World Health Organization

Web supplement

WHO recommendations on antenatal care for a positive pregnancy experience: evidence base*

* The full guideline document and web annexes are available at:
http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/anc-positive-pregnancy-experience/en/

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WHO recommendations on antenatal care for a positive pregnancy experience: evidence base

Acronyms and abbreviations

ANC	antenatal care
CI	confidence interval
EB	evidence base
Hb	haemoglobin
MD	mean difference
RCT	randomized controlled trial
RR	relative risk
UNIMMAP	United Nations international multiple micronutrient preparation

A. Nutritional interventions

A.1. Dietary interventions

EB Table A.1.1: All diet and/or physical activity/exercise interventions versus control (standard or other care)

Source: Muktabhant B, Lawrie TA, Lumbiganon P, Laopaiboon M. Diet or exercise, or both, for preventing excessive weight gain in pregnancy. Cochrane Database Syst Rev. 2015;(6):CD007145.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	All diet and/or exercise interventions	Standard/other care	Relative (95% CI)	Absolute	
Pre-eclampsia – all interventions											
15	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	170/2783 (6.1%)	167/2547 (6.6%)	RR 0.95 (0.77 to 1.16)	3 fewer per 1000 (from 15 fewer to 10 more)	⊕⊕⊕⊕ HIGH
Pre-eclampsia – diet and exercise counselling											
7	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[3]	89/1624 (5.5%)	88/1515 (5.8%)	RR 0.99 (0.74 to 1.31)	1 fewer per 1000 (from 15 fewer to 18 more)	⊕◯◯◯ VERY LOW
Pre-eclampsia – supervised exercise											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	25/540 (4.6%)	22/484 (4.5%)	RR 0.91 (0.52 to 1.6)	4 fewer per 1000 (from 22 fewer to 27 more)	⊕⊕⊕◯ MODERATE
Pre-eclampsia – unsupervised exercise											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	6/143 (4.2%)	2/86 (2.3%)	RR 1.6 (0.38 to 6.73)	14 more per 1000 (from 14 fewer to 133 more)	⊕◯◯◯ VERY LOW
Pre-eclampsia – supervised exercise plus diet											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	23/150 (15.3%)	28/154 (18.2%)	RR 0.84 (0.51 to 1.4)	29 fewer per 1000 (from 89 fewer to 73 more)	⊕⊕⊕◯ MODERATE
Pre-eclampsia – diet counselling/other											
4	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	27/326 (8.3%)	27/308 (8.8%)	RR 0.9 (0.54 to 1.48)	9 fewer per 1000 (from 40 fewer to 42 more)	⊕⊕◯◯ LOW

EB Table A.1.1: All diet and/or physical activity/exercise interventions versus control (standard or other care) (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**All diet and/or exercise interventions**	**Standard/other care**	**Relative (95% CI)**	**Absolute**	
Caesarean section – all interventions											
28	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[3]	1053/3839 (27.4%)	1066/3695 (28.8%)	RR 0.95 (0.88 to 1.03)	14 fewer per 1000 (from 35 fewer to 9 more)	⊕⊕◯◯ LOW
Caesarean section – diet intervention											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,4]	none	15/68 (22.1%)	14/65 (21.5%)	RR 0.99 (0.33 to 3.01)	2 fewer per 1000 (from 144 fewer to 433 more)	⊕⊕◯◯ LOW
Caesarean section – diet and exercise counselling											
9	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	539/1761 (30.6%)	566/1645 (34.4%)	RR 0.87 (0.75 to 1.01)	45 fewer per 1000 (from 86 fewer to 3 more)	⊕⊕⊕⊕ HIGH
Caesarean section – unsupervised exercise intervention											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	56/143 (39.2%)	34/86 (39.5%)	RR 0.91 (0.53 to 1.59)	36 fewer per 1000 (from 186 fewer to 233 more)	⊕⊕◯◯ LOW
Caesarean section – supervised exercise											
8	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	215/1171 (18.4%)	240/1234 (19.4%)	RR 0.96 (0.82 to 1.11)	8 fewer per 1000 (from 35 fewer to 21 more)	⊕⊕⊕◯ MODERATE
Caesarean section – supervised exercise plus diet											
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	42/309 (13.6%)	44/298 (14.8%)	RR 1 (0.69 to 1.45)	0 fewer per 1000 (from 46 fewer to 66 more)	⊕⊕⊕◯ MODERATE
Caesarean section – diet counselling/other											
5	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	186/387 (48.1%)	168/367 (45.8%)	RR 1.06 (0.93 to 1.21)	27 more per 1000 (from 32 fewer to 96 more)	⊕⊕⊕◯ MODERATE
Excessive weight gain – all interventions											
24	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1372/3621 (37.9%)	1573/3475 (45.3%)	RR 0.8 (0.73 to 0.87)	91 fewer per 1000 (from 59 fewer to 122 fewer)	⊕⊕⊕⊕ HIGH

EB Table A.1.1: All diet and/or physical activity/exercise interventions versus control (standard or other care) (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**All diet and/or exercise interventions**	**Standard/other care**	**Relative (95% CI)**	**Absolute**	
Excessive weight gain – diet intervention											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	150/412 (36.4%)	200/423 (47.3%)	RR 0.77 (0.66 to 0.91)	109 fewer per 1000 (from 43 fewer to 161 fewer)	⊕⊕⊕⊕ HIGH
Excessive weight gain – diet and exercise counselling											
9	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	729/1628 (44.8%)	735/1516 (48.5%)	RR 0.86 (0.75 to 0.98)	68 fewer per 1000 (from 10 fewer to 121 fewer)	⊕⊕⊕◯ MODERATE
Excessive weight gain – unsupervised exercise											
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	154/335 (46%)	146/268 (54.5%)	RR 0.83 (0.71 to 0.97)	93 fewer per 1000 (from 16 fewer to 158 fewer)	⊕⊕⊕⊕ HIGH
Excessive weight gain – supervised exercise											
3	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	157/621 (25.3%)	231/677 (34.1%)	RR 0.75 (0.63 to 0.89)	85 fewer per 1000 (from 38 fewer to 126 fewer)	⊕⊕⊕◯ MODERATE
Excessive weight gain – supervised exercise and diet											
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	121/353 (34.3%)	162/336 (48.2%)	RR 0.71 (0.59 to 0.85)	140 fewer per 1000 (from 72 fewer to 198 fewer)	⊕⊕⊕⊕ HIGH
Excessive weight gain – diet counselling/other											
3	randomized trials	no serious risk of bias	serious[5]	no serious indirectness	serious[2]	none	61/272 (22.4%)	99/255 (38.8%)	RR 0.46 (0.17 to 1.23)	210 fewer per 1000 (from 322 fewer to 89 more)	⊕⊕◯◯ LOW
Preterm birth – all interventions											
16	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[3]	143/3025 (4.7%)	166/2898 (5.7%)	RR 0.91 (0.68 to 1.22)	5 fewer per 1000 (from 18 fewer to 13 more)	⊕⊕◯◯ LOW
Preterm birth – diet intervention											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,4]	none	4/396 (1%)	12/408 (2.9%)	RR 0.33 (0.11 to 1.02)	20 fewer per 1000 (from 26 fewer to 1 more)	⊕⊕◯◯ LOW

EB Table A.1.1: All diet and/or physical activity/exercise interventions versus control (standard or other care) (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**All diet and/or exercise interventions**	**Standard/other care**	**Relative (95% CI)**	**Absolute**	
Preterm birth – diet and exercise counselling											
7	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[3]	112/1619 (6.9%)	134/1551 (8.6%)	RR 0.95 (0.6 to 1.51)	4 fewer per 1000 (from 35 fewer to 44 more)	⊕⊕◯◯ LOW
Preterm birth – unsupervised exercise											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	8/143 (5.6%)	4/86 (4.7%)	RR 1.17 (0.35 to 3.85)	8 more per 1000 (from 30 fewer to 133 more)	⊕◯◯◯ VERY LOW
Preterm birth – supervised exercise											
3	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	12/564 (2.1%)	6/565 (1.1%)	RR 1.92 (0.75 to 4.93)	10 more per 1000 (from 3 fewer to 42 more)	⊕◯◯◯ VERY LOW
Preterm birth – diet counselling/other											
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,4]	none	7/303 (2.3%)	10/288 (3.5%)	RR 0.67 (0.26 to 1.73)	11 fewer per 1000 (from 26 fewer to 25 more)	⊕⊕◯◯ LOW
Macrosomia (infant birth weight > 4000 g) – all interventions											
27	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	728/4383 (16.6%)	751/4215 (17.8%)	RR 0.93 (0.86 to 1.02)	12 fewer per 1000 (from 25 fewer to 4 more)	⊕⊕⊕◯ MODERATE
Macrosomia (infant birth weight > 4000 g) – diet intervention											
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	223/739 (30.2%)	242/733 (33%)	RR 0.96 (0.84 to 1.1)	13 fewer per 1000 (from 53 fewer to 33 more)	⊕⊕⊕⊕ HIGH
Macrosomia (infant birth weight > 4000 g) – diet and exercise counselling											
10	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	288/1904 (15.1%)	300/1801 (16.7%)	RR 0.93 (0.77 to 1.12)	12 fewer per 1000 (from 38 fewer to 20 more)	⊕⊕⊕◯ MODERATE
Macrosomia (infant birth weight > 4000 g) – unsupervised exercise											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	42/143 (29.4%)	22/86 (25.6%)	RR 1.16 (0.74 to 1.81)	41 more per 1000 (from 67 fewer to 207 more)	⊕⊕◯◯ LOW

EB Table A.1.1: All diet and/or physical activity/exercise interventions versus control (standard or other care) (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**All diet and/or exercise interventions**	**Standard/other care**	**Relative (95% CI)**	**Absolute**	
Macrosomia (infant birth weight > 4000 g) – supervised exercise intervention											
7	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	110/1218 (9%)	132/1227 (10.8%)	RR 0.81 (0.64 to 1.02)	20 fewer per 1000 (from 39 fewer to 2 more)	⊕⊕◯◯ LOW
Macrosomia (infant birth weight > 4000 g) – supervised exercise plus diet intervention											
3	randomized trials	very serious[6]	no serious inconsistency	no serious indirectness	serious[2]	none	45/200 (22.5%)	45/198 (22.7%)	RR 1.02 (0.71 to 1.46)	5 more per 1000 (from 66 fewer to 105 more)	⊕◯◯◯ VERY LOW
Macrosomia (infant birth weight > 4000 g) – diet counselling/other											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	20/179 (11.2%)	10/170 (5.9%)	RR 1.81 (0.88 to 3.72)	48 more per 1000 (from 7 fewer to 160 more)	⊕⊕◯◯ LOW
Low birth weight (infant birth weight < 2500 g) – all interventions											
12	randomized trials	very serious[6]	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[3]	109/2456 (4.4%)	118/2378 (5%)	RR 0.88 (0.67 to 1.14)	6 fewer per 1000 (from 16 fewer to 7 more)	⊕◯◯◯ VERY LOW
Low birth weight (infant birth weight < 2500 g) – exercise and diet counselling											
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	64/1499 (4.3%)	72/1435 (5%)	RR 0.84 (0.6 to 1.17)	8 fewer per 1000 (from 20 fewer to 9 more)	⊕⊕⊕◯ MODERATE
Low birth weight (infant birth weight < 2500 g) – unsupervised exercise											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	4/143 (2.8%)	1/86 (1.2%)	RR 2.14 (0.24 to 18.8)	13 more per 1000 (from 9 fewer to 207 more)	⊕◯◯◯ VERY LOW
Low birth weight (infant birth weight < 2500 g) – supervised exercise											
4	randomized trials	very serious[6]	no serious inconsistency	no serious indirectness	serious[2]	none	31/664 (4.7%)	33/723 (4.6%)	RR 0.99 (0.61 to 1.63)	0 fewer per 1000 (from 18 fewer to 29 more)	⊕◯◯◯ VERY LOW
Low birth weight (infant birth weight < 2500 g) – supervised exercise plus diet											
1	randomized trials	very serious[6]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	1/26 (3.8%)	0/23 (0%)	RR 2.67 (0.11 to 62.42)	–	⊕◯◯◯ VERY LOW

EB Table A.1.1: All diet and/or physical activity/exercise interventions versus control (standard or other care) (continued)

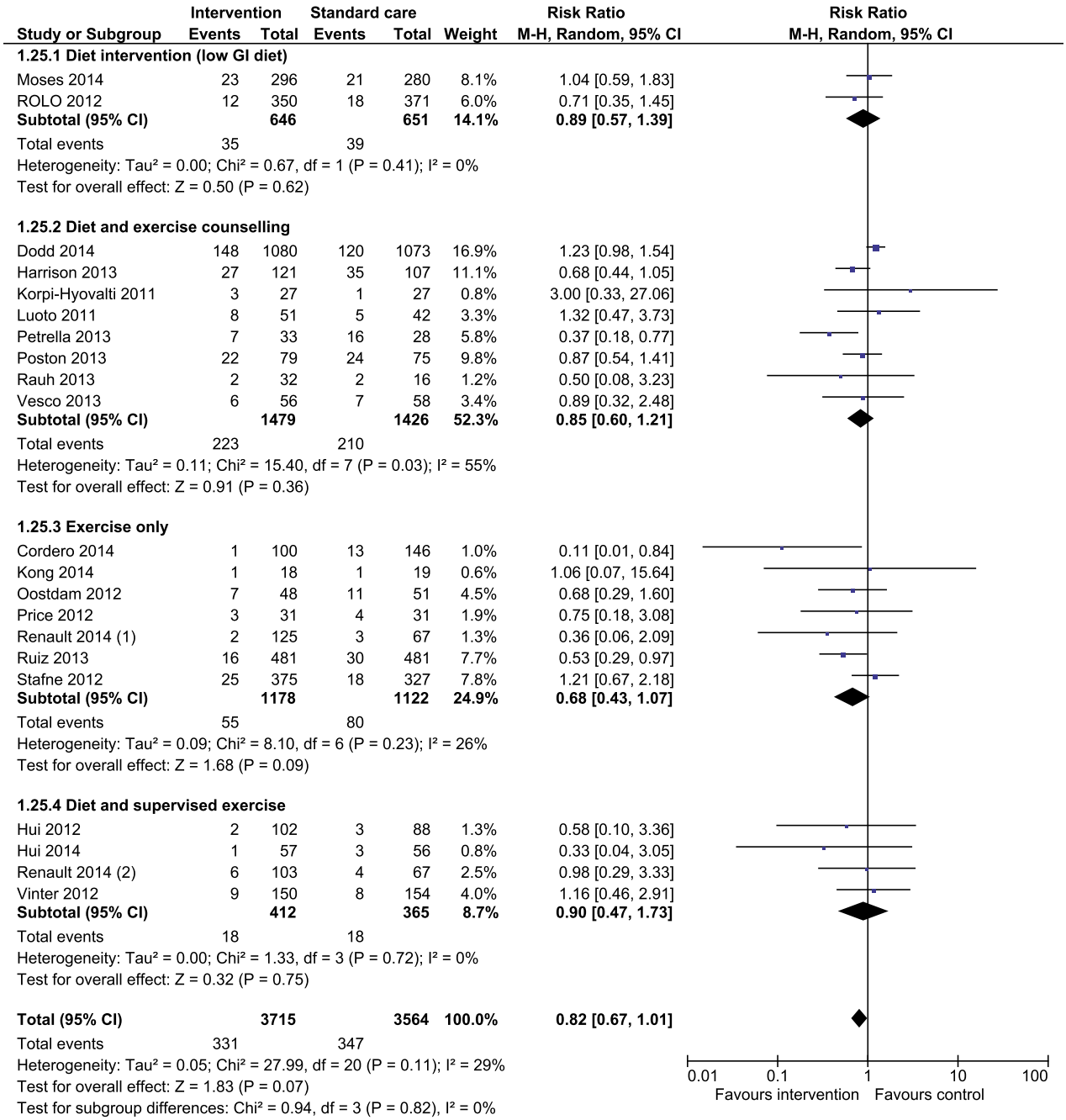
Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**All diet and/or exercise interventions**	**Standard/other care**	**Relative (95% CI)**	**Absolute**	
Low birth weight (infant birth weight < 2500 g) – diet counselling/other											
1	randomized trials	very serious[6]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	9/124 (7.3%)	12/111 (10.8%)	RR 0.67 (0.29 to 1.53)	36 fewer per 1000 (from 77 fewer to 57 more)	⊕○○○ VERY LOW
Induction of labour – all interventions											
8	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[3]	640/2000 (32%)	545/1832 (29.7%)	RR 1.06 (0.94 to 1.19)	18 more per 1000 (from 18 fewer to 57 more)	⊕⊕⊕○ MODERATE
Induction of labour – diet intervention											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	65/361 (18%)	41/373 (11%)	RR 1.64 (1.14 to 2.36)	70 more per 1000 (from 15 more to 149 more)	⊕⊕⊕⊕ HIGH
Induction of labour – diet and exercise counselling											
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	482/1317 (36.6%)	426/1205 (35.4%)	RR 1.03 (0.93 to 1.14)	11 more per 1000 (from 25 fewer to 49 more)	⊕⊕⊕⊕ HIGH
Induction of labour – unsupervised exercise											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	42/125 (33.6%)	23/67 (34.3%)	RR 0.98 (0.65 to 1.48)	7 fewer per 1000 (from 120 fewer to 165 more)	⊕⊕⊕○ MODERATE
Induction of labour – supervised exercise											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/18 (0%)	1/17 (5.9%)	RR 0.32 (0.01 to 7.26)	40 fewer per 1000 (from 58 fewer to 368 more)	⊕○○○ VERY LOW
Induction of labour – diet counselling/other											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	51/179 (28.5%)	54/170 (31.8%)	RR 0.89 (0.59 to 1.35)	35 fewer per 1000 (from 130 fewer to 111 more)	⊕⊕○○ LOW
Shoulder dystocia – all interventions											
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	47/1634 (2.9%)	43/1619 (2.7%)	RR 1.02 (0.57 to 1.83)	1 more per 1000 (from 11 fewer to 22 more)	⊕⊕⊕○ MODERATE

EB Table A.1.1: All diet and/or physical activity/exercise interventions versus control (standard or other care) (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	All diet and/or exercise interventions	Standard/other care	Relative (95% CI)	Absolute	
Shoulder dystocia – diet intervention											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,4]	none	2/372 (0.5%)	4/387 (1%)	RR 0.52 (0.1 to 2.82)	5 fewer per 1000 (from 9 fewer to 19 more)	⊕⊕◯◯ LOW
Shoulder dystocia – diet and exercise counselling											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	44/1075 (4.1%)	35/1067 (3.3%)	RR 1.25 (0.81 to 1.93)	8 more per 1000 (from 6 fewer to 31 more)	⊕⊕⊕◯ MODERATE
Shoulder dystocia – diet counselling/other											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	1/187 (0.5%)	4/165 (2.4%)	RR 0.35 (0.05 to 2.64)	16 fewer per 1000 (from 23 fewer to 40 more)	⊕◯◯◯ VERY LOW
Neonatal hypoglycaemia – all interventions											
4	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	132/1315 (10%)	130/1286 (10.1%)	RR 0.95 (0.76 to 1.18)	5 fewer per 1000 (from 24 fewer to 18 more)	⊕⊕⊕◯ MODERATE
Neonatal hypoglycaemia – diet and exercise counselling											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	107/1131 (9.5%)	104/1125 (9.2%)	RR 1.02 (0.79 to 1.32)	2 more per 1000 (from 19 fewer to 30 more)	⊕⊕◯◯ LOW
Neonatal hypoglycaemia – diet counselling/other											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	25/184 (13.6%)	26/161 (16.1%)	RR 0.88 (0.36 to 2.15)	19 fewer per 1000 (from 103 fewer to 186 more)	⊕⊕◯◯ LOW
Neonatal respiratory distress – all interventions											
2	randomized trials	serious[1]	serious[5]	no serious indirectness	no serious imprecision	none	16/1131 (1.4%)	34/1125 (3%)	RR 0.47 (0.26 to 0.85)	16 fewer per 1000 (from 5 fewer to 22 fewer)	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C" (studies at high risk of bias).
2. Wide confidence interval (CI) crossing the line of no effect.
3. Evident asymmetry in the funnel plot with at least 5 studies.
4. Small sample size and/or few events.
5. Severe unexplained heterogeneity.
6. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (i.e. > 40%) from studies "C" (studies at high risk of bias).

Figure A.1.1: Additional meta-analysis: Effect of diet and/or exercise interventions versus control on gestational diabetes mellitus (GDM) (not included in the systematic review by Muktabhant et al., 2015 [see EB Table A.1.1])



EB Table A.1.2: Energy and protein nutrition education during pregnancy versus control (no nutritional education or normal care)

Source: Ota E, Hori H, Mori R, Tobe-Gai R, Farrar D. Antenatal dietary education and supplementation to increase energy and protein intake. Cochrane Database Syst Rev. 2015;(6):CD000032.

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Nutritional education during pregnancy**	**Control (no nutritional education or normal care)**	**Relative (95% CI)**	**Absolute**	
Total gestational weight gain (kg) (MD; better indicated by higher values)											
2	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	146	87	-	MD 0.41 lower (4.41 lower to 3.59 higher)	⊕◯◯◯ VERY LOW
Small for gestational age											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	12/205 (5.9%)	12/199 (6%)	RR 0.97 (0.45 to 2.11)	2 fewer per 1000 (from 33 fewer to 67 more)	⊕⊕◯◯ LOW
Low birth weight											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	3/150 (2%)	67/150 (44.7%)	RR 0.04 (0.01 to 0.14)	429 fewer per 1000 (from 384 fewer to 442 fewer)	⊕⊕◯◯ LOW
Preterm birth											
2	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[1]	none	9/238 (3.8%)	18/211 (8.5%)	RR 0.46 (0.21 to 0.98)	46 fewer per 1000 (from 2 fewer to 67 fewer)	⊕◯◯◯ VERY LOW
Stillbirth											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	2/223 (0.9%)	5/208 (2.4%)	RR 0.37 (0.07 to 1.9)	15 fewer per 1000 (from 22 fewer to 22 more)	⊕⊕◯◯ LOW
Neonatal death											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	5/221 (2.3%)	4/227 (1.8%)	RR 1.28 (0.35 to 4.72)	5 more per 1000 (from 11 fewer to 66 more)	⊕⊕◯◯ LOW

1. Wide CI crossing the line of no effect.
2. Small sample size and few events.

EB Table A.1.3: Energy and protein dietary supplements versus control

Source: Ota E, Hori H, Mori R, Tobe-Gai R, Farrar D. Antenatal dietary education and supplementation to increase energy and protein intake. Cochrane Database Syst Rev. 2015;(6):CD000032.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Balanced protein/energy supplementation	Control	Relative (95% CI)	Absolute	
Pre-eclampsia											
2	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	25/231 (10.8%)	17/232 (7.3%)	RR 1.48 (0.82 to 2.66)	35 more per 1000 (from 13 fewer to 122 more)	⊕○○○ VERY LOW
Small for gestational age											
7	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[3]	309/2275 (13.6%)	370/2133 (17.3%)	RR 0.79 (0.69 to 0.9)	36 fewer per 1000 (from 17 fewer to 54 fewer)	⊕⊕⊕○ MODERATE
Preterm birth											
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[3]	182/1704 (10.7%)	189/1680 (11.3%)	RR 0.96 (0.8 to 1.16)	5 fewer per 1000 (from 22 fewer to 18 more)	⊕⊕⊕○ MODERATE
Stillbirth											
5	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	31/1759 (1.8%)	49/1649 (3%)	RR 0.6 (0.39 to 0.94)	12 fewer per 1000 (from 2 fewer to 18 fewer)	⊕⊕⊕○ MODERATE
Neonatal death											
5	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	serious[2]	none	32/1747 (1.8%)	43/1634 (2.6%)	RR 0.68 (0.43 to 1.07)	8 fewer per 1000 (from 15 fewer to 2 more)	⊕⊕○○ LOW

1. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (i.e. > 40%) from studies "C".
2. Wide CI crossing the line of no effect.
3. Evident asymmetry in funnel plot.
4. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".

EB Table A.1.4: High-protein supplements versus control

Source: Ota E, Hori H, Mori R, Tobe-Gai R, Farrar D. Antenatal dietary education and supplementation to increase energy and protein intake. Cochrane Database Syst Rev. 2015;(6):CD000032.

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**High-protein supplementation**	**Control**	**Relative (95% CI)**	**Absolute**	
Small for gestational age											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious	none	46/249 (18.5%)	30/256 (11.7%)	RR 1.58 (1.03 to 2.41)	68 more per 1000 (from 4 more to 165 more)	⊕⊕⊕⊕ HIGH
Preterm birth											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	62/249 (24.9%)	56/256 (21.9%)	RR 1.14 (0.83 to 1.56)	31 more per 1000 (from 37 fewer to 122 more)	⊕⊕⊕◯ MODERATE
Stillbirth											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	7/259 (2.7%)	9/270 (3.3%)	RR 0.81 (0.31 to 2.15)	6 fewer per 1000 (from 23 fewer to 38 more)	⊕⊕◯◯ LOW
Neonatal death											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	8/259 (3.1%)	3/270 (1.1%)	RR 2.78 (0.75 to 10.36)	20 more per 1000 (from 3 fewer to 104 more)	⊕⊕◯◯ LOW

1. Wide CI crossing the line of no effect.
2. Small sample size and few events.

A.2. Iron and folic acid supplements

EB Table A.2.1: Daily iron and folic acid supplements versus control (supplements without iron or no treatment/placebo)

Source: Peña-Rosas JP, De-Regil LM, Garcia-Casal MN, Dowswell T. Daily oral iron supplementation during pregnancy. Cochrane Database Syst Rev. 2015;(7):CD004736.

