

# THE LANCET

## Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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## **Appendix 1. Literature review on preconception diet and lifestyle risk factors for adverse maternal and perinatal outcomes**

### **Summary of methods**

The literature review aimed to identify original research articles and reviews reporting on relationships between preconception diet and lifestyle risk factors (across the life course) and maternal and perinatal outcomes. The MEDLINE database was searched using the search strategy presented in Box 1 with restrictions to human studies published in English in the past 5 years (from November 2011). The search was performed in November 2016 and updated in February 2017. Results were imported into Endnote for title and abstract screening, and relevant studies reporting on exposures in the pre- or periconception period were summarised based on study design, population, period (before or between pregnancies), exposure(s), outcome(s), and main study findings.

#### **Box 1. Search strategy**

((preconception OR pre-conception OR preconception care OR prepregnancy OR pre-pregnancy OR pre-existing OR planning OR intrauterine OR infancy OR childhood OR early life OR school age OR puberty OR adolescence OR adulthood OR sensitive period OR critical period OR accumulation OR timing OR lifecourse OR life-course OR life course OR maternal OR mother OR paternal OR father)

AND (lifestyle OR body mass index OR weight OR overweight OR obese OR diet OR nutrition OR physical activity OR smoking OR alcohol OR illicit drug)

AND (maternal outcome OR infant outcome OR miscarriage OR stillbirth OR gestational diabetes OR gestational hypertension OR preeclampsia OR metabolic risk factors OR delivery method OR anemia OR intrauterine growth restriction OR preterm birth OR low birth weight OR macrosomia OR birth defects OR child outcome OR postpartum depression OR breastfeeding OR fertility))

## Periconception exposures

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Case A, 2015 (1)	Cross-sectional N = 954 USA	Teenagers	Periconception	- Pregnancy planning - Folic acid supplements	na	1/3 <sup>rd</sup> of teenagers had intended pregnancy Younger teenagers were less likely to plan and to take preconception folic acid
Caspers K, 2014 (2)	Case-control N = 906 cases N = 8,352 controls USA	Reproductive-aged women	Periconception	- Alcohol	Congenital limb deficiencies (LD)	32% consumed alcohol in periconception period, 12% binge drinking Alcohol consumption was associated with lower odds of LD
Caspers K, 2013 (3)	Case-control N = 906 cases N = 8,352 controls USA	Reproductive-aged women	Periconception	- Cigarette smoking (active and passive)	Congenital limb deficiencies (LD)	21% active smokers 18% passive smokers Active and passive smoking increased odds of LD
Chan F, 2015 (4)	Review	Reproductive-aged women	Periconception	- Opioid use	Birth defects	Prevalence periconceptional opioid use: 2-4% Evidence is inconclusive, and potentially confounded by factors such as SES, stress and alcohol consumption
Deng K, 2013 (5)	Case-control N = 284 cases N = 422 controls China	Reproductive-aged men	Periconception	- Paternal smoking	Congenital heart defects (CHD)	Paternal smoking increased odds of CHD

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Makelarski J, 2013 (6)	Case-control N = 1,223 cases N = 6,807 controls USA	Reproductive-aged women	Periconception	- Alcohol	Neural tube defects (NTD)	No association found between periconceptional alcohol consumption and NTD
Zhu Y, 2015 (7)	Case-control N = 7,076 cases N = 7,972 controls USA	Reproductive-aged women	Periconception	- Alcohol	Congenital heart defects (CHD)	No association found between periconceptional alcohol consumption and CHD
Matusiak K, 2014 (8)	Review	Reproductive-aged women	Periconception	- Maternal periconceptional weight loss	Maternal and perinatal outcomes	Weight loss (undernutrition) in the periconception period may improve maternal outcomes (gestational diabetes and pre-eclampsia), but increase risk of adverse consequences for offspring (currently only based on animal studies)
Steegers R, 2013 (9)	Review	Reproductive-aged women	Periconception	- Age, obesity, liver and renal function, folate and vitamin B12 deficiency, fertility treatment (amongst other factors)	Subfertility, miscarriage, congenital malformations, fetal growth restriction, placental related disorders (such as pre-eclampsia)	All listed exposures were found to be associated with the listed outcomes

## Preconception exposures

### Summary of reviews

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Preconception	- Underweight	Preterm birth	Pooled OR 1.32 (1.22, 1.43) N = 12 studies; I <sup>2</sup> = 50%
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Preconception	- Underweight	Small-for-gestational-age	Pooled OR 1.64 (1.22, 2.21) N studies and I <sup>2</sup> not reported
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Preconception	- Underweight	Low birth weight	Pooled OR 1.37 (0.46, 4.13) N studies and I <sup>2</sup> not reported
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Preconception	- Underweight	Gestational diabetes, gestational hypertension, macrosomia, congenital birth defects	No effects (no pooled estimates reported)
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Preconception	- Overweight	Pre-eclampsia	Pooled OR 2.28 (2.04, 2.55) N = 12 studies; I <sup>2</sup> = 77%
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Preconception	- Overweight	Gestational diabetes	Pooled OR 1.91 (1.58, 2.32) N studies and I <sup>2</sup> not reported

