Cochrane Library

Cochrane Database of Systematic Reviews

Antenatal dietary education and supplementation to increase energy and protein intake (Review)

Ota E, Hori H, Mori R, Tobe-Gai R, Farrar D

Ota E, Hori H, Mori R, Tobe-Gai R, Farrar D.
Antenatal dietary education and supplementation to increase energy and protein intake.
Cochrane Database of Systematic Reviews 2015, Issue 6. Art. No.: CD000032.
DOI: 10.1002/14651858.CD000032.pub3.

www.cochranelibrary.com

WILEY

TABLE OF CONTENTS

[Intervention Review]

Antenatal dietary education and supplementation to increase energy and protein intake

Erika Ota[1], Hiroyuki Hori[2], Rintaro Mori[1], Ruoyan Tobe-Gai[3], Diane Farrar[4]

[1]Department of Health Policy, National Center for Child Health and Development, Tokyo, Japan. [2]Medical Research Division, National Center for Child Health and Development, Setagaya, Japan. [3]School of Public Health, Shandong University, Jinan, China. [4]Maternal and Child Health, Bradford Institute for Health Research, Bradford, UK

Contact address: Erika Ota, Department of Health Policy, National Center for Child Health and Development, 2-10-1 Okura, Setagaya-ku, Tokyo, 157-8535, Japan. e-i@umin.ac.jp.

Editorial group: Cochrane Pregnancy and Childbirth Group.
Publication status and date: New search for studies and content updated (conclusions changed), published in Issue 6, 2015.

Citation: Ota E, Hori H, Mori R, Tobe-Gai R, Farrar D. Antenatal dietary education and supplementation to increase energy and protein intake. *Cochrane Database of Systematic Reviews* 2015, Issue 6. Art. No.: CD000032. DOI: 10.1002/14651858.CD000032.pub3.

ABSTRACT

Background

Gestational weight gain is positively associated with fetal growth, and observational studies of food supplementation in pregnancy have reported increases in gestational weight gain and fetal growth.

Objectives

To assess the effects of education during pregnancy to increase energy and protein intake, or of actual energy and protein supplementation, on energy and protein intake, and the effect on maternal and infant health outcomes.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (31 January 2015), reference lists of retrieved studies and contacted researchers in the field.

Selection criteria

Randomised controlled trials of dietary education to increase energy and protein intake, or of actual energy and protein supplementation, during pregnancy.

Data collection and analysis

Two review authors independently assessed trials for inclusion and assessed risk of bias. Two review authors independently extracted data and checked for accuracy. Extracted data were supplemented by additional information from the trialists we contacted.

Main results

We examined 149 reports corresponding to 65 trials. Of these trials, 17 were included, 46 were excluded, and two are ongoing. Overall, 17 trials involving 9030 women were included. For this update, we assessed methodological quality of the included trials using the standard Cochrane criteria (risk of bias) and the GRADE approach. The overall risk of bias was unclear.

Nutritional education (five trials, 1090 women)

Women given nutritional education had a lower relative risk of having a preterm birth (two trials, 449 women) (risk ratio (RR) 0.46, 95% CI 0.21 to 0.98, *low-quality evidence*), and low birthweight (one trial, 300 women) (RR 0.04, 95% CI 0.01 to 0.14). Head circumference at birth was increased in one trial (389 women) (mean difference (MD) 0.99 cm, 95% CI 0.43 to 1.55), while birthweight was significantly increased among undernourished women in two trials (320 women) (MD 489.76 g, 95% CI 427.93 to 551.59, *low-quality evidence*), but did not significantly increase for adequately nourished women (MD 15.00, 95% CI -76.30 to 106.30, one trial, 406 women). Protein intake increased significantly (three trials, 632 women) (protein intake: MD +6.99 g/day, 95% CI 3.02 to 10.97). No significant differences were observed on any other outcomes such as neonatal death (RR 1.28, 95% CI 0.35 to 4.72, one trial, 448 women, *low-quality evidence*), stillbirth (RR 0.37, 95% CI 0.07 to 1.90, one trial, 431 women, *low-quality evidence*), small-for-gestational age (RR 0.97, 95% CI 0.45 to 2.11, one trial, 404 women, *low-quality evidence*) and total gestational weight gain (MD -0.41, 95% CI -4.41 to 3.59, two trials, 233 women). There were no data on perinatal death.

Balanced energy and protein supplementation (12 trials, 6705 women)

Risk of stillbirth was significantly reduced for women given balanced energy and protein supplementation (RR 0.60, 95% CI 0.39 to 0.94, five trials, 3408 women, *moderate-quality evidence*), and the mean birthweight was significantly increased (random-effects MD +40.96 g, 95% CI 4.66 to 77.26, $Tau^2 = 1744$, $I^2 = 44\%$, 11 trials, 5385 women, *moderate-quality evidence*). There was also a significant reduction in the risk of small-for-gestational age (RR 0.79, 95% CI 0.69 to 0.90, $I^2 = 16\%$, seven trials, 4408 women, *moderate-quality evidence*). No significant effect was detected for preterm birth (RR 0.96, 95% CI 0.80 to 1.16, five trials, 3384 women, *moderate-quality evidence*) or neonatal death (RR 0.68, 95% CI 0.43 to 1.07, five trials, 3381 women, *low-quality evidence*). Weekly gestational weight gain was not significantly increased (MD 18.63, 95% CI -1.81 to 39.07, nine trials, 2391 women, *very low quality evidence*). There were no data reported on perinatal death and low birthweight.

High-protein supplementation (one trial, 1051 women)

High-protein supplementation (one trial, 505 women), was associated with a significantly increased risk of small-for-gestational age babies (RR 1.58, 95% CI 1.03 to 2.41, *moderate-quality evidence*). There was no significant effect for stillbirth (RR 0.81, 95% CI 0.31 to 2.15, one trial, 529 women), neonatal death (RR 2.78, 95% CI 0.75 to 10.36, one trial, 529 women), preterm birth (RR 1.14, 95% CI 0.83 to 1.56, one trial, 505 women), birthweight (MD -73.00, 95% CI -171.26 to 25.26, one trial, 504 women) and weekly gestational weight gain (MD 4.50, 95% CI -33.55 to 42.55, one trial, 486 women, *low-quality evidence*). No data were reported on perinatal death.

Isocaloric protein supplementation (two trials, 184 women)

Isocaloric protein supplementation (two trials, 184 women) had no significant effect on birthweight (MD 108.25, 95% CI -220.89 to 437.40) and weekly gestational weight gain (MD 110.45, 95% CI -82.87 to 303.76, *very low-quality evidence*). No data reported on perinatal mortality, stillbirth, neonatal death, small-for-gestational age, and preterm birth.

Authors' conclusions

This review provides encouraging evidence that antenatal nutritional education with the aim of increasing energy and protein intake in the general obstetric population appears to be effective in reducing the risk of preterm birth, low birthweight, increasing head circumference at birth, increasing birthweight among undernourished women, and increasing protein intake. There was no evidence of benefit or adverse effect for any other outcome reported.

Balanced energy and protein supplementation seems to improve fetal growth, and may reduce the risk of stillbirth and infants born small-for-gestational age. High-protein supplementation does not seem to be beneficial and may be harmful to the fetus. Balanced-protein supplementation alone had no significant effects on perinatal outcomes.

The results of this review should be interpreted with caution. The risk of bias was either unclear or high for at least one category examined in several of the included trials, and the quality of the evidence was low for several important outcomes. Also, as the anthropometric characteristics of the general obstetric population is changing, those developing interventions aimed at altering energy and protein intake should ensure that only those women likely to benefit are included. Large, well-designed randomised trials are needed to assess the effects of increasing energy and protein intake during pregnancy in women whose intake is below recommended levels.

PLAIN LANGUAGE SUMMARY

Antenatal dietary education and supplementation on energy and protein intake in pregnancy to improve infant outcomes

What is the issue?

Does dietary advice or supplementation to increase energy and protein intake in pregnancy improve outcomes for babies, and are there any adverse effects? Do these interventions impact differently on poorly-nourished and well-nourished pregnant women and their infants?

Why is this important?

During pregnancy, a baby developing inside the womb receives all its nutrition from its mother. Inadequate dietary intake during pregnancy can lead to malnutrition and poor outcomes for the baby. Therefore, advising women on their diet and providing food supplements in pregnancy may help babies to grow and thrive.

What evidence did we find

This review includes 17 randomised controlled trials, involving 9030 women. The quality of the included trials is low to moderate. We, examined several aspects of dietary advice and supplementation and produced the following four main findings.

(1) Providing nutritional advice resulted in an increase in the mother's protein intake, there were fewer babies born too early (two trials involving 449 women) and fewer babies with low birthweight (one trial involving 300 women), One study of 389 women showed increases in some babies birth head circumference (in one trial involving 389 women) There were also more babies with a higher birthweight among undernourished women (two trials involving 320 women).

(2) Giving the mothers balanced energy and protein supplements was associated with fewer babies dying during labour (five trials, 3408 women), clear increases in birthweight (11 trials, 5385 women) and fewer babies who were small-for-gestational age (seven trials, 4408 women). However, the impact on the long-term health of the baby was uncertain, including among undernourished women.

(3) High-protein supplementation (one trial involving 1051 women) showed no benefit for women and potential harm for the baby through an increase in the number of babies small for their gestational age at birth.

(4) Isocaloric protein supplementations (i.e. balanced supplements in which the protein replaces an equal quantity of other nutrients, e.g. fat and carbohydrate): in birthweight and weekly gestational weight gain, showed no benefit for women or their babies (two trials involving 184 women).

What does this mean?

Providing nutritional advice or balanced energy and protein supplements to women during pregnancy may be beneficial. However, there is not enough evidence on isocaloric protein supplements which currently appear to be unhelpful and high-protein supplements may be harmful.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Nutritional education compared with no counselling or education during pregnancy for perinatal outcomes

Nutritional education compared with no counselling or education during pregnancy for perinatal outcomes

Population: pregnant women
Settings: USA, Greece, Bangladesh
Intervention: nutritional education to increase energy and protein intake during pregnancy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No. of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Nutritional education during pregnancy				
Perinatal mortality	Not estimable			0 study	See comment	This outcome was not reported in the included studies.
Stillbirth	**Study population**		**RR 0.37** (0.07 to 1.9)	431 (1 study)	⊕⊕⊝⊝ **low** [1,2]	
	24 per 1000	**9 per 1000** (2 to 46)				
	Moderate					
	24 per 1000	**9 per 1000** (2 to 46)				
Neonatal death	**Study population**		**RR 1.28** (0.35 to 4.72)	448 (1 study)	⊕⊕⊝⊝ **low** [1,2]	
	18 per 1000	**23 per 1000** (6 to 83)				
	Moderate					
	18 per 1000	**23 per 1000**				

		(6 to 83)			
Small-for-gestational age	**Study population**		**RR 0.97** (0.45 to 2.11)	404 (1 study)	⊕⊕⊝⊝ **low** [1,2]
	60 per 1000	**58 per 1000** (27 to 127)			
	Moderate				
	60 per 1000	**58 per 1000** (27 to 127)			
Preterm birth	**Study population**		**RR 0.46** (0.21 to 0.98)	449 (2 studies)	⊕⊕⊝⊝ **low** [2,3]
	85 per 1000	**39 per 1000** (18 to 84)			
	Moderate				
	92 per 1000	**42 per 1000** (19 to 90)			
Birthweight (g)	Undernourished women	The mean birthweight (g) in the intervention groups was **489.76 higher** (427.93 lower to 551.59 higher)		320 (2 studies)	⊕⊕⊝⊝ **low** [2,4]
	Adequately nourished women	The mean birthweight (g) in the intervention groups was **15 higher** (76.3 lower to 106.3 higher)		406 (1 study)	⊕⊕⊝⊝ **low** [1,3]
Total gestational weight gain (kg)		The mean gestational weight gain (kg) in the intervention groups was **0.41 lower** (4.41 lower to 3.59 higher)		233 (2 studies)	⊕⊝⊝⊝ **very low** [1,3,5]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in the footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

1 Wide confidence interval crossing the line of no effect.
2 Few events and small sample size.
3 One study with design limitations.
4 Most studies contributing data had design limitations.
5 Statistical heterogeneity ($I^2 > 60\%$).

Summary of findings 2. Balanced protein and energy supplementation compared with control or no intervention in pregnancy for perinatal and maternal outcomes

Balanced protein and energy supplementation compared with control or no intervention in pregnancy for perinatal and maternal outcomes

Population: pregnant women
Settings: USA, UK, Taiwan, Gambia, India, Burkina Faso, Colombia, Indonesia

Intervention: balanced protein/energy supplementation in pregnancy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Balanced protein/energy supplementation in pregnancy				
Perinatal mortality	Not estimable			0 study	See comment	This outcome was not reported in the included studies.
Stillbirth	**Study population**		**RR 0.60** (0.39 to 0.94)	3408 (5 studies)	⊕⊕⊕⊝ **moderate** [1]	
	30 per 1000	**18 per 1000** (12 to 28)				
	Moderate					
	29 per 1000	**18 per 1000** (11 to 28)				
Neonatal death	**Study population**		**RR 0.68** (0.43 to 1.07)	3381 (5 studies)	⊕⊕⊝⊝ **low** [1,2]	
	26 per 1000	**18 per 1000**				

		(11 to 28)			
	Moderate				
	17 per 1000	**12 per 1000** (7 to 18)			
Small-for-gestational age	**Study population**		**RR 0.79** (0.69 to 0.9)	4408 (7 studies)	⊕⊕⊕⊝ **moderate** [1]
	173 per 1000	**137 per 1000** (120 to 156)			
	Moderate				
	163 per 1000	**129 per 1000** (112 to 147)			
Preterm birth	**Study population**		**RR 0.96** (0.8 to 1.16)	3384 (5 studies)	⊕⊕⊕⊝ **moderate** [1]
	112 per 1000	**108 per 1000** (90 to 130)			
	Moderate				
	113 per 1000	**108 per 1000** (90 to 131)			
Birthweight (g)		The mean birthweight (g) in the intervention groups was **40.96 higher** (4.66 to 77.26 higher)		5385 (11 studies)	⊕⊕⊕⊝ **moderate** [1]
Weekly gestational weight gain (g/week)		The mean weekly gestational weight gain (g/week) in the intervention groups was **18.63 higher** (1.81 lower to 39.07 higher)		2391 (9 studies)	⊕⊝⊝⊝ **very low** [1,2,4]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in the footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Most studies contributing data had design limitations.
[2] Wide confidence interval crossing the line of no effect.
[3] Few events and small sample size.
[4] Statistical heterogeneity (I^2 = 57%).

Summary of findings 3. High-protein supplementation in pregnancy and perinatal outcomes

High-protein supplementation in pregnancy and perinatal outcomes

Population: pregnant women
Settings: USA
Intervention: high-protein supplementation in pregnancy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	High-protein supplementation in pregnancy				
Perinatal mortality	Not estimable			0 study	See comment	This outcome was not reported in the included studies.
Stillbirth	**Study population**		RR 0.81 (0.31 to 2.15)	529 (1 study)	⊕⊕⊝⊝ **low** [1,2]	
	33 per 1000	**27 per 1000** (10 to 72)				
	Moderate					
	33 per 1000	**27 per 1000** (10 to 71)				
Neonatal death	**Study population**		RR 2.78 (0.75 to 10.36)	529 (1 study)	⊕⊕⊝⊝ **low** [1,2]	
	11 per 1000	**31 per 1000** (8 to 115)				
	Moderate					

	11 per 1000	**31 per 1000** (8 to 114)			
Small-for-gestational age	**Study population**		**RR 1.58** (1.03 to 2.41)	505 (1 study)	⊕⊕⊕⊝ **moderate** [2]
	117 per 1000	**185 per 1000** (121 to 282)			
	Moderate				
	117 per 1000	**185 per 1000** (121 to 282)			
Preterm birth	**Study population**		**RR 1.14** (0.83 to 1.56)	505 (1 study)	⊕⊕⊝⊝ **low** [1,2]
	219 per 1000	**249 per 1000** (182 to 341)			
	Moderate				
	219 per 1000	**250 per 1000** (182 to 342)			
Birthweight (g)		The mean birthweight (g) in the intervention groups was **73 lower** (171.26 lower to 25.26 higher)		504 (1 study)	⊕⊕⊝⊝ **low** [1,2]
Weekly gestational weight gain (g)		The mean weekly gestational weight gain (g/week) in the intervention groups was **4.5 higher** (33.55 lower to 42.55 higher)		486 (1 study)	⊕⊕⊝⊝ **low** [1,3]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in the footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

1 Wide confidence interval crossing the line of no effect.
2 Few events and small sample size.

[3] One study with design limitations.

Summary of findings 4. Isocaloric balanced protein supplementation in pregnancy and outcomes

Isocaloric balanced protein supplementation in pregnancy and outcomes

Population: pregnant women
Settings: UK
Intervention: isocaloric balanced protein supplementation in pregnancy

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Isocaloric balanced protein supplementation in pregnancy				
Perinatal mortality	Not estimable			0 study	See comment	This outcome was not reported in the one included study.
Stillbirth	Not estimable			0 study	See comment	This outcome was not reported in the one included study.
Neonatal death	Not estimable			0 study	See comment	This outcome was not reported in the one included study.
Small-for-gestational age	Not estimable			0 study	See comment	This outcome was not reported in the one included study.
Preterm birth	Not estimable			0 study	See comment	This outcome was not reported in the one included study.
Birthweight (g)		The mean birthweight (g) in the intervention groups was **108.25 higher** (220.89 lower to 437.4 higher)		184 (2 studies)	⊕⊝⊝⊝ **very low** [1,2,3]	
Weekly gestational weight gain (g/week)		The mean weekly gestational weight gain (g/week) in the intervention groups was **110.45 higher** (82.87 lower to 303.76 higher)		184 (2 studies)	⊕⊝⊝⊝ **very low** [1,2,3]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in the footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] Most studies contributing data had design limitations.
[2] Statistical heterogeneity (I^2 > 60%).
[3] Few events and small sample size.

BACKGROUND

Description of the condition

Pregnancy requires an increased intake of macronutrients and micronutrients for maternal and fetal needs, and malnourishment or inadequate dietary intake during pregnancy can lead to adverse perinatal outcomes. Observational studies (IOM 1990; Kramer 1987; Rush 2001) have indicated that both gestational weight gain and energy intake are strongly and positively associated with fetal growth, and possibly associated with a reduced risk of preterm birth. Moreover, these associations are stronger in undernourished women, i.e. those with low pre-pregnancy body mass index (BMI) (Ota 2011). Fetal development complications, such as low birthweight and infants born small-for-gestational age, are associated with increases in perinatal mortality and morbidities (Ashworth 1998; Kramer 1987). Globally, it is estimated that more than approximately 20 million low birthweight infants are born each year, and more than 95% of these babies are born in developing countries (Unicef-WHO 2004). The effects of poor maternal nutrition on both immediate birth outcomes and longer-term health has been well-described in many epidemiological studies, including the effects from the Dutch winter famine of 1944 to 1945 (Stein 1975). Recognised longer-term health risks associated with poor infant growth include type 2 diabetes, hypertension, cardiovascular disease and obesity (Barker 1998; Barker 2002; Eriksson 2001).

Description of the interventions and how the interventions might work

Undernourished maternal nutritional status at conception and inadequate maternal nutritional status during pregnancy can result in adverse perinatal outcomes (Viswanathan 2008). Dietary education to pregnant women and balanced protein energy supplementation to achieve appropriate energy intake can lead to an increase in maternal weight gain during pregnancy, and fetal growth (de Onis 1998; Kulier 1998; Viller 1998). Protein generally comprises about 10% to 15% of dietary energy (Garlick 2000). Balanced protein energy supplementation (i.e. supplements in which protein provides less than 25% of the total energy content) has been shown to have significant positive impacts on maternal and perinatal birth outcomes, such as reductions in the incidences of preterm birth (Viller 1998), stillbirth (Imdad 2011) and intrauterine growth restriction (de Onis 1998). Furthermore, non-randomised trials have reported beneficial effects on fetal growth (Lechtig 1975; Prentice 1983), although the evidence from properly randomised trials suggests more modest benefits (Rush 1989; Rush 2001). On the other hand, data from women with severe dietary carbohydrate restrictions and very high animal protein intake, which were collected as part of routine antenatal care in a moderately affluent area, suggest that high-protein dietary supplementation may have depressed birthweight by 400 g or more (Grieve 1979: Rush 1989). Isocaloric protein supplementation denotes a supplement, in which the protein content is 'balanced', i.e. provides less than 25% of its total energy content, but the protein replaced an equal quantity of non-protein energy in the control group. The observational findings reported for a non-randomised trial in Guatemala (Lechtig 1975) also suggest that protein supplementation is unlikely to benefit pregnant women or their infants.

Why it is important to do this review

Reliable high-quality information is required about the benefits and harms of energy/protein supplementation during pregnancy both for the woman and her infant. This review updates the previous version by two additional studies (Jahan 2013; Oaks 2014), in order to aid clinical decisions and health policy-making.

OBJECTIVES

To assess the benefits and harms of dietary education, supplementation or restriction on health outcomes for women and their infants. More specifically, the purpose of this review was to evaluate the five items listed below.

1. Effects of advising pregnant women to increase their energy and protein intakes on gestational weight gain and outcomes of pregnancy, including fetal growth, gestational duration, and maternal and fetal/infant morbidity and mortality.
2. Effects of balanced energy and protein supplements during pregnancy on gestational weight gain and outcomes of pregnancy.
3. Effects of high-protein nutritional supplements during pregnancy on gestational weight gain and outcomes of pregnancy.
4. Effects of isocaloric protein supplements (i.e. where the protein replaces an equal quantity of non-protein energy) during pregnancy on gestational weight gain and outcomes of pregnancy.

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised controlled trials with randomisation at either the individual or cluster level. We did not include quasi-randomised trials or cross-over trials.

For assessing dietary education to increase energy and protein intake, we included randomised controlled trials of such education, whether administered on a one-to-one basis or to groups of women.

For assessing dietary supplementation: randomised controlled trials of energy and protein supplementation, with or without placebo.

Types of participants

All pregnant women with no systemic illness.

Types of interventions

1. Specific nutritional education to increase dietary energy and protein intake versus no nutritional education or a different form of consultation.
2. Balanced energy and protein supplementation versus no 'balanced energy and protein' supplementation or placebo. The types of supplements included those that were 'balanced' energy and protein supplements (i.e. an energy supplement in which less than 25% of the energy is from protein).

3. High-protein supplements versus low- or no protein supplements (i.e. an energy supplement in which more than 25% of the energy is from protein).
4. Isocaloric protein supplements versus the protein replacing an equal quantity of non-protein energy (i.e. a supplement in which the protein content is 'balanced', i.e. provides less than 25% of total energy content, but the protein replaced an equal quantity of non-protein energy in the control group).

Types of outcome measures

Primary outcomes

- Perinatal mortality (defined by trialists)
- Stillbirth (death after 20 weeks' gestation and before birth)
- Neonatal death (death of a live infant within the first 28 days of life)

Secondary outcomes

Maternal outcomes

- Pre-eclampsia (defined by trialists)
- Energy intake (kcal/day)
- Protein intake (g/day)
- Gestational weight gain (kg)
- Duration of labour (hours)
- Mode of birth
- Number of antenatal hospital admissions
- Exclusive breastfeeding at six months (defined by trialists)

Fetal/infant outcomes

- Birthweight (g)
- Small-for-gestational weight (defined by trialists)
- Low birthweight (less than 2500 g)
- Macrosomia (birthweight ≥ 4 kg and birth injury)
- Birth length (cm)
- Birth head circumference (cm)
- Neurological development
- Preterm birth (prior to 37 weeks' gestation)
- Respiratory distress syndrome
- Admission to neonatal intensive care unit
- Chronic lung disease
- Periventricular leukomalacia
- Intraventricular haemorrhage
- Necrotising enterocolitis
- Retinopathy of prematurity
- Child growth (weight, height, head circumference, BMI)

Child outcomes

- Child growth (weight, height, head circumference, BMI)
- Neurological development

Search methods for identification of studies

The following methods section of this review is based on a standard template used by the Cochrane Pregnancy and Childbirth Group.

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register by contacting the Trials Search Co-ordinator (31 January 2015).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE (Ovid);
3. weekly searches of Embase (Ovid);
4. monthly searches of CINAHL (EBSCO);
5. handsearches of 30 journals and the proceedings of major conferences;
6. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE, Embase and CINAHL, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

Searching other resources

We searched the reference lists of retrieved studies and contacted authors for additional data.

We did not apply any language or date restrictions.

Data collection and analysis

For the methods used when assessing the trials identified in the previous version of this review, *see* Ota 2012.

For this update, we used the following methods based on a standard template used by the Cochrane Pregnancy and Childbirth Group for assessing the reports that were identified as a result of the updated search.

Selection of studies

Review authors Erika Ota (EO) and Hiroyuki Hori (HH) independently assessed all the potential studies we identified as a result of the updated search strategy for inclusion and resolved any disagreements through discussion or, if required, through consultation with Rintaro Mori (RM).

Data extraction and management

For eligible studies, EO and HH extracted the data independently and entered them into Review Manager software (RevMan 2014). We resolved any discrepancies through discussion or, if required, through consultation with RM. Data were checked for accuracy.

When information regarding any of the above was unclear, we attempted to contact the authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors (EO and HH) independently assessed risk of bias using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved discrepancies through discussion.

(1) Random sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We assessed the method as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

For each included study, we described the method used to conceal the allocation sequence in sufficient detail and determined whether the intervention allocation could have been foreseen in advance of or during recruitment, or changed after assignment.

We assessed the methods as indicated below:

- low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk of bias (e.g. open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded, or if we judged that the lack of blinding would be unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed the methods as:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed methods used to blind outcome assessment as:

- low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, protocol deviations)

For each included study, and each outcome or class of outcomes, we described the completeness of the data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported, the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported or supplied by the trial authors, we re-included missing data in the analyses that we undertook.

We assessed methods as indicated below:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomisation);
- unclear risk of bias.

(5) Selective reporting bias

For each included study, we described how we investigated the possibility of selective outcome reporting bias and what we found.

We assessed the methods as indicated below:

- low risk of bias (where it was clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review had been reported);
- high risk of bias (where not all of the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest were reported incompletely and could not be used; study failed to include results of a key outcome that would have been expected to have been reported);
- unclear risk of bias.

(6) Other bias (checking for bias caused by problems not covered by section (1) to (5) above)

For each included study, we described any important concerns we had about other possible sources of bias.

We assessed whether each study was free of other problems that could put it at risk of bias as indicated below:

- low risk of other bias;
- high risk of other bias;
- unclear risk of other bias.

(7) Overall risk of bias

We made explicit judgements about whether studies were at high risk of bias, according to the criteria given in the *Handbook* (Higgins 2011). With reference to (1) to (6) above, we planned to assess the likely magnitude and direction of the bias and whether we considered it was likely to impact on the findings. In future updates, we will explore the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis.