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Design limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Any supplements containing iron**	**Same supplements without iron or no treatment/ placebo (no iron or placebo)**	**Relative (95% CI)**	**Absolute**	
Maternal anaemia at term (Hb < 110 g/L at 37 weeks of gestation or more)											
14	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[2]	152/1163 (13.1%)	370/1036 (35.7%)	RR 0.3 (0.19 to 0.46)	250 fewer per 1000 (from 193 fewer to 289 fewer)	⊕⊕◯◯ LOW
Maternal death (death during or within 42 days of pregnancy)											
2	randomized trials	no serious design limitations	serious[1]	no serious indirectness	serious[3,4]	none	0/6276 (0%)	1/6284 (0%)	RR 0.33 (0.01 to 8.19)	0 fewer per 1000 (from 0 fewer to 1 more)	⊕⊕◯◯ LOW
Side-effects (any reported throughout the intervention period)											
11	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness	serious[3]	none	281/1298 (21.6%)	202/1125 (18%)	RR 1.29 (0.83 to 2.02)	52 more per 1000 (from 31 fewer to 183 more)	⊕⊕⊕◯ MODERATE
Maternal Hb concentration at or near term (in g/L, at 34 weeks of gestation or more; better indicated by lower values)											
19	randomized trials	serious[1]	serious[5]	no serious indirectness	no serious imprecision	none	1964	1740	-	MD 8.88 higher (6.96 to 10.8 higher)	⊕⊕◯◯ LOW
Maternal high haemoglobin concentrations at or near term (Hb > 130 g/L at 34 weeks of gestation or more)											
8	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[2]	543/1135 (47.8%)	342/1021 (33.5%)	RR 3.07 (1.18 to 8.02)	693 more per 1000 (from 60 more to 1000 more)	⊕⊕◯◯ LOW
Severe postpartum anaemia (Hb < 80 g/L)											
8	randomized trials	very serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/707 (0%)	30/632 (4.7%)	RR 0.04 (0.01 to 0.28)	46 fewer per 1000 (from 34 fewer to 47 fewer)	⊕⊕◯◯ LOW

EB Table A.2.1: Daily iron and folic acid supplements versus control (supplements without iron or no treatment/placebo) (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Design limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Any supplements containing iron**	**Same supplements without iron or no treatment/ placebo (no iron or placebo)**	**Relative (95% CI)**	**Absolute**	
Puerperal infection											
4	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	67/2199 (3%)	100/2175 (4.6%)	RR 0.68 (0.5 to 0.92)	15 fewer per 1000 (from 4 fewer to 23 fewer)	⊕⊕⊕◯ MODERATE
Antepartum haemorrhage											
2	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness	very serious[3,7]	none	8/586 (1.4%)	5/571 (0.9%)	RR 1.48 (0.51 to 4.31)	4 more per 1000 (from 4 fewer to 29 more)	⊕⊕◯◯ LOW
Postpartum haemorrhage											
4	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness	serious1	none	36/776 (4.6%)	31/712 (4.4%)	RR 0.93 (0.59 to 1.49)	3 fewer per 1000 (from 18 fewer to 21 more)	⊕⊕⊕◯ MODERATE
Transfusion provided											
2	randomized trials	very serious[6]	no serious inconsistency	no serious indirectness	very serious[3,7]	none	1/386 (0.3%)	1/373 (0.3%)	RR 0.96 (0.1 to 8.98)	0 fewer per 1000 (from 2 fewer to 21 more)	⊕◯◯◯ VERY LOW
Diarrhoea											
3	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	24/614 (3.9%)	24/474 (5.1%)	RR 0.55 (0.32 to 0.93)	23 fewer per 1000 (from 4 fewer to 34 fewer)	⊕⊕⊕⊕ HIGH
Constipation											
4	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness3	serious[3]	none	84/818 (10.3%)	58/677 (8.6%)	RR 0.95 (0.62 to 1.43)	4 fewer per 1000 (from 33 fewer to 37 more)	⊕⊕⊕◯ MODERATE
Nausea											
4	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	80/735 (10.9%)	59/642 (9.2%)	RR 1.21 (0.72 to 2.03)	19 more per 1000 (from 26 fewer to 95 more)	⊕⊕◯◯ LOW

EB Table A.2.1: Daily iron and folic acid supplements versus control (supplements without iron or no treatment/placebo) (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Design limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Any supplements containing iron**	**Same supplements without iron or no treatment/ placebo (no iron or placebo)**	**Relative (95% CI)**	**Absolute**	
Heartburn											
3	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness	serious[3]	none	166/702 (23.6%)	124/621 (20%)	RR 1.19 (0.86 to 1.66)	38 more per 1000 (from 28 fewer to 132 more)	⊕⊕⊕◯ MODERATE
Vomiting											
4	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness	serious[3]	none	52/747 (7%)	44/645 (6.8%)	RR 0.88 (0.59 to 1.3)	8 fewer per 1000 (from 28 fewer to 20 more)	⊕⊕⊕◯ MODERATE
Maternal satisfaction											
1	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness	serious	none	21/24 (87.5%)	24/25 (96%)	RR 0.91 (0.77 to 1.08)	86 fewer per 1000 (from 221 fewer to 77 more)	⊕⊕⊕◯ MODERATE
Placental abruption											
3	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3,7]	none	11/1516 (0.7%)	7/1435 (0.5%)	RR 1.41 (0.56 to 3.59)	2 more per 1000 (from 2 fewer to 13 more)	⊕◯◯◯ VERY LOW
Pre-eclampsia											
4	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	27/874 (3.1%)	15/830 (1.8%)	RR 1.63 (0.87 to 3.07)	11 more per 1000 (from 2 fewer to 37 more)	⊕⊕◯◯ LOW
Low birth weight (< 2500 g)											
11	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness	serious[3]	reporting bias[2]	446/8809 (5.1%)	516/8804 (5.9%)	RR 0.84 (0.69 to 1.03)	9 fewer per 1000 (from 18 fewer to 2 more)	⊕⊕◯◯ LOW
Preterm birth (< 37 weeks of gestation)											
13	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	651/9698 (6.7%)	698/9588 (7.3%)	RR 0.93 (0.84 to 1.03)	5 fewer per 1000 (from 12 fewer to 2 more)	⊕⊕⊕⊕ HIGH

EB Table A.2.1: Daily iron and folic acid supplements versus control (supplements without iron or no treatment/placebo) (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Design limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Any supplements containing iron**	**Same supplements without iron or no treatment/ placebo (no iron or placebo)**	**Relative (95% CI)**	**Absolute**	
Very preterm birth (< 34 weeks of gestation)											
5	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	17/1861 (0.9%)	35/1882 (1.9%)	RR 0.51 (0.29 to 0.91)	9 fewer per 1000 (from 2 fewer to 13 fewer)	⊕⊕⊕⊕ HIGH
Neonatal death (within 28 days after delivery)											
4	randomized trials	no serious design limitations	no serious inconsistency	no serious indirectness	serious[3]	none	107/8261 (1.3%)	122/8342 (1.5%)	RR 0.91 (0.71 to 1.18)	1 fewer per 1000 (from 4 fewer to 3 more)	⊕⊕⊕◯ MODERATE
Congenital anomalies											
4	randomized trials	no serious design limitations	serious[5]	no serious indirectness	serious[3]	none	41/7358 (0.6%)	48/7278 (0.7%)	RR 0.88 (0.58 to 1.33)	1 fewer per 1000 (from 3 fewer to 2 more)	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by trials "B" or "C" without a substantial proportion (< 40%) from trials "C".
2. Evident asymmetry in funnel plot with at least five trials.
3. Wide CI crossing the line of no effect.
4. More than 3000 women.
5. Severe unexplained heterogeneity.
6. Most of the pooled effect provided by trials "B" or "C" with a substantial proportion (> 40%) from trials "C".
7. Small sample size and/or few events.

EB Table A.2.2: Intermittent iron and folic acid supplements versus daily regimen with no iron

Source: Peña-Rosas JP, De-Regil LM, Gomez Malave H, Flores-Urrutia MC, Dowswell T. Intermittent oral iron supplementation during pregnancy. Cochrane Database Syst Rev. 2015;(19):CD009997.

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Design limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Any intermittent iron regimen (with or without other vitamins and minerals)**	**Daily regimen (with same vitamins and minerals but no iron)**	**Relative (95% CI)**	**Absolute**	
Maternal anaemia at term (Hb < 110 g/L at 37 weeks of gestation or more)											
4	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	54/339 (15.9%)	57/337 (16.9%)	RR 1.22 (0.84 to 1.8)	37 more per 1000 (from 27 fewer to 135 more)	⊕⊕◯◯ LOW
Maternal anaemia at or near term (Hb < 110 g/L at 34 weeks of gestation or more)											
8	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	167/751 (22.2%)	99/634 (15.6%)	RR 1.66 (1.09 to 2.53)	103 more per 1000 (from 14 more to 239 more)	⊕⊕⊕◯ MODERATE
Severe anaemia at or near term (Hb < 70 g/L at 34 weeks of gestation or more)											
6	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/546 (0%)	0/504 (0%)	not estimable	not estimable	⊕⊕⊕◯ MODERATE
Severe postpartum anaemia (Hb < 80 g/L)											
1	randomized trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	1/91 (1.1%)	2/78 (2.6%)	RR 0.43 (0.04 to 4.64)	15 fewer per 1000 (from 25 fewer to 93 more)	⊕◯◯◯ VERY LOW
Maternal haemoglobin concentration at or near term (in g/L at 34 weeks of gestation or more) (MD; better indicated by lower values)											
8	randomized trials	serious[1]	serious[5]	no serious indirectness	serious[2]	none	717	589	MD 2.57 lower (5.18 lower to 0.04 higher)	–	⊕◯◯◯ VERY LOW
Maternal high haemoglobin concentrations during second or third trimester (Hb > 130 g/L)											
15	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	154/1351 (11.4%)	252/1265 (19.9%)	RR 0.53 (0.38 to 0.74)	94 fewer per 1000 (from 52 fewer to 124 fewer)	⊕⊕⊕◯ MODERATE
Antepartum haemorrhage											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	1/55 (1.8%)	1/55 (1.8%)	RR 1 (0.06 to 15.59)	0 fewer per 1000 (from 17 fewer to 265 more)	⊕◯◯◯ VERY LOW

EB Table A.2.2: Intermittent iron and folic acid supplements versus daily regimen with no iron (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Design limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Any intermittent iron regimen (with or without other vitamins and minerals)	Daily regimen (with same vitamins and minerals but no iron)	Relative (95% CI)	Absolute	
Placental abruption											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	0/55 (0%)	1/55 (1.8%)	RR 0.33 (0.01 to 8.01)	12 fewer per 1000 (from 18 fewer to 127 more)	⊕OOO VERY LOW
Any side-effects											
11	randomized trials	very serious[3]	serious[5]	no serious indirectness	no serious imprecision	none	198/916 (21.6%)	284/861 (33%)	RR 0.56 (0.37 to 0.84)	145 fewer per 1000 (from 53 fewer to 208 fewer)	⊕OOO VERY LOW
Diarrhoea											
5	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[6]	38/308 (12.3%)	35/305 (11.5%)	RR 0.8 (0.32 to 2)	23 fewer per 1000 (from 78 fewer to 115 more)	⊕OOO VERY LOW
Constipation											
6	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[6]	89/364 (24.5%)	87/369 (23.6%)	RR 0.85 (0.45 to 1.59)	35 fewer per 1000 (from 130 fewer to 139 more)	⊕OOO VERY LOW
Nausea											
7	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	33/520 (6.3%)	55/514 (10.7%)	RR 0.6 (0.37 to 0.97)	43 fewer per 1000 (from 3 fewer to 67 fewer)	⊕⊕⊕O MODERATE
Heartburn											
4	randomized trials	serious[1]	serious[5]	no serious indirectness	serious[2]	none	54/268 (20.1%)	59/265 (22.3%)	RR 0.75 (0.31 to 1.81)	56 fewer per 1000 (from 154 fewer to 180 more)	⊕OOO VERY LOW
Vomiting											
6	randomized trials	very serious[3]	no serious inconsistency	no serious indirectness	serious[2]	none	69/480 (14.4%)	50/474 (10.5%)	RR 1.3 (0.79 to 2.15)	32 more per 1000 (from 22 fewer to 121 more)	⊕OOO VERY LOW
Preterm rupture of membranes											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	0/40 (0%)	1/40 (2.5%)	RR 0.33 (0.01 to 7.95)	17 fewer per 1000 (from 25 fewer to 174 more)	⊕OOO VERY LOW

EB Table A.2.2: Intermittent iron and folic acid supplements versus daily regimen with no iron (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Design limitations**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Any intermittent iron regimen (with or without other vitamins and minerals)**	**Daily regimen (with same vitamins and minerals but no iron)**	**Relative (95% CI)**	**Absolute**	
Low birth weight (< 2500 g)											
8	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	44/1026 (4.3%)	51/872 (5.8%)	RR 0.82 (0.55 to 1.22)	11 fewer per 1000 (from 26 fewer to 13 more)	⊕⊕OO LOW
Preterm birth (< 37 weeks of gestation)											
5	randomized trials	very serious[3]	no serious inconsistency	no serious indirectness	serious[2]	none	78/613 (12.7%)	72/564 (12.8%)	RR 1.03 (0.76 to 1.39)	4 more per 1000 (from 31 fewer to 50 more)	⊕OOO VERY LOW
Very preterm birth (< 34 weeks of gestation)											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	1/116 (0.9%)	1/111 (0.9%)	RR 0.98 (0.06 to 15.31)	0 fewer per 1000 (from 8 fewer to 129 more)	⊕OOO VERY LOW
Neonatal death (within 28 days after delivery)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	1/400 (0.3%)	2/395 (0.5%)	RR 0.49 (0.04 to 5.42)	3 fewer per 1000 (from 5 fewer to 22 more)	⊕OOO VERY LOW

1. Most of the pooled effect provided by trials "B" or "C" without a substantial proportion (< 40%) from trials "C".
2. Wide CI crossing the line of no effect.
3. Most of the pooled effect provided by trials "B" or "C" with a substantial proportion (> 40%) from trials "C".
4. Small sample size and few events.
5. Severe unexplained heterogeneity.
6. Evident asymmetry in funnel plot with at least five trials.

A.3. Calcium supplements

EB Table A.3: Calcium supplements versus placebo or no treatment

Source: Buppasiri P, Lumbiganon P, Thinkhamrop J, Ngamjarus C, Laopaiboon M, Medley N. Calcium supplementation (other than for preventing or treating hypertension) for improving pregnancy and infant outcomes. Cochrane Database Syst Rev. 2015;(2):CD007079.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Calcium supplementation	Placebo or no treatment	Relative (95% CI)	Absolute	
Maternal anaemia											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	208/544 (38.2%)	203/554 (36.6%)	RR 1.04 (0.9 to 1.22)	15 more per 1000 (from 37 fewer to 81 more)	⊕⊕⊕⊕ HIGH
Caesarean section											
9	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	592/3760 (15.7%)	585/3680 (15.9%)	RR 0.99 (0.89 to 1.1)	2 fewer per 1000 (from 17 fewer to 16 more)	⊕⊕⊕⊕ HIGH
Urinary tract infection											
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	67/865 (7.7%)	72/878 (8.2%)	RR 0.95 (0.69 to 1.3)	4 fewer per 1000 (from 25 fewer to 25 more)	⊕⊕⊕○ MODERATE
Maternal weight gain (grams per week)											
3	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	serious[2]	none	199	205	MD 29.46 lower (119.8 lower to 60.89 higher)	-	⊕⊕○○ LOW
Maternal death											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	2/4481 (0%)	7/4493 (0.2%)	RR 0.29 (0.06 to 1.38)	1 fewer per 1000 (from 1 fewer to 1 more)	⊕⊕⊕○ MODERATE
Side-effects (Including headache, vomiting, backache, swelling, vaginal and urinary complaints, dyspepsia and abdominal pain)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	764/4151 (18.4%)	751/4161 (18%)	RR 1.02 (0.93 to 1.12)	4 more per 1000 (from 13 fewer to 22 more)	⊕⊕⊕⊕ HIGH
Gall stones											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,3]	none	8/257 (3.1%)	6/261 (2.3%)	RR 1.35 (0.48 to 3.85)	8 more per 1000 (from 12 fewer to 66 more)	⊕⊕○○ LOW

EB Table A.3: Calcium supplements versus placebo or no treatment (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Calcium supplementation	Placebo or no treatment	Relative (95% CI)	Absolute	
Urinary stones											
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	11/6703 (0.2%)	10/6716 (0.1%)	RR 1.11 (0.48 to 2.54)	0 more per 1000 (from 1 fewer to 2 more)	⊕⊕⊕◯ MODERATE
Renal colic											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	5/4151 (0.1%)	3/4161 (0.1%)	RR 1.67 (0.4 to 6.99)	0 more per 1000 (from 0 fewer to 4 more)	⊕⊕⊕◯ MODERATE
Impaired renal function											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	21/2295 (0.9%)	23/2294 (1%)	RR 0.91 (0.51 to 1.64)	1 fewer per 1000 (from 5 fewer to 6 more)	⊕⊕⊕◯ MODERATE
Preterm birth – main analysis											
13	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[4]	789/8074 (9.8%)	846/8065 (10.5%)	RR 0.86 (0.7 to 1.05)	15 fewer per 1000 (from 31 fewer to 5 more)	⊕⊕◯◯ LOW
Preterm birth – low dose subgroup											
1	randomized trials	very serious[5]	no serious inconsistency	no serious indirectness	serious[2]	none	45/330 (13.6%)	29/330 (8.8%)	RR 1.55 (1 to 2.41)	48 more per 1000 (from 0 more to 124 more)	⊕◯◯◯ VERY LOW
Preterm birth – high dose subgroup											
12	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[4]	744/7744 (9.6%)	817/7735 (10.6%)	RR 0.81 (0.66 to 0.99)	20 fewer per 1000 (from 1 fewer to 36 fewer)	⊕⊕⊕◯ MODERATE
Low birth weight (< 2500 g)											
6	randomized trials	no serious risk of bias	no serious inconsistency[6]	no serious indirectness	no serious imprecision	reporting bias[4]	808/7089 (11.4%)	823/7073 (11.6%)	RR 0.93 (0.81 to 1.07)	8 fewer per 1000 (from 22 fewer to 8 more)	⊕⊕⊕◯ MODERATE
Stillbirth or fetal death											
6	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	137/7636 (1.8%)	151/7633 (2%)	RR 0.91 (0.72 to 1.14)	2 fewer per 1000 (from 6 fewer to 3 more)	⊕⊕⊕◯ MODERATE

EB Table A.3: Calcium supplements versus placebo or no treatment (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Calcium supplementation**	**Placebo or no treatment**	**Relative (95% CI)**	**Absolute**	
Perinatal mortality											
8	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[4]	179/7870 (2.3%)	206/7915 (2.6%)	RR 0.87 (0.72 to 1.06)	3 fewer per 1000 (from 7 fewer to 2 more)	⊕⊕◯◯ LOW

1. Severe unexplained inconsistency.
2. Wide CI crossing the line of no effect.
3. Small sample size and/or few events.
4. Evident asymmetry in funnel plot.
5. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (i.e. > 40%) from studies "C".
6. Inconsistency explained by publication bias.

A.4. Vitamin A supplements

EB Table A.4: Vitamin A supplements alone versus placebo or no treatment

Source: McCauley ME, van den Broek N, Dou L, Othman M. Vitamin A supplementation during pregnancy for maternal and newborn outcomes. Cochrane Database Syst Rev. 2015;(10):CD008666.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vitamin A alone	Control (placebo or no treatment)	Relative (95% CI)	Absolute	
Maternal anaemia											
3	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	none	2699	1119	RR 0.64 (0.43 to 0.94)	-	⊕⊕⊕◯ MODERATE
Maternal infection											
5	randomized trials	serious[2]	serious[1]	no serious indirectness	no serious imprecision	none	1212	706	RR 0.45 (0.2 to 0.99)	-	⊕⊕◯◯ LOW
Maternal death											
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	54 824	46 750	RR 0.88 (0.65 to 1.2)	-	⊕⊕⊕◯ MODERATE
Low birth weight											
4	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	4210/9580 (43.9%)	2085/5019 (41.5%)	RR 1.02 (0.89 to 1.16)	8 more per 1000 (from 46 fewer to 66 more)	⊕⊕⊕◯ MODERATE
Preterm birth											
5	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[4]	6551/26 562 (24.7%)	3374/13 575 (24.9%)	RR 0.98 (0.94 to 1.01)	5 fewer per 1000 (from 15 fewer to 2 more)	⊕⊕◯◯ LOW
Perinatal mortality											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	38 283	37 893	RR 1.01 (0.95 to 1.07)	-	⊕⊕⊕⊕ HIGH
Neonatal mortality											
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	47 616	41 940	RR 0.97 (0.9 to 1.05)	-	⊕⊕⊕⊕ HIGH

EB Table A.4: Vitamin A supplements alone versus placebo or no treatment (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Vitamin A alone**	**Control (placebo or no treatment)**	**Relative (95% CI)**	**Absolute**	
Stillbirth											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	2680/68 859 (3.9%)	1878/53 991 (3.5%)	RR 1.04 (0.98 to 1.1)	1 more per 1000 (from 1 fewer to 3 more)	⊕⊕⊕⊕ HIGH
Maternal night blindness											
2	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	serious[5]	none	7110	3498	RR 0.79 (0.64 to 0.98)	-	⊕⊕◯◯ LOW

1. Severe unexplained heterogeneity
2. Most of the pooled effect provided by trials "B" or "C" without a substantial proportion (< 40%) from trials "C".
3. Wide CI crossing the line of no effect.
4. Evident asymmetry in funnel plot with at least five trials.
5. Subgroup of participants not generalizable to all pregnant women.

A.5. Zinc supplements

EB Table A.5: Zinc supplements versus no intervention or placebo

Source: Ota E, Mori R, Middleton P, Tobe-Gai R, Mahomed K, Miyazaki C, Bhutta ZA. Zinc supplementation for improving pregnancy and infant outcome. Cochrane Database Syst Rev. 2015;(2):CD000230.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vitamin A alone	Control (placebo or no treatment)	Relative (95% CI)	Absolute	
Any maternal infection											
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	52/585 (8.9%)	50/600 (8.3%)	RR 1.06 (0.74 to 1.53)	5 more per 1000 (from 22 fewer to 44 more)	⊕⊕⊕◯ MODERATE
Pregnancy hypertension or pre-eclampsia											
7	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	reporting bias[3]	89/1483 (6%)	106/1492 (7.1%)	RR 0.83 (0.64 to 1.08)	12 fewer per 1000 (from 26 fewer to 6 more)	⊕◯◯◯ VERY LOW
Caesarean section											
6	randomized trials	serious[2]	serious[4]	no serious indirectness	serious[1]	reporting bias[3]	140/1109 (12.6%)	124/1055 (11.8%)	RR 0.95 (0.58 to 1.53)	6 fewer per 1000 (from 49 fewer to 62 more)	⊕◯◯◯ VERY LOW
Instrumental vaginal birth											
1	randomized trials	very serious[5]	no serious inconsistency	no serious indirectness	serious[1]	none	58/585 (9.9%)	55/621 (8.9%)	RR 1.12 (0.79 to 1.59)	11 more per 1000 (from 19 fewer to 52 more)	⊕◯◯◯ VERY LOW
Side-effect (smell dysfunction)											
1	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	16/82 (19.5%)	17/88 (19.3%)	RR 1.01 (0.55 to 1.86)	2 more per 1000 (from 87 fewer to 166 more)	⊕⊕◯◯ LOW
Side-effect (taste dysfunction)											
1	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[1,2]	none	11/82 (13.4%)	16/88 (18.2%)	RR 0.74 (0.36 to 1.5)	47 fewer per 1000 (from 116 fewer to 91 more)	⊕◯◯◯ VERY LOW
Neonatal infection											
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[6]	none	1/410 (0.2%)	6/326 (1.8%)	RR 0.17 (0.03 to 1.01)	15 fewer per 1000 (from 18 fewer to 0 more)	⊕⊕◯◯ LOW

EB Table A.5: Zinc supplements versus no intervention or placebo (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vitamin A alone	Control (placebo or no treatment)	Relative (95% CI)	Absolute	
Small for gestational age											
8	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[3]	575/2161 (26.6%)	554/2091 (26.5%)	RR 1.02 (0.94 to 1.11)	5 more per 1000 (from 16 fewer to 29 more)	⊕⊕◯◯ LOW
Low birth weight											
14	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[3]	570/2884 (19.8%)	540/2759 (19.6%)	RR 0.93 (0.78 to 1.12)	14 fewer per 1000 (from 43 fewer to 23 more)	⊕⊕◯◯ LOW
Preterm birth											
16	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[3]	427/3851 (11.1%)	489/3786 (12.9%)	RR 0.86 (0.76 to 0.97)	18 fewer per 1000 (from 4 fewer to 31 fewer)	⊕⊕◯◯ LOW
Congenital malformation											
6	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious1	none	13/667 (1.9%)	18/573 (3.1%)	RR 0.67 (0.33 to 1.34)	10 fewer per 1000 (from 21 fewer to 11 more)	⊕⊕◯◯ LOW

1. Wide CI crossing the line of no effect.
2. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C"
3. Evident asymmetry in funnel plot.
4. Severe unexplained heterogeneity.
5. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (i.e. > 40%) from studies "C".
6. Small sample size and few events.

A.6. Multiple micronutrient (MMN) supplements

EB Table A.6: Multiple micronutrient supplements versus iron (with or without folic acid)[1]

Source: Haider BA, Bhutta ZA. Multiple-micronutrient supplementation for women during pregnancy. Cochrane Database Syst Rev. 2015;(11):CD004905.

Quality assessment							No. of women[1]		Effect	Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	13–15 micronutrients	Iron (with or without folic acid)	Relative (95% CI)	
Maternal anaemia (third trimester Hb < 110 g/L)										
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	5132	5134	RR 0.98 (0.85 to 1.13)	⊕⊕⊕⊕ HIGH
Caesarean section										
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	3299	3374	RR 1.03 (0.75 to 1.43)	⊕⊕⊕◯ MODERATE
Maternal mortality										
3	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	serious[2]	none	19 089	17 971	RR 0.97 (0.63 to 1.48)	⊕⊕◯◯ LOW
Small for gestational age										
13	randomized trials	no serious risk of bias	serious inconsistency	no serious indirectness	no serious imprecision	none	49 928	47 979	RR 0.98 (0.96 to 1.00)	⊕⊕⊕◯ MODERATE
Low birth weight										
14	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	56 180	55 077	RR 0.88 (0.85 to 0.91)	⊕⊕⊕⊕ HIGH
Preterm birth										
14	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	56 180	55 077	RR 0.95 (0.88 to 1.03)	⊕⊕⊕⊕ HIGH

1 The evidence presented in this table is for MMN supplements with 13–15 micronutrients versus iron supplements (with or without folic acid). Additional meta-analyses in which included trials were subgrouped according to iron dose can be found at the end of this EB table, as well as meta-analyses of all trials that evaluated the UNIMMAP supplement (United Nations international multiple micronutrient preparation). For these meta-analyses, most data were derived directly from the Cochrane review. An error was detected in the published stillbirth data of one trial and this error was communicated to the Cochrane review authors.

EB Table A.6: Multiple micronutrient supplements versus iron (with or without folic acid) (continued)

Quality assessment							No. of women[1]		Effect	Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**13–15 micronutrients**	**Iron (with or without folic acid)**	**Relative (95% CI)**	
Congenital anomalies										
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	serious[2]	none	600	600	RR 0.99 (0 to 7.00)	⊕⊕◯◯ LOW
Perinatal mortality										
11	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	30 950	29 968	RR 1.00 (0.85 to 1.19)	⊕⊕⊕◯ MODERATE
Stillbirths										
14	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	56 180	55 077	RR 0.97 (0.86 to 1.09)	⊕⊕⊕◯ MODERATE
Neonatal mortality										
11	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	53 015	52 030	RR 0.99 (0.90 to 1.08)	⊕⊕⊕◯ MODERATE

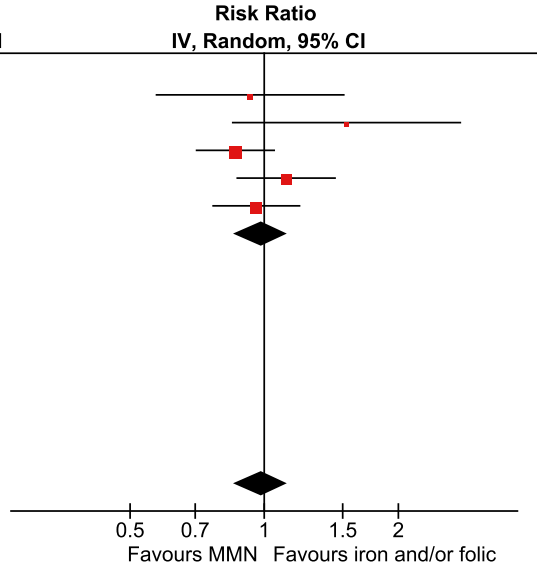
1. These are estimates only due to inverse variance method of analysis.
2. Wide CI crossing the line of no effect.
3. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
4. Clinical heterogeneity between trials.