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Preconception	- Overweight	Caesarean delivery	Pooled OR 1.42 (1.21, 1.66) N studies and I <sup>2</sup> not reported
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Preconception	- Overweight	Macrosomia	Pooled OR 1.63 (1.51, 1.76) N studies and I <sup>2</sup> not reported
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Preconception	- Overweight	Birth defects	Pooled OR 1.15 (1.07, 1.24) N studies and I <sup>2</sup> not reported
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Periconception	- Multivitamin supplementation	Pre-eclampsia	Pooled OR 0.73 (0.58, 0.92) N = 2 studies; I <sup>2</sup> = 23%
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Periconception	- Multivitamin supplementation	Congenital abnormalities	Pooled OR 0.57 (0.34, 0.97) N = 4 studies; I <sup>2</sup> = 57%
Dean S, 2014 (10)	Systematic review (observational studies)	Reproductive-aged women	Periconception	- Multivitamin supplementation	Neural tube defect	Pooled OR 0.51 (0.31, 0.82) N = 7 studies; I <sup>2</sup> = 84%
Lassi Z, 2014 (11)	Systematic review (observational studies)	Reproductive-aged women	Periconception	- Caffeine intake	Spontaneous abortion	Pooled OR 1.77 (0.83, 3.78) N = 6 studies; I <sup>2</sup> = 96%

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Lassi Z, 2014 (11)	Systematic review (observational studies)	Reproductive-aged women	Preconception	- Alcohol intake	Spontaneous abortion	Pooled OR 1.30 (0.85, 1.97) N = 2 studies; I <sup>2</sup> = 0%
Lassi Z, 2014 (11)	Systematic review (observational studies)	Reproductive-aged women	Periconception	- Illicit drug use	Neural tube defects	Pooled OR 0.91 (0.77, 1.07) N = 6 studies; I <sup>2</sup> = 43%
Poston L, 2016 (12)	Review	Reproductive-aged women	Preconception and antenatal periods	- Maternal obesity	Range of maternal, perinatal, delivery and postpartum outcomes	Global overview of maternal obesity rates Studies on associations between maternal obesity and maternal, perinatal, delivery and postpartum outcomes
Hanson M, 2016 (13)	Review	Reproductive-aged women	Preconception and antenatal periods	- Maternal obesity	Range of maternal, perinatal, delivery and postpartum outcomes	Discusses the lack of preconception studies evaluating the effect of preconception weight management on maternal and perinatal outcomes
Temel S, 2014 (14)	Systematic review	Reproductive-aged women	Preconception	- Preconception lifestyle intervention	Maternal and infant health	Evidence on preconception risk factors associated with maternal and infant outcomes is large Evidence on effectiveness of preconception intervention is lacking Identified few preconception trials

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Anderson K, 2010 (15)	Systematic review	Reproductive-aged women who perceived that they may be infertile	Preconception	- Lifestyle intervention	Fertility	No RCTs were identified
Solmi F, 2014 (16)	Systematic review	Pregnant women	Preconception (retrospective)	- History of anorexia nervosa	Low birth weight	Offspring of women with (history of) anorexia nervosa were at increased risk of low birth weight, standardised difference was small (200g)
De-Regil, L 2015 (17)	Systematic review	Pregnant women	Preconception (retrospective)	- Periconceptional folic acid supplement use	Neural tube and other congenital anomalies	Folic acid, alone or in combination with vitamins and minerals, prevents neural tube defects, but did not have a clear effect on other birth defects
Ramakrishnan U, 2012 (18)	Systematic review	Reproductive-aged women (non-pregnant and pregnant)	Peri-conception	- Nutritional factors	Maternal, neonatal and child health outcomes	Pre- and periconceptional intake of multivitamin supplements reduced risk of low birth weight, small-for-gestational-age and preterm delivery. Quality of evidence rated as low
Stang J, 2016 (19)	Review	Reproductive-aged women	Preconception	- Weight	Maternal, neonatal and child health outcomes	There is no evidence evaluating the impact of intentional preconceptional weight loss on pregnancy outcomes



Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Harrison C, 2016 (20)	Review	Reproductive-aged women	Preconception	- Physical activity	Preconception risk factors	55% of young women do not meet physical activity guidelines which may influences fertility, PCOS, weight and mental health, and in turn affect maternal and perinatal health
Tobias D, 2011 (21)	Systematic review	Reproductive-aged women	Preconception	- Physical activity	Gestational diabetes	Pooled OR 0.45 (0.28, 0.75) N = 7 studies, I <sup>2</sup> = 81%
Campbell J, 2015 (22)	Systematic review	Reproductive-aged men	Preconception	- Obesity	Fertility	Obese men were more likely to experience infertility: Pooled OR 1.66 (1.53, 1.79) N = 5 studies; I <sup>2</sup> = 66% Obese men were more likely to have a live birth from assisted reproductive technology: Pooled OR 0.65 (0.44, 0.97) N = 5 studies; I <sup>2</sup> = 54%
Been J, 2014 (23)	Systematic review	Reproductive-aged women	Reproductive years	- Smoke-free legislation	Perinatal outcomes	Smoke-free legislation was associated with low birth weight Pooled risk change (95% CI): -10.4% (-18.8, -2.0), N = 4 studies, I <sup>2</sup> = 83% No associations with low birth weight or small-for-gestational-age