Assessing the quality of the evidence

For this update the quality of the evidence was assessed using the GRADE approach (Guyatt 2008; Schunemann 2009) in order to assess the quality of the body of evidence relating to the following outcomes (*maximum of seven*) for the four main interventions such as dietary education, balanced protein and energy supplementation, high-protein supplementation and isocaloric balanced protein supplementation:

1. perinatal mortality (defined by trialists);
2. stillbirth (death after 20 weeks' gestation and before birth);
3. neonatal death (death of a live infant within the first 28 days of life);
4. small-for-gestational age;
5. preterm birth;
6. birthweight (g);
7. gestational weight gain (kg) (including weekly gestational weight gain (g)).

GRADEprofiler (GRADEpro 2014) was used to import data from Review Manager 5.3 (RevMan 2014) in order to create 'Summary of findings' tables. A summary of the intervention effect and a measure of quality for each of the above outcomes was produced using the GRADE approach. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from 'high quality' by one level for serious (or by two levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias.

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented the results as the summary risk ratio with the 95% confidence intervals.

Continuous data

For continuous data, we used the mean difference if the outcomes were measured in the same way between trials. If necessary, we planned to use the standardised mean difference to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomised trials

We included cluster-randomised trials in the analyses along with individually-randomised trials. We adjusted their sample sizes using the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011) using an estimate of the intra-cluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. Where we used ICCs from other sources, we reported this and conducted sensitivity analyses to investigate the effect of variation in the ICC. We determined that if we identified both cluster-randomised trials and individually-randomised trials, we planned to synthesise the relevant information. We would have considered it reasonable to combine the results from both if there was little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit was considered to be unlikely. Two of the trials (Ceesay 1997; Kafatos 1989) gave no published or unpublished data on the outcome-specific ICC. Therefore, we assumed a value of 0.01 and adjusted the corresponding sample sizes according to the design effect, i.e. by dividing the crude (individual) sample sizes by 1+ (m -1)r, where m is the average cluster size and r is the ICC (assumed to be 0.01). We conducted sensitivity analyses to investigate the effect of variation in the ICC (Figure 1; Figure 2).

Figure 1. Sensitivity analysis of the effect of clustering : Nutritional education during pregnancy (1.7 preterm birth) Kafatos 1989

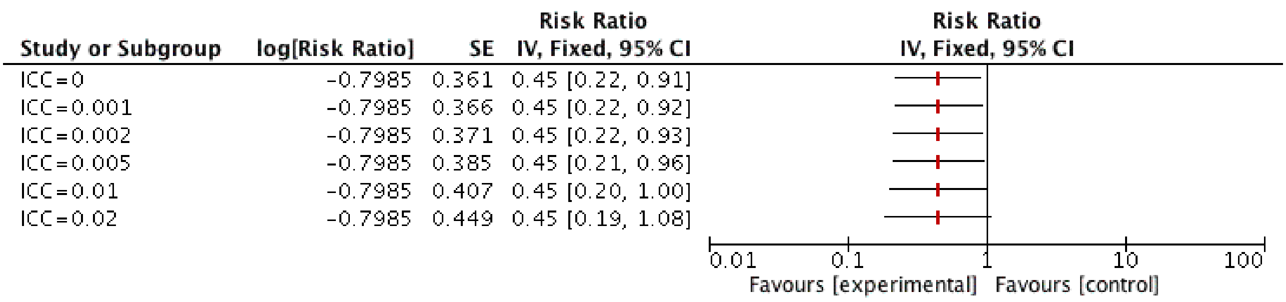
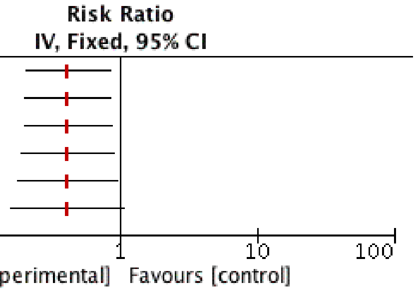


Figure 2. Sensitivity analysis of the effect of clustering : Balanced protein/energy supplementation in pregnancy (2.1 Stillbirth) Ceesay 1997

Study or Subgroup	log[Risk Ratio]	SE	Risk Ratio IV, Fixed, 95% CI
ICC=0	-0.8754	0.3607	0.42 [0.21, 0.84]
ICC=0.001	-0.8754	0.3682	0.42 [0.20, 0.86]
ICC=0.002	-0.8754	0.3755	0.42 [0.20, 0.87]
ICC=0.005	-0.8754	0.3966	0.42 [0.19, 0.91]
ICC=0.01	-0.8754	0.4295	0.42 [0.18, 0.97]
ICC=0.02	-0.8754	0.4886	0.42 [0.16, 1.09]



Cross-over trials

Cross-over trials were not considered in this review.

Dealing with missing data

For included studies, we noted the levels of attrition. The impact of including studies with high levels of missing data in the overall assessment of the treatment effect was explored using a sensitivity analysis.

All outcomes analyses were carried out, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses. The denominator for each outcome in each trial was the randomised number minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed the statistical heterogeneity in each meta-analysis using Tau^2, I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if the I^2 was greater than 30% and either the Tau^2 was greater than zero, or there was a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

Where there were 10 or more studies in the meta-analysis, we investigated the reporting biases (such as publication bias) using funnel plots. We assessed the funnel plot asymmetry visually. If asymmetry was suggested by a visual assessment, we performed exploratory analyses to investigate this.

Data synthesis

We carried out statistical analysis using Review Manager software (RevMan 2014). We used a fixed-effect inverse variance meta-analysis for combining data where trials were examining the same intervention, and the trials' populations and methods were judged to be sufficiently similar. If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, we used a random-effects meta-analysis to produce an overall summary when an average treatment effect across trials was considered clinically meaningful. The random-effects summary was treated as the average of the range of possible treatment effects and we discussed the clinical implications of treatment effects differing between trials. Where the average treatment effect was not clinically meaningful, we did not combine trials.

When we performed random-effects analyses, the results were presented as the average treatment effects with 95% confidence intervals, and the estimates of Tau^2 and I^2.

Subgroup analysis and investigation of heterogeneity

When we identified substantial heterogeneity, we investigated it using subgroup analyses and sensitivity analyses. We considered whether an overall summary was meaningful, and if it was, we used a random-effects analysis to produce such a summary.

Since observational studies (IOM 1990; Kramer 1987) suggest a stronger association between gestational weight gain and fetal growth in women who were under-nourished before pregnancy, we stratified the analysis of the effects on mean birthweight into those trials in which the majority of women had low pre-pregnancy (or early pregnancy) weight (Ceesay 1997; Girija 1984; Kardjati 1988; Mora 1978; Rush 1980), and those in which the participants appeared adequately nourished (Elwood 1981; Ross 1985; Viegas 1982a). For the Taiwan trial (Blackwell 1973) and two other trials (Huybregts 2009; Viegas 1982b),within-trial stratification was possible, based on data contained in the published reports.

The following outcomes were used in subgroup analysis birthweight, weight, height and BMI:

1. women with low pre-pregnancy (or early pregnancy) weight versus adequately nourished women;
2. boy versus girl.

We assessed subgroup differences by interaction tests available within RevMan (RevMan 2014). We reported the results of subgroup analyses quoting the Chi^2 statistic and P value, and the interaction test I^2 value.

Because growth varies with differences in sex (de Onis 2007), it is desirable to compare growth between groups after adjusting for variations by sex. We conducted subgroup analysis on children's data separated by sex for the follow-up results of balanced protein and energy supplementation at the age of 11 to 17 years (height, weight, BMI z-score, and body fat).

Sensitivity analysis

We carried out sensitivity analyses to explore the effects of fixed-effect or random-effects analyses for outcomes with statistical heterogeneity.

RESULTS

Description of studies

Results of the search

Initially we examined 149 reports corresponding to 65 trials. Of these trials, 17 were included and 46 were excluded. Two trials are ongoing (Hambidge 2014; Moore 2011) (*see* Characteristics of ongoing studies).

Included studies

We included 17 trials published between 1973 to 2014 that met the inclusion criteria.

Participants

Seven trials were conducted in an economically disadvantaged area including under-nourished populations (Briley 2002; Ceesay 1997; Girija 1984; Huybregts 2009; Kardjati 1988; Mora 1978; Rush 1980); the other 10 trials included well-nourished populations (Blackwell 1973; Elwood 1981; Hunt 1976; Jahan 2013; Kafatos 1989; Oaks 2014; Ross 1985; Sweeney 1985; Viegas 1982a; Viegas 1982b).

Interventions

Five trials (Briley 2002; Hunt 1976; Jahan 2013; Kafatos 1989; Sweeney 1985) evaluated nutritional education to increase energy and protein intake. Twelve trials (Blackwell 1973; Ceesay 1997; Elwood 1981; Girija 1984; Huybregts 2009; Kardjati 1988; Mora 1978; Oaks 2014; Ross 1985; Rush 1980; Viegas 1982a; Viegas 1982b) assessed the impact of balanced energy/protein supplementation. Only one trial assessed the effects of high-protein nutritional supplements (Rush 1980). Two trials (Viegas 1982a; Viegas 1982b) investigated the effects of isocaloric protein supplements. Interventions for nutritional education included counselling or classes versus no interventions (four trials: Hunt 1976; Jahan 2013; Kafatos 1989; Sweeney 1985) and counselling versus home visits without counselling (one trial: Briley 2002). Interventions for balanced energy and protein supplementation included supplementation versus control supplements (nine trials: Blackwell 1973; Huybregts 2009; Kardjati 1988; Mora 1978; Oaks 2014; Ross 1985; Rush 1980; Viegas 1982a; Viegas 1982b) and supplementation versus no intervention (three trials: Ceesay 1997; Elwood 1981; Girija 1984). Intervention for high-protein nutritional supplements included supplementation versus supplement containing vitamins/minerals (Rush 1980). Intervention for isocaloric-protein nutritional supplements included supplementation versus supplement of flavoured carbonated water containing iron and vitamin C (Viegas 1982a; Viegas 1982b).

Outcomes

Most of the trials focused on assessing the effects of dietary education, supplementation, or restriction on gestational weight gain, pre-eclampsia and/or pregnancy outcomes, or child development.

Setting

Seven trials were from high-income countries such as the USA and UK, and 10 trials from low- and middle-income countries such as Gambia, Taiwan, India, Burkina Faso, Greece, Indonesia, Colombia, South Africa, Ghana and Bangladesh.

For details of the included studies, *see* the Characteristics of included studies table.

Excluded studies

We excluded 46 trials. Of these trials, 15 trials did not match the interventions in this review, 15 trials involved participants who were outside the scope of the review, one did not have a control group, one trial's analysis was based on individual women despite randomising by village, two trials had very high attrition, and 12 trials did not involve randomisation, or the designs were outside the scope of the review.

For details of the excluded studies, *see* the Characteristics of excluded studies table.

Risk of bias in included studies

See Figure 3 and Figure 4.

Figure 3. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

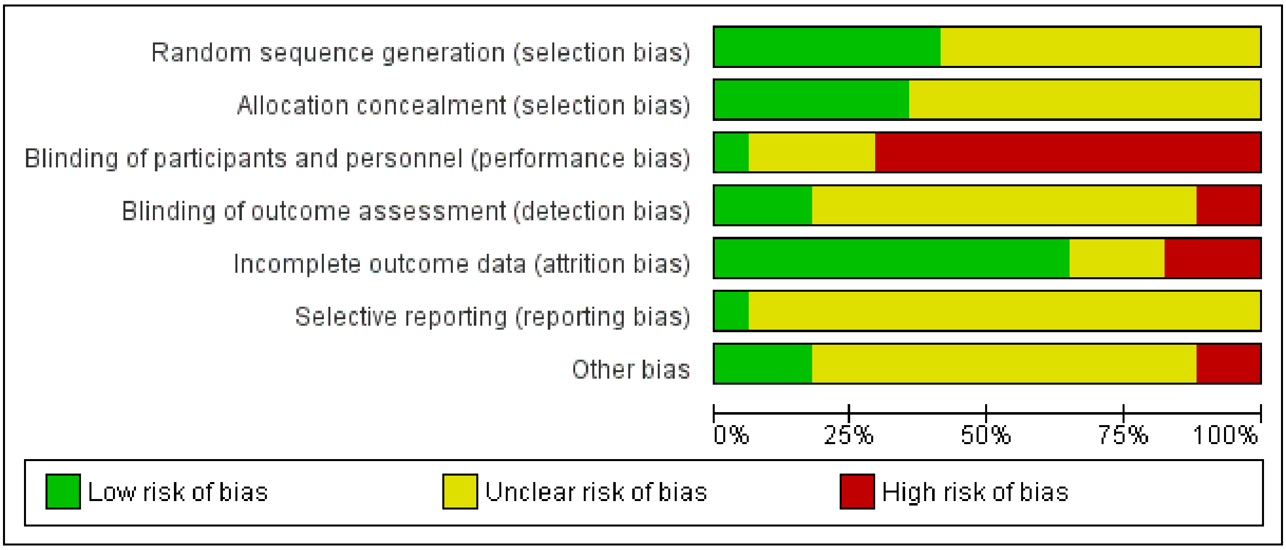
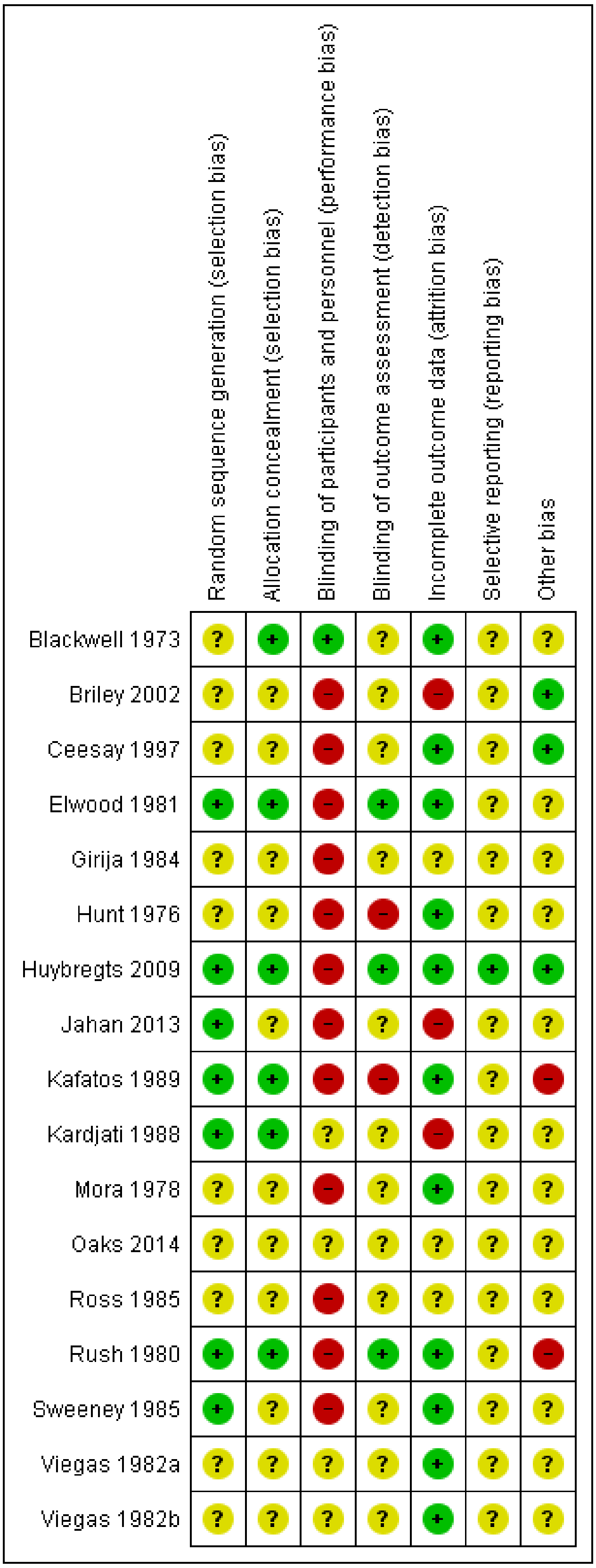


Figure 4. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Sequence generation

Seven trials had a low risk of bias because of adequate randomisation of participants to the intervention groups (Elwood 1981; Huybregts 2009; Jahan 2013; Kafatos 1989; Kardjati 1988; Rush 1980; Sweeney 1985). For 10 trials, risk of bias could not be adequately judged because no detailed information was provided about allocation sequence generation (Blackwell 1973; Briley 2002; Ceesay 1997; Girija 1984; Hunt 1976; Mora 1978; Oaks 2014; Ross 1985; Viegas 1982a; Viegas 1982b).

Allocation concealment

Six trials had a low risk of bias through the use of sequentially numbered, opaque, sealed envelopes or drug containers of identical appearance or central allocation (Blackwell 1973; Elwood 1981; Huybregts 2009; Kafatos 1989; Kardjati 1988; Rush 1980). Eleven trials provided no information about allocation concealment (Briley 2002; Ceesay 1997; Girija 1984; Hunt 1976; Jahan 2013; Mora 1978; Oaks 2014; Ross 1985; Sweeney 1985; Viegas 1982a; Viegas 1982b).

Blinding

Participants and personnel

One trial had a low risk of bias using double blinding (Blackwell 1973). Twelve trials had a high risk of bias owing to a lack of blinding. Four trials could not be judged for the risk because no information was provided (Kardjati 1988; Oaks 2014; Viegas 1982a; Viegas 1982b).

Outcome assessment

Three trials had a low risk of bias (Elwood 1981; Huybregts 2009; Rush 1980). Two trials had a high risk of bias due to the fact that delivery of the intervention and outcome assessment were carried out by the same personnel (Hunt 1976; Kafatos 1989). The other 12 trials were judged unclear due to no information provided about outcome assessors.

Incomplete outcome data

Losses to follow-up ranged from 1.5% in Viegas 1982b to 25.9% in Briley 2002. Eleven trials had a low risk of bias, three trials had a high risk of bias and three trials were judged as unclear bias owing to insufficient information.

Selective reporting

Sixteen trials were judged as unclear risk because the protocol was not available for judgment of this bias. Only one trial (Huybregts 2009) had a protocol and was judged as low risk for selective reporting.

Other potential sources of bias

Two trials had a high risk of bias because no data were presented on compliance or substitution, and for other reasons. Three trials had a low risk of bias and 12 trials had insufficient information and were judged as unclear risk.

The funnel plots (Figure 5; Figure 6) did not show any publication bias.

Figure 5. Funnel plot of comparison: 2 Balanced protein/energy supplementation in pregnancy, outcome: 2.3 Birthweight (g).

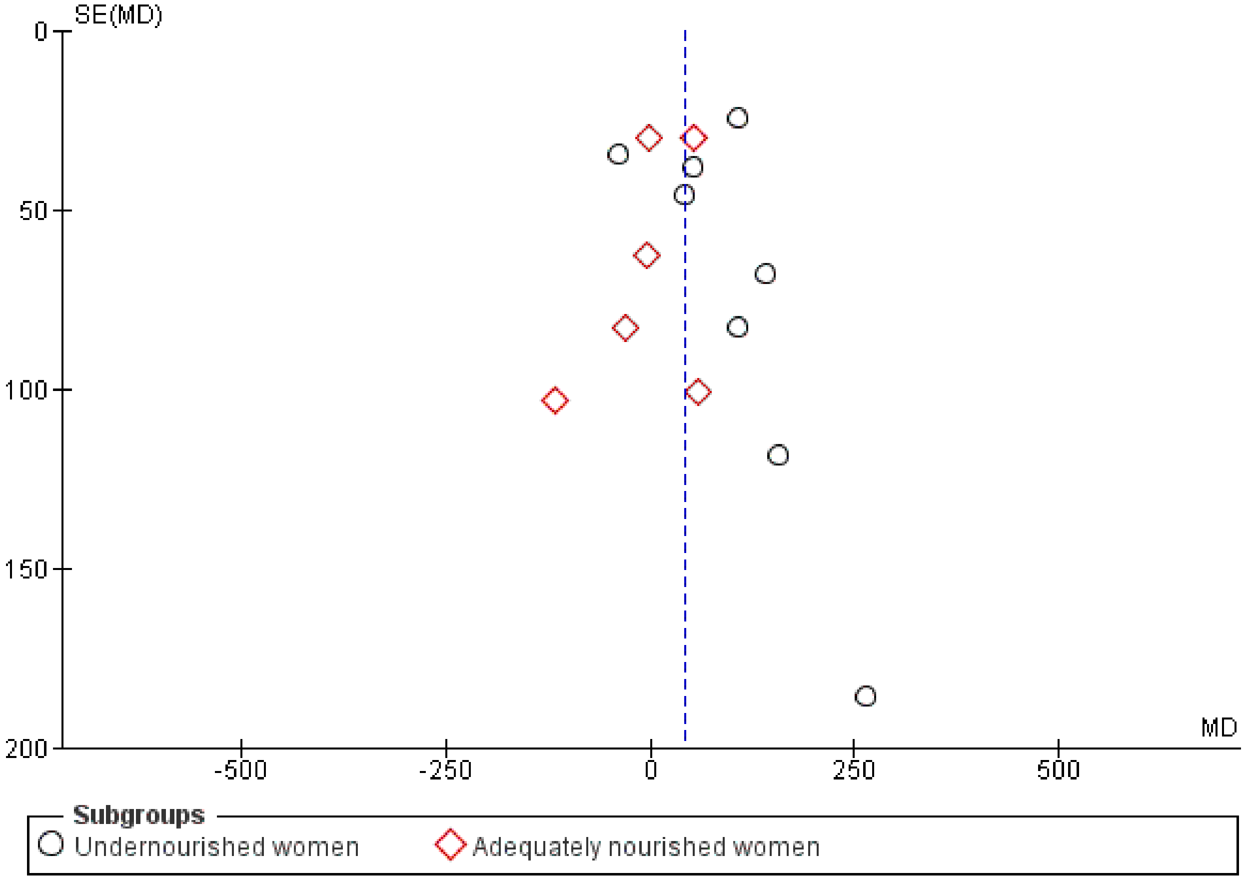
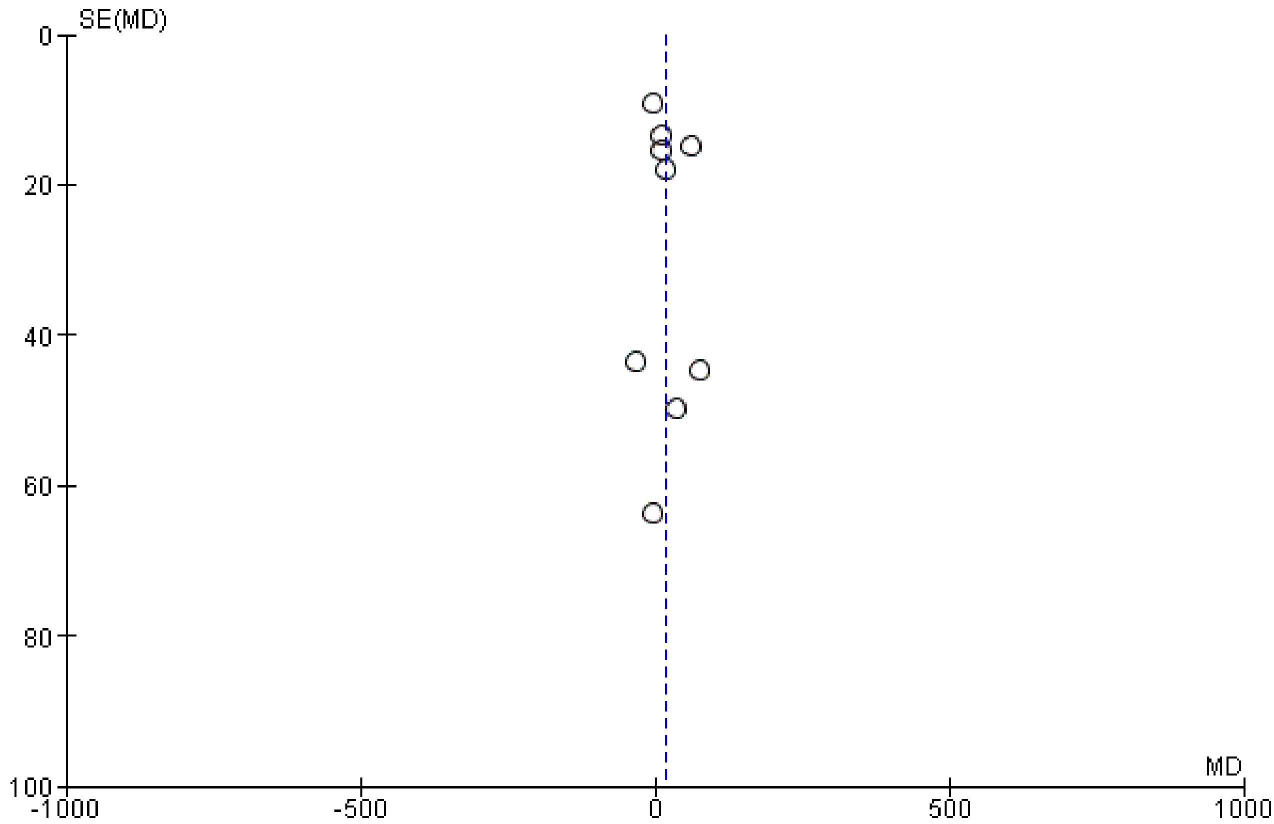


Figure 6. Funnel plot of comparison: 2 Balanced protein/energy supplementation in pregnancy, outcome: 2.9 Weekly gestational weight gain (g/week).



Effects of interventions

See: **Summary of findings for the main comparison** Nutritional education compared with no counselling or education during pregnancy for perinatal outcomes; **Summary of findings 2** Balanced protein and energy supplementation compared with control or no intervention in pregnancy for perinatal and maternal outcomes; **Summary of findings 3** High-protein supplementation in pregnancy and perinatal outcomes; **Summary of findings 4** Isocaloric balanced protein supplementation in pregnancy and outcomes

Nutritional education during pregnancy versus no nutritional education (or normal care)

Five trials of nutritional education, involving 1090 women, were included.

Primary outcomes

For the primary outcomes, there was no significant effect on stillbirth (risk ratio (RR) 0.37, 95% confidence interval (CI) 0.07 to 1.90; one trial, 431 women - Analysis 1.1) or neonatal death (RR 1.28, 95% CI 0.35 to 4.72; one trial, 448 women - Analysis 1.2). Perinatal mortality was not reported in any trials.

Secondary outcomes

There was a significant increase in birthweight among undernourished women (mean difference (MD) 489.76, 95% CI 427.93 to 551.59; two trials, 320 women; I^2 = 0%), although there was no significant increase among adequately nourished women (MD 15.00, 95% CI -76.30 to 106.30; one trial, 406 women) in the subgroup analysis (subgroup differences P < 0.0001) (Analysis 1.3). There was no significant difference in birth length (Analysis 1.4), and small-for-gestational age (Analysis 1.6). The results of total gestational weight gain (Briley 2002; Kafatos 1989) were inconsistent and showed higher heterogeneity (I^2 = 63%) (Analysis 1.12). In Jahan 2013, total body weight gain from seven to nine months was significantly increased in the intervention group compared to control group (8.6 ± 2.3 kg versus 5.4 ± 2.3 kg) among poor urban women in Bangladesh (data not shown in the forest plot). Birth head circumference (cm) was significantly increased in the intervention group (MD 0.99 cm, 95% CI 0.43 to 1.55; one trial, 389 women - Analysis 1.5). The 'significant' reduction in preterm birth associated with education (RR 0.46, 95% CI 0.21 to 0.98, P < 0.05; two trials, 449 women - Analysis 1.7) was not consistent with the total absence of effect on mean gestational age (MD -0.10 weeks, 95% CI -0.48 to 0.28; one trial, 399 women - Analysis 1.8).

