WHO/RHR/15.17

WHO recommendations on interventions to improve preterm birth outcomes:

Evidence base

World Health Organization

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Contents

Abbreviations: CI: confidence interval; MD: mean difference; OR: odds ratio; RR: relative risk

Table 1a. Antenatal corticosteroids (ACS) versus placebo or no treatment for accelerating fetal lung maturation for women at risk of preterm birth (all women and babies)

Source: Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2006;(3):CD004454. (updated for the guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment	Relative (95% CI)	Absolute		
Maternal death												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/188 (0.5%)	1/177 (0.6%)	RR 0.98 (0.06 to 15.50)	0 fewer per 1000 (from 5 fewer to 82 more)	⊕⊕OO LOW	CRITICAL
Maternal admission into intensive care unit												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	6/160 (3.8%)	8/159 (5.0%)	RR 0.74 (0.26 to 2.05)	13 fewer per 1000 (from 37 fewer to 53 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis												
13	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	91/1254 (7.3%)	101/1271 (7.9%)	RR 0.90 (0.69 to 1.17)	8 fewer per 1000 (from 25 fewer to 14 more)	⊕⊕OO LOW	CRITICAL
Puerperal sepsis												
8	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	57/496 (11.5%)	44/507 (8.7%)	RR 1.35 (0.93 to 1.95)	30 more per 1000 (from 6 fewer to 82 more)	⊕⊕⊕O MODERATE	CRITICAL
Mean interval between trial entry and birth (days) (better indicated by higher values)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	749	764	—	MD 0.23 higher (1.86 lower to 2.32 higher)	⊕⊕⊕O MODERATE	CRITICAL
Fetal and neonatal death												
13	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	261/1813 (14.4%)	341/1814 (18.8%)	RR 0.77 (0.67 to 0.89)	43 fewer per 1000 (from 21 fewer to 62 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Fetal death												
13	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	86/1813 (4.7%)	89/1814 (4.9%)	RR 0.98 (0.73 to 1.30)	1 fewer per 1000 (from 13 fewer to 15 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment	Relative (95% CI)	Absolute		
Neonatal death												
21	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	210/2218 (9.5%)	306/2190 (14.0%)	RR 0.68 (0.58 to 0.80)	45 fewer per 1000 (from 28 fewer to 59 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Childhood death												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	16/537 (3.0%)	20/473 (4.2%)	RR 0.68 (0.36 to 1.27)	14 fewer per 1000 (from 27 fewer to 11 more)	⊕⊕⊕O MODERATE	CRITICAL
Death in adulthood												
1	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	serious[3]	none	21/493 (4.3%)	21/495 (4.2%)	RR 1.00 (0.56 to 1.81)	0 fewer per 1000 (from 19 fewer to 34 more)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome												
25	randomized trials	serious2	no serious inconsistency	no serious indirectness	no serious imprecision	none	369/2310 (16.0%)	553/2280 (24.3%)	RR 0.65 (0.58 to 0.73)	85 fewer per 1000 (from 65 fewer to 102 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Moderate/severe respiratory distress syndrome												
6	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	81/835 (9.7%)	145/851 (17.0%)	RR 0.55 (0.43 to 0.71)	77 fewer per 1000 (from 49 fewer to 97 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Mean duration of mechanical ventilation/continuous positive airway pressure (days) (better indicated by lower values)												
3	randomized trials	no serious risk of bias	serious[5]	no serious indirectness	no serious imprecision	none	264	254	—	MD 1.42 lower (2.28 to 0.56 lower)	⊕⊕⊕O MODERATE	CRITICAL
Mean duration of oxygen supplementation (days) (better indicated by lower values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	28	45	—	MD 2.86 lower (5.51 to 0.21 lower)	⊕⊕⊕O MODERATE	CRITICAL
Surfactant use												
4	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	42/392 (10.7%)	56/384 (14.6%)	RR 0.74 (0.52 to 1.05)	38 fewer per 1000 (from 70 fewer to 7 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment	Relative (95% CI)	Absolute		
Chronic lung disease												