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Aune D, 2014 (24)	Systematic review	Reproductive-aged women	Preconception and during early pregnancy	- BMI	Fetal death, stillbirth and infant death	Increases of 5 BMI units were associated with: Fetal death: pooled RR 1.21 (1.09, 1.35), N = 7 studies, I <sup>2</sup> = 78% Stillbirth: pooled RR 1.24 (1.18, 1.30), N = 18 studies, I <sup>2</sup> = 80% Perinatal death: pooled RR 1.16 (1.00, 1.35), N = 11 studies, I <sup>2</sup> = 94% Neonatal death: pooled RR 1.15 (1.07, 1.23), N = 12 studies, I <sup>2</sup> = 79% Infant death: pooled RR 1.18 (1.09, 1.28), N = 4 studies, I <sup>2</sup> = 79%
Yi X, 2015 (25)	Systematic review	Reproductive-aged women	Preconception	- Bariatric surgery	Maternal and fetal outcomes	Compared with obese women who had not undergone bariatric surgery, women who had undergone bariatric surgery were less likely to develop: Gestational diabetes: Pooled OR (95% CI): 0.31 (0.15, 0.65), N = 9 studies, I <sup>2</sup> = 85% Hypertensive disorders: Pooled OR (95% CI): 0.42 (0.23, 0.78), N = 9 studies, I <sup>2</sup> = 83% Macrosomia: Pooled OR (95% CI): 0.40 (0.24, 0.67), N = 6 studies, I <sup>2</sup> = 24% However, they were also more likely to develop:

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
						<p>Small-for-gestational-age infant: Pooled OR (95% CI): 2.16 (1.28, 3.66), N = 5 studies, I<sup>2</sup> = 28%</p> <p>There were no effects on caesarean delivery and preterm birth</p> <p>Sensitivity analyses showed that pregnancy &lt;2 years after surgery was associated with even larger lower risk of hypertensive disorders compared with pregnancy &gt;2 years after surgery</p> <p>Based on current literature, there is no conclusive evidence on the optimal timing for conception after bariatric surgery</p>
Galazis N, 2014 (26)	Systematic review	Reproductive-aged women	Preconception	- Bariatric surgery	Maternal and fetal outcomes	<p>Compared with obese women who had not undergone bariatric surgery, women who had undergone bariatric surgery were less likely to develop:</p> <p>Gestational diabetes: Pooled OR (95% CI): 0.47 (0.40, 0.56), N = 15 studies, I<sup>2</sup> = &gt;50%</p> <p>Pre-eclampsia: Pooled OR (95% CI): 0.45 (0.25, 0.80), N = 11 studies, I<sup>2</sup> = &gt;50%</p> <p>Macrosomia: Pooled OR (95% CI): 0.46 (0.34, 0.62), N = 14 studies, I<sup>2</sup> = &gt;50%</p>

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
						<p>However, they were also more likely to develop:</p> <p>Small-for-gestational-age infant: Pooled OR (95% CI): 1.93 (1.52, 2.44), N = 11 studies, I<sup>2</sup> = &gt;50%</p> <p>Preterm birth: Pooled OR (95% CI): 1.31 (1.08, 1.58), N = 12 studies, I<sup>2</sup> = &gt;50%</p> <p>NICU admission: Pooled OR (95% CI): 1.33 (1.02, 1.72), N = 4 studies, I<sup>2</sup> = &lt;50%</p> <p>Maternal anemia: Pooled OR (95% CI): 3.41 (1.56, 7.44), N = 4 studies, I<sup>2</sup> = &gt;50%</p> <p>There were no effects of bariatric surgery on caesarean delivery and perinatal mortality</p> <p>Laparoscopic adjustable gastric band reduced odds of pre-eclampsia, gestational diabetes, and did not increase risk of small-for-gestational-age and preterm birth</p> <p>This suggests that restrictive rather than mal-absorptive bariatric surgery (like gastric bypass) should be preferred in young women planning pregnancy</p>
Tan O, 2012 (27)	Review	Reproductive-aged women	Preconception	- Bariatric surgery	Fertility	Evidence is suggestive of better ovulatory function and spontaneous pregnancy rates in

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
						obese women who lost weight after bariatric surgery, however, most are small case-control studies Data on improved IVF success rates is similarly limited

**Summary of original research studies according to preconception risk factors**

*Diet and lifestyle risk factors*

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Nykjaer C, 2014 (28)	Prospective cohort N = 1,303 UK	Pregnant women	Preconception (retrospective) During pregnancy	- Alcohol	Birth weight and preterm	2/3 of women before pregnancy and >1/2 in the first trimester reported alcohol intakes above the UK guidelines High alcohol consumption increased risk of low birth weight and preterm birth Strongest association for first trimester
Eagles J, 2012 (29)	Case-control N = 130 cases N = 670 controls UK	Reproductive-aged women	Preconception (retrospective)	- History of anorexia nervosa	Preterm, birth weight, gestational hypertension, antepartum haemorrhage, caesarean section, intrauterine growth restriction	History of anorexia nervosa increased risk of intrauterine growth restriction and antepartum haemorrhage