Additional meta-analyses on the effect of MMN supplements (not included in the systematic review by Haider and Bhutta, 2015)

i. Subgroup analyses grouping trials according to dose of iron in the control group (60 mg, 30 mg or not stated)[2]

1. Maternal anaemia

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.0728	0.2468	7.9%	0.93 [0.57, 1.51]
Christian 2003	0.4253	0.2999	5.5%	1.53 [0.85, 2.75]
Osrin 2005	-0.1491	0.1022	33.6%	0.86 [0.71, 1.05]
Ramakrishnan 2003 (1)	0.1133	0.1288	24.1%	1.12 [0.87, 1.44]
Zeng 2008	-0.0408	0.1138	28.9%	0.96 [0.77, 1.20]
Subtotal (95% CI)			**100.0%**	**0.98 [0.85, 1.13]**
Heterogeneity: Tau² = 0.01; Chi² = 4.94, df = 4 (P = 0.29); I² = 19%				
Test for overall effect: Z = 0.24 (P = 0.81)				
1.1.2 versus 30mg iron plus folic acid				
Subtotal (95% CI)				**Not estimable**
Heterogeneity: Not applicable				
Test for overall effect: Not applicable				
Total (95% CI)			**100.0%**	**0.98 [0.85, 1.13]**
Heterogeneity: Tau² = 0.01; Chi² = 4.94, df = 4 (P = 0.29); I² = 19%				
Test for overall effect: Z = 0.24 (P = 0.81)				
Test for subgroup differences: Not applicable				



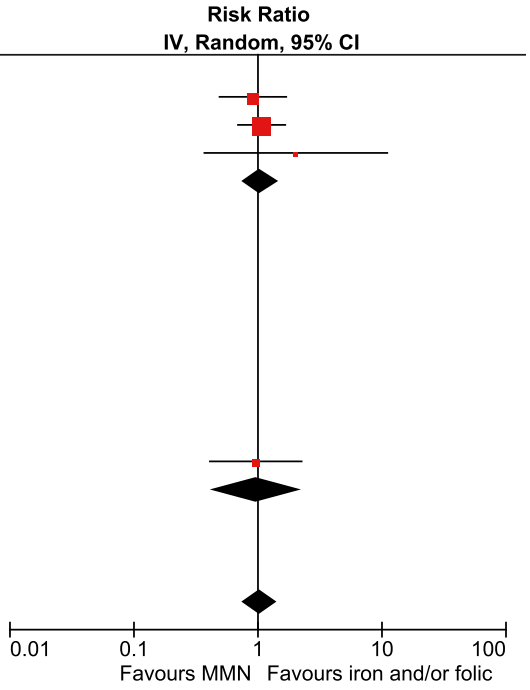
Footnotes

(1) Control group received iron only

2 Folic acid is 0.4 mg in the control group for all trials unless footnoted.

2. Caesarean section

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.2.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.0943	0.3158	27.4%	0.91 [0.49, 1.69]
Osrin 2005	0.0677	0.2238	54.5%	1.07 [0.69, 1.66]
Roberfroid 2008	0.7031	0.866	3.6%	2.02 [0.37, 11.03]
Subtotal (95% CI)			**85.5%**	**1.04 [0.74, 1.48]**
Heterogeneity: Tau² = 0.00; Chi² = 0.78, df = 2 (P = 0.68); I² = 0%				
Test for overall effect: Z = 0.24 (P = 0.81)				
1.2.2 versus 30mg iron plus folic acid				
Subtotal (95% CI)				**Not estimable**
Heterogeneity: Not applicable				
Test for overall effect: Not applicable				
1.2.3 Iron dose not specified				
Friis 2004 (1)	-0.0408	0.4341	14.5%	0.96 [0.41, 2.25]
Subtotal (95% CI)			**14.5%**	**0.96 [0.41, 2.25]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.09 (P = 0.93)				
Total (95% CI)			**100.0%**	**1.03 [0.75, 1.43]**
Heterogeneity: Tau² = 0.00; Chi² = 0.81, df = 3 (P = 0.85); I² = 0%				
Test for overall effect: Z = 0.19 (P = 0.85)				
Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.86), I² = 0%				

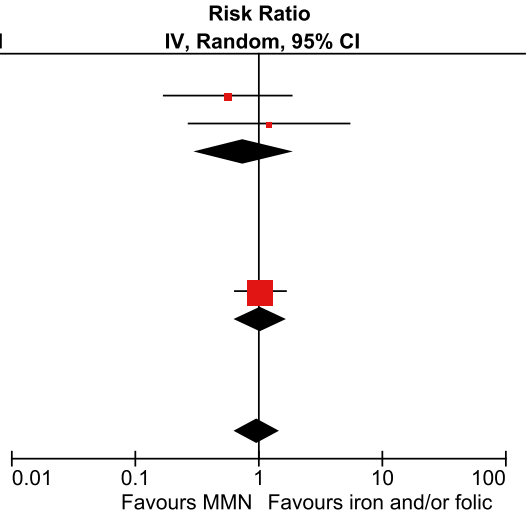


Footnotes

(1) same iron and folic acid supplements in both arms

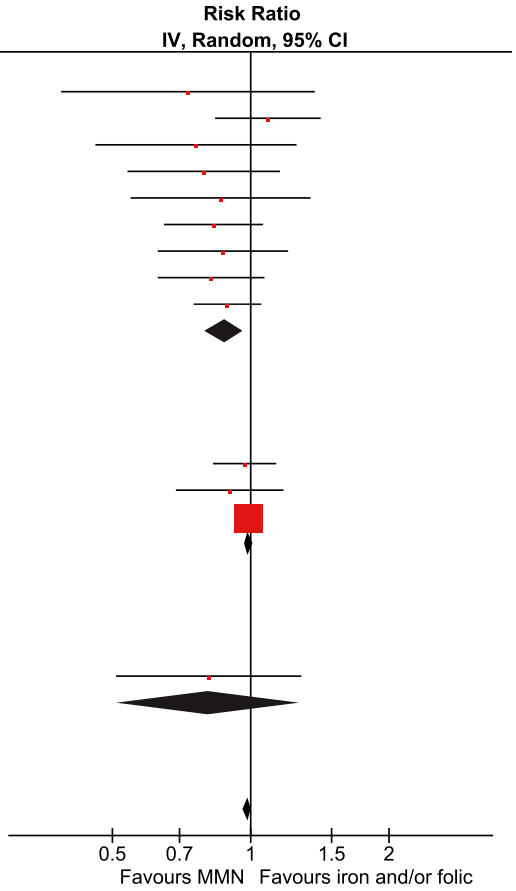
3. Maternal mortality

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.3.1 versus 60mg iron plus folic acid				
Kaestel 2005	-0.5798	0.6082	12.6%	0.56 [0.17, 1.84]
Zagre 2007	0.1906	0.7652	8.0%	1.21 [0.27, 5.42]
Subtotal (95% CI)			**20.6%**	**0.75 [0.30, 1.92]**
Heterogeneity: Tau² = 0.00; Chi² = 0.62, df = 1 (P = 0.43); I² = 0%				
Test for overall effect: Z = 0.59 (P = 0.55)				
1.3.2 versus 30mg iron plus folic acid				
SUMMIT 2008	0.02955	0.2427	79.4%	1.03 [0.64, 1.66]
Subtotal (95% CI)			**79.4%**	**1.03 [0.64, 1.66]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.12 (P = 0.90)				
Total (95% CI)			**100.0%**	**0.97 [0.63, 1.48]**
Heterogeneity: Tau² = 0.00; Chi² = 0.96, df = 2 (P = 0.62); I² = 0%				
Test for overall effect: Z = 0.16 (P = 0.87)				
Test for subgroup differences: Chi² = 0.34, df = 1 (P = 0.56), I² = 0%				



4. Small for gestational age (SGA)

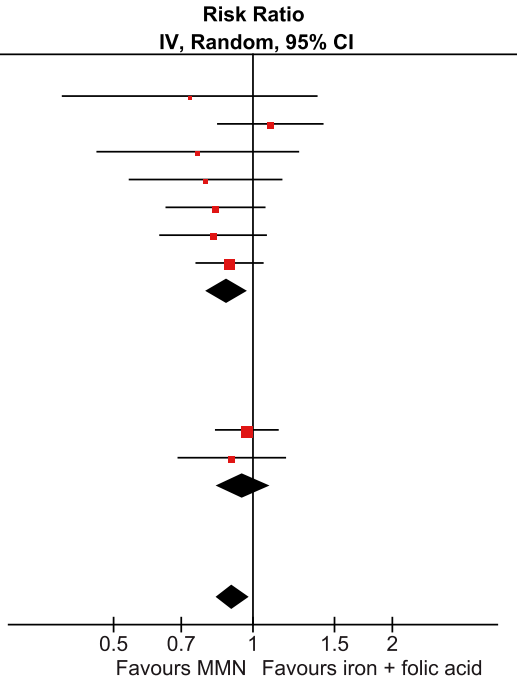
Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.4.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.3147	0.3223	0.1%	0.73 [0.39, 1.37]
Christian 2003	0.0862	0.1329	0.6%	1.09 [0.84, 1.41]
Kaestel 2005	-0.2744	0.255	0.2%	0.76 [0.46, 1.25]
Osrin 2005	-0.2357	0.1928	0.3%	0.79 [0.54, 1.15]
Ramakrishnan 2003 (1)	-0.1508	0.22806	0.2%	0.86 [0.55, 1.34]
Roberfroid 2008	-0.1863	0.1247	0.6%	0.83 [0.65, 1.06]
Sunawang 2009 (2)	-0.1392	0.16468	0.4%	0.87 [0.63, 1.20]
Zagre 2007	-0.1984	0.1344	0.6%	0.82 [0.63, 1.07]
Zeng 2008	-0.1165	0.0843	1.4%	0.89 [0.75, 1.05]
Subtotal (95% CI)			**4.3%**	**0.88 [0.80, 0.96]**
Heterogeneity: Tau² = 0.00; Chi² = 4.09, df = 8 (P = 0.85); I² = 0%				
Test for overall effect: Z = 2.72 (P = 0.007)				
1.4.2 versus 30mg iron plus folic acid				
SUMMIT 2008	-0.0305	0.0787	1.6%	0.97 [0.83, 1.13]
Tofail 2008	-0.1053	0.1355	0.5%	0.90 [0.69, 1.17]
West 2014 (3)	-0.0101	0.0104	93.3%	0.99 [0.97, 1.01]
Subtotal (95% CI)			**95.5%**	**0.99 [0.97, 1.01]**
Heterogeneity: Tau² = 0.00; Chi² = 0.55, df = 2 (P = 0.76); I² = 0%				
Test for overall effect: Z = 1.07 (P = 0.28)				
1.4.3 Iron dose not specified				
Friis 2004 (4)	-0.2107	0.2347	0.2%	0.81 [0.51, 1.28]
Subtotal (95% CI)			**0.2%**	**0.81 [0.51, 1.28]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.90 (P = 0.37)				
Total (95% CI)			**100.0%**	**0.98 [0.96, 1.00]**
Heterogeneity: Tau² = 0.00; Chi² = 11.29, df = 12 (P = 0.50); I² = 0%				
Test for overall effect: Z = 1.65 (P = 0.10)				
Test for subgroup differences: Chi² = 6.64, df = 2 (P = 0.04), I² = 69.9%				



Footnotes
(1) Control group received iron only
(2) Control group received 60 mg iron and 0.25 mg folic acid
(3) Control group received 27 mg of iron and 0.6 mg folic acid
(4) Iron and folic acid provided as separate supplements

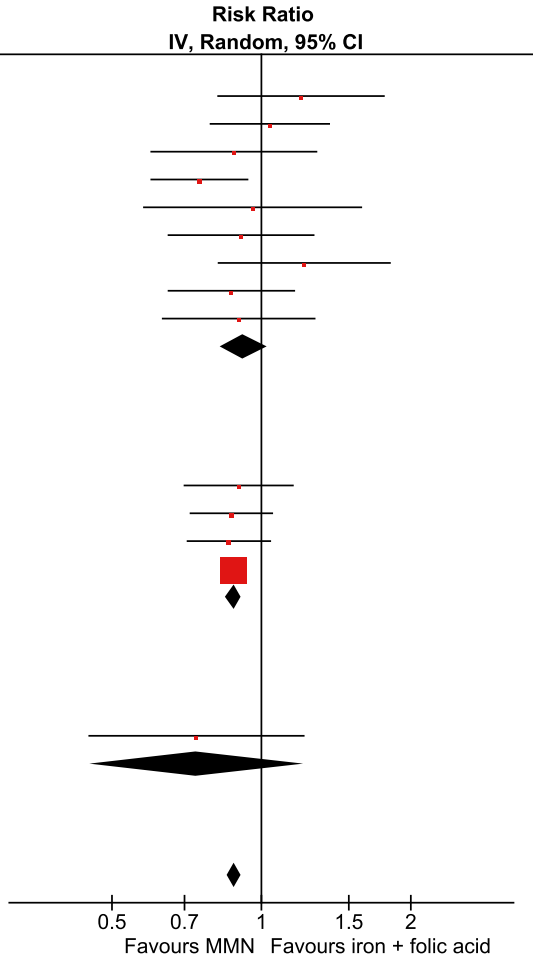
4b. SGA – exploratory analysis, with data restricted to trials with control arms receiving 60 mg or 30 mg iron plus 0.4 mg folic acid.

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
7.4.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.3147	0.3223	1.6%	0.73 [0.39, 1.37]
Christian 2003	0.0862	0.1329	9.7%	1.09 [0.84, 1.41]
Kaestel 2005	-0.2744	0.255	2.6%	0.76 [0.46, 1.25]
Osrin 2005	-0.2357	0.1928	4.6%	0.79 [0.54, 1.15]
Roberfroid 2008	-0.1863	0.1247	11.0%	0.83 [0.65, 1.06]
Zagre 2007	-0.1984	0.1344	9.5%	0.82 [0.63, 1.07]
Zeng 2008	-0.1165	0.0843	24.1%	0.89 [0.75, 1.05]
Subtotal (95% CI)			**63.1%**	**0.88 [0.79, 0.97]**
Heterogeneity: Tau² = 0.00; Chi² = 4.08, df = 6 (P = 0.67); I² = 0%				
Test for overall effect: Z = 2.50 (P = 0.01)				
7.4.2 versus 30mg iron plus folic acid				
SUMMIT 2008	-0.0305	0.0787	27.6%	0.97 [0.83, 1.13]
Tofail 2008	-0.1053	0.1355	9.3%	0.90 [0.69, 1.17]
Subtotal (95% CI)			**36.9%**	**0.95 [0.83, 1.09]**
Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 1 (P = 0.63); I² = 0%				
Test for overall effect: Z = 0.73 (P = 0.47)				
Total (95% CI)			**100.0%**	**0.90 [0.83, 0.98]**
Heterogeneity: Tau² = 0.00; Chi² = 5.20, df = 8 (P = 0.74); I² = 0%				
Test for overall effect: Z = 2.43 (P = 0.02)				
Test for subgroup differences: Chi² = 0.89, df = 1 (P = 0.34), I² = 0%				



5. Low birth weight

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.5.1 versus 60mg iron plus folic acid				
Bhutta 2009a	0.1838	0.19606	0.7%	1.20 [0.82, 1.76]
Christian 2003	0.0392	0.1403	1.3%	1.04 [0.79, 1.37]
Kaestel 2005	-0.1278	0.1954	0.7%	0.88 [0.60, 1.29]
Osrin 2005	-0.2876	0.1138	2.0%	0.75 [0.60, 0.94]
Ramakrishnan 2003 (1)	-0.0408	0.2571	0.4%	0.96 [0.58, 1.59]
Roberfroid 2008	-0.09431	0.17166	0.9%	0.91 [0.65, 1.27]
Sunawang 2009 (2)	0.1988	0.2027	0.6%	1.22 [0.82, 1.81]
Zagre 2007	-0.1392	0.1487	1.2%	0.87 [0.65, 1.16]
Zeng 2008	-0.1054	0.1797	0.8%	0.90 [0.63, 1.28]
Subtotal (95% CI)			**8.7%**	**0.92 [0.83, 1.03]**
Heterogeneity: Tau² = 0.00; Chi² = 8.02, df = 8 (P = 0.43); I² = 0%				
Test for overall effect: Z = 1.50 (P = 0.13)				
1.5.2 versus 30mg iron plus folic acid				
Lui 2013	-0.1054	0.1282	1.6%	0.90 [0.70, 1.16]
SUMMIT 2008	-0.1393	0.0966	2.8%	0.87 [0.72, 1.05]
Tofail 2008	-0.1508	0.09778	2.7%	0.86 [0.71, 1.04]
West 2014 (3)	-0.1278	0.0177	83.8%	0.88 [0.85, 0.91]
Subtotal (95% CI)			**90.9%**	**0.88 [0.85, 0.91]**
Heterogeneity: Tau² = 0.00; Chi² = 0.10, df = 3 (P = 0.99); I² = 0%				
Test for overall effect: Z = 7.56 (P < 0.00001)				
1.5.3 Iron dose not specified				
Friis 2004 (4)	-0.3011	0.2537	0.4%	0.74 [0.45, 1.22]
Subtotal (95% CI)			**0.4%**	**0.74 [0.45, 1.22]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.19 (P = 0.24)				
Total (95% CI)			**100.0%**	**0.88 [0.85, 0.91]**
Heterogeneity: Tau² = 0.00; Chi² = 9.23, df = 13 (P = 0.76); I² = 0%				
Test for overall effect: Z = 7.73 (P < 0.00001)				
Test for subgroup differences: Chi² = 1.11, df = 2 (P = 0.57), I² = 0%				

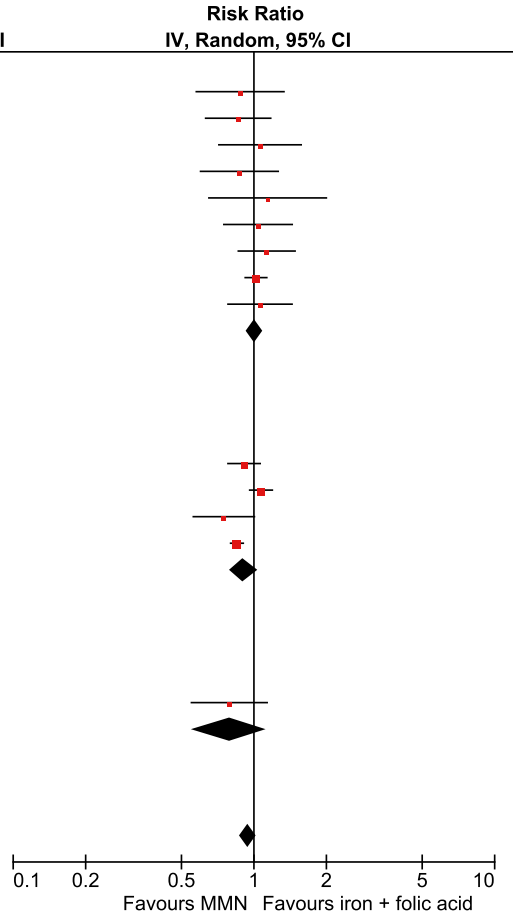


Footnotes

(1) Control group received iron only
(2) Control arm received 60 mg iron and 0.25 mg folic acid
(3) Control arm received 27 mg iron and 0.6 mg folic acid
(4) Iron and folic acid provided as separate supplements in both arms

6. Preterm birth

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.6.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.13196	0.2139	2.9%	0.88 [0.58, 1.33]
Christian 2003	-0.1508	0.1588	4.8%	0.86 [0.63, 1.17]
Kaestel 2005	0.0583	0.2008	3.3%	1.06 [0.72, 1.57]
Osrin 2005	-0.1392	0.1895	3.6%	0.87 [0.60, 1.26]
Ramakrishnan 2003 (1)	0.131	0.2866	1.8%	1.14 [0.65, 2.00]
Roberfroid 2008	0.03922	0.16678	4.4%	1.04 [0.75, 1.44]
Sunawang 2009 (2)	0.1222	0.1385	5.9%	1.13 [0.86, 1.48]
Zagre 2007	0.019802	0.05264	15.1%	1.02 [0.92, 1.13]
Zeng 2008	0.0583	0.1563	4.9%	1.06 [0.78, 1.44]
Subtotal (95% CI)			**46.7%**	**1.01 [0.94, 1.10]**
Heterogeneity: Tau² = 0.00; Chi² = 3.14, df = 8 (P = 0.93); I² = 0%				
Test for overall effect: Z = 0.31 (P = 0.76)				
1.6.2 versus 30mg iron plus folic acid				
Lui 2013	-0.0943	0.0786	11.4%	0.91 [0.78, 1.06]
SUMMIT 2008	0.0677	0.0553	14.7%	1.07 [0.96, 1.19]
Tofail 2008	-0.2876	0.14904	5.3%	0.75 [0.56, 1.00]
West 2014 (3)	-0.1625	0.0309	18.3%	0.85 [0.80, 0.90]
Subtotal (95% CI)			**49.6%**	**0.91 [0.79, 1.04]**
Heterogeneity: Tau² = 0.01; Chi² = 14.67, df = 3 (P = 0.002); I² = 80%				
Test for overall effect: Z = 1.36 (P = 0.18)				
1.6.3 Iron dose not specified				
Friis 2004 (4)	-0.2357	0.1847	3.8%	0.79 [0.55, 1.13]
Subtotal (95% CI)			**3.8%**	**0.79 [0.55, 1.13]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 1.28 (P = 0.20)				
Total (95% CI)			**100.0%**	**0.95 [0.88, 1.03]**
Heterogeneity: Tau² = 0.01; Chi² = 25.33, df = 13 (P = 0.02); I² = 49%				
Test for overall effect: Z = 1.30 (P = 0.19)				
Test for subgroup differences: Chi² = 3.16, df = 2 (P = 0.21), I² = 36.7%				



Footnotes

(1) Control group received iron only

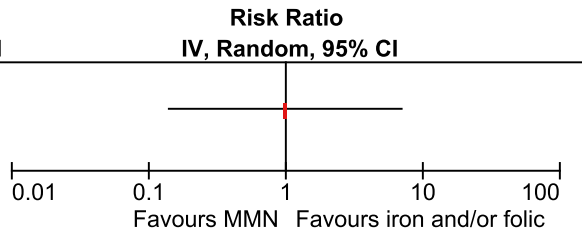
(2) Control arm received 60 mg iron and 0.25 mg folic acid

(3) Control arm received 27 mg iron and 0.6 mg folic acid

(4) Iron and folic acid provided as separate supplements in both arms

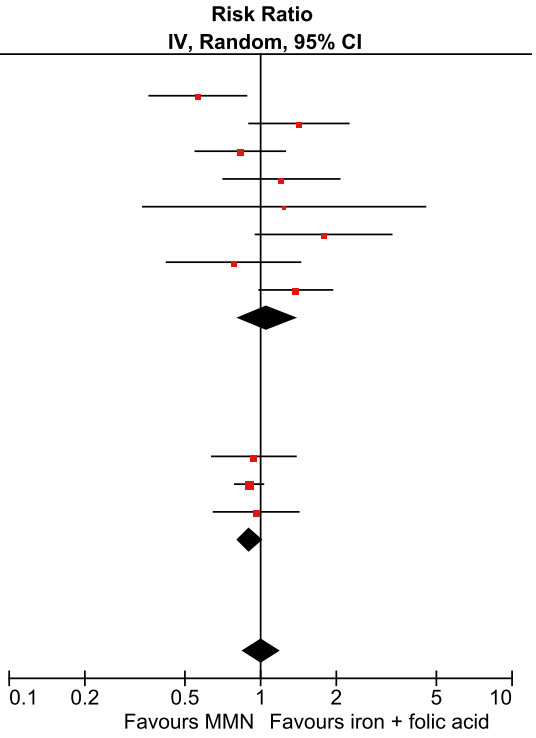
7. Congenital anomalies

Study or Subgroup	log[Risk Ratio]	SE	Risk Ratio IV, Random, 95% CI
1.7.1 versus 60mg iron plus folic acid			
Osrin 2005	-0.01005	0.9979	0.99 [0.14, 7.00]



8. Perinatal mortality

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.8.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.5749	0.22696	8.9%	0.56 [0.36, 0.88]
Christian 2003	0.3507	0.2327	8.6%	1.42 [0.90, 2.24]
Kaestel 2005	-0.1863	0.2099	9.8%	0.83 [0.55, 1.25]
Osrin 2005	0.1906	0.2719	7.1%	1.21 [0.71, 2.06]
Ramakrishnan 2003 (1)	0.2151	0.6601	1.6%	1.24 [0.34, 4.52]
Roberfroid 2008	0.5766	0.318	5.6%	1.78 [0.95, 3.32]
Sunawang 2009 (2)	-0.2485	0.3125	5.8%	0.78 [0.42, 1.44]
Zeng 2008	0.3221	0.1711	12.0%	1.38 [0.99, 1.93]
Subtotal (95% CI)			**59.4%**	**1.06 [0.80, 1.41]**
Heterogeneity: Tau² = 0.09; Chi² = 17.01, df = 7 (P = 0.02); I² = 59%				
Test for overall effect: Z = 0.42 (P = 0.67)				
1.8.2 versus 30mg iron plus folic acid				
Lui 2013	-0.0619	0.1961	10.5%	0.94 [0.64, 1.38]
SUMMIT 2008	-0.10536	0.06651	19.7%	0.90 [0.79, 1.03]
Tofail 2008	-0.04082	0.19895	10.3%	0.96 [0.65, 1.42]
Subtotal (95% CI)			**40.6%**	**0.91 [0.81, 1.02]**
Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 2 (P = 0.94); I² = 0%				
Test for overall effect: Z = 1.59 (P = 0.11)				
Total (95% CI)			**100.0%**	**1.00 [0.85, 1.19]**
Heterogeneity: Tau² = 0.03; Chi² = 19.38, df = 10 (P = 0.04); I² = 48%				
Test for overall effect: Z = 0.04 (P = 0.97)				
Test for subgroup differences: Chi² = 1.00, df = 1 (P = 0.32), I² = 0%				



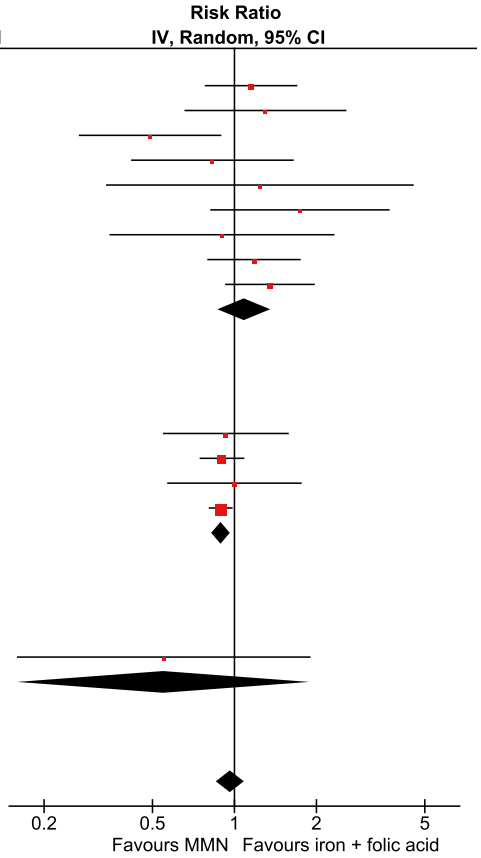
Footnotes

(1) Control group received iron only

(2) Control arm received 60 mg iron and 0.25 mg folic acid

9. Stillbirth

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.10.1 versus 60mg iron plus folic acid				
Bhutta 2009a	0.1403	0.1962	7.7%	1.15 [0.78, 1.69]
Christian 2003	0.2624	0.3459	2.8%	1.30 [0.66, 2.56]
Kaestel 2005	-0.7133	0.304	3.6%	0.49 [0.27, 0.89]
Osrin 2005	-0.1863	0.3475	2.8%	0.83 [0.42, 1.64]
Ramakrishnan 2003 (1)	0.2151	0.6601	0.8%	1.24 [0.34, 4.52]
Roberfroid 2008	0.5539	0.3835	2.3%	1.74 [0.82, 3.69]
Sunawang 2009 (2)	-0.1053	0.4818	1.5%	0.90 [0.35, 2.31]
Zagre 2007	0.1655	0.1982	7.5%	1.18 [0.80, 1.74]
Zeng 2008	0.3001	0.1902	8.0%	1.35 [0.93, 1.96]
Subtotal (95% CI)			**37.0%**	**1.09 [0.88, 1.36]**
Heterogeneity: Tau² = 0.03; Chi² = 10.92, df = 8 (P = 0.21); I² = 27%				
Test for overall effect: Z = 0.79 (P = 0.43)				
1.10.2 versus 30mg iron plus folic acid				
Lui 2013	-0.0726	0.268	4.5%	0.93 [0.55, 1.57]
SUMMIT 2008	-0.1053	0.09302	20.8%	0.90 [0.75, 1.08]
Tofail 2008	0	0.2867	4.0%	1.00 [0.57, 1.75]
West 2014 (3)	-0.1165	0.0481	32.8%	0.89 [0.81, 0.98]
Subtotal (95% CI)			**62.1%**	**0.90 [0.82, 0.97]**
Heterogeneity: Tau² = 0.00; Chi² = 0.19, df = 3 (P = 0.98); I² = 0%				
Test for overall effect: Z = 2.65 (P = 0.008)				
1.10.3 Iron dose not specified				
Friis 2004 (4)	-0.5978	0.6299	0.9%	0.55 [0.16, 1.89]
Subtotal (95% CI)			**0.9%**	**0.55 [0.16, 1.89]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.95 (P = 0.34)				
Total (95% CI)			**100.0%**	**0.97 [0.86, 1.09]**
Heterogeneity: Tau² = 0.01; Chi² = 16.52, df = 13 (P = 0.22); I² = 21%				
Test for overall effect: Z = 0.53 (P = 0.60)				
Test for subgroup differences: Chi² = 3.39, df = 2 (P = 0.18), I² = 41.0%				

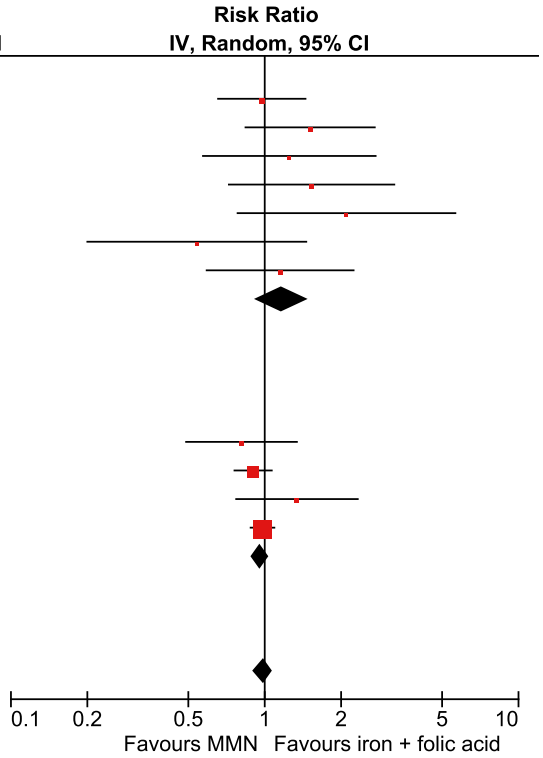


Footnotes

(1) Control group received iron only
(2) Control arm received 60 mg iron and 0.25 mg folic acid
(3) Control arm received 27 mg iron and 0.6 mg folic acid
(4) Iron and folic acid provided as separate supplements in both arms

10. Neonatal mortality

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.9.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.0266	0.2023	5.5%	0.97 [0.66, 1.45]
Christian 2003	0.4121	0.2992	2.6%	1.51 [0.84, 2.71]
Kaestel 2005	0.2231	0.3996	1.4%	1.25 [0.57, 2.74]
Osrin 2005	0.4253	0.3829	1.6%	1.53 [0.72, 3.24]
Roberfroid 2008	0.7419	0.5041	0.9%	2.10 [0.78, 5.64]
Sunawang 2009 (1)	-0.61618	0.5067	0.9%	0.54 [0.20, 1.46]
Zeng 2008	0.1398	0.3401	2.0%	1.15 [0.59, 2.24]
Subtotal (95% CI)			**14.9%**	**1.17 [0.91, 1.49]**
Heterogeneity: Tau² = 0.00; Chi² = 5.75, df = 6 (P = 0.45); I² = 0%				
Test for overall effect: Z = 1.24 (P = 0.22)				
1.9.2 versus 30mg iron plus folic acid				
Lui 2013	-0.2107	0.2564	3.5%	0.81 [0.49, 1.34]
SUMMIT 2008	-0.1053	0.08626	26.3%	0.90 [0.76, 1.07]
Tofail 2008	0.2927	0.2814	2.9%	1.34 [0.77, 2.33]
West 2014 (2)	-0.0202	0.0549	52.5%	0.98 [0.88, 1.09]
Subtotal (95% CI)			**85.1%**	**0.96 [0.88, 1.05]**
Heterogeneity: Tau² = 0.00; Chi² = 2.54, df = 3 (P = 0.47); I² = 0%				
Test for overall effect: Z = 0.92 (P = 0.36)				
Total (95% CI)			**100.0%**	**0.99 [0.90, 1.08]**
Heterogeneity: Tau² = 0.00; Chi² = 10.46, df = 10 (P = 0.40); I² = 4%				
Test for overall effect: Z = 0.29 (P = 0.77)				
Test for subgroup differences: Chi² = 2.17, df = 1 (P = 0.14), I² = 54.0%				