Sensitivity analyses (Figure 1) was conducted to explore different values of the ICC used for adjustments of data from the cluster trial, Kafatos 1989. Using different values for the ICC, the risk became non-significant when the ICC was more than 0.01; however, overall results did not qualitatively change the relative risks for preterm in Kafatos 1989.

Antenatal nutritional education was associated with a significant reduction in low birthweight (RR 0.04, 95% CI 0.01 to 0.14; one trial, 300 women; Analysis 1.9). Within the methodological limitations discussed above, education to increase protein intake seems to be successful in achieving its goal (protein intake: MD +6.99 g/day, 95% CI 3.02 to 10.97, $P < 0.05$; three trials, 632 women - Analysis 1.10), but there was no significant increase in energy intake (energy intake: MD +105.61 kcal/day, 95% CI -18.94 to 230.15, P = 0.10; three trials, 342 women - Analysis 1.11).

Balanced protein/energy supplementation versus control or no intervention in pregnancy

Twelve trials, involving 6705 women, were included.

Primary outcomes

Providing balanced energy and protein supplementation significantly reduced the risk of stillbirth (RR 0.60, 95% CI 0.39 to 0.94; five trials, 3408 women - Analysis 2.1). Neonatal death was unaffected (RR 0.68, 95% CI 0.43 to 1.07; five trials, 3381 women - Analysis 2.2).

Sensitivity analysis was conducted to explore different values of ICC used for adjustments of data from the cluster trial, Ceesay 1997. Sensitivity analyses (Figure 2) for ICCs of 0.02 to 0 made little difference; using values of 0.01 for the ICC did not qualitatively change the relative risks for stillbirth in Ceesay 1997. We also conducted the analysis using ICC = 0.02 for risk of stillbirth (RR 0.62, 95% CI 0.39 to 0.99), but this did not change the overall risk.

Secondary outcomes

Supplementation was also associated with significant increases in mean birthweight (random-effects MD +40.96 g, 95% CI 4.66 to 77.26, $Tau^2 = 1744$, $I^2 = 44\%$, P = 0.03; 11 trials, 5385 infants - Analysis 2.3 , funnel plot Figure 5). Although clinically small, no statistically significant difference (random-effects MD 0.18, 95% CI -0.04 to 0.40; five trials, 3370 women; $I^2 = 44\%$ - Analysis 2.4) was observed in birth length (cm), and also no significant difference was found for birth head circumference (Analysis 2.5). The incidence of small-for-gestational age birth was significantly reduced (RR 0.79, 95% CI 0.69 to 0.90, $I^2 = 16\%$; seven trials, 4408 women - Analysis 2.6). There were no significant effects observed on preterm birth (Analysis 2.7), gestational age (week) (Analysis 2.8), or weekly gestational weight gain (g/week) ((MD 18.63, 95% CI -1.81 to 39.07, $I^2 = 57\%$; Nine trials, 2391 women, Analysis 2.9, funnel plot Figure 6). The rather meagre data on pre-eclampsia did not suggest a reduction in risk with supplementation (RR 1.48, 95% CI 0.82 to 2.66; two trials, 463 women - Analysis 2.10). The funnel plots (Figure 5; Figure 6) did not show any publication bias.

Although postnatal follow-up was limited to a small number of trials, the enhancement of fetal growth observed in those trials was not reflected in larger size or improved neurocognitive development at one year. The Bayley mental score at one year had no significant effect in one trial (Rush 1980; Analysis 2.11). The Taiwan trial (Blackwell 1973) detected no effect on the Stanford-Binet IQ score at five years (Analysis 2.12), and weight at one year (Analysis 2.13). As the data of the standard deviation of length at one year for Blackwell 1973 were not credible compared with the Rush 1980 study, we omitted the former from the analysis and only showed the data from Rush 1980 (Analysis 2.14). There was no significant effect on head circumference at one year from either the Taiwan (Blackwell 1973) or Harlem trials (Rush 1980) (Analysis 2.15). Mortality from birth to age 12 months follow-up showed no significant difference between prenatal lipid-based nutrient supplements versus prenatal multiple micronutrients (Huybregts 2009) (RR 1.10, 95% CI 0.58 to 2.10; one study, 1023 women; Analysis 2.17). A follow-up study at age 12 months of Huybregts 2009 showed no significant difference for infant growth (length for age growth, weight per month, length per month, head circumference per month, chest circumference per month), mortality, or morbidity between groups (Lanou 2014).

Maternal outcomes other than weight gain were reported infrequently. Only two trials reported results on other outcomes. The Bogota trial (Mora 1978) detected no significant reduction in duration of labour with supplementation (Analysis 2.16). The East Java trial (Kardjati 1988) found no increase in maternal weight at four weeks postpartum (Analysis 2.18).

In this update, we found one trial of 1320 pregnant women for lipid-based nutrient supplementation (only the conference abstract was available). However, we could not incorporate this trial in the meta-analysis as the only outcome was maternal salivary cortisol at 36 gestational weeks (Oaks 2014).

Follow-up at 6.5 to 9.5 years of age for approximately 25% of the children randomised in Ceesay 1997 found no difference in immune function (delayed-hypersensitivity skin tests, antibody responses to pneumococcal and rabies vaccines, and salivary IgA concentration) between the intervention and control groups (data not shown in data and analysis table). Follow-up at 11 to 17 years of age for approximately two-thirds of the children who were still alive found no significant differences in height (Analysis 2.19), weight (Analysis 2.20), or systolic or diastolic blood pressure (data not shown), but did find a small increase in the mean BMI z-score (MD +0.16, 95% CI +0.01 to +0.31; one trial, 855 children - Analysis 2.21) in the control group. However, the difference in BMI was in contrast with the absence of the effect on per cent body fat (Analysis 2.22). Follow-up at 16 to 22 years of age of Ceesay 1997 showed no evidence (data not shown) that maternal protein-energy supplementation during pregnancy compared with supplementation during lactation (controlled group were supplemented protein-energy during lactation) affected the cognitive ability or school performance of offspring in rural Gambia (Alderman 2014).

In a follow-up study of offspring at the mean age of 22 to 23 years (Viegas 1982a), 236 (83%) offspring were traced and 118 (50%) were assessed as being at risk of cardiovascular and metabolic disease; however, nutritional supplementation (protein/energy/vitamins; energy/vitamins or vitamins only) showed no strong association (data not shown) with any markers of adult disease risk in either unselected or undernourished mothers (Macleod 2013).

High-protein supplementation versus low or no protein supplements in pregnancy

Only one trial (Rush 1980), involving 1051 women, was included.

Primary outcomes

For primary outcomes, the Harlem trial (Rush 1980) reported non-significant effects in stillbirth (RR 0.81, 95% CI 0.31 to 2.15; one trial, 529 women - Analysis 3.1) and neonatal death (RR 2.78, 95% CI

0.75 to 10.36; one trial, 529 women - Analysis 3.2) with high-protein supplementation.

Secondary outcomes

The only available trial (Rush 1980) provided evidence of significant increases in infants born small-for-gestational age (RR 1.58, 95% CI 1.03 to 2.41, P = 0.04; one trial, 505 women - Analysis 3.3), although there was no significant effect for birthweight ((MD -73.00, 95% CI -171.26 to 25.26, I^2 = 0%, one study, 504 women, Analysis 3.4) or preterm birth (RR 1.14, 95% CI 0.83 to 1.56, I^2 = 0%, one study, 505 women, Analysis 3.5).

High-protein supplementation had no effect on weekly gestational weight gain (MD +4.50 g/week, 95% CI -33.55 to +42.55; one trial, 486 women - Analysis 3.6). At one-year follow-up in the Harlem trial (Rush 1980), high-protein supplementation was not associated with detectable differences in weight (Analysis 3.7), length (Analysis 3.8), head circumference (Analysis 3.9) or Bayley mental score (Analysis 3.10).

Isocaloric balanced protein supplementation versus protein replaced an equal quantity of non-protein energy in pregnancy

Two trials, involving 184 women, were included.

Primary outcomes

Primary outcomes were not reported.

Secondary outcomes

Owing to the significant heterogeneity in the results for birthweight and gestational weight gain, the data were pooled using a random-effects model. There was no significant effect on birthweight or gestational weight gain of isocaloric protein supplementation. For mean birthweight the MD was +108.25 g (95% CI -220.89 to 437.40, Tau^2 = 47211, I^2 = 84%; two trials, 184 infants - Analysis 4.1), while for gestational weight gain, the MD was +110.45 g/week (95% CI -82.87 to 303.76, Tau^2 = 16542, I^2 = 85%; two trials, 184 women - Analysis 4.2).

Subgroup analysis in balanced energy/protein supplementation

Since observational studies (IOM 1990; Kramer 1987) suggested a stronger association between gestational weight gain and fetal growth in women who were under-nourished before pregnancy, we stratified the analysis of the effects on mean birthweight into those trials in which the majority of women had low pre-pregnancy (or early pregnancy) weight (Ceesay 1997; Girija 1984; Kardjati 1988; Mora 1978; Rush 1980) and those in which the participants appeared adequately nourished (Elwood 1981; Ross 1985; Viegas 1982a). For the Taiwan trial (Blackwell 1973), and two others (Huybregts 2009, Viegas 1982b), within-trial stratification was possible, based on the data contained in the published reports. Only the mean birthweight in balanced energy/protein supplementation was analysed for the subgroups of undernourished and nourished women. However, there was no clear evidence of a subgroup difference between the malnourished and adequately nourished groups (test for subgroup differences: Chi^2 = 2.35. df = 1(P = 0.12), I^2 = 57.5%), Analysis 2.3.

DISCUSSION

Summary of main results

Nutritional education was successful in reducing the risk of preterm birth, low birthweight, increasing head circumference at birth, increasing birthweight among undernourished women and increasing protein intake; however, there was no evidence of benefit or adverse effect for any other outcome reported.

Balanced energy/protein supplementation was associated with a significantly reduced risk of stillbirth, increased mean birthweight, and a significant reduction in the risk of small-for-gestational-age birth. No significant effect was detected for preterm birth, or neonatal death.

High-protein supplementation was associated with a significantly increased risk of infants born small-for-gestational age, but this is based on only one trial including 1051 women. Based on two trials including only 184 women, isocaloric protein supplementation had no significant effect on birthweight or weekly gestational weight gain.

Overall completeness and applicability of evidence

Nutritional education appears effective in increasing pregnant women's protein intake, as well as significantly increasing birth head circumference and birthweight among undernourished women, and reducing preterm birth and low birthweight. No data have been reported on other important maternal pregnancy outcomes, such as duration of labour, caesarean section, or postpartum weight retention.

The modest increase in birthweight associated with balanced energy/protein supplementation may well be explained by the rather small net increases in energy intake achieved in most of the trials. Non-compliance and dietary substitution are likely explanations for these small net increases, and the much higher energy supplement provided in the Gambia trial (Ceesay 1997) appeared to have a much larger effect on mean birthweight. Of the seven sizeable trials with the highest methodological quality (Blackwell 1973; Ceesay 1997; Elwood 1981; Huybregts 2009; Kardjati 1988; Mora 1978; Rush 1980), only the East Java trial (Kardjati 1988) failed to show any benefit for mean birthweight (Analysis 2.3), despite convincing evidence that the trial participants were undernourished prior to the intervention. Owing to the large sample size, chance is an unlikely explanation for the absence of benefit in the East Java trial (Kardjati 1988), and an undetected substitution of the normal home diet by the supplement seems more likely. Due to the significant effect on mean birthweight (Analysis 2.3), the reduction in the risk of infants born small-for-gestational age (Analysis 2.6) was substantial. Nonetheless, that reduction did not appear to be associated with long-term benefits for child growth or development, and long-term follow-up was only reported in two trials (Ceesay 1997; Rush 1980). Of greatest importance is the evidence indicating reduced risk of stillbirth (Analysis 2.1). However, this evidence is based on five trials and is classified as low quality, and the biological mechanism for such risk reduction remains unclear, given the modest effects observed on the indices of fetal growth.

Most of the supplements/dietary manipulations also involved changes to the micronutrient (vitamins and minerals) content of the diet in both the intervention and control. As micronutrient supplementation may also alter some pregnancy outcomes independent of protein and energy, it is difficult to separate the contribution to the effects, particularly in the "balanced protein and energy" studies.

The available evidence from one trial provides no justification for prescribing high-protein nutritional supplements to pregnant women. Not only do such supplements appear to lack beneficial effects, but the evidence suggests that they may even be harmful. Furthermore, the data derived from these trials suggest that isocaloric protein supplementation alone (i.e. without energy supplementation) is unlikely to be of benefit to pregnant women or their infants. The two included trials had high heterogeneity, probably because amounts of energy supplementation were different (273 kcal in Viegas 1982a; 425 kcal in Viegas 1982b). The finding of the excluded trial of Mardones-Santander 1988, which reported increases in the risk of small-for-gestational age infants, remains uncertain, given the methodological limitations of the trial. Moreover, the normal-protein "control" supplement in Mardones-Santander 1988 contained much higher quantities of iron and other micronutrients than the high-protein supplement.

The results of this review should be interpreted with caution considering that the majority of trials were published in the 1970s and 1980s. The incidence of inadequate nutrition and overweight and obesity is likely to be different today, and most trials included a mixed population of those considered to have poor nutritional status and potentially those with adequate nutrition or over-nutrition. Indeed, seven trials were from high-income countries where recent reports suggest that two-thirds of the general population and half of pregnant women are overweight or obese (Haslehurst 2006; Wang 2011).

Quality of the evidence

We included 17 trials involving 9030 women. The quality of the evidence in this review was assessed using the GRADE approach (Guyatt 2008) and the results are presented in Summary of findings for the main comparison; Summary of findings 2; Summary of findings 3; and Summary of findings 4. The GRADE uses four levels of quality (very low, low, moderate and high) over several domains covering limitations in the design and implementation of the studies, indirectness of evidence, unexplained heterogeneity or inconsistency in the results, imprecision of the results and high probability of publication bias. Weekly gestational weight gain was used when total gestational weight gain was not available. In studies on a nutritional education during pregnancy (Summary of findings for the main comparison), the evidence was judged to be of low quality (stillbirth, neonatal death, preterm birth, birthweight and infants born small-for-gestational age) and very low quality (total gestational weight gain) which includes two of the primary outcomes. The studies on balanced protein and energy supplementation in pregnancy (Summary of findings 2), including significant reductions in stillbirth and infants born small-for-gestational age, and significant increase in birthweight, were considered to be of moderate quality. Preterm birth was also of moderate quality. Neonatal death was low quality, and weekly gestational weight gain was very low quality. In studies on high-protein supplementation in pregnancy studies (Summary of findings 3), the significant increase in infants born small-for-gestational age was of moderate quality in only one study (Rush 1980) and weekly gestational weight gain was of low quality. In the isocaloric balanced protein supplementation in pregnancy studies (Summary of findings 4), the evidence was judged to be of very low quality (birthweight, weekly gestational weight gain) meaning that the estimates were very uncertain.

Potential biases in the review process

We made efforts to limit potential biases in the review process in several ways. Two review authors assessed the eligibility for inclusion and the risks of bias independently. Although the authors' views varied, we decided to accept the final conclusions after extensive discussion and reaching a consensus. Carrying out reviews, however, may require a number of subjective judgements, and it is possible that a different review team may have reached different decisions regarding the assessments of eligibility and risks of bias. Feedback from readers will serve to improve the next review update.

Agreements and disagreements with other studies or reviews

We have included only randomised controlled trials (RCTs) and excluded the quasi-RCTs previously included in the review (Kramer 2003). The new findings of this review are that balanced energy and protein supplementation was associated with significant increases in mean birthweight, while the other major findings are consistent with those of the previous Cochrane review (Kramer 2003). Prenatal supplementation with multi-micronutrients was associated with a significantly reduced risk of low-birthweight infants and with improved birthweight when compared with iron-folic acid supplementation, although there was no effect on the risk of preterm birth or small-for-gestational age infants (Shah 2009). Researchers should aim to include only those women in trials to increase energy and protein intake who have the potential to benefit. Observational data suggest women who are overweight or obese or who exceed their daily energy and protein requirements during pregnancy are at increased risk of adverse pregnancy outcomes including: stillbirth and large-for-gestational age and macrosomia (birthweight $\geq$ 4 kg) (Chen 2009; Heslehurst 2008; Thangaratinam 2012), therefore, the effect of increasing protein and energy intake could have opposite effects on different populations within the same trial if those included are not adequately defined and selected.

In this update, we found a follow-up study of Ceesay 1997 participants aged 16 to 22 years that assessed the cognitive ability or school performance of offspring (Alderman 2014). Although balanced protein-energy supplementation provided a benefit for short-term pregnancy outcomes, no long-term effects on cognitive ability were observed in the follow-up study. We could not conclude if the benefits of supplementation during pregnancy lasted for a long period, and we also need to consider the effect of the intervention given postpartum in the control group. Some studies showed that nutrition in the early postnatal period was important for brain development, prolonged and exclusive breastfeeding improved cognitive development at 6.5 years of age (Kramer 2008), and stunting in early childhood was related to poor cognitive development (Grantham-McGregor 1991).

AUTHORS' CONCLUSIONS

Implications for practice

This review provides encouraging evidence that nutritional education to increase protein and energy intake and balanced energy and protein supplementation may reduce some perinatal adverse outcomes. The long-term effects are unclear and it seems likely that targeting undernourished women rather than the whole obstetric population would convey the most benefit. For most of the included trials in this review, the risk of bias was either unclear or high for at least one category examined, and the results of this review should therefore be interpreted with caution.

Nutritional education appears to be effective in increasing pregnant women's protein intake, and increases fetal growth, such as birth head circumference and birthweight among undernourished women. The 54% relative reduction in preterm birth, and also the reduction in low birthweight for nutritional education in energy and protein compared with no nutritional counselling may be beneficial to pregnant women.

Balanced energy and protein supplementation appears to reduce the risks of stillbirth, although the biological mechanisms underlying these reductions remain unclear. Furthermore, balanced protein and energy interventions, as provided in most trials, result in significant increases in maternal weight gain and infant birthweight, and decrease the risk of infants born small-for-gestational age These effects do not seem to confer long-term benefits to the child in terms of growth, neurocognitive development, and diseases in adulthood, such as adiposity or blood pressure. The available evidence is inadequate to evaluate the potential effects on preterm birth, neonatal death or maternal health.

Based on the available evidence, there is no justification for prescribing high-protein and isocaloric nutritional supplements to pregnant women, although the number of trials and women included are few.

Implications for research

High-quality randomised trials that target those women who are nutritionally deprived or underweight with reduced energy intake are needed; and long-term follow-up is also required.

Given the modest benefits in birthweight among undernourished women, preterm delivery and low birthweight documented for balanced energy and protein education during pregnancy, future randomised trials need to assess the effects on perinatal outcomes such as stillbirth and neonatal death. Effective interventions, such as the content and frequency of nutritional education, need to be clarified.

Future energy and protein supplementation trials should focus on outcomes other than fetal growth, especially in undernourished women, and should give particular attention to confirming evidence on interventions for reducing the risks of stillbirth and small-for-gestational age. Such trials will require large sample sizes. Any future trials should also assess the effects on women, including duration of labour, caesarean section, macrosomia and postpartum weight retention. Increased protein intake during pregnancy seems to be effective for increasing birthweight; however, future interventions need to consider how women and families can learn to integrate more protein in daily meals.

The lack of evidence of benefit, coupled with the possibility of harm, suggests that future trials of high-protein supplementation and isocaloric protein supplementation should not be considered.

ACKNOWLEDGEMENTS

We are grateful to Michael S Kramer and Ritsuko Kakuma who developed the original review (Kramer 2003) and subsequent updates upon which this updated review is based.

The review authors would like to acknowledge the Pregnancy and Childbirth team for assistance with the preparation of the original review and its update, including the Trials Search Co-ordinator for assistance in developing the search strategy, the editors, co-editors and other staff within the team.

As part of the pre-publication editorial process, this review has been commented on by two peers (an editor and referee who is external to the editorial team), a member of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

Erika Ota's work was financially supported by the UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), Department of Reproductive Health and Research (RHR), World Health Organization. The named authors alone are responsible for the views expressed in this publication.

This project was supported by the National Institute for Health Research via Cochrane Infrastructure funding to Cochrane Pregnancy and Childbirth. The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIIHR, NHS or the Department of Health.

REFERENCES

References to studies included in this review

Blackwell 1973 *{published data only}*

Adair LS, Pollitt E. Outcome of maternal nutritional supplementation: a comprehensive review of the Bacon Chow Study. *American Journal of Clinical Nutrition* 1985;**41**:948-78.

Adair LS, Pollitt E, Mueller WH. The Bacon Chow Study: effect of nutritional supplementation on maternal weight and skinfold thickness during pregnancy and lactation. *British Journal of Nutrition* 1984;**51**:357-69.

* Blackwell RQ, Chow BF, Chinn KSK, Blackwell BN, Hsu SC. Prospective maternal nutrition study in Taiwan: rationale, study design, feasibility and preliminary findings. *Nutrition Reports International* 1973;**7**:517-32.

Joos SK, Pollitt E, Mueller WH, Albright DL. The Bacon Chow Study: maternal nutritional supplementation and infant behavioral development. *Child Development* 1983;**54**:669-76.

McDonald EC, Pollitt E, Mueller W, Hsueh AM, Sherwin R. The Bacon Chow study: maternal nutritional supplementation and birth weight of offspring. *American Journal of Clinical Nutrition* 1981;**34**:2133-44.

Mueller WH, Pollitt E. The Bacon Chow Study: effects of nutrition supplementation on sibling-sibling anthropometric correlations. *Human Biology* 1982;**54**:455-68.

Mueller WH, Pollitt E. The Bacon Chow study: effects of maternal nutritional supplementation on birth measurements of children, accounting for the size of a previous (unsupplemented) child. *Early Human Development* 1984;**10**:127-36.

Pollitt E, Mueller W. Maternal nutrition supplementation during pregnancy interferes with physical resemblance of siblings at birth according to infant sex. *Early Human Development* 1982;**7**:251-6.

Wohlleb JC, Pollitt E, Mueller WH, Bigelow R. The Bacon Chow Study: maternal supplementation and infant growth. *Early Human Development* 1983;**9**:79-91.

Briley 2002 *{published data only}*

Briley C, Flanagan NL, Lewis NM. In-home prenatal nutrition intervention increased dietary iron intakes and reduced low birthweight in low-income African-American women. *Journal of the American Dietetic Association* 2002;**102**(7):984-7.

Ceesay 1997 *{published data only}*

Alderman H, Hawkesworth S, Lundberg M, Tasneem A, Mark H, Moore SE. Supplemental feeding during pregnancy compared with maternal supplementation during lactation does not affect schooling and cognitive development through late adolescence. *American Journal of Clinical Nutrition* 2014;**99**(1):122-9.

Ceesay SM, Saidykhan S, Prentice AM, Cole TJ, Day KC, Rowland MGM, et al. Effect on birth weight of a community-based supplementation programme for pregnant Gambian women: first year results. *Proceedings of the Nutrition Society* 1992;**51**:77A.

* Ceesay SN, Prentice AM, Cole TJ, Foord F, Weaver LT, Poskitt EME, et al. Effects on birth weight and perinatal mortality of maternal dietary supplements in rural Gambia: 5 year randomised controlled trial. *BMJ* 1997;**315**:786-90.

Hawkesworth S, Prentice AM, Fulford AJ, Moore SE. Dietary supplementation of rural Gambian women during pregnancy does not affect body composition in offspring at 11-17 years of age. *Journal of Nutrition* 2008;**138**(12):2468-73.

Hawkesworth S, Prentice AM, Fulford AJ, Moore SE. Maternal protein-energy supplementation does not affect adolescent blood pressure in The Gambia. *International Journal of Epidemiology* 2009;**38**(1):119-27.

Hawkesworth S, Walker CG, Sawo Y, Fulford AJ, Jarjou LM, Goldberg GR, et al. Nutritional supplementation during pregnancy and offspring cardiovascular disease risk in The Gambia. *American Journal of Clinical Nutrition* 2011;**94**(6 Suppl):1853S-1860S.

Moore SE, Collinson AC, Prentice AM. Immune function in rural Gambian children is not related to season of birth, birth size, or maternal supplementation status. *American Journal of Clinical Nutrition* 2001;**74**:840-7.

Elwood 1981 *{published and unpublished data}*

Ben-Shlomo Y, Holly J, McCarthy A, Savage P, Davies D, Davey Smith G. Prenatal and postnatal milk supplementation and adult insulin-like growth factor I: long-term follow-up of a randomized controlled trial. *Cancer Epidemiology, Biomarkers & Prevention* 2005;**14**(5):1336-9.

Ben-Shlomo Y, McCarthy A, Hughes R, Tilling K, Davies D, Smith GD. Immediate postnatal growth is associated with blood pressure in young adulthood: the Barry Caerphilly growth study. *Hypertension* 2008;**52**:638-44.

Elwood PC, Haley TJL, Hughes SJ, Sweetnam PM, Gray OP, Davies DP. Child growth (0-5 years), and the effect of entitlement to a milk supplement. *Archives of Disease in Childhood* 1981;**56**:831-5.

Williams DM, Martin RM, Davey Smith G, Alberti KG, Ben-Shlomo Y, McCarthy A. Associations of infant nutrition with insulin resistance measures in early adulthood: evidence from the Barry-Caerphilly Growth (BCG) study. *PLoS ONE* 2012;**7**(3):e34161.

Girija 1984 *{published and unpublished data}*

Girija A, Geervani P, Rao GN. Influence of dietary supplementation during pregnancy on lactation performance. *Journal of Tropical Pediatrics* 1984;**30**:79-83.

Hunt 1976 *{published data only}*

Hunt IF, Jacob M, Ostergard NJ, Masri G, Clark VA, Coulson AH. Effect of nutrition education on the nutritional status of low-income pregnant women of Mexican descent. *American Journal of Clinical Nutrition* 1976;**29**:675-84.

Huybregts 2009 *{published data only}*

Huybregts L, Roberfroid D, Lanou H, Kolsteren P, Camp J. Prenatal lipid-based nutrient supplements increase cord leptin concentration in pregnant women from rural Burkina Faso. *Annals of Nutrition & Metabolism* 2013;**63**(Suppl 1):799, Abstract no: PO1134.

Huybregts L, Roberfroid D, Lanou H, Meda N, Taes Y, Valea I, et al. Prenatal lipid-based nutrient supplements increase cord leptin concentration in pregnant women from rural Burkina Faso. *Journal of Nutrition* 2013;**143**(5):576-83.

* Huybregts L, Roberfroid D, Lanou H, Menten J, Meda N, Van Camp J, et al. Prenatal food supplementation fortified with multiple micronutrients increases birth length: a randomized controlled trial in rural Burkina Faso. *American Journal of Clinical Nutrition* 2009;**90**(6):1593-600.

Lanou H, Huybregts L, Roberfroid D, Kolsteren P. Effect of prenatal lipid-based nutrient supplementation on gestational weight gain. *Annals of Nutrition & Metabolism* 2013;**63**(Suppl 1):783, Abstract no: PO1099.

