamb as a main dish
Study type	Part of a longitudinal prospective birth cohort study
Level of evidence	II (aetiology)
Setting	Denver, Colorado, US (part of the Diabetes Autoimmunity Study in the Young (the DAISY))
Funding	National Institutes of Health, Diabetes Endocrine Research Center
Participants	642 newborns at increased risk for type 1 diabetes (based on HLA genotype and family history), enrolled in the study from 1993 to 2004; 27 cases defined as testing positive for islet autoantibodies at two consecutive blood draws and still positive (diabetic) at last follow-up
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	From 1997 to 2004, mothers of infants enrolled in DAISY completed FFQ soon after birth, reflecting diet in the last trimester of pregnancy (but could submit FFQ before child reached one year of age)
Comparison	Monthly servings of meat
Outcomes	Islet autoimmunity (a precursor of type 1 diabetes) at 9 months, 15 months, 2 years and annually thereafter up to the age of 15
Results	**Meat:** aHR (for one standard deviation change in reported consumption) 0.91 95% CI 0.54 to 1.51 (40 mean monthly servings)
Followup	Up to 15 years
Confounding	Size for gestational age, ethnicity, maternal education, household income, exposure to type 1 diabetes or GDM in utero, gender of child, maternal age at birth, total calories of maternal diet
Risk of bias	Moderate risk of bias: subset of DAISY only (later enrolments); and women were not reminded to submit FFQ, leading to possible selection bias; of the 661 FFQs returned, 5 were excluded because incomplete, and 14 for implausible dietary intakes, leaving 642 FFQs for analysis; child's diet not controlled for (except partially for first introduction to cereals in the maternal potato consumption analysis)
Relevance	Likely to be relevant to some Australian women, although women in this study may have been at higher risk of diabetes
Other comments	

Reference	**Latva-Pukkila 2009**
Dietary patterns	Meat
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Turku, Finland (cohort from Piirainen 2006)
Funding	Social Insurance Institution of Finland, the Sigrid Juselius Foundation and the Academy of Finland
Participants	256 pregnant women
Baseline comparisons	Women with NVP were older and tended to be primiparous compared to those without
Dietary assessment	3 day food diaries
Timing	Three times during pregnancy (mean 14, 24 and 34 weeks gestation)
Comparison	With nausea and vomiting in pregnancy (NVP) versus no NVP; 134 (72%) women reporting experiencing nausea; with 40 (30%) vomiting (9 (4.8%) more than once a day) during the first trimester
Outcomes	Influence of nausea and vomiting in pregnancy on dietary intake; Severity of NVP assessed as having no nausea and vomiting, only nausea, vomiting once a day or vomiting more than once a day, with the primary outcome being presence or absence of nausea
Results	| | ***With NVP (n = 134)*** | ***Without NVP (n = 53)*** | ***p*** | | **Meat products (g), median (IQR) daily** | **98 (66 to 138)** | **121 (95 to 164)** | **0.004** |
Followup	To 34 weeks gestation
Confounding	Not reported if any of the analyses were adjusted
Risk of bias	Moderate risk of bias: not clear if analyses were adjusted for potential confounders
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Maconochie 2007**
Food groups	Meat: red meat
Study type	Case-control study (postal survey sampled from the electoral roll – National Women's Health Study)
Level of evidence	III-3 (aetiology)
Setting	UK general population
Funding	National Lottery Community Fund, Miscarriage Association
Participants	Cases: 603 women aged 18 to 55 years whose most recent pregnancy had ended in first trimester miscarriage (< 13 weeks gestation); Controls: 6116 women aged 18 to 55 years whose most recent pregnancy had progressed beyond 12 weeks
Baseline Comparisons	BMI < 18.5 was significantly associated with odds of miscarriage *Also see Confounding below*
Dietary Assessment	questionnaire
Timing	Diet in the three months prior to conception and the first 12 weeks of pregnancy
Comparison	At least twice weekly
Outcomes	First trimester miscarriage
Results	**Meat twice weekly or more** (see table below)
Length of followup	n/a
Confounding	Adjusted for year of conception, maternal age, previous miscarriage and previous live birth; and further adjusted for nausea in the first 12 weeks of pregnancy
Risk of bias	Low risk of bias: 88% of eligible women responding to stage 1 agreed to participate in the second stage of the study; and 71% responded to the stage 2 questionnaire. 1071/7790 records (7508 women) were excluded (mostly due to index pregnancy being conceived prior to 1980), leaving 6719 records (86%) available for analysis
Relevance	L ikely to be relevant to Australian women
Other comments	Women who suffered from nausea in the first 12 weeks of pregnancy were almost 70% less likely to miscarry

Meat twice weekly or more

	Cases	*Controls*	*aOR (95% CI)*	*aOR further adjusted for nausea*
No	262 (47%)	2324 (40%)	1.00	1.00
Yes	299 (53%)	3435 (60%)	1.03 (0.86 to 1.23)	0.98 (0.81 to 1.18)

Reference	**Mikkelsen 2008**
Dietary patterns	Mediterranean diet (consumption of fish twice a week or more, intake of olive or canola oil, high consumption of fruits and vegetables (5 a day or more), **meat (other than poultry or fish) at most twice a week**, and at most 2 cups of coffee a day)
Study type	Prospective cohort study
Level of evidence	II
Setting	Denmark (part of the Danish National Birth Cohort (DBNC))
Funding	March of Dimes Birth Defects Foundation, Danish National Research Foundation, Danish Medical Research Foundation, Danish Health Foundation, Danish Heart Foundation, EU FP7 consortium (EARNEST), Pharmacy Foundation, Egmont Foundation, Augustinus Foundation.
Participants	35,530 pregnant women recruited from 1996 to 2002 Exclusions: women who smoked, women aged < 21 and > 38 years, BMI < 19 and > 32, a history of more than 3 abortions, twin pregnancies, chronic hypertension, women with a calculated energy intake < 4,200 kJ and > 16,700 kJ
Baseline comparisons	BMIs were significantly lower in the MD and none groups.
Dietary assessment	FFQ
Timing	FFQ mailed to all DBNC participants in 25th week of gestation
Comparison	Meat ≤ 2 times a week v 3 or more times a week
Outcomes	Preterm birth
Results	**Preterm birth < 37 weeks** OR 0.97 95% CI 0.86 to 1.11 aOR 0.92 95% CI 0.81 to 1.05 **Early preterm birth < 35 weeks** OR 0.92 95% CI 0.74 to 1.14 aOR 0.86 95% CI 0.68 to 1.07 **Late preterm birth 35-36 weeks** OR 1.00 95% CI 0.86 to 1.17 aOR 0.96 95% CI 0.82 to 1.13
Followup	To birth
Confounding	Adjusted for parity, BMI, maternal height, socioeconomic status and cohabitant status
Risk of bias	Low risk of bias; GA based mostly on ultrasound; 0.36% missing data (127/35657)
Relevance	Relevance limited by exclusion of smokers and obese women
Other comments	

Reference	**Mitchell 2004**
Dietary patterns	Meat (including meat products)
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Waitemata Health or Auckland Healthcare regions, New Zealand
Funding	Health Research Council of New Zealand, Foundation for the Newborn, Child Health Research Foundation
Participants	Mothers of 1138 children born between October 1995 and November 1997 (844 born SGA and 870 born appropriate for GA); only term infants (> 37 weeks); Exclusions: preterm births (< 37 weeks), multiple births and those with congenital anomalies
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered after birth (to cover the periconception period and the last month of pregnancy)
Comparison	0-2 v > 2-4 v > 4-5 v > 5-6 v > 6 serves of meat per week
Outcomes	SGA (≤ 10^{th} centile for GA and gender)
Results	**SGA (Meat consumption at time of conception)**

	SGA	AGA	aOR	p value for trend
0-2	60/533 (11.3%)	42/598 (7.0%)	1.36 (0.80 to 2.29)	
>2-4	180/533 (33.8%)	193/598 (32.3%)	1.07 (0.76 to 1.51)	
>4-5	85/533 (15.9%)	114/598 (19.1%)	0.97 (0.64 to 1.45)	
>5-6	71/533 (13.3%)	81/598 (13.6%)	1.01 (0.65 to 1.56)	
>6	137/533 (25.7%)	168/598 (28.1%)	1	0.79

SGA (Meat consumption in last month of pregnancy)

	SGA	AGA	aOR (95% CI)	p value for trend
0-2	56/534 (10.5%)	57/597 (9.5%)	0.70 (0.43 to 1.16)	
>2-4	177/534 (33.1%)	202/597 (33.8%)	0.84 (0.59 to 1.19)	
>4-5	102/534 (19.1%)	123/597 (20.6%)	0.85 (0.57 to 1.26)	
>5-6	66/534 (12.4%)	72/597 (12.1%)	0.97 (0.62 to 1.53)	
>6	133/534 (24.9%	143/597 (24.0%)	1	0.66

Followup	NA
Confounding	Adjusted for socio-economic status, ethnicity, maternal height, maternal weight before pregnancy, maternal hypertension and maternal smoking; but folate supplementation was not controlled for (periconception folate was significantly associated with reduced SGA risk).
Risk of bias	Low-moderate risk of bias: Of the 2182 eligible infants, parents of 1714 (78.6%) completed the FFQ; 1138 (67%) of women completed the FFQ; missing items in completed FFQ treated as woman not consuming any meat
Relevance	Likely to be relevant to Australian women
Other comments	Only term infants included

Reference	**Miyake 2009 (follow-up of Saito 2009)**

Dietary patterns	Meat
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Osaka, Japan
Funding	Ministry of Education, Culture, Sports, Science, and Technology and Health and Labour Sciences Research Grants, Ministry of Health, Labour and Welfare, Japan
Participants	763 mother-child pairs (part of the Osaka Maternal and Child Health Study). Pregnant women recruited between November 2001 and March 2003
Baseline comparisons	*See below*
Dietary assessment	Diet history questionnaire (DHQ)
Timing	DHQ at mean 17.7 [SD 6.7] weeks gestation to reflect dietary intake for the previous month
Comparison	Quartiles of maternal meat consumption during pregnancy (medians in g/day adjusted energy intake; Q1 33.8; Q2 49.0; Q3 63.6; Q4 90.8
Outcomes	Wheeze and eczema in infants aged 16-24 months (ISAAC definitions)
Results	**Infant wheeze at 16-24 months (n=763)** ***OR (95% CI)*** / ***aOR (95% CI)*** Q1: 1.00 / 1.00 Q2: **0.61 (0.37 to 0.97)** / 0.67 (0.40 to 1.11) Q3: **0.57 (0.35 to 0.91)** / **0.57 (0.33 to 0.95)** Q4: 0.73 (0.46 to 1.16) / 0.77 (0.47 to 1.27) p for trend: 0.16 / 0.22 **Infant eczema at 16-24 months (n=763)** Q1: 1.00 / 1.00 Q2: 0.59 (0.34 to 1.01) / 0.68 (0.38 to 1.21) Q3: 0.76 (0.45 to 1.26) / 0.80 (0.46 to 1.39) Q4: 1.12 (0.69 to 1.83) / 1.31 (0.78 to 2.22) p for trend: 0.47 / 0.28
Followup	16-24 months after birth
Confounding	Adjusted for maternal age, gestation at baseline, place of residence at baseline, family income, maternal and paternal income, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, maternal intake of vitamin D and E during pregnancy, changes in maternal diet during the previous month, season when baseline data were collected, maternal smoking during pregnancy, baby's older siblings, baby's sex, baby's birthweight, household smoking, breastfeeding duration and time of birth before third follow-up survey
Risk of bias	Low risk of bias: of the 1002 women initially recruited, 763 mother-child pairs (76.3%) completed all three surveys (compared with non-participants, participants had higher incomes, higher education levels and were more likely higher intakes of fat, cholesterol, vitamin D & E
Relevance	Fish intake in Japan likely to be higher than in Australia
Other comments	75% of infants were breastfed for 6 months or longer.

Reference	**Miyake 2006**
Food groups	Meat
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Women who became pregnant in November 2001-March 2003 Neyagawa City, Osaka Prefecture and several surrounding municipalities (Osaka Maternal and Child Health Study, Japan)
Funding	Grant-in-Aid for Scientific Research (Government grant)
Participants	865 pregnant Japanese women
Baseline comparisons	*See Confounding below*
Dietary Assessment	Dietary history questionnaire-self administered
Timing	Diet survey for previous month at baseline (period of baseline not stated), EPDS at 2-9 months post partum
Comparison	Daily intake of meat Note: other dietary intakes analysed: dairy, fish, eggs, total fat, saturated fatty acids, cholesterol, LA, ALA and AA
Outcomes	Postpartum depression (EPDS with postpartum depression when score ≥ 9)
Results	No significant association between meat intake and postpartum depression on adjusted analysis
Length of follow up	2-9 months postpartum
Confounding	Age, gestation, parity, smoking, family structure, occupation, family income, education, changes in diet in previous month, season when baseline data collected, BMI, time of delivery, medical problems in pregnancy, baby's sex, baby's birthweight
Risk of bias	Low risk of bias: data for 865/1002 (86.5%) women available for analysis
Relevance	Australian diets very different to Japanese - much less seafood intake in Australia and more white fish rather than fatty fish
Other comments	Originally 1002 women enrolled only 865 completed (note: depressed persons less likely to participate), low rate of enrolment into study (17.2% of those eligible in Neyagawa)

Reference	**Peters 1994**
Food groups	Meat: breakfast meats (bacon, sausage, ham); luncheon meats (salami, pastrami, lunch meat, corned beef, bologna); hot dogs; charcoal broiled meats
Study type	Case control study
Level of evidence	III-3 (aetiology)
Setting	Los Angeles County, CA, USA
Funding	Electric Power Research Institute, National Institutes of Occupational Safety and Health
Participants	232 cases from birth to 10 years of age, ascertained through a population-based tumour registry from 1980 to 1987 232 controls (friends and random-digit dialling); matched on age, gender and ethnicity
Baseline comparisons	*See Confounding below*
Dietary Assessment	Dietary history questionnaire - interview
Timing	n/a
Comparison	Monthly servings – see results
Outcomes	Childhood leukemia
Results	See table below
Length of followup	n/a
Confounding	Analyses of mother's diet were not adjusted
Risk of bias	Moderate risk of bias: interviews were completed for 252/331 (76.1%) of the cases identified (22 physician refusals, 24 parent refusals and 33 untraceable cases); controls could not be found for 20 cases; adjusted analyses only presented for results that were significant on unadjusted analyses (therefore no there were no maternal diet analyses presented); not clear if mothers were asked to recall present diet or diet during pregnancy
Relevance	Likely to be reasonably similar to Australian diets
Other comments	Child's and father's diet assessed in addition to mother's diet

Results

	Servings per month				**CI for highest category**	**P for trend**
	None (0)	**Low (1 to 3.9)**	**Medium (4 to 11.9)**	**High (12+)**		
Ham, bacon, sausage						
Case/control (N)	75/67	65/84	64/55	25/23		
OR	1.0	0.7	1.0	1.0	0.5 to 2.0	0.8
Hot dogs						
Case/control (N)	106/110	79/92	30/18	37/29		
OR	1.0	0.9	1.8	2.4	0.7 to 8.1	0.1
Bologna, pastrami, salami, corned beef, lunch meat						
Case/control (N)	103/107	49/48	41/46	37/29		
OR	1.0	1.0	1.0	1.3	0.8 to 2.4	0.5
Hamburgers						
Case/control (N)	53/56	82/71	73/83	23/21		
OR	1.0	1.2	0.9	1.2	0.5 to 2.5	0.9
Charbroiled meats						
Case/control (N)	66/72	91/83	44/42	25/29		
OR	1.0	1.2	1.1	0.9	0.5 to 1.8	1.0

Reference	**Petridou 2005**
Food type	Meat and meat products
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Greece
Funding	The Childhood Hematology-Oncology Group: Athens University Medical School, Aristotle University of Thessaloniki, University Hospital of Heraklion
Participants	Cases: 131 children with acute lymphoblastic leukemia, aged 12 to 59 months, gender and age matched to Controls: 131 children hospitalised for minor conditions between 1999 and 2003
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During index pregnancy
Comparison	Quintiles of meat and meat products – median Q1; 25 g/day: median Q5 61 g/day
Outcomes	Acute lymphoblastic leukemia (ALL)
Results	see below
Followup	NA
Confounding	Total energy intake (but not mutually among food groups); matching variables; maternal age at birth; birthweight; maternal smoking during pregnancy; maternal years of schooling, maternal occupation
Risk of bias	Moderate: moderate risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy some time previously; Cases: 171 children with ALL were identified; 21 had missing data, consent was not given in 9 cases and 10 were unable to be matched, leaving 131 (77%) of cases available
Relevance	Diets of Greek women may differ from current diets of Australian women
Other comments	

Results:

	Median g/day	**Cases**	**Controls**	**P for trend**
Q1:	25	23	30	
Q2:	33	28	30	
Q3:	39	17	31	
Q4:	46	29	24	
Q5:	61	34	16	**0.01**

Logistic regression: one quintile more of meat/meat products: aOR 1.25 95% CI 1.09 to 1.57

Reference	**Petridou 1998**
Food type	Meat and meat products: pork, veal, lamb, goat,chicken, turkey, ham, salami and sauages, liver and other offal, eggs, meat pie (0.5), moussaka (0.5), pastitsio (0.5).
Study type	Case-control study
Level of evidence	III-3
Setting	Greater Athens area, Greece
Funding	Greek Ministry of Health and Welfare, and Foundation for Research in Childhood 'S. Doxiadis'
Participants	Cases: 109 children with cerebral palsy (CP), born between 1984 and 1988 (estimated to be two-thirds of the children with CP born during this period) Controls (1): 155 neighbouring children of similar sex and age (± 12 months) Controls (2): 99 healthy siblings of similar sex and age (± 12 months) of the first neurological patient seen by the attending physician after a visit by the CP patient
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During pregnancy
Comparison	≤ 4 versus 5-6 versus 7-8 versus > 8 serves of meat per week; regression analysis: risk of cerebral palsy with change in consumption by one unit (= consumption of meat twice weekly)
Outcomes	Cerebral palsy
Results	≤ 4 serves of meat per week: 7/91 (7.7%) cases v 35/246 (14.2%) controls 5-6 serves of meat per week: 23/91 (25.3%) cases v 88/246 (35.8%) controls 7-8 serves of meat a week: 24/91 (26.4%) cases v 72/246 (29.3%) controls > 8 serves of meat a week: 37/91 (40.6%) cases v 51 (20.7%) controls Regression analysis for each unit of consumption of meat 2 times per week: **aOR 1.45 95% CI 1.11 to 1.89** **aOR 1.42 95% CI 1.07 to 1.88 (additionally adjusted for all food groups)**
Followup	8 years
Confounding	Age and sex of child, maternal age at birth, maternal age at menarche, maternal chronic disease, previous spontaneous abortions, persistent vomiting during index pregnancy, multiple pregnancy, number of obstetric visits; timing of membrane rupture in index birth, use of general anaesthesia in the index birth, mode of birth, abnormal placenta, infant head circumference at birth, congenital malformation, place of index birth, use of supplementary iron during index pregnancy, physical exercise during index pregnancy, painless childbirth classes. The following were not included in the model: - Smoking or consumption of coffee or alcohol during pregnancy (stated to be "unrelated to CP and had no confounding influence"); - Gestational age, birthweight and maternal weight gain (stated to be "strong predictors of CP, but were not included in the model, since they are probably intermediate stages in a possible link between diet and CP (mediators) rather than genuine confounders"
Risk of bias	Moderate-high: High risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy 8 years previously; Cases: 109 children with CP were identified; for 6 children either collaboration with their guardian or a diagnosis of CP was not confirmed; and reliable maternal dietary intakes were not available for 12 women, leaving 91 cases available for analysis. Controls: 278 mother-child pairs were approached; 16 refused to participate; matching controls were not available in 8 instances, and reliable maternal dietary intakes were not available for 8 women, leaving 246 controls available for analysis. Regression analysis and use of consumption does not indicate any threshold effects e.g. benefit/harm differences at different levels of consumption.
Relevance	Diets of Greek women in 1998 may differ from current diets of Australian women
Other comments	Eggs included under 'Meat' category

Reference	**Pogoda 2009**
Food type	Meat: cured meat; noncured meat
Study type	Case-control study Separate centre reports: Preston-Martin 1996 (Los Angeles); Lubin 2000 (Israel); Cordier 1994 (France); McCredie 1994 (Australia)
Level of evidence	III-3 (aetiology)
Setting	International (seven countries – USA, Israel, Italy, Spain, Australia, France and Canada (International Collaborative Study of Childhood Brain Tumors)
Funding	NIH, California Department of Health, Southern California Environmental Health Sciences Center, National Cancer Institutes, Cancer Surveillance System of Western Washington, Fred Hutchinson Cancer Research Center, Fondo de Investigaciones Sanitarias of Spain, Conselleria de Sanitat i Consum of Valencian Autonomous Community for the Childhood Cancer Registry of the Province of Valencia, Spanish Society of Paediatric Oncology with the National Childhood Cancer Registry, ISCIII-RTIC, Villavecchia Foundation and Scientific Foundation of the AECC
Participants	Cases: 1281 Controls: 2223 Years of diagnosis varied between centres, ranging from 1976 to 1992 (with most diagnosed between 1982 and 1992) Controls were frequency matched to cases in US centres and in France; otherwise they were individually matched (by region of residence, age, sex, and geographic area (except for Sydney and Los Angeles))
Baseline comparisons	*See confounding below*
Dietary assessment	Standardised study questionnaire using detailed dietary recall methods and abstract food models to gauge portion size
Timing	Diet during the past year and during the index pregnancy
Comparison	Quartiles
Outcomes	Childhood brain tumours
Results	

Results

	Controls	**Cases**	**aOR 95% CI**
<u>All tumours (n = 1204 cases)</u>			
Cured meat			
Q1	873 (40%)	375 (32%)	1.0
Q2	545 (21%)	236 (20%)	1.1 (0.9 to 1.2)
Q3	430 (20%)	261 (23%)	**1.2 (1.0 to 1.5)**
Q4	413 (19%)	284 (25%)	**1.5 (1.1 to 2.1)**
P for trend = 0.03			
Noncured meat			
Q1	1187 (54%)	652 (55%)	1.0
Q2	285 (13%)	145 (12%)	1.0 (0.9 to 1.2)
Q3	274 (13%)	133 (11%)	1.0 (0.8 to 1.2)
Q4	437 (20%)	247 (21%)	**1.2 (1.0 to 1.3)**
P for trend = 0.19			
<u>Astroglials (n = 621 cases)</u>			
Cured meat			
Q1	873 (40%)	170 (29%)	1.0
Q2	454 (21%)	128 (22%)	**1.1 (1.0 to 1.3)**
Q3	430 (20%)	132 (22%)	**1.3 (1.0 to 1.9)**
Q4	413 (19%)	161 (27%)	**1.8 (1.2 to 2.6)**
P for trend = 0.01			
Noncured meat			
Q1	1187 (54%)	345 (57%)	1.0
Q2	285 (13%)	73 (12%)	1.0 (0.9 to 1.1)
Q3	274 (13%)	58 (10%)	0.9 (0.6 to 1.3)

	Q4	437 (20%)	128 (21%)	**1.2 (1.0 to 1.4)**	
	P for trend = 0.49				
	Primitive neural ectodermal tumors (PNETs) (n = 257 cases)				
	Cured meat				
	Q1	873 (40%)	87 (36%)	1.0	
	Q2	454 (21%)	43 (18%)	1.1 (0.8 to 1.4)	
	Q3	430 (20%)	59 (24%)	1.1 (0.9 to 1.4)	
	Q4	413 (19%)	52 (22%)	1.2 (0.9 to 1.6)	
	P for trend = 0.15				
	Noncured meat				
	Q1	1187 (54%)	137 (55%)	1.0	
	Q2	285 (13%)	27 (11%)	0.9 (0.6 to 1.5)	
	Q3	274 (13%)	34 (14%)	**1.2 (1.0 to 1.4)**	
	Q4	437 (20%)	49 (20%)	1.0 (0.8 to 1.3)	
	P for trend = 0.45				
	<u>Tumour subtypes</u>				
	Astrocytomas				
		Pilocytic (142 cases)	**Anaplastic (96 cases)**	**Other (199 cases)**	
	Cured meat	***2.5 (1.1 to 5.8)***	***2.1 (1.1 to 4.3)***	***1.8 (1.2 to 2.7)***	
	P for trend	***0.03***	***0.004***	***0.008***	
	Noncured meat	1.1 (0.5 to 2.8)	1.2 (0.3 to 4.6)	***1.2 (1.1 to 1.3)***	
	P for trend	0.54	0.72	0.46	
	Other types				
		Malignant gliomas (122 cases)	**Medulloblastomas (193 cases)**	**PNET (64 cases)**	**Ependymomas (104 cases)**
	Cured meat	1.9 (0.9 to 3.9)	1.1 (0.9 to 1.3)	1.5 (0.5 to 4.8)	2.0 (1.4 to 2.9)
	P for trend	0.13	0.43	0.38	0.03
	Noncured meat	0.9 (0.7 to 1.3)	1.0 (0.7 to 1.5)	1.1 (0.6 to 1.9)	1.3 (0.7 to 2.2)
	P for trend	0.74	0.41	0.65	0.70
Followup	n/a				
Confounding	Analyses adjusted for age and sex of child, study centre and each food group; Adjustment for total intake of foods had little effect on estimates				
Risk of bias	Low-moderate risk of bias: 75% of eligible cases and 71% of eligible controls participated (based on centres for which these data were available); some lack of standardisation in dietary assessments between study centres; potentially high risk of recall bias for women whose pregnancies may have been at least 10 years previously.				
Relevance	Likely to be relevant to Australian women				
Other comments					