6	randomized trials	serious[2]	serious[5]	no serious indirectness	serious[3]	none	48/413 (11.6%)	50/405 (12.3%)	RR 0.86 (0.61 to 1.22)	17 fewer per 1000 (from 48 fewer to 27 more)	⊕OOO VERY LOW	CRITICAL
Cerebroventricular haemorrhage												
13	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	88/1445 (6.1%)	155/1427 (10.9%)	RR 0.54 (0.43 to 0.69)	50 fewer per 1000 (from 34 fewer to 62 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Systemic infection in the first 48 hours of life												
6	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	33/685 (4.8%)	57/674 (8.5%)	RR 0.57 (0.38 to 0.86)	36 fewer per 1000 (from 12 fewer to 52 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Necrotizing enterocolitis												
8	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	25/853 (2.9%)	52/822 (6.3%)	RR 0.46 (0.29 to 0.74)	34 fewer per 1000 (from 16 fewer to 45 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Small for gestational age												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	73/367 (19.9%)	63/331 (19%)	RR 1.05 (0.78 to 1.42)	10 more per 1000 (from 42 fewer to 80 more)	⊕⊕⊕O MODERATE	CRITICAL
Mean birth weight (g) (better indicated by higher values)												
13	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	1498	1463	—	MD 6.93 lower (39.41 lower to 25.55 higher)	⊕⊕OO LOW	CRITICAL
Admission to neonatal intensive care unit												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	112/314 (35.7%)	127/315 (40.3%)	RR 0.88 (0.73 to 1.06)	48 fewer per 1000 (from 109 fewer to 24 more)	⊕⊕⊕O MODERATE	IMPOR-TANT
Mean duration of neonatal hospitalization (days) (better indicated by lower values)												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	323	318	—	MD 0 higher (1.08 lower to 1.09 higher)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment	Relative (95% CI)	Absolute		
Cerebral palsy in childhood												
5	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	20/490 (4.1%)	28/414 (6.8%)	RR 0.60 (0.34 to 1.03)	27 fewer per 1000 (from 45 fewer to 2 more)	⊕⊕OO LOW	CRITICAL
Developmental delay in childhood												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	11/266 (4.1%)	19/252 (7.5%)	RR 0.49 (0.24 to 1.00)	38 fewer per 1000 (from 57 fewer to 0 more)	⊕⊕⊕O MODERATE	CRITICAL
Visual impairment in childhood												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	9/100 (9.0%)	11/66 (16.7%)	RR 0.55 (0.24 to 1.23)	75 fewer per 1000 (from 127 fewer to 38 more)	⊕⊕OO LOW	CRITICAL
Hearing impairment in childhood												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[7]	none	1/100 (1.0%)	1/66 (1.5%)	RR 0.64 (0.04 to 9.87)	5 fewer per 1000 (from 15 fewer to 134 more)	⊕OOO VERY LOW	CRITICAL
Neurodevelopmental delay in childhood												
1	randomized trials	serious4	no serious inconsistency	no serious indirectness	very serious[7]	none	3/50 (6.0%)	3/32 (9.4%)	RR 0.64 (0.14 to 2.98)	34 fewer per 1000 (from 81 fewer to 186 more)	⊕OOO VERY LOW	CRITICAL
Intellectual impairment in childhood												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	16/409 (3.9%)	17/369 (4.6%)	RR 0.86 (0.44 to 1.69)	6 fewer per 1000 (from 26 fewer to 32 more)	⊕⊕OO LOW	CRITICAL
Behavioural/learning difficulties in childhood												
1	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[7]	none	9/54 (16.7%)	7/36 (19.4%)	RR 0.86 (0.35 to 2.09)	27 fewer per 1000 (from 126 fewer to 212 more)	⊕OOO VERY LOW	CRITICAL
Visual impairment in adulthood												
1	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[8]	none	18/87 (20.7%)	24/105 (22.9%)	RR 0.91 (0.53 to 1.55)	21 fewer per 1000 (from 107 fewer to 126 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment	Relative (95% CI)	Absolute		
Hearing impairment in adulthood												
1	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[7]	none	1/87 (1.1%)	5/105 (4.8%)	RR 0.24 (0.03 to 2.03)	36 fewer per 1000 (from 46 fewer to 49 more)	⊕OOO VERY LOW	CRITICAL
Intellectual impairment in adulthood												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[7]	none	0/135 (0.0%)	2/138 (1.4%)	RR 0.24 (0.01 to 4.95)	11 fewer per 1000 (from 14 fewer to 57 more)	⊕OOO VERY LOW	CRITICAL