Lanou H, Huybregts L, Roberfroid D, Nikiema L, Kouanda S, Van Camp J, et al. Prenatal nutrient supplementation and postnatal growth in a developing nation: an RCT. *Pediatrics* 2014;**133**(4):e1001-8.

Jahan 2013 *{published data only}*

Jahan K, Roy SK, Israt S, Ferdouse K, Salam SB. Impact of nutrition education on pregnancy weight gain and birth outcome. *Annals of Nutrition & Metabolism* 2013;**63**(Suppl 1):756, Abstract no: PO1043.

* Jahan K, Roy SK, Mihrshahi S, Sultana N, Khatoon S, Roy H, et al. Short-term nutrition education reduces low birthweight and improves pregnancy outcomes among urban poor women in Bangladesh. *Food and Nutrition Bulletin* 2014;**35**(4):414-21. [PUBMED: 25639126]

Kafatos 1989 *{published and unpublished data}*

Kafatos AG, Vlachonikolis IG, Codrington CA. Nutrition during pregnancy: the effects of an educational intervention program in Greece. *American Journal of Clinical Nutrition* 1989;**50**:970-9.

Kardjati 1988 *{published data only}*

* Kardjati S, Kusin JA, De With C. Energy supplementation in the last trimester of pregnancy in East Java: I. Effect on birthweight. *British Journal of Obstetrics and Gynaecology* 1988;**95**:783-94.

Kardjati S, Kusin JA, Schofield WM, De With C. Energy supplementation in the last trimester of pregnancy in East Java, Indonesia: effect on maternal anthropometry. *American Journal of Clinical Nutrition* 1990;**52**:987-94.

Kusin JA, Kardjati S, Houtkooper JM, Renqvist UH. Energy supplementation during pregnancy and postnatal growth. *Lancet* 1992;**340**:623-6.

Van Steenbergen WM, Kusin JA, Kardjati S, De With C. Energy supplementation in the last trimester of pregnancy in East Java, Indonesia: effect on breast-milk output. *American Journal of Clinical Nutrition* 1989;**50**:274-9.

Mora 1978 *{published data only}*

Christiansen N, Mora JO, Navarro L, Herrera MG. Effects of nutritional supplementation during pregnancy upon birth weight: the influence of pre-supplementation on diet. *Nutrition Reports International* 1980;**21**:615-24.

Herrera MG, Mora JO, De Paredes B, Wagner M. Maternal weight/height and the effect of food supplementation during pregnancy and lactation. Maternal nutrition during pregnancy and lactation. A Nestlé Foundation workshop; 1979 April 26-27; Lausanne, Switzerland. Bern: Hans Huber, 1980:252-63.

Mora JO, Clement J, Christiansen N, Suescun J, Wagner M, Herrera MG. Nutritional supplementation and the outcome of pregnancy. III. Perinatal and neonatal mortality. *Nutrition Reports International* 1978;**18**:167-75.

* Mora JO, De Navarro L, Clement J, Wagner M, De Paredes B, Herrera MG. The effect of nutritional supplementation on calorie and protein intake of pregnant women. *Nutrition Reports International* 1978;**17**:217-28.

Mora JO, De Paredes B, Wagner M, De Navarro L, Suescun J, Christiansen N, et al. Nutritional supplementation and the outcome of pregnancy. I. Birth weight. *American Journal of Clinical Nutrition* 1979;**32**:455-62.

Mora JO, Herrera MG, Suescun J, De Navarro L, Wagner M. The effects of nutritional supplementation on physical growth of children at risk of malnutrition. *American Journal of Clinical Nutrition* 1981;**34**:1885-92.

Mora JO, Sanchez R, De Paredes B, Herrera MG. Sex related effects of nutritional supplementation during pregnancy on fetal growth. *Early Human Development* 1981;**5**:243-51.

Overholt C, Sellers SG, Mora JO, de Paredes B, Herrera MG. The effects of nutritional supplementation on the diets of low-income families at risk of malnutrition. *American Journal of Clinical Nutrition* 1982;**36**:1153-61.

Vuori L, Christiansen N, Clement J, Mora JO, Wagner M, Herrera MG. Nutritional supplementation and the outcome of pregnancy. II. Visual habituation at 15 days. *American Journal of Clinical Nutrition* 1979;**32**:463-9.

Vuori L, De Navarro L, Christiansen N, Mora JO, Herrera MG. Food supplementation of pregnant women at risk of malnutrition and their newborns' responsiveness to stimulation. *Developmental Medicine and Child Neurology* 1980;**22**:61-71.

Waber DP, Vuori-Christiansen L, Ortiz N, Clement JR, Christiansen NE, Mora JO, et al. Nutritional supplementation, maternal education, and cognitive development of infants at risk of malnutrition. *American Journal of Clinical Nutrition* 1981;**34**:807-13.

Oaks 2014 *{published data only}*

Oaks B, Adu-Afarwuah S, Lartey A, Stewart C, Ashorn P, Vosti S, et al. Lipid-based nutrient supplementation during pregnancy decreases maternal cortisol in younger women. *FASEB Journal* 2014;**28**(1 Suppl 1):[Abstract no. 389.6].

Ross 1985 *{published data only}*

Ross SM, Nel E, Naeye RL. Differing effects of low and high bulk maternal dietary supplements during pregnancy. *Early Human Development* 1985;**10**:295-302.

Rush 1980 *{published and unpublished data}*

Jacobson HN. A randomized controlled trial of prenatal nutritional supplementation. *Pediatrics* 1980;**65**:835-6.

Pereira M, Rush D, Campbell-Brown M, Rosso P, Winick M, Brasel JA, et al. Effects of prenatal nutritional supplementation on the placenta: report of a randomized controlled trial. *American Journal of Clinical Nutrition* 1982;**36**:229-34.

Rush D, Kristal A, Blanc W, Navarro C, Chauham P, Campbell-Brown M, et al. The effects of maternal cigarette smoking on placental morphology, histomorphometry, and biochemistry. *American Journal of Perinatology* 1986;**3**:263-72.

Rush D, Kristal A, Navarro C, Chauhan P, Blanc W, Naeye R, et al. The effects of dietary supplementation during pregnancy on placental morphology, pathology, and histomorphometry. *American Journal of Clinical Nutrition* 1984;**39**:863-71.

* Rush D, Stein Z, Susser M. A randomized controlled trial of prenatal nutritional supplementation in New York City. *Pediatrics* 1980;**65**:683-97.

Rush D, Stein Z, Susser M. Controlled trial of prenatal nutrition supplementation defended. *Pediatrics* 1980;**66**:656-8.

Rush D, Stein Z, Susser M. Diet in pregnancy: a randomized controlled trial of nutritional supplements. *Birth Defects* 1980;**16**:1-187.

Rush D, Stein Z, Susser, M. The rationale for, and design of, a randomized controlled trial of nutritional supplementation in pregnancy. *Nutrition Reports International* 1973;**7**:547-53.

Stein Z, Susser M, Rush D. Prenatal nutrition and birth weight: experiments and quasi-experiments in the past decade. *Journal of Reproductive Medicine* 1978;**21**:287-97.

Sweeney 1985 *{published data only}*

Sweeney C, Smith H, Foster JC, Specht J, Kochenour NK, Prater BM. Effects of a nutrition intervention program during pregnancy: maternal data phases 1 and 2. *Journal of Nurse Midwifery* 1985;**30**:149-58.

Viegas 1982a *{published data only}*

Macleod J, Tang L, Hobbs FD, Wharton B, Holder R, Hussain S, et al. Effects of nutritional supplementation during pregnancy on early adult disease risk: follow up of offspring of participants in a randomised controlled trial investigating effects of supplementation on infant birth weight. *PLoS ONE [Electronic Resource]* 2013;**8**(12):e83371.

Viegas OAC, Scott PH, Cole TJ, Mansfield HN, Wharton P, Wharton BA. Dietary protein energy supplementation of pregnant Asian mothers at Sorrento, Birmingham. I. Unselective during second and third trimesters. *British Medical Journal* 1982;**285**:589-92.

Viegas 1982b *{published data only}*

Viegas OAC, Scott PH, Cole TJ, Eaton P, Needham PG, Wharton BA. Dietary protein energy supplementation of pregnant Asian mothers at Sorrento, Birmingham. II. Selective during third trimester only. *British Medical Journal* 1982;**285**:592-5.

References to studies excluded from this review

Aaltonen 2005 *{published data only}*

* Aaltonen J, Ojala T, Laitinen K, Isolauri E. Programming of infants systolic blood pressure by accelerated foetal growth during early pregnancy. *Journal of Pediatric Gastroenterology and Nutrition* 2005;**40**(5):624.

Aaltonen J, Ojala T, Laitinen K, Pirainen TJ, Poussa TA, Isolauri E. Evidence of infant blood pressure programming by maternal nutrition during pregnancy: a prospective randomized controlled intervention study. *Journal of Pediatrics* 2008;**152**:79-84.

Aaltonen J, Ojala T, Laitinen K, Poussa T, Ozanne S, Isolauri E. Impact of maternal diet during pregnancy and breastfeeding on infant metabolic programming: a prospective randomized controlled study. *European Journal of Clinical Nutrition* 2011;**65**(1):10-9.

Huurre A, Laitinen K, Rautava S, Korkeamaki M, Isolauri E. Impact of maternal atopy and probiotic supplementation during pregnancy on infant sensitization: a double-blind placebo-controlled study. *Clinical and Experimental Allergy* 2008;**38**(8):1342-8.

Isolauri E. The effects of maternal nutrition during pregnancy and breast feeding on the risk of allergic disease in child (NAMI). ClinicalTrials.gov (http://clinicaltrials.gov/) (accessed 6 Nov 2007).

Laitinen K, Poussa T, Isolauri E, Nutrition, Allergy, Mucosal Immunology and Intestinal Microbiota Group. Probiotics and dietary counselling contribute to glucose regulation during and after pregnancy: a randomised controlled trial. *British Journal of Nutrition* 2009;**101**:1679–87.

Luoto R, Laitinen K, Nermes M, Isolauri E. Impact of maternal probiotic-supplemented dietary counselling on pregnancy outcome and prenatal and postnatal growth: a double-blind, placebo-controlled study. *British Journal of Nutrition* 2010;**103**(12):1792-9.

Luoto R, Nermes M, Laitinen K, Isolauri E. Impact of maternal probiotic-supplemented dietary counselling on pregnancy outcome and prenatal and postnatal growth: a double-blind, placebo-controlled study. Pediatric Academic Societies Annual Meeting; 2009 May 2-5; Baltimore, USA. 2009.

Piirainen T, Isolauri E, Lagstrom H, Laitinen K. Impact of dietary counselling on nutrient intake during pregnancy: a prospective cohort study. *British Journal of Nutrition* 2006;**96**:1095-104.

Vahamiko S, Isolauri E, Laitinen K. Weight status and dietary intake determine serum leptin concentrations in pregnant and lactating women and their infants. *British Journal of Nutrition* 2013;**110**(6):1098-106.

Adams 1978 *{published data only}*

Adams SO, Barr GD, Huenemann RL. Effect of nutritional supplementation in pregnancy. *Journal of the American Dietetic Association* 1978;**72**:144-7.

Anderson 1995 *{published data only}*

Anderson AS, Campbell DM, Shepherd R. The influence of dietary advice on nutrient intake during pregnancy. *British Journal of Nutrition* 1995;**73**:163-77.

Astrup 2013 *{published data only}*

Astrup AV. An optimized programming of healthy children (APPROACH). ClinicalTrials.gov (http://clinicaltrials.gov/) [accessed 5 February 2014] 2013.

Atkinson 2013 *{published data only}*

Atkinson SA. Be healthy in pregnancy (B-HIP): a trial to study nutrition and exercise approaches for healthy (B-HIP). ClinicalTrials.gov (accessed 21 May 2013) 2013.

Atton 1990 *{published data only}*

* Atton C, Watney PJM. Selective supplementation in pregnancy: effect on birth weight. *Journal of Human Nutrition and Dietetics* 1990;**3**:381-92.

Watney PJM, Atton C. Dietary supplementation in pregnancy. *British Medical Journal* 1986;**293**:1102.

Badrawi 1993 *{published data only}*

Badrawi H, Hassanein MK, Badraoui MHH, Wafa YA, Shawky HA, Badrawi N. Pregnancy outcome in obese pregnant mothers. *Journal of Perinatal Medicine* 1992;**20**(Suppl 1):203.

* Badrawi H, Hassanein MK, Badrroui MHH, Wafa YA, Shawky HA, Badrawi N. Pregnancy outcome in obese pregnant mothers. *New Egypt Journal of Medicine* 1993;**8**(6):1717-26.

Bosaeus 2015 *{published data only}*

Bosaeus M, Hussain A, Karlsson T, Andersson L, Hulthen L, Svelander C, et al. A randomized longitudinal dietary intervention study during pregnancy: effects on fish intake, phospholipids, and body composition. *Nutrition Journal* 2015;**14**(1):1.

Campbell 1975 *{published data only}*

Blumenthal I. Diet and diuretics in pregnancy and subsequent growth of offspring. *British Medical Journal* 1976;**2**:733.

* Campbell DM, MacGillivray I. The effect of a low calorie diet or a thiazide diuretic on the incidence of pre-eclampsia and on birthweight. *British Journal of Obstetrics and Gynaecology* 1975;**82**:572-7.

Campbell 1983 *{published data only}*

Campbell DM. Dietary restriction in obesity and its effect on neonatal outcome. Nutrition in pregnancy. Proceedings of 10th Study Group of the RCOG; 1983; London, UK. London: RCOG, 1983:243-50.

Campbell Brown 1983 *{published data only}*

Campbell Brown M. Protein energy supplements in primigravid women at risk of low birthweight. In: Campbell DM, Gillmer MDG editor(s). Nutrition in pregnancy. Proceedings of the 10th Study Group of the RCOG. London: RCOG, 1983:85-98.

Clapp 1997 *{published data only}*

* Clapp JF. Diet, exercise, and feto-placental growth. *Archives of Gynecology and Obstetrics* 1997;**260**:101-8.

Clapp JF. Effects of dietary carbohydrate on the glucose and insulin response to mixed caloric intake and exercise in both nonpregnant and pregnant women. *Diabetes Care* 1998;**21**(Suppl 2):B107-B112.

Dirige 1987 *{published data only}*

Dirige OV, McNutt SW, Hamatake CK, McGee RI, Manayan CA. The effect of nutrition education on the nutritional status of pregnant Filipino women in Hawaii. *Nutrition Research* 1987;**7**:197-209.

Ebbs 1941 *{published data only}*

Ebbs JH, Scott WA, Tisdall FF, Moyle WJ, Bell M. Nutrition in pregnancy. *Canadian Medical Association Journal* 1942;**46**:1-6.

* Ebbs JH, Tisdall FF, Scott WA. The influence of prenatal diet on the mother and child. *Journal of Nutrition* 1941;**22**:515-6.

Eneroth 2010 *{published data only}*

Eneroth H, El Arifeen S, Persson LA, Lonnerdal B, Hossain MB, Stephensen CB, et al. Maternal multiple micronutrient supplementation has limited impact on micronutrient status of Bangladeshi infants compared with standard iron and folic acid supplementation. *Journal of Nutrition* 2010;**140**(3):618-24.

Fard 2004 *{published data only}*

Fard NM, Mehrabian F, Sarraf-zadegan N, Sajadi F. Fat-modified diets during pregnancy and lactation and serum lipids after birth. *Indian Journal of Pediatrics* 2004;**71**:683-7.

Fung 2010 *{published data only}*

Fung EB, Ritchie LD, Walker BH, Gildengorin G, Crawford PB. Randomized, controlled trial to examine the impact of providing yogurt to women enrolled in WIC. *Journal of Nutrition Education and Behavior* 2010;**42**(3 Suppl):S22-29.

Guelinckx 2010 *{published data only}*

Guelinckx I, Devlieger R, Mullie P, Vansant G. Effect of lifestyle intervention on dietary habits, physical activity, and gestational weight gain in obese pregnant women: a randomized controlled trial. *American Journal of Clinical Nutrition* 2010;**91**(2):373-80.

Hankin 1962 *{published data only}*

Hankin ME, Symonds EM. Body weight, diet and pre-eclamptic toxaemia of pregnancy. *Australian and New Zealand Journal of Obstetrics and Gynaecology* 1962;**4**:156-60.

Hautero 2013 *{published data only}*

Hautero U, Laakso P, Linderborg K, Niinivirta K, Poussa T, Isolauri E, et al. Proportions and concentrations of serum n-3 fatty acids can be increased by dietary counseling during pregnancy. *European Journal of Clinical Nutrition* 2013;**67**(11):1163-8.

Iyengar 1967 *{published data only}*

Iyengar L. Effects of dietary supplements late in pregnancy on the expectant mother and her newborn. *Indian Journal of Medical Research* 1967;**55**:85-9.

Kaseb 2002 *{published data only}*

Kaseb F, Kimiagar M, Ghafarpoor M, Valaii N. Effect of traditional food supplementation during pregnancy on maternal weight gain and birthweight. *International Journal for Vitamin & Nutrition Research* 2002;**72**(6):389-93.

Kinra 2008 *{published data only}*

Kinra S, Rameshwar Sarma KV, Ghafoorunissa, Mendu VV, Ravikumar R, Mohan V, et al. Effect of integration of supplemental nutrition with public health programmes in pregnancy and early childhood on cardiovascular risk in rural Indian adolescents: long term follow-up of hyderabad nutrition trial. *BMJ* 2008;**337**:a605.

Kinra S, Sarma KV, Hards M, Smith GD, Ben-Shlomo Y. Is relative leg length a biomarker of childhood nutrition? Long-term follow-up of the Hyderabad Nutrition Trial. *International Journal of Epidemiology* 2011;**40**(4):1022-9.

Lechtig 1975 *{published data only}*

Behrman JR, Calderon MC, Preston SH, Hoddinott J, Martorell R, Stein AD. Nutritional supplementation in girls influences the growth of their children: prospective study in Guatemala. *American Journal of Clinical Nutrition* 2009;**90**(5):1372-9.

Conlisk AJ, Barnhart HX, Martorell R, Grajeda R, Stein AD. Maternal and child nutritional supplementation are inversely associated with fasting plasma glucose concentration in young Guatemalan adults. *Journal of Nutrition* 2004;**134**(4):890-7.

Delgado H, Martorell R, Brineman E, Klein RE. Nutrition and length of gestation. *Nutrition Research* 1982;**2**:117-26.

Delgado HL, Martorell R, Klein RE. Nutrition, lactation, and birth interval components in rural Guatemala. *American Journal of Clinical Nutrition* 1982;**35**:1468-76.

Hoddinott J, Maluccio JA, Behrman JR, Flores R, Martorell R. Effect of a nutrition intervention during early childhood on economic productivity in Guatemalan adults. *Lancet* 2008;**371**(9610):411-6.

* Lechtig A, Habicht JP, Delgado H, Klein RE, Yarbrough C, Martorell R. Effect of food supplementation during pregnancy on birthweight. *Pediatrics* 1975;**56**:508-20.

Lechtig A, Klein RE, Daza CH, Read MS, Kahn SG. Effects of maternal nutrition on infant health: implications for action. *Archivos Latinoamericanos de Nutricion* 1979;**29**:1-26.

Lechtig A, Yarbrough C, Delgado H, Martorell R, Klein RE, Behar M. Effect of moderate maternal malnutrition on the placenta. *American Journal of Obstetrics and Gynecology* 1975;**123**:191-201.

Merchant K, Martorell R, Haas J. Maternal and fetal responses to the stresses of lactation concurrent with pregnancy and of short recuperative intervals. *American Journal of Clinical Nutrition* 1990;**52**:280-8.

Rasmussen KM, Habicht JP. Maternal supplementation differentially affects the mother and newborn. *Journal of Nutrition* 2010;**140**(2):402-6.

Stein AD, Barnhart HX, Hickey M, Ramakrishnan U, Schroeder DG, Martorell R. Prospective study of protein-energy supplementation early in life and of growth in the subsequent generation in Guatemala. *American Journal of Clinical Nutrition* 2003;**78**:162-7.

Stein AD, Wang M, Ramirez-Zea M, Flores R, Grajeda R, Melgar P, et al. Exposure to a nutrition supplementation intervention in early childhood and risk factors for cardiovascular disease in adulthood: evidence from Guatemala. *American Journal of Epidemiology* 2006;**164**(12):1160-70.

Webb AL, Conlisk AJ, Barnhart HX, Martorell R, Grajeda R, Stein AD. Maternal and childhood nutrition and later blood pressure levels in young Guatemalan adults. *International Journal of Epidemiology* 2005;**34**(4):898-904.

Li 2014 *{published data only}*

Li YF, Hu NS, Tian XB, Li L, Wang SM, Xu XB, et al. Effect of daily milk supplementation on serum and umbilical cord blood folic acid concentrations in pregnant Han and Mongolian women and birth characteristics in China. *Asia Pacific Journal of Clinical Nutrition* 2014;**23**(4):567-74.

Luke 2001 *{published data only}*

Luke B, Misiunas R, Anderson E, Hediger M, Burpee B, Gogliotti S, et al. Prenatal program to improve neonatal and early childhood outcomes in twins [abstract]. American Journal of Obstetrics and Gynecology 2001; Vol. 185, issue 6 Suppl:S105.

Magon 2014 *{published data only}*

Magon A, Collin SM, Joshi P, Davys Late G, Attlee A, Mathur B. Leaf concentrate fortification of antenatal protein-calorie snacks improves pregnancy outcomes. *Journal of Health, Population and Nutrition* 2014;**32**(3):430-40.

Maleta 2014 *{published data only}*

Maleta K. Randomized controlled trial of the impact of treating moderately malnourished women in pregnancy. ClinicalTrials.gov (http://clinicaltrials.gov/) [accessed 27 August 2014] 2014.

Mardones-Santander 1988 *{published and unpublished data}*

Mardones-Santander F, Rosso P, Stekel A, Ahumada E, Llaguno S, Pizzaro F, et al. Effect of a milk-based food supplement on maternal nutritional status and fetal growth in underweight Chilean women. *American Journal of Clinical Nutrition* 1988;**47**:413-9.

Metcoff 1985 *{published and unpublished data}*

Metcoff J, Costiloe P, Crosby WM, Dutta S, Sandstead H, Milne D, et al. Effects of WIC supplement on maternal nutritional status between 19 and 36 weeks pregnancy. *American Journal of Clinical Nutrition* 1983;**37**:703.

Metcoff J, Costiloe P, Crosby WM, Dutta S, Sandstead H, Milne D, et al. Interaction between birth weight and smoking altered by WIC supplementation during pregnancy. *American Journal of Clinical Nutrition* 1983;**37**:710.

* Metcoff J, Costiloe P, Crosby WM, Dutta S, Sandstead HH, Milne D, et al. Effect of food supplementation (WIC) during pregnancy on birth weight. *American Journal of Clinical Nutrition* 1985;**41**:933-47.

Mirmolaei 2010 *{published data only}*

Mirmolaei ST, Moshrefi M, Kazemnejad A, Farivar F, Morteza H. The effect of nutrition education on nutritional behaviors in pregnant women. *HAYAT* 2010;**15**(4):35-42.

Moses 2006 *{published data only}*

Moses RG, Barker M, Winter M, Petocz P, Brand-Miller JC. Can a low-glycemic index diet reduce the need for insulin in gestational diabetes mellitus? A randomized trial. *Diabetes Care* 2009;**32**(6):996-1000.

Moses RG, Casey S, Cleary J, Milosavljevic M, Quinn E, Tapsell L, et al. Effect of low glycaemic index dietary advice in normal pregnancy: The PREGGIO study. *Obesity Research and Clinical Practice* 2013;**7**:e34-5.

Moses RG, Casey SA, Quinn EG, Cleary JM, Tapsell LC, Milosavljevic M, et al. Pregnancy and Glycemic Index Outcomes study: effects of low glycemic index compared with conventional dietary advice on selected pregnancy outcomes. *American Journal of Clinical Nutrition* 2014;**99**(3):517-23.

* Moses RG, Luebcke M, Davis WS, Coleman KJ, Tapsell LC, Petocz P, et al. Effect of a low-glycemic-index diet during pregnancy on obstetric outcomes. *American Journal of Clinical Nutrition* 2006;**84**(4):807-12.

Moses RG, Luebke M, Petocz P, Brand-Miller JC. Maternal diet and infant size 2 y after the completion of a study of a low-glycemic-index diet in pregnancy. *American Journal of Clinical Nutrition* 2007;**86**(6):1806.

Oken 2013 *{published data only}*

Oken E, Guthrie LB, Bloomingdale A, Platek DN, Price S, Haines J, et al. A pilot randomized controlled trial to promote healthful fish consumption during pregnancy: the Food for Thought Study. *Nutrition Journal* 2013;**12**:33.

Potdar 2014 *{published data only}*

Potdar RD, Sahariah SA, Gandhi M, Kehoe SH, Brown N, Sane H, et al. Improving women's diet quality preconceptionally and during gestation: effects on birth weight and prevalence of low birth weight-a randomized controlled efficacy trial in India (Mumbai Maternal Nutrition Project). *American Journal of Clinical Nutrition* 2014;**100**(5):1257-68.

Qureshi 1973 *{published data only}*

Qureshi S, Rao NP, Madhavi V, Mathur YC, Reddi YR. Effect of maternal nutrition supplementation on the birth weight of the newborn. *Indian Journal of Pediatrics* 1973;**10**:541-4.

Ross 1938 *{published data only}*

Ross RA, Perlzweig WA, Taylor HM, McBryde A, Yates A, Kondritzer AA, et al. A study of certain dietary factors of possible etiologic significance in toxemias of pregnancy. *American Journal of Obstetrics and Gynecology* 1938;**35**:426-40.

Thangaratinam 2014 *{published data only}*

Thangaratinam S. Effect of simple, targeted diet in pregnant women with metabolic risk factors on pre-eclampsia (ESTEEM): a randomised trial. ClinicalTrials.gov (http://clinicaltrials.gov/) [accessed 2 September 2014] 2014.

Tompkins 1954 *{published data only}*

Kasius RV, Randall A, Tompkins WT, Wiehl DG. Maternal and newborn nutrition studies at Philadelphia Lying-In Hospital. Newborn studies I. Size and growth of babies and mothers receiving nutritional supplements. *Milbank Memorial Fund Quarterly* 1955;**33**:230-45.

* Tompkins WT, Wiehl DG. Effect of nutrient supplements on obese patients during pregnancy. *Obstetrics & Gynecology* 1954;**4**(4):365-74.

Wiehl DG, Tompkins WT. Size of babies of obese mothers receiving nutrient supplements. *Milbank Memorial Fund Quarterly* 1954;**32**:125-40.

Tontisirin 1986 *{published data only}*

Tontisirin K, Booranasubkajorn U, Hongsumarn A, Thewtong D. Formulation and evaluation of supplementary foods for Thai pregnant women. *American Journal of Clinical Nutrition* 1986;**43**:931-9.

Tu 2013 *{published data only}*

Tu N, King JC, Dean D, Dirren H. Effect of food-based supplement prior to and during pregnancy on birth weight and prematurity in rural Vietnam (VINAVAC study). *Annals of Nutrition & Metabolism* 2013;**63**(Suppl 1):806, Abstract no: PO3314.