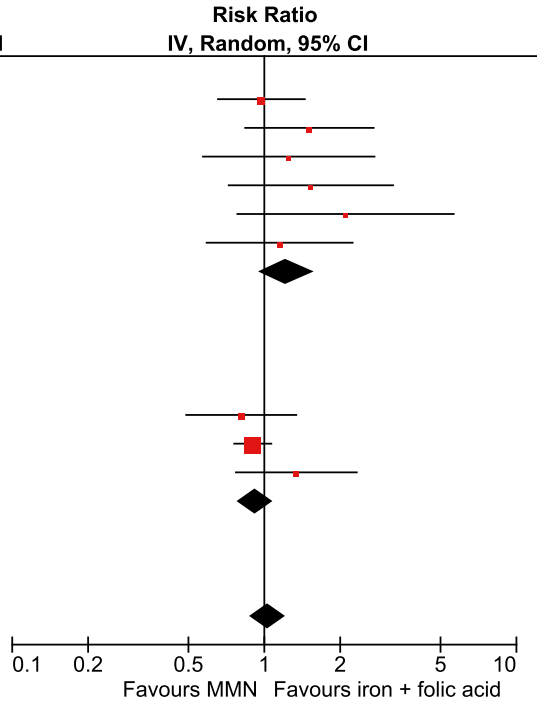
Footnotes

(1) Control arm received 60 mg iron and 0.25 mg folic acid

(2) Control arm received 27 mg iron and 0.6 mg folic acid

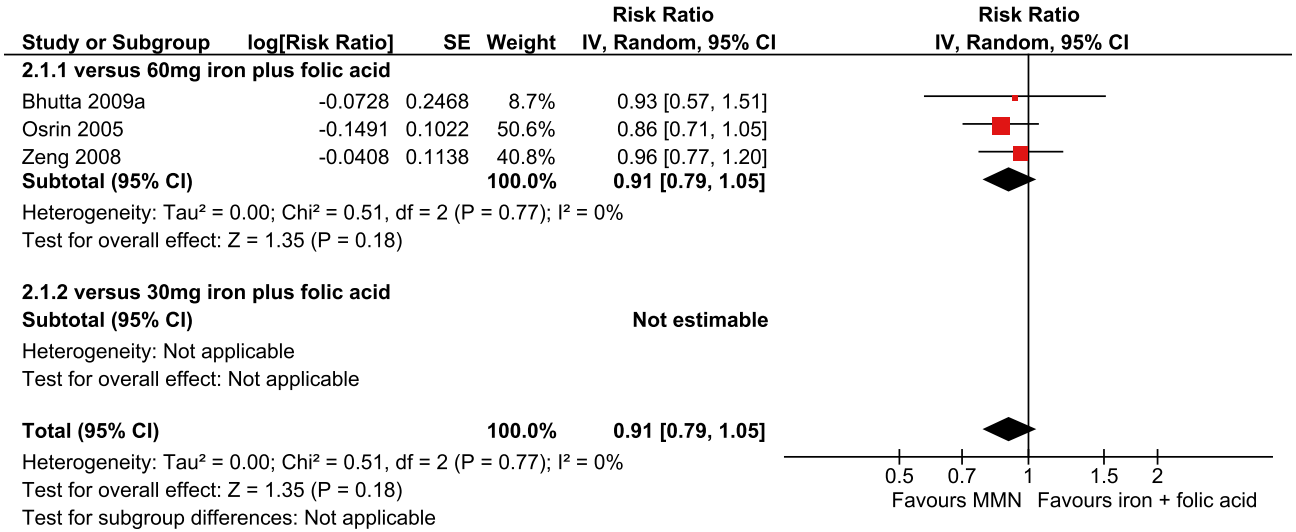
10b. Neonatal mortality – exploratory analysis, with data restricted to trials with control arms receiving 60 mg or 30 mg iron plus 0.4 mg folic acid

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
7.9.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.0266	0.2023	14.0%	0.97 [0.66, 1.45]
Christian 2003	0.4121	0.2992	7.0%	1.51 [0.84, 2.71]
Kaestel 2005	0.2231	0.3996	4.1%	1.25 [0.57, 2.74]
Osrin 2005	0.4253	0.3829	4.4%	1.53 [0.72, 3.24]
Roberfroid 2008	0.7419	0.5041	2.6%	2.10 [0.78, 5.64]
Zeng 2008	0.1398	0.3401	5.5%	1.15 [0.59, 2.24]
Subtotal (95% CI)			**37.6%**	**1.22 [0.95, 1.57]**
Heterogeneity: Tau² = 0.00; Chi² = 3.29, df = 5 (P = 0.65); I² = 0%				
Test for overall effect: Z = 1.58 (P = 0.11)				
7.9.2 versus 30mg iron plus folic acid				
Lui 2013	-0.2107	0.2564	9.3%	0.81 [0.49, 1.34]
SUMMIT 2008	-0.1053	0.08626	45.3%	0.90 [0.76, 1.07]
Tofail 2008	0.2927	0.2814	7.8%	1.34 [0.77, 2.33]
Subtotal (95% CI)			**62.4%**	**0.92 [0.78, 1.09]**
Heterogeneity: Tau² = 0.00; Chi² = 2.10, df = 2 (P = 0.35); I² = 5%				
Test for overall effect: Z = 0.92 (P = 0.36)				
Total (95% CI)			**100.0%**	**1.04 [0.88, 1.22]**
Heterogeneity: Tau² = 0.01; Chi² = 9.03, df = 8 (P = 0.34); I² = 11%				
Test for overall effect: Z = 0.43 (P = 0.67)				
Test for subgroup differences: Chi² = 3.34, df = 1 (P = 0.07), I² = 70.1%				



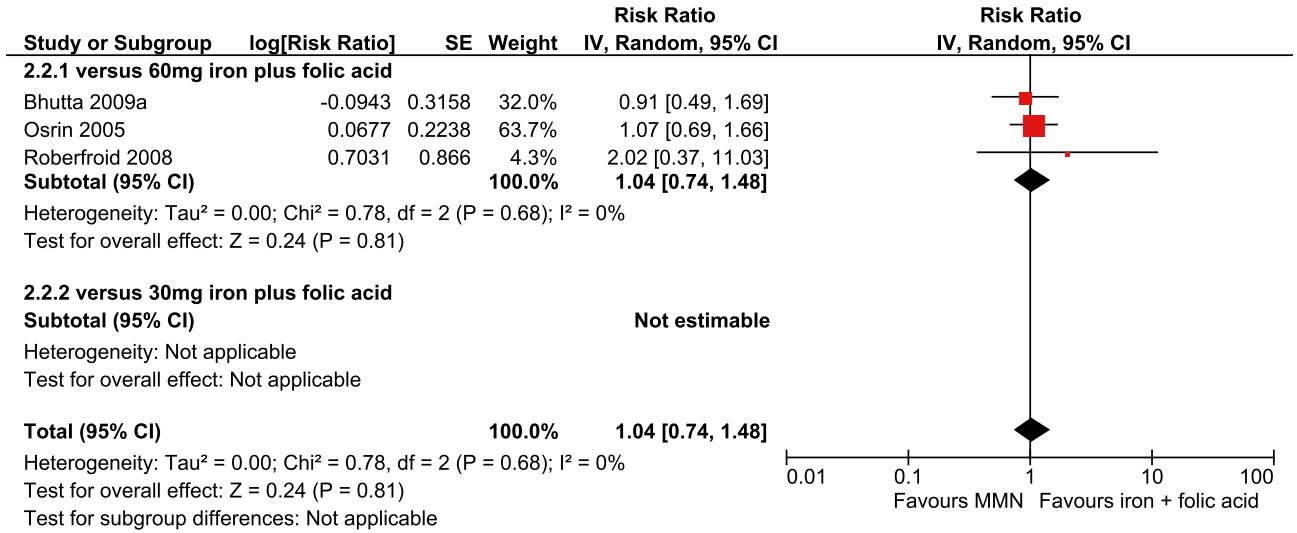
ii. Meta-analyses of trials evaluating UNIMMAP supplements with trials grouped according to dose of iron in the control group (60 mg, 30 mg or not stated)[3]

1. Maternal anaemia

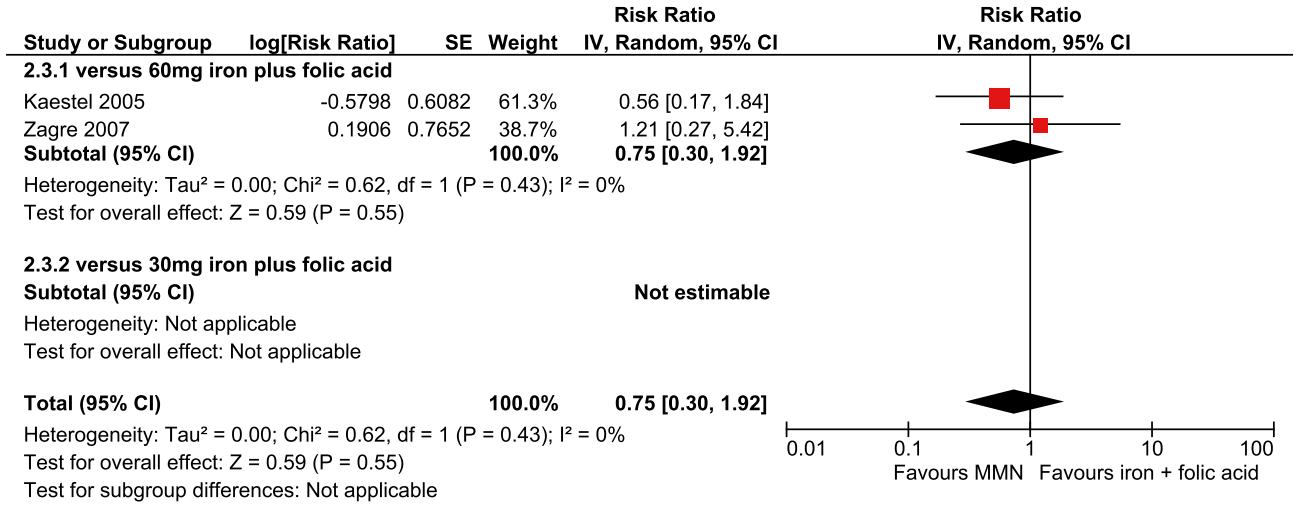


3 Folic acid is 0.4 mg in the control group for all trials unless footnoted.

2. Caesarean section

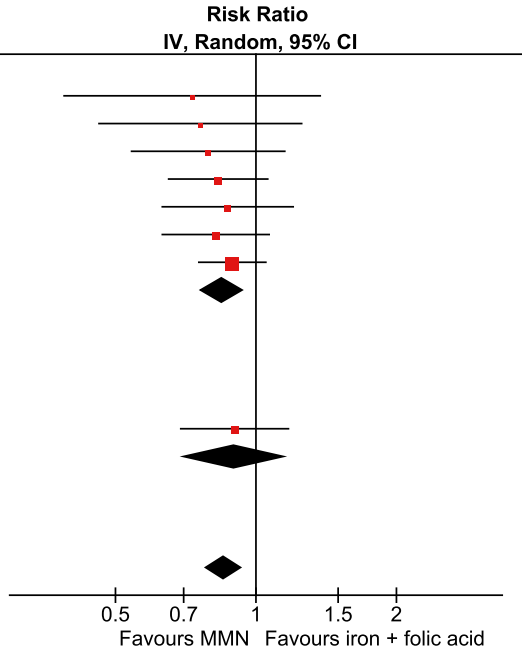


3. Maternal mortality



4. SGA

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
2.4.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.3147	0.3223	2.4%	0.73 [0.39, 1.37]
Kaestel 2005	-0.2744	0.255	3.8%	0.76 [0.46, 1.25]
Osrin 2005	-0.2357	0.1928	6.7%	0.79 [0.54, 1.15]
Roberfroid 2008	-0.1863	0.1247	15.9%	0.83 [0.65, 1.06]
Sunawang 2009 (1)	-0.1392	0.16468	9.1%	0.87 [0.63, 1.20]
Zagre 2007	-0.1984	0.1344	13.7%	0.82 [0.63, 1.07]
Zeng 2008	-0.1165	0.0843	34.9%	0.89 [0.75, 1.05]
Subtotal (95% CI)			**86.5%**	**0.85 [0.76, 0.94]**
Heterogeneity: Tau² = 0.00; Chi² = 0.98, df = 6 (P = 0.99); I² = 0%				
Test for overall effect: Z = 3.11 (P = 0.002)				
2.4.2 versus 30mg iron plus folic acid				
Tofail 2008	-0.1053	0.1355	13.5%	0.90 [0.69, 1.17]
Subtotal (95% CI)			**13.5%**	**0.90 [0.69, 1.17]**
Heterogeneity: Not applicable				
Test for overall effect: Z = 0.78 (P = 0.44)				
Total (95% CI)			**100.0%**	**0.85 [0.77, 0.94]**
Heterogeneity: Tau² = 0.00; Chi² = 1.16, df = 7 (P = 0.99); I² = 0%				
Test for overall effect: Z = 3.18 (P = 0.001)				
Test for subgroup differences: Chi² = 0.18, df = 1 (P = 0.68), I² = 0%				

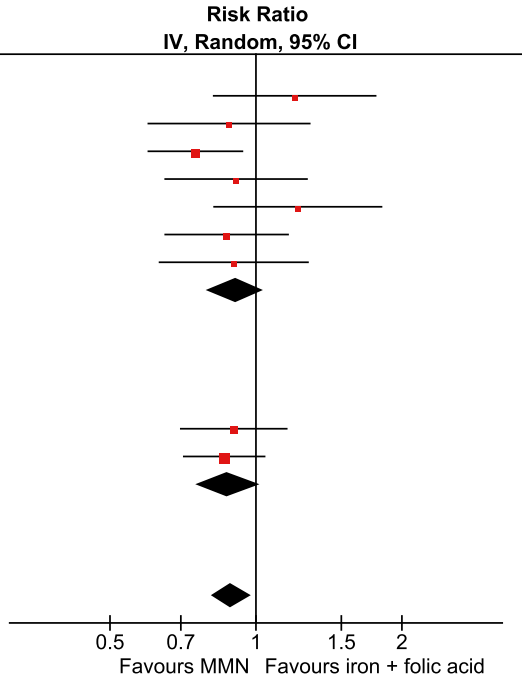


Footnotes

(1) Control arm received 60 mg iron and 0.25 mg folic acid

5. Low birth weight

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
2.5.1 versus 60mg iron plus folic acid				
Bhutta 2009a	0.1838	0.19606	6.1%	1.20 [0.82, 1.76]
Kaestel 2005	-0.1278	0.1954	6.1%	0.88 [0.60, 1.29]
Osrin 2005	-0.2876	0.1138	18.0%	0.75 [0.60, 0.94]
Roberfroid 2008	-0.09431	0.17166	7.9%	0.91 [0.65, 1.27]
Sunawang 2009 (1)	0.1988	0.2027	5.7%	1.22 [0.82, 1.81]
Zagre 2007	-0.1392	0.1487	10.5%	0.87 [0.65, 1.16]
Zeng 2008	-0.1054	0.1797	7.2%	0.90 [0.63, 1.28]
Subtotal (95% CI)			**61.5%**	**0.91 [0.79, 1.04]**
Heterogeneity: Tau² = 0.00; Chi² = 7.06, df = 6 (P = 0.32); I² = 15%				
Test for overall effect: Z = 1.44 (P = 0.15)				
2.5.2 versus 30mg iron plus folic acid				
Lui 2013	-0.1054	0.1282	14.2%	0.90 [0.70, 1.16]
Tofail 2008	-0.1508	0.09778	24.4%	0.86 [0.71, 1.04]
Subtotal (95% CI)			**38.5%**	**0.87 [0.75, 1.02]**
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%				
Test for overall effect: Z = 1.72 (P = 0.08)				
Total (95% CI)			**100.0%**	**0.89 [0.81, 0.98]**
Heterogeneity: Tau² = 0.00; Chi² = 7.20, df = 8 (P = 0.51); I² = 0%				
Test for overall effect: Z = 2.46 (P = 0.01)				
Test for subgroup differences: Chi² = 0.12, df = 1 (P = 0.73), I² = 0%				

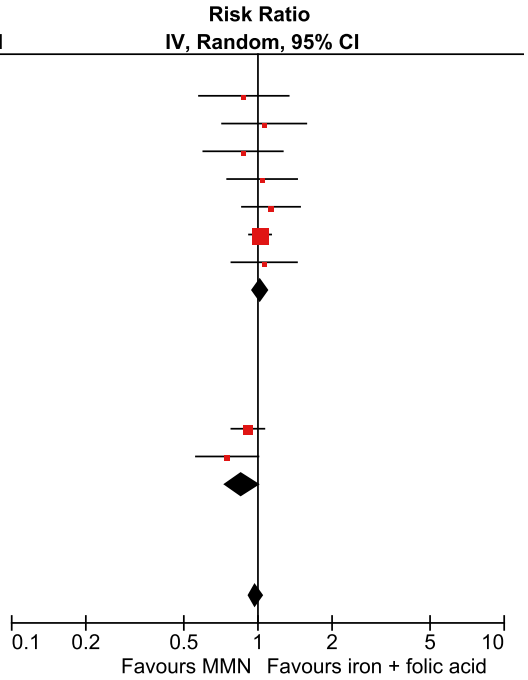


Footnotes

(1) Control arm received 60 mg iron and 0.25 mg folic acid

6. Preterm birth

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
2.6.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.13196	0.2139	2.8%	0.88 [0.58, 1.33]
Kaestel 2005	0.0583	0.2008	3.2%	1.06 [0.72, 1.57]
Osrin 2005	-0.1392	0.1895	3.6%	0.87 [0.60, 1.26]
Roberfroid 2008	0.03922	0.16678	4.7%	1.04 [0.75, 1.44]
Sunawang 2009 (1)	0.1222	0.1385	6.8%	1.13 [0.86, 1.48]
Zagre 2007	0.019802	0.05264	46.8%	1.02 [0.92, 1.13]
Zeng 2008	0.0583	0.1563	5.3%	1.06 [0.78, 1.44]
Subtotal (95% CI)			**73.2%**	**1.02 [0.94, 1.11]**
Heterogeneity: Tau² = 0.00; Chi² = 1.86, df = 6 (P = 0.93); I² = 0%				
Test for overall effect: Z = 0.51 (P = 0.61)				
2.6.2 versus 30mg iron plus folic acid				
Lui 2013	-0.0943	0.0786	21.0%	0.91 [0.78, 1.06]
Tofail 2008	-0.2876	0.14904	5.8%	0.75 [0.56, 1.00]
Subtotal (95% CI)			**26.8%**	**0.86 [0.73, 1.02]**
Heterogeneity: Tau² = 0.00; Chi² = 1.32, df = 1 (P = 0.25); I² = 24%				
Test for overall effect: Z = 1.71 (P = 0.09)				
Total (95% CI)			**100.0%**	**0.98 [0.91, 1.05]**
Heterogeneity: Tau² = 0.00; Chi² = 6.94, df = 8 (P = 0.54); I² = 0%				
Test for overall effect: Z = 0.58 (P = 0.56)				
Test for subgroup differences: Chi² = 3.10, df = 1 (P = 0.08), I² = 67.8%				

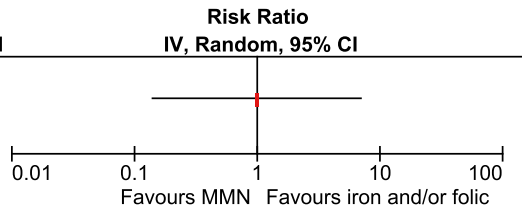


Footnotes

(1) Control arm received 60 mg iron and 0.25 mg folic acid

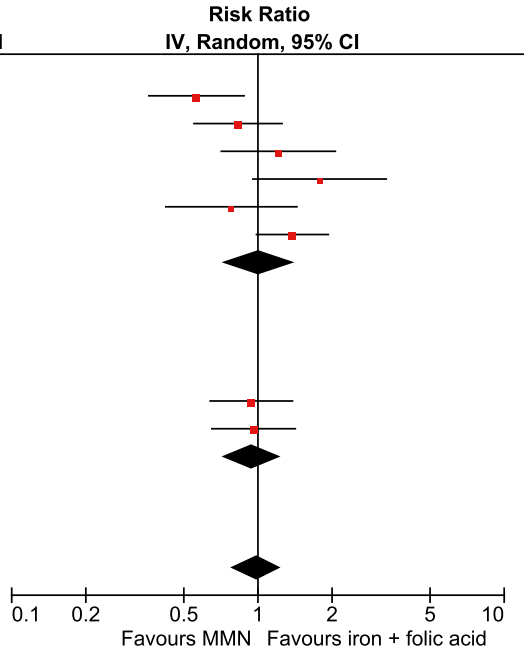
7. Congenital anomalies

Study or Subgroup	log[Risk Ratio]	SE	Risk Ratio IV, Random, 95% CI
2.7.1 versus 60mg iron plus folic acid			
Osrin 2005	-0.01005	0.9979	0.99 [0.14, 7.00]



8. Perinatal mortality

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
2.8.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.5749	0.22696	12.8%	0.56 [0.36, 0.88]
Kaestel 2005	-0.1863	0.2099	13.7%	0.83 [0.55, 1.25]
Osrin 2005	0.1906	0.2719	10.7%	1.21 [0.71, 2.06]
Roberfroid 2008	0.5766	0.318	8.9%	1.78 [0.95, 3.32]
Sunawang 2009 (1)	-0.2485	0.3125	9.1%	0.78 [0.42, 1.44]
Zeng 2008	0.3221	0.1711	16.0%	1.38 [0.99, 1.93]
Subtotal (95% CI)			**71.1%**	**1.00 [0.72, 1.41]**
Heterogeneity: Tau² = 0.12; Chi² = 15.14, df = 5 (P = 0.010); I² = 67%				
Test for overall effect: Z = 0.02 (P = 0.98)				
2.8.2 versus 30mg iron plus folic acid				
Lui 2013	-0.0619	0.1961	14.5%	0.94 [0.64, 1.38]
Tofail 2008	-0.04082	0.19895	14.3%	0.96 [0.65, 1.42]
Subtotal (95% CI)			**28.9%**	**0.95 [0.72, 1.25]**
Heterogeneity: Tau² = 0.00; Chi² = 0.01, df = 1 (P = 0.94); I² = 0%				
Test for overall effect: Z = 0.37 (P = 0.71)				
Total (95% CI)			**100.0%**	**0.99 [0.78, 1.25]**
Heterogeneity: Tau² = 0.06; Chi² = 15.29, df = 7 (P = 0.03); I² = 54%				
Test for overall effect: Z = 0.11 (P = 0.91)				
Test for subgroup differences: Chi² = 0.06, df = 1 (P = 0.80), I² = 0%				

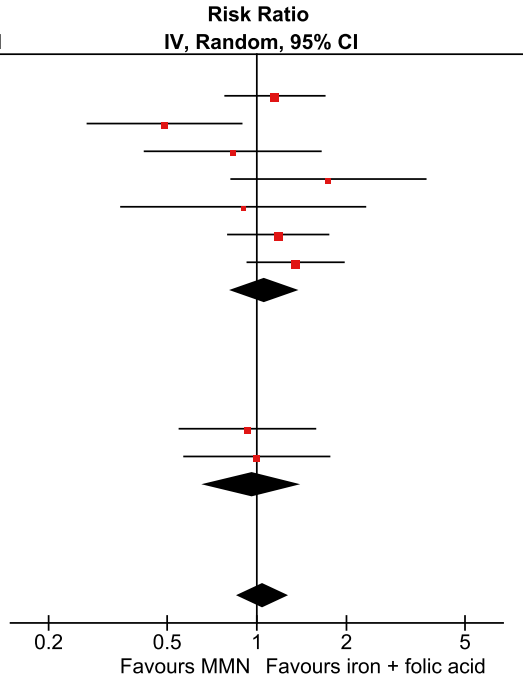


Footnotes

(1) Control arm received 60 mg iron and 0.25 mg folic acid

9. Stillbirth

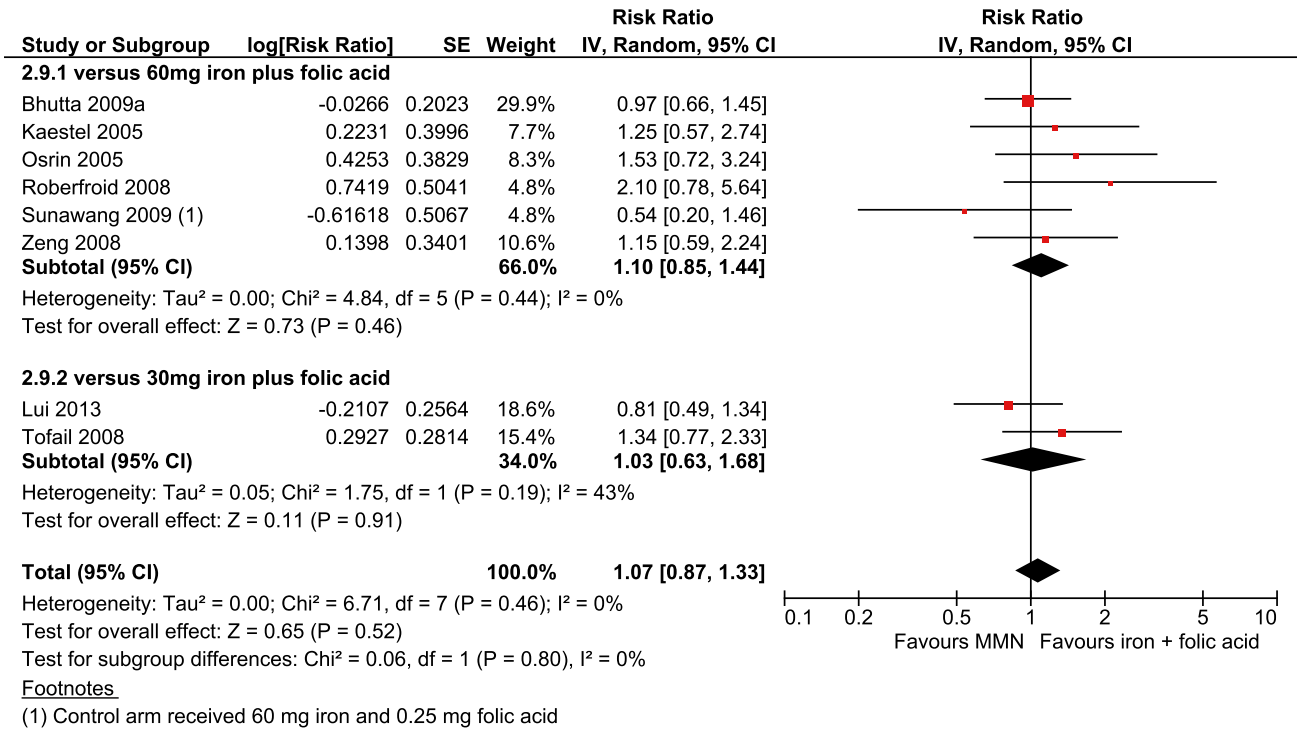
Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
2.10.1 versus 60mg iron plus folic acid				
Bhutta 2009a	0.1403	0.1962	17.0%	1.15 [0.78, 1.69]
Kaestel 2005	-0.7133	0.304	9.3%	0.49 [0.27, 0.89]
Osrin 2005	-0.1863	0.3475	7.5%	0.83 [0.42, 1.64]
Roberfroid 2008	0.5539	0.3835	6.4%	1.74 [0.82, 3.69]
Sunawang 2009 (1)	-0.1053	0.4818	4.3%	0.90 [0.35, 2.31]
Zagre 2007	0.1655	0.1982	16.7%	1.18 [0.80, 1.74]
Zeng 2008	0.3001	0.1902	17.6%	1.35 [0.93, 1.96]
Subtotal (95% CI)			**78.6%**	**1.06 [0.81, 1.38]**
Heterogeneity: Tau² = 0.05; Chi² = 10.67, df = 6 (P = 0.10); I² = 44%				
Test for overall effect: Z = 0.42 (P = 0.67)				
2.10.2 versus 30mg iron plus folic acid				
Lui 2013	-0.0726	0.268	11.2%	0.93 [0.55, 1.57]
Tofail 2008	0	0.2867	10.1%	1.00 [0.57, 1.75]
Subtotal (95% CI)			**21.4%**	**0.96 [0.66, 1.41]**
Heterogeneity: Tau² = 0.00; Chi² = 0.03, df = 1 (P = 0.85); I² = 0%				
Test for overall effect: Z = 0.20 (P = 0.84)				
Total (95% CI)			**100.0%**	**1.05 [0.85, 1.29]**
Heterogeneity: Tau² = 0.03; Chi² = 11.07, df = 8 (P = 0.20); I² = 28%				
Test for overall effect: Z = 0.44 (P = 0.66)				
Test for subgroup differences: Chi² = 0.16, df = 1 (P = 0.69), I² = 0%				