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Linna M, 2014 (30)	Prospective cohort N = 11,285 Finland	Reproductive-aged women	Preconception (retrospective)	- History of anorexia nervosa, bulimia nervosa, binge eating disorder	Gestational diabetes, anemia, gestational hypertension, pre-eclampsia, fetal growth, caesarean section, preterm, birth weight	~10% had an eating disorder history A history of eating disorders was associated with several pregnancy, obstetric and perinatal complications. Strongest associations with birth outcomes
Micali N, 2014 (31)	Prospective cohort N = 6,318 Netherlands	Pregnant women	Preconception (retrospective)	- History of anorexia nervosa, bulimia nervosa,	Fertility treatment and pregnancy planning	~9% had an eating disorder history Women with eating disorders were more likely to receive fertility treatment and not have an unplanned pregnancy
Pasternak Y, 2012 (32)	Retrospective cohort N = 117,875 Israel	Pregnant women	Preconception (retrospective)	- History of eating disorder	Pregnancy, obstetric and delivery complications	~0.1% had an eating disorder history History of eating disorder increased risk of low birth weight, preterm delivery and caesarean section
Khodr Z, 2014 (33)	Cohort N = 6,570 USA	Pregnant women	Preconception (retrospective)	- Range of risk factors	Preconceptional folic acid - containing supplement use	~32% took preconceptional folic acid-containing supplements Low education, non-white ethnic group and younger women were less likely to take preconceptional folic acid-containing supplements

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Malek L, 2016 (34)	Cohort N = 857 Australia	Pregnant women	Preconception (retrospective)	- Range of risk factors	Periconceptual folic acid and iodine supplement use	27% and 23% took preconceptional folic acid and iodine supplements, respectively Pregnancy planning was the only significant risk factor
Mannien J, 2014 (35)	Cohort N = 5,975 Netherlands	Pregnant women	Preconception (retrospective)	- Range of risk factors	Preconceptional folic acid supplement use	55% took preconceptional folic acid supplements Non-Western ethnicity, unemployed and not having a partner were the strongest risk factors for not using preconceptional folic acid supplements
Tort J, 2013 (36)	Cohort N = 12,646 France	Pregnant women	Preconception (retrospective)	- Range of risk factors	Preconceptional folic acid supplement use	~15% took preconceptional folic acid supplements Younger age, multiparous, single, low education, smoking before pregnancy were risk factors for not using preconceptional folic acid supplements
Nurses' Health Study II (37-45)	Prospective cohort N = ~13,000 USA	Reproductive-aged women	Pre- and inter-conception (up to 2 years prior to pregnancy)	- Range of dietary patterns	Gestational diabetes	A diet rich in fruit, vegetables, legumes, nuts and fish; and low in red and processed meat and discretionary foods, was associated with lower risk of gestational diabetes

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Schoenaker D, 2015 (46-48)	Prospective cohort N = ~3,500 Australia	Reproductive-aged women	Pre- and inter-conception (up to 3 years prior to pregnancy)	- Range of dietary patterns	Gestational diabetes and hypertensive disorders of pregnancy	A diet rich in fruit, vegetables, legumes, nuts and fish; and low in red and processed meat and discretionary foods, was associated with lower risk of gestational diabetes and hypertensive disorders of pregnancy
Mishra G, 2014 (49)	Prospective cohort N = 5,760 Australia	Reproductive-aged women	Pre- and inter-conception	- Food groups	Adherence to Australian Dietary Guidelines	Less than 30% of women adhered to Meat and Fruit guidelines, less than 12% adhered to Dairy and Cereal guidelines, less than 2% adhered to guideline for Vegetables
Grieger J, 2014 (50)	Retrospective cohort N = 309 Australia	Reproductive-aged women	Preconception (retrospective)	- Dietary patterns in the 12 months before conception	Fetal growth and preterm delivery	A dietary pattern containing protein-rich food sources, fruit, and whole-grains was associated with reduced likelihood for preterm delivery, whereas a dietary pattern mainly consisting of discretionary items was associated with preterm delivery, shorter birth length, and earlier gestation
Hatch E, 2012 (51)	Prospective cohort N = 3,628 Denmark	Reproductive-aged women planning a pregnancy	Preconception	- Caffeinated beverages and soda consumption	Fertility	No association found after adjustment for confounders between caffeinated beverages and soda consumption and time to pregnancy



Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Twigt J, 2012 (52)	Prospective cohort N = 199 Netherlands	Reproductive-aged women undergoing IVF	Preconception	- Adherence to dietary guidelines	Ongoing pregnancy	Better adherence to dietary guidelines increased the chance of ongoing pregnancy
Xie Y, 2015 (53)	Cohort N = 833 USA	Reproductive-aged women	Preconception	- Food intake and physical activity	Birth weight and gestational age	54% reported eating 2 pieces of fruit or vegetables 37% reported 7 or more occasions of physical activity Food intake was not associated with birth outcomes Higher physical activity levels were associated with higher birthweight (lower likelihood of low birth weight)
Hauff L, 2014 (54)	Cohort N = 2,824 USA	Pregnant and postpartum women	Preconception (retrospectively)	- Pre-pregnancy BMI and psychosocial factors	Breastfeeding intension, initiation and duration	Obese women had similar breastfeeding intension, but low odds of ever breastfeeding and increased risk of earlier cessation of breastfeeding compared with normal-weight women. Psychosocial factors largely explained these associations
Krogsgaard S, 2013 (55)	Cohort N = 2,026 Norway	Reproductive-aged women	Preconception	- Physical activity	Birth weight	No associations for leisure time physical activity No exercise reduced risk of macrosomia