1 Wide confidence interval crossing the line of no effect and few events.
2 Most of the pooled effect provided by studies with design limitations.
3 Wide confidence interval crossing the line of no effect.
4 One study with design limitations.
5 Statistical heterogeneity ($I^2 > 60\%$).
6 Estimate based on small sample size.
7 Wide confidence interval crossing the line of no effect, few events and small sample size.
8 Wide confidence interval crossing the line of no effect and small sample size.

Table 1b. Antenatal corticosteroids (ACS) versus placebo or no treatment for accelerating fetal lung maturation for women at risk of preterm birth (gestational age at first dose)

Source: Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2006;(3):CD004454. (updated for the guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at 1st dose)	Relative (95% CI)	Absolute		
Chorioamnionitis — in women < 26 weeks of gestation at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	6/22 (27.3%)	3/24 (12.5%)	RR 2.18 (0.62 to 7.69)	148 more per 1000 (from 47 fewer to 836 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women between 26 and < 30 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	17/129 (13.2%)	14/113 (12.4%)	RR 1.06 (0.55 to 2.06)	7 more per 1000 (from 56 fewer to 131 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women between 30 and < 33 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	2/150 (1.3%)	10/144 (6.9%)	RR 0.19 (0.04 to 0.86)	56 fewer per 1000 (from 10 fewer to 67 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Chorioamnionitis — in women between 33 and < 35 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	3/158 (1.9%)	7/175 (4.0%)	RR 0.47 (0.12 to 1.80)	21 fewer per 1000 (from 35 fewer to 32 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women between 35 and < 37 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	0/81 (0.0%)	3/100 (3.0%)	RR 0.18 (0.01 to 3.36)	25 fewer per 1000 (from 30 fewer to 71 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women > 36 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	0/16 (0.0%)	0/24 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies < 26 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	15/23 (65.2%)	17/26 (65.4%)	RR 1.00 (0.66 to 1.50)	0 fewer per 1000 (from 222 fewer to 327 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at 1st dose)	Relative (95% CI)	Absolute		
Fetal and neonatal deaths — in babies between 26 and < 30 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	50/140 (35.7%)	54/121 (44.6%)	RR 0.80 (0.59 to 1.08)	89 fewer per 1000 (from 183 fewer to 36 more)	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies between 30 and < 33 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	19/165 (11.5%)	30/154 (19.5%)	RR 0.59 (0.35 to 1.01)	80 fewer per 1000 (from 127 fewer to 2 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal and neonatal deaths — in babies between 33 and < 35 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	18/168 (10.7%)	18/185 (9.7%)	RR 1.10 (0.59 to 2.05)	10 more per 1000 (from 40 fewer to 102 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal and neonatal deaths — in babies between 35 and < 37 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	3/87 (3.4%)	3/107 (2.8%)	RR 1.23 (0.25 to 5.94)	6 more per 1000 (from 21 fewer to 139 more)	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies > 36 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	3/18 (16.7%)	0/24 (0.0%)	RR 9.21 (0.51 to 167.82)	—	⊕⊕OO LOW	CRITICAL
Fetal deaths — in babies < 26 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	8/23 (34.8%)	14/26 (53.8%)	RR 0.65 (0.33 to 1.25)	188 fewer per 1000 (from 361 fewer to 135 more)	⊕⊕OO LOW	CRITICAL
Fetal deaths — in babies between 26 and < 30 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	20/140 (14.3%)	14/121 (11.6%)	RR 1.23 (0.65 to 2.34)	27 more per 1000 (from 40 fewer to 155 more)	⊕⊕OO LOW	CRITICAL
Fetal deaths — in babies between 30 and < 33 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	10/165 (6.1%)	14/154 (9.1%)	RR 0.67 (0.31 to 1.46)	30 fewer per 1000 (from 63 fewer to 42 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at 1st dose)	Relative (95% CI)	Absolute		
Fetal deaths — in babies between 33 and < 35 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	7/168 (4.2%)	7/185 (3.8%)	RR 1.10 (0.39 to 3.07)	4 more per 1000 (from 23 fewer to 78 more)	⊕⊕OO LOW	CRITICAL
Fetal deaths — in babies between 35 and < 37 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	2/87 (2.3%)	1/107 (0.9%)	RR 2.46 (0.23 to 26.68)	14 more per 1000 (from 7 fewer to 240 more)	⊕⊕OO LOW	CRITICAL
Fetal deaths — in babies > 36 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	0/18 (0.0%)	0/24 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Neonatal deaths — in babies < 26 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	7/15 (46.7%)	3/12 (25.0%)	RR 1.87 (0.61 to 5.72)	218 more per 1000 (from 97 fewer to 1000 more)	⊕⊕OO LOW	CRITICAL
Neonatal deaths — in babies between 26 and < 30 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	30/120 (25.0%)	40/107 (37.4%)	RR 0.67 (0.45 to 0.99)	123 fewer per 1000 (from 4 fewer to 206 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal deaths — in babies between 30 and < 33 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	9/155 (5.8%)	16/140 (11.4%)	RR 0.51 (0.23 to 1.11)	56 fewer per 1000 (from 88 fewer to 13 more)	⊕⊕OO LOW	CRITICAL