Walsh 2012 *{published data only}*

Donnelly J, Horan M, Walsh J, McGowan C, Byrne J, Molloy EJ, et al. Impact of a low GI diet on neonatal body composition (ROLO Kids). Pediatric Academic Societies Annual Meeting; 2013 May 4-7; Washington DC, USA. 2013.

Donnelly JM, Walsh JM, Byrne J, Molloy E, McAuliffe FM. Altered neonatal anthropometric measurements following maternal low GI diet in pregnancy (ROLO study). *Acta Obstetricia et Gynecologica Scandinavica* 2013;**92**(s160):13.

Horan M, McGowan C, Donnelly J, Gibney E, McAuliffe F. Maternal diet and weight at 3 months partum following a pregnancy intervention with a low glycaemic index diet: Results from the ROLO randomised control trial. *Archives of Disease in Childhood. Fetal and Neonatal Edition* 2014;**99**(Suppl 1):A129-A130 [Abstract no: PMM.20].

Horan MK, McGowan CA, Donnelly J, Gibney E, McAuliffe FM. The association of maternal characteristics and macronutrient intake in pregnancy with neonatal body composition. *Archives of Disease in Childhood. Fetal and Neonatal Edition* 2014;**99**(Suppl 1):A11.

Horan MK, McGowan CA, Doyle O, McAuliffe FM. Well-being in pregnancy: An examination of the effect of socioeconomic, dietary and lifestyle factors including impact of a low glycaemic index dietary intervention. *European Journal of Clinical Nutrition* 2014;**68**(1):19-24.

Horan MK, McGowan CA, Gibney ER, Donnelly JM, McAuliffe FM. Maternal diet and weight at 3 months postpartum following a pregnancy intervention with a low glycaemic index diet: results from the ROLO randomised control trial. *Nutrients* 2014;**6**(7):2946-55.

Horan MK, McGowan CA, Gibney ER, Donnelly JM, McAuliffe FM. Maternal low glycaemic index diet, fat intake and postprandial glucose influences neonatal adiposity - secondary analysis from the ROLO study. *Nutrition Journal* 2014;**13**(1):78.

McGowan CA, Walsh JM, Byrne J, Curran S, McAuliffe FM. The influence of a low glycemic index dietary intervention on maternal dietary intake, glycemic index and gestational weight gain during pregnancy: a randomized controlled trial. *Nutrition Journal* 2013;**12**(1):140.

Walsh J, Mahony R, Foley M, McAuliffe F. ROLO study: a randomized control trial of low glycemic index diet to prevent macrosomia in euglycemic women. *American Journal of Obstetrics and Gynecology* 2012;**206**(Suppl 1):S4.

Walsh JM, Mahony RM, Canty G, Foley ME, McAuliffe FM. Identification of those most likely to benefit from a low-glycaemic index dietary intervention in pregnancy. *British Journal of Nutrition* 2014;**112**:583-9.

Walsh JM, Mahony RM, Culliton M, Foley ME, McAuliffe FM. Impact of a low glycemic index diet in pregnancy on markers of maternal and fetal metabolism and inflammation. *Reproductive Sciences* 2014;**21**(11):1378-81.

* Walsh JM, McGowan CA, Mahony R, Foley ME, McAuliffe FM. Low glycaemic index diet in pregnancy to prevent macrosomia (ROLO study): randomised control trial. *BMJ* 2012;**345**:e5605.

Wijaya-Erhardt 2011 *{published data only}*

Wijaya-Erhardt M, Muslimatun S, Erhardt G. Effect of an educational intervention related to health and nutrition on pregnant women in the villages of Central Java Province, Indonesia. *Health Education Journal* 2014;**73**(4):370-81.

Wijaya-Erhardt M, Muslimatun S, Erhardt JG. Fermented soyabean and vitamin C-rich fruit: a possibility to circumvent the further decrease of iron status among iron-deficient pregnant women in Indonesia. *Public Health Nutrition* 2011;**14**(12):2185-96.

Wolever 2010 *{published data only}*

Wolever T. The effect of a low glycemic index diet on blood sugar control in pregnant women at risk for gestational diabetes. ClinicalTrials.gov (accessed 21 May 2013) 2010.

Wolff 2008 *{published data only}*

Wolff S, Legarth J, Vangsgaard K, Toubro S, Astrup A. A randomized trial of the effects of dietary counseling on gestational weight gain and glucose metabolism in obese pregnant women. *International Journal of Obesity* 2008;**32**(3):495-501.

Woods 1995 *{published data only}*

Woods LL, Gaboury CL. Importance of baseline diet in modulating renal reserve in pregnant women [abstract]. *Journal of the American Society of Nephrology* 1995;**6**(3):688.

Yan 2012 *{published data only}*

Yan W. Low glycemic index diet management for overweight pregnant women (LGIDMOPW). ClinicalTrials.gov (accessed 21 May 2013) 2012.

References to ongoing studies

Hambidge 2014 *{published data only}*

Hambidge KM, Krebs NF, Westcott JE, Garces A, Goudar SS, Kodkany BS, et al. Preconception maternal nutrition: a multi-site randomized controlled trial. *BMC Pregnancy and Childbirth* 2014;**14**(1):111.

Moore 2011 *{published data only}*

Moore S. Investigating the effects of pre-natal and infancy nutritional supplementation on infant immune development in The Gambia: the early nutrition and immune development (ENID) trial. Current Clinical Trials (http://www.current-trials.com) [accessed 8 July 2011] 2011.

Moore SE, Fulford AJC, Darboe MK, Jobarteh ML, Jarjou LM, Prentice AM. A randomized trial to investigate the effects of pre-natal and infant nutritional supplementation on infant immune development in rural Gambia: The ENID trial: Early Nutrition and Immune Development. *BMC Pregnancy and Childbirth* 2012;**12**:107.

Additional references

Aaltonen 2011

Aaltonen J, Ojala T, Laitinen K, Poussa T, Ozanne S, Isolauri E. Impact of maternal diet during pregnancy and breastfeeding on infant metabolic programming: a prospective randomized controlled study. *European Journal of Clinical Nutrition* 2011;**65**(1):10-9.

Alderman 2014

Alderman H, Hawkesworth S, Lundberg M, Tasneem A, Mark H, Moore SE. Supplemental feeding during pregnancy compared with maternal supplementation during lactation does not affect schooling and cognitive development through late adolescence. *American Journal of Clinical Nutrition* 2014;**99**(1):122-9.

Ashworth 1998

Ashworth A. Effects of intrauterine growth retardation on mortality and morbidity in infants and young children. *European Journal of Clinical Nutrition* 1998;**52**(1):S34-41.

Barker 1998

Barker DJP. Mothers, Babies and Health in Later Life. Edinburgh: Churchill Livingstone, 1998.

Barker 2002

Barker DJP, Eriksson JG, Forsén T, Osmond C. Fetal origins of adult disease: strength of effects and biological basis. *International Journal of Epidemiology* 2002;**31**:1235–9.

Behrman 2009

Behrman JR, Calderon MC, Preston SH, Hoddinott J, Martorell R, Stein AD. Nutritional supplementation in girls influences the growth of their children: prospective study in Guatemala. *American Journal of Clinical Nutrition* 2009;**90**(5):1372-9.

Chen 2009

Chen A, Feresu S, Fernandez C, Rogan W. Maternal obesity and the risk of infant death in the United States. *Epidemiology* 2009;**20**:74-81.

de Onis 1998

de Onis M, Villar J, Gülmezoglu M. Nutritional intervention to prevent intrauterine growth retardation: evidence from randomized controlled trials. *European Journal of Clinical Nutrition* 1998;**52**(1):S83–S93.

de Onis 2007

de Onis M, Onyango AW, Borghi E, Siyam A, Nishida C, Siekmann J. Development of a WHO growth reference for school-aged children and adolescents. *Bulletin of the World Health Organization* 2007;**85**(9):660-7.

Eriksson 2001

Eriksson JG, Forsén T, Tuomilehto J, Osmond C, Barker DJ. Early growth and coronary heart disease in later life: longitudinal study. *BMJ* 2001;**322**(7292):949-53.

Garlick 2000

Garlick PJ, Reeds PJ. Proteins. Human Nutrition and Dietetics. 10th Edition. UK: Churchill Livingstone, 2000:77.

GRADEpro 2014 [Computer program]

McMaster University. GRADEpro. [Computer program on www.gradepro.org]. Version 2015. McMaster University, 2014.

Grantham-McGregor 1991

Grantham-McGregor SM, Powell CA, Walker SP, Himes JH. Nutritional supplementation, psychosocial stimulation, and mental development of stunted children: the Jamaican Study. *Lancet* 1991;**338**(8758):1-5. [PUBMED: 1676083]

Grieve 1979

Grieve JFK, Campbell Brown BM, Johnsotone FD. Dieting in pregnancy: a study of the effect of a high protein low carhobydrate diet on birthweight on an obstetric population. In: Sutherland MW, Stowers JM editor(s). Carbohydrate Metabolism in Pregnancy and the Newborn 1978. Berlin: Springer Verlag, 1979:518-33.

Guyatt 2008

Guyatt GH, Oxman AD, Kunz R, Vist GE, Falck-Ytter Y, Schunemann HJ. GRADE Working Group. Rating quality of evidence and strength of recommendations: What is "quality of evidence" and why is it important to clinicians?. *BMJ* 2008;**336**(7651):995-8.

Haslehurst 2006

Heslehurst N, Ells LJ, Simpson H, Batterham A, Wilkinson J, Summerbell CD. Trends in maternal obesity incidence rates, demographic predictors, and health inequalities in 36 821 women over a 15-year period. *An International Journal of Obstetrics and Gynaecology* 2006;**114**:187-94.

Heslehurst 2008

Heslehurst N, Simpson H, Ells LJ, Rankin J, Wilkinson J, Lang R, et al. The impact of maternal BMI status on pregnancy outcomes with immediate short-term obstetric resource implications: a meta-analysis. *Obesity Reviews* 2008;**9**:635-83.

Higgins 2011

Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Imdad 2011

Imdad A, Yakoob MY, Bhutta ZA. The effect of folic acid, protein energy and multiple micronutrient suppleme *BMC Public Health* 2011;**11**(Suppl3):S4.

IOM 1990

Institute of Medicine. Nutrition in Pregnancy. Washington, DC: National Academy Press, 1990:137-75.

Kardjati 1983

Kardjati S, Kusin JA, de With C. Food consumption of rural women in East Java. *Nutrition Reports International* 1983;**28**:1341-9.

Kramer 1987

Kramer MS. Determinants of low birth weight: methodological assessment and meta-analysis. *Bulletin of the World Health Organization* 1987;**65**:663-737.

Kramer 2008

Kramer MS, Aboud F, Mironova E, Vanilovich I, Platt RW, Matush L, et al. Breastfeeding and child cognitive development: new evidence from a large randomized trial. *Archives of General Psychiatry* 2008;**65**(5):578-84. [PUBMED: 18458209]

Kulier 1998

Kulier R, de Onis M, Gülmezoglu AM, Villar J. Nutritional interventions for the prevention of maternal morbidity. *International Journal of Gynaecology and Obstettrics* 1998;**63**(3):231-46.

Laitinen 2009

Laitinen K, Poussa T, Isolauri E, Nutrition, Allergy, Mucosal Immunology and Intestinal Microbiota Group. Probiotics and dietary counselling contribute to glucose regulation during and after pregnancy: a randomised controlled trial. *British Journal of Nutrition* 2009;**101**:1679–87.

Lanou 2014

Lanou H, Huybregts L, Roberfroid D, Nikiema L, Kouanda S, Van Camp J, et al. Prenatal nutrient supplementation and postnatal growth in a developing nation: an RCT. *Pediatrics* 2014;**133**(4):e1001-8.

Luoto 2010

Luoto R, Laitinen K, Nermes M, Isolauri E. Impact of maternal probiotic-supplemented dietary counselling on pregnancy outcome and prenatal and postnatal growth: a double-blind, placebo-controlled study. *British Journal of Nutrition* 2010;**103**(12):1792-9.

Macleod 2013

Macleod J, Tang L, Hobbs FD, Wharton B, Holder R, Hussain S, et al. Effects of nutritional supplementation during pregnancy on early adult disease risk: follow up of offspring of participants in a randomised controlled trial investigating effects of supplementation on infant birth weight. *PLoS ONE [Electronic Resource]* 2013;**8**(12):e83371.

Ota 2011

Ota E, Haruna M, Suzuki M, Anh DD, Tho HL, Thanh Tam NT, et al. The association of gestational weight gain and maternal body mass index on perinatal outcomes in Vietnamese women. *Bulletin of the World Health Organization* 2011;**89**(2):127-36.

Prentice 1983

Prentice AM, Whitehead RG, Watkinson M, Lamb WH, Cole TJ. Prenatal dietary supplementation of African women and birth weight. *Lancet* 1983;**321**(8323):489-92.

Rasmussen 2010

Rasmussen KM, Habicht JP. Maternal supplementation differentially affects the mother and newborn. *Journal of Nutrition* 2010;**140**(2):402-6.

RevMan 2014 [Computer program]

The Cochrane Collaboration. Review Manager (RevMan). Version 5.3. Copenhagen, The Nordic Cochrane Centre: The Cochrane Collaboration, 2014.

Rush 1989

Rush D. Effects of changes in protein and calorie intake during pregnancy on the growth of the human fetus. In: Chalmers I, Enkin MW, Keirse MJNC editor(s). Effective Care in Pregnancy and Childbirth. Oxford: Oxford University Press, 1989:255-80.

Rush 2001

Rush D. Maternal nutrition and perinatal survival. *Journal of Health, Population and Nutrition* 2001;**19 Suppl**:S217-S264.

Schunemann 2009

Schunemann HJ. GRADE: from grading the evidence to developing recommendations. A description of the system and a proposal regarding the transferability of the results of clinical research to clinical practice [GRADE: Von der Evidenz zur Empfehlung. Beschreibung des Systems und Losungsbeitrag zur Ubertragbarkeit von Studienergebnissen]. *Zeitschrift fur Evidenz, Fortbildung und Qualitat im Gesundheitswesen* 2009;**103**(6):391-400. [PUBMED: 19839216]

Shah 2009

Shah PS, Ohlsson A, Knowledge Synthesis Group on Determinants of Low Birth Weight and Preterm Births. Effects of prenatal multimicronutrient supplementation on pregnancy outcomes: a meta-analysis. *Canadian Medical Association Journal* 2009;**180**(21):E99-E108.

Stein 1975

Stein Z, Susser M, Saenger G, Marolla F. Famine and Human Development: the Dutch Hunger Winter of 1944-45. New York: Oxford University Press, 1975.

Thangaratinam 2012

Thangaratinam S, Rogozińska E, Jolly K, Glinkowski S, Roseboom T, Tomlinson JW, et al. Effects of interventions in pregnancy on maternal weight and obstetric outcomes: meta-analysis of randomised evidence. *BMJ* 2012;**344**:e2088.

Unicef-WHO 2004

United Nations Children's Fund and World Health Organization. Low Birth Weight; Country and Global Estimates. New York: UNICEF, 2004.

Viller 1998

Villar J, Gülmezoglu AM, de Onis M. Nutritional and antimicrobial interventions to prevent preterm birth: an overview of randomized controlled trials. *Obstetrical & Gynecological Survey* 1998;**53**(9):575-85.

Viswanathan 2008

Viswanathan M, Siega-Riz AM, Moos MK, Deierlein A, Mumford S, Knaack J, et al. Outcomes of maternal weight gain. *Evidence Report/Technology Assessment* 2008;**168**:1-223.

Wang 2011

Wang TC, McPherson K, Marsh T, Gortmaker SL, Borown M. Health and economic burden of the projected obesity trends in the USA and the UK. *Lancet* 2011;**378**:815-25.

References to other published versions of this review

CDSR 1996a

Kramer MS. Energy/protein restriction for high weight-for-height or weight gain during pregnancy. *Cochrane Database of Systematic Reviews* 1996, Issue 3. [DOI: 10.1002/14651858.CD000080]

CDSR 1996b

Kramer MS. High protein supplementation in pregnancy. *Cochrane Database of Systematic Reviews* 1996, Issue 4. [DOI: 10.1002/14651858.CD000105]

CDSR 1996c

Kramer MS. Isocaloric balanced protein supplementation in pregnancy. *Cochrane Database of Systematic Reviews* 1996, Issue 4. [DOI: 10.1002/14651858.CD000118]

CDSR 1996d

Kramer MS. Nutritional advice in pregnancy. *Cochrane Database of Systematic Reviews* 1996, Issue 4. [DOI: 10.1002/14651858.CD000149]

Kramer 2003

Kramer MS, Kakuma R. Energy and protein intake in pregnancy. *Cochrane Database of Systematic Reviews* 2003, Issue 4. [DOI: 10.1002/14651858.CD000032]

Ota 2012

Ota E, Tobe-Gai R, Mori R, Farrar D. Antenatal dietary advice and supplementation to increase energy and protein intake. *Cochrane Database of Systematic Reviews* 2012, Issue 9. [DOI: 10.1002/14651858.CD000032.pub2]

* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Blackwell 1973

Methods	Interventions 'assigned randomly and blindly', but method not specified.
Participants	Well-nourished rural Taiwanese women with 'marginal' diets (a preliminary food survey in 1965 in this area estimated a daily energy intake of approximately 2000 kcal and protein intake <= 40 g for adult women). Women who were married, and planned to have at least one more child, and were classified as low socioeconomic status (defined as a lack of electric appliances in the home) were recruited in the last trimester of pregnancy. 294 women were recruited and 225 women gave birth to another child (114 in intervention group, 111 in control group). This study is known as the Bacon Chow study.
Interventions	Experimental: chocolate-flavoured liquid supplement given twice daily beginning after prior birth and continuing during index pregnancy until 15 months postpartum; supplement contained 40 g protein and 800 kcal energy plus vitamins/minerals. Control: supplement containing vitamins and minerals only, but given at the same time and for the same duration.
Outcomes	Gestational weight gain, preterm birth, birthweight, SGA, length, head circumference, and IQ at age 5.
Notes	1) Data presented on dietary substitution, but based on meal survey only. 2) High alleged net energy supplement not associated with significantly higher gestational weight gain. 3) Discrepancies in first-infant LBW rates in 1981 vs 1973 reports. 4) Significant correlation between birthweight and energy (and supplement) intake in controls only. 5) Supplementation continued until 15 months postpartum; data on maternal postpartum weight were therefore omitted from review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Although details are not described, it says the study participants were randomly assigned.
Allocation concealment (selection bias)	Low risk	The study states that ”The other person in Taipei who knew the code and directed the labelling did not disclose details to any one else in the study”.

Blackwell 1973 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	The 2 supplements were similar and no women were considered to be able to distinguish between them. Participants and personnel were blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description was given.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The cause of attrition was described with reasons and did not differ between studies.
Selective reporting (reporting bias)	Unclear risk	No description was given. Not mentioned on registered protocol.
Other bias	Unclear risk	No data were provided for background characteristics.

Briley 2002

Methods	Randomisation method not reported.
Participants	27 low-income African-American women. Mean pre-pregnancy BMI is within the normal range for both groups (intervention, 24.7 ± 3.4, control, 23.2 ± 4.1 kg/m^2).
Interventions	Experimental: minimum of 6 individualised in-home nutrition assessments and counselling visits. Control: 2 home visits without counselling.
Outcomes	Energy intake, gestational weight gain, birthweight, and preterm birth.
Notes	1) 7 of 27 randomised women dropped out and were not included in the analysis. 2) Neither participants nor observers were apparently blinded to the allocation.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Women were randomly assigned, though no detailed methods on randomisation were described.
Allocation concealment (selection bias)	Unclear risk	Insufficient information, the method of concealment was not described.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Counselling group was evident and interventions could not be blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information was given.
Incomplete outcome data (attrition bias) All outcomes	High risk	7 women dropped out of 27 women (74.1%) and no ITT.

Briley 2002 *(Continued)*

Selective reporting (reporting bias)	Unclear risk	Uncertain; if the protocol was registered, etc., this was not described.
Other bias	Low risk	There was no significant difference in the demographic background between the groups.

Ceesay 1997

Methods	Cluster randomisation by village "using a stratified design according to village size", but no details provided on method of random allocation or concealment.
Participants	Rural Gambian women from 28 villages with "chronically" marginal nutrition. Undernutrition more pronounced from June to October (the 'hungry' season involving low food supply and heavy agricultural work) than from November to May (the dry harvest season with adequate food supply and less strenuous work). The mean maternal BMI measured after delivery was 20.7 ± 2.3 kg/m^2 in the control group and 21.3 ± 2.8 kg/m^2 in the intervention group.
Interventions	Experimental villages: 2 supplement biscuits containing roasted groundnuts, rice flour, sugar, and groundnut oil (4250 kJ (1017 kcal) energy, 22 g protein, 56 g fat, 47 mg calcium, and 1.8 mg iron) consumed daily in presence of birth attendants. Supplementation began at 20 weeks' gestation. Control villages: no supplement.
Outcomes	Gestational weight gain, GA, birthweight, birth length, head circumference, stillbirth, and neonatal death.
Notes	1) Randomisation by cluster (village), but effects reported for individual births, based on multilevel (3-stage random-effects) modelling with separate error terms for the village, mother and, for mothers with more than 1 pregnancy during study, the baby. 2) Results reported both overall and stratified by season (hungry vs harvest), but this review was based on overall data. Note that definitions of seasons are not entirely consistent with previous (non-randomised) studies from this group and were chosen because "post hoc analysis indicated that this selection yielded the greatest discrimination between hungry and harvest season effects". 3) Many outcome analyses are based on individual women and therefore do not account for the intra-class correlation among women living in the same village. Sample sizes in these outcomes have therefore been adjusted downward to the nearest integer by dividing by 1+(m-1)r, where m is the average number of women per village and r = 0.01 is the (assumed) intra-class correlation co-efficient. 4) Data on LBW used in the analysis of infants born SGA. 5) Number of intervention and control participants reversed in column headings of Table 5.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Villages were randomly assigned, but no details provided on method of random allocation.
Allocation concealment (selection bias)	Unclear risk	Insufficient information; the method of allocation concealment was not described.
Blinding of participants and personnel (performance bias) All outcomes	High risk	The supplement biscuits were provided in intervention group only. Intervention was evident.

Ceesay 1997 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Measurements were carried out by 8 field workers, but no information was provided on their blinding status.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Over 95% agreed and remained in the trial throughout. The analysis presented here covers 2047 normal singleton live births from 1460 different women who delivered during October 1989 to October 1994.
Selective reporting (reporting bias)	Unclear risk	Not clear if the protocol was registered prior to the study.
Other bias	Low risk	Similar between the groups and multilevel multiple regression was employed.

Elwood 1981

Methods	Randomisation based on random numbers with sealed envelopes.
Participants	1251 pregnant Welsh women in 2 small towns recruited at time of first reporting of pregnancy in South Wales, UK. No information available for pregnant women's pre-pregnancy BMI.
Interventions	Experimental: free tokens worth ½ pint milk each. Control: no intervention.
Outcomes	GA, preterm birth, birthweight, LBW, length, and head circumference.
Notes	1) 24% of women lost to follow-up, with evidence of higher losses in control group. 2) No adjustment for higher percentage of smokers in control group. 3) Trial also includes postnatal milk supplement (tokens) in children; all data on postnatal growth in children were therefore omitted from review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation based on random numbers with sealed envelopes.
Allocation concealment (selection bias)	Low risk	Randomisation based on random numbers with sealed envelopes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Allocation was evident.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Anthropometric measurements were carried out by 2 blinded nurses.
Incomplete outcome data (attrition bias) All outcomes	Low risk	212 were lost to follow-up. 82% were analysed.
Selective reporting (reporting bias)	Unclear risk	Not enough information was provided.

Elwood 1981 *(Continued)*

Other bias	Unclear risk	Not enough information was provided.

Girija 1984

Methods	Randomly allocated.
Participants	20 poor Indian women in last trimester. Pregnant women's weight at last trimester was approximately 47 kg in both intervention group and control group.
Interventions	Experimental: supplement containing 50 g sesame cake, 40 g jaggery, and 10 g oil (417 kcal energy and 30 g protein). Control: normal (unsupplemented) diet.
Outcomes	Gestational weight gain, birthweight, length, head circumference, breast milk output, and weight, length, and head circumference, through 3 months of age.
Notes	1) Large losses to follow-up for breast milk output. 2) No SDs reported on postnatal anthropometric outcomes, so data not included in review. 3) No data reported on compliance or dietary substitution. 4) Energy and protein intakes appear higher before supplementation, even in supplemented group. 5) Mean GA (between 36 and 37 weeks in both groups) is incompatible with reported rates of preterm birth (0 of 10 in both groups), so data on preterm birth are omitted from review.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	The participants were randomly assigned, though no other details were provided.
Allocation concealment (selection bias)	Unclear risk	Insufficient information; the method of concealment was not described.
Blinding of participants and personnel (performance bias) All outcomes	High risk	The allocation was evident.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No description on the blinding of outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information was given.
Selective reporting (reporting bias)	Unclear risk	Not enough information was given.
Other bias	Unclear risk	No description on demographic characteristics and others.

Hunt 1976

Methods	Method of randomisation not reported.
Participants	344 Spanish-speaking women with first prenatal clinic visit <= 21 weeks' gestation in Los Angeles. Pre-pregnancy self-report weight for intervention group was 127 ± 19 lb, and control group was 126 ± 23 lb.
Interventions	Experimental: nutrition classes (average of 3 per woman). Control: no classes.
Outcomes	Protein and energy intakes; no data on gestational weight gain or pregnancy outcome.
Notes	1) 65 women excluded or lost (not interviewed) post-randomisation. 2) Possible 'contamination' via contact between women in 2 groups. 3) No blinding.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	The women were randomly assigned to a control or treatment group. Method of randomisation not reported.
Allocation concealment (selection bias)	Unclear risk	Insufficient information; the method of concealment was not described.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding, possible ‘contamination’ via contact between women in the groups.
Blinding of outcome assessment (detection bias) All outcomes	High risk	The same nutritionist provided nutrition education (intervention) and interview for outcome assessment.
Incomplete outcome data (attrition bias) All outcomes	Low risk	279 (81%) women were followed. Reasons for missing outcome data balanced in numbers across groups.
Selective reporting (reporting bias)	Unclear risk	No protocol, insufficient information to permit judgement.
Other bias	Unclear risk	Insufficient information to assess whether an important risk of bias exists.

Huybregts 2009

Methods	A non-blinded, individually randomised controlled trial. A randomisation scheme was generated by a computer program in permuted blocks of 4. Randomisation numbers were sealed in opaque envelopes by administrative staff. MISAME2 study.
Participants	1296 pregnant women in 2 villages in rural Burkina Faso. BMI at entry of the trial for intervention group was 20.8 ± 2.2 kg/m^2, and control group was 21.0 ± 2.2 kg/m^2.
Interventions	Intervention: prenatal multiple micronutrient + fortified food supplement. Control: multiple micronutrient.
Outcomes	Anthropometric measures at birth, LBW, infant born SGA, LGA, GA, preterm.