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Been J, 2015 (56)	Cohort N = 10,291,113 England	Reproductive- aged women	Reproductive years	- Smoke-free legislation	Low birth weight, stillbirth, neonatal mortality, sudden infant death syndrome	Compared with period before July 2007, odds ratios for birth outcomes after July 2007 (when smoke-free legislation was introduced) indicate lower likelihood of low birth weight, stillbirth and neonatal mortality, but not sudden infant death syndrome. Magnitude of risk reductions were small (4-8%), but significant number of absolute cases were prevented
Cox B, 2013 (57)	Cohort N = 606,877 Belgium	Reproductive- aged women	Reproductive years	- Smoke-free legislation (stepwise introduction)	Preterm birth	Consistent patterns of reductions in preterm birth were observed with stepwise introductions of smoking bans (workplace, restaurants, and bars)
McKinnon B, 2015 (58)	Cohort N = 470,199 Canada	Reproductive- aged women	Reproductive years	- Smoke-free legislation and education	Preterm birth, small-for- gestational-age, low birth weight	Smoke-free legislation was associated with improved birth outcomes in all categories of maternal education

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Suzuki K, 2014 (59)	Cohort N = 2,663 Japan	Reproductive-aged women	Preconception and early pregnancy	- Smoking cessation before or in early pregnancy	Birth weight and small-for-gestational-age	Smoking during pregnancy was associated with lower birth weight compared with non-smokers. Smoking cessation before or during early pregnancy was associated with a much smaller difference in low birth weight compared with continued smoking. Smoking during pregnancy was associated with small-for-gestational-age, ex-smokers who quit before or during pregnancy were not at increased risk of small-for-gestational-age. Birth weight and the proportion of small-for-gestational-age infants were similar in non-smoking mothers and mothers who quit smoking before or during early pregnancy.

Weight-related factors

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Adane A, 2016 (60)	Prospective cohort N = 3,111 Australia	Reproductive-aged women	Pre- and inter-conception	- Weight change	Gestational diabetes	Small (1.5-2.5% annual weight change), moderate (2.5-5%) and high (>5%) weight gain prior to pregnancy were associated with higher risk of gestational diabetes (independent of baseline BMI) Weight loss was not associated with gestational diabetes risk (low numbers)
Hure A, 2017 (61)	Prospective cohort N = 5,275 Australia	Reproductive-aged women	Preconception	- Maternal age, BMI, height, lifestyle, anxiety, health insurance	Caesarean delivery	Higher maternal age, overweight and obesity and short stature were associated with higher risk of both emergency and elective caesarean delivery; diagnosis of anxiety and private health insurance were associated with higher risk of elective caesarean delivery
Honein M, 2013 (62)	Simulation USA	Reproductive-aged women	Preconception	- Obesity	Fetal death, birth defects	Reports on the number of fetal deaths and infants born with birth defects that would be prevented if interventions would be successful in eliminating or reducing (10%) rates of obesity

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Kim S, 2013 (63)	Cohort N = 1,228,265 USA	Reproductive-aged women	Preconception (retrospectively)	- Overweight and obesity	Gestational diabetes	Preconception overweight and obesity contribute to gestational diabetes in all ethnic groups but magnitude of percentage gestational diabetes attributable to obesity varied for different ethnic groups. Asian ethnic groups had the highest gestational diabetes prevalence, but the lowest percentage attributable to obesity
Kachoria R, 2015 (64)	Cohort N = 244,196 USA	Reproductive-aged women	Preconception (retrospectively)	- BMI	Breastfeeding initiation, continuations and exclusivity	Decreasing number of women initiated, continued and breastfed exclusively with increasing BMI Over time (2009 to 2011), breastfeeding initiation and continuation increased for all women; exclusive breastfeeding increased over time for normal weight and overweight women, but decreased for obese women
Kirkegaard H, 2015 (65)	Cohort N = 1,024 USA	Reproductive-aged women	Preconception (retrospectively)	- Waist circumference (WC) and BMI	Gestational weight gain and breastfeeding behaviour	Preconception BMI and WC were differently associated with GWG and breastfeeding intension Higher BMI, but lower WC, were associated with higher GWG and never breastfeeding

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Makela J, 2014 (66)	Cohort N = 848 Finland	Reproductive-aged women (postpartum)	Preconception (retrospectively)	- Overweight and obesity	Breastfeeding and infant feeding	Overweight women had a shorter exclusive breastfeeding time and introduced complementary foods earlier compared with normal weight women Longer duration of exclusive and partial breastfeeding, and later introduction of complementary foods were associated with lower risk of childhood obesity
Thompson L, 2013 (67)	Cohort N = 1,161,949 USA	Reproductive-aged women	Preconception (retrospectively)	- BMI	Breastfeeding initiation	Underweight and obese women were less likely to initiate breastfeeding than women with normal BMI, (OR 0.87, 95 % CI 0.85, 0.89 for underweight; OR 0.84, 95 % CI 0.83, 0.85 for obese). The magnitude of these findings did not significantly vary by race, ethnicity or income (indicating interventions are needed in all populations)