Neonatal deaths — in babies between 33 and < 35 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	11/161 (6.8%)	11/178 (6.2%)	RR 1.11 (0.49 to 2.48)	7 more per 1000 (from 32 fewer to 91 more)	⊕⊕OO LOW	CRITICAL
Neonatal deaths — in babies between 35 and < 37 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/85 (1.2%)	2/106 (1.9%)	RR 0.62 (0.06 to 6.76)	7 fewer per 1000 (from 18 fewer to 109 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at 1st dose)	Relative (95% CI)	Absolute		
Neonatal deaths — in babies between 34 and <37 weeks at 1st dose												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	1/248 (0.4%)	4/263 (1.5%)	RR 0.37 (0.06 to 2.26)	10 fewer per 1000 (from 14 fewer to 19 more)	⊕⊕OO LOW	CRITICAL
Neonatal deaths — in babies > 36 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	3/18 (16.7%)	0/24 (0.0%)	RR 9.21 (0.51 to 167.82)	—	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome — in babies < 26 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	4/14 (28.6%)	1/10 (10.0%)	RR 2.86 (0.37 to 21.87)	186 more per 1000 (from 63 fewer to 1000 more)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome — in babies between 26 and < 30 weeks at 1st dose												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious7	none	27/129 (20.9%)	50/113 (44.2%)	RR 0.49 (0.34 to 0.72)	226 fewer per 1000 (from 124 fewer to 292 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome — in babies between 30 and < 33 weeks at 1st dose												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	25/186 (13.4%)	43/175 (24.6%)	RR 0.56 (0.36 to 0.87)	108 fewer per 1000 (from 32 fewer to 157 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Respiratory distress syndrome — in babies between 33 and < 35 weeks at 1st dose												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	18/212 (8.5%)	34/222 (15.3%)	RR 0.53 (0.31 to 0.91)	72 fewer per 1000 (from 14 fewer to 106 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Respiratory distress syndrome — in babies between 35 and < 37 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	2/85 (2.4%)	4/104 (3.8%)	RR 0.61 (0.11 to 3.26)	15 fewer per 1000 (from 34 fewer to 87 more)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome — in babies between 34 and <37 weeks at 1st dose												
3	randomized trials	serious[8]	no serious inconsistency	no serious indirectness	very serious[4]	none	6/298 (2.0%)	13/311 (4.2%)	RR 0.49 (0.19 to 1.26)	21 fewer per 1000 (from 34 fewer to 11 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at 1st dose)	Relative (95% CI)	Absolute		
Respiratory distress syndrome — in babies > 36 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	0/16 (0.0%)	0/24 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies < 26 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	3/15 (20.0%)	2/12 (16.7%)	RR 1.20 (0.24 to 6.06)	33 more per 1000 (from 127 fewer to 843 more)	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies between 26 and < 30 weeks at 1st dose												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[7]	none	9/121 (7.4%)	18/108 (16.7%)	RR 0.45 (0.21 to 0.95)	92 fewer per 1000 (from 8 fewer to 132 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Cerebroventricular haemorrhage — in babies between 30 and < 33 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/155 (0.6%)	4/140 (2.9%)	RR 0.23 (0.03 to 2.00)	22 fewer per 1000 (from 28 fewer to 29 more)	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies between 33 and < 35 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	3/161 (1.9%)	3/178 (1.7%)	RR 1.11 (0.23 to 5.40)	2 more per 1000 (from 13 fewer to 74 more)	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies between 35 and < 37 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	0/85 (0.0%)	0/106 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies > 36 weeks at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	0/18 (0.0%)	0/24 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies < 26 weeks at 1st dose (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	23	26	—	MD 63.14 higher (607.37 lower to 733.65 higher)	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies between 26 and < 30 weeks at 1st dose (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	140	121	—	MD 26.41 higher (215.55 lower to 268.37 higher)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at 1st dose)	Relative (95% CI)	Absolute		
Mean birth weight (g) — in babies between 30 and < 33 weeks at 1st dose (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	165	154	—	MD 190.64 lower (359.98 to 21.30 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Mean birth weight (g) — in babies between 33 and < 35 weeks at 1st dose (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	168	185	—	MD 38.72 lower (172.29 lower to 94.85 higher)	⊕⊕⊕O MODERATE	CRITICAL
Mean birth weight (g) — in babies between 35 and < 37 weeks at 1st dose (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	87	107	—	MD 13.57 lower (175.45 lower to 148.31 higher)	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies between 34 and <37 weeks at 1st dose (better indicated by higher values)												
3	randomized trials	serious8	no serious inconsistency	no serious indirectness	serious[6]	none	280	287	—	MD 3.51 higher (41.98 lower to 49 higher)	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies > 36 weeks at 1st dose (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	18	24	—	MD 73.89 higher (270.89 lower to 418.67 higher)	⊕⊕OO LOW	CRITICAL