Huybregts 2009 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A randomisation scheme was generated by a computer program in permuted blocks of 4. Randomisation numbers were sealed in opaque envelopes by administrative staff.
Allocation concealment (selection bias)	Low risk	Sequentially numbered, opaque, sealed envelopes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Care was taken to blind staff who performed the anthropometric measurements at delivery.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Analysis for 87% of the 1175 live singleton deliveries enrolled.
Selective reporting (reporting bias)	Low risk	The trial was registered at clinical trials.gov as NCT00909974.
Other bias	Low risk	The compliance was closely verified by using a community-based network of home visitors.

Jahan 2013

Methods	A non-blinded, individually randomised controlled trial. Randomisation was conducted using a computer-generated randomised table.
Participants	384 pregnant women were randomised at a gestational age of 24 weeks at the government Maternal and Child Health Training Institute, Azimpur, and the Marie Stopes Clinic, Bashbari, Dhaka, Bangladesh. Intervention group: 150/192 (78.1%), control group: 150/192 (78.1%). Study conducted from Nov 2007 to Aug 2008.
Interventions	Monthly 1-hour education session at the clinic for 3 months. The content included the nutritional value of food including benefits of adequate energy, protein vitamins, and regular iron intake, the importance of exclusive breastfeeding, establishing an adequate diet during pregnancy and lactation, cooking practices for optimum retention of nutrients and a cooking demonstration of local foods called khichuri (highly nutritious local dish).
Outcomes	Gestational weight gain (7 to 9 months), birth weight of newborn, LBW, the rate of initiation of breastfeeding within 1 hour after birth.
Notes	

Risk of bias

Jahan 2013 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was conducted using a computer-generated randomised table.
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Intervention was evident to participants and personnel.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned.
Incomplete outcome data (attrition bias) All outcomes	High risk	Intervention group: 150/192 (78.1%), control group: 150/192 (78.1%). High attrition rate but comparison of characteristics between women who continued the study and who dropped out was not significant.
Selective reporting (reporting bias)	Unclear risk	Protocol is not available.
Other bias	Unclear risk	No information for compliance or behaviour change.

Kafatos 1989

Methods	Randomisation of 20 clinics using computer-generated random numbers.
Participants	568 pregnant women in rural area in Northern Greece < 27 weeks' gestation. Initial BMI was 23.10 ± 0.2 kg/m^2 in intervention group, and 22.7 ± 0.2 kg/m^2 in control group.
Interventions	Experimental: nutrition counselling to improve 'quality' of diet ('high nutrient value'). Control: no counselling.
Outcomes	Energy and protein intake, serum vitamin and mineral levels, gestational weight gain, birthweight, birth length and head circumference, GA, LBW, infant born SGA, preterm birth, stillbirth, and neonatal death.
Notes	1) Analysis based on individual women, rather than the clinic. To account for the intra-class correlation among women attending the same clinic, sample sizes have been adjusted downward to the nearest integer by dividing by 1+(m-1)r, where m is the average number of women per clinic (30.0 intervention and 26.8 control) and r = 0.01 is the (assumed) intra-class correlation. 2) Dietary intake unblinded, and energy intake higher in experimental group prior to intervention. 3) Inconsistent results: lower preterm rate, yet no difference in mean GA; higher head and chest circumferences but no difference in birthweight. 4) Discrepancies in sample sizes for different outcomes, even birthweight vs LBW rate. 5) SEM of GA in intervention (experimental) group assumed to be 0.10, not the 0.01 shown in Table 3.

Risk of bias

Bias	Authors' judgement	Support for judgement

Kafatos 1989 *(Continued)*

Random sequence generation (selection bias)	Low risk	A cluster randomisation of 20 clinics using computer-generated random numbers.
Allocation concealment (selection bias)	Low risk	Randomisation by clinic using computer-generated random numbers; clinic enrolled all women to minimise selection bias for allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding, but possible contamination effects of the educational program in that women from the same village or neighbourhood attended different clinics.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Delivery of intervention and outcome assessment were carried out by the same nurses, but periodical spot supervision provided by the program's nurse coordinator did not reveal suspect discrepancies between food weighting logs and dietary histories or suspect variations between records collated by individual nurses at different points in time.
Incomplete outcome data (attrition bias) All outcomes	Low risk	For dietary records, intervention group 216 (86.7%), control group 180(94.2%) were followed up after allocation.
Selective reporting (reporting bias)	Unclear risk	Insufficient information to permit judgement.
Other bias	High risk	Energy intake higher in experimental group prior to intervention.

Kardjati 1988

Methods	"Blind" randomisation based on household numbers, with use of a random-numbers table.
Participants	747 women in 3 villages in rural East Java (an area known to be 'nutritionally vulnerable' (Kardjati 1983) at 26-28 weeks' gestation. Total mean ± SD pre-pregnant BMI was 18.7 ± 2.0 kg/m^2.
Interventions	Experimental: supplement containing a dry powder (50% fat, 10% casein, and 40% glucose) providing 465 kcal energy and 7.1 g protein ('high energy'). Control: supplement containing 52 kcal energy and 6.2 g protein ('low energy').
Outcomes	Gestational weight gain, birthweight, and breast milk output.
Notes	1) Although data on birthweight were not analysed according to ITT, they are included in this review because birthweight was similar in the 2 study groups and in non-compliers (both groups combined). 2) Data on gestational weight gain are based on the combined results in all 3 compliance strata, but are missing for approximately one-third of study participants. 3) Data on breast milk output based on a selection of 50% of 'randomly'-selected study participants (only 10% of total study sample). Data excluded on 16 'uncooperative' or 'repeatedly absent' participants. 4) Data on postnatal infant growth reported in Kusin 1992 have been excluded from review, because poor compliers were excluded from the analysis (i.e. not based on ITT).

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The household numbers were the basis for allocation using random number tables.

Kardjati 1988 *(Continued)*

Allocation concealment (selection bias)	Low risk	The characteristics of the pregnant women cannot be inferred from the household numbers, which were used for randomisation.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	While participants and personnel were not blinded, the randomisation was, since the characteristics of the pregnant women cannot be inferred from the household numbers.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to permit judgment.
Incomplete outcome data (attrition bias) All outcomes	High risk	Birthweight was recorded in 419 liveborn singletons (87%). Gestational weight gain is missing for approximately one-third of study participants.
Selective reporting (reporting bias)	Unclear risk	Protocol not available.
Other bias	Unclear risk	The absence of a difference in mean birthweight between the HE and LE groups as a whole may be attributed to a masking effect of the better home diet in the experimental period.

Mora 1978

Methods	Allocation method not reported.
Participants	456 poor first-or second-trimester women from Bogota slum, for whom at least 50% of previous children had weight-for-height < 85% of the Colombian standard. No information about maternal anthropometry (weight or BMI) was provided.
Interventions	Experimental: supplement containing 60 g dried skim milk, 150 g enriched bread, and 20 g vegetable oil (856 kcal energy and 38.4 g protein) beginning in third trimester. Control: normal (unsupplemented) diet.
Outcomes	Pre-eclampsia, GA, preterm birth, birthweight, LBW, stillbirth, perinatal mortality, neonatal mortality.
Notes	1) Compliance assessed but data not presented. 2) Substitution assessed by single 24-hour recall 8 weeks after starting supplement. 3) Preterm birth rate not increased, but higher mortality reported among those born preterm. 4) Data on term LBW used in analysis of infant born SGA.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomly assigned either to a supplemented or an unsupplemented group.
Allocation concealment (selection bias)	Unclear risk	Allocation method not reported.
Blinding of participants and personnel (performance bias)	High risk	No blinding.

Mora 1978 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information was given.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Supplemented group (186/226, 82.3%), unsupplemented group(173/230, 75.2%) were followed. Total sample and subsample in table 2 showed no significant difference in characteristics.
Selective reporting (reporting bias)	Unclear risk	No protocol available, insufficient information to judge this.
Other bias	Unclear risk	Compliance not mentioned.

Oaks 2014

Methods	Allocation method not reported (only abstract available).
Participants	1320 pregnant Ghanaian women
Interventions	From 20 weeks of gestation, women were assigned to receive daily supplementation during pregnancy either: 1) 60 mg iron + 400µg folic acid (IFA) 2) multiple micronutrients, 3) 20g lipid based nutrient supplementation (containing 118 kcal, 22 micronutrients and protein).
Outcomes	Morning salivary cortisol at baseline and 36 weeks of gestation.
Notes	Only conference proceeding abstract available.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"A randomized controlled trial". Only abstract available, detail methods not mentioned.
Allocation concealment (selection bias)	Unclear risk	Not described.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not described.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information provided for attrition.
Selective reporting (reporting bias)	Unclear risk	Protocol is not available.

Oaks 2014 *(Continued)*

Other bias	Unclear risk	No data presented on compliance or base-line differences.

Ross 1985

Methods	Allocation method not reported.
Participants	127 Black South African women < 20 weeks' gestation. Study women averaged > 70 kg at 20 weeks.
Interventions	Experimental: supplement containing 700-800 kcal energy and 36-44 g protein. 2 types of supplements were given: a high-bulk mixture of beans and maize, given as mush with added vitamins, and a low-bulk porridge containing dried skimmed milk, maize, flour, vitamins, and minerals; the high- and low-bulk groups are combined in the experimental group for this review. Control: placebo pills (zinc-supplemented group is excluded from review).
Outcomes	Gestational weight gain (after 20 weeks), GA, and birthweight.
Notes	1) Higher gestational weight gain in the control group argues against causal association with birth-weight. 2) No data presented on compliance or substitution. 3) Number of women originally randomised not reported ('90% continued ... to delivery'). 4) Original sample size, nor its justification, were given.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	127 Zulu women were randomly assigned to 4 groups.
Allocation concealment (selection bias)	Unclear risk	Allocation method not reported.
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information was given.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of women originally randomised not reported, or no missing case.
Selective reporting (reporting bias)	Unclear risk	Protocol is not available.
Other bias	Unclear risk	No data presented on compliance or substitution.

Rush 1980

Methods	Stratified randomisation based on table of random numbers, with allocation in sealed envelope and blinding of all research staff.
Participants	1051 low-income black women in Harlem (New York City) <= 30 weeks' gestation 'at risk' for LBW based on 1 or more of the following criteria: 1) pre-pregnancy weight < 110 lbs; 2) pre-pregnancy weight 110-139 lbs plus low gestational weight gain as of recruitment; 3) pre-pregnancy weight 110-139 lbs plus previous history of LBW; or 4) pre-pregnancy weight 110-139 lbs plus protein intake < 50 g in the 24 hours preceding registration.
Interventions	Experimental (1): balanced energy/protein 16-oz beverage supplement containing 322 kcal energy, 6 g protein, and vitamins/minerals ('complement'). Experimental (2): high-protein 16-oz beverage supplement containing 470 kcal + 40 g protein per day + vitamins and minerals. Control: supplement containing vitamins/minerals only.
Outcomes	Gestational weight gain, GA, preterm birth, infant born SGA, birthweight, LBW, stillbirth, neonatal mortality, and weight, length, head circumference, and Bayley scores at 1 year.
Notes	Almost no data presented on the (approximately) 25% of participants who failed to comply, dropped out, or moved away.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random assignment.
Allocation concealment (selection bias)	Low risk	Based on table of random numbers, with allocation in sealed envelope.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Blinding of all research staff and participants of beverage interventions, although control group could not be blinded.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Most of the outcome data from hospital records, and outcome assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	94% follow-up, 48 whose mothers chose to discontinue supplements and 1 infant with Down's syndrome excluded.
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	High risk	Almost no data presented on the (approximately) 25% of recruited participants who failed to comply, dropped out, or moved away.

Sweeney 1985

Methods	Stratified randomisation 'using biased coin methodology'.

Sweeney 1985 *(Continued)*

Participants	47 healthy women < 20 weeks' gestation in Salt Lake, USA. Maternal height ranged from 152 to 180 cm, and pre-pregnant weight ranged from 41 to 113 kg.
Interventions	Experimental: Higgins' method of protein/energy 'prescription' (i.e. advice only, no supplementation). Control: no advice.
Outcomes	Protein and energy intake, gestational weight gain, birthweight and GA.
Notes	1) Slight discrepancy in number of women allocated. 2) Mean and SD weight gain, birthweight, and GA not reported by allocation group. 3) Probable non-blinding of intake (protein and energy) histories.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Stratified random allocation using a biased coin methodology.
Allocation concealment (selection bias)	Unclear risk	Insufficient information to permit judgement for allocation concealment.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Probable non-blinding.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Collection of newborn data was carried out by blinded researcher, but no other information was given on assessment of other outcomes.
Incomplete outcome data (attrition bias) All outcomes	Low risk	43 out of 47 (91.5%) women were analysed.
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	Unclear risk	Slight discrepancy in number of women allocated.

Viegas 1982a

Methods	Allocation method not reported.
Participants	153 Asian women in Birmingham, UK < 20 weeks' gestation who appeared well-nourished based on their weight and height. The mean ± SD height and weight for intervention group was 154.6 ± 4.4 cm, 53.0 ± 9.1 kg and control group was 156.5 ± 5.8 cm, 56.3 ± 10.6 kg.
Interventions	Experimental: supplement of flavoured carbonated glucose drink providing 273 kcal energy (with 11% of energy as protein) plus vitamins from 18 to 38 weeks. Control: supplement of flavoured carbonated water containing iron and vitamin C.
Outcomes	Gestational weight gain and birthweight, placental weight, maternal skin folds and arm circumference.
Notes	1) Designed as 3-arm trial, but group receiving supplement with 11% of energy provided as protein were combined with energy-only group for this review.

Viegas 1982a *(Continued)*

	2) No evidence that study women were undernourished. 3) No data presented on compliance or dietary substitution. 4) Results presented only in graphic form; extracted data are therefore approximate.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Minimisation. Allocation to a particular regimen was designed to give as closely as possible the same distribution of parity, abnormal past obstetric history and history of early bleeding in the current pregnancy.
Allocation concealment (selection bias)	Unclear risk	Allocation method not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information was given.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Protein energy vitamin group: 47/51(92.1%); energy vitamin group: 50/57(87.7%); vitamin group: 45, no missing.
Selective reporting (reporting bias)	Unclear risk	No protocol available.
Other bias	Unclear risk	No data presented on compliance.

Viegas 1982b

Methods	Allocation method not reported.
Participants	130 Asian women in Birmingham, UK < 20 weeks' gestation (who appeared well-nourished (based on height and weight) prior to pregnancy, 45 of whom were later considered "nutritionally at risk" based on inadequate increase in triceps skin folds (between 18 and 28 weeks) stratified at 28 weeks according to increase in triceps skinfold during second trimester (<= 0.02 vs > 0.02 mm/week).
Interventions	Experimental: supplement of flavoured carbonated glucose drink + skim milk powder providing 425 kcal energy (with 10% of energy as protein), plus vitamins from 28 to 38 weeks. Control: supplement of flavoured carbonated water containing iron and vitamin C.
Outcomes	Gestational weight gain, GA, birthweight, length, and head circumference, placental weight, and maternal skin folds.
Notes	1) Designed as 3-arm trial, but group receiving supplement with 10% of energy provided as protein were combined with energy-only group for this review. 2) No data presented on compliance or dietary substitution. 3) Results for gestational weight gain presented only in graphic form; extracted data are therefore approximate. 4) Probable misprint in Table II: mean GA in supplemented (EnVi = energy plus vitamins) group assumed to be 39.2 weeks, rather than the 29.2 weeks indicated in the table.

Viegas 1982b *(Continued)*

	5) Data on outcomes stratified according to increase in triceps skin folds from 18-28 weeks. Because of harmful effect in those with normal skin folds, and as there was no statement that threshold was established a priori, outcomes from both strata have been combined in the review. 6) Data from ITT analysis extracted from graph; not presented in tabular form. 7) Probable misprint in GA for control group (adequate skinfold stratum) in Table II.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Members of each group were then assigned at random to 1 of 3 supplement groups.
Allocation concealment (selection bias)	Unclear risk	Allocation method not reported.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Blinding not reported.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	No information was given.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only 2 missing in EnVi group; reasons for perinatal death were detailed. 128 out of 130 (98.5%) were included.
Selective reporting (reporting bias)	Unclear risk	Protocol not available.
Other bias	Unclear risk	No data for compliance.

BMI: body mass index
GA: gestational age
IQ: intelligence quotient
ITT: intention-to-treat
LBW: low birthweight
LGA: large-for-gestational age
SD: standard deviation
SEM: standard error of the mean
SGA: small-for-gestational age
UK: United Kingdom
vs: versus

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Aaltonen 2005	Intervention involved advice to alter fat composition of the diet, but not to change its energy or protein content.
Adams 1978	Participants were high-risk women only.
Anderson 1995	The nutritional advice studied does not relate to energy or protein intake, or both.

Study	Reason for exclusion
Astrup 2013	Participants were high-risk women only (pre-pregnancy BMI 30-45).
Atkinson 2013	Participants were high-risk women only (pre-pregnancy BMI of > 25 and < 35 kg/m^2).
Atton 1990	Not randomised, alternate allocation.
Badrawi 1993	Studies of calorie/energy restriction for women who are overweight or obese are beyond the scope of this review.
Bosaeus 2015	The dietary counselling does not relate to energy or protein intake, but focused on increasing fish intake. This study called the Pregnancy Obesity Nutrition and Child Health (PONCH) study.
Campbell 1975	Studies of calorie/energy restriction for women who are overweight or obese are beyond the scope of this review.
Campbell 1983	Studies of calorie/energy restriction for women who are overweight or obese are beyond the scope of this review.
Campbell Brown 1983	Not randomised, alternate allocation.
Clapp 1997	Experimental intervention involved no change in energy or protein intake, but only in the type of carbohydrate in the diet. Moreover, the only outcomes studied were glycaemic (blood glucose) responses to diet and exercise.
Dirige 1987	The nutritional advice studied does not relate to energy or protein intake, or both.
Ebbs 1941	Not randomised.
Eneroth 2010	Follow-up analysis of Matlab (MINIMat) study, intervention is not relevant to our review.
Fard 2004	RCT of maternal dietary fat modification with no net supplementation of energy or protein.
Fung 2010	Participants are not only pregnant women and outcome is not relevant to our review.
Guelinckx 2010	Studies of calorie/energy restriction for women who are overweight or obese are beyond the scope of this review.
Hankin 1962	Not randomised, allocation by day of week.
Hautero 2013	The intervention is out of scope for this review (improving intake of n-3 long chain polyunsaturated fatty acids (LC-PUFA)).
Iyengar 1967	Not randomised.
Kaseb 2002	Not randomised, quasi-randomised study.
Kinra 2008	Intervention was not randomised and included both prenatal and postnatal (for the infant/child) supplementation.
Lechtig 1975	Despite the original RCT design, the reported results were based on observational analyses of the data. In one report of this trial (Delgado 1982), the results were indeed presented according to randomised treatment. This report was also excluded, however, because the analysis was based on individual women despite randomisation by village, and was limited to women with data on length of gestation, and showed evidence of major problems in validity of gestational age measurements. Stein 2003, Webb 2005, Stein 2006, and Hodinott 2008 were also based on the treatment allocation as randomised but were excluded from analysis of long-term outcomes because the offspring were

Study	Reason for exclusion
	also supplemented, making it impossible to distinguish effects of prenatal maternal supplementation from those of postnatal supplementation of the infant/child.n-3 long chain polyunsaturated fatty acids (LC-PUFA).
Li 2014	Parallel group design. Participants were first divided into ethnic group, Hand and Mongolian. Then they were divided into 4 groups; group 1 (folic acid + milk), group 2 (milk), group 3 (folic acid), and group 4 (control). Although the population and intervention were eligible, we excluded this trial due to its high attrition rate 2016/3526 (57%) and no reasons described.
Luke 2001	Not randomised or quasi-randomised trial.
Magon 2014	The intervention is out of scope for this review; both the intervention group received a similar amount of protein but intervention group received leaf concentrate (additional calcium, iron, β-carotene, folate).
Maleta 2014	Participants were high-risk women only. Intervention for treatment of moderately malnourished women in pregnancy. Mamachiponde study.
Mardones-Santander 1988	Not randomised, alternate allocation.
Metcoff 1985	Participants were high-risk women only.
Mirmolaei 2010	This paper focused on the impact of education on nutritional behaviour and worked with a scale related to nutritional behaviour. There was no specific question about energy or protein intake.
Moses 2006	RCT of diets with high vs low glycaemic index, with no net supplementation of energy or protein.
Oken 2013	This study aimed to increase DHA, and fish consumption. Intervention was different.
Potdar 2014	This study aim was to improve women's dietary micronutrient quality before conception and during pregnancy. Intervention group received an average of 6.4 g protein and control group received an average of 2.4 g protein with co-intervention micronutrient (high vs low) content snack before and after pregnancy. We decided to exclude this trial from our review due to very high attrition rate (Intervention group only remain 20.7%, and control group remain 21.1% from randomisation (preconception) and intervention group 59.8%, and control group 58.9% after pregnancy).
Qureshi 1973	Not randomised, alternate allocation.
Ross 1938	Not randomised, alternate allocation.
Thangaratinam 2014	The target population was beyond the scope of this review. Only including pregnant women with pre-eclampsia.
Tompkins 1954	The target population was beyond the scope of this review.
Tontisirin 1986	Not randomised.
Tu 2013	Intervention was out of scope for this review, this study focused on zinc, iron, vitamin A, B12 and folic acid. VINAVAC study.
Walsh 2012	ROLO study, the target population was high-risk. Participants had previously delivered an infant weighing greater than 4 kg.
Wijaya-Erhardt 2011	Intervention focused on increasing the consumption of Fe-rich foods to prevent maternal iron deficiency during pregnancy. The intervention is beyond the scope of this review.

Study	Reason for exclusion
Wolever 2010	Educational intervention (low glycaemic index diet) aimed to prevent GDM among a high-risk population (e.g. any 1 of: BMI >= 25 kg/m^2, or age >= 35 years, or high-risk ethnicity (Asian, South Asian, Hispanic, African, Aboriginal).
Wolff 2008	The current inclusion of information about caloric restriction for women who are overweight or obese only serves to increase confusion as it requires discussion of the clinical implications for 2 different populations, thus we excluded the outcome of "energy and protein restriction in women who were overweight or showed high weight gain". This trial previously included in the analysis, has now been excluded because the target population was out of scope for this review.
Woods 1995	Small (n = 10) cross-over trial of high- vs low-protein diet without control group, but no pregnancy or offspring outcomes are analysed. The only outcomes reported are renal haemodynamic responses to a meat meal.
Yan 2012	The intervention is different. Dietary advice for low glycaemic index diet management for overweight pregnant women.

BMI: body mass index
DHA: docosahexaenoic acid
FE: iron
GDM: gestational diabetes mellitus
RCT: randomised controlled trial
vs: versus

Characteristics of ongoing studies *[ordered by study ID]*

Hambidge 2014

Trial name or title	Preconception maternal nutrition: a multi-site randomised controlled trial.
Methods	3-armed randomised controlled trial.
Participants	Women (16-35 years of age, parity 0-5) identified primarily thorough the Global Network Maternal Newborn Registry in India (Belgaum, Karnataka), Pakistan (Thatta, Sind Province), Democratic Republic of Congo (DRC, Equateur Province), and Guatemala (Chimaltenango Department) who expect to have first or additional pregnancy within the next 2 years and without intent to utilise contraception.
Interventions	Arm-1: daily 20 g MMN fortified lipid-based (118 kcal) supplement (Nutriset, Malauney, France) beginning 3 or more months prior to conception until delivery. Arm-2: the same daily nutrition supplement beginning at 12 weeks of gestation until delivery. Arm-3: no nutrition supplement.
Outcomes	Primary outcome: birth length-for-age Z-score. Secondary outcomes: infant length-for-age Z-score at age 0.5, 1, 3 and 6 months postnatal; fetal length at 12 and 34 weeks gestation; mean birthweight and incidence of low birthweight infants; perinatal mortality; incidence of severe neonatal and infant infectious disease, epigenome of mother, fetus and offspring; deep phenotyping of metabolic and nutritional status; maternal and infant microbiome; and nutritive compounds in breast milk.
Starting date	1 January 2014.
Contact information	K Michael Hambidge.

Hambidge 2014 *(Continued)*

	Michael.Hambidge@ucdenver.edu
Notes	ClinicalTrials.gov NCT01883193, Anticipated date of follow-up completion: 30 May 2017.

Moore 2011

Trial name or title	Investigating the effects of pre-natal and infancy nutritional supplementation on infant immune development in The Gambia: the early nutrition and immune development (ENID) trial.
Methods	3-way randomised controlled trial.
Participants	Women (aged 18 to 45 years) resident in Kiang West Region, The Gambia, with pregnancy confirmed by urine test and ultrasound examination and with gestational age approximately 10-20 weeks.
Interventions	4 pregnancy interventions, to be given daily from 12 weeks' gestation until delivery. 1. FeFol: iron-folate, 60 mg iron 400 µg folate, representing the usual standard of care during pregnancy, as per Gambian Government guidelines (control group). 2. MMNs: a combination of 15 micronutrients, specifically designed for use during pregnancy, and as formulated by UNICEF. A single tablet provides the recommended dietary allowance for each micronutrient, but we will supplement women in this arm of the trial with 2 daily MMN tablets. 3. PE + FeFol: protein-energy and iron-folate. A food-based supplement developed by Valid International, providing a comparable level of iron and folate to the FeFol only arm, but with the addition of energy, protein and lipids. 4. PE + MMN: protein-energy and MMNs. A micronutrient fortified food-based supplement also developed by Valid International, and providing comparable levels of micronutrients to the MMN arm (including FeFol), in addition to the energy and protein and lipid content.
Outcomes	Infant immunity development.
Starting date	01/10/2009.
Contact information	Dr Sophie Moore. smoore@mrc.gm
Notes	ISRCTN49285450, Anticipated end date 30/09/2013.

MMN: multiple micronutrient

DATA AND ANALYSES

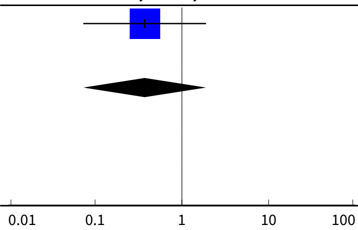
Comparison 1. Nutritional education during pregnancy versus no nutritional education (or normal care)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Stillbirth	1	431	Risk Ratio (M-H, Fixed, 95% CI)	0.37 [0.07, 1.90]
2 Neonatal death	1	448	Risk Ratio (M-H, Fixed, 95% CI)	1.28 [0.35, 4.72]
3 Birthweight (g)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
3.1 Undernourished women	2	320	Mean Difference (IV, Random, 95% CI)	489.76 [427.93, 551.59]
3.2 Adequately nourished women	1	406	Mean Difference (IV, Random, 95% CI)	15.0 [-76.30, 106.30]
4 Birth length (cm)	1	399	Mean Difference (IV, Fixed, 95% CI)	0.17 [-0.72, 1.06]
5 Birth head circumference (cm)	1	389	Mean Difference (IV, Fixed, 95% CI)	0.99 [0.43, 1.55]
6 Small-for-gestational age	1	404	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.45, 2.11]
7 Preterm birth	2	449	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.21, 0.98]
8 Gestational age (week)	1	399	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.48, 0.28]
9 Low birthweight	1	300	Risk Ratio (M-H, Fixed, 95% CI)	0.04 [0.01, 0.14]
10 Protein intake (g/day)	3	632	Mean Difference (IV, Fixed, 95% CI)	6.99 [3.02, 10.97]
11 Energy intake (kcal/day)	3	342	Mean Difference (IV, Fixed, 95% CI)	105.61 [-18.94, 230.15]
12 Total gestational weight gain (kg)	2	233	Mean Difference (IV, Random, 95% CI)	-0.41 [-4.41, 3.59]

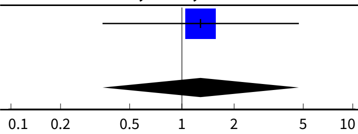
Analysis 1.1. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 1 Stillbirth.