Reference	**Pogoda 2001**
Food type	Cured meat
Study type	Case-control
Level of evidence	III-3 (aetiology)
Setting	From a study about childhood brain tumours in 19 counties on the U.S. West Coast (U.S. West Coast Childhood Brain Tumour Study) Cases: This study includes 3 U.S. centres (Los Angeles County, the five counties in the San Francisco-Oakland metropolitan area, 13 counties in western Washington state) and approximately half the total number of children with brain tumours
Funding	Grants from National Cancer Institute and Cancer Research Foundation of America
Participants	**Cases**: 540 children aged 0-19 years old and diagnosed with a primary brain tumour between January 1984-December 1990 (Seattle and San Francisco) or 1991 (Los Angeles) identified from the cancer registry in each area. 813 cases were identified, physicians permission to contact family for 790 (97%) cases, 51 of these ineligible. Of the remaining 739 cases 106 (14%) family could not be located, 73 (10%) declined, 20 (3%) did not participate. 540/739 (73%) mothers eligible and interviewed. **Controls**: 801 children whose biological mothers had to be available for interview in English or Spanish, have a telephone, provide informed consent. Controls were selected from the same geographic areas as cases using 2-step random digit dialling procedure and were similar in age and gender. A screening interview to determine eligibility into study conducted on 88.3%(6170 of 6990) residents called, 67% (801) of those eligible (1196) agreed and were interviewed Ratio= approximately 2 controls for every case
Baseline comparisons	*See Confounding below*
Dietary Assessment Method	Detailed dietary recall in-person interview for the past year and during the pregnancy
Timing	Interview after diagnosis and contact and consent with family (up to 19 years after pregnancy)
Comparison	Estimated daily nitrate intake (using literature of nitrate content of meats and amounts reported in food recall interview) from cured meats: Ham, Bacon, Hot dogs, Sausage and other cured meats (Lunch meat, meatloaf, pork)
Outcomes	Childhood (0-19 years old) diagnosis of tumour of the brain, cranial nerves or cranial meninges
Results	See Table 2 below

Table 2 Comparison of odds ratios (OR) and 95% confidence intervals (CI) at fixed categories of maternal nitrite exposure from consumption of cured meats during pregnancy by source of nitrite estimation, US West Coast Childhood Brain Tumour case-control study, 1984-1991

Average daily nitrite from cured meats (mg)	Time-specific nitrite estimates from literature review			Nitrate estimates from dietary conversion software		
	No. of cases (%)	No. of controls (%)	OR (95%CI)	No. of cases (%)	No. of controls (%)	OR (95%CI)
0	102 (20)	161 (20)	1.0	102 (20)	161 (20)	1.0
0.01-0.49	293 (57)	499 (63)	1.1 (0.8, 1.5)	377 (73)	601 (75)	1.2 (0.9, 1.6)
0.50-0.99	68 (13)	79 (9)	1.9 (1.2, 2.9)	27 (5)	24 (3)	2.3 (1.3, 4.4
1.00-1.99	28 (5)	43 (5)	1.3 (0.8, 2.3)	6 (1)	10 (1)	1.3 (0.5, 3.3)*
2.00-2.99	12 (2)	13 (2)	1.8 (0.8, 4.1)	2 (0.4)	0 (0)	-
≥3.0	11 (2)	9 (1)	3.0 (1.2, 7.9	0 (0)	1 (0.1)	-

* Includes two cases and one control with exposure ≥2 mg day $^{-1}$.

Follow-up	0-19 years (age of diagnosis)
Confounding	None mentioned
Risk of bias	Low
Relevance	Nitrate levels in cured meats likely to be similar to Australian??
Other comments	Note this is an updated analysis (of nitrite) of the same sample/study in Preston-Martin 1996 **Note: no direct link between meat intake and brain tumour risk, only nitrite intake (via cured meat intake) and brain tumour risk**

Reference	**Radesky 2008**
Food type	Meat: red meat (beef, lamb, pork or hamburger); processed meat (bacon, hot dogs, sausage, salami, bologna and other processed meats)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Boston, MA, USA
Funding	NIH, March of Dimes Birth Defects Foundation, Harvard Medical School Division of Nutrition, Harvard Pilgrim Health Care Foundation
Participants	1773 women with singleton pregnancies enrolled in Project Viva (initial antenatal visit before 22 weeks gestation, able to complete study forms in English, did not plan to move out of the study area before birth
Baseline comparisons	Included women had lower pregnancy BMIs than excluded women, were less likely to be African-American or Hispanic, to have low SES *See confounding below*
Dietary assessment	FFQ
Timing	FFQ completed at first antenatal visit at a mean 11.8 weeks GA (range 5-25.6 weeks) - to assess diet during first trimester
Comparison	Daily intake of red meat; and processed meat
Outcomes	Glucose tolerance testing at 26-28 weeks gestation – GDM; impaired glucose tolerance (IGT) Normal glucose tolerance defined as: < 140 mg/dL 1 hour after a 50 g glucose load (non-fasting oral glucose challenge test); IGT defined as ≥ 140 mg/dL on non-fasting oral glucose challenge test but 0 or 1 abnormal result for a fasting glucose tolerance test (100g oral glucose load where normal = < 95 mg/dL at baseline, < 180 mg/dL at 1 h, < 155 mg/dL at 2 h and < 140 mg/dL at 3 h; GDM defined as ≥ 140 mg/dL on non-fasting oral glucose challenge test with 2 or more abnormal GTT results (For the 39 women with incomplete glucose testing data, medical records were used to assign them to normal glucose tolerance (n = 7), IGT (n = 10), or GDM (n = 22).
Results	**Impaired glucose tolerance (per weekly serving of red meat):** aOR 1.01 95% CI 0.95 to 1.08 **GDM (per weekly serving of red meat):** aOR 1.01 95% CI 0.91 to 1.12 **Impaired glucose tolerance (per weekly serving of processed meat):** aOR 1.02 95% CI 0.94 to 1.10 **GDM (per weekly serving of processed meat):** aOR 0.95 95% CI 0.85 to 1.06
Followup	To birth
Confounding	Adjusted for maternal age, pre-pregnancy BMI, ethnicity, family history of diabetes, history of GDM in a prior pregnancy, smoking in index pregnancy; Used energy partition models and nutrient density substitution models to study the simultaneous effects of different macronutrients on GDM and IGT risk; Other studies have not adjusted for different types of fats – which may have opposing effects on risk of GDM
Risk of bias	Low risk of bias: Of 2128 women who gave birth to a live infant, 24 were excluded for missing or incomplete glucose tolerance testing records; 18 with a history of previous type 1 or 2 DM or PCOS with glucose intolerance, 342 missing or implausible first trimester diet information; 11 completion of FFQ after 26 weeks GA (i.e. after glucose tolerance screening) or on an unknown date; leaving 1773 (83.3%) available for analysis
Relevance	Likely to be relevant to Australian women
Other comments	Paper concludes that “nutritional status entering pregnancy, as reflected by pre-pregnancy BMI, is probably more important than pregnancy diet in development of GDM”

Reference	**Saito 2010**
Food type	Meat
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Neyagawa City, Japan
Funding	Ministry of Education, Culture, Sports, Science and Technology and Health and Labour Sciences, Ministry of Health, Labour and Welfare, Japan
Participants	771 mother-child pairs recruited from November 2001 to March 2003 at any stage of pregnancy – mean GA 18 weeks (part of the Osaka Maternal and Child Health Study)
Baseline comparisons	*See confounding below*
Dietary assessment	Diet history questionnaire (DHQ)
Timing	DHQ to assess dietary habits during the preceding month
Comparison	Quartiles of meat consumption
Outcomes	Suspected atopic eczema
Results	**Suspected atopic eczema** *n/N* / *OR (95% CI)* / *aOR (95% CI)* Q1 (33.4 g/day): 10/192; 1.00; 1.00 Q2 (49.1 g/day): 14/193; 1.42 (0.62 to 3.38); 1.46 (0.61 to 3.62) Q3 (63.6 g/day): 19/193; 1.99 (0.92 to 4.56); **2.41 (1.06 to 5.75)** **Q4 (89.8 g/day): 22/193; 2.34 (1.10 to 5.30); 2.59 (1.15 to 6.17)** **p value for trend (unadjusted): 0.02** **p value for trend (adjusted): 0.01**
Followup	3-4 months
Confounding	Adjusted for maternal age, gestation at baseline, family income, maternal and paternal education, maternal and paternal history of asthma, atopic eczema and allergic rhinitis, mite allergen level from maternal bedclothes, vacuuming living room, mould in kitchen, changes in maternal diet in previous month, season when baseline data collected, baby's older siblings, baby's sex, baby's birthweight, breastfeeding and bathing or showering infant
Risk of bias	Low risk of bias: Of 1002 eligible women, a final sample of 771 (77%) was available for analysis
Relevance	Fish intake in Japan likely to be higher than in Australia
Other comments	

Results (Suspected atopic eczema):

	n/N	*OR (95% CI)*	*aOR (95% CI)*
Q1 (33.4 g/day)	10/192	1.00	1.00
Q2 (49.1 g/day)	14/193	1.42 (0.62 to 3.38)	1.46 (0.61 to 3.62)
Q3 (63.6 g/day)	19/193	1.99 (0.92 to 4.56)	**2.41 (1.06 to 5.75)**
Q4 (89.8 g/day)	**22/193**	**2.34 (1.10 to 5.30)**	**2.59 (1.15 to 6.17)**

Reference	**Sarasua 1994**
Food type	Meat – cured or broiled [grilled] (ham, bacon or sausage; hot dogs, hamburgers; bologna, pastrami, corned beef, salami or lunch meat; charcoal broiled foods)
Study type	Case-control
Level of evidence	III-3 (aetiology)
Setting	Denver, Colorado, US
Funding	Not reported
Participants	234 cancer cases (including 56 acute lymphoblastic leukemia, 45 brain tumour, 25 lymphoma, 24 soft tissue sarcoma) diagnosed between 1976 to 1983 in children 0 to 14 years of age; 206 controls, selected by random-digit dialling
Baseline comparisons	*See confounding below*
Dietary assessment	In-home interview with a parent (generally the mother)
Timing	To assess how often each of the meat groups was eaten by the mother during pregnancy
Comparison	Generally < once per week versus more than once a week; Hot dogs and charcoal broiled foods: never versus more than 0 times a week
Outcomes	Cancers
Results	

	No. of controls	n (cases)	aOR (95% CI)
Acute lymphoblastic leukemia			
Ham, bacon, sausage			
< 1/week	82	17	1.0
1+/week	124	39	1.5 (0.7 to 3.0)
Hot dogs			
0/week	81	21	1.0
>0/week	125	35	0.9 (0.4 to 1.8)
Hamburgers			
< 1/week	55	11	1.0
1+/week	151	45	1.2 (0.5 to 2.7)
Lunch meats			
< 1/week	90	24	1.0
1+/week	116	32	1.0 (0.5 to 2.0)
Charcoal-broiled foods			
0/week	84	25	1.0
>0/week	122	31	1.0 (0.5 to 1.9)
Brain tumors			
Ham, bacon, sausage			
< 1/week	82	18	1.0
1+/week	124	27	1.0 (0.5 to 2.1)
Hot dogs			
0/week	81	12	1.0
>0/week	125	33	2.3 (1.0 to 5.4)
Hamburgers			
< 1/week	55	14	1.0
1+/week	121	31	0.7 (0.3 to 1.6)

	Lunch meats			
	< 1/week	90	26	1.0
	1+/week	116	19	**0.4 (0.2 to 0.8)**
	Charcoal-broiled foods			
	0/week	84	24	1.0
	>0/week	122	21	0.6 (0.3 to 1.2)
	Lymphomas – no significant association with lunch meat OR 2.3 95% CI 0.9 to 6.0; or with ham, bacon, sausage or hamburgers (OR 1.3 to 1.5) [CIs not given] **Soft tissue sarcoma** - no significant associations with meats (exact numbers not reported)			
Followup	n/a			
Confounding	Adjusted for other types of meat, age at diagnosis, and per capita income			
Risk of bias	Low to moderate risk of bias: Of the 356 eligible cases, 252 (708%) were interviewed; mothers asked to recall diet during a pregnancy up to 14 years previously			
Relevance	Likely to be relevant to Australian women			
Other comments	Mothers in lower income households were more frequent consumers of hamburgers and ham, bacon or sausage (1.5 versus 1.1 serves per week); Maternal vitamin supplementation attenuated the adverse effects of meat consumption; Associations with children's diets were stronger than those with maternal diets during pregnancy			

Reference	**Shiell 2001**
Food groups	Meat
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Motherwell, Scotland
Funding	Dunhill Medical Trust
Participants	626 (274 men and 352 women) whose mothers' food intakes had been recorded during pregnancy during 1967 to 1968. These women had been advised to eat 0.45 kg of red meat a day and to avoid carbohydrate-rich foods during pregnancy
Baseline comparisons	*See confounding below*
Dietary assessment	Mothers asked about consumption of 10 foods
Timing	Early pregnancy (≤ 20 weeks); late pregnancy (> 20 weeks)
Comparison	Maternal consumption of meat (mean consumption in late pregnancy was 13.3 [SD 5.8] serves per week – nearly double that of early pregnancy)
Outcomes	Systolic and diastolic blood pressure at in offspring aged 27 to 30 years
Results	**<u>Systolic blood pressure at 27 to 30 years</u>** **Regression coefficient for amount of maternal meat consumption; ß 0.21 95% CI 0.04 to 0.37, p = 0.01** **<u>Diastolic blood pressure at 27 to 30 years</u>** Regression coefficient for amount of maternal meat consumption; ß 0.00 95% CI -0.12 to 0.13, p = 0.96
Length of followup	27 to 30 years
Confounding	Analyses adjusted for offspring's gender, BMI, alcohol consumption, and cuff size used for blood pressure
Risk of bias	Moderate risk of bias: For the 1432 records from 1967-8 recorded liveborn, singleton births with complete names, birth measurements and ≥ 1 diet record. 965 offspring were alive and living locally; and after attrition or declining to participate, 626 (43.7%) were available for analysis.
Relevance	Very high intake of meat and very low carbohydrate intake limits the relevance to current dietary intakes of Australian women
Other comments	Authors state that "low intake of green vegetables, a source of folate, accentuated the effect of high meat and fish consumption on systolic blood pressure"

Reference	Stuebe 2009
Dietary patterns	Meat: red and processed meats
Study type	Prospective cohort study (Project Viva)
Level of evidence	II (aetiology)
Setting	8 urban and suburban obstetric offices of a multispecialty group practice in eastern Massachusetts, USA
Funding	US NIH, Harvard Medical School, Harvard Pilgrim Health Care Foundation
Participants	1338 women giving birth to a live singleton infant, < 22 weeks gestation at study entry; 379 (27%) were overweight (BMI ≥ 26); 703 (51%) experienced excessive weight gain Exclusions: not fluent in English
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Administered in first and second trimesters of pregnancy
Comparison	Red and processed meats (serves per day)
Outcomes	Excessive gestational weight gain (IOM 1990)
Results	**Excessive gestational weight gain: red and processed meat** **Serves per day, median** — **Inadequate/adequate GWG**; **excessive GWG**; **aOR (95% CI)** Meat: 0.53 [SD0.40]; 0.56 [SD0.39]; 1.00 (0.74 to 1.34)
Followup	To birth
Confounding	Adjusted for pre-pregnancy BMI, maternal age, race/ethnicity, smoking status, gestational age at birth, nausea in first trimester in pregnancy
Risk of bias	Low risk of bias: Of 2083 eligible women, 1388 (67%) of women had data available for analysis (31 had missing information on pre-pregnancy BMI and gestational weight gain; 226 had missing covariate information and 438 had missing data on either first or second-trimester diet and mid-pregnancy physical activity); included women were less likely to be African-American or Hispanic, to be younger, multiparous and obese
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Yin 2010 (see also Jones 2000)**
Food type	Meat
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Southern Tasmania, Australia
Funding	NHMRC, Tasmanian Government, Royal Hobart Hospital Acute Care Program
Participants	216 adolescents born in 1988 (part of a larger infant health study of babies at high risk of SIDS) Exclusions: multiple pregnancies
Baseline comparisons	Children with unemployed fathers more likely to have been excluded due to missing data
Dietary assessment	FFQ
Timing	Dietary intake during third trimester of pregnancy
Comparison	Linear regression of density (portions per kJ)
Outcomes	Bone mass (bone mineral density (BMD) and bone mineral content*) in 16 year old adolescents
Results	**BMD at 16 years;** **Total body (g/cm^2)** r^2 -0.002; ß +10.4 (pns) adjusted r^2 0.3324; ß +6.1 (pns) **Femoral neck (g/cm^2)** r^2 0.000 ß +17.3 (pns) adjusted r^2 0.349; ß +11.1 (pns) **Lumbar spine (g/cm^2)** r^2 -0.004; ß -8.4 (pns) adjusted r^2 0.200; ß -12.5 (pns)
Followup	16 years
Confounding	Analyses were adjusted for sex, weight at age 16 years, sunlight exposure in winter at age 16 years, smoking during pregnancy, sports participation, ever breast-fed, current calcium intake, Tanner stage, maternal age at the time of childbirth and "other factors" [these other factors were not listed in the paper]
Risk of bias	Moderate-high: 415 children were followed from birth to age 16. This dropped to 216 (dietary information missing or unreliable for 138 mothers, 47 multiple births, 14 participants had missing data for confounders) representing 52% of participants followed from birth to age 16. 70% of the 216 participants were male. Gender imbalance suggests potential selection bias (due to original selection of infants at high risk of SIDS)
Relevance	Infants at high risk of SIDS represent a selected group (more males, preterm births, teenage mothers, smoking during pregnancy)
Other comments	*Bone mineral content results not reported; Study flow figures differ between 2000 and 2010 reports (e.g. numbers of multiple births)

Reference	**Zhang 2006**
Food type	Meat: meat (beef, pork, lamb, hamburger); processed meat (bacon, hot dogs, sausage, salami, bologna and other processed meats)
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	USA
Funding	NIH
Participants	13,110 women who were free of cardiovascular disease, cancer, type 2 diabetes and history of GDM with at least one singleton pregnancy between 1992 to 1998 (part of the Nurses' Health Study II); Exclusions: incomplete FFQ, implausible dietary intake
Baseline comparisons	*See Confounding below* Sensitivity analyses done for nulliparous women as they were over-represented (due to exclusion of women with a history of GDM)
Dietary assessment	FFQ
Timing	Dietary intake over previous year (i.e. at least some pre-pregnancy coverage)
Comparison	Quintiles of red meat and processed meat consumption; single meat item intakes were divided into none; < 0.14 serve per day (one serve per week); ≥ 0.14 serve per day
Outcomes	GDM
Results	**GDM (RR 95% CI)**

	Q1	**Q**	**Q3**	**Q4**	**□5**	**P for trend**
Red meat (servings/day)						
Median (range)	0.14 (0-0.21)	0.35 (0.28-0.35)	0.49 (0.42-0.56)	0.71 (0.57-0.85)	1.07 (0.86-3.50)	
Number of cases of GDM	118	135	173	152	180	
Person-years	21,965	20,925	21,955	16,691	18,366	
aRR (age, parity)	1.00	**1.37 (1.07 to 1.76)**	**1.78 (1.40 to 2.25)**	**2.16 (1.69 to 2.75)**	**2.36 (1.86 to 2.99)**	**<0.0001**
aRR (age, parity, BMI)	1.00	**1.28 (1.00 to 1.64)**	**1.59 (1.26 to 2.02)**	**1.87 (1.46 to 2.38)**	**1.92 (1.52 to 2.44)**	**<0.0001**
aRR (see below)	1.00	1.25 (0.97 to 1.60)	**1.52 (1.19 to 1.94)**	**1.73 (1.35 to 2.23)**	**1.74 (1.35 to 2.26)**	**<0.0001**

After adjustment for fatty acids and cholesterol, p for trend = 0.006
After adjustment for dietary haem iron, p for trend = 0.08

RR 1.61 95% CI 1.25 to 2.07 for each serve increment

Total processed meat						
Serves/day	0	0.07	0.14	0.21 – 0.35	0.42 – 4.47	
Number of cases of GDM	104	107	147	185	195	
Person-years	18,411	18,136	21,341	21,022	20,722	
aRR (age, parity)	1.00	**1.42 (1.03 to 1.73)**	**1.55 (1.20 to 1.99)**	**1.90 (1.49 to 2.42)**	**2.21 (1.73 to 2.81)**	**<0.001**
aRR (age, parity, BMI)	1.00	**1.33 (1.03 to 1.73)**	**1.40 (1.08 to 1.80)**	**1.68 (1.31 to 2.14)**	**1.87 (1.46 to 2.38)**	**<0.001**
aRR (see below)	1.00	1.29 (0.99 to 1.67)	**1.33 (1.03 to 1.72)**	**1.58 (1.23 to 2.02)**	**1.68 (1.30 to 2.16)**	**0.0003**

After adjustment for fatty acids and cholesterol, p for trend = 0.049
After adjustment for dietary haem iron, p for trend = 0.01

Bacon						
Serves/day		0	0.07	≥0.14		

	Number of cases of GDM	328	333	97	
	Person-years	48,102	41,701	9829	
	aRR (age, parity)	1.00	**1.43 (1.23 to 1.67)**	**1.51 (1.20 to 1.89)**	**<0.0001**
	aRR (age, parity, BMI)	1.00	**1.35 (1.16 to 1.58)**	**1.37 (1.10 to 1.73)**	**0.0002**
	aRR (see below)	1.00	**1.32 (1.13 to 1.55)**	**1.29 (1.02 to 1.63)**	**0.002**
	Hotdogs				
	Serves/day	0	0.07	≥0.14	
	Number of cases of GDM	271	355	122	
	Person-years	37,770	47,685	14,177	
	aRR (age, parity)	**1.00**	**1.41 (1.20 to 1.66)**	**1.60 (1.29 to 1.99)**	**<0.0001**
	aRR (age, parity, BMI)	**1.00**	**1.29 (1.10 to 1.52)**	**1.38 (1.11 to 1.72)**	**0.0007**
	aRR (see below)	**1.00**	**1.22(1.04 to 1.44)**	**1.25 (1.00 to 1.56)**	**0.02**
	Sausages, salami, bologna and other processed meats				
	Serves/day	0	0.07	≥0.14	
	Number of cases of GDM	183	309	266	
	Person-years	28,484	44,538	26,610	
	aRR (age, parity)	**1.00**	**1.40 (1.16 to 1.68)**	**1.92 (1.59 to 2.32)**	**<0.0001**
	aRR (age, parity, BMI)	**1.00**	**1.30 (1.08 to 1.57)**	**1.72 (1.42 to 2.08)**	**<0.0001**
	aRR (see below)	**1.00**	**1.26 (1.05 to 1.52)**	**1.60 (1.31 to 1.95)**	**<0.0001**
Followup	Variable				
Confounding	Analyses were adjusted for parity, age, BMI, smoking status, race/ethnicity, family history of diabetes, physical activity, dietary variables including total fat (% energy), cereal fibre, alcohol consumption, glycaemic load and total energy intake				
Risk of bias	Low risk of bias				
Relevance	Likely to be relevant to Australian women				
Other comments	Based on assumption that a woman's diet remains similar over time				

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Nuts and Seeds

Included Studies

Study	Outcomes
1. Chatzi 2008	Child persistent wheeze, atopic wheeze, atopy (all at 6.5 years)
2. Haggarty 2009	Deprivation
3. Hourihane 1996	Childhood allergy
4. Jensen 2004	Childhood acute lymphoblastic leukemia
5. Sausenthaler 2007	Allergic sensitisation, eczema at 2 yrs
6. Thompson 2010 (SR)	Childhood allergy
7. Vadas 2001	Peanut protein in breast milk
8. Venter 2009	Infant food allergy sensitisation
9. Willers 2008	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable 'asthma symptoms' in the last 12 months (measured longitudinally from 1 to 8 years age)