1 Wide confidence interval crossing the line of no effect, few events and small sample size.
2 Wide confidence interval crossing the line of no effect and small sample size.
3 Estimate based on few events and small sample size.
4 Wide confidence interval crossing the line of no effect and few events.
5 No events.
6 Wide confidence interval crossing the line of no effect.
7 Few events and small sample size.
8 Most studies contributing data had design limitations.

Table 1c. Antenatal corticosteroids (ACS) versus placebo or no treatment for accelerating fetal lung maturation for women at risk of preterm birth (gestational age at birth)

Source: Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2006;(3):CD004454. (updated for the guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at birth)	Relative (95% CI)	Absolute		
Chorioamnionitis — in women delivering < 28 weeks of gestation												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	10/45 (22.2%)	11/46 (23.9%)	RR 0.93 (0.44 to 1.97)	17 fewer per 1000 (from 134 fewer to 232 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women delivering < 30 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	19/91 (20.9%)	18/93 (19.4%)	RR 1.08 (0.61 to 1.92)	15 more per 1000 (from 75 fewer to 178 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women delivering < 32 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	21/165 (12.7%)	25/154 (16.2%)	RR 0.78 (0.46 to 1.34)	36 fewer per 1000 (from 88 fewer to 55 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women delivering < 34 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	25/283 (8.8%)	34/264 (12.9%)	RR 0.69 (0.42 to 1.12)	40 fewer per 1000 (from 75 fewer to 15 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women delivering < 36 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	27/401 (6.7%)	37/392 (9.4%)	RR 0.71 (0.44 to 1.15)	27 fewer per 1000 (from 53 fewer to 14 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women delivering ≥ 34 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	5/337 (1.5%)	10/391 (2.6%)	RR 0.58 (0.20 to 1.68)	11 fewer per 1000 (from 20 fewer to 17 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at birth)	Relative (95% CI)	Absolute		
Chorioamnionitis — in women delivering ≥ 36 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	2/202 (1.0%)	2/240 (0.8%)	RR 1.19 (0.17 to 8.36)	2 more per 1000 (from 7 fewer to 61 more)	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies born < 28 weeks												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	39/60 (65%)	53/69 (76.8%)	RR 0.81 (0.65 to 1.01)	146 fewer per 1000 (from 269 fewer to 8 more)	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies born < 30 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	59/99 (59.6%)	71/102 (69.6%)	RR 0.86 (0.7 to 1.05)	97 fewer per 1000 (from 209 fewer to 35 more)	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies born < 32 weeks												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	82/230 (35.7%)	110/223 (49.3%)	RR 0.71 (0.57 to 0.88)	143 fewer per 1000 (from 59 fewer to 212 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Fetal and neonatal deaths — in babies born < 34 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	90/312 (28.8%)	113/286 (39.5%)	RR 0.73 (0.58 to 0.91)	107 fewer per 1000 (from 36 fewer to 166 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Fetal and neonatal deaths — in babies born < 36 weeks												
2	randomized trials	no serious risk of bias	serious2	no serious indirectness	no serious imprecision	none	107/498 (21.5%)	135/471 (28.7%)	RR 0.75 (0.61 to 0.94)	72 fewer per 1000 (from 17 fewer to 112 fewer)	⊕⊕OO MODERATE	CRITICAL
Fetal and neonatal deaths — in babies born ≥ 34 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	24/361 (6.6%)	24/409 (5.9%)	RR 1.13 (0.66 to 1.96)	8 more per 1000 (from 20 fewer to 56 more)	⊕⊕OO MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at birth)	Relative (95% CI)	Absolute		
Fetal and neonatal deaths — in babies born ≥ 36 weeks												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	10/234 (4.3%)	3/264 (1.1%)	RR 3.25 (0.99 to 10.66)	26 more per 1000 (from 0 fewer to 110 more)	⊕⊕OO LOW	CRITICAL
Fetal deaths — in babies born < 28 weeks												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	15/60 (25.0%)	25/69 (36.2%)	RR 0.65 (0.39 to 1.09)	127 fewer per 1000 (from 221 fewer to 33 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths — in babies born < 30 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	23/99 (23.2%)	28/102 (27.5%)	RR 0.85 (0.53 to 1.36)	41 fewer per 1000 (from 129 fewer to 99 more)	⊕⊕OO LOW	CRITICAL
Fetal deaths — in babies born < 32 weeks												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	37/230 (16.1%)	38/223 (17.0%)	RR 0.92 (0.62 to 1.38)	14 fewer per 1000 (from 65 fewer to 65 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths — in babies born < 34 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	39/312 (12.5%)	44/286 (15.4%)	RR 0.81 (0.54 to 1.21)	29 fewer per 1000 (from 71 fewer to 32 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths — in babies born < 36 weeks												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	47/498 (9.4%)	53/471 (11.3%)	RR 0.85 (0.59 to 1.23)	17 fewer per 1000 (from 46 fewer to 26 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths — in babies born ≥ 34 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	10/361 (2.8%)	14/409 (3.4%)	RR 0.81 (0.36 to 1.80)	7 fewer per 1000 (from 22 fewer to 27 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at birth)	Relative (95% CI)	Absolute		
Fetal deaths — in babies born ≥ 36 weeks												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	2/234 (0.9%)	0/264 (0.0%)	RR 5.92 (0.29 to 122.63)	—	⊕⊕OO LOW	CRITICAL
Neonatal deaths — in babies born < 28 weeks												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	24/45 (53.3%)	28/44 (63.6%)	RR 0.79 (0.56 to 1.12)	134 fewer per 1000 (from 280 fewer to 76 more)	⊕⊕OO LOW	CRITICAL
Neonatal deaths — in babies born < 30 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	36/76 (47.4%)	43/74 (58.1%)	RR 0.82 (0.60 to 1.11)	105 fewer per 1000 (from 232 fewer to 64 more)	⊕⊕OO LOW	CRITICAL