Footnotes

(1) Control arm received 60 mg iron and 0.25 mg folic acid

10a. Neonatal mortality

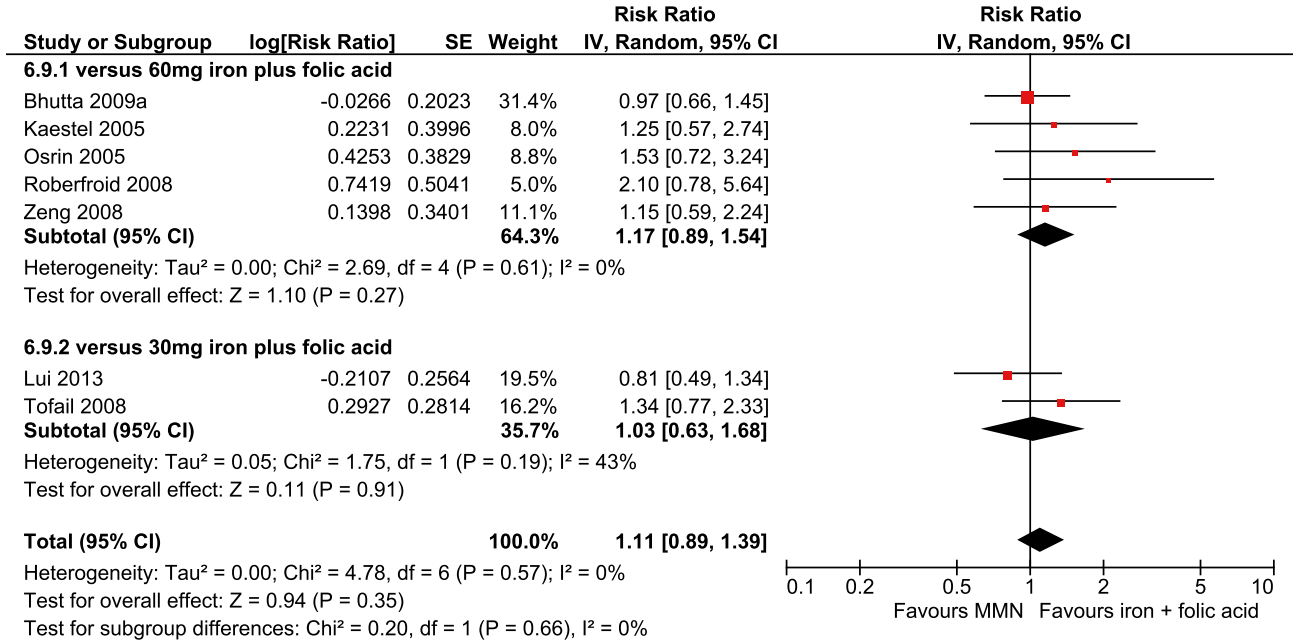


Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
2.9.1 versus 60mg iron plus folic acid				
Bhutta 2009a	-0.0266	0.2023	29.9%	0.97 [0.66, 1.45]
Kaestel 2005	0.2231	0.3996	7.7%	1.25 [0.57, 2.74]
Osrin 2005	0.4253	0.3829	8.3%	1.53 [0.72, 3.24]
Roberfroid 2008	0.7419	0.5041	4.8%	2.10 [0.78, 5.64]
Sunawang 2009 (1)	-0.61618	0.5067	4.8%	0.54 [0.20, 1.46]
Zeng 2008	0.1398	0.3401	10.6%	1.15 [0.59, 2.24]
Subtotal (95% CI)			**66.0%**	**1.10 [0.85, 1.44]**
Heterogeneity: Tau² = 0.00; Chi² = 4.84, df = 5 (P = 0.44); I² = 0%				
Test for overall effect: Z = 0.73 (P = 0.46)				
2.9.2 versus 30mg iron plus folic acid				
Lui 2013	-0.2107	0.2564	18.6%	0.81 [0.49, 1.34]
Tofail 2008	0.2927	0.2814	15.4%	1.34 [0.77, 2.33]
Subtotal (95% CI)			**34.0%**	**1.03 [0.63, 1.68]**
Heterogeneity: Tau² = 0.05; Chi² = 1.75, df = 1 (P = 0.19); I² = 43%				
Test for overall effect: Z = 0.11 (P = 0.91)				
Total (95% CI)			**100.0%**	**1.07 [0.87, 1.33]**
Heterogeneity: Tau² = 0.00; Chi² = 6.71, df = 7 (P = 0.46); I² = 0%				
Test for overall effect: Z = 0.65 (P = 0.52)				
Test for subgroup differences: Chi² = 0.06, df = 1 (P = 0.80), I² = 0%				

Footnotes

(1) Control arm received 60 mg iron and 0.25 mg folic acid

10b. Neonatal mortality – exploratory analysis with data restricted to trials with control arms receiving 60 mg or 30 mg iron plus 0.4 mg folic acid



A.7. Vitamin B6 (pyridoxine) supplements

EB Table A.7: Vitamin B6 (pyridoxine) supplements versus control

Source: Salam RA, Zuberi NF, Bhutta ZA. Pyridoxine (vitamin B6) supplementation during pregnancy or labour for maternal and neonatal outcomes. Cochrane Database Syst Rev. 2015;(6):CD000179.

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Pyridoxine (B6)**	**Control**	**Relative (95% CI)**	**Absolute**	
Pre-eclampsia – antenatal oral pyridoxine tablets											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	21/604 (3.5%)	12/593 (2%)	RR 1.71 (0.85 to 3.45)	14 more per 1000 (from 3 fewer to 50 more)	⊕⊕◯◯ LOW
Pre-eclampsia – antenatal pyridoxine lozenges											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	11/368 (3%)	12/576 (2.1%)	RR 1.43 (0.64 to 3.22)	9 more per 1000 (from 7 fewer to 46 more)	⊕◯◯◯ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Wide CI crossing the line of no effect.
3. Small sample size and few events.

A.8. Vitamin E and C supplements

EB Table A.8a: Vitamin E and C supplementation versus placebo or no treatment

Source: Rumbold A, Ota E, Hori H, Miyazaki C, Crowther CA. Vitamin E supplementation in pregnancy. Cochrane Database Syst Rev. 2015;(9):CD004069.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any vitamin E and C supplementation	Control (placebo or no treatment)	Relative (95% CI)	Absolute	
Pre-eclampsia											
14	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[1]	968/10 423 (9.3%)	997/10 455 (9.5%)	RR 0.91 (0.79 to 1.06)	9 fewer per 1000 (from 20 fewer to 6 more)	⊕⊕⊕◯ MODERATE
Eclampsia											
8	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	19/9729 (0.2%)	11/9742 (0.1%)	RR 1.67 (0.82 to 3.41)	1 more per 1000 (from 0 fewer to 3 more)	⊕⊕⊕◯ MODERATE
Any caesarean section											
6	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	2307/7641 (30.2%)	2272/7656 (29.7%)	RR 1.02 (0.97 to 1.07)	6 more per 1000 (from 9 fewer to 21 more)	⊕⊕⊕⊕ HIGH
Induction of labour											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	311/935 (33.3%)	283/942 (30%)	RR 1.11 (0.97 to 1.26)	33 more per 1000 (from 9 fewer to 78 more)	⊕⊕⊕◯ MODERATE
Maternal death											
7	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness[3]	serious[2,4]	none	2/8566 (0%)	4/8554 (0%)	RR 0.6 (0.14 to 2.51)	0 fewer per 1000 (from 0 fewer to 1 more)	⊕⊕⊕◯ MODERATE
Placental abruption											
7	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[1]	45/7471 (0.6%)	70/7451 (0.9%)	RR 0.64 (0.44 to 0.93)	3 fewer per 1000 (from 1 fewer to 5 fewer)	⊕⊕⊕◯ MODERATE
Antepartum haemorrhage											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	60/6123 (1%)	48/6133 (0.8%)	RR 1.25 (0.85 to 1.82)	2 more per 1000 (from 1 fewer to 6 more)	⊕⊕⊕◯ MODERATE

EB Table A.8a: Vitamin E and C supplementation versus placebo or no treatment (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Any vitamin E and C supplementation**	**Control (placebo or no treatment)**	**Relative (95% CI)**	**Absolute**	
Any side-effects											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,5]	none	7/355 (2%)	6/352 (1.7%)	RR 1.16 (0.39 to 3.41)	3 more per 1000 (from 10 fewer to 41 more)	⊕⊕◯◯ LOW
Side-effects – abdominal pain											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	74/935 (7.9%)	45/942 (4.8%)	RR 1.66 (1.16 to 2.37)	32 more per 1000 (from 8 more to 65 more)	⊕⊕⊕⊕ HIGH
Small for gestational age (Intrauterine growth restriction – various definitions)											
11	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1052/10 095 (10.4%)	1076/10 107 (10.6%)	RR 0.98 (0.91 to 1.06)	2 fewer per 1000 (from 10 fewer to 6 more)	⊕⊕⊕⊕ HIGH
Preterm birth (< 37 weeks of gestation)											
11	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[1]	1614/10 265 (15.7%)	1638/10 300 (15.9%)	RR 0.98 (0.88 to 1.09)	3 fewer per 1000 (from 19 fewer to 14 more)	⊕⊕⊕◯ MODERATE
Congenital malformations											
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	69/2725 (2.5%)	61/2786 (2.2%)	RR 1.16 (0.83 to 1.63)	4 more per 1000 (from 4 fewer to 14 more)	⊕⊕⊕◯ MODERATE
Stillbirth											
9	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[1]	100/9493 (1.1%)	86/9530 (0.9%)	RR 1.17 (0.88 to 1.56)	2 more per 1000 (from 1 fewer to 5 more)	⊕⊕◯◯ LOW
Neonatal death											
9	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	61/9283 (0.7%)	75/9334 (0.8%)	RR 0.81 (0.58 to 1.13)	2 fewer per 1000 (from 3 fewer to 1 more)	⊕⊕⊕◯ MODERATE
Perinatal death											
6	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	reporting bias[1]	139/8448 (1.6%)	133/8475 (1.6%)	RR 1.09 (0.77 to 1.54)	1 more per 1000 (from 4 fewer to 8 more)	⊕⊕◯◯ LOW

EB Table A.8a: Vitamin E and C supplementation versus placebo or no treatment (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Any vitamin E and C supplementation**	**Control (placebo or no treatment)**	**Relative (95% CI)**	**Absolute**	
PROM – preterm (< 37 weeks of gestation)											
5	randomized trials	no serious risk of bias	serious[6]	no serious indirectness	serious[2]	none	257/992 (25.9%)	222/1007 (22%)	RR 1.27 (0.93 to 1.75)	60 more per 1000 (from 15 fewer to 165 more)	⊕⊕◯◯ LOW
PROM – term (≥ 37 weeks of gestation)											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness[3]	no serious imprecision	none	146/1227 (11.9%)	86/1277 (6.7%)	RR 1.77 (1.37 to 2.28)	52 more per 1000 (from 25 more to 86 more)	⊕⊕⊕⊕ HIGH

1. Evident asymmetry in funnel plot.
2. Wide CI crossing the line of no effect.
3. No explanation was provided.
4. Total number of women over 3000.
5. Small sample size and/or few events.
6. Severe unexplained heterogeneity.

EB Table A.8b: Vitamin C supplementation alone versus placebo or no treatment

Source: Rumbold A, Ota E, Hori H, Miyazaki C, Crowther CA. Vitamin E supplementation in pregnancy. Cochrane Database Syst Rev. 2015;(9):CD004069.

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Vitamin C alone**	**Placebo or no treatment**	**Relative (95% CI)**	**Absolute**	
Prelabour rupture of membranes (PROM)											
6	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	64/722 (8.9%)	105/730 (14.4%)	RR 0.63 (0.48 to 0.83)	53 fewer per 1000 (from 24 fewer to 75 fewer)	⊕⊕⊕◯ MODERATE
PROM – preterm											
5	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	48/637 (7.5%)	76/645 (11.8%)	RR 0.66 (0.48 to 0.91)	40 fewer per 1000 (from 11 fewer to 61 fewer)	⊕⊕⊕◯ MODERATE
PROM – term											
1	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	16/85 (18.8%)	29/85 (34.1%)	RR 0.55 (0.32 to 0.94)	154 fewer per 1000 (from 20 fewer to 232 fewer)	⊕⊕◯◯ LOW

1. 47.8% of the events come from a single study ranked as "B".
2. The included study ranked as "B".
3. Small sample size.

A.9. Vitamin D supplements

EB Table A.9: Vitamin D supplementation alone or with calcium versus placebo or no treatment

Source: De-Regil LM, Palacios C, Lombardo LK, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. Cochrane Database Syst Rev. 2016;(1):CD008873.

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Intervention**	**Control**	**Relative (95% CI)**	**Absolute**	
Vitamin D supplementation alone versus placebo or no treatment											
Pre-eclampsia											
2	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	12/135 (8.9%)	13/84 (15.5%)	RR 0.52 (0.25 to 1.05)	74 fewer per 1000 (from 116 fewer to 8 more)	⊕◯◯◯ VERY LOW
Gestational diabetes											
2	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	1/135 (0.7%)	2/84 (2.4%)	RR 0.43 (0.05 to 3.45)	14 fewer per 1000 (from 23 fewer to 58 more)	⊕◯◯◯ VERY LOW
Caesarean section											
2	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	55/181 (30.4%)	53/131 (40.5%)	RR 0.95 (0.69 to 1.31)	20 fewer per 1000 (from 125 fewer to 125 more)	⊕◯◯◯ VERY LOW
Maternal death											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/120 (0%)	0/60 (0%)	not pooled	not pooled	⊕◯◯◯ VERY LOW
Preterm birth (< 37 weeks of gestation)											
3	randomized trials	serious[5]	no serious inconsistency	no serious indirectness	serious[2]	none	10/306 (3.3%)	17/171 (9.9%)	RR 0.36 (0.14 to 0.93)	64 fewer per 1000 (from 7 fewer to 85 fewer)	⊕⊕◯◯ LOW
Low birth weight (< 2500 g)											
3	randomized trials	very serious[1,5]	no serious inconsistency	no serious indirectness	no serious imprecision	none	20/267 (7.5%)	45/226 (19.9%)	RR 0.4 (0.24 to 0.67)	119 fewer per 1000 (from 66 fewer to 151 fewer)	⊕⊕◯◯ LOW
Stillbirth											
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,3]	none	1/334 (0.3%)	3/206 (1.5%)	RR 0.35 (0.06 to 1.99)	9 fewer per 1000 (from 14 fewer to 14 more)	⊕⊕◯◯ LOW

EB Table A.9: Vitamin D supplementation alone or with calcium versus placebo or no treatment (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intervention	Control	Relative (95% CI)	Absolute	
Neonatal death											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,3]	none	1/163 (0.6%)	4/119 (3.4%)	RR 0.27 (0.04 to 1.67)	25 fewer per 1000 (from 32 fewer to 23 more)	⊕⊕◯◯ LOW
Vitamin D plus calcium supplementation versus placebo or no treatment											
Pre-eclampsia											
3	randomized trials	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	26/557 (4.7%)	52/557 (9.3%)	RR 0.51 (0.32 to 0.8)	46 fewer per 1000 (from 19 fewer to 63 fewer)	⊕⊕⊕◯ MODERATE
Gestational diabetes											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,3]	none	0/27 (0%)	1/27 (3.7%)	RR 0.33 (0.01 to 7.84)	25 fewer per 1000 (from 37 fewer to 253 more)	⊕⊕◯◯ LOW
Preterm birth (< 37 weeks of gestation)											
3	randomized trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	46/400 (11.5%)	29/398 (7.3%)	RR 1.57 (1.02 to 2.43)	42 more per 1000 (from 1 more to 104 more)	⊕⊕⊕◯ MODERATE
Neonatal death											
1	randomized trials	serious[6]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	0/330 (0%)	2/330 (0.6%)	RR 0.2 (0.01 to 4.15)	5 fewer per 1000 (from 6 fewer to 19 more)	⊕◯◯◯ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (> 40%) from studies "C".
2. Small sample size and few events.
3. Wide CI crossing the line of no effect.
4. No events.
5. 76% of data come from two studies with high risk of bias.
6. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C".
7. 98% of data come from one study with risk of bias.

A.10. Restricting caffeine intake

EB Table A.10a: Caffeinated coffee versus decaffeinated coffee

Source: Jahanfar S, Jaafar SH. Effects of restricted caffeine intake by mother on fetal, neonatal and pregnancy outcomes. Cochrane Database Syst Rev. 2015;(6):CD006965.

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Caffeinated coffee**	**Decaffeinated coffee**	**Relative (95% CI)**	**Absolute**	
Preterm birth											
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	23/552 (4.2%)	31/601 (5.2%)	RR 0.81 (0.48 to 1.37)	10 fewer per 1000 (from 27 fewer to 19 more)	⊕⊕⊕◯ MODERATE
Small for gestational age											
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	25/552 (4.5%)	28/598 (4.7%)	RR 0.97 (0.57 to 1.64)	1 fewer per 1000 (from 20 fewer to 30 more)	⊕⊕⊕◯ MODERATE

1. Intervention arm did not restrict all types of caffeine intake, only caffeinated coffee.
2. Wide CI crossing the line of no effect.

EB Table A.10b: Non-randomized evidence of effect of caffeine on low birth weight – 1

Source: Chen LW, Wu Y, Neelakantan N, Chong MF, Pan A, van Dam RM. Maternal caffeine intake during pregnancy is associated with risk of low birth weight: a systematic review and dose-response meta-analysis. BMC Med. 2014;12:174. doi:10.1186/s12916-014-0174-6.

Quality assessment							Effect	Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative (95% CI)**	
Low birth weight – high caffeine intake vs very low or no caffeine intake								
8	observational studies[1]	no serious risk of bias	serious[2]	no serious indirectness	no serious imprecision	none	RR 1.60 (1.24 to 2.08)	⊕○○○ VERY LOW
Low birth weight – moderate caffeine intake vs very low or no caffeine intake								
7	observational studies[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	RR 1.38 (1.18 to 1.62)	⊕⊕○○ LOW
Low birth weight – low caffeine intake vs very low or no caffeine intake								
5	observational studies[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	dose-response gradient[2]	RR 1.13 (1.06 to 1.21)	⊕⊕⊕○ MODERATE

1. Case-control.
2. Severe unexplained heterogeneity (I2 65.8%).

EB Table A.10b: Non-randomized evidence of effect of caffeine on low birth weight – 2

Source: Rhee J, Kim R, Kim Y, Tam M, Lai Y, Keum N, Oldenburg CE. Maternal caffeine consumption during pregnancy and risk of low birth weight: a dose-response meta-analysis of observational studies. PLoS One. 2015;10(7):e0132334. doi:10.1371/journal.pone.0132334.

Quality assessment							Effect	Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative (95% CI)**	
Low birth weight – higher caffeine intake vs lower caffeine intake								
12	observational studies[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	dose response gradient[2]	OR 1.38 (1.1 to 1.73)	⊕⊕⊕○ MODERATE

1. Case-control and other observational studies.
2. Linear relationship.

EB Table A.10c: Non-randomized evidence of effect of caffeine on pregnancy loss – 1

Source: Chen LW, Wu Y, Neelakantan N, Chong MF, Pan A, van Dam RM. Maternal caffeine intake during pregnancy and risk of pregnancy loss: a categorical and dose-response meta-analysis of prospective studies. Public Health Nutr. 2016:19(7):1233–44. doi:10.1017/S1368980015002463.

Quality assessment							Effect	Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative (95% CI)**	
Pregnancy loss – very high caffeine intake vs very low or no caffeine intake								
4	observational studies[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[2]	OR 1.72 (1.4 to 2.13)	⊕OOO VERY LOW
Pregnancy loss – high caffeine intake vs very low or no caffeine intake								
8	observational studies[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[2]	OR 1.40 (1.16 to 1.68)	⊕OOO VERY LOW
Pregnancy loss – moderate caffeine intake vs very low or no caffeine intake								
12	observational studies[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	reporting bias[2]	OR 1.16 (0.94 to 1.41)	⊕OOO VERY LOW
Pregnancy loss – low caffeine intake vs very low or no caffeine intake								
8	serious risk of bias[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[2]	OR 1.02 (0.85 to 1.24)	⊕OOO VERY LOW

1. Case–control and other observational studies.
2. Evident asymmetry in funnel plot.
3. Wide CI crossing the line of no effect.

EB Table A.10c: Non-randomized evidence of effect of caffeine on pregnancy loss – 2

Source: Li J, Zhao H, Song JM, Zhang J, Tang YL, Xin CM. A meta-analysis of risk of pregnancy loss and caffeine and coffee consumption during pregnancy. Int J Gynaecol Obstet. 2015;130(2):116-22. doi:10.1016/j.ijgo.2015.03.033.

Quality assessment							Effect	Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Relative (95% CI)**	
Pregnancy loss – any caffeine intake vs low or no caffeine intake								
18	observational studies[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	dose response gradient[2]	OR 1.32 (1.24 to 1.40)	⊕⊕⊕◯ MODERATE
Pregnancy loss – high caffeine intake vs low or no caffeine intake								
17	observational studies[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	dose response gradient[2]	OR 1.6 (1.46 to 1.76)	⊕⊕⊕◯ MODERATE
Pregnancy loss – moderate caffeine intake vs low or no caffeine intake								
18	observational studies[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	dose response gradient[2]	OR 1.28 (1.16 to 1.42)	⊕⊕⊕◯ MODERATE
Pregnancy loss – low caffeine intake vs very low or no caffeine intake								
13	observational studies[1]	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	dose response gradient[2]	OR 1.04 (0.94 to 1.15)	⊕⊕⊕◯ MODERATE

1. Case–control and other study designs together.
2. Linear relationship (the risk of pregnancy loss increased by 19% for every 150 mg/day increase in caffeine consumption in the random effect dose–response model, assuming linearity).

B. Maternal and fetal assessment

B.1. Maternal assessment

EB Table B.1.1a: Anaemia (test accuracy): haemoglobinometer method for diagnosing anaemia (Hb < 11 g/dL) in pregnancy

Source: Sobhy S, Rogozinska E, Khan KS. Accuracy of on-site tests to detect anaemia in antenatal care: a systematic review. BJOG. 2016 (in press).

Pooled sensitivity: 0.85 (95% CI: 0.79–0.90); pooled specificity: 0.80 (95% CI: 0.76–0.83).

Test result (anaemia is defined as Hb < 11 g/dL)	No. of results per 1000 women tested (95% CI)			No. of participants (studies)	Certainty
	Prevalence 24%	Prevalence 42%	Prevalence 57%		
True positives (women with anaemia)	204 (190 to 216)	357 (332 to 378)	484 (450 to 513)	157 (1)	⊕⊕⊕◯ MODERATE[1,2]
False negatives (women incorrectly classified as not having anaemia)	36 (50 to 24)	63 (88 to 42)	86 (120 to 57)		
True negatives (women without anaemia)	608 (578 to 631)	464 (441 to 481)	344 (327 to 357)	514 (1)	⊕⊕⊕◯ MODERATE[1,2]
False positives (women incorrectly classified as having anaemia)	152 (182 to 129)	116 (139 to 99)	86 (103 to 73)		

1. Unclear selection of study population.
2. Not assessed, only one study available.

EB Table B.1.1b: Anaemia (test accuracy): Hb Colour Scale method for diagnosing anaemia (Hb < 11 g/dL) in pregnancy

Source: Sobhy S, Rogozinska E, Khan KS. Accuracy of on-site tests to detect anaemia in antenatal care: a systematic review. BJOG. 2016 (in press).

Pooled sensitivity: 0.75 (95% CI: 0.71–0.80); pooled specificity: 0.47 (95% CI: 0.41–0.53).

Test result (anaemia is defined as Hb < 11 g/dL)	No. of results per 1000 women tested (95% CI)			No. of participants (studies)	Certainty
	Prevalence 24%	Prevalence 42%	Prevalence 57%		
True positives (women with anaemia)	204 (190 to 216)	357 (332 to 378)	484 (450 to 513)	157 (1)	⊕⊕⊕◯ MODERATE[1,2]
False negatives (women incorrectly classified as not having anaemia)	36 (50 to 24)	63 (88 to 42)	86 (120 to 57)		
True negatives (women without anaemia)	608 (578 to 631)	464 (441 to 481)	344 (327 to 357)	514 (1)	⊕⊕⊕◯ MODERATE[1,2]
False positives (women incorrectly classified as having anaemia)	152 (182 to 129)	116 (139 to 99)	86 (103 to 73)		

1. Unclear selection of study population.
2. Not assessed, only one study available.

Web supplement:
WHO recommendations on antenatal care for a positive pregnancy experience: evidence base

EB Table B.1.2a: Asymptomatic bacteriuria (ASB): dipstick (nitrites or leukocytes) for diagnosing ASB in pregnancy

Source: Rogozinska E, Formina S, Zamora J, Mignini L, Khan KS. Accuracy of on-site tests to detect asymptomatic bacteriuria in pregnancy: a systematic review and meta-analysis. Obstet Gynecol. 2016;128(3):495–503. doi:10.1097/AOG.0000000000001597.

Pooled sensitivity: 0.73 (95% CI: 0.59–0.83); pooled specificity: 0.89 (95% CI: 0.79–0.94).

Test result	No. of results per 1000 women tested (95% CI)			No. of participants (studies)	Certainty
	Prevalence 3%	Prevalence 9%	Prevalence 19%		
True positives (women with ASB)	21 (17 to 24)	62 (50 to 72)	131 (106 to 152)	603 (7)	⊕OOO VERY LOW [1,2,3]
False negatives (women incorrectly classified as not having ASB)	9 (6 to 13)	28 (18 to 40)	59 (38 to 84)		
True negatives (women without ASB)	844 (737 to 902)	792 (692 to 846)	705 (616 to 753)	5087 (7)	⊕OOO VERY LOW [1,2,3,4]
False positives (women incorrectly classified as having ASB)	126 (68 to 233)	118 (64 to 218)	105 (57 to 194)		

1. Majority of studies of moderate certainty and one of low certainty.
2. Visible inconsistency in estimates between studies.
3. Visible imprecision, wide CI.

EB Table B.1.2b: Asymptomatic bacteriuria (ASB): Gram staining for diagnosing ASB in pregnancy

Pooled sensitivity: 0.86 (95% CI: 0.80–0.91); pooled specificity: 0.97 (95% CI: 0.93–0.99).

Test result	No. of results per 1000 women tested (95% CI)			No. of participants (studies)	Certainty
	Prevalence 3%	Prevalence 9%	Prevalence 19%		
True positives (women with ASB)	25 (23 to 27)	76 (68 to 81)	160 (143 to 171)	156 (4)	⊕OOO VERY LOW [1,2,3]
False negatives (women incorrectly classified as not having ASB)	5 (3 to 7)	14 (9 to 22)	30 (19 to 47)		
True negatives (women without ASB)	951 (902 to 960)	892 (846 to 901)	794 (753 to 802)	1748 (4)	⊕OOO VERY LOW [1,2,4]
False positives (women incorrectly classified as having ASB)	19 (10 to 68)	18 (9 to 64)	16 (8 to 57)		

1. Unclear risk of bias in population selection.
2. High concern over applicability of reference standard in two of four studies.
3. Visible imprecision, wide CI.
4. Not overlapping CI.

EB Table B.1.3: Intimate partner violence (IPV): screening women for IPV

Source: Rogozinska E, Formina S, Zamora J, Mignini L, Khan KS. Accuracy of on-site tests to detect asymptomatic bacteriuria in pregnancy: a systematic review and meta-analysis. Obstet Gynecol. 2016;128(3):495–503. doi:10.1097/AOG.0000000000001597.

Outcome	No. of participants (studies)	Anticipated absolute effects		Relative effect (95% CI)	Certainty
		Risk with usual antenatal care	Risk difference with universal screening for IPV		
Identification of IPV	663 (2 RCTs)	17 per 1000	57 more per 1000 (13 more to 162 more)	RR 4.28 (1.77 to 10.36)	⊕⊕◯◯ LOW[1]

1. Studies with high risk of bias.

B.2. Fetal assessment

EB Table B.2.1: Routine daily fetal movement counting versus usual practice (mixed or undefined fetal movement counting)

Source: Mangesi L, Hofmeyr GJ, Smith V, Smyth RMD. Fetal movement counting for assessment of fetal wellbeing. Cochrane Database Syst Rev. 2015;(10):CD004909.

Outcome	No. of participants (studies)	Anticipated absolute effects*		Relative effect (95% CI)	Certainty
		Risk with mixed or undefined fetal movement counting	Risk difference with routine fetal movement counting*		
Caesarean section	1076 (1 RCT)	71 per 1000	5 fewer per 1000 (29 fewer to 31 more)	RR 0.93 (0.60 to 1.44)	⊕◯◯◯ VERY LOW [1,2,3]
Assisted birth (vaginal)	1076 (1 RCT)	60 per 1000	2 more per 1000 (21 fewer to 40 more)	RR 1.04 (0.65 to 1.66)	⊕⊕◯◯ LOW [1,2]
Perinatal death	1076 (1 RCT)	0 per 1000	0 fewer per 1000 (0 fewer to 0 fewer)	not estimable	⊕⊕◯◯ LOW [1,4]
Preterm birth	1076 (1 RCT)	45 per 1000	9 fewer per 1000 (24 fewer to 21 more)	RR 0.81 (0.46 to 1.46)	⊕◯◯◯ VERY LOW [1,2,3]
Mean anxiety score	1013 (1 RCT)	not estimated	not estimated	SMD -0.22 (-0.35 to -0.10)	⊕⊕◯◯ LOW [2,5]
Low birth weight (< 2500 g or < 10th centile)	1076 (1 RCT)	87 per 1000	2 fewer per 1000 (30 fewer to 38 more)	RR 0.98 (0.66 to 1.44)	⊕◯◯◯ VERY LOW [1,2,3]

* The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

1. Analyses were performed by the researcher without blinding to group assignment.
2. Only one RCT available.
3. Wide CI, sample size > 300, total number of events > 30.
4. No events.
5. Risk of bias.