Evidence Summaries

	N	Level	References
Maternal Outcomes			
1. In a Scottish cohort study, maternal intake of nuts and seeds during pregnancy was not associated with **deprivation**	1277	II	Haggarty 2009
Breastfeeding Outcomes			
2. In a small before and after study from North America, peanut protein persisted longer than 6 hours in the **breastmilk** of only one out of 23 women	23	IV	Vadas 2001
Childhood – Asthma, Eczema and Other Allergy Outcomes			
3. In a German cohort study, maternal intake of nuts or seeds during pregnancy was not associated with **eczema** or **allergic sensitisation** (food or inhalant) in children at two years of age	3097	II	Sausenthaler 2007
4. In a systematic review of two case-control studies, maternal peanut consumption during pregnancy and breastfeeding was not associated with **sensitisation and peanut allergy**	2 studies	I (SR)	Thompson 2010
5. In a cross-sectional survey from the UK there was some indication that **peanut allergy** presents earlier in children of women consuming peanuts regularly (at least weekly) during pregnancy and lactation	622	IV	Hourihane 1996
6. In a cohort study from the UK, no association was seen between maternal consumption of peanuts during pregnancy and development of **food hypersensitivity** in infants up to three years of age	969	II	Venter 2009
7. In a Spanish cohort study, maternal intake under two serves of nuts a week compared with two or more serves a week did not show any significant differences in the rates of **persistent wheeze, atopic wheeze or atopy** in children at 6.5 years of age	482 children	II	Chatzi 2008
8. In a Dutch cohort study, maternal consumption of nut products (but not nuts) during pregnancy was associated with a significant increase in **asthma symptoms** in children at eight years of age: aOR 1.47 95% CI 1.08 to 1.99 for daily versus rare consumption of nut products	2832 children	II	Willers 2008
Other Childhood Outcomes			
9. In a US case-control study, maternal consumption of peanuts and peanut butter (mean of 3 serves a day) during pregnancy was not associated with **childhood acute lymphoblastic leukemia**	138 cases; 138 controls	III-3	Jensen 2004

Evidence Tables

Reference	**Chatzi 2008**
Food type	Nuts
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women presenting antenatal care at general practices in Menorca, a Mediterranean island in Spain (mid 1997 to mid 1998)
Funding	Instituto de Salud Carlos III red de Grupos Infancia y Media Ambiente, the Fundacio “La Caixa” , Instituto de Salud Carlos III, red de Centros de Investigacion en Epidemiologica y Salud Publica, EU, National Center for Environmental Health, USA, the GA^2LEN project, Ministry of Education and Science, Spain, Oficina de Ciencia y Tecnologia, Generalitat Valenciana.
Participants	482 children of 507 women who had attended antenatal care in Menorca
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	not clear when women did FFQ and period of pregnancy it was intended to cover
Comparison	≤ 1 v > 1 serves of nuts per week
Outcomes	Persistent wheeze, atopic wheeze and atopy at 6.5 years
Results	***Persistent wheeze at 6.5 years*** Low 19 (12.50%) v high 18 (14.06%); pns (also adjusted for firstborn and lower respiratory tract infections at age 1) ***Atopic wheeze at 6.5 years*** Low 9 (4.71%) v high 11 (7.24%); pns (also adjusted for birthweight and maternal atopy) ***Atopy at 6.5 years*** Low 37 (16.09%) v high 33 (18.23%) pns (also adjusted for birthweight and maternal atopy)
Followup	6.5 years
Confounding	Analyses adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years and total energy intake at 6.5 years
Risk of bias	Low risk of bias: Results from 468/482 children (97%) able to be analysed (4 incomplete data and 8 implausible values);
Relevance	Diets in Menorca may differ from diets of Australian women, particularly urban women

Reference	**Haggarty 2009**
Dietary patterns	Nuts and seeds
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Aberdeen, Scotland
Funding	UK Food Standards Agency
Participants	1277 sequentially enrolled pregnant women attending Aberdeen Maternity Hospital for ultrasound (a further 184 women were recruited later in pregnancy). Exclusions: diabetic women, women with multiple pregnancies, women who conceived as a result of fertility treatment, or clinical data not available
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	Assessed at 19 weeks gestation
Comparison	Intake of nuts and seeds by deciles of deprivation
Outcomes	Deprivation (assessed using the Scottish Index of Multiple Deprivation); Low birthweight (defined as < 2500 g or lowest decile for birthweight z score adjusted for gestational age, sex and parity) Preterm birth (< 37 weeks) Admission to neonatal unit
Results	**Deprivation** Intake of nuts and seeds did not differ significantly between deciles of deprivation on regression analysis
Followup	To neonatal period
Confounding	(Some?) analyses adjusted for energy intake
Risk of bias	Low to moderate risk of bias: low attrition, some lack of detail in reporting of outcomes
Relevance	Likely to be relevant to Australian women
Other comments	About 40-50% of the least deprived women reported taking folic acid supplements compared with about 20% for the most deprived women; Most birth outcome associations were reported by nutrient rather than food group; Not easy to deduce quantities of intake of foods (main graphs reported as change in intake by deprivation decile)

Reference	**Hourihane 1996**
Dietary patterns	Nuts: peanuts
Study type	Cross-sectional survey
Level of evidence	IV (aetiology)
Setting	Southampton, UK; 1994/5
Funding	UK Ministry of Agriculture, Fisheries and Food
Participants	622 respondents known to have a peanut allergy (mostly children)
Baseline comparisons	n/a
Dietary assessment	questionnaire
Timing	Variable – after birth
Comparison	Intake of peanuts at least weekly during pregnancy and lactation versus no peanut consumption
Outcomes	Peanut allergy, time of development of peanut allergy
Results	Mothers of younger probands (5 years or younger) were significantly more likely than mothers of older probands to have regularly consumed peanuts (at least weekly) during pregnancy and lactation (104 (50.7%) v 138 (33.1%); $p < 0.005$). In other words, peanut allergy presents earlier in women consuming peanuts during pregnancy and lactation.
Followup	n/a
Confounding	n/a
Risk of bias	Moderate-high risk of bias: 622/833 (75%) usable responses to questionnaire; maternal recall of peanut consumption during pregnancy and lactation subject to bias
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Jensen 2004**
Food type	Nuts: peanuts and peanut butter (also in legumes)
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study)
Funding	PHS
Participants	138 matched cases and controls: Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, parental occupation and smoking during pregnancy – no evidence of confounding was seen for these variables. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of nuts
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Peanuts, peanut butter**: aOR 1.00 95% CI 0.86 to 1.18: mean consumption 2.99 [SD 1.89] serves per day*
Followup	n/a
Confounding	Analyses were adjusted for variables previously shown to be significantly associated with ALL in the overall study – income, prior fetal loss, child’s exposure to other children under age five, and maternal exposure to indoor insecticides during pregnancy; along with portion size and energy consumption
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 1999, 83% consented to participate; 69% of the eligible controls agreed to participate. Of the 161 matched pairs, seven pairs were excluded as the respondent was not the biological mother, 16 pairs were excluded due to questionable dietary questionnaire data, leaving 138 matched pairs (86%); some recall bias likely
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	*Some consumption levels seem high – possibly per week rather than per day?

Reference	**Sausenthaler 2007**
Food groups	Nuts and seeds
Study type	Prospective cohort study: from the LISA birth cohort
Level of evidence	II (aetiology)
Setting	4 German cities (Munich, Leipzig, Wesel, Bad Honnef)
Funding	Federal Ministry for Education, Science, Research and Technology, Germany
Participants	3097 newborns recruited
Baseline comparisons	*See Confounding below*
Dietary assessment	FFQ
Timing	Maternal diet during the last 4 weeks of pregnancy (obtained shortly after birth, median 3 days)
Variable	Low intake group as reference group compared with high intake group: • Nuts high intake = 1-2 times/week • Seeds high intake = 1-2 times/week
Outcomes	Allergic sensitisation, eczema at 2 yrs
Results	(see below)

	Doctor-diagnosed eczema	**Any allergen sensitisation**	**Food allergens**	**Inhalant allergens**
	Adjusted OR (95% CI)			
Nuts	0.85 (0.63, 1.14)	0.92 (0.62, 1.34)	1.10 (0.72, 1.67)	0.84 (0.46, 1.53)
Seeds	1.24 (0.94, 1.64)	0.78 (0.53, 1.14)	0.72 (0.47, 1.12)	0.75 (0.42, 1.33)

Length of followup	2 years
Confounding	Crude and adjusted results reported (adjusted for study area, sex, maternal age, maternal smoking, level of parental education, exclusive breastfeeding ≥ 4 months, parental history of atopic diseases, season of birth and all dietary variables
Risk of bias	Low risk of bias: two year data available for 2641/3097 children (85%): 433 lost to follow-up, 9 excluded due to chronic disease, 14 missing maternal FFQ
Relevance	Likely to be reasonably similar to dietary intakes of Australian women in Australia
Other comments	

Reference	**Thompson 2010**
Food groups	Nuts: peanuts
Study type	Systematic review of studies published between 1 January 1999 and 7 March 2008
Level of evidence	III (aetiology)
Setting	International
Funding	UK Food Standards Agency
Participants	Two included studies: Frank 1999 (case control); Lack 2003 (case-control)
Baseline comparisons	*See risk of bias*
Dietary assessment	Questionnaire/telephone interview
Timing	Questionnaire relating to pregnancy, lactation and child administered when child food allergy diagnosed
Comparison	Frequency of peanut consumption during pregnancy and lactation
Outcomes	1) Sensitisation (positive peanut-specific IgE) 2) Peanut allergy (double blind placebo-controlled food challenge)
Results	<u>**Pregnancy**</u> **Frank 1999: Peanut consumption during pregnancy** — **> once per week** / **< once per week** Peanut-sensitive group (n=23): 11 / 12 Control group (n=16): 3 / 13 Crude OR=3.97 (95% CI 0.73 to 24.0) p=0.063 **Lack 2003: % of mothers consuming peanuts during pregnancy** Cases (n = 23) – 65%; Controls (atopic; n = 70) – 71%; Controls (non-atopic; n = 140) – 61%: pns <u>**Lactation**</u> **Frank 1999: Peanut consumption during lactation** — **> once per week** / **< once per week** Crude OR 2.19 95% CI 0.39 to 13.47 **Lack 2003: % of mothers consuming peanuts at least seven times a week** Cases – 17%; Controls (atopic) – 5%; Controls (non-atopic) – 5%: p = 0.03, pns after adjustment
Length of followup	Three years
Confounding	*See risk of bias*
Risk of bias	Low risk of bias for conduct of systematic review although studies published prior to 1999 not discussed); moderate risk of bias for included studies (one study did not adjust for confounders; while the other study did, it did not report which confounders were adjusted for
Relevance	Likely to be reasonably similar to dietary intakes of Australian women in Australia
Other comments	Mentions ongoing studies such as LEAP (Learning Early About Peanut Allergy) – findings due 2013

Reference	**Vadas 2001**
Food groups	Peanuts (dry roasted)
Study type	Before and after study
Level of evidence	IV (intervention)
Setting	North America (women recruited from March 1999 to October 2000)
Funding	Health Canada, the Peanut Foundation, Allergy, Asthma and Immunology Society of Ontario, and Nestle Canada
Participants	23 healthy lactating women aged 21-35 years, excluding women with known peanut or tree nut allergy
Baseline comparisons	*NA*
Dietary assessment	NA
Timing	*See below*
Variable	Ingestion of 50 g dry roasted peanuts after initial breast milk collection compared with breast milk collected at 1, 2, 3, 4, 6, 8 and 12 hours after peanut ingestion
Outcomes	Peanut protein in breast milk
Results	Detection of peanut protein in 11/23 women (47.8%); In these 11 women, peanut protein appeared within 1 hour to 6 hours; and cleared rapidly for all but one of the 11 women
Length of followup	n/a
Confounding	n/a
Risk of bias	Low risk of bias: women acted as their own controls (they were instructed to avoid legumes 24 hours prior to start of the study)
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Venter 2009**
Food groups	Nuts: peanuts
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Portsmouth, UK
Funding	Food Standards Agency
Participants	969 pregnant women at 12 weeks gestation (with estimated birth date between 1 September 2001 and 31 August 2002)
Baseline comparisons	Pregnant women with a maternal history of atopic disease were more likely to smoke
Dietary assessment	FFQ
Timing	FFQ at 36 weeks gestation
Comparison	No (54% of women) versus moderate (44%) versus frequent (2%) versus uncertain (<1%) consumption of peanuts during pregnancy
Outcomes	Food hypersensitivity (FHS) in infants up to three years of age
Results	11/925 infants showed FHS to peanuts in the first three years (6 where mothers never consumed peanuts during pregnancy, 4 where mothers reported moderate consumption of peanuts during pregnancy, and 1 where mothers reported frequent consumption of peanuts during pregnancy) "Statistical inferences could not be measured due to the small numbers"
Length of followup	Up to three years
Confounding	Analyses do not appear to have been adjusted
Risk of bias	Moderate-high risk of bias: Data were obtained from 91% (n = 969) of the birth cohort; at 1 year follow-up data were available for 77.6% (752/969) and for 65.2% (632/969) at 3 years; analyses probably not adjusted for confounders
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Willers 2008**
Food type	Nuts and nut products
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Netherlands
Funding	Netherlands Organization for Health Research and Development, Netherlands Organization for Scientific Research; Netherlands Asthma Fund; Netherlands Ministry of Spatial Planning, Housing, and the Environment; Netherlands Ministry of Health, Welfare and Sport, GlaxoSmithKline
Participants	2,832 children (part of the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered at antenatal recruitment (mean gestational ages not reported) to cover dietary intake over the previous month
Comparison	Nuts: daily (once per day or more) or regular v rare consumption; Nut products: daily v regular v rare consumption
Outcomes	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable 'asthma symptoms' in the last 12 months (measured longitudinally from 1 to 8 years age); IgE at 8 years for a subset of children
Results	**NUTS** **Wheeze from 1 to 8 years age (n = 2806)** OR 0.96 95% CI 0.83 to 1.12 aOR 0.99 95% CI 0.86 to 1.15 **Dyspnoea from 1 to 8 years age (n = 2806)** OR 1.00 95% CI 0.82 to 1.19 aOR 1.04 95% CI 0.88 to 1.23 **Steroid use from 1 to 8 years age (n = 2806)** OR 0.95 95% CI 0.75 to 1.19 aOR 1.03 95% CI 0.81 to 1.29 **Asthma symptoms (composite of previous three outcomes) from 1 to 8 years age (n = 2806)** OR 0.96 95% CI 0.82 to 1.11 aOR 1.00 95% CI 0.86 to 1.17 **NUT PRODUCTS** **Wheeze from 1 to 8 years age (n = 2806)** ***Regular v rare*** OR 1.04 95% CI 0.90 to 1.21 aOR 1.01 95% CI 0.88 to 1.18 ***Daily v rare*** **OR 1.39 95% CI 1.05 to 1.86** **aOR 1.42 95% CI 1.06 to 1.89** **Dyspnoea from 1 to 8 years age (n = 2806)** ***Regular v rare*** OR 0.99 95% CI 0.82 to 1.18

	aOR 0.98 95% CI 0.82 to 1.16 ***Daily v rare*** **OR 1.52 95% CI 1.12 to 2.06** **aOR 1.58 95% CI 1.16 to 2.15** **<u>Steroid use from 1 to 8 years age (n = 2806)</u>** ***Regular v rare*** OR 0.94 95% CI 0.74 to 1.18 aOR 0.94 95% CI 0.74 to 1.19 ***Daily v rare*** **OR 1.48 95% CI 0.98 to 2.22** **aOR 1.62 95% CI 1.06 to 2.46** **<u>Asthma symptoms (composite of previous three outcomes) from 1 to 8 years age (n = 2806)</u>** ***Regular v rare*** OR 0.99 95% CI 0.85 to 1.15 aOR 0.98 95% CI 0.84 to 1.14 ***Daily v rare*** **OR 1.41 95% CI 1.05 to 1.89** **aOR 1.47 95% CI 1.08 to 1.99**
Followup	8 years
Confounding	The child's dietary data on fruit, vegetables, fish, eggs, full cream milk, butter and peanut butter consumption at 2 years of age were used to check for potential confounding by the child's diet. Results were adjusted for by sex, maternal education, parental allergy, maternal smoking during pregnancy, smoking in the home at 8 years of age, breastfeeding, presence of older siblings, birthweight, maternal overweight 1 year after pregnancy, maternal supplement use during pregnancy, region and study arm (intervention or natural history arm).
Risk of bias	Moderate risk of bias: Initial study population of 4,146 mothers dropped to 2,832 participants with complete data (68.3%) (pregnancy questionnaire, at least one of the outcome time points and all confounders). Participants with complete data were more likely to have a high education level, to have daily dairy and fruit intake during pregnancy and to have breastfed and less likely to have maternal asthma or maternal atopy, smoked during pregnancy, be from a south western region compared with participants who did not have complete data.
Relevance	Dietary intakes likely to be different from Australian e.g. low fish consumption in study participants
Other comments	Not clear when women assessed their diet during pregnancy; 83% of pregnant women used supplements (50% used folic acid/iron)

References

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Salt/Sodium

Included studies

Study	Outcomes
1. Bower 1961	Induction, caesarean, perinatal death, mean stay in hospital, birthweight, eclampsia, blood pressure change
2. Duley 1999 & 2005	Hypertension, pre-eclampsia and birth outcomes
3. Jensen 2004	Childhood acute lymphoblastic leukemia
4. Morris 2001	Pre-eclampsia; pregnancy-associated hypertension

Evidence summaries

	N	Level	References
Maternal Outcomes			
1. In a quasi-RCT from the UK and Canada, no significant differences were seen between maternal intake of 2 g versus 10 g versus 25 g per day in hospitalised pregnant women for **eclampsia or caesarean section**	1082	III-1 (intervention)	Bower 1961
2. In a Cochrane systematic review, no significant differences were seen between a low salt diet or no dietary advice for pregnant women for **pre-eclampsia or caesarean section**	2 RCTs (603 women)	I (Cochrane SR)	Duley 1999; Duley 2005
3. In a US cohort study, amount of sodium in pregnant women's diet was not associated with increased risk of **pre-eclampsia or pregnancy-associated hypertension**	4314	II	Morris 2001
Birth Outcomes			
4. In a quasi-RCT from the UK and Canada, no significant differences were seen between maternal intake of 2 g versus 10 g versus 25 g per day in hospitalised pregnant women for **perinatal death or birthweight**	1082	III-1 (intervention)	Bower 1961
5. In a Cochrane systematic review, no significant differences were seen between a low salt diet or no dietary advice for pregnant women for **perinatal death, preterm birth or birthweight**	2 RCTs (603 women)	I (Cochrane SR)	Duley 1999; Duley 2005
Childhood Outcomes			
6. In a US case control study, maternal sodium intake during pregnancy was not associated with an increase in number of cases of **childhood acute lymphoblastic leukemia** in their offspring	138 cases; 138 controls	III-3	Jensen 2004

Evidence Tables

Reference	**Bower 1964**
Food type	Salt
Study type	Quasi-RCT (allocated by booking or admission date or by ward) with historical arm
Level of evidence	III-1 (intervention)
Setting	London, UK & Toronto, Canada
Funding	Berkeley Fellowship Committee of Caius College, Cambridge and Middlesex Hospital, UK
Participants	UK: 739 women (341 in 2 g group (1958); 201 in 10 g group (1959-60); 197 in 25 g group (1959-60); with at least two of 1) blood pressure > 140 systolic or 90 diastolic, providing that the systolic BP was not less than 120 and the diastolic BP was not less than 80; 2) definite oedema; 3) more than 'a trace' of albuminuria Canada: 243 women (113 low salt diet in 1960 and 130 normal diet in 1961)
Baseline comparisons	Not reported
Dietary assessment	NA
Timing	NA
Comparison	2 g versus 10 g versus 25 g salt per day
Outcomes	Induction, caesarean, perinatal death, mean stay in hospital, birthweight, eclampsia, blood pressure change (first v second half of admission)
Results	See tables below
Followup	NA
Confounding	Not reported
Risk of bias	Moderate to high risk of bias: no adjustments made for potential confounders
Relevance	Limited relevance from old study
Other comments	

Results:

UK	**2g**	**10g**	**25g**	**p (2 v 10g)**	**p (2 v 25g)**
Induction	213/341 (63%)	118/201 (59%)	115/197 (58%)	ns	ns
Caesarean	19/341 (5.6%)	10 (5.0%)	10 (5.1%)	ns	ns
Perinatal death	20/341 (5.9%)	11/201 (5.5%)	9/197 (6.4%)	ns	ns
Hospital stay (days)	9.9	10	8.7	ns	ns
Birthweight (lbs)	6.7	6.9	6.9	ns	ns
Eclampsia	4/341	2/201	2/197	ns	ns
BP Change					
- Systolic	+0.101	-0.129	-0.019	ns	ns
- Diastolic	+0.103	+0.020	+0.131	ns	ns

Canada	**Low salt (1.5g)**	**Normal salt (10g)**	**p**
Induction	48/113 (42.5%)	47/130 (31.5%)	ns
Caesarean	19/113 (16.8)	16/130 (12.3%)	ns
Perinatal death	8/118 (7.1%)	5/133 (3.8%)	ns
Hospital stay (days)	7.6	7.6	ns
Birthweight (lbs)	7.0	6.8	ns
BP Change			
- Systolic	-0.055	+0.02	ns
- Diastolic	+0.017	-0.013	ns

Reference	**Duley 1999 and 2005**
Food type	Salt
Study type	SR (2 Cochrane reviews) of two RCTs: 1) Steegers 1991; van Buul 1995; van Buul 1997; van Buul 1992; van Buul 1991; van der Maten 1995; van der Post 1997 2) Knuist 1998
Level of evidence	I (intervention)
Setting	Netherlands (both trials)
Funding	Department for International Development, UK; MRC, UK
Participants	603 pregnant nulliparous women
Baseline comparisons	n/a
Dietary assessment	n/a
Timing	From 12 weeks gestation in one trial and after 20 weeks gestation in the other trial
Comparison	Low salt diet (20 or 50 mmol/day) versus no dietary advice
Outcomes	Hypertension, pre-eclampsia and birth outcomes (see results)
Results	Hypertension — RR 0.98 95% CI 0.49 to 1.94 — 1 trial (n = 242) Pre-eclampsia — RR 1.11 95% CI 0.46 to 2.66 — 2 trials (n = 603) Referral to hospital, no admission — RR 1.05 95% CI 0.48 to 2.32 — 1 trial (n = 361) Admission to hospital — RR 0.82 95% CI 0.56 to 1.22 — 1 trial (n = 361) Placental abruption — RR 0.19 95% CI 0.01 to 3.98 — 1 trial (n = 361) Caesarean section — RR 0.75 95% CI 0.44 to 1.27 — 1 trial (n = 361) Perinatal mortality — RR 1.92 95% CI 0.18 to 21.03 — 2 trials (n = 409) Birthweight < 10th centile — RR 1.5 95% CI 0.73 to 3.07 — 1 trial (n = 242) Birthweight <2500 g — RR 0.84 95% CI 0.42 to 1.67 — 1 trial (n = 361) Preterm birth — RR 1.08 95% CI 0.47 to 2.56 — 1 trial (n = 242) Apgar < 7 at 5 mins — RR 1.37 95% CI 0.53 to 3.53 — 1 trial (n = 361) Paediatric admission — RR 0.98 95% CI 0.69 to 1.40 — 1 trial (n = 361)
Followup	To birth
Confounding	n/a
Risk of bias	One trial at moderate risk of bias (unclear allocation concealment; 28/270 (10.4%) losses to followup, including 17 women in the low salt group refusing the diet: One trial at low risk of bias: adequate allocation concealment; no losses to followup reported
Relevance	Restriction of salt to this level likely to be unpalatable and therefore hard for women to achieve
Other comments	In one trial 13% of women in the salt restriction arm did not want to follow the diet and in the other trial only 24% of womene met the target levels of reduced salt intake

Reference	**Jensen 2004**
Food type	Sodium
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study)
Funding	PHS
Participants	138 matched cases and controls: Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, parental occupation and smoking during pregnancy – no evidence of confounding was seen for these variables. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Sodium intake per day
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Childhood acute lymphoblastic leukemia** aOR 0.29 95% CI 0.05 to 1.84; mean daily intake of sodium 2603.7 mg [SD 1052.4]
Followup	n/a
Confounding	Analyses were adjusted for variables previously shown to be significantly associated with ALL in the overall study – income, prior fetal loss, child's exposure to other children under age five, and maternal exposure to indoor insecticides during pregnancy; along with portion size and energy consumption
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 1999, 83% consented to participate; 69% of the eligible controls agreed to participate. Of the 161 matched pairs, seven pairs were excluded as the respondent was not the biological mother, 16 pairs were excluded due to questionable dietary questionnaire data, leaving 138 matched pairs (86%); some recall bias likely
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	

Reference	**Morris 2001**
Food type	Salt
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	USA (part of RCT of calcium, CPEP); both arms of the RCT were pooled as no significant differences were seen between calcium and placebo
Funding	NICHHD, National Heart, Lung and Blood Institute
Participants	4314 women recruited at 13 to 21 weeks gestation
Baseline comparisons	*See confounding below*
Dietary assessment	24 hour dietary recall
Timing	Dietary recall at time of recruitment
Comparison	Amount of dietary sodium
Outcomes	Pre-eclampsia and pregnancy-associated hypertension (diastolic BP ≥ 90 mmHg on 2 occasions from 4 to 168 hours apart)
Results	*Unadjusted (univariate analysis)* — 4322 mg/day SE 123; p < 0.15 compared with normotensive pregnancy Pre-eclampsia (n = 311): 4215 mg/day SE 77 Pregnancy-associated hypertension (n = 721): 4242 mg/day SE 39 Normotensive pregnancy (n = 3215): **Pre-eclapsia** < 2544 mg/day — 1.00 **2544 – 3451 — 1.65 95% CI 1.11 to 2.46** 3452 – 4328 — 1.23 95% CI 0.79 to 1.87 4329 – 5706 — 1.35 95% CI 0.87 to 2.10 5707 — 1.49 95% CI 0.90 to 2.48 **Pregnancy-associated hypertension** < 2544 mg/day — 1.00 2544 – 3451 — 1.02 95% CI 0.78 to 1.34 3452 – 4328 — 1.11 95% CI 0.84 to 1.46 4329 – 5706 — 1.05 95% CI 0.78 to 1.41 5707 — 1.06 95% CI 0.75 to 1.51
Followup	To 24 hours postpartum
Confounding	Adjusted for total energy intake and for variables found to be significant in univariate analysis (race/ethnicity and BMI)
Risk of bias	Low-moderate risk of bias: Of the 4589 women recruited, 253 (5.5%) could not be followed up for the outcomes of pre-eclampsia and pregnancy-associated hypertension; 22 women (0.5%) were excluded because pregnancy terminated < 20 weeks gestation; Accuracy of 24 hour dietary recall unknown
Relevance	Likely to be similar to Australian women
Other comments	Not clear if OR or RR used in multivariate analyses (graph shows as RR; legend shows as OR)

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Duley L, Henderson-Smart D and Meher S. "Altered dietary salt for preventing pre-eclampsia, and its complications." ***Cochrane Database Syst Rev*** 2005: (4): CD005548.