Neonatal deaths — in babies born < 32 weeks												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	45/193 (23.3%)	72/185 (38.9%)	RR 0.59 (0.43 to 0.80)	160 fewer per 1000 (from 78 fewer to 222 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal deaths — in babies born < 34 weeks												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	65/372 (17.5%)	86/343 (25.1%)	RR 0.69 (0.52 to 0.92)	78 fewer per 1000 (from 20 fewer to 120 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal deaths — in babies born < 36 weeks												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	60/451 (13.3%)	82/418 (19.6%)	RR 0.68 (0.50 to 0.92)	63 fewer per 1000 (from 16 fewer to 98 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal deaths — in babies born <37 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	0/163 (0.0%)	2/157 (1.3%)	RR 0.19 (0.01 to 3.98)	10 fewer per 1000 (from 13 fewer to 38 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at birth)	Relative (95% CI)	Absolute		
Neonatal deaths — in babies born ≥ 34 weeks												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	14/382 (3.7%)	10/426 (2.3%)	RR 1.58 (0.71 to 3.50)	14 more per 1000 (from 7 fewer to 59 more)	⊕⊕OO LOW	CRITICAL
Neonatal deaths — in babies born ≥ 36 weeks												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	8/241 (3.3%)	3/273 (1.1%)	RR 2.62 (0.77 to 8.96)	18 more per 1000 (from 3 fewer to 87 more)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome — in babies born < 28 weeks												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	20/48 (41.7%)	29/54 (53.7%)	RR 0.79 (0.53 to 1.18)	113 fewer per 1000 (from 252 fewer to 97 more)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome — in babies born < 30 weeks												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	46/108 (42.6%)	71/110 (64.5%)	RR 0.67 (0.52 to 0.87)	213 fewer per 1000 (from 84 fewer to 310 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome — in babies born < 32 weeks												
6	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	75/292 (25.7%)	134/291 (46.0%)	RR 0.56 (0.45 to 0.71)	203 fewer per 1000 (from 134 fewer to 253 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Respiratory distress syndrome — in babies born < 34 weeks												
5	randomized trials	serious[7]	no serious inconsistency	no serious indirectness	no serious imprecision	none	109/600 (18.2%)	179/577 (31.0%)	RR 0.58 (0.47 to 0.72)	130 fewer per 1000 (from 87 fewer to 164 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome — in babies born < 36 weeks												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	66/525 (12.6%)	121/497 (24.3%)	RR 0.52 (0.40 to 0.69)	117 fewer per 1000 (from 75 fewer to 146 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at birth)	Relative (95% CI)	Absolute		
Respiratory distress syndrome — in babies born <37 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	2/163 (1.2%)	1/157 (0.6%)	RR 1.93 (0.18 to 21.03)	6 more per 1000 (from 5 fewer to 128 more)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome — in babies born ≥ 34 weeks												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	19/618 (3.1%)	30/643 (4.7%)	RR 0.66 (0.38 to 1.16)	16 fewer per 1000 (from 29 fewer to 7 more)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome — in babies born ≥ 36 weeks												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	1/261 (0.4%)	4/296 (1.4%)	RR 0.30 (0.03 to 2.67)	9 fewer per 1000 (from 13 fewer to 23 more)	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies born < 28 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[8]	none	5/34 (14.7%)	12/28 (42.9%)	RR 0.34 (0.14 to 0.86)	283 fewer per 1000 (from 60 fewer to 369 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Cerebroventricular haemorrhage — in babies born < 30 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	11/76 (14.5%)	19/74 (25.7%)	RR 0.56 (0.29 to 1.10)	113 fewer per 1000 (from 182 fewer to 26 more)	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies born < 32 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	13/144 (9.0%)	23/133 (17.3%)	RR 0.52 (0.28 to 0.99)	83 fewer per 1000 (from 2 fewer to 125 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Cerebroventricular haemorrhage — in babies born < 34 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	16/273 (5.9%)	27/242 (11.2%)	RR 0.53 (0.29 to 0.95)	52 fewer per 1000 (from 6 fewer to 79 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at birth)	Relative (95% CI)	Absolute		
Cerebroventricular haemorrhage — in babies born < 36 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	16/394 (4.1%)	27/373 (7.2%)	RR 0.56 (0.31 to 1.02)	32 fewer per 1000 (from 50 fewer to 1 more)	⊕⊕⊕O MODERATE	CRITICAL
Cerebroventricular haemorrhage — in babies born ≥ 34 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	1/351 (0.3%)	1/395 (0.3%)	RR 1.13 (0.07 to 17.92)	0 more per 1000 (from 2 fewer to 43 more)	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies born ≥ 36 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[9]	none	0/209 (0.0%)	0/250 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies born < 28 weeks (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	49	51	—	MD 71.2 higher (42.54 lower to 184.94 higher)	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies born < 30 weeks (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	99	102	—	MD 0.89 higher (98.17 lower to 99.95 higher)	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies born < 32 weeks (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	179	168	—	MD 1.15 higher (91.77 lower to 94.07 higher)		CRITICAL
Mean birth weight (g) — in babies born < 34 weeks (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	312	286	—	MD 30.28 lower (115.06 lower to 54.5 higher)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by gestational age at birth)	Relative (95% CI)	Absolute		
Mean birth weight (g) — in babies born < 36 weeks (better indicated by higher values)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	524	520	—	MD 8.32 lower (51.31 lower to 34.67 higher)	⊕⊕⊕O MODERATE	CRITICAL
Mean birth weight (g) — in babies born <37 weeks (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	143	130	—	MD 13 higher (93.57 lower to 119.57 higher)	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies born ≥ 34 weeks (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	361	409	—	MD 12 lower (107.48 lower to 83.48 higher)	⊕⊕⊕O MODERATE	CRITICAL
Mean birth weight (g) — in babies born ≥36 weeks (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	390	367	—	MD 34.84 lower (117.23 lower to 47.55 higher)	⊕⊕⊕O MODERATE	CRITICAL