EB Table B.2.2: Symphysis-fundal height (SFH) measurement versus clinical palpation

Source: Robert Peter J, Ho JJ, Valliapan J, Sivasangari S. Symphysial fundal height (SFH) measurement in pregnancy for detecting abnormal fetal growth. Cochrane Database Syst Rev. 2015;(9):CD008136.

Outcome	No. of participants (studies)	Anticipated absolute effects*		Relative effect (95% CI)	Certainty
		Risk with clinical palpation	Risk difference with tape measurement		
Caesarean section	1639 (1 RCT)	16 per 1000	4 fewer per 1000 (11 fewer to 10 more)	RR 0.72 (0.31 to 1.67)	⊕⊕◯◯ LOW [1,2]
Induction of labour	1639 (1 RCT)	25 per 1000	4 fewer per 1000 (14 fewer to 15 more)	RR 0.84 (0.45 to 1.58)	⊕⊕◯◯ LOW [1,2]
Small for gestational age	1639 (1 RCT)	57 per 1000	18 more per 1000 (5 fewer to 52 more)	RR 1.32 (0.92 to 1.90)	⊕⊕⊕◯ MODERATE [1,3]
Perinatal mortality	1639 (1 RCT)	6 per 1000	1 more per 1000 (4 fewer to 18 more)	RR 1.25 (0.38 to 4.07)	⊕⊕◯◯ LOW [1,2]

* The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

1. Only one RCT available.
2. Wide CI, total event rate < 30.
3. Wide CI, total event rate > 30.

EB Table B.2.3: Routine antenatal cardiotocography (CTG) versus no routine antenatal CTG

Source: Grivell RM, Alfirevic Z, Gyte GML, Devane D. Antenatal cardiotocography for fetal assessment. Cochrane Database Syst Rev. 2015;(9):CD007863.

There was no direct evidence on effects for this intervention.

EB Table B.2.4a: Early ultrasound scan (< 24 weeks of gestation) versus selective/concealed ultrasound scan in early pregnancy)

Source: Whitworth M, Bricker L, Mullan C. Ultrasound for fetal assessment in early pregnancy. Cochrane Database Syst Rev. 2015;(7):CD007058.

Outcome	No. of participants (studies)	Anticipated absolute effects*		Relative effect (95% CI)	Certainty
		Risk with selective/concealed ultrasound in early pregnancy	Risk difference with routine/ revealed		
Caesarean section	22 193 (5 RCTs)	132 per 1000	7 more per 1000 (3 fewer to 16 more)	RR 1.05 (0.98 to 1.12)	⊕⊕⊕◯ MODERATE [1]
Induction of labour (for post-term pregnancy)	25 516 (8 RCTs)	31 per 1000	13 fewer per 1000 (18 fewer to 5 fewer)	RR 0.59 (0.42 to 0.83)	⊕⊕◯◯ LOW [2,3]
Mothers not satisfied with care (worried about pregnancy)	634 (1 RCT)	395 per 1000	79 fewer per 1000 (138 fewer to 4 fewer)	RR 0.80 (0.65 to 0.99)	⊕⊕◯◯ LOW [1,4]
Perinatal death	35 735 (10 RCTs)	8 per 1000	1 fewer per 1000 (2 fewer to 1 more)	RR 0.89 (0.70 to 1.12)	⊕⊕◯◯ LOW [2]
Detection of major anomaly before birth	387 (2 RCTs)	99 per 1000	218 more per 1000 (98 more to 409 more)	RR 3.19 (1.99 to 5.11)	⊕⊕◯◯ LOW [1,5]
Detection of fetal abnormality before 24 weeks of gestation	387 (2 RCTs)	44 per 1000	109 more per 1000 (30 more to 271 more)	RR 3.46 (1.67 to 7.14)	⊕⊕◯◯ LOW [1,5]
Small for gestational age	17 105 (3 RCTs)	29 per 1000	1 more per 1000 (5 fewer to 10 more)	RR 1.05 (0.81 to 1.35)	⊕⊕⊕◯ MODERATE [1]
Low birth weight (< 2500 g)	15 868 (4 RCTs)	33 per 1000	6 fewer per 1000 (13 fewer to 5 more)	RR 0.83 (0.60 to 1.15)	⊕⊕◯◯ LOW [1,3]

* The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

1. Data coming from studies with moderate risk of bias.
2. > 40% of data from studies of high risk of bias.
3. Severe heterogeneity; I2 > 60%.
4. Only one RCT available.
5. Wide CI, sample size > 300, total event rate > 30.

EB Table B.2.4b: Late ultrasound scan (> 24 weeks of gestation) versus no, concealed or selective late ultrasound scan

Source: Bricker L, Medley N, Pratt JJ. Routine ultrasound in late pregnancy (after 24 weeks of gestation). Cochrane Database Syst Rev. 2015;(6):CD001451.

Outcome	No. of participants (studies)	Anticipated absolute effects*		Relative effect (95% CI)	Certainty
		Risk with no/concealed/ selective ultrasound	Risk difference with routine ultrasound		
Caesarean section	22 663 (6 RCTs)	139 per 1000	4 more per 1000 (11 fewer to 21 more)	RR 1.03 (0.92 to 1.15)	⊕⊕⊕○ MODERATE [1,2]
Induction of labour	22 663 (6 RCTs)	238 per 1000	17 fewer per 1000 (45 fewer to 17 more)	RR 0.93 (0.81 to 1.07)	⊕⊕⊕○ MODERATE [1]
Instrumental delivery	12 310 (5 RCTs)	102 per 1000	5 more per 1000 (5 fewer to 16 more)	RR 1.05 (0.95 to 1.16)	⊕⊕⊕○ MODERATE [1]
Perinatal mortality	30 675 (8 RCTs)	6 per 1000	0 fewer per 1000 (2 fewer to 3 more)	RR 1.01 (0.67 to 1.54)	⊕⊕⊕○ MODERATE [1,3]
Preterm birth	17 151 (2 RCTs)	59 per 1000	2 fewer per 1000 (9 fewer to 5 more)	RR 0.96 (0.85 to 1.08)	⊕⊕⊕○ MODERATE [4]
Small for gestational age	20 293 (4 RCTs)	39 per 1000	1 fewer per 1000 (10 fewer to 11 more)	RR 0.98 (0.74 to 1.28)	⊕⊕○○ LOW [2,3,4]
Low birth weight	4510 (3 RCTs)	53 per 1000	4 fewer per 1000 (15 fewer to 10 more)	RR 0.92 (0.71 to 1.18)	⊕⊕○○ LOW [1,3]
Low birth weight (< 2500 g)	15 868 (4 RCTs)	33 per 1000	6 fewer per 1000 (13 fewer to 5 more)	RR 0.83 (0.60 to 1.15)	⊕⊕○○ LOW [1,3]

* The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

1. > 40% of data from studies of high risk of bias.
2. I^2 > 60%.
3. Wide CI despite large sample size.
4. Data coming from studies with moderate risk of bias.

EB Table B.2.5a: All routine Doppler ultrasound (of fetal blood vessels) versus no Doppler ultrasound in normal pregnancy

Source: Alfirevic Z, Stampalija T, Medley N. Fetal and umbilical Doppler ultrasound in normal pregnancy. Cochrane Database Syst Rev. 2015;(4):CD001450.

Outcome	No. of participants (studies)	Anticipated absolute effects		Relative effect (95% CI)	Certainty
		Risk with no Doppler ultrasound	Risk difference with all routine Doppler ultrasound		
Caesarean section	6373 (2 RCTs)	108 per 1000	2 fewer per 1000 (16 fewer to 14 more)	RR 0.98 (0.85 to 1.13)	⊕⊕⊕◯ MODERATE [1]
Operative vaginal birth	6884 (2 RCTs)	252 per 1000	10 more per 1000 (10 fewer to 30 more)	RR 1.04 (0.96 to 1.12)	⊕⊕⊕◯ MODERATE [1]
Perinatal death	11 183 (4 RCTs)	9 per 1000	2 fewer per 1000 (6 fewer to 7 more)	RR 0.80 (0.35 to 1.83)	⊕⊕◯◯ LOW [2,3]
Preterm birth (before 37 weeks)	12 162 (4 RCTs)	51 per 1000	1 more per 1000 (7 fewer to 9 more)	RR 1.02 (0.87 to 1.18)	⊕⊕⊕◯ MODERATE [1]

1. > 40% of data from studies with high risk of bias.
2. I^2 > 60%.
3. Wide CI, total sample size >300, total event rate >30.

EB Table B.2.5b: Multiple Doppler ultrasound versus no Doppler ultrasound in normal pregnancy

Outcome	No. of participants (studies)	Anticipated absolute effects		Relative effect (95% CI)	Certainty
		Risk with no Doppler ultrasound	Risk difference with multiple Doppler ultrasound		
Caesarean section*	2475 (1 RCT)	75 per 1000	1 fewer per 1000 (19 fewer to 22 more)	RR 0.98 (0.74 to 1.29)	⊕⊕⊕◯ MODERATE [1]
Operative vaginal birth	not available	not available	not available	not available	not available
Perinatal death	7292 (3 RCTs)	9 per 1000	0 fewer per 1000 (6 fewer to 16 more)	RR 1.04 (0.40 to 2.66)	⊕⊕◯◯ LOW [2,3]
Preterm birth (< 37 weeks)	8264 (3 RCTs)	62 per 1000	2 fewer per 1000 (11 fewer to 9 more)	RR 0.97 (0.82 to 1.15)	⊕⊕⊕◯ MODERATE[4]

* Data only for: Fetal/umbilical vessels + uterine artery.

1. High risk of bias in blinding of participants and outcomes assessment, unclear risk of bias in randomization procedure.
2. $I^2 > 60\%$.
3. Wide CI, total sample size >300, total event rate > 30.
4. 40% of data from studies of high risk of bias.

EB Table B.2.5c: Single Doppler ultrasound versus no Doppler ultrasound in normal pregnancy

Outcome	No. of participants (studies)	Anticipated absolute effects		Relative effect (95% CI)	Certainty
		Risk with no Doppler ultrasound	Risk difference with single Doppler ultrasound		
Caesarean section	3891 (1 RCT)	129 per 1000	1 fewer per 1000 (21 fewer to 21 more)	RR 0.99 (0.84 to 1.16)	⊕⊕⊕◯ MODERATE [1]
Operative vaginal birth	3891 (1 RCT)	154 per 1000	15 more per 1000 (8 fewer to 40 more)	RR 1.10 (0.95 to 1.26)	⊕⊕⊕◯ MODERATE [2]
Perinatal death	3891 (1 RCT)	7 per 1000	5 fewer per 1000 (6 fewer to 0 fewer)	RR 0.36 (0.13 to 0.99)	⊕⊕◯◯ LOW [3]
Preterm birth (< 37 weeks)	3891 (1 RCT)	30 per 1000	6 more per 1000 (4 fewer to 21 more)	RR 1.20 (0.86 to 1.69)	⊕◯◯◯ VERY LOW [1,3,4]

1. Only one RCT available.
2. Wide CI, total sample size > 300, total event rate > 30.
3. Wide CI, total sample size > 300, total event rate < 30.
4. High risk of bias in blinding of participants and outcomes assessment, unclear risk of bias in randomization procedure.

C. Preventive measures

C.1. Antibiotics for asymptomatic bacteriuria (ASB)

EB Table C.1: Antibiotics for ASB versus no treatment

Source: Smaill FM, Vazquez JC. Antibiotics for asymptomatic bacteriuria in pregnancy. Cochrane Database Syst Rev. 2015;(8):CD000490.

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Antibiotic**	**No treatment**	**Relative (95% CI)**	**Absolute**	
Pyelonephritis – any antibiotic regimen											
11	randomized trials	very serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	55/983 (5.6%)	197/949 (20.8%)	RR 0.23 (0.13 to 0.41)	160 fewer per 1000 (from 122 fewer to 181 fewer)	⊕OOO VERY LOW
Pyelonephritis – single dose regimen											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	9/87 (10.3%)	20/86 (23.3%)	RR 0.44 (0.21 to 0.92)	130 fewer per 1000 (from 19 fewer to 184 fewer)	⊕⊕OO LOW
Pyelonephritis – short course (3–7 days) regimen											
3	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	9/235 (3.8%)	33/248 (13.3%)	RR 0.31 (0.09 to 1.16)	92 fewer per 1000 (from 121 fewer to 21 more)	⊕OOO VERY LOW
Pyelonephritis – intermediate course (3–6 weeks) regimen											
2	randomized trials	very serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	7/209 (3.3%)	44/224 (19.6%)	RR 0.17 (0.08 to 0.37)	163 fewer per 1000 (from 124 fewer to 181 fewer)	⊕OOO VERY LOW
Pyelonephritis – continuous treatment regimen											
5	randomized trials	very serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	30/452 (6.6%)	100/391 (25.6%)	RR 0.16 (0.04 to 0.57)	215 fewer per 1000 (from 110 fewer to 246 fewer)	⊕OOO VERY LOW
Persistent bacteriuria											
4	randomized trials	serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	60/296 (20.3%)	199/300 (66.3%)	RR 0.3 (0.18 to 0.53)	464 fewer per 1000 (from 312 fewer to 544 fewer)	⊕⊕OO LOW

EB Table C.1: Antibiotics for ASB versus no treatment (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Antibiotic**	**No treatment**	**Relative (95% CI)**	**Absolute**	
Birth weight < 2500 g											
6	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	63/729 (8.6%)	96/708 (13.6%)	RR 0.64 (0.45 to 0.93)	49 fewer per 1000 (from 9 fewer to 75 fewer)	⊕⊕◯◯ LOW
Preterm birth < 37 weeks											
2	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	7/120 (5.8%)	27/122 (22.1%)	RR 0.27 (0.11 to 0.62)	162 fewer per 1000 (from 84 fewer to 197 fewer)	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by trials "B" or "C" with a substantial proportion (i.e. > 40%) from trials "C".
2. Severe unexplained heterogeneity.
3. Small sample size and/or few events.
4. Wide CI crossing the line of no effect.

C.2. Antibiotic prophylaxis to prevent recurrent urinary tract infections (RUTI)

EB Table C.2: Antibiotic prophylaxis to prevent recurrent urinary tract infections (RUTI) versus control

Source: Schneeberger C, Geerlings SE, Middleton P, Crowther CA. Interventions for preventing recurrent urinary tract infection during pregnancy. Cochrane Database Syst Rev. 2015;(7):CD009279.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Nitrofurantoin and close surveillance	Control (close surveillance alone)	Relative (95% CI)	Absolute	
Recurrent pyelonephritis											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	6/82 (7.3%)	7/85 (8.2%)	RR 0.89 (0.31 to 2.53)	9 fewer per 1000 (from 57 fewer to 126 more)	⊕OOO VERY LOW
Urinary tract infection (cystitis)											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	2/82 (2.4%)	7/85 (8.2%)	RR 0.3 (0.06 to 1.38)	58 fewer per 1000 (from 77 fewer to 31 more)	⊕OOO VERY LOW
Preterm birth (< 37 weeks)											
1	randomized trials	very serious[1,4]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	7/73 (9.6%)	6/74 (8.1%)	RR 1.18 (0.42 to 3.35)	15 more per 1000 (from 47 fewer to 191 more)	⊕OOO VERY LOW
Low birth weight (birth weight < 2500 g)											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	6/73 (8.2%)	3/74 (4.1%)	RR 2.03 (0.53 to 7.8)	42 more per 1000 (from 19 fewer to 276 more)	⊕OOO VERY LOW
Asymptomatic bacteriuria in women with 90% clinical attendance											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14/43 (32.6%)	35/59 (59.3%)	RR 0.55 (0.34 to 0.89)	267 fewer per 1000 (from 65 fewer to 392 fewer)	⊕⊕OO LOW

1. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (> 40%) from studies "C".
2. Small sample size and few events.
3. Wide CI crossing the line of no effect.
4. Severe unexplained heterogeneity.

C.3. Antenatal anti-D immunoglobulin prophylaxis

EB Table C.3: Antenatal anti-D immunoglobulin prophylaxis versus control

Source: McBain RD, Crowther CA, Middleton P. Anti-D administration in pregnancy for preventing Rhesus alloimmunization. Cochrane Database Syst Rev. 2015;(9):CD000020.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Anti-D administration in pregnancy	Control (no routine antenatal anti-D administration)	Relative (95% CI)	Absolute	
Rhesus D alloimmunization during pregnancy – any regimen											
2	randomized trials	very serious[1,2]	no serious inconsistency	no serious indirectness	serious[3]	none	5/1879 (0.3%)	13/2023 (0.6%)	RR 0.42 (0.15 to 1.17)	4 fewer per 1000 (from 5 fewer to 1 more)	⊕OOO VERY LOW
Rhesus D alloimmunization during pregnancy – 100 micrograms at 28 and 34 weeks											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	1/927 (0.1%)	6/955 (0.6%)	RR 0.17 (0.02 to 1.42)	5 fewer per 1000 (from 6 fewer to 3 more)	⊕OOO VERY LOW
Rhesus D alloimmunization during pregnancy – 50 micrograms at 28 and 34 weeks											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	4/952 (0.4%)	7/1068 (0.7%)	RR 0.64 (0.19 to 2.18)	2 fewer per 1000 (from 5 fewer to 8 more)	⊕OOO VERY LOW
Rhesus D alloimmunization postpartum (at birth of Rh-positive infant) – any regimen											
2	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	5/1112 (0.4%)	13/1185 (1.1%)	RR 0.42 (0.15 to 1.17)	6 fewer per 1000 (from 9 fewer to 2 more)	⊕OOO VERY LOW
Rhesus D alloimmunization postpartum (at birth of Rh-positive infant) – 100 micrograms at 28 and 34 weeks											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	1/599 (0.2%)	6/590 (1%)	RR 0.16 (0.02 to 1.36)	9 fewer per 1000 (from 10 fewer to 4 more)	⊕OOO VERY LOW
Rhesus D alloimmunization postpartum (at birth of Rh-positive infant) – 50 micrograms at 28 and 34 weeks											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	4/513 (0.8%)	7/595 (1.2%)	RR 0.66 (0.2 to 2.25)	4 fewer per 1000 (from 9 fewer to 15 more)	⊕OOO VERY LOW
Rhesus D alloimmunization postpartum (at birth of Rh-positive infant and follow up, up to 12 months) – any regimen											
2	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	6/985 (0.6%)	16/1063 (1.5%)	RR 0.39 (0.1 to 1.62)	9 fewer per 1000 (from 14 fewer to 9 more)	⊕OOO VERY LOW

EB Table C.3: Antenatal anti-D immunoglobulin prophylaxis versus control (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Anti-D administration in pregnancy	Control (no routine antenatal anti-D administration)	Relative (95% CI)	Absolute	
Rhesus D alloimmunization postpartum (at birth of Rh-positive infant and follow up, up to 12 months) – 100 micrograms at 28 and 34 weeks											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	1/472 (0.2%)	7/468 (1.5%)	RR 0.14 (0.02 to 1.15)	13 fewer per 1000 (from 15 fewer to 2 more)	⊕◯◯◯ VERY LOW
Rhesus D alloimmunization postpartum (at birth of Rh-positive infant and follow up, up to 12 months) – 50 micrograms at 28 and 34 weeks											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	5/513 (1%)	9/595 (1.5%)	RR 0.64 (0.22 to 1.91)	5 fewer per 1000 (from 12 fewer to 14 more)	⊕◯◯◯ VERY LOW
Rhesus D alloimmunization postpartum (after birth of Rh-positive infant at 2 to 12 months): primigravidae											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	0/362 (0%)	4/360 (1.1%)	RR 0.11 (0.01 to 2.04)	10 fewer per 1000 (from 11 fewer to 12 more)	⊕◯◯◯ VERY LOW
Incidence of positive Kleihauer test at 32–35 weeks of gestation											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	39/927 (4.2%)	67/957 (7%)	RR 0.6 (0.41 to 0.88)	28 fewer per 1000 (from 8 fewer to 41 fewer)	⊕⊕◯◯ LOW
Incidence of positive Kleihauer test at birth of Rh-positive infant											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	73/599 (12.2%)	119/590 (20.2%)	RR 0.6 (0.46 to 0.79)	81 fewer per 1000 (from 42 fewer to 109 fewer)	⊕⊕◯◯ LOW
Neonatal morbidity (jaundice)											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	1/927 (0.1%)	4/955 (0.4%)	RR 0.26 (0.03 to 2.3)	3 fewer per 1000 (from 4 fewer to 5 more)	⊕◯◯◯ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (> 40%) from studies "C".
2. Severe unexplained heterogeneity.
3. Wide CI crossing the line of no effect.
4. Small sample size and few events.

C.4. Preventive anthelminthic treatment

EB Table C.4: Preventive anthelminthic treatment versus control

Source: Salam RA, Haider BA, Humayun Q, Bhutta ZA. Effect of administration of anthelminthics for soil-transmitted helminths during pregnancy. Cochrane Database Syst Rev. 2015;(6):CD005547.

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Antihelminthics**	**Control (no routine anthelminthics)**	**Relative (95% CI)**	**Absolute**	
Maternal anaemia in third trimester (< 110 g/L)											
4	randomized trials	serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	715/2121 (33.7%)	390/1145 (34.1%)	RR 0.94 (0.81 to 1.1)	20 fewer per 1000 (from 65 fewer to 34 more)	⊕⊕◯◯ LOW
Low birth weight											
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	183/2128 (8.6%)	99/1127 (8.8%)	RR 1 (0.79 to 1.27)	0 fewer per 1000 (from 18 fewer to 24 more)	⊕⊕⊕◯ MODERATE
Preterm birth											
2	randomized trials	serious[1]	serious[2]	no serious indirectness	serious[3]	none	14/659 (2.1%)	16/659 (2.4%)	RR 0.88 (0.43 to 1.78)	3 fewer per 1000 (from 14 fewer to 19 more)	⊕◯◯◯ VERY LOW
Perinatal mortality											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	76/2289 (3.3%)	30/1096 (2.7%)	RR 1.09 (0.71 to 1.67)	2 more per 1000 (from 8 fewer to 18 more)	⊕⊕⊕◯ MODERATE

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C".
2. Severe unexplained heterogeneity.
3. Wide CI crossing the line of no effect.

C.5. Tetanus toxoid vaccination

EB Table C.5: Tetanus toxoid (TT) vaccination versus influenza vaccination

Source: Demicheli V, Barale A, Rivetti A. Vaccines for women for preventing neonatal tetanus. Cochrane Database Syst Rev. 2015;(7):CD002959.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	TT vaccine	Influenza vaccine	Relative (95% CI)	Absolute	
Neonatal tetanus cases – any dose											
1	randomized trials	serious[1]	serious[2]	no serious indirectness	serious[3]	none	9/565 (1.6%)	49/617 (7.9%)	RR 0.2 (0.1 to 0.4)	64 fewer per 1000 (from 48 fewer to 71 fewer)	⊕⊕◯◯ LOW
Neonatal tetanus deaths – one dose											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	9/224 (4%)	19/270 (7%)	RR 0.57 (0.26 to 1.24)	30 fewer per 1000 (from 52 fewer to 17 more)	⊕◯◯◯ VERY LOW
Neonatal tetanus deaths – two or three doses											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	0/341 (0%)	27/347 (7.8%)	RR 0.02 (0 to 0.3)	76 fewer per 1000 (from 54 fewer to 78 fewer)	⊕⊕◯◯ LOW
All causes of death – one dose											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	25/224 (11.2%)	28/270 (10.4%)	RR 1.08 (0.65 to 1.79)	8 more per 1000 (from 36 fewer to 82 more)	⊕⊕◯◯ LOW
All causes of death – two or three doses											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	14/341 (4.1%)	46/347 (13.3%)	RR 0.31 (0.17 to 0.55)	91 fewer per 1000 (from 60 fewer to 110 fewer)	⊕⊕⊕◯ MODERATE

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. 2evere heterogeneity.
3. Small sample size and/or few events.
4. Wide CI crossing the line of no effect.

D. Interventions for common physiological symptoms

D.1. Nausea and vomiting

Source: Matthews A, Haas DM, O'Mathúna DP, Dowswell T. Interventions for nausea and vomiting in early pregnancy. Cochrane Database Syst Rev. 2015;(9):CD007575.

EB Table D.1a: P6 acupressure versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**P6 acupressure**	**Control (placebo)**	**Relative (95% CI)**	**Absolute**	
Severity of nausea after treatment (of 4 days) using a 10 cm visual analogue scale (VAS; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	50	50	MD 1.7 lower (2.41 to 0.99 lower)	-	⊕⊕◯◯ LOW
No improvement in intensity of symptoms											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	15/53 (28.3%)	16/44 (36.4%)	RR 0.78 (0.44 to 1.39)	80 fewer per 1000 (from 204 fewer to 142 more)	⊕⊕◯◯ LOW
Mean nausea score after day 3 using VAS (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency[3]	no serious indirectness	very serious[2]	none	20	20	MD 0.1 higher (1.49 lower to 1.69 higher)	-	⊕⊕◯◯ LOW
Mean nausea score days 1–3 (average) (MD; better indicated by lower values)											
1	randomized trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	30	30	MD 0.39 higher (0.8 lower to 1.58 higher)	-	⊕◯◯◯ VERY LOW
Mean total scores (Rhodes Index) days 1–3 (average) (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	30	30	MD 1.17 higher (1.52 lower to 3.86 higher)	-	⊕◯◯◯ VERY LOW
Total Rhodes Index score on the 3rd day of intervention (MD; better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	48	45	MD 1.48 lower (4.1 lower to 1.14 higher)	-	⊕◯◯◯ VERY LOW

EB Table D.1a: P6 acupressure versus placebo (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**P6 acupressure**	**Control (placebo)**	**Relative (95% CI)**	**Absolute**	
Severity of vomiting after treatment (of 4 days) as number of vomiting episodes (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	50	50	MD 0.9 lower (1.06 to 0.74 lower)	-	⊕⊕OO LOW
Mean emesis scores days 1–3 (average) (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	30	30	MD 0.26 higher (1.06 lower to 1.58 higher)	-	⊕⊕OO LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Wide CI crossing the line of no effect and sample size < 300.
3. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (i.e. > 40%) from studies "C".
4. Sample size < 300.

EB Table D.1b: Auricular acupressure versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Auricular acupressure**	**Control (placebo)**	**Relative (95% CI)**	**Absolute**	
Nausea/vomiting score (combined Rhodes Index score) on day 6 (3 days after treatment started) (MD; better indicated by lower values)											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious	none	45	46	MD 3.6 lower (6.62 to 0.58 lower)	-	⊕⊕OO LOW

1. Baseline imbalance in scores favouring intervention group and unblinded [–2].

EB Table D.1c: Acustimulation therapy at P6 point versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Acustimulation therapy at P6 point**	**Control (placebo)**	**Relative (95% CI)**	**Absolute**	
Weight gain (in lbs) over 3 week period (MD; better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	95	92	MD 1.7 higher (0.23 to 3.17 higher)	-	⊕⊕◯◯ LOW
Dehydration: occurrences reported											
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[3]	none	3/95 (3.2%)	12/92 (13%)	RR 0.24 (0.07 to 0.83)	99 fewer per 1000 (from 22 fewer to 121 fewer)	⊕⊕◯◯ LOW

1. Indirect outcome.
2. Small sample size.
3. Small sample size and/or few events.

EB Table D.1d: Traditional acupuncture versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Traditional acupuncture**	**Control (placebo)**	**Relative (95% CI)**	**Absolute**	
Mean nausea score on day 7 (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	148	148	MD 0.7 lower (1.36 to 0.04 lower)	-	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Small sample size.

EB Table D.1e: P6 acupuncture versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**P6 acupuncture**	**Control (placebo)**	**Relative (95% CI)**	**Absolute**	
Mean nausea score on day 7 (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	148	148	MD 0.3 lower (1 lower to 0.4 higher)	-	⊕⊕◯◯ LOW
Mean dry retching score on day 7 (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	148	148	MD 0.1 higher (0.3 lower to 0.5 higher)	-	⊕⊕◯◯ LOW
Mean vomiting score on day 7 (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2,3]	none	148	148	MD 0.3 lower (0.78 lower to 0.18 higher)	-	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Wide CI crossing the line of no effect.
3. Small sample size.

EB Table D.1f: Ginger versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ginger	Control (placebo)	Relative (95% CI)	Absolute	
Mean nausea score (using Rhodes Index) on day 3 (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	34	34	MD 1.38 lower (2.73 to 0.03 lower)	-	⊕⊕◯◯ LOW
Mean vomiting score (using Rhodes Index) on day 3 (better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	34	34	MD 1.14 lower (1.91 to 0.37 lower)	-	⊕⊕◯◯ LOW
Total Rhodes Index score on day 3 (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	34	34	MD 2.52 lower (4.5 to 0.54 lower)	-	⊕⊕◯◯ LOW
Total Rhodes Index score after 1 week treatment (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	35	35	MD 4.19 lower (6.65 to 1.73 lower)	-	⊕⊕◯◯ LOW
Little improvement in nausea											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	3/13 (23.1%)	8/10 (80%)	RR 0.29 (0.1 to 0.82)	568 fewer per 1000 (from 144 fewer to 720 fewer)	⊕⊕⊕◯ MODERATE
Symptoms improved (better or much better versus same)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,3]	none	28/32 (87.5%)	21/30 (70%)	RR 1.25 (0.96 to 1.63)	175 more per 1000 (from 28 fewer to 441 more)	⊕⊕◯◯ LOW
Number of women continuing vomiting at day 6											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	4/12 (33.3%)	8/10 (80%)	RR 0.42 (0.18 to 0.98)	464 fewer per 1000 (from 16 fewer to 656 fewer)	⊕⊕⊕◯ MODERATE

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Small sample size and/or few events.
3. Wide CI crossing the line of no effect.