Jensen CD, Block G, Buffler P, Ma X, Selvin S and Month S. "Maternal dietary risk factors in childhood acute lymphoblastic leukemia (United States)." ***Cancer Causes Control*** 2004: **15**(6): 559-70.

Morris CD, Jacobson SL, Anand R, Ewell MG, Hauth JC, Curet LB, Catalano PM, Sibai BM and Levine RJ. "Nutrient intake and hypertensive disorders of pregnancy: Evidence from a large prospective cohort." ***Am J Obstet Gynecol*** 2001: **184**(4): 643-51.

Sugar

Included Studies

Study	Outcomes
1. Chen 2009	GDM
2. George 2005	Breastfeeding
3. Haggarty 2009	Deprivation, SGA
4. Herrick 2003	Cortisol concentrations in offspring aged 30 years
5. Kwan 2009	Childhood acute lymphoblastic leukemia
6. Lenders 1994	Gestational weight gain, preterm birth, birthweight, SGA
7. Lenders 1996	SGA
8. Nwaru 2010	Allergic sensitisation in offspring by 5 years
9. Olafsdottir 2006	GWG
10. Petridou 2005	Childhood acute lymphoblastic leukemia
11. Petridou 1998a	Cerebral palsy at 8 years
12. Petridou 1998b	Birthweight
13. Stuebe 2009	GWG

Evidence Summaries

	N	Level	References
Maternal Outcomes			
1. In a Scottish cohort study, confectionery intake did not differ significantly between deciles of **deprivation** on regression analysis and sugar sweetened beverages (soft drinks) showed significantly higher intake with higher levels of deprivation ($p < 0.001$)	1277	II	Haggarty 2009
2. In a US cohort study, maternal consumption of sugar sweetened beverages was not associated with an increased risk of **excessive gestational weight gain** under a multivariate logistic regression model: aOR 0.87 95% CI 0.72 to 1.05 (serves per day)	1338	II	Stuebe 2009
3. In a cohort study from USA, differing maternal consumption of sugar (low versus high) during pregnancy was not associated with differences in **gestational weight gain**	337	II	Lenders 1994
4. In a cohort study from Iceland, eating more sweets in early pregnancy was associated with increased risk of **excessive gestational weight gain**: aOR 2.52 95% CI 1.10 to 5.77	495	II	Olafsdottir 2006
5. In a US cohort study, consumption of sugar-sweetened beverages overall during pregnancy was not associated with an increased risk of **gestational diabetes mellitus**, although it was for sugar-sweetened cola beverages (but not diet cola): • aOR for SSBs overall: 1.16 95% CI 0.98 to 1.37; $p_{trend} = 0.06$ • aOR for GDM with sugar-sweetened cola beverages: 1.22 95% CI 1.01 to 1.47; $p_{trend} = 0.04$ • aOR for GDM with diet cola beverages: 0.90 95% CI 0.78 to 1.03; $p_{trend} = 0.07$	13,475	II	Chen 2009
Breastfeeding			
6. In a cohort study from the US, no significant differences were seen in postpartum added sugar consumtion between **lactating and nonlactating** women	149	II	George 2005
Birth Outcomes			
7. In a Scottish cohort study, low maternal sugar intake during pregnancy was associated with **SGA** (being in the lowest decile for standardised birthweight): OR 0.78 95% CI 0.64 to 0.96)	1277	II	Haggarty 2009
8. In a cohort study from USA, differing maternal consumption of sugar (low versus high) during pregnancy was not associated with differences in **SGA** ($p = 0.08$)	337	II	Lenders 1994
9. In a cohort study from USA, high sugar consumption by pregnant teenagers was associated with a higher rate of **SGA**: aOR 2.01 95% CI 1.05 to 7.53	594	II	Lenders 1996
10. In a cohort study from USA, differing maternal consumption of sugar (low versus high) during pregnancy was not associated with differences in **preterm birth** (11% versus 12%)	337	II	Lenders 1994
Asthma And Allergy Outcomes			
11. In a Finnish cohort study, no significant associations were seen between maternal consumption of sweets and chocolates and **allergic sensitisation in their children at five**	931 children	II	Nwaru 2009

years of age			
Other Childhood Outcomes			
12. In a US case-control study maternal intake of sugar during pregnancy was not associated with increased risk of **acute lymphoblastic leukemia in children up to 15 years of age:** aOR 0.99 95% CI 0.96 to 1.02 for sweets as % energy (median consumption 8.00% energy per day)	282 cases; 282 controls	III-3	Kwan 2009
13. In a Greek case-control study, maternal intake of sugars and syrups was associated with increased risk of **acute lymphoblastic leukemia in children up to 5 years of age:** logistic regression: one quintile more of sugars/syrups: aOR 1.32 95% CI 1.05 to 1.67	131 cases and 131 controls	III-3	Petridou 2005
14. In a Greek case-control study, **cerebral palsy in children up to eight years of age** was not associated with maternal consumption of sugars and syrups during pregnancy; regression analysis for each unit (once a week) aOR 1.21 95% CI 0.77 to 1.90	138 cases; 138 controls	III-3	Petridou 1998a
15. In a cohort study from Scotland, no significant associations was seen between maternal consumption of sweets and **cortisol concentrations in offspring at 30 years of age**	251	II	Herrick 2003

Evidence Tables

Reference	**Chen 2009**
Food groups	Sugar: sugar-sweetened beverages (SSB); [results for low calorie beverages included under 'Beverages']
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	US (Nurses' Health Study)
Funding	NIH
Participants	13,475 women who reported at least one singleton pregnancy between 1992 and 2001 Exclusions: history of diabetes, cancer, cardiovascular disease or GDM on 1989 or 1991 questionnaires
Baseline comparisons	*See confounding below*
Dietary assessments	FFQ
Timing	Consumption of SSBs before pregnancy
Comparison	0.3 serves of SSBs a month versus 1-4 a week versus ≥ 5 a week versus 1 a day
Outcomes	GDM
Results	(see below)

GDM (RR 95% CI)
SSB consumption

	0-3 serves/month	**1-4 serves/week**	**≥5 serves/week**	**1 serve/day**	**p trend**
All S SBs					
Cases/person-years	323/185,682	229/173,189	208/185,757		
Model 1	1.00	1.01 (0.85 to 1.20)	**1.23 (1.05 to 1.45)**	**1.25 (1.07 to 1.45)**	**0.005**
Model 2	1.00	1.02 (0.86 to 1.21)	**1.17 (1.00 to 1.37)**	**1.18 (1.01 to 1.37)**	**0.04**
Model 3	1.00	1.06 (0.89 to 1.25)	**1.23 (1.05 to 1.44)**	**1.23 (1.05 to 1.43)**	**0.01**
Model 4	1.00	1.03 (0.87 to 1.23)	1.16 (0.98 to 1.37)	1.16 (0.99 to 1.36)	0.06
Sugar-sweetened cola					
Cases/person-years	544/332,516	168/113,899	148/98,214		
Model 1	1.00	1.12 (0.94 to 1.33)	**1.39 (1.16 to 1.67)**	**1.39 (1.16 to 1.67)**	**< 0.001**
Model 2	1.00	1.07 (0.90 to 1.28)	**1.26 (1.04 to 1.51)**	**1.25 (1.04 to 1.51)**	**0.02**
Model 3	1.00	1.11 (0.93 to 1.32)	**1.29 (1.07 to 1.56)**	**1.29 (1.07 to 1.55)**	**0.007**
Model 4	1.00	1.08 (0.90 to 1.28)	**1.22 (1.01 to 1.47)**	**1.22 (1.01 to 1.47)**	**0.04**
Other S SBs					
Cases/person-years	448/254,751	256/195,695	156/94,182		
Model 1	1.00	1.00 (0.86 to 1.17)	0.98 (0.81 to 1.17)	0.97 (0.77 to 1.22)	0.78
Model 2	1.00	1.00 (0.86 to 1.17)	0.95 (0.79 to 1.14)	0.94 (0.74 to 1.18)	0.58
Model 3	1.00	1.06 (0.90 to 1.23)	0.99 (0.82 to 1.19)	0.99 (0.78 to 1.25)	0.92
Model 4	1.00	1.02 (0.87 to 1.19)	0.94 (0.78 to 1.13)	0.92 (0.78 to 1.16)	0.48

Length of followup	10 years
Confounding	Model 1: adjusted for age and parity Model 2: adjusted for age and parity; plus race/ethnicity; smoking status, family history of diabetes in a first degree relative, alcohol intake, physical activity Model 3: adjusted for age and parity, race/ethnicity; smoking status, family history of diabetes in a first degree relative, alcohol intake, physical activity;

	plus BMI Model 4: adjusted for age and parity, race/ethnicity; smoking status, family history of diabetes in a first degree relative, alcohol intake, physical activity; BMI, plus Western dietary pattern
Risk of bias	Low-moderate risk of bias: typically 90% followup rate; analyses did not adjust for other caffeine use
Relevance	Likely to be relevant to Australian women
Other comments	Caramel colouring in cola drinks is rich in advanced glycation end products, but positive association was not seen for diet cola (see Caffeine food group)

Reference	**George 2005**
Food type	Foods with added sugar (Coke/Sprite; fruit drinks; Gatorade, Snapple; sugar, syrup, jams, honey); chocolate candy
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Texas, US
Funding	Not reported
Participants	149 Medicaid-qualified women (30% white, 24% African American, 46% Hispanic) – recruited from a larger study on postpartum weight retention Inclusion criteria: 18 years or older; non-Hispanic white, African American or Hispanic ethnicity; birth of a health term infant, fluency and literacy in English; absence of pregnancy-related abnormalities and disease conditions.
Baseline comparisons	Significant differences between lactating and non-lactating women – higher parity, BMI and lower education levels in non-lactating women.
Dietary assessment	Semiquantitative FFQ to cover pregnancy and first six months postpartum
Timing	FFQ administered at 6 weeks and 6 months postpartum
Comparison	Number of serves of foods with added sugar
Outcomes	Breastfeeding (exclusive or partial at 6 months postpartum)
Results	Lactating women and nonlactating women did not show significant differences in the amount of foods with added sugar that they consumed postpartum
Followup	6 months postpartum
Confounding	No adjustment for potential confounding
Risk of bias	Moderate-to-high risk of bias; no attempt to control for confounding despite significant baseline differences between lactating and non-lactating women.
Relevance	Possibly relevant to low-income women in Australia
Other comments	Minimal reporting of results

Reference	**Haggarty 2009**
Dietary patterns	Sugar: total sugars, confectionery, soft drinks
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Aberdeen, Scotland
Funding	UK Food Standards Agency
Participants	1277 sequentially enrolled pregnant women attending Aberdeen Maternity Hospital for ultrasound (a further 184 women were recruited later in pregnancy). Exclusions: diabetic women, women with multiple pregnancies, women who conceived as a result of fertility treatment, or clinical dat not available
Baseline comparisons	*See confounding below*
Assessment	FFQ
Timing	Assessed at 19 weeks gestation
Comparison	Intake of sugar by deciles of deprivation
Outcomes	Deprivation (assessed using the Scottish Index of Multiple Deprivation); Low birthweight (defined as < 2500 g or lowest decile for birthweight z score adjusted for gestational age, sex and parity) Preterm birth (< 37 weeks) Admission to neonatal unit
Results	**Deprivation** Confectionery intake did not differ significantly between deciles of deprivation on regression analysis Soft drinks: significantly higher intake with higher levels of deprivation ($p < 0.001$) **Lowest decile for standardised birthweight:** OR for diets low in sugars: **0.78 95% CI 0.64 to 0.96**
Followup	To neonatal period
Confounding	(Some?) analyses adjusted for energy intake
Risk of bias	Low to moderate risk of bias: low attrition, some lack of detail in reporting of outcomes
Relevance	Likely to be relevant to Australian women
Other comments	About 40-50% of the least deprived women reported taking folic acid supplements compared with about 20% for the most deprived women; Most birth outcome associations were reported by nutrient rather than food group; Not easy to deduce quantities of intake of foods (main graphs reported as change in intake by deprivation decile)

Reference	**Herrick 2003**
Food groups	Sugar; sweets
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Motherwell, Scotland
Funding	Dunhill Medical Trust, NIH
Participants	251 men and women whose mothers' food intakes had been recorded during pregnancy during 1967 to 1968. These women had been advised to eat 0.45 kg of red meat a day and to avoid carbohydrate-rich foods during pregnancy
Baseline comparisons	*See confounding below*
Dietary assessment	Mothers asked about consumption of 10 foods
Timing	Early pregnancy (≤ 20 weeks); late pregnancy (> 20 weeks)
Comparison	portions of sweets (1/4 pound) per week; mean 1.1 [SD 0.8] portions
Outcomes	Cortisol concentrations in offspring aged 30 years
Results	Cortisol (change per unit change in maternal sweet consumption during pregnancy) No significant association
Length of followup	30 years
Confounding	Analyses adjusted for offspring's gender, social class at birth, BMI, alcohol consumption, and activity level
Risk of bias	Moderate risk of bias: For the 1432 records from 1967-8 recorded liveborn, singleton births with complete names, birth measurements and ≥ 1 diet record. 965 offspring were alive and living locally; and after attrition or declining to participate, 251 (17.5%) were available for analysis.
Relevance	Very high intake of meat and very low carbohydrate intake limits the relevance to current dietary intakes of Australian women
Other comments	Authors state that "in the setting of advice to follow a pregnancy diet high in protein and low in carbohydrate, an unbalanced pattern of higher meat/fish and lower green vegetable consumption in late pregnancy leads to elevated cortisol concentrations in the offspring"

Reference	**Kwan 2009**
Food type	Sugar (energy from sweets)
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study – phase 1 and 2 (phase 1 reported in Jensen 2004)
Funding	PHS; Paul O'Gorman Foundation for Children with Leukemia
Participants	866 individuals - 282 matched cases and controls (205 pairs and 77 trios): Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth (in phase 1 (1995-99) only due to concerns about overmatching on potential environmental exposures linked to leukemia risk) Data collected from August 1995 to November 2002
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, and smoking during pregnancy. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Daily intake of sweets (% energy)
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Sweets (% energy):** aOR 0.99 95% CI 0.96 to 1.02: median consumption 8.00% energy per day (25^{th}, 75^{th} percentiles 4.09, 14.5)
Followup	n/a
Confounding	Analyses were adjusted for total energy intake, household income, indoor insecticide exposure during pregnancy; and proportion of foods reported as large or extra-large portion size Also adjusted for child's diet, with little effect seen on results
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 2002, 86% consented to participate; 56% of the eligible controls agreed to participate. 190 participants excluded: leukemia diagnosis was not ALL (n = 127); no dietary data (n = 4); a case or a control respondent was not the biological mother (n = 14), questionable dietary questionnaire data (n = 45), leaving 282 matched sets (86%).
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	Regular use of any dietary supplement was not associated with risk of ALL

Reference	**Lenders 1994**
Food groups	Sugar: total sum of simple carbohydrates (does not include complex carbohydrates such as starch or fibre)
Study type	Prospective cohort study (part of the Camden County Adolescent Family Health Program)
Level of evidence	II (aetiology)
Setting	Camden, New Jersey, USA
Funding	NICHHD, Heinz Pediatric Fellowship Program
Participants	337 pregnant adolescents from low-income families giving birth to live singleton babies > 20 weeks gestation (1982 to 1987);
Baseline comparisons	Participants were divided into two groups: high sugar intake (≥ 206 g, n = 34); low sugar intake group (< 206 g, n = 303) *See confounding below*
Dietary assessment	24 hour dietary recall
Timing	First antenatal visit
Comparison	high sugar intake (≥ 206 g = 90th centile of sugar intake) versus low sugar intake group (< 206 g)
Outcomes	Maternal BMI, gestational weight gain, preterm birth, gestational age, birthweight, SGA
Results	see below

	Low sugar (n = 303)	**High sugar (n = 34)**	**p**
Maternal BMI, mean	22 [SD4]	21 [SD3]	
Gestation weight gain, mean	11 [SD8]	10 [SD4]	
SGA	32 (11%)	7 (21%)	0.083
Preterm birth	33 (11%)	4 (12%)	
Gestational age at birth, weeks, mean	39 [SD3]	39 [SD2]	
Birthweight, g, mean	3204 [SD672]	3056 [SD603]	

Effect of high sugar intake on birthweight (multiple regression analysis): -216.6 g (SE10.3.9) p < 0.05*

Length of followup	To birth
Confounding	*adjusted for gestational age, ethnicity, marital status, age, parity, cigarette smoking, new weight gain, BMI, energy
Risk of bias	Low risk of bias: of the 425 adolescents randomly selected from the total cohort of 2789 to provide dietary information, 88 (21%)were excluded mostly due to lack of weight gain values and pre-pregnancy weight gain data
Relevance	Likely to be relevant to pregnant adolescent women in Australia
Other comments	In the high sugar intake group, the five most commonly listed products contributing to total sugar intake were carbonated beverages, fruit juices, icecream, syrup added to pancakes, and sweetened cereals

Reference	**Lenders 1996**
Food groups	sugar
Study type /method	Prospective cohort
Level of evidence	II (aetiology)
Setting	City of Camden, NJ, USA; 1985 to 1990
Funding	NICHHD
Participants	594 pregnant teens aged 12-15 y at first pregnancy (Mean age 16.2 [1.9]); 61% black, 30% Hispanic, 9% white; nondiabetic; low substance use; 69% primiparas; 97% unmarried
Baseline comparisons	After adjusting for energy intake, adolescents with a BMI ≥ 26 were three times more likely to consume high sugar diets *Also see confounding below*
Dietary assessment	24 hour dietary recalls
Timing	At entry, 28 weeks and 36 weeks gestation
Comparison	High sugar diet defined as daily intake of total (simple carbohydrates) at or above the 90th percentile (≥206 g); [n = 60] Reference group < 206 g total sugar/day [n = 534]
Outcomes	SGA (< 10th percentile of birthweight for gestational age)
Results	**SGA** **N** / **%SGA** / **aOR (95% CI)** Reference: 534 / 7 / 1.00 High sugar: 60 / 13 / **2.01 (1.05 to 7.35)**
Length of followup	To birth
Confounding	Adjusted for ethnicity, age, smoking, inadequate weight gain, BMI, total energy intake, low gynaecological age, parity, pregnancy-induced hypertension and inadequate antenatal care
Risk of bias	Low risk of bias: uncertain how accurate 24 hour dietary recalls are
Relevance	Reasonably relevant to teenage women in Australia; note that study found ethnic differences (Puerto Rican adolescents showed a strong association between high sugar intake and shortened gestation)
Other comments	High sugar group consumed 44% of their total dietary energy as total sugar compared with 195 in the reference group

Results (SGA):

	N	%SGA	aOR (95% CI)
Reference	534	7	1.00
High sugar	60	13	**2.01 (1.05 to 7.35)**

Reference	**Nwaru 2010**
Food type	Sugar: chocolate and sweets
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Tampere, Finland
Funding	Academy of Finland, Finnish Pediatric Research Foundation, the Juho Vainio Foundation, the Yrjo Jahnsson Foundation, Turku, Oulu and Tampere University Hospitals, JDRF, Novo Nordisk Foundation, EU Biomed 2 Program
Participants	931 mother-infant pairs (children with human leukocyte antigen-conferred susceptibility to type 1 diabetes) participating in the Finnish type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study between September 1996 and October 1997
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ given to women after birth, for return at the three month visit (FFQ intended to cover maternal diet during pregnancy and lactation)
Comparison	Amount of intake of chocolate and sweets
Outcomes	Allergic sensitisation in offspring by 5 years: food allergens (egg, cow's milk, fish, wheat); inhalant allergens (house dust mite, cat, timothy grass, birch)
Results	**Chocolates and sweets** ***Food allergens*** / ***Inhalant allergens*** OR 1.00 95% CI 0.88 to 1.16 / OR 1.01 95% CI 0.90 to 1.13 aOR 0.99 95% CI 0.86 to 1.14 / aOR 1.00 95% CI 0.88 to 1.14
Followup	To 5 years
Confounding	Adjusted for energy intake, place of birth, season of birth, sex of the child, number of siblings, gestational age at birth, parental asthma, parental allergic rhinitis, maternal age at birth, maternal smoking during pregnancy, maternal education
Risk of bias	Low risk of bias: data available for 931/1175 (79.2%) children recruited – 108 did not participate in survey, a further 49 did not have IgE measurements, a further 87 had no FFQ or an incomplete FFQ
Relevance	Likely to be relevant to Australian women; some differences in individual types of vegetables between Finland and Australia
Other comments	28% of women took vitamin D supplements, 73% took iron supplements; HLA genotype not likely to have any impact on the development of allergic diseases.