1 Wide confidence interval crossing the line of no effect, few events and small sample size.
2 Statistical heterogeneity ($I^2 > 60\%$).
3 Wide confidence interval crossing the line of no effect.
4 Wide confidence interval crossing the line of no effect and few events.
5 Wide confidence interval crossing the line of no effect and small sample size.
6 Estimate based on small sample size.
7 Most studies contributing data had design limitations.
8 Estimate based on small sample size and few events.
9 No events.

Table 1d. Antenatal corticosteroids (ACS) versus placebo or no treatment for accelerating fetal lung maturation for women at risk of preterm birth (interval to delivery)

Source: Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2006;(3):CD004454. (updated for the guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by interval to delivery)	Relative (95% CI)	Absolute		
Chorioamnionitis — in women delivering < 24 hours after 1st dose												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	8/113 (7.1%)	10/126 (7.9%)	RR 0.92 (0.38 to 2.27)	6 fewer per 1000 (from 49 fewer to 101 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women delivering < 48 hours after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	11/150 (7.3%)	18/191 (9.4%)	RR 0.78 (0.38 to 1.60)	21 fewer per 1000 (from 58 fewer to 57 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women delivering 1—7 days after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	11/242 (4.5%)	20/240 (8.3%)	RR 0.55 (0.27 to 1.11)	37 fewer per 1000 (from 61 fewer to 9 more)	⊕⊕⊕O MODERATE	CRITICAL
Chorioamnionitis — in women delivering > 7 days after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	11/229 (4.8%)	7/232 (3.0%)	RR 1.59 (0.63 to 4.03)	18 more per 1000 (from 11 fewer to 91 more)	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies born < 24 hours after 1st dose												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	23/142 (16.2%)	44/151 (29.1%)	RR 0.60 (0.39 to 0.94)	117 fewer per 1000 (from 17 fewer to 178 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Fetal and neonatal deaths — in babies born < 48 hours after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	31/165 (18.8%)	66/208 (31.7%)	RR 0.59 (0.41 to 0.86)	130 fewer per 1000 (from 44 fewer to 187 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by interval to delivery)	Relative (95% CI)	Absolute		
Fetal and neonatal deaths — in babies born 1—7 days after 1st dose												
3	randomized trials	no serious risk of bias	serious5	no serious indirectness	serious[3]	none	62/310 (20.0%)	74/296 (25.0%)	RR 0.81 (0.6 to 1.09)	47 fewer per 1000 (from 100 fewer to 23 more)	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies born > 7 days after 1st dose												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	42/308 (13.6%)	28/290 (9.7%)	RR 1.42 (0.91 to 2.23)	41 more per 1000 (from 9 fewer to 119 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths — in babies born < 24 hours after 1st dose												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	10/142 (7.0%)	18/151 (11.9%)	RR 0.68 (0.34 to 1.38)	38 fewer per 1000 (from 79 fewer to 45 more)	⊕⊕OO LOW	CRITICAL
Fetal deaths — in babies born < 48 hours after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	13/165 (7.9%)	21/208 (10.1%)	RR 0.78 (0.4 to 1.51)	22 fewer per 1000 (from 61 fewer to 51 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths — in babies born 1—7 days after 1st dose												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	22/310 (7.1%)	21/296 (7.1%)	RR 1.01 (0.58 to 1.76)	1 more per 1000 (from 30 fewer to 54 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths — in babies born > 7 days after 1st dose												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	22/308 (7.1%)	15/290 (5.2%)	RR 1.36 (0.73 to 2.53)	19 more per 1000 (from 14 fewer to 79 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal deaths — in babies born < 24 hours after 1st dose												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	14/152 (9.2%)	27/143 (18.9%)	RR 0.53 (0.29 to 0.96)	89 fewer per 1000 (from 8 fewer to 134 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by interval to delivery)	Relative (95% CI)	Absolute		
Neonatal deaths — in babies born < 48 hours after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	18/152 (11.8%)	45/187 (24.1%)	RR 0.49 (0.30 to 0.81)	123 fewer per 1000 (from 46 fewer to 168 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal deaths — in babies born 1—7 days after 1st dose												
3	randomized trials	no serious risk of bias	serious[5]	no serious indirectness	serious[3]	none	40/288 (13.9%)	53/275 (19.3%)	RR 0.74 (0.51 to 1.07)	50 fewer per 1000 (from 94 fewer to 13 more)	⊕⊕OO LOW	CRITICAL
Neonatal deaths — in babies born > 7 days after 1st dose												
3	randomized trials	no serious risk of bias	serious[5]	no serious indirectness	serious[3]	none	20/286 (7.0%)	13/275 (4.7%)	RR 1.45 (0.75 to 2.80)	21 more per 1000 (from 12 fewer to 85 more)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome — in babies born < 24 hours after 1st dose												
9	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	68/260 (26.2%)	74/257 (28.8%)	RR 0.87 (0.66 to 1.15)	37 fewer per 1000 (from 98 fewer to 43 more)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome — in babies born < 48 hours after 1st dose												
3	randomized trials	no serious risk of bias	serious[5]	no serious indirectness	no serious imprecision	none	38/171 (22.2%)	68/203 (33.5%)	RR 0.67 (0.49 to 0.93)	111 fewer per 1000 (from 23 fewer to 171 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome — in babies born 1—7 days after 1st dose												
9	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	57/563 (10.1%)	126/547 (23.0%)	RR 0.46 (0.35 to 0.60)	124 fewer per 1000 (from 92 fewer to 150 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Respiratory distress syndrome — in babies born > 7 days after 1st dose												
8	randomized trials	serious[6]	no serious inconsistency	no serious indirectness	serious[3]	none	32/498 (6.4%)	37/490 (7.6%)	RR 0.82 (0.53 to 1.28)	14 fewer per 1000 (from 35 fewer to 21 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by interval to delivery)	Relative (95% CI)	Absolute		
Moderate/severe respiratory distress syndrome — in babies born < 24 hours after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	13/82 (15.9%)	23/100 (23.0%)	RR 0.69 (0.37 to 1.27)	71 fewer per 1000 (from 145 fewer to 62 more)	⊕⊕OO LOW	CRITICAL
Moderate/severe respiratory distress syndrome — in babies born < 48 hours after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	18/147 (12.2%)	49/179 (27.4%)	RR 0.45 (0.27 to 0.73)	151 fewer per 1000 (from 74 fewer to 200 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Moderate/severe respiratory distress syndrome — in babies born 1—7 days after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	17/237 (7.2%)	44/225 (19.6%)	RR 0.37 (0.22 to 0.62)	123 fewer per 1000 (from 74 fewer to 153 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Moderate/severe respiratory distress syndrome — in babies born > 7 days after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	11/223 (4.9%)	6/223 (2.7%)	RR 1.83 (0.69 to 4.87)	22 more per 1000 (from 8 fewer to 104 more)	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies born < 24 hours after 1st dose												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	7/133 (5.3%)	11/131 (8.4%)	RR 0.54 (0.21 to 1.36)	39 fewer per 1000 (from 66 fewer to 30 more)	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies born < 48 hours after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[8]	none	4/152 (2.6%)	19/187 (10.2%)	RR 0.26 (0.09 to 0.75)	75 fewer per 1000 (from 25 fewer to 92 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Cerebroventricular haemorrhage — in babies born 1—7 days after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	9/245 (3.7%)	17/237 (7.2%)	RR 0.51 (0.23 to 1.13)	35 fewer per 1000 (from 55 fewer to 9 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by interval to delivery)	Relative (95% CI)	Absolute		
Cerebroventricular haemorrhage — in babies born > 7 days after 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	4/226 (1.8%)	2/227 (0.9%)	RR 2.01 (0.37 to 10.86)	9 more per 1000 (from 6 fewer to 87 more)	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies born < 24 hours after 1st dose (better indicated by higher values)												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	112	130	—	MD 46.52 higher (94.26 lower to 187.29 higher)	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies born < 48 hours after 1st dose (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	165	208	—	MD 5.9 lower (131.95 lower to 120.15 higher)	⊕⊕⊕O MODERATE	CRITICAL
Mean birth weight (g) — in babies born 1—7 days after 1st dose (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	264	256	—	MD 105.92 lower (212.52 lower to 0.68 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Mean birth weight (g) — in babies born > 7 days after 1st dose (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	245	241	—	MD 147.01 lower (291.97 to 2.05 lower)	⊕⊕⊕⊕ HIGH	CRITICAL