Study or subgroup	Nutritional advice n/N	No advice n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Kafatos 1989	2/223	5/208		100%	0.37[0.07,1.9]
Total (95% CI)	**223**	**208**		**100%**	**0.37[0.07,1.9]**
Total events: 2 (Nutritional advice), 5 (No advice)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.19(P=0.24)					



Analysis 1.2. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 2 Neonatal death.

Study or subgroup	Nutritional advice n/N	No advice n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Kafatos 1989	5/221	4/227		100%	1.28[0.35,4.72]
Total (95% CI)	**221**	**227**		**100%**	**1.28[0.35,4.72]**



Study or subgroup	Nutritional advice	No advice	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
Total events: 5 (Nutritional advice), 4 (No advice)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.38(P=0.71)					

Favours Nutritional advice 0.1 0.2 0.5 1 2 5 10 Favours No advice

Analysis 1.3. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 3 Birthweight (g).

Study or subgroup	Nutritional advice N	Nutritional advice Mean(SD)	No advice N	No advice Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.3.1 Undernourished women							
Briley 2002	10	3540 (400)	10	3060 (500)		2.43%	480[83.14,876.86]
Jahan 2013	150	2980 (330)	150	2490 (210)		97.57%	490[427.4,552.6]
Subtotal ***	**160**		**160**			**100%**	**489.76[427.93,551.59]**
Heterogeneity: Tau²=0; Chi²=0, df=1(P=0.96); I²=0%							
Test for overall effect: Z=15.52(P<0.0001)							
1.3.2 Adequately nourished women							
Kafatos 1989	211	3391 (434.4)	195	3376 (498.7)		100%	15[-76.3,106.3]
Subtotal ***	**211**		**195**			**100%**	**15[-76.3,106.3]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.32(P=0.75)							
Test for subgroup differences: Chi²=71.22, df=1 (P<0.0001), I²=98.6%							

Favours Nutritional advice -1000 -500 0 500 1000 Favours No advice

Analysis 1.4. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 4 Birth length (cm).

Study or subgroup	Nutritional advice N	Nutritional advice Mean(SD)	No advice N	No advice Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kafatos 1989	206	50.1 (3.3)	193	49.9 (5.5)		100%	0.17[-0.72,1.06]
Total ***	**206**		**193**			**100%**	**0.17[-0.72,1.06]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.37(P=0.71)							

Favours No advice -10 -5 0 5 10 Favours Nutritional advice

Analysis 1.5. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 5 Birth head circumference (cm).

Study or subgroup	Nutritional advice N	Nutritional advice Mean(SD)	No advice N	No advice Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kafatos 1989	197	34.4 (2.9)	192	33.4 (2.8)		100%	0.99[0.43,1.55]

Favours No advice -10 -5 0 5 10 Favours Nutritional advice

Study or subgroup	Nutritional advice N	Nutritional advice Mean(SD)	No advice N	No advice Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Total ***	**197**		**192**			**100%**	**0.99[0.43,1.55]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.45(P=0)							

Favours No advice -10 -5 0 5 10 Favours Nutritional advice

Analysis 1.6. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 6 Small-for-gestational age.

Study or subgroup	Nutritional advice n/N	No advice n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Kafatos 1989	12/205	12/199		100%	0.97[0.45,2.11]
Total (95% CI)	**205**	**199**		**100%**	**0.97[0.45,2.11]**
Total events: 12 (Nutritional advice), 12 (No advice)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.08(P=0.94)					

Favours Nutritional advice 0.1 0.2 0.5 1 2 5 10 Favours No advice

Analysis 1.7. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 7 Preterm birth.

Study or subgroup	Nutritional advice n/N	No advice n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Briley 2002	0/10	1/10		7.66%	0.33[0.02,7.32]
Kafatos 1989	9/228	17/201		92.34%	0.47[0.21,1.02]
Total (95% CI)	**238**	**211**		**100%**	**0.46[0.21,0.98]**
Total events: 9 (Nutritional advice), 18 (No advice)					
Heterogeneity: Tau²=0; Chi²=0.04, df=1(P=0.84); I²=0%					
Test for overall effect: Z=2.02(P=0.04)					

Favours Nutritional advice 0.01 0.1 1 10 100 Favours No advice

Analysis 1.8. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 8 Gestational age (week).

Study or subgroup	Nutritional advice N	Nutritional advice Mean(SD)	No advice N	No advice Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kafatos 1989	205	39.6 (1.6)	194	39.7 (2.2)		100%	-0.1[-0.48,0.28]
Total ***	**205**		**194**			**100%**	**-0.1[-0.48,0.28]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.52(P=0.61)							

Favours No advice -10 -5 0 5 10 Favours Nutritional advice

Analysis 1.9. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 9 Low birthweight.

Study or subgroup	Nutritional education n/N	Normal care n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Jahan 2013	3/150	67/150		100%	0.04[0.01,0.14]
Total (95% CI)	**150**	**150**		**100%**	**0.04[0.01,0.14]**
Total events: 3 (Nutritional education), 67 (Normal care)					
Heterogeneity: Not applicable					
Test for overall effect: Z=5.37(P<0.0001)					

Nutritional education 0.01 0.1 1 10 100 Routine hospital services

Analysis 1.10. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 10 Protein intake (g/day).

Study or subgroup	Nutritional advice N	Nutritional advice Mean(SD)	No advice N	No advice Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Hunt 1976	147	73 (27)	132	68 (28)		37.75%	5[-1.47,11.47]
Kafatos 1989	167	78.4 (16.5)	143	70.8 (30.2)		51.37%	7.65[2.1,13.2]
Sweeney 1985	18	91.6 (18.3)	25	80.8 (21.9)		10.89%	10.8[-1.25,22.85]
Total ***	**332**		**300**			**100%**	**6.99[3.02,10.97]**
Heterogeneity: Tau²=0; Chi²=0.8, df=2(P=0.67); I²=0%							
Test for overall effect: Z=3.45(P=0)							

Favours No advice -100 -50 0 50 100 Favours Nutritional advice

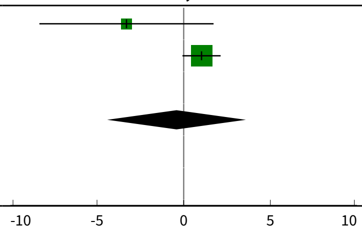
Analysis 1.11. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 11 Energy intake (kcal/day).

Study or subgroup	Nutritional advice N	Nutritional advice Mean(SD)	No advice N	No advice Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Briley 2002	10	2082 (612)	10	2227 (871)		3.56%	-145[-804.78,514.78]
Hunt 1976	147	1851 (632)	132	1754 (572)		77.71%	97[-44.28,238.28]
Sweeney 1985	18	2562 (423.9)	25	2373 (538)		18.73%	189[-98.79,476.79]
Total ***	**175**		**167**			**100%**	**105.61[-18.94,230.15]**
Heterogeneity: Tau²=0; Chi²=0.89, df=2(P=0.64); I²=0%							
Test for overall effect: Z=1.66(P=0.1)							

Favours No advice -1000 -500 0 500 1000 Favours Nutritional advice

Analysis 1.12. Comparison 1 Nutritional education during pregnancy versus no nutritional education (or normal care), Outcome 12 Total gestational weight gain (kg).

Study or subgroup	Nutritional advice		No advice		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
Briley 2002	10	11.9 (6.3)	10	15.2 (5.1)		33.32%	-3.3[-8.32,1.72]
Kafatos 1989	136	11.3 (4.1)	77	10.3 (3.8)		66.68%	1.03[-0.07,2.13]
Total ***	**146**		**87**			**100%**	**-0.41[-4.41,3.59]**
Heterogeneity: Tau²=5.93; Chi²=2.72, df=1(P=0.1); I²=63.27%							
Test for overall effect: Z=0.2(P=0.84)							



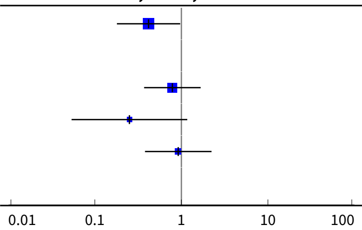
Comparison 2. Balanced protein/energy supplementation versus control or no intervention in pregnancy

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Stillbirth	5	3408	Risk Ratio (M-H, Fixed, 95% CI)	0.60 [0.39, 0.94]
2 Neonatal death	5	3381	Risk Ratio (M-H, Fixed, 95% CI)	0.68 [0.43, 1.07]
3 Birthweight (g)	11	5385	Mean Difference (IV, Random, 95% CI)	40.96 [4.66, 77.26]
3.1 Undernourished women	8	2903	Mean Difference (IV, Random, 95% CI)	66.96 [13.13, 120.78]
3.2 Adequately nourished women	6	2482	Mean Difference (IV, Random, 95% CI)	15.93 [-20.83, 52.69]
4 Birth length (cm)	5	3370	Mean Difference (IV, Random, 95% CI)	0.18 [-0.04, 0.40]
5 Birth head circumference (cm)	5	3352	Mean Difference (IV, Random, 95% CI)	0.04 [-0.08, 0.17]
6 Small-for-gestational age	7	4408	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.69, 0.90]
7 Preterm birth	5	3384	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.80, 1.16]
8 Gestational age (week)	6	3471	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.22, 0.01]
9 Weekly gestational weight gain (g/week)	9	2391	Mean Difference (IV, Random, 95% CI)	18.63 [-1.81, 39.07]
10 Pre-eclampsia	2	463	Risk Ratio (M-H, Fixed, 95% CI)	1.48 [0.82, 2.66]
11 Bayley mental score at 1 year	1	411	Mean Difference (IV, Fixed, 95% CI)	-0.74 [-1.95, 0.47]
12 IQ at 5 years	1	153	Mean Difference (IV, Fixed, 95% CI)	0.0 [-4.98, 4.98]
13 Weight at 1 year (g)	2	623	Mean Difference (IV, Fixed, 95% CI)	30.43 [-139.67, 200.53]
14 Length at 1 year (cm)	1	428	Mean Difference (IV, Fixed, 95% CI)	0.0 [-5.69, 5.69]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
15 Head circumference at 1 year (cm)	2	627	Mean Difference (IV, Fixed, 95% CI)	-0.13 [-0.35, 0.10]
16 Duration of labour (hours)	1	345	Mean Difference (IV, Fixed, 95% CI)	-0.09 [-1.18, 1.00]
17 Mortality from birth to age 12 months	1	1023	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.58, 2.10]
18 Maternal weight 4 weeks' postpartum (kg)	1	354	Mean Difference (IV, Fixed, 95% CI)	-0.90 [-1.92, 0.12]
19 Height at age 11-17 years (cm)	1	855	Mean Difference (IV, Random, 95% CI)	-0.36 [-2.12, 1.41]
19.1 Boys	1	445	Mean Difference (IV, Random, 95% CI)	0.60 [-1.40, 2.60]
19.2 Girls	1	410	Mean Difference (IV, Random, 95% CI)	-1.20 [-3.00, 0.60]
20 Weight at 11-17 years (kg)	1	855	Mean Difference (IV, Fixed, 95% CI)	0.46 [-0.77, 1.69]
20.1 Boys	1	445	Mean Difference (IV, Fixed, 95% CI)	0.70 [-0.89, 2.29]
20.2 Girls	1	410	Mean Difference (IV, Fixed, 95% CI)	0.10 [-1.86, 2.06]
21 BMI z-score at age 11-17 years	1	855	Mean Difference (IV, Fixed, 95% CI)	0.16 [0.01, 0.31]
21.1 Boys	1	445	Mean Difference (IV, Fixed, 95% CI)	0.20 [0.00, 0.40]
21.2 Girls	1	410	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.13, 0.33]
22 % body fat at 11-17 years	1	847	Mean Difference (IV, Fixed, 95% CI)	0.06 [-0.41, 0.52]
22.1 Boys	1	440	Mean Difference (IV, Fixed, 95% CI)	0.0 [-0.54, 0.54]
22.2 Girls	1	407	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.68, 1.08]

Analysis 2.1. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 1 Stillbirth.

Study or subgroup	Balanced protein/energy n/N	Control/ no intervention n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Ceesay 1997	8/652	16/545		34.57%	0.42[0.18,0.97]
Girija 1984	0/10	0/10			Not estimable
Huybregts 2009	12/606	15/596		29.99%	0.79[0.37,1.67]
Mora 1978	2/221	8/222		15.83%	0.25[0.05,1.17]
Rush 1980	9/270	10/276		19.61%	0.92[0.38,2.23]



Study or subgroup	Balanced protein/energy	Control/ no intervention	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
Total (95% CI)	**1759**	**1649**		**100%**	**0.6[0.39,0.94]**
Total events: 31 (Balanced protein/energy), 49 (Control/ no intervention)					
Heterogeneity: Tau²=0; Chi²=3.34, df=3(P=0.34); I²=10.12%					
Test for overall effect: Z=2.26(P=0.02)					
		Balanced protein/energy	0.01 0.1 1 10 100	Control/ no intervention	

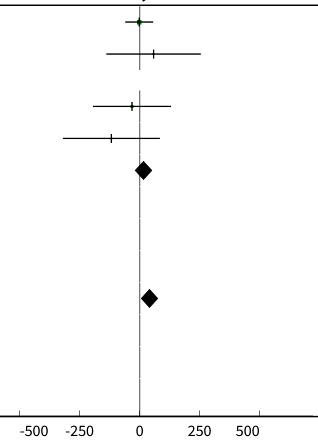
Analysis 2.2. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 2 Neonatal death.

Study or subgroup	Balanced protein/energy	Control/ no intervention	Risk Ratio	Weight	Risk Ratio
	n/N	n/N	M-H, Fixed, 95% CI		M-H, Fixed, 95% CI
Ceesay 1997	15/652	21/545		50.91%	0.6[0.31,1.15]
Girija 1984	0/10	0/10			Not estimable
Huybregts 2009	9/594	10/581		22.5%	0.88[0.36,2.15]
Mora 1978	5/221	9/222		19.98%	0.56[0.19,1.64]
Rush 1980	3/270	3/276		6.6%	1.02[0.21,5.02]
Total (95% CI)	**1747**	**1634**		**100%**	**0.68[0.43,1.07]**
Total events: 32 (Balanced protein/energy), 43 (Control/ no intervention)					
Heterogeneity: Tau²=0; Chi²=0.85, df=3(P=0.84); I²=0%					
Test for overall effect: Z=1.67(P=0.1)					
		Balanced protein/energy	0.1 0.2 0.5 1 2 5 10	Control/ no intervention	

Analysis 2.3. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 3 Birthweight (g).

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Control/ no intervention N	Control/ no intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.3.1 Undernourished women							
Blackwell 1973	55	3082 (401)	55	2942 (307)		5.38%	140[6.53,273.47]
Ceesay 1997	620	2966 (422)	553	2860 (427)		14.53%	106[57.32,154.68]
Girija 1984	10	2939 (376)	10	2676 (451)		0.95%	263[-100.93,626.93]
Huybregts 2009	64	2916 (408)	54	2810 (480)		3.98%	106[-56.42,268.42]
Kardjati 1988	258	2908 (397)	252	2948 (392)		11.57%	-40[-108.48,28.48]
Mora 1978	207	2978 (377)	200	2927 (392)		10.73%	51[-23.76,125.76]
Rush 1980	256	3011 (508)	264	2970 (535)		8.94%	41[-48.65,130.65]
Viegas 1982b	31	3184 (540)	14	3027 (255)		2.17%	157[-75.33,389.33]
Subtotal ***	**1501**		**1402**			**58.25%**	**66.96[13.13,120.78]**
Heterogeneity: Tau²=2725.45; Chi²=15.35, df=7(P=0.03); I²=54.41%							
Test for overall effect: Z=2.44(P=0.01)							
2.3.2 Adequately nourished women							
Blackwell 1973	57	3184 (335)	56	3190 (333)		6.03%	-6[-129.17,117.17]
Elwood 1981	591	3378 (519)	562	3325 (498)		12.99%	53[-5.7,111.7]
				Control/ no intervention	-500 -250 0 250 500	Balanced protein/energy	

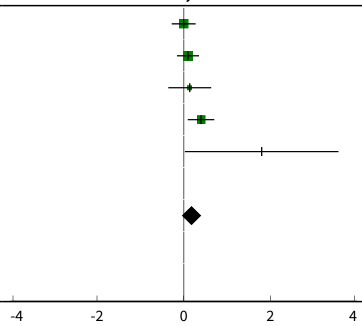
Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Control/ no intervention N	Control/ no intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Huybregts 2009	457	2945 (463)	439	2947 (425)		13.07%	-2[-60.16,56.16]
Ross 1985	62	3229 (432.5)	33	3171 (483)		2.9%	58[-138.84,254.84]
Viegas 1982a	97	3028 (431)	45	3060 (472)		3.98%	-32[-194.4,130.4]
Viegas 1982b	56	3115 (454)	27	3233 (433)		2.77%	-118[-320.03,84.03]
Subtotal ***	**1320**		**1162**			**41.75%**	**15.93[-20.83,52.69]**
Heterogeneity: Tau²=0; Chi²=4.22, df=5(P=0.52); I²=0%							
Test for overall effect: Z=0.85(P=0.4)							
Total ***	**2821**		**2564**			**100%**	**40.96[4.66,77.26]**
Heterogeneity: Tau²=1743.47; Chi²=23.35, df=13(P=0.04); I²=44.33%							
Test for overall effect: Z=2.21(P=0.03)							
Test for subgroup differences: Chi²=2.35, df=1 (P=0.12), I²=57.53%							



Control/ no intervention — Balanced protein/energy

Analysis 2.4. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 4 Birth length (cm).

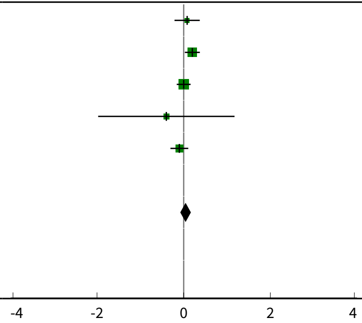
Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Control/ no intervention N	Control/ no intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Ceesay 1997	540	49.3 (2.3)	481	49.3 (2.2)		28.22%	0[-0.28,0.28]
Elwood 1981	562	51.8 (2.2)	535	51.7 (2.1)		30.19%	0.1[-0.15,0.35]
Blackwell 1973	108	49.2 (1.9)	105	49.1 (1.8)		14.43%	0.14[-0.36,0.64]
Huybregts 2009	522	48 (2.6)	497	47.6 (2.4)		25.62%	0.4[0.09,0.71]
Girija 1984	10	47.7 (1.7)	10	45.9 (2.3)		1.54%	1.8[0.03,3.57]
Total ***	**1742**		**1628**			**100%**	**0.18[-0.04,0.4]**
Heterogeneity: Tau²=0.03; Chi²=7.14, df=4(P=0.13); I²=44.01%							
Test for overall effect: Z=1.58(P=0.11)							



Control/ no intervention — Balanced protein/energy

Analysis 2.5. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 5 Birth head circumference (cm).

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Control/ no intervention N	Control/ no intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Blackwell 1973	108	33.4 (1.1)	105	33.4 (1.1)		14.18%	0.08[-0.21,0.37]
Ceesay 1997	533	33.6 (1.4)	475	33.4 (1.4)		29.38%	0.2[0.03,0.37]
Elwood 1981	561	35.9 (1.4)	536	35.9 (1.3)		32.16%	0[-0.16,0.16]
Girija 1984	6	37.1 (1.6)	9	37.5 (1.4)		0.6%	-0.4[-1.97,1.17]
Huybregts 2009	522	33.4 (1.8)	497	33.5 (1.6)		23.67%	-0.1[-0.31,0.11]
Total ***	**1730**		**1622**			**100%**	**0.04[-0.08,0.17]**
Heterogeneity: Tau²=0.01; Chi²=5.65, df=4(P=0.23); I²=29.22%							
Test for overall effect: Z=0.7(P=0.48)							



Control/ no intervention — Balanced protein/energy

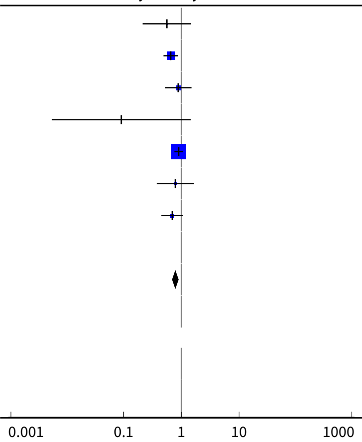
Analysis 2.6. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 6 Small-for-gestational age.

Study or subgroup	Balanced protein/energy n/N	Control/ no intervention n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Blackwell 1973	6/94	10/88		2.71%	0.56[0.21,1.48]
Ceesay 1997	69/620	94/553		26.03%	0.65[0.49,0.87]
Elwood 1981	25/591	27/562		7.25%	0.88[0.52,1.5]
Girija 1984	0/10	5/10		1.44%	0.09[0.01,1.45]
Huybregts 2009	167/518	177/494		47.46%	0.9[0.76,1.07]
Mora 1978	12/177	14/162		3.83%	0.78[0.37,1.65]
Rush 1980	30/265	43/264		11.28%	0.7[0.45,1.07]
Total (95% CI)	**2275**	**2133**		**100%**	**0.79[0.69,0.9]**

Total events: 309 (Balanced protein/energy), 370 (Control/ no intervention)

Heterogeneity: Tau²=0; Chi²=7.19, df=6(P=0.3); I²=16.49%

Test for overall effect: Z=3.55(P=0)



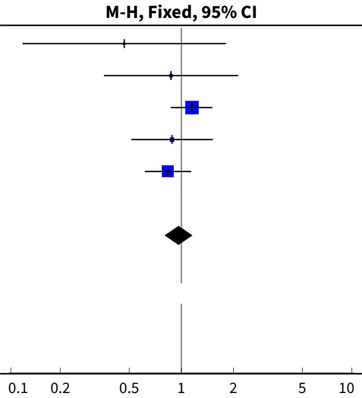
Analysis 2.7. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 7 Preterm birth.

Study or subgroup	Balanced protein/energy n/N	Control/ no intervention n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Blackwell 1973	3/94	6/88		3.28%	0.47[0.12,1.81]
Elwood 1981	9/557	10/539		5.38%	0.87[0.36,2.13]
Huybregts 2009	92/576	79/567		42.16%	1.15[0.87,1.51]
Mora 1978	22/221	25/222		13.21%	0.88[0.51,1.52]
Rush 1980	56/256	69/264		35.97%	0.84[0.62,1.14]
Total (95% CI)	**1704**	**1680**		**100%**	**0.96[0.8,1.16]**

Total events: 182 (Balanced protein/energy), 189 (Control/ no intervention)

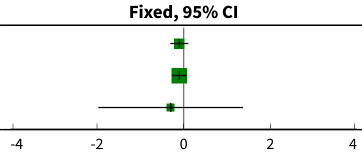
Heterogeneity: Tau²=0; Chi²=3.55, df=4(P=0.47); I²=0%

Test for overall effect: Z=0.39(P=0.69)



Analysis 2.8. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 8 Gestational age (week).

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Control/ no intervention N	Control/ no intervention Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Ceesay 1997	359	39.9 (1.4)	316	40 (1.4)		32.6%	-0.1[-0.31,0.11]
Elwood 1981	557	40 (1.5)	539	40.1 (1.4)		47.11%	-0.1[-0.27,0.07]
Girija 1984	10	36.5 (2)	10	36.8 (1.9)		0.5%	-0.3[-1.97,1.37]



Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Control/ no intervention N	Control/ no intervention Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Huybregts 2009	576	38.9 (3)	567	39.1 (2.5)		13.57%	-0.2[-0.52,0.12]
Mora 1978	221	39.4 (2.5)	222	39.3 (2.9)		5.47%	0.1[-0.4,0.6]
Ross 1985	62	38.9 (2.5)	32	38.9 (3.5)		0.75%	0[-1.36,1.36]
Total ***	**1785**		**1686**			**100%**	**-0.1[-0.22,0.01]**
Heterogeneity: Tau²=0; Chi²=1.05, df=5(P=0.96); I²=0%							
Test for overall effect: Z=1.71(P=0.09)							

Control/ no intervention -4 -2 0 2 4 Balanced protein/energy

Analysis 2.9. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 9 Weekly gestational weight gain (g/week).

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Control/ no intervention N	Control/ no intervention Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Blackwell 1973	107	193 (71)	105	198 (64)		20.63%	-5[-23.19,13.19]
Ceesay 1997	304	283 (158)	266	271.3 (162.7)		17.47%	11.67[-14.74,38.08]
Girija 1984	10	325 (100)	10	329.2 (175)		2.42%	-4.2[-129.12,120.72]
Kardjati 1988	174	168.3 (146.7)	180	158.3 (145.8)		15.93%	10[-20.48,40.48]
Mora 1978	190	322.5 (157.6)	179	260 (126)		16.47%	62.52[33.49,91.55]
Ross 1985	62	433.5 (203.5)	33	465.6 (201.1)		4.66%	-32.11[-117.38,53.16]
Rush 1980	246	431.3 (199.8)	255	413.1 (204.3)		14.18%	18.2[-17.19,53.59]
Viegas 1982a	97	411 (220.4)	45	335 (258)		4.49%	76[-11.21,163.21]
Viegas 1982b	87	437.6 (291)	41	402 (247)		3.75%	35.6[-61.64,132.84]
Total ***	**1277**		**1114**			**100%**	**18.63[-1.81,39.07]**
Heterogeneity: Tau²=441.14; Chi²=18.41, df=8(P=0.02); I²=56.54%							
Test for overall effect: Z=1.79(P=0.07)							

Control/ no intervention -1000 -500 0 500 1000 Balanced protein/energy

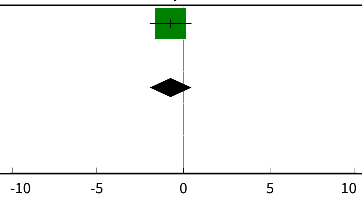
Analysis 2.10. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 10 Pre-eclampsia.

Study or subgroup	Balanced protein/energy n/N	No supplementation n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Girija 1984	0/10	0/10			Not estimable
Mora 1978	25/221	17/222		100%	1.48[0.82,2.66]
Total (95% CI)	**231**	**232**		**100%**	**1.48[0.82,2.66]**
Total events: 25 (Balanced protein/energy), 17 (No supplementation)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.3(P=0.19)					

Balanced protein/energy 0.1 0.2 0.5 1 2 5 10 Control/ no intervention

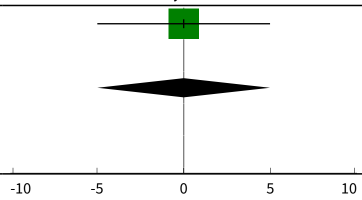
Analysis 2.11. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 11 Bayley mental score at 1 year.