Reference	**Olafsdottir 2006**
Dietary patterns	Sugar: eating more sweets in early pregnancy
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Iceland
Funding	Icelandic Research Council, University of Iceland Research Fund
Participants	495 randomly selected healthy pregnant women attending a routine first antenatal visit
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	At 11-15 weeks gestation; and 34-37 weeks gestation (to reflect food intake for the last 3 months)
Comparison	Eating more sweets versus not eating more sweets than usual (in early pregnancy)
Outcomes	Gestational weight gain (optimal weight gain defined as 12.1 to 18.0 kg for women with normal pre-pregnancy weight; and 7.1 to 12.0 kg for overweight women)
Results	20% of the 301 women with BMI < 25 at first visit had excessive gestational weight gain; 55% of the 194 women with BMI ≥ 25 at first visit had excessive gestational weight gain **Eating more sweets in early pregnancy** At least optimal weight gain: aOR 2.78 95% 0.84 to 9.27 **Excessive weight gain: aOR 2.52 95% CI 1.10 to 5.77**
Followup	To birth
Confounding	Adjusted for maternal age, gestational length and smoking
Risk of bias	Low to moderate risk of bias: of the 549 women enrolled, 495 (90%) completed the study; 54 women were excluded (17 miscarriage/stillbirths, 5 sets of twins or triplets, 17 preterm births, 15 missing data); 89 women did not complete FFQ at the second timepoint and so only 406 women could be included for measures relating to late pregnancy; limited number of confounders used in adjusted analyses
Relevance	Likely to be reasonably relevant to Australian women
Other comments	

<table>
<tr><td>Reference</td><td>Petridou 2005</td></tr>
<tr><td>Food type</td><td>Sugars and syrups</td></tr>
<tr><td>Study type</td><td>Case-control study</td></tr>
<tr><td>Level of evidence</td><td>III-3</td></tr>
<tr><td>Setting</td><td>Greece</td></tr>
<tr><td>Funding</td><td>The Childhood Hematology-Oncology Group: Athens University Medical School, Aristotle University of Thessaloniki, University Hospital of Heraklion</td></tr>
<tr><td>Participants</td><td>Cases: 131 children with acute lymphoblastic leukemia, aged 12 to 59 months, gender and age matched to
Controls: 131 children hospitalised for minor conditions between 1999 and 2003</td></tr>
<tr><td>Baseline comparisons</td><td>See confounding below</td></tr>
<tr><td>Dietary assessment</td><td>FFQ</td></tr>
<tr><td>Timing</td><td>During index pregnancy</td></tr>
<tr><td>Comparison</td><td>Quintiles of sugars/syrups – median Q1; 10 g/day: median Q5 152 g/day</td></tr>
<tr><td>Outcomes</td><td>Acute lymphoblastic leukemia (ALL)</td></tr>
<tr><td>Results</td><td><table>
<tr><td></td><td>Median g/day</td><td>Cases</td><td>Controls</td><td>p for trend</td></tr>
<tr><td>Q1:</td><td>10</td><td>21</td><td>31</td><td></td></tr>
<tr><td>Q2:</td><td>25</td><td>19</td><td>34</td><td></td></tr>
<tr><td>Q3:</td><td>44</td><td>29</td><td>23</td><td></td></tr>
<tr><td>Q4:</td><td>79</td><td>29</td><td>23</td><td></td></tr>
<tr><td>Q5:</td><td>152</td><td>33</td><td>20</td><td>0.004</td></tr>
</table>
Logistic regression: one quintile more of sugars/syrups: aOR 1.32 95% CI 1.05 to 1.67</td></tr>
<tr><td>Followup</td><td>NA</td></tr>
<tr><td>Confounding</td><td>Total energy intake (but not mutually among food groups); matching variables; maternal age at birth; birthweight; maternal smoking during pregnancy; maternal years of schooling, maternal occupation</td></tr>
<tr><td>Risk of bias</td><td>Moderate: moderate risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy some time previously;
Cases: 171 children with ALL were identified; 21 had missing data, consent was not given in 9 cases and 10 were unable to be matched, leaving 131 (77%) of cases available</td></tr>
<tr><td>Relevance</td><td>Diets of Greek women may differ from current diets of Australian women</td></tr>
<tr><td>Other comments</td><td></td></tr>
</table>

Reference	**Petridou 1998a**
Food type	Sugars and syrups: sugar, cookies, chocolate bars, wafers, baklava, kataifi and other Greek sweets with syrup, spoonful sweets, jellies, glazed fruits, cream pastries, pancakes with syrup, bonbons, honey, compote (0.5).
Study type	Case-control study
Level of evidence	III-3
Setting	Greater Athens area, Greece
Funding	Greek Ministry of Health and Welfare, and Foundation for Research in Childhood 'S. Doxiadis'
Participants	Cases: 109 children with cerebral palsy (CP), born between 1984 and 1988 (estimated to be two-thirds of the children with CP born during this period) Controls (1): 155 neighbouring children of similar sex and age (± 12 months) Controls (2): 99 healthy siblings of similar sex and age (± 12 months) of the first neurological patient seen by the attending physician after a visit by the CP patient
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During pregnancy
Comparison	≤ 1 versus 2 versus > 2 serves of sugars and syrups per day; regression analysis: risk of cerebral palsy with change in consumption by one unit (= consumption of sugars and syrup once daily)
Outcomes	Cerebral palsy
Results	≤ 1 serve of sugars and syrups per day: 11/91 (12.1%) cases v 21/246 (8.5%) controls 2 serves of sugars and syrups per day: 31/91 (34.0%) cases v 104/246 (42.3) controls > 2 serves of sugars and syrups per day: 49/91 (53.9%) cases v 121/246 (49.2%) controls Regression analysis for each unit of consumption of sugars and syrups once daily: aOR 1.08 95% CI 0.73 to 1.62 aOR 1.21 95% CI 0.77 to 1.90 (additionally adjusted for all food groups)
Followup	8 years
Confounding	Age and sex of child, maternal age at birth, maternal age at menarche, maternal chronic disease, previous spontaneous abortions, persistent vomiting during index pregnancy, multiple pregnancy, number of obstetric visits; timing of membrane rupture in index birth, use of general anaesthesia in the index birth, mode of birth, abnormal placenta, infant head circumference at birth, congenital malformation, place of index birth, use of supplementary iron during index pregnancy, physical exercise during index pregnancy, painless childbirth classes. The following were not included in the model: - Smoking or consumption of coffee or alcohol during pregnancy (stated to be "unrelated to CP and had no confounding influence"); - Gestational age, birthweight and maternal weight gain (stated to be "strong predictors of CP, but were not included in the model, since they are probably intermediate stages in a possible link between diet and CP (mediators) rather than genuine confounders"
Risk of bias	Moderate-high: High risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy 8 years previously; Cases: 109 children with CP were identified; for 6 children either collaboration with their guardian or a diagnosis of CP was not confirmed; and reliable maternal dietary intakes were not available for 12 women, leaving 91 cases available for analysis. Controls: 278 mother-child pairs were approached; 16 refused to participate; matching controls were not available in 8 instances, and reliable maternal dietary intakes were not available for 8 women, leaving 246 controls available for analysis.
Relevance	Diets of Greek women in 1998 may differ from current diets of Australian women
Other comments	

Reference	**Petridou 1998b**

Food type	Sugars and syrups: sugar, cookies, chocolate bars, wafers, baklava, kataifi and other Greek sweets with syrup, spoonful sweets, jellies, glazed fruits, cream pastries, pancakes with syrup, bonbons, honey, compote (0.5).
Study type	Retrospective cohort study
Level of evidence	III-2
Setting	Two cities (Athens and Larissa) in Greece
Funding	Not reported
Participants	368 nondiabetic women giving birth to healthy singleton babies from March to October 1995
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Immediately after birth
Comparison	< 1 versus 1-2 versus 3-4 versus > 4 serves of sugars and syrups per day; < 1 serve of sugars and syrups per day: 156/268 (42.4%) 1-2 serves of sugars and syrups per day: 95/268 (25.8%) 3-4 serves of sugars and syrups per day: 84/268 (22.8%) >4 serves of sugars and syrups per day: 33/268 (9.0%) Regression analysis: mean change in birthweight (g) for each unit change in consumption (= consumption of sugars and syrup once daily)
Outcomes	Birthweight
Results	**Regression analysis for each unit of consumption of sugars and syrups (once daily):** 4 g [SE33], p = 0.90 -2 g [SE32], p = 0.96 without controlling for total energy intake
Followup	To birth
Confounding	Gender of child, birth order, maternal age, maternal education, maternal height, history of miscarriages, history of abortions, bleeding, smoking during pregnancy, coffee drinking, alcohol drinking, maternal weight gain, total energy intake, folic acid supplements
Risk of bias	Low-moderate risk of bias: of the 400 eligible women, 368 (92%) were available for analysis – 32 were unwilling or unable to participate; women would have been aware of the birthweight of their baby before completing the FFQ
Relevance	Diets of Greek women in 1995 may differ from current diets of Australian women
Other comments	

Reference	Stuebe 2009
Dietary patterns	Sugar: sugar-sweetened beverages
Study type	Prospective cohort study (Project Viva)
Level of evidence	II (aetiology)
Setting	8 urban and suburban obstetric offices of a multispecialty group practice in eastern Massachusetts, USA
Funding	US NIH, Harvard Medical School, Harvard Pilgrim Health Care Foundation
Participants	1338 women giving birth to a live singleton infant, < 22 weeks gestation at study entry; 379 (27%) were overweight (BMI ≥ 26); 703 (51%) experienced excessive weight gain Exclusions: not fluent in English
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Administered in first and second trimesters of pregnancy
Comparison	Sugar sweetened beverages (serves per day)
Outcomes	Excessive gestational weight gain (IOM 1990)
Results	**Excessive gestational weight gain: sugar-sweetened beverages (SSBs)** **Serves per day, median** — **aOR (95% CI)** **Inadequate/adequate GWG** / **excessive GWG** SSBs: 0.36 (IQR 0.11 to 0.75) / 0.37 (IQR 0.12 to 0.75) / 0.93 (0.78 to 1.11) **SSBs, per serving per day: multivariate logistic regression model:** aOR 0.87 95% CI 0.72 to 1.05 **-0.46 kg 95% CI -0.87 to -0.05**
Followup	To birth
Confounding	Adjusted for pre-pregnancy BMI, maternal age, race/ethnicity, smoking status, gestational age at birth, nausea in first trimester in pregnancy
Risk of bias	Low risk of bias: Of 2083 eligible women, 1388 (67%) of women had data available for analysis (31 had missing information on pre-pregnancy BMI and gestational weight gain; 226 had missing covariate information and 438 had missing data on either first or second-trimester diet and mid-pregnancy physical activity); included women were less likely to be African-American or Hispanic, to be younger, multiparous and obese
Relevance	Likely to be relevant to Australian women
Other comments	Surprising results for SSBs – one explanation given was that women gaining excessive weight may cut back SSBs, but this does not appear to hold for other foods such as fried foods.

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Vegetables

Included Studies

Study	Outcomes
1. Brekke 2009	Beta-cell autoimmunity
2. Chatzi 2008	Child persistent wheeze, atopic wheeze, atopy (all at 6.5 years)
3. George 2005	Breastfeeding at 6 months
4. Giordano 2010	Child hypospadias
5. Giordano 2008	Child hypospadias and cryptorchidism
6. Herrick 2003	Cortisol concentrations in offspring at 30 years
7. Jensen 2004	Childhood acute lymphoblastic leukemia
8. Jones 2000	Bone mass at 8 years
9. Knox 1972	Anencephalus
10. Kwan 2009	Childhood acute lymphoblastic leukemia – update of Jensen 2004
11. Lagiou 2006	Maternal pregnancy hormones
12. Lamb 2008	Islet autoimmunity
13. Laraia 2007	“Pre-pregnancy BMI”
14. Li 2009	Maternal URTI
15. Martindale 2005	Eczema, wheeze in first 2 years of child’s life
16. Mikkelsen 2006	Birthweight
17. Mitchell 2004	SGA
18. Miyake 2010	Infant wheeze and eczema up to 24 months
19. Nwaru 2010	Allergic sensitisation in offspring by 5 years
20. Oien 2010	Childhood eczema and asthma at 2 years
21. Petridou 2005	Childhood acute lymphoblastic leukemia
22. Petridou 1998	Cerebral palsy at 8 years
23. Pierik 2004	Cryptorchidism and hypospadias
24. Pogoda 2009	Childhood brain tumours
25. Ramon 2009	Birthweight, SGA
26. Sausenthaler 2007	Allergic sensitisation, eczema at 2 years of age
27. Shiell 2001	Blood pressure in offspring at 27 to 30 years
28. Willers 2007	Respiratory and atopic symptoms
29. Willers 2008	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable ‘asthma symptoms’ in the last

	12 months (measured longitudinally from 1 to 8 years age)
30. Yin 2010	Bone mass at 16 y
31. Zhang 2006	GDM

Evidence Statements

	N	Level	References
Maternal Outcomes			
1. In a US cohort study, women who were **obese before pregnancy** were significantly less likely to meet recommendations for vegetable intake compared with overweight women: • Adherence for overweight women was 101.3% [SD 80.1] compared with 86.4% [SD 64.5] for obese women ($p < 0.03$)	2394	II	Laraia 2007
2. In a US cohort study, **increased maternal sex hormone binding globulin (SHBG)** was significantly associated with increasing intake of vegetables and legumes during pregnancy: • 16 completed weeks GA: 4.2 % SHBG change 95% CI 0.6 to 7.9; 27 completed weeks GA: 4.2 % SHBG change 95% CI 0.2 to 8.4 No significant associations were seen between vegetable intake and maternal oestradiol, oestriol, progesterone, or prolactin	270	II	Lagiou 2006
3. In a US cohort study, no association was seen between women having **gestational diabetes mellitus (GDM)** and their intake of vegetable fibre intake in fully adjusted analyses (p for trend = 0.24)	13,110	II	Zhang 2006
4. In a North American retrospective cohort study, no association was seen between **upper respiratory infections** in women during the first half of pregnancy and their intake of vegetables (p value for trend of 5 month risk = 0.33)	1034	III-2	Li 2006
Congenital Anomalies			
5. In a case-control study from the UK, stillbirths and infant death due to **anencephalus** were negatively associated with canned beans, onions/shallots, brussel sprouts and old potatoes; and positively associated with new potatoes, tomatoes, cabbages, and canned peas	Not stated	III-3	Knox 1972
6. In an Italian case-control study, no associations were seen between maternal intake of vegetables and risk of **hypospadias** in offspring: aOR 0.89 95% CI 0.38 to 2.10	80 cases; 80 controls	III-3	Giordano 2010
7. In an Italian case-control study, no associations were seen between maternal intake of vegetables during pregnancy (less than once a week versus more than once a week) and **hypospadias and cryptorchidism** in offspring: • Raw vegetables: aOR 1.12 95% CI 0.57 to 2.21 • Cooked vegetables: OR 0.76 95% CI 0.39 to 1.46	90 cases; 243 controls	III-3	Giordano 2008

• Mostly market vegetables: OR 1.31 95% CI 0.69 to 2.51			
8. In a Dutch case-control study, a vegetable-rich diet during pregnancy reduced the risk of **cryptorchidism** in male offspring (aOR 0.4 95% CI 0.2 to 0.9) but no influence was seen on risk of **hypospadias** (OR 0.7 95% CI 1.2)	443 pairs	III-3	Pierik 2004
Birth Outcomes			
9. In a New Zealand case-control study, no significant association was seen between **SGA** and vegetable intake at the time of conception ($p = 0.32$) or in the last month of pregnancy ($p = 0.12$)	1138	III-3	Mitchell 2004
10. In a Danish cohort study, **birthweight** was not significantly associated with maternal intake of green leafy vegetables during pregnancy: • Adjusted regression coefficient 5.5 95% CI -0.23 to -11.3 (additionally energy-adjusted)	43,585	II	Mikkelsen 2006
11. In a Spanish cohort study: • lower **birthweight and birth length** were associated with lower maternal vegetable intake in the first and third trimester • Lower **SGA for weight and for length (customised < 10th percentile)** were associated with lower maternal vegetable intake in the first trimester ($p < 0.001$ and $p < 0.03$ for adjusted trend) and third trimester ($p = 0.01$ and $p = 0.02$) for adjusted trend across quintiles.	787 infants	II	Ramon 2009
Breastfeeding			
12. In a US study, lactating women: • consumed more vegetables than non-lactating women (2.6 v 1.8 serves a day, $p < 0.02$); • had significantly higher intakes of lettuce than women who bottle-fed exclusively ($p < 0.0\%$)	149	II	George 2005
Childhood – Eczema And Other Allergy Outcomes			
13. In a Japanese cohort study: • **Eczema in children at 16-24 months** was not associated with maternal intake of total vegetables or other vegetables, but increased intake of green and yellow vegetables was associated with fewer cases of eczema (compared with lowest quartile): o 2nd quartile aOR 0.30 95% 0.16 to 0.52 o 3rd quartile aOR 0.53 95% CI 0.31 to 0.89 o 4th quartile aOR 0.41 95% CI 0.24 to 0.71 ($p = 0.01$) • **Wheeze in children at 16-24 months** was not associated with maternal intake of total vegetables, green and yellow vegetables or other vegetables during pregnancy.	763	II	Miyake 2010
14. In a Scottish cohort study, vegetable intake during pregnancy was not associated with either **eczema or wheeze** in children in their 2nd year of life	1300 children	II	Martindale 2005

15. In a German cohort study: **Allergen sensitisation or eczema in children at 2 years of age** were not generally associated with maternal intake of specific vegetables in pregnancy except for: • Significantly increased allergen sensitisation with **celery** intake 2-3 times a month or more (aOR for any sensitisation 1.61 95% CI 1.07 to 2.41 and 1.81 95% CI 1.18 to 2.89 for food allergens; • Significantly increased allergen sensitisation with **raw sweet pepper** intake 2-3 months or more (aOR for any sensitisation 1.45 95% CI 1.03 to 2.06 and 2.16 95% 95% CI 1.20 to 3.90).	3097 children	II	Sausenthaler 2007
16. In a retrospective cohort study from Norway, neither **asthma nor eczema** at two years was associated with vegetable intake during pregnancy: • **Asthma**: almost daily versus ≤ once a week: OR 1.02 95% CI 0.58 to 1.81 • **Eczema**: almost daily versus ≤ once a week: OR 0.72 95% CI 0.51 to 1.02	3086 children	III-2	Oien 2010
17. In a Scottish cohort study, high vegetable intake during pregnancy (≥ once per week) was not significantly associated with **respiratory and atopic outcomes in 5 year old children** (pns; actual numbers not reported)	1212	II	Willers 2007
18. In a Finnish cohort study, vegetable intake during pregnancy was not associated with **allergen sensitisation in children at 5 years of age:** • Food allergen sensitisation aOR 0.80 95% CI 0.49 to 1.31 • Inhalant sensitisation aOR 1.28 95% CI 0.82 to 1.99	931 children	II	Nwaru 2010
19. In a Spanish cohort study, **persistent wheeze and atopy** (but not atopic wheeze) **in children at 6.5 years** were significantly associated with low maternal vegetable intake during pregnancy: • Persistent wheeze aOR 0.36 95% CI 0.14 to 0.92 (> 8 v ≤ 8 serves/week) • Atopy aOR 0.40 95% CI 0.22 to 0.72 (> 8 v ≤ 8 serves/week)	482 children	II	Chatzi 2008
20. In a cohort study from the Netherlands, **wheeze, dyspnoea, steroid use or asthma symptoms** (composite of previous three) **in children longitudinally over 1 to 8 years of age** were not associated with maternal vegetable intake during pregnancy (once per day or more v 1-4 times a week or fewer): • Wheeze aOR 0.97 95% CI 0.83 to 1.12 • Dyspnoea aOR 0.99 95% CI 0.84 to 1.17 • Steroid use aOR 0.96 95% CI 0.76 to 1.20 • Asthma symptoms aOR 0.98 95% CI 0.84 to 1.14	2830 children	II	Willers 2008
Childhood – Other Outcomes			
21. In a Swedish cohort study, **beta-cell autoimmunity in children up to 5 years** was	5,724	II	Brekke 2009

significantly associated with low maternal vegetable intake during pregnancy: • aOR 2.89 95% CI 1.18 to 7.05 (daily v less than daily) (No significant associations were seen for potatoes/root vegetables, fried potatoes or mushrooms)	children		
22. In a cohort study from the US, **islet autoimmunity in children up to 15 years of age** was not associated with maternal vegetable intake during pregnancy; • except for potatoes where an increased consumption was protective (delayed time to onset of islet autoimmunity): aHR 0.49 95% CI 0.28 to 0.87	642 children	II	Lamb 2008
23. In one Australian cohort study, **bone mineral density of children at 8 years** was not associated with maternal vegetable intake during pregnancy: • Total body bone mineral density – p = 0.53 for adjusted regression of portions per week	173 children	II	Jones 2000
24. In a Greek case-control study, **cerebral palsy in children at 8 years** was not associated with maternal vegetable intake during pregnancy: • Regression analysis for each unit of consumption of vegetables once per day: aOR 1.19 95% CI 0.88 to 1.61 (additionally adjusted for all food groups)	109 children	III-3	Petridou 1998
25. In a US case-control study, lower risk of **childhood acute lymphoblastic leukemia** was associated with higher maternal intake of vegetables in the year prior to pregnancy: • aOR 0.53 95% CI 0.33 to 0.85; mean consumption of vegetables 0.74 [SD 0.48] serves per day	138 cases; 138 controls	III-3	Jensen 2004
26. In a US case-control study (phase 1 reported in Jensen 2004), lower risk of **childhood acute lymphoblastic leukemia** was associated with higher maternal intake of vegetables in the year prior to pregnancy: • aOR 0.65 95% CI 0.50 to 0.84: median consumption 0.74 (25^{th} 75^{th} percentiles 0.4, 1.0) serves per day	866 (282 cases)	III-3	Kwan 2009
27. In a Greek case-control study, lower risk of **childhood acute lymphoblastic leukemia** was associated with higher maternal intake of vegetables in the year prior to pregnancy: • logistic regression: one quintile more of milk/dairy products: aOR 0.76 95% CI 0.60 to 0.95	131 cases; 131 controls	III-3	Petridou 2005
28. In an international case-control study, maternal vegetable consumption prior to, and during pregnancy was not generally associated with risk of **childhood brain tumours**, except for decreased risk of primitive neural ectodermal tumours, anaplastic astrocytomas and medulloblastomas with yellow-orange vegetables and anaplastic astrocytomas with cruciferous vegetables	1281 cases; 2223 controls	III-3	Pogoda 2009

29. In one Australian cohort study **bone mineral density of children at 8 years** was not associated with maternal intake of vegetables prior to pregnancy: • Total body bone mineral density – $p = 0.52$ for adjusted regression of portions per week	173 children	II	Jones 2000
30. In an Australian cohort study (follow-up of Jones 2000) **bone mass in 16 year-old adolescents** was not associated with maternal vegetable intake during pregnancy: • Total body bone mineral density r^2 0.324; ß -2.3 (pns) for adjusted regression of portions per week	216 children	II	Yin 2010
31. In a cohort study from Scotland, **systolic blood pressure** was significantly increased in 27 to 30 year old offspring of women with low intake of vegetables during pregnancy (in conjunction with a high red meat and low carbohydrate diet): • < 7 serves per week of green vegetables: ß 0.26 95% CI 0.03 to 0.50	626 adult off-spring	II	Shiell 2001
32. In a cohort study from Scotland, **cortisol concentrations in offspring aged 30 years** were highest in women consuming less than 7 portions of green vegetables (and more than 21 portions of meat/fish < per week) in late pregnancy	251 adult off-spring	II	Herrick 2003

Evidence Tables

Reference	**Brekke 2009**
Food type	Vegetables
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	5 years follow up of babies born in Southeast Sweden between 1 October 1997 and 1 October 1999 and invited to be in the Southeast Sweden (ABIS) study.
Funding	JDRF-Wallenberg foundations, Swedish Medical Research Council, Swedish Child Diabetes Foundation, Swedish Diabetes Association, Swedish Dairy Association R & D, Majblomman Foundation and the Novo Nordisk Foundation.
Participants	5 year follow up of 5724 children who completed 2 of the 3 possible blood samplings (study cohort), 36% of the total 16004 children participating in ABIS (the primary cohort).
Dietary assessment	FFQ performed after delivery, but used to recall diet during pregnancy, Food groups classified according to daily, 3-5 times/week, 1-2 times/wk or <1 time/wk.
Baseline comparisons	*See confounding below*
Timing	After birth women recalled their diet in pregnancy, covering the whole pregnancy.
Comparison	Frequency of consumption of foods in pregnancy amongst the group of infants with beta-cell autoimmunity vs infants without beta-cell autoimmunity.
Outcomes	Beta-cell autoimmunity in the child up to 5 years defined as being positive for two or more autoantibodies (GADA, IA-2A, IAA) at any of the three follow up time points or being diagnosed with diabetes during the 5 year follow up period.
Results	Summary: less than daily vegetable consumption was associated with an increased risk of beta-cell autoimmunity; these findings were robust to adjustment for confounding. 191/5724 (3.3%) children were classified as having beta-cell autoimmunity. **Beta-cell autoimmunity in the child up to 5 years** **Unadjusted OR** / **Adjusted OR** (95% CI) **Vegetables** <1 time/wk: **2.28 (1.08-4.80)** / **2.89 (1.18-7.05)** 1-2 times/wk: 1.20 (0.72-1.99) / 1.30 (0.69-2.45) 3-5 times/wk: **1.71 (1.24-2.35)** / **2.23 (1.52-3.30)** Daily (ref): 1.00 / 1.00 In univariate analyses, when combining the three lower frequency categories and compared with daily vegetable consumption the OR for auto-immunity associated with less than daily consumption was 1.63 (1.20-2.17), p=0.002. 56% of all women consumed vegetables daily in pregnancy, the power to show differences in the 2 bottom categories is limited due to small numbers. None of the following vegetable groups showed any association with risk of autoimmunity in the child: potatoes/root vegetables, fried potatoes, mushroom (field).
Followup	1, 2.5 and 5 years
Confounding	Analyses adjusted for maternal education, weight increase from birth to 2.5 yr, breastfeeding duration and introduction of cow's milk protein. Authors comment that 'adjusting for additional possible confounders like type 1 diabetes in first degree relative, maternal age, delivery mode, smoking during pregnancy, use of vitamin D containing multivitamin supplement in pregnancy and time for introduction of gluten did not change the results.'
Risk of bias	Moderate risk of bias (recall, ascertainment) Study cohort differed significantly from the primary cohort. Mothers of women in the study cohort were generally higher on measures of SES (age,

	education, country of birth, marital status). There was no adjustment for the child's dietary intake during the follow up period.
Relevance	Diets in Sweden may differ from diets of Australian women, particularly in relation to access to seafood. National data collected during ABIS suggested during pregnancy the most frequently consumed vegetables in Sweden were tomatoes, cabbage, onions, lettuce and cucumbers. Intake of fruit was not assessed, therefore it is possible there could be combined effects of fruits and vegetables, (if we suspect a diet high in vegetables is also high in fruit).
Other comments	Some funding from Swedish Dairy Association.