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Dekker-Nitert M, 2011 (68)	Cohort N = 412 Australia	Reproductive-aged women (early pregnancy)	Preconception (retrospectively)	-	Knowledge regarding the risks of overweight and obesity in pregnancy	>75% of women identified obesity as risk factor for gestational diabetes and hypertension >60% of women identified obesity as risk factor for caesarean delivery <50% of women identified obesity as risk factor for adverse neonatal outcomes Education level, but not BMI status, was associated with knowledge of risks of overweight and obesity in pregnancy

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Schummers L, 2015 (69)	Cohort N = 226,958 Canada	Reproductive-aged women	Preconception (retrospectively)	- BMI	Maternal and perinatal outcomes	Presents absolute risk of maternal perinatal outcomes according to change in preconception BMI A 10% difference in preconception BMI was associated with clinically meaningful risk differences for pre-eclampsia, gestational diabetes, preterm delivery, macrosomia, and stillbirth Larger differences in preconception BMI (20-30% differences or shifting at least a BMI category) would be necessary to see meaningfully lower risks of caesarean delivery, shoulder dystocia, NICU stay, and neonatal mortality
Yachi Y, 2013 (70)	Cohort N = 624 Japan	Reproductive-aged women	Preconception (retrospectively)	- BMI at age 20 and BMI change since age 20	Gestational diabetes	Low BMI at age 20 and larger BMI increase since age 20 were associated with higher gestational diabetes risk



*Paternal diet and lifestyle factors*

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Mutsaerts M, 2012 (71)	Cohort N = 1,924 Netherlands	Reproductive-aged men	Preconception (retrospective)	- Age, BMI, smoking, alcohol, vitamin use, working hours, physical activity	Time to pregnancy (from date the couple set out to conceive)	No significant associations
Mutsaerts M, 2014 (72)	Cohort N = 2,264 Netherlands	Reproductive-aged men	Preconception (retrospective)	- Age, BMI, smoking, alcohol, working hours, physical activity	Gestational hypertension, gestational diabetes, preterm birth, small-for-gestational-age	Paternal lifestyle factors were not associated with pregnancy and birth outcomes; Maternal and paternal lifestyle were highly correlated: both partners should be involved in preconception counselling

## Inter-pregnancy exposures

### Summary of reviews

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Adegboye A, 2013 (73)	Systematic review (RCTs)	Reproductive-aged women	Inter-pregnancy (postpartum)	- Diet and physical activity intervention	Weight	Women in intervention, compared with standard care: - lost more weight: Mean difference: -1.93 kg (-2.96, -0.89), N = 7 studies - were more likely to return to pre-pregnancy weight: Risk ratio 2.00 (1.31, 3.05), N = 3 studies
He X, 2015 (74)	Systematic review (RCTs and observational studies)	Reproductive-aged women	Inter-pregnancy	- Breastfeeding	Inter-pregnancy weight loss at 3-6 months postpartum	Breastfeeding compared with formula feeding did not significantly reduce postpartum weight, large heterogeneity between studies depending on study design, breastfeeding duration and confounding factors taken into account
Neville C, 2014 (75)	Systematic review (RCTs)	Reproductive-aged women (breastfeeding)	Inter-pregnancy	- Diet and physical activity intervention	Inter-pregnancy weight loss	Diet and physical activity interventions may be effective in reducing postpartum weight in breastfeeding women (no meta-analysis)

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Neville C, 2014 (76)	Systematic review (observational studies)	Reproductive-aged women	Inter-pregnancy	- Breastfeeding	Inter-pregnancy weight loss	Insufficient evidence to suggest an association between breastfeeding and postpartum weight loss. Study findings varied depending on the time at which the postpartum measurements were carried out, duration and intensity of breastfeeding Few studies rated as high quality showed a positive association
Hadar E, 2015 (77)	Review (observational studies)	Reproductive-aged women with obesity	Inter-pregnancy	- Inter-pregnancy weight loss	Maternal and perinatal outcomes	Evidence suggests a risk reduction for large-for-gestational-age, pre-eclampsia, gestational diabetes, gestational hypertension

**Summary of original research studies**

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Perni U, 2012 (78)	Cohort N = 371,627 Sweden	Reproductive-aged women	Inter-pregnancy	- Inter-pregnancy change in smoking habits	Pre-eclampsia	Compared with women who did not smoke in either pregnancy, risk of preeclampsia was reduced in women who smoked in both pregnancies, in those who only smoked in second pregnancy and, to a lesser extent, in women who smoked only in the first pregnancy
Bogaerts A, 2013 (79)	Cohort N = 7,897 Belgium	Reproductive-aged women	Inter-pregnancy	- Inter-pregnancy weight change	Maternal and perinatal complications	Weight retention between first and second pregnancy was associated with increased risk of gestational diabetes, gestational hypertension and caesarean delivery Among normal weight women, inter-pregnancy weight loss decreased risk of macrosomia, but increased risk of low birth weight
Cnattingius S, 2016 (80)	Cohort N = 456,711 Sweden	Reproductive-aged women	Inter-pregnancy	- Inter-pregnancy weight change	Stillbirth and infant mortality	Women who gained weight between pregnancies had increased risk of stillbirth and infant mortality In overweight women, weight loss between pregnancies reduced risk of infant mortality