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Rush 1980	197	98.7 (6.2)	214	99.4 (6.2)		100%	-0.74[-1.95,0.47]
Total ***	**197**		**214**			**100%**	**-0.74[-1.95,0.47]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.2(P=0.23)							



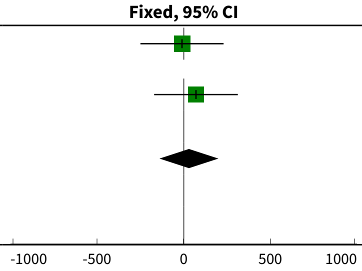
Analysis 2.12. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 12 IQ at 5 years.

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Blackwell 1973	64	89 (15.3)	89	89 (15.8)		100%	0[-4.98,4.98]
Total ***	**64**		**89**			**100%**	**0[-4.98,4.98]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							



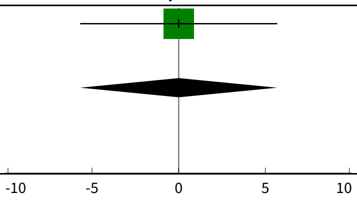
Analysis 2.13. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 13 Weight at 1 year (g).

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Blackwell 1973	97	8125.8 (861.7)	102	8135.5 (864.1)		50.29%	-9.67[-249.52,230.18]
Rush 1980	207	9568 (1267)	217	9497 (1267)		49.71%	71[-170.26,312.26]
Total ***	**304**		**319**			**100%**	**30.43[-139.67,200.53]**
Heterogeneity: Tau^2=0; Chi^2=0.22, df=1(P=0.64); I^2=0%							
Test for overall effect: Z=0.35(P=0.73)							



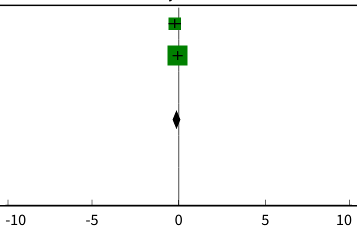
Analysis 2.14. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 14 Length at 1 year (cm).

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Rush 1980	208	74.7 (30)	220	74.7 (30)		100%	0[-5.69,5.69]
Total ***	**208**		**220**			**100%**	**0[-5.69,5.69]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							



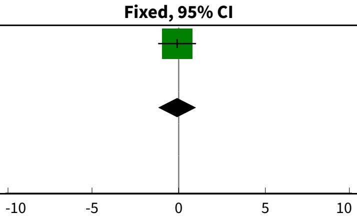
Analysis 2.15. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 15 Head circumference at 1 year (cm).

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Blackwell 1973	98	44.6 (1.4)	102	44.8 (1.3)		38.77%	-0.23[-0.59,0.13]
Rush 1980	208	46 (1.5)	219	46 (1.5)		61.23%	-0.06[-0.35,0.23]
Total ***	**306**		**321**			**100%**	**-0.13[-0.35,0.1]**
Heterogeneity: $Tau^2=0$; $Chi^2=0.51$, df=1(P=0.47); $I^2=0\%$							
Test for overall effect: Z=1.09(P=0.28)							



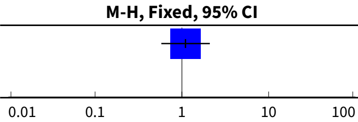
Analysis 2.16. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 16 Duration of labour (hours).

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	No supplementation N	No supplementation Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Mora 1978	184	6.2 (5.6)	161	6.3 (4.7)		100%	-0.09[-1.18,1]
Total ***	**184**		**161**			**100%**	**-0.09[-1.18,1]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.16(P=0.87)							



Analysis 2.17. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 17 Mortality from birth to age 12 months.

Study or subgroup	Balanced protein/energy n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Huybregts 2009	19/515	17/508		100%	1.1[0.58,2.1]



Study or subgroup	Balanced protein/energy n/N	Control n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Total (95% CI)	**515**	**508**		**100%**	**1.1[0.58,2.1]**
Total events: 19 (Balanced protein/energy), 17 (Control)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.3(P=0.77)					

Balanced protein/energy 0.01 0.1 1 10 100 Control

Analysis 2.18. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 18 Maternal weight 4 weeks' postpartum (kg).

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	Low energy diet N	Low energy diet Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Kardjati 1988	176	43.2 (4.5)	178	44.1 (5.3)		100%	-0.9[-1.92,0.12]
Total ***	**176**		**178**			**100%**	**-0.9[-1.92,0.12]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%							
Test for overall effect: Z=1.73(P=0.08)							

Low energy diet -10 -5 0 5 10 Balanced protein/energy

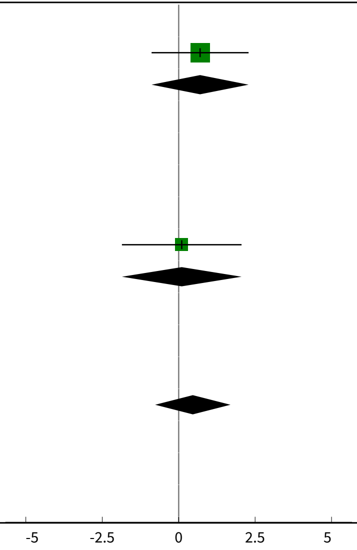
Analysis 2.19. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 19 Height at age 11-17 years (cm).

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	No supplementation N	No supplementation Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
2.19.1 Boys							
Ceesay 1997	230	150.7 (10.5)	215	150.1 (11)		46.94%	0.6[-1.4,2.6]
Subtotal ***	**230**		**215**			**46.94%**	**0.6[-1.4,2.6]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.59(P=0.56)							
2.19.2 Girls							
Ceesay 1997	206	151.6 (9.2)	204	152.8 (9.4)		53.06%	-1.2[-3,0.6]
Subtotal ***	**206**		**204**			**53.06%**	**-1.2[-3,0.6]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.31(P=0.19)							
Total ***	**436**		**419**			**100%**	**-0.36[-2.12,1.41]**
Heterogeneity: Tau²=0.68; Chi²=1.72, df=1(P=0.19); I²=41.79%							
Test for overall effect: Z=0.4(P=0.69)							
Test for subgroup differences: Chi²=1.72, df=1 (P=0.19), I²=41.79%							

No supplementation -5 -2.5 0 2.5 5 Balanced protein/energy

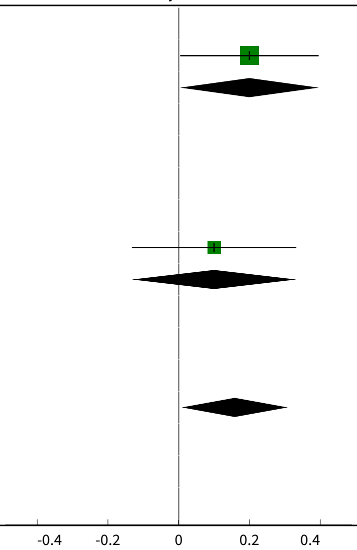
Analysis 2.20. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 20 Weight at 11-17 years (kg).

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	No supplementation N	No supplementation Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
2.20.1 Boys							
Ceesay 1997	230	37.5 (8)	215	36.8 (9)		60.34%	0.7[-0.89,2.29]
Subtotal ***	**230**		**215**			**60.34%**	**0.7[-0.89,2.29]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.86(P=0.39)							
2.20.2 Girls							
Ceesay 1997	206	41.3 (10.5)	204	41.2 (9.7)		39.66%	0.1[-1.86,2.06]
Subtotal ***	**206**		**204**			**39.66%**	**0.1[-1.86,2.06]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.1(P=0.92)							
Total ***	**436**		**419**			**100%**	**0.46[-0.77,1.69]**
Heterogeneity: Tau²=0; Chi²=0.22, df=1(P=0.64); I²=0%							
Test for overall effect: Z=0.73(P=0.46)							
Test for subgroup differences: Chi²=0.22, df=1 (P=0.64), I²=0%							



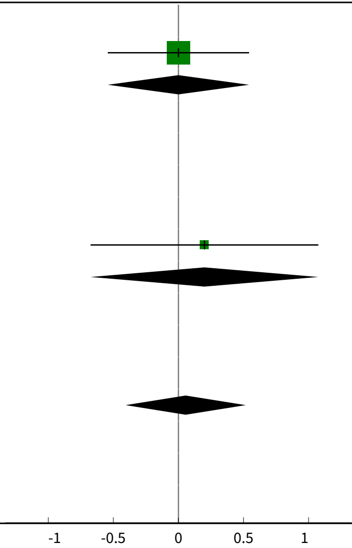
Analysis 2.21. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 21 BMI z-score at age 11-17 years.

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	No supplementation N	No supplementation Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
2.21.1 Boys							
Ceesay 1997	230	-1.4 (1)	215	-1.6 (1.1)		58.48%	0.2[0,0.4]
Subtotal ***	**230**		**215**			**58.48%**	**0.2[0,0.4]**
Heterogeneity: Not applicable							
Test for overall effect: Z=2(P=0.05)							
2.21.2 Girls							
Ceesay 1997	206	-1 (1.2)	204	-1.1 (1.2)		41.52%	0.1[-0.13,0.33]
Subtotal ***	**206**		**204**			**41.52%**	**0.1[-0.13,0.33]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.84(P=0.4)							
Total ***	**436**		**419**			**100%**	**0.16[0.01,0.31]**
Heterogeneity: Tau²=0; Chi²=0.42, df=1(P=0.52); I²=0%							
Test for overall effect: Z=2.07(P=0.04)							
Test for subgroup differences: Chi²=0.42, df=1 (P=0.52), I²=0%							



Analysis 2.22. Comparison 2 Balanced protein/energy supplementation versus control or no intervention in pregnancy, Outcome 22 % body fat at 11-17 years.

Study or subgroup	Balanced protein/energy N	Balanced protein/energy Mean(SD)	No supplementation N	No supplementation Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
2.22.1 Boys							
Ceesay 1997	226	12.6 (2.8)	214	12.6 (3)		72.2%	0[-0.54,0.54]
Subtotal ***	**226**		**214**			**72.2%**	**0[-0.54,0.54]**
Heterogeneity: Not applicable							
Test for overall effect: Not applicable							
2.22.2 Girls							
Ceesay 1997	204	19.5 (4.7)	203	19.3 (4.3)		27.8%	0.2[-0.68,1.08]
Subtotal ***	**204**		**203**			**27.8%**	**0.2[-0.68,1.08]**
Heterogeneity: Tau²=0; Chi²=0, df=0(P<0.0001); I²=100%							
Test for overall effect: Z=0.45(P=0.65)							
Total ***	**430**		**417**			**100%**	**0.06[-0.41,0.52]**
Heterogeneity: Tau²=0; Chi²=0.14, df=1(P=0.7); I²=0%							
Test for overall effect: Z=0.24(P=0.81)							
Test for subgroup differences: Chi²=0.14, df=1 (P=0.7), I²=0%							

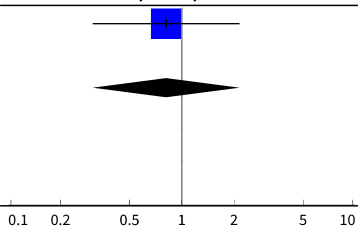


Comparison 3. High protein supplementation versus low or no protein supplements in pregnancy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Stillbirth	1	529	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.31, 2.15]
2 Neonatal death	1	529	Risk Ratio (M-H, Fixed, 95% CI)	2.78 [0.75, 10.36]
3 Small-for-gestational age	1	505	Risk Ratio (M-H, Fixed, 95% CI)	1.58 [1.03, 2.41]
4 Birthweight (g)	1	504	Mean Difference (IV, Fixed, 95% CI)	-73.0 [-171.26, 25.26]
5 Preterm birth	1	505	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.83, 1.56]
6 Weekly gestational weight gain (g/week)	1	486	Mean Difference (IV, Fixed, 95% CI)	4.5 [-33.55, 42.55]
7 Weight at 1 year (g)	1	409	Mean Difference (IV, Fixed, 95% CI)	61.0 [-184.60, 306.60]
8 Length at 1 year (cm)	1	412	Mean Difference (IV, Fixed, 95% CI)	0.20 [-5.59, 5.99]
9 Head circumference at 1 year	1	412	Mean Difference (IV, Fixed, 95% CI)	0.11 [-0.19, 0.41]
10 Bayley mental score at 1 year	1	396	Mean Difference (IV, Fixed, 95% CI)	0.32 [-0.91, 1.55]

Analysis 3.1. Comparison 3 High protein supplementation versus low or no protein supplements in pregnancy, Outcome 1 Stillbirth.

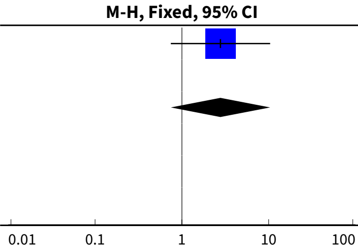
Study or subgroup	High protein n/N	Vitamins/minerals n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rush 1980	7/259	9/270		100%	0.81[0.31,2.15]
Total (95% CI)	**259**	**270**		**100%**	**0.81[0.31,2.15]**
Total events: 7 (High protein), 9 (Vitamins/minerals)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.42(P=0.67)					



High protein | Vitamins/minerals

Analysis 3.2. Comparison 3 High protein supplementation versus low or no protein supplements in pregnancy, Outcome 2 Neonatal death.

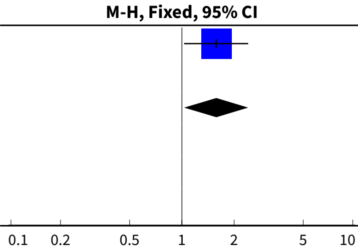
Study or subgroup	High protein n/N	Vitamins/minerals n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rush 1980	8/259	3/270		100%	2.78[0.75,10.36]
Total (95% CI)	**259**	**270**		**100%**	**2.78[0.75,10.36]**
Total events: 8 (High protein), 3 (Vitamins/minerals)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.52(P=0.13)					



High protein | Vitamins/minerals

Analysis 3.3. Comparison 3 High protein supplementation versus low or no protein supplements in pregnancy, Outcome 3 Small-for-gestational age.

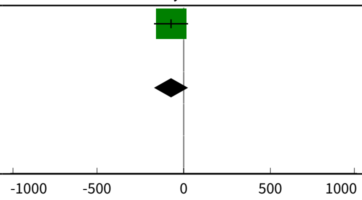
Study or subgroup	High protein n/N	Vitamins/minerals n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rush 1980	46/249	30/256		100%	1.58[1.03,2.41]
Total (95% CI)	**249**	**256**		**100%**	**1.58[1.03,2.41]**
Total events: 46 (High protein), 30 (Vitamins/minerals)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.1(P=0.04)					



High protein | Vitamins/minerals

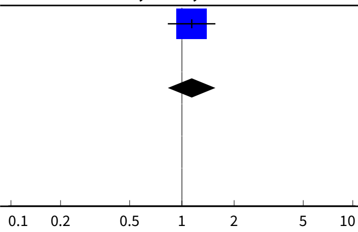
Analysis 3.4. Comparison 3 High protein supplementation versus low or no protein supplements in pregnancy, Outcome 4 Birthweight (g).

Study or subgroup	High protein N	High protein Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Rush 1980	248	2938 (611)	256	3011 (508)		100%	-73[-171.26,25.26]
Total ***	**248**		**256**			**100%**	**-73[-171.26,25.26]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.46(P=0.15)							



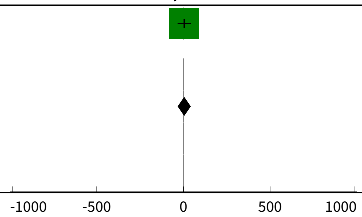
Analysis 3.5. Comparison 3 High protein supplementation versus low or no protein supplements in pregnancy, Outcome 5 Preterm birth.

Study or subgroup	High protein n/N	Vitamins/minerals n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Rush 1980	62/249	56/256		100%	1.14[0.83,1.56]
Total (95% CI)	**249**	**256**		**100%**	**1.14[0.83,1.56]**
Total events: 62 (High protein), 56 (Vitamins/minerals)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.8(P=0.42)					



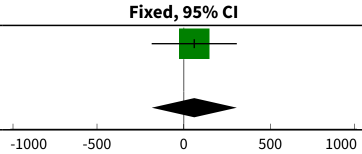
Analysis 3.6. Comparison 3 High protein supplementation versus low or no protein supplements in pregnancy, Outcome 6 Weekly gestational weight gain (g/week).

Study or subgroup	High protein N	High protein Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Rush 1980	240	435.8 (227)	246	431.3 (199.8)		100%	4.5[-33.55,42.55]
Total ***	**240**		**246**			**100%**	**4.5[-33.55,42.55]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.23(P=0.82)							



Analysis 3.7. Comparison 3 High protein supplementation versus low or no protein supplements in pregnancy, Outcome 7 Weight at 1 year (g).

Study or subgroup	High protein N	High protein Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Rush 1980	202	9629 (1267)	207	9568 (1267)		100%	61[-184.6,306.6]
Total ***	**202**		**207**			**100%**	**61[-184.6,306.6]**



Study or subgroup	High protein N	High protein Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Heterogeneity: Not applicable							
Test for overall effect: Z=0.49(P=0.63)							

Vitamins/minerals -1000 -500 0 500 1000 High protein

Analysis 3.8. Comparison 3 High protein supplementation versus low or no protein supplements in pregnancy, Outcome 8 Length at 1 year (cm).

Study or subgroup	High protein N	High protein Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Rush 1980	204	74.9 (30)	208	74.7 (30)		100%	0.2[-5.59,5.99]
Total ***	**204**		**208**			**100%**	**0.2[-5.59,5.99]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.07(P=0.95)							

Vitamins/minerals -10 -5 0 5 10 High protein

Analysis 3.9. Comparison 3 High protein supplementation versus low or no protein supplements in pregnancy, Outcome 9 Head circumference at 1 year.

Study or subgroup	High protein N	High protein Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Rush 1980	204	46.1 (1.5)	208	46 (1.5)		100%	0.11[-0.19,0.41]
Total ***	**204**		**208**			**100%**	**0.11[-0.19,0.41]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.73(P=0.47)							

Vitamins/minerals -10 -5 0 5 10 High protein

Analysis 3.10. Comparison 3 High protein supplementation versus low or no protein supplements in pregnancy, Outcome 10 Bayley mental score at 1 year.

Study or subgroup	High protein N	High protein Mean(SD)	Vitamins/minerals N	Vitamins/minerals Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Rush 1980	199	99 (6.2)	197	98.7 (6.2)		100%	0.32[-0.91,1.55]
Total ***	**199**		**197**			**100%**	**0.32[-0.91,1.55]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.51(P=0.61)							

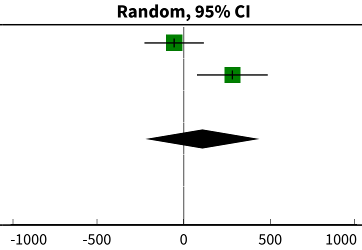
Vitamins/minerals -10 -5 0 5 10 High protein

Comparison 4. Isocaloric balanced protein supplementation versus protein replaced an equal quantity of non-protein energy in pregnancy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Birthweight (g)	2	184	Mean Difference (IV, Random, 95% CI)	108.25 [-220.89, 437.40]
2 Weekly gestational weight gain (g/week)	2	184	Mean Difference (IV, Random, 95% CI)	110.45 [-82.87, 303.76]

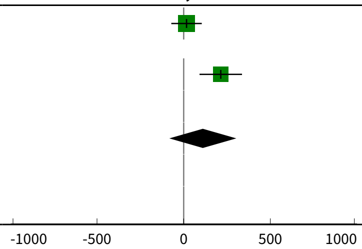
Analysis 4.1. Comparison 4 Isocaloric balanced protein supplementation versus protein replaced an equal quantity of non-protein energy in pregnancy, Outcome 1 Birthweight (g).

Study or subgroup	Isocaroric balanced N	Isocaroric balanced Mean(SD)	Iron/ Vitamins N	Iron/ Vitamins Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Viegas 1982a	47	3000 (417)	50	3055 (444)		51.41%	-55[-226.34,116.34]
Viegas 1982b	44	3415 (471)	43	3134 (499)		48.59%	281[77.01,484.99]
Total ***	**91**		**93**			**100%**	**108.25[-220.89,437.4]**
Heterogeneity: Tau²=47210.48; Chi²=6.11, df=1(P=0.01); I²=83.64%							
Test for overall effect: Z=0.64(P=0.52)							



Analysis 4.2. Comparison 4 Isocaloric balanced protein supplementation versus protein replaced an equal quantity of non-protein energy in pregnancy, Outcome 2 Weekly gestational weight gain (g/week).

Study or subgroup	Isocaroric balanced N	Isocaroric balanced Mean(SD)	Iron/ vitamins N	Iron/ vitamins Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Viegas 1982a	47	419.5 (226.2)	50	403 (214.9)		52.43%	16.5[-71.42,104.42]
Viegas 1982b	44	494 (298.5)	43	280 (284.7)		47.57%	214[91.44,336.56]
Total ***	**91**		**93**			**100%**	**110.45[-82.87,303.76]**
Heterogeneity: Tau²=16541.97; Chi²=6.59, df=1(P=0.01); I²=84.82%							
Test for overall effect: Z=1.12(P=0.26)							



WHAT'S NEW

Date	Event	Description
31 January 2015	New citation required and conclusions have changed	Antenatal nutritional education appears to reduce low birthweight and, in a subgroup analysis of birthweight, there was an increase in birthweight among undernourished women. However, these conclusions are based on two small trials of low quality.

Date	Event	Description
31 January 2015	New search has been performed	Search updated: two new trials included (Jahan 2013; Oaks 2014) and 16 excluded. Methods updated and GRADE 'Summary of findings' tables have been incorporated.

HISTORY

Protocol first published: Issue 2, 1997
Review first published: Issue 2, 1997

Date	Event	Description
22 July 2011	New search has been performed	A new team of review authors prepared this updated review. Search updated. Ten new trials identified: one has been included (Huybregts 2009) and eight excluded (Aaltonen 2011; Behrman 2009; Eneroth 2010; Fung 2010; Guelinckx 2010; Laitinen 2009; Luoto 2010; Rasmussen 2010). One trial is ongoing (Moore 2011). The methods section has changed to include only RCTs and exclude quasi-RCTs or cross-over trials. Six trials (Atton 1990; Campbell Brown 1983; Hankin 1962; Iyengar 1967; Mardones-Santander 1988; Ross 1938), previously included in the analysis, have now been excluded because of their quasi-RCT design. The current inclusion of information about caloric restriction for women who are overweight or obese only serves to increase confusion as it requires discussion of the clinical implications for two different populations, thus we excluded the outcome of "energy and protein restriction in women who were overweight or showed high weight gain". Five trials (Badrawi 1993; Campbell 1975; Campbell 1983; Guelinckx 2010; Wolff 2008), previously included in the analysis, have now been excluded because the target population was out of focus. Three reports from an updated search in July 2012 have been added to Studies awaiting classification for consideration at the next update.
22 July 2011	New citation required and conclusions have changed	Nutritional advice to increase energy and protein intakes is associated with significant increases in protein intake. Balanced energy and protein supplementation is associated with significant increases in mean birthweight, although this difference disappeared after excluding one trial of weekly gestational weight gain. The other findings have not changed.
22 December 2009	New search has been performed	Search updated. One new trial included (Wolff 2008) and two excluded (Aaltonen 2005; Kinra 2008).
2 September 2008	Amended	Converted to new review format.

Date	Event	Description
30 November 2006	New search has been performed	New search conducted in November 2006 identified eight new reports to evaluate (Anderson 1995; an additional report of Clapp 1997; Fard 2004; Kaseb 2002; Moses 2006; additional reports of Lechtig 1975; Woods 1995), none of which were eligible for inclusion in the update. We have substantially updated the Methods of the review section.
1 August 2003	New search has been performed	This updated review combines and replaces five previous Cochrane reviews entitled ''Balanced protein/energy supplementation in pregnancy', 'Energy/protein restriction for high weight-for-height or weight gain during pregnancy' (CDSR 1996a), 'High protein supplementation in pregnancy' (CDSR 1996b), 'Isocaloric balanced protein supplementation in pregnancy' (CDSR 1996c) and 'Nutritional advice in pregnancy' (CDSR 1996d). This combination was suggested by colleagues in the field, the PCG editors, and by the Cochrane Pregnancy and Childbirth Group's Consumer Panel.

CONTRIBUTIONS OF AUTHORS

Erika Ota (EO) and Hiroyuki Hori (HH) independently rated all the included studies for the 'Risk of bias' tables from the previous review. EO, HH and Rintaro Mori (RM) jointly applied the study selection criteria and extracted data from the included studies for updated trials. EO edited the updated results. HH, RT, RM and Diane Farrar revised the manuscript. All the authors read and approved the final version to be published.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- The Grant of National Center for Child Health and Development 27B-10, 26A-5, Japan.

External sources

- Ministry of Health, Labour and Welfare, Japan.

  Health Labour Sciences Research Grant (No.26260101, No.13800128)
- Japan Agency for Medical Research and development, Japan.

  AMED No.27300101
- UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), Department of Reproductive Health and Research, World Health Organization, Switzerland.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

The methods section has changed to include only randomised controlled trials (RCTs) and to exclude quasi-RCTs or cross-over trials. Six trials (Atton 1990; Campbell Brown 1983; Hankin 1962; Iyengar 1967; Mardones-Santander 1988; Ross 1938), previously included in the analysis, have now been excluded because of their quasi-RCT design. The current inclusion of information about caloric restriction for women who are overweight or obese only serves to increase confusion as it requires discussion of the clinical implications for two different populations, thus we excluded the outcome of "energy and protein restriction in women who were overweight or showed high weight gain". Five trials (Badrawi 1993; Campbell 1975; Campbell 1983; Guelinckx 2010; Wolff 2008), previously included in the analysis, have now been excluded because the target population was out of scope for this review. Six trials (Atton 1990; Campbell Brown 1983; Hankin 1962; Iyengar 1967; Mardones-Santander 1988; Ross 1938), previously included in the review, have now been excluded because of their quasi-RCT design.

We have added subgroup analysis that were not specified in the original protocol. Observational studies (IOM 1990; Kramer 1987) suggest a stronger association between gestational weight gain and fetal growth in women who were under-nourished before pregnancy. We therefore stratified the analysis of the effects on mean birthweight into those trials in which the majority of women had low pre-pregnancy (or early pregnancy) weight (Ceesay 1997; Girija 1984; Kardjati 1988; Mora 1978; Rush 1980), and those in which the participants appeared adequately nourished (Elwood 1981; Ross 1985; Viegas 1982a). For the Taiwan trial (Blackwell 1973) and two others (Huybregts 2009; Viegas 1982b), within-trial stratification was possible, based on data contained in the published reports. Because growth varies with differences in sex (de Onis 2007), it is desirable to compare growth between groups after adjusting for variations by sex. We conducted subgroup analysis separated by sexes for follow-up results of balanced protein and energy supplementation at the age of 11 to 17 years (height, weight, systolic blood pressure, diastolic blood pressure, BMI z-score, and body fat).

INDEX TERMS

Medical Subject Headings (MeSH)

*Energy Intake; Diet [*methods]; Dietary Proteins [*administration & dosage]; Dietary Supplements; Fetal Development; Pregnancy Outcome; Premature Birth [prevention & control]; Prenatal Care [*methods]; Prenatal Education [*methods]; Randomized Controlled Trials as Topic; Stillbirth; Weight Gain

MeSH check words

Female; Humans; Pregnancy