Reference	**Chatzi 2008**
Food type	Vegetables
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women presenting antenatal care at general practices in Menorca, a Mediterranean island in Spain (mid 1997 to mid 1998)
Funding	Instituto de Salud Carlos III red de Grupos Infancia y Media Ambiente, the Fundacio "La Caixa" , Instituto de Salud Carlos III, red de Centros de Investigacion en Epidemiologica y Salud Publica, EU, National Center for Environmental Health, USA, the GA2LEN project, Ministry of Education and Science, Spain, Oficina de Ciencia y Tecnologia, Generalitat Valenciana.
Participants	482 children of 507 women who had attended antenatal care in Menorca
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	not clear when women did FFQ and period of pregnancy it was intended to cover
Comparison	≤ 8 v > 8 serves of vegetables per week
Outcomes	Persistent wheeze, atopic wheeze and atopy at 6.5 years
Results	***Persistent wheeze at 6.5 years*** **aOR 0.36 95% CI 0.14 to 0.92** (also adjusted for firstborn and lower respiratory tract infections at age 1) ***Atopic wheeze at 6.5 years*** aOR pns (also adjusted for birthweight and maternal atopy) ***Atopy at 6.5 years*** **aOR 0.40 95% CI 0.22 to 0.72** (also adjusted for birthweight and maternal atopy)
Followup	6.5 years
Confounding	Analyses adjusted for gender, maternal and paternal asthma, maternal social class and education, BMI at age 6.5 years and total energy intake at 6.5 years
Risk of bias	Low risk of bias: results from 468/482 children (97%) able to be analysed (4 incomplete data and 8 implausible values);
Relevance	Diets in Menorca may differ from diets of Australian women, particularly urban women
Other comments	

Reference	**George 2005**
Food type	Vegetables
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Texas, US
Funding	Not reported
Participants	149 Medicaid-qualified women (30% white, 24% African American, 46% Hispanic) – recruited from a larger study on postpartum weight retention Inclusion criteria: 18 years or older; non-Hispanic white, African American or Hispanic ethnicity; birth of a health term infant, fluency and literacy in English; absence of pregnancy-related abnormalities and disease conditions.
Baseline comparisons	Significant differences between lactating and non-lactating women – higher parity, BMI and lower education levels in non-lactating women.
Dietary assessment	Semiquantitative FFQ to cover pregnancy and first six months postpartum
Timing	FFQ administered at 6 weeks and 6 months postpartum
Comparison	Number of daily serves of vegetables (mostly potatoes, corn, tomatoes and lettuce).
Outcomes	Breastfeeding (exclusive or partial at 6 months postpartum)
Results	**Lactating women consumed more vegetables in the postpartum period than non-lactating women (2.6 v 1.8 serves a day, $p < 0.02$)** **After childbirth, lactating women had significantly higher intakes of lettuce than women who bottle-fed exclusively ($p < 0.05$)**
Followup	6 months postpartum
Confounding	No adjustment for potential confounding
Risk of bias	Moderate-to-high risk of bias; no attempt to control for confounding despite significant baseline differences between lactating and non-lactating women.
Relevance	Possibly relevant to low-income women in Australia
Other comments	Minimal reporting of results

Reference	**Giordano 2010**
Food type	Vegetables
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Rome, Italy
Funding	Not reported
Participants	80 cases of hypospadias requiring surgical treatment in children aged 0 to 24 months (mean age 57.62 weeks) 80 controls: healthy males without any congenital defect, aged 0 to 24 months (mean age 36.52 weeks); recruited between September 2005 and May 2007
Baseline comparisons	*See confounding below*
Dietary assessment	Interview on 'typical' maternal diet habits in relation to the index pregnancy and food frequencies
Timing	FFQ administered on recruitment for mothers of cases and during vaccination visits for mothers of controls
Comparison	Rare versus frequent consumption of vegetables
Outcomes	Hypospadias
Results	**Vegetables** **Cases** / **Controls** / **OR** / **aOR** **Rare**: **64** (80.0%) / 66 (82.5%) / 1.00 / 1.00 **Frequent**: **16** (20.0%) / 14 (17.5%) / 1.18 95% CI 0.53 to 2.61 / 0.89 95% CI 0.38 to 2.10
Followup	n/a
Confounding	Adjusted for mother's BMI at conception and education of the father; Gestational age, birthweight and SGA were not included among the covariates in the regression models, as they may share a common aetiology with hypospadias
Risk of bias	Moderate risk of bias: Participation rate of parents of cases was higher than that of controls (85% versus 70%); very few potential confounders used in adjusted analyses
Relevance	Likely to be reasonably relevant for Australian women
Other comments	Likely to be underpowered

Results table:

Vegetables	Cases	Controls	OR	aOR
Rare	**64** (80.0%)	66 (82.5%)	1.00	1.00
Frequent	**16** (20.0%)	14 (17.5%)	1.18 95% CI 0.53 to 2.61	0.89 95% CI 0.38 to 2.10

Reference	**Giordano 2008**
Food type	Vegetables: raw vegetables, cooked vegetables, mostly market vegetables
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Sicily, Italy
Funding	Sicilian Congenital Malformation Registry
Participants	90 cases: 43 cases of hypospadias and 48 cases of cryptorchidism (both in one infant) 202 controls: randomly selected controls born in the same year and the same region Births between 1998 to 2003
Baseline comparisons	Low birthweight, low maternal education, mother's history of gynaecological disease and father's history of urogenital diseases differed significantly between cases and controls *See confounding below*
Dietary assessment	Interview on maternal diet and food frequencies
Timing	FFQ
Comparison	Consumption of vegetables once a week or less versus more than once a week
Outcomes	Hypospadias and cryptorchidism
Results	**Raw vegetables** **Hypospadias** Cases / Controls / OR **≤ 1/week**: 12 (27.9%) / 42 (20.9%) / 1.00 **> 1/week**: 31 (72.1%) / 159 (79.1%) / 0.68 95% CI 0.32 to 1.44 **Cryptorchidism** **≤ 1/week**: 7 (14.9%) / 42 (20.9%) / 1.00 **> 1/week**: 40 (85.1%) / 159 (79.1%) / 1.51 95% CI 0.53 to 1.79 **Hypospadias and cryptorchidism** **≤ 1/week**: 19 (21.3%) / 42 (20.9%) / 1.00 **> 1/week**: 70. (78.7%) / 159 (79.1% / 0.76 95% CI 0.39 to 1.46 **Cooked vegetables** **Hypospadias** **≤ 1/week**: 16 (37.2%) / 63 (31.2%) / 1.00 **> 1/week**: 27 (62.8%) / 139 (68.8%) / 0.76 95% CI 0.39 to 1.52 **Cryptorchidism** **≤ 1/week**: 18 (37.5%) / 63 (31.2%) / 1.00 **> 1/week**: 30 (62.5%) / 139 (68.8%) / 0.76 95% CI 0.39 to 1.46 **Hypospadias and cryptorchidism** **≤ 1/week**: 34 (37.8%) / 63 (31.2%) / 1.00 **> 1/week**: 56 (62.2%) / 139 (68.8%) / 0.75 95% CI 0.44 to 1.26 **Mostly market vegetables** **Hypospadias**

	≤ 1/week	15 (34.9%)	78 (38.6%)	1.00
	> 1/week	28 (65.1%)	124 (61.4%)	1.17 95% CI 0.59 to 2.34
	<u>Cryptorchidism</u>			
	≤ 1/week	18 (37.5%)	78 (38.6%)	1.00
	> 1/week	30 (62.5%)	124 (61.4%)	1.05 95% CI 0.55 to 2.01
	<u>Hypospadias and cryptorchidism</u>			
	≤ 1/week	15 (16.7%)	78 (38.6%)	1.00
	> 1/week	75 (83.3%)	124 (61.4%)	1.31 95% CI 0.69 to 2.51
	<u>Raw vegetables (adjusted analysis)*</u>			
		aOR		
	Hypospadias			
	>1/week	1.59 95% CI 0.68 to 3.74		
	Cryptorchidism			
	>1/week	0.82 95% CI 0.32 to 2.12		
	Hypospadias and cryptorchidism			
	>1/week	1.12 95% CI 0.57 to 2.21		
Followup	n/a			
Confounding	Results for this food group were not presented as adjusted analyses *Analysis of raw vegetables adjusted for mother's age, parity, education, gynaecological diseases; paternal urogenital diseases, and use of pesticides; birthweight			
Risk of bias	Moderate risk of bias: Participation rate of parents and data collection rate of cases was lower than that of controls (76% versus 91%); no adjusted results presented for this food group			
Relevance	Likely to be reasonably relevant for Australian women, although hypospadias rates very high and unlikely that most Australian women will have such high pesticide exposure; threshold of vegetable consumption very low (once a week versus more than once a week)			
Other comments	Ragusa region in Sicily is a region of intensive agriculture (involving high rates of pesticide and other chemical use) with high rates of hypospadias and cryptorchidism			

Reference	**Herrick 2003**
Food groups	Vegetables: green vegetables; potatoes
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Motherwell, Scotland
Funding	Dunhill Medical Trust, NIH
Participants	251 men and women whose mothers' food intakes had been recorded during pregnancy during 1967 to 1968. These women had been advised to eat 0.45 kg of red meat a day and to avoid carbohydrate-rich foods during pregnancy
Baseline comparisons	*See confounding below*
Dietary assessment	Mothers asked about consumption of 10 foods
Timing	Early pregnancy (≤ 20 weeks); late pregnancy (> 20 weeks)
Comparison	portions of green vegetables and potatoes per week
Outcomes	Cortisol concentrations in offspring aged 30 years
Results	**Green Vegetables** ***Cortisol concentrations highest in women consuming more than 21 portions of meat/fish and < 7 portions of green vegetables per week in late pregnancy*** **Potatoes**: no significant association seen with cortisol concentrations (exact numbers not reported in paper)
Length of followup	30 years
Confounding	Analyses adjusted for offspring's gender, social class at birth, BMI, alcohol consumption, and activity level
Risk of bias	Moderate risk of bias: For the 1432 records from 1967-8 recorded liveborn, singleton births with complete names, birth measurements and ≥ 1 diet record. 965 offspring were alive and living locally; and after attrition or declining to participate, 251 (17.5%) were available for analysis.
Relevance	Very high intake of meat and very low carbohydrate intake limits the relevance to current dietary intakes of Australian women
Other comments	Authors state that "in the setting of advice to follow a pregnancy diet high in protein and low in carbohydrate, an unbalanced pattern of higher meat/fish and lower green vegetable consumption in late pregnancy leads to elevated cortisol concentrations in the offspring"

Reference	**Jensen 2004**
Food type	Vegetables: all; specific vegetables (string beans or peas; tomatoes or tomato juice; coleslaw or cabbage; mustard greens, turnip greens, collards, kale; carrots or mixed vegetables containing carrots; broccoli; spinach; cauliflower or brussel sprouts
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study)
Funding	PHS
Participants	138 matched cases and controls: Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, parental occupation and smoking during pregnancy – no evidence of confounding was seen for these variables. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of vegetables
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Vegetables as a group:** **aOR 0.53 95% CI 0.33 to 0.85**: mean consumption 0.74 [SD 0.48] serves per day **String beans or peas:** **aOR 0.84 95% CI 0.71 to 1.00**: mean consumption 3.40 [SD 1.81] serves per day* **Tomatoes, tomato juice:** aOR 0.94 95% CI 0.82 to 1.08: mean consumption 4.24 [SD 2.17] serves per day* **Coleslaw, cabbage**: aOR 0.88 95% CI 0.71 to 1.08: mean consumption 2.07 [SD 1.51] serves per day* **Mustard greens, etc.:** aOR 0.88 95% CI 0.58 to 1.34: mean consumption 1.23 [SD 0.80] serves per day* **Carrots, etc.:** **aOR 0.79 95% CI 0.67 to 0.94**: mean consumption 4.14 [SD 1.86] serves per day* **Broccoli:** aOR 1.00 95% CI 0.84 to 1.19: mean consumption 3.72 [SD 1.81] serves per day* **Spinach**: aOR 1.02 95% CI 0.81 to 1.27: mean consumption 2.18 [SD 1.51] serves per day* **Cauliflower or b. Sprouts** aOR 1.03 95% CI 0.83 to 1.27: mean consumption 2.13 [SD 1.49] serves per day*
Followup	n/a
Confounding	Analyses were adjusted for variables previously shown to be significantly associated with ALL in the overall study – income, prior fetal loss, child's exposure to other children under age five, and maternal exposure to indoor insecticides during pregnancy; along with portion size and energy consumption
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 1999, 83% consented to participate; 69% of the eligible controls agreed to participate. Of the 161 matched pairs, seven pairs were excluded as the respondent was not the biological mother, 16 pairs were excluded due to questionable dietary questionnaire data, leaving 138 matched pairs (86%); some recall bias likely
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	*Some consumption levels seem high – possibly per week rather than per day?

Reference	**Jones 2000 (see also Yin 2010)**
Food type	Vegetables
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Southern Tasmania, Australia
Funding	NHMRC, Tasmanian Government, Royal Hobart Hospital Acute Care Program
Participants	173 mothers; and their infants born in 1988 (part of a larger infant health study of babies at high risk of SIDS) Exclusions: multiple pregnancies
Baseline comparisons	Mothers with no tertiary education more likely to have been excluded due to missing data
Dietary assessment	FFQ
Timing	Dietary intake during third trimester of pregnancy
Comparison	Linear regression of density (portions per kJ)
Outcomes	Bone mass (bone mineral density (BMD) and bone mineral content*) in 8 year old children
Results	**BMD at 8 years;** **Total body (g/cm^2)** r^2 0% 0.002 (p = 0.42) adjusted r^2 23% 0.001 (p = 0.52) **Femoral neck (g/cm^2)** r^2 1% 0.002 (p = 0.50) adjusted r^2 33% 0.001 (p = 0.67) **Lumbar spine (g/cm^2)** r^2 2% 0.005 (p = 0.1 adjusted r^2 33% 0.004 (p = 0.11)
Followup	8 years
Confounding	Analyses were adjusted for method of dietary assessment, maternal education, parental unemployment, sex, weight at age 8 years, height at age 8 years, weekend sunlight exposure in winter at age 8 years, smoking during pregnancy, sports participation, ever breast-fed and current calcium intake.
Risk of bias	Moderate-high: 330 (215 males, 115 females) representing a 60% response rate from those available in 1996; 47% of the original 1988 cohort, This dropped to 173 (dietary information missing or unreliable for 115 mothers, 32 multiple births, 10 participants had missing data for confounders) representing 52% of participants from 1996 and 25% of those in the original cohort. 72% of the 173 participants were male. Gender imbalance suggests potential selection bias (due to original selection of infants at high risk of SIDS)
Relevance	Infants at high risk of SIDS represent a selected group (more males, preterm births, teenage mothers, smoking during pregnancy)
Other comments	*Bone mineral content not reported – stated to be similar to bone mineral density results

Reference	**Knox 1972**
Food type	Vegetables (canned beans, onions/shallots, brussel sprouts, old potatoes, new potatoes, tomatoes, cabbages, canned peas)
Study type	Case control (cases matched to food consumption at population level for a particular period)
Level of evidence	III-3 (aetiology)
Setting	Birmingham, UK
Funding	Not reported
Cases	Stillbirths and infant deaths due to anencephalus between 1961 and 1967
Baseline comparisons	n/a
Dietary assessment	Population surveys
Timing	Each quarter
Comparison	Monthly stillbirths and infant deaths due to anencephalus matched to quarterly consumption of main food stuffs (in previous five to nine months)
Outcomes	Anencephalus
Results	**Canned beans negatively associated with cases of anencephalus: r = -0.67 after a lag interval of five months** **Onions/shallots negatively associated with cases of anencephalus: r = -0.55 after a lag interval of five months** **Brussel sprouts negatively associated with cases of anencephalus: r = -0.54 after a lag interval of five months** **Old potatoes negatively associated with cases of anencephalus: r = -0.53 after a lag interval of five months** **New potatoes positively associated with cases of anencephalus: r = +0.64 after a lag interval of five months** **Tomatoes positively associated with cases of anencephalus: r = +0.62 after a lag interval of five months** **Cabbages positively associated with cases of anencephalus: r = +0.60 after a lag interval of five months** **Canned peas positively associated with cases of anencephalus: r = +0.54 after a lag interval of nine months***
Followup	n/a
Confounding	Analyses were not adjusted
Risk of bias	High risk of bias: links between population consumption of foods and anencephalus very distal and no control for potential confounders
Relevance	Likely to differ from a modern Australian diet
Other comments	Food consumption of total population not likely to reflect food consumption of pregnant women; and will not be able to reflect differences between diets of individual or specific groups *Positive association with canned peas may be due to magnesium salts used in processing and canning

Reference	**Kwan 2009**
Food type	Vegetables: string beans or peas; tomatoes or tomato juice; coleslaw or cabbage; mustard greens, turnip greens, collards, kale; carrots or mixed vegetables containing carrots; broccoli; spinach; cauliflower or brussel sprouts; cooked green peppers, chilli peppers, hot chilli sauce
Study type	Case control
Level of evidence	III-3 (aetiology)
Setting	California, USA (part of the Northern California Childhood Leukemia Study – phase 1 and 2 (phase 1 reported in Jensen 2004)
Funding	PHS; Paul O'Gorman Foundation for Children with Leukemia
Participants	866 individuals - 282 matched cases and controls (205 pairs and 77 trios): Cases: Children under 15 years of age, with a parent who spoke English or Spanish, were resident in the study area at the time of diagnosis of acute lymphoblastic leukemia (ALL), with no prior diagnosis of cancer Controls: identified from birth certificates matched to the case on date of birth, sex, maternal race, Hispanic ethnicity of mother or father, and county of residence at birth (in phase 1 (1995-99) only due to concerns about overmatching on potential environmental exposures linked to leukemia risk) Data collected from August 1995 to November 2002
Baseline comparisons	A priori potential confounders were identified as birthweight, breastfeeding, maternal age and education, and smoking during pregnancy. *Also see Confounding below*.
Dietary assessment	FFQ
Timing	Dietary intake to reflect the year before the index pregnancy (to indicate dietary status at the start of pregnancy)
Comparison	Serves of vegetables
Outcomes	Childhood acute lymphoblastic leukemia
Results	**Vegetables (garden vegetable only – excludes salad, potatoes, soup and stew):** **aOR 0.65 95% CI 0.50 to 0.84**: median consumption 0.74 (25^{th} 75^{th} percentiles 0.4, 1.0) serves per day **Green beans: aOR 0.85 95% CI 0.74 to 0.98** **Carrots: aOR 0.82 95% CI 0.71 to 0.96**
Followup	n/a
Confounding	Analyses were adjusted for total energy intake, household income, indoor insecticide exposure during pregnancy; and proportion of foods reported as large or extra-large portion size Also adjusted for child's diet, with little effect seen on results
Risk of bias	Low-moderate risk of bias: Of eligible cases identified from January 1995 to November 2002, 86% consented to participate; 56% of the eligible controls agreed to participate. 190 participants excluded: leukemia diagnosis was not ALL (n = 127); no dietary data (n = 4); a case or a control respondent was not the biological mother (n = 14), questionable dietary questionnaire data (n = 45), leaving 282 matched sets (86%).
Relevance	Likely to be relevant for Australian women, though some diet components may differ e.g. high bean consumption
Other comments	Regular use of any dietary supplement was not associated with risk of ALL.

Reference	**Lagiou 2006**
Food type	Vegetables and pulses
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Boston, USA
Funding	NIH
Participants	277 pregnant women who were Caucasian, < 40 years old and parity no more than two (recruited between March 1994 and October 1995). Exclusions: women who had taken any kind of hormonal medication during the index pregnancy, with a prior diagnosis of diabetes mellitus or thyroid disease, or if the fetus had a known major anomaly.
Dietary assessment	FFQ
Timing	Mailed to women prior to a routine antenatal visit around 27 weeks GA, to reflect women's dietary intake during the second trimester of pregnancy
Baseline comparisons	Women in the study likely to be older, better educated, primiparae, lower BMI and less likely to smoke than pregnant women in the general US population
Comparison	Vegetables and pulses – times consumed per month (mean 103.9 SD (increment) 60.7); potatoes
Outcomes	Maternal pregnancy oestradiol, unconjugated oestriol, sex hormone binding globulin (SHBG), progesterone, prolactin – women's blood was taken at 16 and 27 completed weeks GA.
Results	**<u>Maternal oestradiol</u>** 16 completed weeks GA: $p < 0.10$ 27 completed weeks GA: $p < 0.10$ **<u>Maternal oestriol</u>** 16 completed weeks GA: $p < 0.10$ 27 completed weeks GA: $p < 0.10$ **<u>Maternal SHBG</u>** **16 completed weeks GA: 4.2% change 95% CI 0.6 to 7.9** **27 completed weeks GA: 4.2% change 95% CI 0.2 to 8.4** **<u>Maternal progesterone</u>** 16 completed weeks GA: $p < 0.10$ 27 completed weeks GA: $p < 0.10$ **<u>Maternal prolactin</u>** 16 completed weeks GA: -4.5% change 95% CI -10.7 to 2.1 27 completed weeks GA: -4.4% change 95% CI -9.2 to 0.6
Followup	27 completed weeks GA
Confounding	Adjusted for age, parity, gender of offspring, smoking and GA at blood measurement, BMI before pregnancy, energy, coffee and alcohol intake during pregnancy
Risk of bias	Low to moderate risk of bias: 277 of 402 (68.9%) eligible women were included – 77 refused to participate, 9 were subsequently excluded because the index pregnancy was terminated through a spontaneous or induced abortion, 2 were excluded because of twin birth and 10 were lost to follow-up after the initial meeting.
Relevance	Indirect outcomes for (risk of) breast cancer
Other comments	Study authors postulate that the association between increased birthweight and increased breast cancer risk are mediated through endocrine hormones; SHBG is inversely associated with pre-pregnancy BMI and maternal weight gain during pregnancy

Reference	**Lamb 2008**
Dietary patterns	Vegetables (alfalfa sprouts, beans or lentils, Brussel sprouts, celery, cabbage or coleslaw, kale, mustard or chard greens, romaine or leaf lettuce, mixed vegetables, string beans, cooked spinach, raw spinach, yellow squash, iceberg or head lettuce, garlic, eggplant, zucchini or other summer squash, peas or lima beans, cauliflower, broccoli, tofu or soybeans, and red chilli sauce); potatoes (baked/boiled/mashed potatoes, French fried potatoes, potato chips); other root vegetables (beets, cooked carrots, raw carrots, yams or sweet potatoes)
Study type	Part of a longitudinal prospective birth cohort study
Level of evidence	II (aetiology)
Setting	Denver, Colorado, US (part of the Diabetes Autoimmunity Study in the Young (the DAISY))
Funding	National Institutes of Health, Diabetes Endocrine Research Center
Participants	642 newborns at increased risk for type 1 diabetes (based on HLA genotype and family history), enrolled in the study from 1993 to 2004; 27 cases defined as testing positive for islet autoantibodies at two consecutive blood draws and still positive (diabetic) at last follow-up
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	From 1997 to 2004, mothers of infants enrolled in DAISY completed FFQ soon after birth, reflecting diet in the last trimester of pregnancy (but could submit FFQ before child reached one year of age)
Comparison	Monthly servings of vegetables, potatoes and other root vegetables
Outcomes	Islet autoimmunity (a precursor of type 1 diabetes) at 9 months, 15 months, 2 years and annually thereafter up to the age of 15
Results	**Vegetables:** aHR (for one standard deviation change in reported consumption) 0.61 95% CI 0.34 to 1.09 (59 mean monthly servings) **Potatoes**: aHR (for one standard deviation change in reported consumption) 0.58 95% CI 0.34 to 1.01 (18 mean monthly servings) additionally adjusted for breastfeeding duration and first introduction to cereals: **aHR 0.49 95% CI 0.28 to 0.87**
Followup	Up to 15 years
Confounding	Size for gestational age, ethnicity, maternal education, household income, exposure to type 1 diabetes or GDM in utero, gender of child, maternal age at birth, total calories of maternal diet
Risk of bias	Moderate risk of bias: subset of DAISY only (later enrolments); and women were not reminded to submit FFQ, leading to possible selection bias; of the 661 FFQs returned, 5 were excluded because incomplete, and 14 for implausible dietary intakes, leaving 642 FFQs for analysis; child's diet not controlled for (except partially for first introduction to cereals in the maternal potato consumption analysis)
Relevance	Likely to be relevant to some Australian women, although women in this study may have been at higher risk of diabetes
Other comments	