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Jain A, 2013 (81)	Cohort N = 10,444 USA	Reproductive-aged women (obese)	Inter-pregnancy	- Inter-pregnancy weight change	Birthweight	Inter-pregnancy weight loss of >2 BMI units was associated with lower risk of large-for-gestational-age infant Inter-pregnancy weight gain of >2 BMI units was associated with higher risk of large-for-gestational-age infant No associations with small-for-gestational-age
Mostello D, 2010 (82)	Cohort N = 17,773 USA	Reproductive-aged women (history of pre-eclampsia)	Inter-pregnancy	- Inter-pregnancy weight change	Recurrent pre-eclampsia	Decrease in BMI between pregnancies was associated with lower risk of recurrent pre-eclampsia, increase in BMI with higher risk of recurrent pre-eclampsia Dose-response observed: linear increase in pre-eclampsia risk with increasing inter-pregnancy BMI
Getahun D, 2007 (83)	Cohort N = 136,884 USA	Reproductive-aged women	Inter-pregnancy	- Inter-pregnancy weight change	Incidence of pre-eclampsia	Change in BMI category between pregnancies was associated with increased risk of pre-eclampsia

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Villamor E, 2006 (84)	Cohort N = 151,025 Sweden	Reproductive-aged women	Inter-pregnancy	- Inter-pregnancy weight change	Maternal and perinatal outcomes	BMI loss >1 unit: lower risk of pre-eclampsia and large-for-gestational-age BMI increase: higher risk of pre-eclampsia, gestational hypertension, gestational diabetes, caesarean delivery, stillbirth and large-for-gestational-age Also among women remaining in the normal weight category No increased risks for decrease in BMI units
Glazer N, 2004 (85)	Cohort N = 4,102 USA	Reproductive-aged women (obese)	Inter-pregnancy	- Inter-pregnancy weight change	Gestational diabetes	32% of women lost weight between pregnancies Weight loss more than 10 pounds (~4 kg) was associated with lower risk of gestational diabetes (OR 0.63, 95% CI 0.38, 1.02) 61% gained weight between pregnancies Weight gain more than 4 kg was associated with higher risk of gestational diabetes (OR 1.47, 95% CI 1.05, 2.04)
Whiteman V, 2011 (86)	Cohort N = 232,272 USA	Reproductive-aged women	Inter-pregnancy	- Inter-pregnancy weight change	Gestational diabetes	Increase in BMI category between pregnancies increased risk of gestational diabetes Decrease in BMI category was associated with lower risk of gestational diabetes

Reference	Study design	Population	Period	Exposure(s)	Outcome(s)	Finding(s)
Whiteman V, 2011 (87)	Cohort N = 218,389 USA	Reproductive-aged women	Inter-pregnancy	- Inter-pregnancy weight change	Stillbirth	Increase in BMI category between pregnancies moderately increased risk of stillbirth Decrease in BMI category was not associated with risk of stillbirth
Whiteman V, 2011 (88)	Cohort N = 100,828 USA	Reproductive-aged women	Inter-pregnancy	- Inter-pregnancy weight change	Caesarean delivery	Increase in BMI category between pregnancies moderately increased risk of caesarean delivery Decrease in BMI category was not associated with risk of caesarean delivery

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## **Appendix 2. Overview of behaviour change interventions in pregnancy with a dietary component.**

### **Background to overview of systematic reviews**

Systematic reviews aim to support evidence-based decision making due to the ever increasing, often unmanageable volume of healthcare research published. However, the volume of systematic reviews being published (approximately 11/day) compounds the problem already faced by decision makers (JBI 2014). An overview of existing systematic reviews (also known as an umbrella review or systematic review of systematic reviews) can compare and contrast published reviews and is an ideal way to highlight if the evidence base is consistent or contradictory. As systematic reviews will have some degree of overlap in their included studies, a meta-analysis to pool summary estimates across systematic reviews is not appropriate. The evidence-synthesis should instead compare results between individual systematic reviews to explore consistency in findings when the same research question is investigated by different groups of researchers.

### **Summary of overview methods**

The review aimed to identify relevant international systematic review evidence on the effectiveness of dietary behaviour change changes interventions in pregnancy, published in peer-reviewed journals or as grey literature. Systematic reviews reporting either a meta-analyses or narrative syntheses were included if published between January 2005 to the date of the searches (January 2016), and in English language. An adapted PICOS framework was used to develop search terms. As we expected to find reviews with multiple Comparator groups (e.g. based on BMI categories) and were not restricting the review to specific behavioural or pregnancy outcomes, the adapted PIS was used to define the Population (pregnancy), Intervention (weight management or diet or obesity), and Study design (systematic review). The databases searched included systematic review repositories (The Cochrane Library: including Cochrane Database of Systematic Reviews, The Database of Abstracts of Reviews of Effectiveness (DARE), Joanna Briggs Institute (JBI) Database of Systematic Reviews and Implementation Reports, PROSPERO), electronic databases (Medline, EMBASE, CINAHL, Maternity and Infant Care, PsycINFO), and grey literature sources (Google Scholar, NICE Evidence Search (<http://www.evidence.nhs.uk>), National Institute for Health Research Journals library, Health Technology Assessment Database). Results were imported into Endnote for title and abstract screening. Narrative and meta-analyses results reported in the included systematic reviews are presented in tables and forest plots. Data are presented in the table of included studies for the effect of interventions on explicit dietary behaviour change during pregnancy. The figures (in the manuscript and web appendices) present the meta-analyses for the effect of dietary interventions on gestational weight gain and the most relevant clinical outcomes which impact on offspring health (gestational diabetes, preterm birth, preeclampsia and large for gestational age).