EB Table D.1g: Lemon oil versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Lemon oil	Control (placebo)	Relative (95% CI)	Absolute	
Mean nausea and vomiting (PUQE) score on day 3 of intervention (better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	50	50	MD 0.46 lower (1.27 lower to 0.35 higher)	-	⊕⊕◯◯ LOW
Total nausea and vomiting (PUQE) scores from baseline to day 3 of intervention (better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	50	50	MD 1.5 lower (2.41 to 0.59 lower)	-	⊕⊕◯◯ LOW
Satisfaction with the given treatment											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	25/50 (50%)	17/50 (34%)	RR 1.47 (0.91 to 2.37)	160 more per 1000 (from 31 fewer to 466 more)	⊕⊕◯◯ LOW

PUQE: pregnancy-unique quantification of emesis/nausea.

1. Wide CI crossing the line of no effect.
2. Small sample size, continuous data.

EB Table D.1h: Mint oil versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mint oil	Control (placebo)	Relative (95% CI)	Absolute	
Severity of nausea on day 4 (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2,3]	none	30	30	MD 0.88 lower (1.93 lower to 0.17 higher)	-	⊕◯◯◯ VERY LOW
Vomiting intensity on day 4 (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2,3]	none	30	30	MD 0.32 lower (1.45 lower to 0.81 higher)	-	⊕◯◯◯ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Wide CI crossing the line of no effect.
3. Small sample size.

EB Table D.1i: Chamomile versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Chamomile**	**Control (placebo)**	**Relative (95% CI)**	**Absolute**	
Rhodes Index score after 1 week treatment (Better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	35	35	MD 5.74 lower (8.31 to 3.17 lower)	-	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".

EB Table D.1j: Vitamin B6 versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Vitamin B6**	**Control (placebo)**	**Relative (95% CI)**	**Absolute**	
Mean reduction in nausea score after 3 days (better indicated by lower values)											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none[1]	199	194	MD 0.92 higher (0.4 to 1.44 higher)	-	⊕⊕⊕◯ MODERATE
Number of women with emesis post-therapy											
2	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	serious[3]	none	69/199 (34.7%)	71/193 (36.8%)	RR 0.76 (0.35 to 1.66)	88 fewer per 1000 (from 239 fewer to 243 more)	⊕⊕◯◯ LOW

1. Small sample size, continuous data.
2. Severe unexplained heterogeneity.
3. Wide CI crossing the line of no effect.

EB Table D.1k: P6 acupressure versus vitamin B6

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**P6 acupressure**	**Control (vitamin B6)**	**Relative (95% CI)**	**Absolute**	
Nausea scores on day 3 (better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	33	33	MD 0.2 higher (2.24 lower to 2.64 higher)	-	⊕⊕◯◯ LOW
Poor symptom relief/amount of rescue medication (number of tablets; better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	30	30	MD 2.2 lower (3.98 to 0.42 lower)	-	⊕⊕⊕◯ MODERATE

1. Wide CI crossing the line of no effect.
2. Small sample size.

EB Table D.1l: Traditional acupuncture versus P6 acupuncture

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Traditional acupuncture**	**Control (P6 acupuncture)**	**Relative (95% CI)**	**Absolute**	
Mean nausea score on day 7 (better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	148	148	MD 0.4 lower (1.12 lower to 0.32 higher)	-	⊕⊕◯◯ LOW
Mean dry retching score on day 7 (better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	148	148	MD 0.3 lower (0.65 lower to 0.05 higher)	-	⊕⊕◯◯ LOW
Mean vomiting score on day 7 (better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	148	148	MD 0.2 higher (0.26 lower to 0.66 higher)	-	⊕⊕◯◯ LOW

1. Wide CI crossing the line of no effect.
2. Small sample size.

EB Table D.1m: Ginger versus P6 acupressure

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ginger versus P6 acupressure	Control	Relative (95% CI)	Absolute	
Total Rhodes Index score on the 3rd day of intervention (better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	50	48	MD 2.27 higher (0.01 lower to 4.55 higher)	-	⊕⊕◯◯ LOW

1. Wide CI crossing the line of no effect.
2. Small sample size.

EB Table D.1n: Ginger versus chamomile

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ginger	Chamomile	Relative (95% CI)	Absolute	
Rhodes Index score after 1 week treatment (better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	35	35	MD 1.55 higher (0.34 lower to 3.44 higher)	-	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Wide CI crossing the line of no effect.

EB Table D.1o: Ginger versus vitamin B6

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ginger	Vitamin B6	Relative (95% CI)	Absolute	
Nausea vomiting score day 3 (better indicated by lower values)											
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	125	126	SMD 0 higher (0.25 lower to 0.25 higher)	-	⊕⊕◯◯ LOW
Nausea vomiting score day 3 – Rhodes Index (better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	61	62	SMD 0.09 lower (0.44 lower to 0.27 higher)	-	⊕⊕◯◯ LOW
Nausea vomiting score day 3 – 10 cm VAS (better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	64	64	SMD 0.08 higher (0.27 lower to 0.43 higher)	-	⊕⊕◯◯ LOW
Post-treatment number of vomiting episodes: day 3 (better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1,2]	none	64	64	MD 0 higher (0.6 lower to 0.6 higher)	-	⊕⊕◯◯ LOW
No improvement in symptoms											
2	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	serious[1]	none	84/181 (46.4%)	87/179 (48.6%)	RR 0.84 (0.47 to 1.52)	78 fewer per 1000 (from 258 fewer to 253 more)	⊕⊕◯◯ LOW

SMD: standardized mean difference; VAS: visual analogue scale

1. Wide CI crossing the line of no effect.
2. Small sample size and/or few events.
3. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".

EB Table D.1p: Vitamin B6 (high dose) versus vitamin B6 (low dose)

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vitamin B6 (high dose)	Vitamin B6 (low dose)	Relative (95% CI)	Absolute	
Mean change in PUQE score from baseline to 2 weeks (better indicated by lower values)											
1	randomized trials	serious	no serious inconsistency	no serious indirectness	no serious imprecision	none	30	30	MD 1.06 lower (2.05 to 0.07 lower)	-	⊕⊕◯◯ LOW

PUQE: pregnancy-unique quantification of emesis/nausea

EB Table D.1q: Ginger versus metoclopramide

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ginger	Metoclopramide	Relative (95% CI)	Absolute	
Mean score for nausea (using Rhodes Index) on day 3 (better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	34	34	MD 1.56 higher (0.22 lower to 3.34 higher)	-	⊕⊕◯◯ LOW
Mean score for vomiting (using Rhodes Index) on day 3 (better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	34	34	MD 0.33 higher (0.69 lower to 1.35 higher)	-	⊕⊕◯◯ LOW
Rhodes Index score on day 3 (better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	34	34	MD 1.89 higher (0.78 lower to 4.56 higher)	-	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Wide CI crossing the line of no effect.

EB Table D.1r: Doxylamine and pyridoxine versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Doxylamine and pyridoxine**	**Control (placebo)**	**Relative (95% CI)**	**Absolute**	
Mean difference in nausea/vomiting/retching (PUQE score) baseline to day 15 (better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	131	125	MD 0.9 lower (1.55 to 0.25 lower)	-	⊕⊕⊕◯ MODERATE
Headache											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1,2]	none	17/131 (13%)	20/125 (16%)	RR 0.81 (0.45 to 1.48)	30 fewer per 1000 (from 88 fewer to 77 more)	⊕⊕◯◯ LOW
Somnolence											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1,2]	none	19/131 (14.5%)	15/125 (12%)	RR 1.21 (0.64 to 2.27)	25 more per 1000 (from 43 fewer to 152 more)	⊕⊕◯◯ LOW

PUQE: pregnancy-unique quantification of emesis/nausea

1. Wide CI crossing the line of no effect.
2. Small sample size and/or few events.

EB Table D.1s: Metoclopramide versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Metoclopramide**	**Control (placebo)**	**Relative (95% CI)**	**Absolute**	
Mean score for nausea (using Rhodes Index) on day 3 (better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	34	34	MD 2.94 lower (4.55 to 1.33 lower)	-	⊕⊕⊕◯ MODERATE

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".

EB Table D.1t: Ondansetron versus metoclopramide

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ondansetron	Metoclopramide	Relative (95% CI)	Absolute	
Average number of nausea episodes on day 3 after treatment (better indicated by lower values)											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	35	35	MD 0.12 lower (0.44 lower to 0.2 higher)	-	⊕◯◯◯ VERY LOW
Average number of vomiting episodes on day 3 after treatment (better indicated by lower values)											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	35	35	MD 0.2 lower (0.57 lower to 0.17 higher)	-	⊕◯◯◯ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (i.e. > 40%) from studies "C".
2. Wide CI crossing the line of no effect.

EB Table D.1u: Ondansetron versus pyridoxine-doxylamine

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Ondansetron	Pyridoxine-doxylamine	Relative (95% CI)	Absolute	
Clinically significant (≥ 25 mm on VAS) reduction in nausea after 5 days of treatment											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	12/13 (92.3%)	7/17 (41.2%)	RR 2.24 (1.24 to 4.04)	511 more per 1000 (from 99 more to 1000 more)	⊕⊕◯◯ LOW
Sedation											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,3]	none	4/13 (30.8%)	7/17 (41.2%)	RR 0.75 (0.28 to 2.02)	103 fewer per 1000 (from 296 fewer to 420 more)	⊕⊕◯◯ LOW
Constipation											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,3]	none	5/13 (38.5%)	3/17 (17.6%)	RR 2.18 (0.63 to 7.5)	208 more per 1000 (from 65 fewer to 1000 more)	⊕⊕◯◯ LOW

1. High risk of bias for this outcome (arbitrary threshold, inappropriate dose and type of doxylamine-pyridoxine).
2. Small sample size and/or few events.
3. Wide CI crossing the line of no effect.

D.2. Interventions for heartburn

Source: Phupong V, Hanprasertpong T. Interventions for heartburn in pregnancy. Cochrane Database Syst Rev. 2015;(9):CD011379.

EB Table D.2a: Any pharmacological treatment versus placebo or no treatment

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Any pharmacological treatment**	**Control (placebo or no treatment)**	**Relative (95% CI)**	**Absolute**	
Complete relief of heartburn											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	75/133 (56.4%)	37/123 (30.1%)	RR 1.85 (1.36 to 2.5)	256 more per 1000 (from 108 more to 451 more)	⊕⊕⊕◯ MODERATE
Partial relief of heartburn											
2	randomized trials	serious[1]	serious[2]	no serious indirectness	serious[3]	none	40/133 (30.1%)	31/123 (25.2%)	RR 1.35 (0.38 to 4.76)	88 more per 1000 (from 156 fewer to 948 more)	⊕◯◯◯ VERY LOW
Side-effects											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3,4]	none	5/133 (3.8%)	7/123 (5.7%)	RR 0.63 (0.21 to 1.89)	21 fewer per 1000 (from 45 fewer to 51 more)	⊕◯◯◯ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Severe unexplained heterogeneity.
3. Wide CI crossing the line of no effect. 4 Small sample size and few events.

EB Table D.2b: Pharmacological treatment versus lifestyle change

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Pharmacological treatment**	**Lifestyle change**	**Relative (95% CI)**	**Absolute**	
Complete relief of heartburn											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious	none	37/41 (90.2%)	9/24 (37.5%)	RR 2.41 (1.42 to 4.07)	529 more per 1000 (from 157 more to 1000 more)	⊕⊕◯◯ LOW
Side-effects											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	1/42 (2.4%)	0/24 (0%)	RR 1.74 (0.07 to 41.21)	-	⊕◯◯◯ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Wide CI crossing the line of no effect.
3. Small sample size and few events.

EB Table D.2c: Acupuncture versus no treatment

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Acupuncture**	**Control (no treatment)**	**Relative (95% CI)**	**Absolute**	
Quality of life – improvement in the ability to sleep											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	14/20 (70%)	4/16 (25%)	RR 2.8 (1.14 to 6.86)	450 more per 1000 (from 35 more to 1000 more)	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Small sample size and few events.

D.3. Interventions for leg cramps

Source: Zhou K, West HM, Zhang J, Xu L, Li W. Interventions for leg cramps in pregnancy. Cochrane Database Syst Rev. 2015;(8):CD010655.

EB Table D.3a: Oral magnesium versus placebo or no treatment

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral magnesium	Placebo/no treatment	Relative (95% CI)	Absolute	
No leg cramps after treatment											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	11/34 (32.4%)	2/35 (5.7%)	RR 5.66 (1.35 to 23.68)	266 more per 1000 (from 20 more to 1000 more)	⊕⊕◯◯ LOW
50% reduction in number of leg cramps											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	37/43 (86%)	26/43 (60.5%)	RR 1.42 (1.09 to 1.86)	254 more per 1000 (from 54 more to 520 more)	⊕⊕⊕⊕ HIGH
Partial improvement: decrease in intensity and frequency											
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	15/21 (71.4%)	14/21 (66.7%)	RR 1.07 (0.71 to 1.61)	47 more per 1000 (from 193 fewer to 407 more)	⊕◯◯◯ VERY LOW
Complete recovery: no leg cramps after treatment											
1	randomized trials	very serious[3]	no serious inconsistency	no serious indirectness	very serious[2,4]	none	6/21 (28.6%)	2/21 (9.5%)	RR 3 (0.68 to 13.2)	190 more per 1000 (from 30 fewer to 1000 more)	⊕◯◯◯ VERY LOW
Side-effects – nausea											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,4]	none	11/43 (25.6%)	6/43 (14%)	RR 1.83 (0.75 to 4.51)	116 more per 1000 (from 35 fewer to 490 more)	⊕⊕◯◯ LOW
Side-effects – diarrhoea											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,4]	none	6/43 (14%)	1/43 (2.3%)	RR 6 (0.75 to 47.76)	116 more per 1000 (from 6 fewer to 1000 more)	⊕⊕◯◯ LOW

EB Table D.3a: Oral magnesium versus placebo or no treatment (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oral magnesium	Placebo/no treatment	Relative (95% CI)	Absolute	
Any side-effects (including nausea, flatulence, diarrhoea and intestinal air)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2,4]	none	6/23 (26.1%)	6/22 (27.3%)	RR 0.96 (0.36 to 2.52)	11 fewer per 1000 (from 175 fewer to 415 more)	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Small sample size and few events.
3. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (i.e. > 40%) from studies "C".
4. Wide CI crossing the line of no effect.

EB Table D.3b: Oral calcium versus no treatment

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Oral calcium**	**No treatment**	**Relative (95% CI)**	**Absolute**	
No leg cramps after treatment											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	9/22 (40.9%)	1/21 (4.8%)	RR 8.59 (1.19 to 62.07)	361 more per 1000 (from 9 more to 1000 more)	⊕⊕◯◯ LOW
Composite outcome: symptoms of leg cramps (intensity and frequency) – partial improvement: decrease in intensity and frequency											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[1,3]	none	9/21 (42.9%)	14/21 (66.7%)	RR 0.64 (0.36 to 1.15)	240 fewer per 1000 (from 427 fewer to 100 more)	⊕◯◯◯ VERY LOW
Composite outcome: symptoms of leg cramps (intensity and frequency) – complete recovery: no leg cramps after treatment											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	11/21 (52.4%)	2/21 (9.5%)	RR 5.5 (1.38 to 21.86)	429 more per 1000 (from 36 more to 1000 more)	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Small sample size and few events.
3. Wide CI crossing the line of no effect.

EB Table D.3c: Vitamin B1 and B6 versus no treatment

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Oral vitamin B1 and B6**	**No treatment**	**Relative (95% CI)**	**Absolute**	
Partial improvement: decrease in intensity and frequency											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	4/21 (19%)	14/21 (66.7%)	RR 0.29 (0.11 to 0.73)	473 fewer per 1000 (from 180 fewer to 593 fewer)	⊕⊕◯◯ LOW
Complete recovery: no leg cramps after treatment											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	15/21 (71.4%)	2/21 (9.5%)	RR 7.5 (1.95 to 28.81)	619 more per 1000 (from 90 more to 1000 more)	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Small sample size and few events.

EB Table D.3d: Oral calcium versus oral vitamin C

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Oral calcium**	**Oral vitamin C**	**Relative (95% CI)**	**Absolute**	
No leg cramps after treatment											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2,3]	none	8/30 (26.7%)	6/30 (20%)	RR 1.33 (0.53 to 3.38)	66 more per 1000 (from 94 fewer to 476 more)	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
2. Small sample size and few events.
3. Wide CI crossing the line of no effect.

D.4. Interventions for low back and pelvic pain

Source: Liddle SD, Pennick V. Interventions for preventing and treating low-back and pelvic pain during pregnancy. Cochrane Database Syst Rev. 2015;(9):CD001139.

EB Table D.4a: Any exercise plus usual antenatal care (ANC) versus usual ANC

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Any exercise + usual ANC**	**Usual ANC**	**Relative (95% CI)**	**Absolute**	
Low back pain intensity (better indicated by lower values)											
7	randomized trials	very serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	321	324	SMD 0.64 lower (1.03 to 0.25 lower)	-	⊕◯◯◯ VERY LOW
Functional disability (better indicated by lower values)											
2	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	74	72	SMD 0.56 lower (0.89 to 0.23 lower)	-	⊕⊕◯◯ LOW
Women who reported pain on visual analogue scale (VAS)											
4	randomized trials	serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	376/598 (62.9%)	409/578 (70.8%)	RR 0.66 (0.45 to 0.97)	241 fewer per 1000 (from 21 fewer to 389 fewer)	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (> 40%) from studies "C".
2. Severe unexplained heterogeneity.
3. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C".
4. Small sample size.

EB Table D.4b: Bellybra versus Tubigrip support belts

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Bellybra**	**Tubigrip**	**Relative (95% CI)**	**Absolute**	
Low-back pain – measured with visual analogue scale (VAS) (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2,3]	none	46	48	MD 0.2 lower (1.19 lower to 0.79 higher)	-	⊕○○○ VERY LOW
Functional disability – (MD; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2,3]	none	46	48	MD 0.9 lower (1.81 lower to 0.01 higher)	-	⊕○○○ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C".
2. Wide CI crossing the line of no effect.
3. Small sample size.

EB Table D.4c: Acupuncture plus usual ANC versus usual ANC

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Acupuncture + usual ANC**	**Usual ANC**	**Relative (95% CI)**	**Absolute**	
Decreased low back and pelvic pain											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	22/37 (59.5%)	5/35 (14.3%)	RR 4.16 (1.77 to 9.78)	451 more per 1000 (from 110 more to 1000 more)	⊕⊕○○ LOW

1. No explanation was provided.
2. Small sample size and few events.

EB Table D.4d: Acupuncture plus usual ANC versus individualized physiotherapy plus usual ANC

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Acupuncture + usual ANC**	**Individualized physiotherapy + usual ANC**	**Relative (95% CI)**	**Absolute**	
Women rating treatment as good or excellent											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	27/28 (96.4%)	14/18 (77.8%)	RR 1.24 (0.96 to 1.6)	187 more per 1000 (from 31 fewer to 467 more)	⊕◯◯◯ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (> 40%) from studies "C".
2. Wide CI crossing the line of no effect.

EB Table D.4e: Multimodal intervention (manual therapy/chiropractic, exercise at home and education) versus usual care (rest, exercise, heat pads and analgesics)

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Bellybra**	**Tubigrip**	**Relative (95% CI)**	**Absolute**	
Pain (MD; better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	serious[1]	87	82	MD 2.7 lower (3.54 to 1.86 lower)	-	⊕⊕⊕◯ MODERATE
Functional disability (MD; better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	serious[1]	87	82	MD 1.4 lower (2.09 to 0.71 lower)	-	⊕⊕⊕◯ MODERATE

1. Small sample size.

D.5. Interventions for constipation

Source: Rungsiprakarn P, Laopaiboon M, Sangkomkamhang US, Lumbiganon P, Pratt JJ. Interventions for treating constipation in pregnancy. Cochrane Database Syst Rev. 2015;(9):CD011448.

EB Table D.5a: Fibre supplementation versus no intervention

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any exercise + usual ANC	Usual ANC	Relative (95% CI)	Absolute	
Frequency of stools (per week) (better indicated by higher values)											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	27	13	MD 2.24 higher (0.96 to 3.52 higher)	-	⊕◯◯◯ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (> 40%) from studies "C".
2. Wide CI crossing the line of no effect".

EB Table D.5b: Stimulant laxatives versus bulk-forming laxatives

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Stimulant laxatives**	**Bulk-forming laxatives**	**Relative (95% CI)**	**Absolute**	
Improvement in constipation											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	54/70 (77.1%)	34/70 (48.6%)	RR 1.59 (1.21 to 2.09)	287 more per 1000 (from 102 more to 529 more)	⊕⊕◯◯ LOW
Abdominal discomfort											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	21/70 (30%)	9/70 (12.9%)	RR 2.33 (1.15 to 4.73)	171 more per 1000 (from 19 more to 480 more)	⊕⊕◯◯ LOW
Diarrhoea											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	9/70 (12.9%)	2/70 (2.9%)	RR 4.5 (1.01 to 20.09)	100 more per 1000 (from 0 more to 545 more)	⊕◯◯◯ VERY LOW
Women's satisfaction											
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	37/70 (52.9%)	35/70 (50%)	RR 1.06 (0.77 to 1.46)	30 more per 1000 (from 115 fewer to 230 more)	⊕◯◯◯ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (> 40%) from studies "C".
2. Small sample size and few events.
3. Wide CI crossing the line of no effect.

D.6. Interventions for varicose veins and oedema

Source: Smyth RMD, Aflaifel N, Bamigboye AA. Interventions for varicose veins and leg oedema in pregnancy. Cochrane Database Syst Rev. 2015;(10):CD001066.

EB Table D.6a: Rutoside versus placebo

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Rutoside**	**Placebo**	**Relative (95% CI)**	**Absolute**	
Relief of symptoms associated with varicose veins											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	24/37 (64.9%)	11/32 (34.4%)	RR 1.89 (1.11 to 3.22)	306 more per 1000 (from 38 more to 763 more)	⊕⊕◯◯ LOW
Side-effects											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	3/37 (8.1%)	2/32 (6.3%)	RR 1.3 (0.23 to 7.28)	19 more per 1000 (from 48 fewer to 393 more)	⊕◯◯◯ VERY LOW
Complications associated with varicose veins (deep vein thrombosis)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	0/37 (0%)	2/32 (6.3%)	RR 0.17 (0.01 to 3.49)	52 fewer per 1000 (from 62 fewer to 156 more)	⊕◯◯◯ VERY LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C".
2. Small sample size and/or few events.
3. Wide CI crossing the line of no effect.

EB Table D.6b: External pneumatic intermittent compression versus rest

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**External pneumatic intermittent compression**	**Rest**	**Relative (95% CI)**	**Absolute**	
Symptoms associated with oedema (change in lower leg volume, unit of analysis not stated) (MD; better indicated by lower values)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	17	18	MD 258.8 lower (566.91 lower to 49.31 higher)	-	⊕⊕OO LOW

1. Wide CI crossing the line of no effect.

EB Table D.6c: Reflexology versus rest

Quality assessment							No. of women		Effect		Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Reflexology**	**Rest**	**Relative (95% CI)**	**Absolute**	
Woman's satisfaction											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2,3]	none	27/45 (60%)	1/10 (10%)	RR 6 (0.92 to 39.11)	500 more per 1000 (from 8 fewer to 1000 more)	⊕OOO VERY LOW
Symptoms associated with oedema											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	30/33 (90.9%)	1/10 (10%)	RR 9.09 (1.41 to 58.54)	809 more per 1000 (from 41 more to 1000 more)	⊕⊕OO LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C".
2. Small sample size and/or few events.
3. Wide CI crossing the line of no effect.

EB Table D.6d: Water immersion versus leg elevation

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Water immersion	Leg elevation	Relative (95% CI)	Absolute	
Women with reduction in leg volume (oedema)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	6/16 (37.5%)	14/16 (87.5%)	RR 0.43 (0.22 to 0.83)	499 fewer per 1000 (from 149 fewer to 683 fewer)	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C".
2. Small sample size and few events.

EB Table D.6e: Foot massage versus "routine care"

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Foot massage	Routine care	Relative (95% CI)	Absolute	
Symptoms associated with oedema (lower leg circumference in centimetres; better indicated by lower values)											
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	40	40	MD 0.11 lower (1.02 lower to 0.8 higher)	-	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C".
2. Wide CI crossing the line of no effect.

E. Health systems interventions to improve antenatal care utilization and quality

E.1. Woman-held case notes

EB Table E.1: Woman-held case notes versus control

Source: Brown HC, Smith HJ, Mori R, Noma H. Giving women their own case notes to carry during pregnancy. Cochrane Database Syst Rev. 2015;(10):CD002856.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Women carrying their own case notes	Control (facility-held case notes)	Relative (95% CI)	Absolute	
Women who felt in control											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	87/229 (38%)	52/221 (23.5%)	RR 1.56 (1.18 to 2.06)	132 more per 1000 (from 42 more to 249 more)	⊕⊕⊕◯ MODERATE
Women's satisfaction with ANC											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	0/348 (0%)	0/350 (0%)	RR 1.02 (0.92 to 1.29)	-	⊕⊕◯◯ LOW
Notes lost or left at home											
2	randomized trials	serious[1]	serious[3]	no serious indirectness	very serious[2,4]	none	6/169 (3.6%)	15/178 (8.4%)	RR 0.38 (0.04 to 3.84)	52 fewer per 1000 (from 81 fewer to 239 more)	⊕◯◯◯ VERY LOW
Caesarean section (cluster-randomized trials)											
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2,4]	serious[5]	253	248	RR 1.51 (1.1 to 2.08)	-	⊕◯◯◯ VERY LOW
Stillbirth or neonatal death											
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	357	356	RR 0.77 (0.17 to 3.48)	-	⊕⊕◯◯ LOW

1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C".
2. Wide CI crossing the line of no effect.
3. Severe unexplained heterogeneity.
4. Small sample size and/or few events.
5. Unexplained data discrepancy (queried with investigators).

E.2. Midwife-led continuity of care (MLCC)

EB Table E.2: MLCC versus other models

Source: Sandall J, Soltani H, Gates S, Shennan A, Devane D. Midwife-led continuity models versus other models of care for childbearing women. Cochrane Database Syst Rev. 2015;(9):CD004667.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	MLCC	Other models	Relative (95% CI)	Absolute	
Caesarean birth											
14	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[2]	1281/9667 (13.3%)	1242/8007 (15.5%)	RR 0.92 (0.84 to 1)	12 fewer per 1000 (from 25 fewer to 0 more)	⊕⊕◯◯ LOW
Instrumental vaginal birth (forceps/vacuum)											
13	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[2]	1176/9586 (12.3%)	1133/7915 (14.3%)	RR 0.9 (0.83 to 0.97)	14 fewer per 1000 (from 4 fewer to 24 fewer)	⊕⊕◯◯ LOW
Spontaneous vaginal birth (as defined by trial authors)											
12	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	6485/9181 (70.6%)	4937/7506 (65.8%)	RR 1.05 (1.03 to 1.07)	33 more per 1000 (from 20 more to 46 more)	⊕⊕⊕◯ MODERATE
Preterm birth (< 37 weeks)											
8	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	360/7440 (4.8%)	367/5798 (6.3%)	RR 0.76 (0.64 to 0.91)	15 fewer per 1000 (from 6 fewer to 23 fewer)	⊕⊕⊕◯ MODERATE
Overall fetal loss and neonatal death											
13	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	257/9611 (2.7%)	273/7950 (3.4%)	RR 0.84 (0.71 to 0.99)	5 fewer per 1000 (from 0 fewer to 10 fewer)	⊕⊕⊕◯ MODERATE
Low birth weight (< 2500 g)											
7	randomized trials	very serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	324/6577 (4.9%)	263/4881 (5.4%)	RR 0.96 (0.82 to 1.13)	2 fewer per 1000 (from 10 fewer to 7 more)	⊕⊕◯◯ LOW
Satisfaction with antenatal care											
4	randomized trials	serious[1]	serious[2]	no serious indirectness	no serious imprecision	none	1882/3150 (59.7%)	1150/2269 (50.7%)	RR 1.31 (1.11 to 1.54)	157 more per 1000 (from 56 more to 274 more)	⊕⊕◯◯ LOW

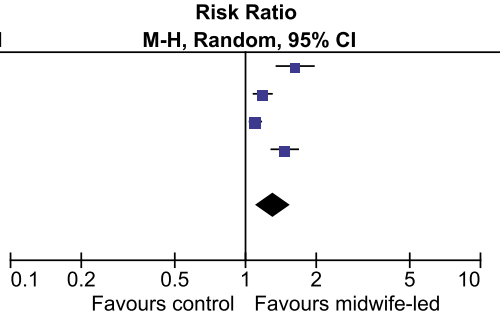
1. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C".
2. Evident asymmetry in funnel plot.
3. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (> 40%) from studies "C".