Reference	**Laraia 2007**
Dietary patterns	% of vegetable serving recommendation
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	North Carolina, US (part of the Pregnancy, Infection and Nutrition (PIN) cohort)
Funding	National Institute of Child Health and Human Development; NIH
Participants	2394 predominantly lower to middle income women, recruited between 24 and 29 weeks gestation (1995-2000)
Baseline comparisons	Mean DQI-P score varied significantly by socio-demographic characteristics; there were higher mean DQI-scores for women who engaged in pre-pregnancy vigorous exercise and pre-pregnancy vitamin use
Dietary assessment	Modified block FFQ
Timing	Self-report at 26-28 weeks gestation covering previous 3 months (corresponding to the 2nd trimester)
Comparison	BMI categories
Outcomes	Pregravid weight status (not an outcome but there is an association)
Results	**<u>Average % of vegetable serving recommendation [SD]</u>** Underweight 98.5 [72.0] Normal weight 90.8 [65.6] Overweight 101.3 [80.1] Obese 86.4 [64.5] **Obese group significantly different from overweight (p < 0.03) and underweight (p < 0.01)** *adjusted for age, ethnicity, level of education, poverty, number of children, smoking during pregnancy only
Followup	26 to 31 weeks gestation
Confounding	Age, ethnicity, level of education, poverty, number of children, smoking during pregnancy, regular vitamin use prior to pregnancy, vigorous leisure activity 3 months prior to pregnancy
Risk of bias	Low risk of bias: better to have used normal weight women as the reference rather than underweight women DQI-P tertile comparison
Relevance	Likely to be relevant to Australian women
Other comments	

Reference	**Li 2009**
Dietary patterns	Vegetables
Study type	Retrospective cohort study
Level of evidence	III-2 (aetiology)
Setting	North America
Funding	National Institute of Dental and Craniofacial Research
Participants	1034 mothers who had participated in a case-control study of children with congenital craniofacial malformations
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Fruit and vegetable intake in the six months before pregnancy
Comparison	Quartiles of vegetable consumption (never to four or more times a day) Serves per day, median (range) 1st quartile 0.73 (0 to 1.11) 2nd quartile 1.53 (1.12 to 2.00) 3rd quartile 2.47 (2.01 to 3.03) 4th quartile 4.00 (3.04 to 13.46)
Outcomes	Upper respiratory infection in women during the first half of pregnancy (not including asthma or allergy) [44 URTI episodes without a known start date were excluded from hazards analysis]
Results	**<u>URTI (five month risk)</u>** **HR (95% CI) aHR (95% CI) p-value for trend** Q1 1.00 1.00 Q2 1.12 (0.82 to 1.51) 1.11 (0.81 to 1.51) Q3 1.13 (0.84 to 1.52) 1.15 (0.84 to 1.58) Q4 1.10 (0.81 to 1.49) 1.17 (0.84 to 1.64) 0.33 **<u>URTI (three month risk)</u>** **HR (95% CI) aHR (95% CI) p-value for trend** Q1 1.00 1.00 Q2 0.97 (0.66 to 1.44) 0.97 (0.65 to 1.46) Q3 0.81 (0.54 to 1.22) 0.84 (0.55 to 1.30) Q4 0.93 (0.62 to 1.38) 0.98 (0.63 to 1.52) 0.78
Followup	5 months since last menstrual period
Confounding	Adjusted for age, race, energy intake, fruit intake
Risk of bias	Low-moderate risk of bias: 1034/1163 (88.9%) women included in analysis – 88 with an incomplete FFQ, 41 with implausible energy intakes); women were interviewed at an average of 8 months after birth, but up to 36 months, so some risk of recall bias; some evidence of increased fruit and vegetable consumption once pregnancy was known (misclassification bias)
Relevance	Likely to be relevant to Australian women
Other comments	URTI during pregnancy may be associated with preterm birth and congenital abnormalities

Reference	**Martindale 2005**
Dietary patterns	Vegetables
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Aberdeen, Scotland
Funding	Asthma UK
Participants	1300 singleton children born to women recruited between October 1997 and April 1999 (at a median gestational age of 12 weeks)
Baseline comparisons	Study population were slightly older, more likely to be primiparous, less likely to be current smokers, and more likely to be from nonmanual social classes than the corresponding general population
Dietary assessment	FFQ at 34 weeks gestation (also enquired about use of vitamin and mineral supplements during the previous 3 months
Timing	Timing of FFQ at 34 weeks was chosen to "avoid the dietary disruption of early pregnancy and to provide an indication of the habitual dietary intake in middle and late pregnancy"
Comparison	Not clearly stated
Outcomes	Symptoms of wheeze, doctor-diagnosed eczema
Results	**Eczema in 2nd year of life**: Vegetables: no significant association **Wheeze in 2nd year of life**: Vegetables: no significant association
Followup	6, 12 and 24 months
Confounding	Analyses adjusted for gender, maternal age, paternal social class, maternal smoking, other children in the home and antibiotic use
Risk of bias	Low-moderate risk of bias: 1924 singletons were born to the 2000 women recruited (34 twins, 42 miscarriage, stillbirth or neonatal death), 1751 (87.6%) of women completed the FFQ, with complete data sets from all three questionnaires available at 24 months for 1300 children (67.6%)
Relevance	Reasonably relevant, probably lower fruit and vegetable intake than in Australia
Other comments	Most results reported as intake of vitamin C and E, not by number of serves of fruit and vegetables

<table>
<tr><td>Reference</td><td>Mikkelsen 2006</td></tr>
<tr><td>Food type</td><td>Fruit and vegetables</td></tr>
<tr><td>Study type</td><td>Prospective cohort study</td></tr>
<tr><td>Level of evidence</td><td>II (aetiology)</td></tr>
<tr><td>Setting</td><td>Women participating in the Danish National Birth Cohort, i.e. became pregnant during January 1997-October 2002 and recruited through general practitioners.</td></tr>
<tr><td>Funding</td><td>Danish National Research Foundation, March of Dimes Birth Defects Foundation, European Union, Novonordic Foundation, ISMF, the Health Foundation, Danish National Medical Research Foundation, Danish Heart Association.</td></tr>
<tr><td>Participants</td><td>43,585 pregnant women with singleton pregnancies for whom complete dietary information and birth records were available.</td></tr>
<tr><td>Dietary assessment</td><td>FFQ compared mid-pregnancy, validated in Danish men and women. Timeframe for food consumption unclear (i.e. consumption in last week, month etc).</td></tr>
<tr><td>Baseline comparisons</td><td>See Confounding below.</td></tr>
<tr><td>Timing</td><td>FFQ completed at 25 weeks gestational age.</td></tr>
<tr><td>Comparison</td><td>Birth weights in quintiles of intake of green leafy vegetables (GLV).
Subgroup analyses performed on a group of thin women (BMI < 20).</td></tr>
<tr><td>Outcomes</td><td>Birth weight and z-scores (in singletons only)</td></tr>
<tr><td>Results</td><td>Mean birthweight and Z-scores were consistently lowest in the lowest quintile.
<u>Regression coefficients of the dietary exposures and birthweight</u>
<table>
<tr><td></td><td>Crude (95% CI)</td><td>Adjusted (95% CI)</td></tr>
<tr><td>GLV</td><td>6.6 (0.75-12.5) pns</td><td>6.1 (0.35-11.5)*</td></tr>
<tr><td>GLV – Energy-adjusted</td><td>6.0 (0.094-11.9)*</td><td>5.5 (-0.23-11.3) pns</td></tr>
</table>
*p < 0.05

Among lean women, substantially stronger associations were seen between the dietary exposures and outcomes.</td></tr>
<tr><td>Followup</td><td>Until child was 18 months old (but birth weight only data reported here).</td></tr>
<tr><td>Confounding</td><td>Analyses adjusted for dietary supplements, maternal smoking, maternal height, pre-pregnant weight, paternal height, parity and maternal age.
Separate analyses also adjusted for energy intake.</td></tr>
<tr><td>Risk of bias</td><td>Large population based cohort. Prospective ascertainment of outcomes.
Low risk of bias.</td></tr>
<tr><td>Relevance</td><td>It is possible that the contribution of GLV to total vegetable intake may be different in Danish and Australian women (possible less in Danish women and this could explain the weak effect seen for GLV in this study).</td></tr>
<tr><td>Other comments</td><td></td></tr>
</table>

Reference	**Mitchell 2004**
Dietary patterns	Vegetables (green and root vegetables, peas, corn, lentils)
Study type	Case-control study
Level of evidence	III-3 (aetiology)
Setting	Waitemata Health or Auckland Healthcare regions, New Zealand
Funding	Health Research Council of New Zealand, Foundation for the Newborn, Child Health Research Foundation
Participants	Mothers of 1138 children born between October 1995 and November 1997 (844 born SGA and 870 born appropriate for GA); only term infants (> 37 weeks); Exclusions: preterm births (< 37 weeks), multiple births and those with congenital anomalies
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered after birth (to cover the periconception period and the last month of pregnancy)
Comparison	0-0.75 v > 0.75-1.25 v > 1.25-2.0 v > 2.0-3.0 v > 3 serves of vegetables per day
Outcomes	SGA (≤ 10th centile for GA and gender)
Results	

SGA (Vegetable consumption at time of conception)

	SGA	**AGA**	**aOR (95% CI)**	**p value for trend**
0-0.75	138/539 (25.6%)	137/598 (22.9%)	1.25 **(0.79 to 1.97)**	
>0.75-1.25	93/539 (17.3%)	81/598 (13.5%)	1.58 (0.97 to 2.58)	
>1.25-2.0	87/539 (16.1%)	104/598 (17.4%)	1.12 (0.70 to 1.80)	
>2.0-3.0	126/539 (15.5%)	190/598 (31.8%)	1.40 (0.91 to 2.14)	
>3	99/539 (18.4%)	86/598 (14.4%)	1	0.32

SGA (Vegetable consumption in last month of pregnancy)

	SGA	**AGA**	**aOR (95% CI)**	**p value for trend**
0-0.75	146/539 (27.1%)	126/598 (21.1%)	1.20 (0.76 to 1.92)	
>0.75-1.25	76/539 (14.1%)	84/598 (14.1%)	0.94 (0.57 to 1.56)	
>1.25-2.0	91/539 (16.9%)	132/598 (22.1%)	0.69 (0.43 to 1.10)	
>2.0-3.0	159/539 (29.5%)	183/598 (30.6%)	0.98 (0.64 to 1.51)	
>3	67/539 (12.4%)	73/598 (12.2%)	1	0.12

Followup	NA
Confounding	Adjusted for socio-economic status, ethnicity, maternal height, maternal weight before pregnancy, maternal hypertension and maternal smoking; but folate supplementation was not controlled for (periconception folate was significantly associated with reduced SGA risk).
Risk of bias	Low-moderate risk of bias: Of the 2182 eligible infants, parents of 1714 (78.6%) completed the FFQ; 1138 (67%) of women completed the FFQ; missing items in completed FFQ treated as woman not consuming any vegetables
Relevance	Likely to be relevant to Australian women
Other comments	Only term infants included

Reference	**Miyake 2010**
Food type	Fruit and vegetables
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women recruited antenatally from hospital obstetric clinics in Neyagawa city and surround municipalities, Osaka Prefecture, Japan, from November 2001 to March 2003.
Funding	Ministry of Education, Culture, Sports, Science and Technology; and Health and Labour Sciences Research Grants, Research on Allergic Disease and Immunology, Ministry of Health, Labour and Welfare, Japan.
Participants	763 mother-infant pairs follow up until 24 months postpartum.
Dietary assessment	Self-administered FFQ undertaken during pregnancy. FFQ validated amongst 92 women against weighed dietary records.
Baseline comparisons	*See confounding below* *Vitamin C supplements or multivitamin supplements were only used by 5.6% and 4.2% of participants at least once a week, therefore contribution of micronutrients from supplements was not considered in the analysis.*
Timing	FFQ undertaken at baseline recruitment relating to diet in the month prior, but varying time of diet assessment as women were recruited from between 5 and 39 weeks gestation.
Comparison	Quartile of dietary intakes and infant wheeze and eczema at 16-24 months.
Outcomes	Infant wheeze and eczema, based on symptoms defined according to ISAAC criteria.
Results	Prevalence of wheeze and asthma at 16-24 months was 22.1% and 18.6% respectively. 75% of infants were breastfed for at least 6 months. No significant association between maternal intake of total vegetables, green and yellow vegetables, vegetables other than green and yellow vegetables - and wheeze. Similar for eczema with the exception of green and yellow vegetables. **Eczema** Green and Yellow Vegetables — Crude OR (CI) — Adjusted OR (CI) **Q1** — **1.00** — **1.00** **Q2** — **0.33 (0.19-0.56)** — **0.30 (0.16-0.52)** **Q3** — **0.55 (0.33-0.88)** — **0.53 (0.31-0.89)** **Q4** — **0.51 (0.31-0.83)** — **0.41 (0.24-0.71)** **P** — **0.02** — **0.01**
Followup	Until 24 months postpartum
Confounding	Quartile median adjusted for energy intake. Analyses adjusted for maternal age, gestation at baseline, residence, income, maternal and parental education, maternal and parental history of asthma, atopic eczema and allergic rhinitis, changes in maternal diet in the previous month, season, maternal smoking, baby's older siblings, baby's birthweight, household smoking in the same room as infant, breastfeeding duration, and age of infant at third survey.
Risk of bias	Moderate risk of bias (selection, ascertainment and attrition): low participation rate, women participating had higher education levels; close to 25% losses to follow up at 24 months assessment; Wheeze was assessed at varying ages between 16 and 24 months.
Relevance	High prevalence of wheeze and eczema (22.1% and 18.6%) in this population aged 16-24 months - ?higher than that reported in Australia. Wheeze in infancy is not a reliable predictor of asthma in older ages.
Other comments	

Reference	**Nwaru 2010**

Food type	Vegetables (cabbages, canned vegetables, cucumber, tomaoto, sweet pepper, courgette, eggplant, salads, spinach, celery, corn, Chinese cabbage, fresh herbs, onions, leek, garlic, carrot, swede, turnip, beetroot, parsnip, Jerusalem, artichoke, potatoes)
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Tampere, Finland
Funding	Academy of Finland, Finnish Pediatric Research Foundation, the Juho Vainio Foundation, the Yrjo Jahnsson Foundation, Turku, Oulu and Tampere University Hospitals, JDRF, Novo Nordisk Foundation, EU Biomed 2 Program
Participants	931 mother-infant pairs (children with human leukocyte antigen-conferred susceptibility to type 1 diabetes) participating in the Finnish type 1 Diabetes Prediction and Prevention (DIPP) Nutrition Study between September 1996 and October 1997
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ given to women after birth, for return at the three month visit (FFQ intended to cover maternal diet during pregnancy and lactation)
Comparison	Amount of vegetable intake
Outcomes	Allergic sensitisation in offspring by 5 years: food allergens (egg, cow's milk, fish, wheat); inhalant allergens (house dust mite, cat, timothy grass, birch)
Results	**Total vegetables and roots** ***Food allergens*** OR 0.77 95% CI 0.50 to 1.18 aOR 0.80 95% CI 0.49 to 1.31 ***Inhalant allergens*** OR 1.16 95% CI 0.79 to 1.69 aOR 1.28 95% CI 0.82 to 1.99 - **Potatoes** ***Food allergens*** OR 0.74 95% CI 0.51 to 1.07 aOR 0.73 95% CI 0.48 to 1.23 ***Inhalant allergens*** OR 0.74 95% CI 0.54 to 1.03 aOR 0.92 95% CI 0.63 to 1.35
Followup	To 5 years
Confounding	Adjusted for energy intake, place of birth, season of birth, sex of the child, number of siblings, gestational age at birth, parental asthma, parental allergic rhinitis, maternal age at birth, maternal smoking during pregnancy, maternal education
Risk of bias	Low risk of risk of bias: data available for 931/1175 (79.2%) children recruited – 108 did not participate in survey, a further 49 did not have IgE measurements, a further 87 had no FFQ or an incomplete FFQ
Relevance	Likely to be relevant to Australian women; some differences in individual types of vegetables between Finland and Australia
Other comments	28% of women took vitamin D supplements, 73% took iron supplements; HLA genotype not likely to have any impact on the development of allergic diseases.

Reference	**Oien 2010**
Food type	Vegetables
Study type	Retrospective* cohort study (Prevention of Allergy among Children in Trondheim (PACT) study)
Level of evidence	III-2 (aetiology)
Setting	Trondheim, Norway
Funding	Norwegian Department of Health and Social Affairs, Astra Zeneca Norway, Norwegian Medical Association, SINTEF Unimed 1999
Participants	3086 children
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	Administered when child was one year of age
Comparison	≤ 1/week versus 2-5/week versus almost daily
Outcomes	Childhood eczema, asthma at two years
Results	**Eczema at 2 years** 2-5/week (n = 1505) versus ≤ 1/week (n = 275) : OR 0.76 95% CI 0.55 to 1.06 almost daily (n = 985) versus ≤ 1/week (n = 275): OR 0.72 95% CI 0.51 to 1.02 **Asthma at 2 years** 2-5/week (n = 1505) versus ≤ 1/week (n = 275) : OR 0.98 95% CI 0.56 to 1.69 almost daily (n = 992) versus ≤ 1/week (n = 275): OR 1.02 95% CI 0.58 to 1.81
Followup	To two years
Confounding	Maternal intake during pregnancy analyses were not adjusted
Risk of bias	Moderate to high risk of bias: of the 5171 eligible children, questionnaires were completed for 3086 children (59.7%); analyses were not adjusted; mothers needed to recall their diet more than a year previously
Relevance	Likely to be relevant to Australian women
Other comments	Children were followed prospectively from one year of age to approximately two years of age; *information on exposure was assessed retrospectively when the child was one year of age; Mothers' consumption of fish and vegetables and children's consumption of fish and vegetables were highly correlated;

Reference	**Petridou 1998**
Food type	Vegetables: raw tomatoes, cooked tomatoes, cucumbers, peppers, raw cabbage, cooked cabbage, lettuce, raw carrots, cooked carrots, zucchini, onions, green beans, eggplants, spinach, leeks, okra, dandelions, artichokes, fresh broad beans, peas, cauliflower, broccoli, beets, mushrooms, vegetable pie (0.5), moussaka (0.5).
Study type	Case-control study
Level of evidence	III-3
Setting	Greater Athens area, Greece
Funding	Greek Ministry of Health and Welfare, and Foundation for Research in Childhood 'S. Doxiadis'
Participants	Cases: 109 children with cerebral palsy (CP), born between 1984 and 1988 (estimated to be two-thirds of the children with CP born during this period) Controls (1): 155 neighbouring children of similar sex and age (± 12 months) Controls (2): 99 healthy siblings of similar sex and age (± 12 months) of the first neurological patient seen by the attending physician after a visit by the CP patient
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	During pregnancy
Comparison	≤ 4 versus 5 versus > 5 serves of vegetables per day; regression analysis: risk of cerebral palsy with change in consumption by one unit (= consumption of vegetables once per day)
Outcomes	Cerebral palsy
Results	≤ 4 serves of vegetables per day: 18/91 (19.8%) cases 63/246 (25.6%) controls 5 serves of vegetables per day: 22/91 (24.2%) cases 86/246 (35.0%) controls > 5 serves of vegetables per day: 51/91 (56.0%) cases v 97/246 (39.4%) controls Regression analysis for each unit of consumption of vegetables once per day: **aOR 1.36 95% CI 1.07 to 1.73** aOR 1.19 95% CI 0.88 to 1.61 (additionally adjusted for all food groups)
Followup	8 years
Confounding	Age and sex of child, maternal age at birth, maternal age at menarche, maternal chronic disease, previous spontaneous abortions, persistent vomiting during index pregnancy, multiple pregnancy, number of obstetric visits; timing of membrane rupture in index birth, use of general anaesthesia in the index birth, mode of birth, abnormal placenta, infant head circumference at birth, congenital malformation, place of index birth, use of supplementary iron during index pregnancy, physical exercise during index pregnancy, painless childbirth classes. The following were not included in the model: - Smoking or consumption of coffee or alcohol during pregnancy (stated to be "unrelated to CP and had no confounding influence"); - Gestational age, birthweight and maternal weight gain (stated to be "strong predictors of CP, but were not included in the model, since they are probably intermediate stages in a possible link between diet and CP (mediators) rather than genuine confounders"
Risk of bias	Moderate-high: High risk of recall bias for women being able to accurately remember their dietary intake during a pregnancy 8 years previously; Cases: 109 children with CP were identified; for 6 children either collaboration with their guardian or a diagnosis of CP was not confirmed; and reliable maternal dietary intakes were not available for 12 women, leaving 91 cases available for analysis. Controls: 278 mother-child pairs were approached; 16 refused to participate; matching controls were not available in 8 instances, and reliable maternal dietary intakes were not available for 8 women, leaving 246 controls available for analysis.
Relevance	Diets of Greek women in 1998 may differ from current diets of Australian women
Other comments	

Reference	**Pierik 2004**
Food type	Vegetable rich diet
Study type	Case-control study (1999-2001)
Level of evidence	III-3
Setting	Rotterdam, Netherlands
Funding	Endocrine Modulators Study Group of the European Chemical Industry Council and Nutricia Research Foundation
Participants	Cases: 78 cryptorchidism and 56 hypospadias cases (diagnosed at first child health visit) Controls: 313 controls = 443 mother-child pairs (including four boys with both abnormalities)
Baseline comparisons	*See confounding below*
Dietary assessment	Phyto-oestrogen specific food questionnaire
Timing	During index pregnancy
Comparison	Vegetable rich diet: yes versus no
Outcomes	Cryptorchidism and hypospadias
Results	**Cryptorchidism: yes versus no for vegetable rich diet** **aOR 0.4 95% CI 0.2 to 0.9** **Hypospadias** | | **Cases** | **Controls** | **OR (95% CI)** | | Yes | 24 | 125 | 0.7 (0.4 to 1.2) | | No | 54 | 186 | 1.0 |
Followup	NA
Confounding	Cryptorchidism analysis adjusted for a range of maternal and paternal risk factors; only univariate (unadjusted) analysis presented for hypospadias
Risk of bias	Moderate risk of bias: Participation rate was 85% for cases and 68% for controls; hypospadias analysis was unadjusted for potential confounders
Relevance	Reasonably relevant to Australian women although likely to be different ethnic mix
Other comments	

Reference	**Pogoda 2009**
Food type	Vegetables: all vegetables, yellow-orange vegetables, cruciferous vegetables, leafy green vegetables
Study type	Case-control study Separate centre reports: Preston-Martin 1996 (Los Angeles); Lubin 2000 (Israel); Cordier 1994 (France); McCredie 1994 (Australia)
Level of evidence	III-3 (aetiology)
Setting	International (seven countries – USA, Israel, Italy, Spain, Australia, France and Canada (International Collaborative Study of Childhood Brain Tumors)
Funding	NIH, California Department of Health, Southern California Environmental Health Sciences Center, National Cancer Institutes, Cancer Surveillance System of Western Washington, Fred Hutchinson Cancer Research Center, Fondo de Investigaciones Sanitarias of Spain, Conselleria de Sanitat i Consum of Valencian Autonomous Community for the Childhood Cancer Registry of the Province of Valencia, Spanish Society of Paediatric Oncology with the National Childhood Cancer Registry, ISCIII-RTIC, Villavecchia Foundation and Scientific Foundation of the AECC
Participants	Cases: 1281 Controls: 2223 Years of diagnosis varied between centres, ranging from 1976 to 1992 (with most diagnosed between 1982 and 1992) Controls were frequency matched to cases in US centres and in France; otherwise they were individually matched (by region of residence, age, sex, and geographic area (except for Sydney and Los Angeles))
Baseline comparisons	*See confounding below*
Dietary assessment	Standardised study questionnaire using detailed dietary recall methods and abstract food models to gauge portion size
Timing	Diet during the past year and during the index pregnancy
Comparison	Quartiles
Outcomes	Childhood brain tumours
Results	

All tumours (n = 1203 cases)

	Controls	**Cases**	**aOR 95% CI**
Cruciferous vegetables			
Q1	1195 (55%)	652 (55%)	1.0
Q2	318 (15%)	189 (16%)	1.0 (0.9 to 1.2)
Q3	332 (15%)	175 (15%)	0.9 (0.8 to 1.1)
Q4	339 (16%)	159 (14%)	0.9 (0.6 to 1.4)
P for trend = 0.45			
Leafy green vegetables			
Q1	964 (44%)	535 (46%)	1.0
Q2	405 (19%)	221 (19%)	0.9 (0.6 to 1.5)
Q3	425 (19%)	193 (16%)	0.9 (0.6 to 1.2)
Q4	392 (18%)	226 (19%)	1.1 (0.9 to 1.4)
P for trend = 0.60			
Yellow-orange vegetables			
Q1	710 (36%)	420 (40%)	1.0
Q2	426 (21%)	215 (20%)	0.9 (0.7 to 1.1)
Q3	404 (20%)	214 (20%)	**0.8 (0.7 to 1.0)**
Q4	444 (22%)	208 (20%)	**0.8 (0.6 to 1.0)**
P for trend = 0.04			

Astroglials (n = 621 cases)

Cruciferous vegetables			
Q1	1195 (55%)	309 (52%)	1.0
Q2	318 (15%)	109 (18%)	**1.2 (1.0 to 1.4)**