Reference: Joanna Briggs Institute (2014) Reviewers' Manual: Methodology for JBI Umbrella Reviews. [www.joannabriggs.org](http://www.joannabriggs.org) [accessed 06/11/2017]

**Table: Characteristics of systematic reviews of behaviour change interventions in pregnancy with a dietary component**

Systematic review author, year	Type of intervention	Intervention targeted by maternal weight	Behaviour outcomes reported*	Evidence synthesis methods	Number of included studies	Sample size of pooled data	Publication date range of included studies	Country economy of included studies <sup>#</sup>	Results: Maternal dietary behaviours
Agha et al 2014	Diet +/- PA	Any weight	proxy	Meta-analysis	14	2,734	1998-2008	High n=14	Not reported
Campbell et al 2011	Diet +/- PA	Any weight	proxy	Meta-analysis	5	390	2002-2010	High n=5	Not reported
Dodd et al 2008	Diet +/- PA	Overweight and obese	proxy	Narrative	2	174	2000-2002	High n=2	Not reported
Dodd et al 2010	Diet +/- PA	Overweight and obese	proxy	Meta-analysis	9	743	1992-2008	Upper-middle n=1 High n=8	Not reported
Furber et al 2013	Diet +/- PA	Obese	proxy	Narrative	0	0	n/a	n/a	Not reported
Gardner et al 2011	Diet +/- PA	Any weight	proxy + explicit	Meta-analysis	10	1,656	2000-2010	High n=10	Diet behaviour significantly improved (n=1 study), no significant difference (n=5 studies)
Hill et al 2013	Diet +/- PA	Any weight	proxy	Meta-analysis	22	3,823	2002-2012	Upper-middle n=2 High n=20	Not reported
Kuhlmann et al 2008	Diet +/- PA	Any weight	proxy	Narrative	1	120	2002	High n=1	Not reported
Liu et al 2005	Diet +/- PA	Any weight	proxy	Narrative	3	706	1995-2004	High n=3	Not reported
Muktabhant et al 2015	Diet +/- PA	Any weight	proxy + explicit	Meta-analysis	44	11,444	1990-2014	Upper-middle n=1 High n=43	Weighted mean difference (95% CI): Energy intake (KJ) -570.77 (-894.28, -247.26) Fibre (g) 1.53 (0.94, 2.12)
Olander et al 2015	Diet +/- PA	Obese	proxy	Narrative	10	N/S	2008-2014	High n=10	Not reported
Oteng-Ntim et al 2012	Diet +/- PA	Overweight and obese	proxy	Meta-analysis	19	3,619	2002-2011	Upper-middle n=1 High n=18	Not reported
Quinlivan et al 2011	Diet	Obese	proxy	Meta-analysis	4	537	2008-2011	High n=4	Not reported

Ronnberg et al 2010	Diet +/- PA	Any weight	proxy	Narrative	8	1,538	2000-2009	High n=8	Not reported
SCHARR 2009	Diet +/- PA	Any weight	proxy + explicit	Meta-analysis	12	1,845	1991-2009	High n=12	Significantly increased: protein, fruit & vegetables, high-fibre bread Significantly reduced: total energy intake, fat, carbohydrate No significant difference: diet behaviour, high sugar snacks
Skouteris et al 2010	Diet +/- PA	Any weight	proxy	Narrative	10	1,852	2000-2010	High n=10	Not reported
Streuling et al 2010	Diet +/- PA	Any weight	proxy	Meta-analysis	9	1,549	2000-2010	High n=9	Not reported
Tanentsapf et al 2011	Diet	Any weight	proxy	Meta-analysis	13	1,802	1975-2011	Lower-middle n=1 High n=12	Not reported
Thangaratinam et al 2012a	Diet +/- PA	Any weight	proxy	Meta-analysis	26	5,426	1976-2011	Not reported	Not reported
Thangaratinam et al 2012b	Diet +/- PA	Any weight	proxy	Meta-analysis	88	182,139	1976-2010	Not reported	Not reported

\*Explicit outcomes following dietary behaviour change intervention are the reported dietary behaviours (e.g. energy intake, fibre consumption). Proxy outcomes are maternal or infant health outcomes (e.g. gestational diabetes, preterm birth) or weight outcomes (e.g. gestational weight gain, birthweight) rather than the explicit dietary behaviour change.

# World Bank list of economies: low-income economies, lower-middle-income economies, upper-middle-income economies, and high-income economies. High-income study populations were from Australia, Belgium, Canada, Denmark, Finland, Germany, Ireland, Italy, Netherlands, Norway, Spain, Sweden, Taiwan, UK and USA. Upper-middle-income populations were from Brazil. Lower-middle-income populations were from Egypt.

Abbreviations: PA – physical activity, CI – confidence interval, KJ – kilojoules, g – grams

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**Intervention effects on Large-for-Gestational-Age births**

**High Birthweight**