Web supplement:
WHO recommendations on antenatal care for a positive pregnancy experience: evidence base

Figure E.2: Additional analysis: MLCC model versus other models of care: satisfaction

Study or Subgroup	Midwife-led Events	Total	Control Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Biro 2000	195	344	100	287	21.3%	1.63 [1.35, 1.95]
MacVicar 1993	865	1663	363	826	26.5%	1.18 [1.08, 1.29]
Turnbull 1996	534	648	487	651	27.8%	1.10 [1.04, 1.17]
Waldenstrom 2001	288	495	200	505	24.4%	1.47 [1.29, 1.67]
Total (95% CI)		**3150**		**2269**	**100.0%**	**1.31 [1.11, 1.54]**
Total events	1882		1150			

Heterogeneity: Tau² = 0.02; Chi² = 31.65, df = 3 (P < 0.00001); I² = 91%
Test for overall effect: Z = 3.18 (P = 0.001)



E.3. Group antenatal care (ANC)

EB Table E.3: Group ANC versus individual ANC

Source: Catling CJ, Medley N, Foureur M, Ryan C, Leap N, Teate A, Homer CSE. Group versus conventional antenatal care for women. Cochrane Database Syst Rev. 2015;(2):CD007622.

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Group ANC	Individual antenatal care (adjusted data)	Relative (95% CI)	Absolute	
Spontaneous vaginal birth											
1	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	94/162 (58%)	97/160 (60.6%)	RR 0.96 (0.8 to 1.15)	24 fewer per 1000 (from 121 fewer to 91 more)	⊕⊕⊕◯ MODERATE
Caesarean section											
2	randomized trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	118/427 (27.6%)	137/415 (33%)	RR 0.83 (0.68 to 1.02)	56 fewer per 1000 (from 106 fewer to 7 more)	⊕◯◯◯ VERY LOW
Satisfaction with antenatal care (MD; better indicated by higher values)											
1	randomized trials	serious[4]	no serious inconsistency	serious[1]	no serious imprecision	none	623	370	MD 4.9 higher (3.1 to 6.7 higher)	-	⊕⊕◯◯ LOW
Small for gestational age											
2	randomized trials	very serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	94/868 (10.8%)	63/605 (10.4%)	RR 0.92 (0.68 to 1.24)	8 fewer per 1000 (from 33 fewer to 25 more)	⊕◯◯◯ VERY LOW
Low birth weight											
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	96/1101 (8.7%)	74/834 (8.9%)	RR 0.92 (0.68 to 1.23)	7 fewer per 1000 (from 28 fewer to 20 more)	⊕⊕⊕◯ MODERATE
Preterm birth											
3	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	serious[3]	none	90/1077 (8.4%)	85/811 (10.5%)	RR 0.75 (0.57 to 1)	26 fewer per 1000 (from 45 fewer to 0 more)	⊕⊕⊕◯ MODERATE

EB Table E.3: Group ANC versus individual ANC (continued)

Quality assessment							No. of women		Effect		Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Group ANC	Individual antenatal care (adjusted data)	Relative (95% CI)	Absolute	
Perinatal mortality											
3	randomized trials	no serious risk of bias	serious[5]	no serious indirectness	serious[3]	none	15/1105 (1.4%)	18/838 (2.1%)	RR 0.63 (0.32 to 1.25)	8 fewer per 1000 (from 15 fewer to 5 more)	⊕⊕◯◯ LOW

1. Single study of specific type of intervention (CenteringPregnancy) in USA setting – may not be generalizable.
2. Most of the pooled effect provided by studies "B" or "C" with a substantial proportion (i.e. > 40%) from studies "C".
3. Wide CI crossing the line of no effect.
4. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
5. Severe unexplained heterogeneity.

E.4. Community-based interventions to improve communication and support

EB Table E.4: Community-based interventions (women's groups, home visits or intervention packages with home visits and community mobilization) versus control

Source: Mbuagbaw L, Medley N, Darzi AJ, Richardson M, Habiba Garga K, Ongolo-Zogo P. Health system and community level interventions for improving antenatal care coverage and health outcomes. Cochrane Database Syst Rev. 2015;(12):CD010994.

Quality assessment							No. of women[1]		Effect[2]	Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Community-based interventions	Control	Relative (95% CI)	
ANC coverage: four or more visits – women's groups										
3	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	29 574	29150	RR 1.05 (0.78 to 1.41)	⊕⊕◯◯ LOW
ANC coverage: four or more visits – home visits										
4	randomized trials	no serious risk of bias[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	9960	10 167	RR 1.09 (0.99 to 1.22)	⊕⊕⊕⊕ HIGH
ANC coverage: four or more visits – home visits and community mobilization										
1	randomized trials	no serious risk of bias[5]	no serious inconsistency	no serious indirectness	serious[4]	none	2339	2135	RR 1.51 (0.5 to 4.59)	⊕⊕⊕◯ MODERATE
ANC coverage: one or more visits – women's groups										
3	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	33 210	32 879	RR 1.77 (1.21 to 2.58)	⊕⊕⊕◯ MODERATE
ANC coverage: one or more visits – home visits										
2	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	5694	6365	RR 1.53 (0.56 to 4.17)	⊕⊕◯◯ LOW
ANC coverage: one or more visits – home visits and community mobilization										
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	92 394	50 704	RR 1.76 (1.43 to 2.16)	⊕⊕⊕⊕ HIGH

EB Table E.4: Community-based interventions (women's groups, home visits or intervention packages with home visits and community mobilization) versus control (continued)

Quality assessment							No. of women[1]		Effect[2]	Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Community-based interventions**	**Control**	**Relative (95% CI)**	
Deliveries in a health facility – women's groups										
5	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	reporting bias[5]	45 199	44 190	RR 1.04 (0.89 to 1.22)	⊕⊕◯◯ LOW
Deliveries in a health facility – home visits										
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	13 985	15 104	RR 1.08 (0.87 to 1.35)	⊕⊕⊕◯ MODERATE
Deliveries in a health facility – home visits and community mobilization										
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	16 167	13 106	RR 1.46 (0.87 to 2.46)	⊕⊕⊕◯ MODERATE
Maternal deaths – women's groups										
7	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	58 773	58 032	RR 0.78 (0.6 to 1.03)	⊕⊕◯◯ LOW
Maternal deaths – home visits										
0	no evidence available					none	-	-	not pooled	
Maternal deaths – home visits and community mobilization										
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	20 362	17 532	RR 0.76 (0.44 to 1.31)	⊕⊕⊕◯ MODERATE
Perinatal deaths – women's groups										
6	randomized trials	serious[3]	serious[6]	no serious indirectness	no serious imprecision	none	49 972	49 249	RR 0.91 (0.82 to 1.01)	⊕⊕◯◯ LOW
Perinatal deaths – home visits										
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	14 472	15 522	RR 0.91 (0.79 to 1.05)	⊕⊕⊕⊕ HIGH

EB Table E.4: Community-based interventions (women's groups, home visits or intervention packages with home visits and community mobilization) versus control (continued)

Quality assessment							No. of women[1]		Effect[2]	Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Community-based interventions**	**Control**	**Relative (95% CI)**	
Perinatal deaths – home visits and community mobilization										
3	randomized trials	no serious risk of bias	serious[6]	no serious indirectness	no serious imprecision	none	16 176	13 106	RR 0.65 (0.48 to 0.88)	⊕⊕⊕◯ MODERATE
Low birth weight – home visits										
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	2246	2202	RR 0.78 (0.61 to 1.01)	⊕⊕⊕◯ MODERATE
Preterm birth – home visits										
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	1033	1040	RR 0.88 (0.54 to 1.44)	⊕⊕⊕◯ MODERATE

1. These numbers are crude estimates only as most trials were cluster RCTs.
2. The inverse variance method of analysis was used as most trials were cluster RCTs.
3. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (< 40%) from studies "C".
4. Wide CI crossing the line of no effect.
5. Evident asymmetry in funnel plot.
6. Severe unexplained heterogeneity.

E.7. Antenatal care contact schedules

EB Table E.7: Focused ANC (FANC) model (minimum of four visits) versus standard ANC model (minimum of eight visits)

Source: Dowswell T, Carroli G, Duley L, Gates S, Gülmezoglu AM, Khan-Neelofur D, Piaggio G. Alternative versus standard packages of antenatal care for low-risk pregnancy. Cochrane Database Syst Rev. 2015;(7):CD000934.

Quality assessment							No. of women[1]		Effect[2]	Certainty
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**FANC model**	**Standard ANC model**	**Relative (95% CI)**	
Caesarean section										
1	cluster-randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	11 624	11 121	RR 1 (0.89 to 1.11)	⊕⊕⊕⊕ HIGH
Maternal death										
3	cluster-randomized trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	27 762	23 742	RR 1.13 (0.5 to 2.57)	⊕⊕◯◯ LOW
Pre-eclampsia (various definitions)										
3	cluster-randomized trials	serious[3]	serious4	no serious indirectness	serious[4]	none	26 390	22 463	RR 0.94 (0.73 to 1.22)	⊕◯◯◯ VERY LOW
Low birth weight (> 2500 g)										
3	cluster-randomized trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	25 208	21 012	RR 1.04 (0.97 to 1.12)	⊕⊕⊕◯ MODERATE
Small for gestational age										
2	cluster-randomized trials	serious[3]	serious[5]	no serious indirectness	no serious imprecision	none	20 837	17 114	RR 1.01 (0.9 to 1.14)	⊕⊕◯◯ LOW
Preterm birth										
3	cluster-randomized trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	25 986	22 108	RR 0.99 (0.91 to 1.08)	⊕⊕⊕◯ MODERATE

EB Table E.7: Focused ANC (FANC) model (minimum of four visits) versus standard ANC model (minimum of eight visits) (continued)

Quality assessment							No. of women[1]		Effect[2]	Certainty
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	FANC model	Standard ANC model	Relative (95% CI)	
Perinatal death										
3	cluster-randomized trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	27 680	23 643	RR 1.15 (1.01 to 1.32)	⊕⊕⊕◯ MODERATE

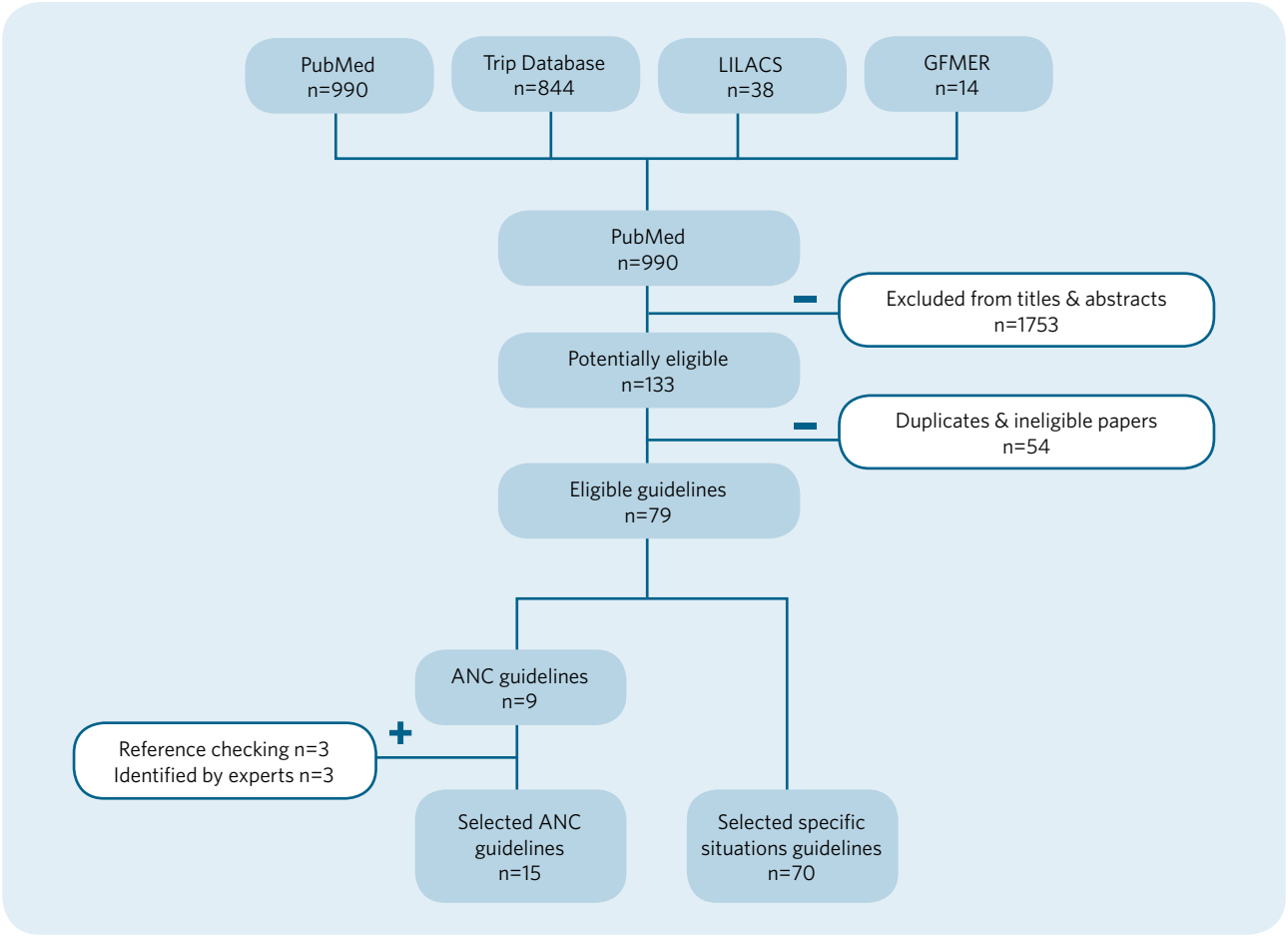
1. These numbers are crude estimates only as all trials were cluster RCTs.
2. The inverse variance method was used for meta-analyses.
3. Most of the pooled effect provided by studies "B" or "C" without a substantial proportion (i.e. < 40%) from studies "C".
4. Wide CI crossing the line of no effect.
5. Severe unexplained heterogeneity.

Search strategies for the evidence base

1. Search strategy to identify existing ANC guidelines[4]

In December 2013, a systematic search was conducted for evidence-based guidelines in the following databases: PubMed,[5] LILACS[6] (an index of scientific and technical literature of Latin America and the Caribbean) and Trip[7] (Turning Research into Practice), and in the guidelines repository maintained by the Geneva Foundation for Medical Education and Research (GFMER). To identify as many relevant guidelines as possible, a broad search strategy was chosen. In PubMed, the words "pregnancy or prenatal or antenatal", and "care or management or screening" were used, selecting guideline/practice guideline (for article type), human (for species) and female (for sex) in the advanced search. For LILACS the words on the category DeCS N04.761.700.350.650 (clinical practice guidelines and all its synonyms in Portuguese, Spanish and English) were combined with "prenatal or antenatal or pregnancy". In Trip Database, the words "antenatal or prenatal or pregnancy" were combined with "clinical or practice" and "guideline* or guidance* or recommendation* or advice". Additionally, all the references from the retrieved papers were checked. The search was limited to all clinical practice guidelines published after January 2000.

Search results



4 Abalos A, Chamillard M, Diaz V, Tunçalp Ö, Gülmezoglu AM. Antenatal care for healthy pregnant women: a mapping of interventions from existing guidelines to inform the development of new WHO guidance on antenatal care. BJOG. 2016;123(4):519–28. doi:10.1111/1471-0528.13820.

5 Available at: https://www.ncbi.nlm.nih.gov/pubmed/

6 Available at: http://lilacs.bvsalud.org/en/

7 Available at: https://www.tripdatabase.com/

2. Search strategy for qualitative meta-synthesis of women's views[8]

Inclusion criteria

i. Study design

- Studies using qualitative designs, including ethnography, phenomenology, case studies, grounded theory and mixed methods.
- Studies using interviews, focus group discussions, open-ended survey questions, diaries and other narrative-based data collection methods.

ii. Study topic/focus

- Studies focused on, or with substantial sections focused on, views, attitudes, experiences, facilitators and/or barriers related to routine ANC (studies that only reported on these aspects of care in the context of services that are provided for women/fetuses with particular health or social conditions – such as HIV, malaria, or in-utero interventions for malformation – were not included).

iii. Population

- Pregnant or postnatal women, including those who had been pregnant at some time since 1998 (allowing for these accounts to be published by 2000 or subsequently).

iv. Date range

- Studies published between 1 January 2000 and August 2014. This date range was intended to capture women's views and experiences of care provision since the introduction of focused antenatal care (FANC) programmes.

v. Language restrictions

- No language restrictions were imposed. Where possible, identified studies published in languages other than English were translated in full. At a minimum, the abstracts were translated where available.

Search terms

Participants	Area of Interest	Context	Phenomenon of interest	Study design
woman OR women* OR patient* OR consumer* OR service user*]	Antenatal* or prenatal* or antepartum or perinatal or pregnan*	care OR support* OR health* OR clinic* or outpatient* OR session* OR matern* OR service* OR office or education*	want* OR like OR desire* OR require* OR expect* OR anticipat* OR view* OR experience* OR perspective* OR perception* OR opinion* OR assum* OR know* OR understand* OR encounter* OR belief* OR believe* OR attitude* OR help* OR promot* OR enable* OR empower* OR permi* OR encourage* OR barrier* OR prevent* OR obstacle* OR delay* OR deny OR denial	Review or qualitative or survey or questionnaire or interview or group or qualitative OR ethnograph* OR phenomenol* OR grounded theory OR hermeneutic* OR lived experience* OR symbolic interaction* OR narrative* OR life experience* OR action research OR observation* OR focus group* OR interview* OR mixed method OR multimethod

The search was adapted to fit with the syntax of each specific database searched. In each case, the search string included title/abstract/keywords at a minimum.

8 Downe S, Finlayson K, Tunçalp Ö, Gülmezoglu AM. Factors that influence the uptake of routine antenatal services by pregnant women: a qualitative evidence synthesis (protocol). Cochrane Database Syst Rev. 2016;(10):CD012392. (http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012392/epdf, accessed 16 November 2016).

Following scrutiny of the initial hits, at each subsequent stage (abstract and full text examination) two members of the qualitative systematic review team determined inclusion independently, and then agreed on the final inclusion list by consensus. In the event of continuing lack of agreement for a particular study, a third team member adjudicated.

The reference lists and key authors in the reference lists were scrutinized and back-chaining and forward-checking were undertaken for any references not identified in the search that may be relevant. These papers were then subject to the same inclusion/exclusion and quality checking criteria as those identified using the search terms above.

Databases and other sources

African Journals OnLine (AJOL)[9], The Allied and Complementary Medicine Database (AMED)[10], Cumulative Index to Nursing and Allied Health Literature (CINAHL)[11], Embase,[12] Online Regional Information System for Scientific Journals from Latin America, the Caribbean, Spain and Portugal (Latindex)[13], MEDLINE[14] and PsycINFO.[15] In addition, Zetoc alerts were set up for over 50 relevant journals.

9 Available at: http://www.ajol.info/
10 Available at: https://www.ebscohost.com/academic/amed-the-allied-and-complementary-medicine-database
11 Available at: https://health.ebsco.com/products/the-cinahl-database/allied-health-nursing
12 Available at: https://www.embase.com/login
13 Available at: http://www.latindex.org/latindex/inicio?lang=en
14 Available at: https://www.medline.com/
15 Available at: http://www.apa.org/pubs/databases/psycinfo/index.aspx

3. Search strategy for qualitative meta-synthesis of health-care providers' views[16]

Inclusion criteria

i. Study design

- Studies using qualitative designs, including ethnography, phenomenology, case studies, grounded theory and mixed methods.
- Studies using interviews, focus group discussions, open-ended survey questions, diaries and other narrative-based data collection methods.

ii. Study topic/focus

- Studies focused on, or with substantial sections focused on, views, attitudes, experiences, facilitators and/or barriers related to routine antenatal care (studies that only reported on these aspects of care in the context of services that are provided for women/fetuses with particular health or social conditions – such as HIV, malaria, or in-utero interventions for malformation – were not included).

iii. Population

- Staff based in primary, secondary and tertiary care settings who were employed by public, private or charity funders to provide routine ANC services.
- Staff were to fulfil the WHO 2004 definition of a skilled birth attendant,[17] or were identified by the study authors as being skilled birth attendants.
- Auxiliary and lay health workers were also included where they were paid directly or indirectly to provide ANC. Staff who were commenting on their experiences and views of delivering babies or of providing specialist ANC services for women/babies with specific risk factors were not included.

iv. Date range

- Studies published between 1 January 2000 and August 2014. This date range was intended to capture staff views and experiences of care provision since the introduction of FANC programmes.

v. Language restrictions

- No language restrictions were imposed. Where possible, identified studies published in languages other than English were translated in full. At a minimum, the abstracts were translated where available.

16 Downe S, Finlayson K, Tunçalp Ö, Gülmezoglu AM. Factors that influence the provision of good quality routine antenatal care services by health staff: a qualitative evidence synthesis. Cochrane Database Syst Rev. 2016 (in press).

17 A skilled birth attendant is "an accredited health professional – such as a midwife, doctor or nurse – who has been educated and trained to proficiency in the skills needed to manage normal (uncomplicated) pregnancies, childbirth and the immediate postnatal period, and in the identification, management and referral of complications in women and newborns". Making pregnancy safer: the critical role of the skilled birth attendant: a joint statement by WHO, ICM and FIGO. Geneva: World Health Organization; 2004 (http://www.who.int/maternal_child_adolescent/documents/9241591692/en/, accessed 16 November 2016).

Search terms

Participants	Area of Interest	Context	Phenomenon of interest	Study design
Staff or provider or health care provider or nurs* or midwife* or physician or doctor or medical or faculty or skilled birth attendant or auxiliary or lay or obstet* or workforce or personnel	Antenatal* or prenatal* or antepartum or perinatal or pregnan*	Care or support or health or clinic or outpatient* or office or education* or parentcraft or home or birth centre or village or communit* or hospital or institution* or session or maternal health services	Want or like or desire or require or expect* or anticipate or view or experienc* or perspective or opinion or assum* or know* or understand* or encounter or belief or attitude or judge* or facilitator or help or promote or provide or provision or enable* or empower* or allow or permi* or encourage* or positive or barrier or prevent* or deter* or obstacle or block or delay or deny or hinder*	Review or qualitative or survey or questionnaire or interview or group or focus group or self-report or life-world or meta-* or ethnograph* or phenomenol* or grounded theory or symbolic interaction*

The search was adapted to fit with the syntax of each specific database searched. In each case, the search string included title/abstract/keywords at a minimum.

Following scrutiny of the initial hits, at each subsequent stage (abstract and full text examination) two members of the qualitative systematic review team determined inclusion independently, and then agreed on the final inclusion list by consensus. In the event of continuing lack of agreement for a particular study, a third team member adjudicated.

The reference lists and key authors in the reference lists were scrutinized and back-chaining and forward-checking were undertaken for any references not identified in the search that may have been relevant. These papers were then subject to the same inclusion/exclusion and quality checking criteria as those identified using the search terms above.

Databases and other sources

African Journals OnLine (AJOL), The Allied and Complementary Medicine Database (AMED), Cumulative Index to Nursing and Allied Health Literature (CINAHL), Embase, Online Regional Information System for Scientific Journals from Latin America, the Caribbean, Spain and Portugal (Latindex), MEDLINE and PsycINFO. In addition, Zetoc alerts were set up for over 50 relevant journals.

4. Search strategy for the review of factors affecting implementation of the WHO ANC guideline/recommendations (i.e. the 2016 WHO ANC model) – large-scale programme evaluation

Search strategy

i. Electronic database searching and grey literature

For peer-reviewed literature, searches were conducted in the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, CINAHL Plus, Global Health and POPLINE, using a broad search strategy, with a date restriction to include studies published after 2000 (when the WHO focused ANC Trial was registered) or 2002 (when the WHO ANC implementation guide was published)[18]. The search string for MEDLINE, which was tailored for each database, was as follows:

1. (antenatal or (ANC and pregnan*) or prenatal or pre-natal or perinatal or peri-natal).ti,ab,kf,hw.
2. exp Perinatal Care/ or exp Prenatal Care/
3. 1 or 2
4. "country name".ti,ab,kf,hw.
5. 3 and 4
6. limit 5 to yr="2000 – Current

The "antenatal care" block was adapted from the search strings used in the Cochrane reviews of ANC and the country keywords were from the MEDLINE low- and middle-income country (LMIC) filter. The reference lists of all relevant studies were checked and the bibliographies of relevant systematic reviews identified during the search were examined. Reports had to be available in English or the primary language spoken in the selected country cases.

For unpublished literature, information was gathered from the following sources:

- ministry of health documents (via web search as well as through local contacts);
- online databases and websites of organizations involved in maternal and child health issues, and if applicable, websites of donors and/or implementation or evaluation partners for selected cases;
- web searches, with keywords "antenatal care" and country name.

Formal appraisal of study quality was not carried out because substantial variability was expected in the quality, scope and format of the available literature. A narrative description of the studies and reports included was undertaken.

ii. Interviews with relevant stakeholders

Primary data collection through key informant interviews ensured comprehensiveness as relevant information on factors that facilitate and hinder implementation (enablers and barriers) was scarce in published literature or online sources, in particular for cases with limited adoption or unsuccessful implementation of the WHO focused ANC model (FANC). Depending on the availability and comprehensiveness of published and unpublished literature, up to five stakeholders were identified for each country case.

The selection of stakeholders used a purposive sampling approach to achieve maximum variation, allowing for the exploration of a range of experiences with the 2016 WHO ANC model. Sampling included people both within and outside of the formal health system and represented key constituencies including policy-makers, managers, donors, researchers, private sector stakeholders, health-care providers and service users.

Face-to-face or phone interviews were conducted with the identified stakeholders. Copious notes were taken during the interviews. The interviews were conducted in English (or if conducted by a local interviewer, then in the primary spoken language of the country). The topic guide was informed by existing data (or lack thereof) for each case,

18 WHO antenatal care randomized trial: manual for the implementation of the new model. Geneva: World Health Organization; 2002 (http://www.who.int/reproductivehealth/publications/maternal_perinatal_health/RHR_01_30/en/, accessed 6 October 2016).

and broadly aimed to explore in detail any gaps in knowledge identified in the literature searches. The interviews were sufficiently open and flexible to ensure participants were able to talk at length about their experience with and perceptions about the FANC model. The project team conducted thematic analysis utilizing the conceptual framework including the Supporting the use of research evidence (SURE) checklist (from the SURE guides for preparing and using evidence-based policy briefs, version 2.1).[19]

iii. Data for country case description

A short profile was developed for each country case. The profile included demographics (e.g. population, country size), economic variables, maternal and neonatal health indicators (e.g. mortality), resource availability (human and capital), ANC coverage and content, and other relevant indicators on access, equity and development. Where possible, time trends for key variables were provided. These indicators were compiled from WHO, World Bank and other publicly available datasets.

19 Available at: http://www.who.int/evidence/sure/guides/en/

5. Search strategy for indirect evidence for health systems interventions

Background

The technical team considered the evidence base for the priority questions on health systems interventions and made the judgement that indirect evidence of effects, to add to the existing direct evidence, should be searched for three of the questions being considered:

1. Should group ANC be recommended as an alternative to standard ANC?
2. What kind of interventions should be recommended to communicate with, and support, pregnant women, their partners and communities about keeping healthy in pregnancy and using ANC services?
3. Should pregnant women carry their own ANC case notes?

These three questions were chosen based on there being a sparsity of direct evidence for one or more of the criteria in the DECIDE Evidence to Decision (EtD) framework,[20] and/or direct evidence from low-income settings.

Inclusion criteria

It was agreed that indirect evidence would be considered if it had been included in a systematic review, and met the following criteria:

- the review was published in the last five years (from the beginning of 2011)
- the interventions were relevant to the ANC guideline question
- the outcomes were relevant to the outcomes agreed from the scoping stage of this guideline.

Exclusion criteria

Reviews would be excluded if the following applied:

- there were major or important limitations to the reliability of the review (e.g. no search strategy reported, no assessment of risk of bias, inappropriate meta-analysis or synthesis of the results of the included studies);
- the findings were assessed to be of low or very low certainty, because further downgrading would be necessary when indirectness was taken into account;
- they related to communication and support interventions targeted at health-care providers, including those involving communication media (e.g. electronic media and mobile phones).

Methods

Members of the technical team discussed how to maximize the possibility of finding relevant indirect evidence in the time available. The following was agreed upon:

For questions 1 and 3 above, PDQ ("pretty darn quick") Evidence[21] was initially searched for relevant reviews for group ANC (searching for "group care" for question 1, and "patient-held notes" for question 3). It was then determined to search terms by looking at the PubMed index terms and the MeSH terms of the reviews of direct evidence (Catling et al., 2015, and Ruiz-Merazo et al., 2012, for question 1; and Brown et al., 2015, and Mori et al., 2015, for question 3), and studies included in them. The same was done for the relevant reviews from the initial searches of PDQ Evidence. From the list of search terms generated, those that were relevant to the question were selected. Searches were then run for reviews published in the last five years in PDQ Evidence using those terms. The titles (and abstracts, if necessary) were screened to find potentially relevant reviews. The matrix (the analysis and search function for the evidence) and related review functions in PDQ Evidence were checked for the reviews of direct and relevant indirect evidence.

For question 2 above, all the reviews carried out by the Cochrane Consumers and Communication Review Group were screened, with search dates no more than five years ago, for relevant indirect evidence.

Each review that met the inclusion and exclusion criteria, and those reviews the technical team was unsure about, was summarized and the relevance of these reviews was discussed within the team.

20 Further information is available at: http://www.decide-collaboration.eu/evidence-decision-etd-framework
21 Available at: http://www.pdq-evidence.org/

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