Q3	332 (15%)	94 (16%)	0.9 (0.8 to 1.2)
Q4	339 (16%)	87 (15%)	1.0 (0.6 to 1.5)
P for trend = 0.64			
Leafy green vegetables			
Q1	946 (44%)	251 (42%)	1.0
Q2	405 (19%)	111 (19%)	1.0 (0.7 to 1.3)
Q3	425 (19%)	112 (19%)	1.0 (0.7 to 1.4)
Q4	392 (18%)	123 (21%)	1.2 (0.8 to 1.6)
P for trend = 0.45			
Yellow-orange vegetables			
Q1	710 (36%)	209 (39%)	1.0
Q2	426 (21%)	95 (18%)	0.7 (0.5 to 1.1)
Q3	404 (20%)	121 (23%)	0.9 (0.7 to 1.3)
Q4	444 (22%)	111 (21%)	0.8 (0.6 to 1.1)
P for trend = 0.24			
Primitive neural ectodermal tumours (PNETs) (n = 257 cases)			
Cruciferous vegetables			
Q1	1195 (55%)	146 (59%)	1.0
Q2	318 (15%)	34 (14%)	0.9 (0.7 to 1.3)
Q3	332 (15%)	35 (15%)	0.9 (0.7 to 1.4)
Q4	339 (16%)	34 (14%)	1.0 (0.5 to 1.7)
P for trend = 0.88			
Leafy green vegetables			
Q1	964 (44%)	125 (50%)	1.0
Q2	405 (19%)	46 (18%)	0.9 (0.4 to 1.9)
Q3	425 (19%)	34 (14%)	0.6 (0.3 to 1.3)
Q4	392 (18%)	44 (18%)	1.0 (0.7 to 1.5)
P for trend = 0.71			
Yellow-orange vegetables			
Q1	710 (36%)	87 (38%)	1.0
Q2	318 (15%)	59 (26%)	1.2 (0.9 to 1.5)
Q3	332 (15%)	38 (17%)	**0.7 (0.5 to 0.8)**
Q4	339 (16%)	42 (19%)	**0.6 (0.4 to 0.9)**
P for trend = 0.0002			

Tumour Subtypes
Astrocytomas

	Pilocytic (142 cases)	Anaplastic (96 cases)	Other (199 cases)
Cruciferous vegetables	1.2 (0.6 to 2.6)	**0.4 (0.3 to 0.7)**	0.8 (0.5 to 1.5)
P for trend	*0.57*	***< 0.0001***	*0.45*
Yellow-orange vegetables	**0.5 (0.4 to 0.6)**	**0.6 (0.4 to 1.0)**	0.7 (0.5 to 1.1)
P for trend	***0.0004***	***0.03***	*0.21*

Other types

		Malignant gliomas (122 cases)	**Medulloblastomas (193 cases)**	**PNET (64 cases)**	**Ependymomas (104 cases)**
	Cruciferous vegetables	1.1 (0.6 to 2.3)	0.6 (0.3 to 1.3)	1.7 (0.7 to 3.7)	0.8 (0.3 to 2.2)
	P for trend	*0.79*	*0.44*	*0.51*	*0.74*
	Yellow-orange vegetables	1.1 (0.9 to 1.3)	**0.5 (0.3 to 0.8)**	0.8 (0.4 to 1.7)	0.7 (0.3 to 1.4)
	P for trend	*0.18*	***0.0004***	*0.45*	*0.22*
Followup	n/a				
Confounding	Analyses adjusted for age and sex of child, study centre and each food group; Adjustment for total intake of foods had little effect on estimates				
Risk of bias	Moderate risk of bias: 75% of eligible cases and 71% of eligible controls participated (based on centres for which these data were available); some lack of standardisation in dietary assessments between study centres; potentially high risk of recall bias for women whose pregnancies may have been at least 10 years previously.				
Relevance	Likely to be relevant to Australian women				
Other comments					

Reference	**Ramon 2009**
Food type	Vegetables
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	Women attending hospital for fetal anomaly screening in Valencia, Spain between February 2004 and June 2005 (INMA-Valencia cohort)
Funding	Instituto de Salud Carlos III, Ministerio Sanidad y Consumo, Ministerio Educacion y Ciencia.
Participants	787 infants born between May 2004 and February 2006 to women at least 16 y, singleton pregnancy, antenatal visit at 10-13 weeks, no assisted conception, no chronic hypertension Mean age 30 y (range 16 to 43); 55% primiparous, 67% completed secondary education; 62% employed; 24% overweight or obese Daily intake fruit 293.0 [216.1] g/day Daily intake veg. 213.3 [121.0] g/day
Dietary assessment	FFQ to assess diet in the first trimester (administered at 10-13 weeks) and then diet since the first assessment (administered at 28-32 weeks). FFQ validated for Spanish population.
Baseline comparisons	*See Confounding below*
Timing	FFQ administered at 10-13 wks and then again at 28-32 weeks gestation.
Comparison	Quintiles of vegetable intake in first and third trimester and birthweight, birth length, SGA (weight), SGA (length). First trimester vegetable intake was 72.8 g/day (range 0 to 114) for quintile 1 and 394.7 g/day (range 299.4 to 948.8) in quintile 5
Outcomes	Birthweight standardised for gender and GA; SGA (weight or length) defined as below 10th percentile based on growth reference charts standardised for both gender and GA for the Spanish population
Results	Summary: lower vegetable intake in the first and third trimester is associated with SGA (strongest in first trimester), lower vegetable intake in the first trimester is associated with SGA for length. Lower intake of vegetables was associated with decreased birthweight and length. **<u>Adjusted OR of the dietary exposures and SGA for weight and length (crude not reported)</u>**

	SGA for weight (95% CI)	**SGA for length (95% CI)**
Vegetable – first trimester		
Q1	**3.7 (1.5-8.9)**	**1.6 (0.6-4.5)**
Q2	**3.0 (1.2-7.0)**	**1.9 (0.7-5.3)**
Q3	**1.7 (0.7-4.3)**	**0.3 (0.1-1.3)**
Q4	**1.0 (0.4-2.7)**	**0.8 (0.2-2.3)**
Q5	**1**	**1**
P	**<0.001**	**0.03**
Vegetable – 3rd trimester		
Q1	**2.1 (1.0-4.7)**	**5.5 (1.7-17.7)**
Q2	**1.3 (0.6-2.8)**	**1.9 (0.6-6.5)**
Q3	**0.6 (0.2-1.4)**	**1.4 (0.4-5.1)**
Q4	**0.7 (0.3-1.6)**	**1.8 (0.6-6.1)**
Q5	**1**	**1**
p	**0.01**	**0.02**

The associations for birth weight and birth length were similar for vegetable intake (lower intake – lower birthweight and length):
<u>Birthweight</u> (**first trimester dietary intake, p for trend across quintiles = 0.04**; 3rd trimester dietary intake, p for trend across quintiles = 0.09
<u>Birth length</u> first trimester dietary intake, p for trend across quintiles = 0.05; **3rd trimester dietary intake, p for trend across quintiles = 0.05**

Followup	Until birth.
Confounding	Analyses adjusted for energy intake, maternal age, maternal pre-pregnancy weight, maternal height, paternal height, weight gain, parity, smoking during pregnancy, caffeine intake, working, country of origin, infant sex, socioeconomic status.
Risk of bias	Low/moderate risk of selection bias due to 54% participation rate. (Women who worked were more likely to participate).
Relevance	More generalisable to Australian women than some of the other studies of veg. Undertaken in a 'horticultural area' where fruit and vegetables are widely available.
Other comments	Authors suggest that low vegetable consumption may affect the lower tail of the birthweight and length distribution.

Reference	**Sausenthaler 2007**
Food groups	Vegetables (also nuts and seeds, fats and oils, dairy, fish, eggs, fruit)
Study type	Prospective cohort study: from the LISA birth cohort
Level of evidence	II (aetiology)
Setting	4 German cities (Munich, Leipzig, Wesel, Bad Honnef)
Funding	Federal Ministry for Education, Science, Research and Technology, Germany
Participants	3097 newborns recruited
Baseline comparisons	*See Confounding below*
Dietary assessment	FFQ
Timing	Maternal diet during the last 4 weeks of pregnancy (obtained shortly after birth, median 3 days)
Variable	Low intake group as reference group compared with high intake group: • Raw carrots high intake = 1-2 times/week • Spinach high intake = 2-3 times/month • Cabbage high intake = 1-2 times/week • Celery high intake = 2-3 times/month • Raw tomatoes high intake = 3-4 times/week • Raw sweet pepper high intake = 2-3 times/month • Salad high intake = 3-4 times/week • Vegetable juice high intake = 2-3 times/month
Outcomes	Allergic sensitisation, eczema at 2 years of age
Results	

Vegetables	Doctor-diagnosed eczema	Any allergen sensitisation	Food allergens	Inhalant allergens
		Adjusted OR (95% CI)		
Raw carrots	1.12 (0.85, 1.46)	0.85 (0.61, 1.18)	1.02 (0.69, 1.49)	0.77 (0.47, 1.28)
Spinach	1.26 (0.99, 1.61)	0.97 (0.71, 1.32)	0.82 (0.58, 1.17)	1.18 (0.73, 1.91)
Cabbage	1.24 (0.96, 1.59)	0.92 (0.66, 1.28)	0.84 (0.58, 1.22)	1.16 (0.71, 1.90)
Celery	0.94 (0.67, 1.31)	**1.61 (1.07, 2.41)**	**1.85 (1.18, 2.89)**	1.39 (0.74, 2.58)
Raw tomatoes	0.83 (0.63, 1.10)	0.81 (0.57, 1.16)	0.74 (0.49, 1.11)	1.05 (0.62, 1.77)
Raw sweet pepper	0.97 (0.75, 1.27)	**1.45 (1.03, 2.06)**	1.16 (0.79, 1.69)	**2.16 (1.20, 3.90)**
Salad	0.92 (0.69, 1.22)	1.09 (0.76, 1.57)	1.14 (0.76, 1.72)	0.92 (0.52, 1.62)
Vegetable juice	0.91 (0.68, 1.22)	0.78 (0.53, 1.16)	0.85 (0.56, 1.31)	0.85 (0.46, 1.56)

Length of followup	2 years
Confounding	Crude and adjusted results reported (adjusted for study area, sex, maternal age, maternal smoking, level of parental education, exclusive breastfeeding ≥ 4 months, parental history of atopic diseases, season of birth and all dietary variables
Risk of bias	Low risk of bias: two year data available for 2641/3097 children (85%): 433 lost to follow-up, 9 excluded due to chronic disease, 14 missing maternal FFQ
Relevance	Likely to be reasonably similar to dietary intakes of Australian women in Australia
Other comments	

Reference	**Shiell 2001**

Food groups	Green vegetables
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Motherwell, Scotland
Funding	Dunhill Medical Trust
Participants	626 (274 men and 352 women) whose mothers' food intakes had been recorded during pregnancy during 1967 to 1968. These women had been advised to eat 0.45 kg of red meat a day and to avoid carbohydrate-rich foods during pregnancy
Baseline comparisons	*See confounding below*
Dietary assessment	Mothers asked about consumption of 10 foods
Timing	Early pregnancy (≤ 20 weeks); late pregnancy (> 20 weeks)
Comparison	Maternal consumption of green vegetables (mean consumption in late pregnancy was 5.4 [SD 2.8] serves per week
Outcomes	Systolic and diastolic blood pressure at in offspring aged 27 to 30 years
Results	**Systolic blood pressure at 27 to 30 years** Regression coefficient for amount of maternal green vegetable consumption; ß -0.29 95% CI -0.62 to 0.05 **Diastolic blood pressure at 27 to 30 years** Regression coefficient for amount of maternal green vegetable consumption; ß -0.12 95% CI -0.38 to 0.14 **Systolic blood pressure for < 7 serves of maternal green vegetable consumption/week at 27 to 30 years*** **Regression coefficient: ß 0.26 95% CI 0.03 to 0.50**
Length of followup	27 to 30 years
Confounding	Analyses adjusted for offspring's gender, BMI, alcohol consumption, and cuff size used for blood pressure
Risk of bias	Moderate risk of bias: For the 1432 records from 1967-8 recorded liveborn, singleton births with complete names, birth measurements and ≥ 1 diet record. 965 offspring were alive and living locally; and after attrition or declining to participate, 626 (43.7%) were available for analysis.
Relevance	Very high intake of meat and very low carbohydrate intake limits the relevance to current dietary intakes of Australian women
Other comments	*Authors state that "low intake of green vegetables, a source of folate, accentuated the effect of high meat and fish consumption on systolic blood pressure"

Reference	**Willers 2007**
Food type	Vegetables
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Antenatal clinics at Aberdeen Maternity Hospital, Aberdeen, Scotland
Funding	Asthma UK, GA^{2}LEN European Network of Excellence on Global Allergy and Asthma
Participants	1212 children (singleton births) whose mothers were recruited between October 1997 and April 1999 at a median gestational age of 12 weeks
Baseline comparisons	Women were representative of the local obstetric population *See confounding below*
Dietary assessment	FFQ
Timing	FFQ mailed at 32 weeks gestation to cover dietary intake over the previous 2-3 months
Comparison	Tertiles:
Outcomes	Wheeze, (asthma), allergic rhinitis, atopic eczema, hay fever at 5 years
Results	**Vegetables (total) and green leafy vegetables** – no consistent linear associations with respiratory and atopic outcomes in 5 year old children (exact numbers not reported in the paper).
Followup	5 years
Confounding	Adjusted for maternal age, paternal social class, maternal education, maternal smoking during pregnancy, smoking in the child’s home at 5 years, energy intake, maternal asthma, maternal atopy, child’s birthweight, child’s sex, presence of older siblings, and breastfeeding
Risk of bias	Low risk of bias: Initial study population of 1924 children dropped to 1212 participants with complete data (63.0%) (questionnaire, at least one of the outcome time points).
Relevance	Likely to be reasonably relevant to Australian women
Other comments	Inclusion of maternal supplement use during pregnancy did not materially change the results

Reference	**Willers 2008**
Food type	Vegetables
Study type	Prospective cohort (longitudinal)
Level of evidence	II (aetiology)
Setting	Netherlands
Funding	Netherlands Organization for Health Research and Development, Netherlands Organization for Scientific Research; Netherlands Asthma Fund; Netherlands Ministry of Spatial Planning, Housing, and the Environment; Netherlands Ministry of Health, Welfare and Sport, GlaxoSmithKline
Participants	2,832 children (part of the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort study
Baseline comparisons	*See confounding below*
Dietary assessment	FFQ
Timing	FFQ administered at antenatal recruitment (mean gestational ages not reported) to cover dietary intake over the previous month
Comparison	Daily (once per day or more) v 1-4 times a week or fewer
Outcomes	Wheeze, dyspnoea, prescription of inhaled steroids for respiratory problems, composite variable 'asthma symptoms' in the last 12 months (measured longitudinally from 1 to 8 years age)
Results	**Wheeze from 1 to 8 years age (n = 2830)** OR 0.97 95% CI 0.85 to 1.12 aOR 0.97 95% CI 0.83 to 1.12 **Dyspnoea from 1 to 8 years age (n = 2830)** OR 1.01 95% CI 0.86 to 1.19 aOR 0.99 95% CI 0.84 to 1.17 **Steroid use from 1 to 8 years age (n = 2830)** OR 0.93 95% CI 0.75 to 1.15 aOR 0.96 95% CI 0.76 to 1.20 **Asthma symptoms (composite of previous three outcomes) from 1 to 8 years age (n = 2830)** OR 0.98 95% CI 0.85 to 1.13 aOR 0.98 95% CI 0.84 to 1.14
Followup	8 years
Confounding	The child's dietary data on fruit, vegetables, fish, eggs, full cream milk, butter and peanut butter consumption at 2 years of age were used to check for potential confounding by the child's diet. Results were adjusted for by sex, maternal education, parental allergy, maternal smoking during pregnancy, smoking in the home at 8 years of age, breastfeeding, presence of older siblings, birthweight, maternal overweight 1 year after pregnancy, maternal supplement use during pregnancy, region and study arm (intervention or natural history arm).
Risk of bias	Moderate risk of bias: Initial study population of 4,146 mothers dropped to 2,832 participants with complete data (68.3%) (pregnancy questionnaire, at least one of the outcome time points and all confounders). Participants with complete data were more likely to have a high education level, to have daily dairy and fruit intake during pregnancy and to have breastfed and less likely to have maternal asthma or maternal atopy, smoked during pregnancy, be from a south western region compared with participants who did not have complete data.
Relevance	Dietary intakes likely to be different from Australian e.g. low fish consumption in study participants
Other comments	Not clear when women assessed their diet during pregnancy; 83% of pregnant women used supplements (50% used folic acid/iron)

Reference	**Yin 2010 (see also Jones 2000)**
Food type	Vegetables
Study type	Prospective cohort
Level of evidence	II (aetiology)
Setting	Southern Tasmania, Australia
Funding	NHMRC, Tasmanian Government, Royal Hobart Hospital Acute Care Program
Participants	216 adolescents born in 1988 (part of a larger infant health study of babies at high risk of SIDS) Exclusions: multiple pregnancies
Baseline comparisons	Children with unemployed fathers more likely to have been excluded due to missing data
Dietary assessment	FFQ
Timing	Dietary intake during third trimester of pregnancy
Comparison	Linear regression of density (portions per kJ)
Outcomes	Bone mass (bone mineral density (BMD) and bone mineral content*) in 16 year old adolescents
Results	**BMD at 16 years;** **Total body (g/cm^2)** r^2 -0.003; ß + 2.5 (pns) adjusted r^2 0.324; ß – 2.3 (pns) **Femoral neck (g/cm^2)** r^2 0.004 ß + 7.7 (pns) adjusted r^2 0.348; ß + 2.7 (pns) **Lumbar spine (g/cm^2)** r^2 – 0.004; ß + 2.1 (pns) adjusted r^2 0.197; ß -1.8 (pns)
Followup	16 years
Confounding	Analyses were adjusted for sex, weight at age 16 years, sunlight exposure in winter at age 16 years, smoking during pregnancy, sports participation, ever breast-fed, current calcium intake, Tanner stage, maternal age at the time of childbirth and “other factors” [these other factors were not listed in the paper]
Risk of bias	Moderate-high: 415 children were followed from birth to age 16. This dropped to 216 (dietary information missing or unreliable for 138 mothers, 47 multiple births, 14 participants had missing data for confounders) representing 52% of participants followed from birth to age 16. 70% of the 216 participants were male. Gender imbalance suggests potential selection bias (due to original selection of infants at high risk of SIDS)
Relevance	Infants at high risk of SIDS represent a selected group (more males, preterm births, teenage mothers, smoking during pregnancy)
Other comments	*Bone mineral content results not reported; Study flow figures differ between 2000 and 2010 reports (e.g. numbers of multiple births)

Reference	**Zhang 2006**
Food type	Vegetable fibre
Study type	Prospective cohort study
Level of evidence	II (aetiology)
Setting	USA (Nurses' Health Study II)
Funding	NIH
Participants	13,110 women who reported having at least one singleton pregnancy lasting ≥ 6 months, between 1992 and 1998 Exclusions: implausible total energy intake (< 500 kcal/day or > 3,500 kcal/day); multiple gestation; history of diabetes, cancer, cardiovascular disease, or GDM on the 1989 or 1991 questionnaire.
Baseline comparisons	*See results*
Dietary assessment	FFQ
Timing	FFQs administered in 1991 or 1995 to reflect dietary intake over the past year
Comparison	Quintiles of vegetable fibre intake (lowest quintile = reference)
Outcomes	Self-reported diagnosis of gestational diabetes mellitus (GDM)
Results	 **<u>GDM (adjusted for age, parity, BMI)</u>** g/day — cases/person-years — RR (95% CI) — p-value for trend Q1 (< 4.1) — 168/20,201 — 1.00 Q2 (4.2 to 5.4) — 163/20,591 — 1.02 (0.83 to 1.26) Q3 (5.5 to 6.8) — 161/19,734 — 0.99 (0.80 to 1.23) Q4 (6.9 to 8.8) — 140/18,826 — 0.95 (0.76 to 1.19) Q5 (> 8.8) — 126/19,280 — **0.77 (0.61 to 0.98)** — **0.03** **<u>GDM (adjusted for age, parity, BMI, race/ethnicity, smoking, family history of diabetes, alcohol intake, physical activity, total energy, protein intake, saturated fat, and polyunsaturated, monounsaturated and trans fatty acids)</u>** g/day — cases/person-years — RR (95% CI) — p-value for trend Q1 (< 4.1) — 168/20,201 — 1.00 Q2 (4.2 to 5.4) — 163/20,591 — 1.04 (0.84 to 1.28) Q3 (5.5 to 6.8) — 161/19,734 — 1.00 (0.80 to 1.24) Q4 (6.9 to 8.8) — 140/18,826 — 0.97 (0.77 to 1.22) Q5 (>8.8) — 126/19,280 — 0.83 (0.64 to 1.08) — pns **<u>GDM (adjusted for age, parity, BMI, physical activity, race/ethnicity, smoking, family history of diabetes, alcohol intake, total energy, protein intake, saturated fat, and polyunsaturated, monounsaturated and trans fatty acids, and vegetable and fruit fibre)</u>** g/day — cases/person-years — RR (95% CI) — p-value for trend Q1 (< 4.1) — 168/20,201 — 1.00 Q2 (4.2 to 5.4) — 163/20,591 — 1.06 (0.86 to 1.32) Q3 (5.5 to 6.8) — 161/19,734 — 1.04 (0.83 to 1.29) Q4 (6.9 to 8.8) — 140/18,826 — 1.01 (0.80 to 1.28) Q5 (> 8.8) — 126/19,280 — 0.87 (0.67 to 1.13) — pns
Followup	Variable
Confounding	*See results*
Risk of bias	Low risk of bias: actual attrition figures for this substudy not reported but overall attrition reported to be 10%

Relevance	Likely to be relevant to Australian women
Other comments	Dietary assessment periods will differ in relation to timing of pregnancies – need to assume a woman's diet will remain similar over time and whether or she is pregnant or planning to become pregnant. This assumption may not apply to alcohol intake, for example

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Excluded Studies

Excluded studies

STUDY

Narrative review

1. Jackson 2001
2. Kind 2006

No perinatal outcomes

3. Bolton 1968
4. Cuco 2006
5. Ereman 1987
6. Glueck 1980
7. Kankaanpaa 2001
8. Miyake 2008
9. Myers 2009
10. Northstone 2008
11. Palmer 2005
12. Petrakos 2006
13. Petridou 1992
14. Pinto 2009
15. Rogers 1998
16. Scopesi 2001
17. Snook Parrott 2009
18. Specker 1994
19. Storro 2010
20. Talai Rad 2009
21. Vahmiko 2010
22. Vance 2005

Nutrient not food based

23. Al 1995
24. Algert 1985
25. Bakker 2008
26. Belfort 2008
27. Bo 2001
28. Brender 2004
29. Brion 2008a
30. Brion 2010
31. Campbell 1996
32. Chan 1987
33. Chierici 1999
34. Clausen 2001
35. Devereux 2007
36. Devereux 2006
37. Duggleby 2010
38. Duggleby 2002
39. Erkkola 2009
40. Ferland 2003
41. Gale 2008
42. Javid 2006
43. Lagiou 2004
44. Litonjua 2006
45. Mahon 2010
46. Major 1998
47. Mathews 1999
48. Miyake 2010
49. Moses 1997
50. Newson 2004
51. Nilsen 2010
52. O'Neil 2009
53. Philipps 1977
54. Qiu 2008
55. Rocha 2010
56. Sabel 2009
57. Saldana 2004
58. Sanders 1992
59. Scholl 2004
60. Shaw 2008
61. Shiell 2000
62. Skajaa 1991
63. Sloan 2001
64. Smedts 2009
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66. Tobias 2005
67. Van Eijsden 2008
68. Verkleij-hagoort 2006
69. Wijendran 1999
70. Wolff 2008
71. Yazdy 2010

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72. Adair 1996
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78. Geppert 2008
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80. Klinger 2006
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82. Krauss-Etschmann 2007
83. Liu 2010
84. Lucia Bergman 2007
85. Luoto 2010
86. Makrides 2006
87. Olafsdottir 2005
88. Olsen 2008
89. Picciano 2003
90. Rees 2008
91. Szajewska 2006
92. Tofail 2006

Other

93. Alm 2009
94. Arkkola 2008
95. Arshad 1992
96. Artal 2007
97. Atkinson 1998
98. Baker 2009
99. Carmichael 2003
100. Catov 2007
101. Chandra 1989
102. Conangelo 2009
103. Conti 1998
104. Harvey 2007
105. Jahanfar 2009
106. Kramer 2006
107. Liu 2009
108. Lopez-Exposito 2009
109. Marques 2008
110. Oberlander 2010
111. Olafsdottir 2005
112. Romon 2001
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114. Schulze 2003
115. Shaw 2003
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