1 Wide confidence interval crossing the line of no effect, few events and small sample size.
2 Wide confidence interval crossing the line of no effect and few events.
3 Wide confidence interval crossing the line of no effect.
4 Estimate based on small sample size.
5 Statistical Heterogeneity ($I^2 > 60\%$).
6 Most studies contributing data had design limitations.
7 Wide confidence interval crossing the line of no effect and small sample size.
8 Few events.

Table 1e. Antenatal corticosteroids (ACS) versus placebo or no treatment for accelerating fetal lung maturation for women at risk of preterm birth (singleton and multiple pregnancy subgroups)

Source: Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2006;(3):CD004454. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by singleton/ multiple pregnancy)	Relative (95% CI)	Absolute		
Chorioamnionitis — in women delivering singleton babies												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	50/823 (6.1%)	61/838 (7.3%)	RR 0.82 (0.58 to 1.18)	13 fewer per 1000 (from 31 fewer to 13 more)	⊕⊕⊕O MODERATE	CRITICAL
Chorioamnionitis — in women delivering multiple babies												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	1/40 (2.5%)	2/34 (5.9%)	RR 0.43 (0.04 to 4.49)	34 fewer per 1000 (from 56 fewer to 205 more)	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies born from singleton pregnancies												
3	randomized trials	no serious risk of bias	serious[3]	no serious indirectness	no serious imprecision	none	140/702 (19.9%)	180/723 (24.9%)	RR 0.79 (0.65 to 0.96)	52 fewer per 1000 (from 10 fewer to 87 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Fetal and neonatal deaths — in babies born from multiple pregnancies												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	19/131 (14.5%)	24/121 (19.8%)	RR 0.71 (0.41 to 1.22)	58 fewer per 1000 (from 117 fewer to 44 more)	⊕⊕OO LOW	CRITICAL
Fetal deaths — in babies born from singleton pregnancies												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	55/702 (7.8%)	51/723 (7.1%)	RR 1.12 (0.78 to 1.61)	8 more per 1000 (from 16 fewer to 43 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths — in babies born from multiple pregnancies												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	6/131 (4.6%)	10/121 (8.3%)	RR 0.53 (0.20 to 1.40)	39 fewer per 1000 (from 66 fewer to 33 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by singleton/ multiple pregnancy)	Relative (95% CI)	Absolute		
Neonatal deaths — in babies born from singleton pregnancies												
7	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	94/957 (9.8%)	141/968 (14.6%)	RR 0.67 (0.53 to 0.85)	48 fewer per 1000 (from 22 fewer to 68 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal deaths — in babies born from multiple pregnancies												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	13/125 (10.4%)	14/111 (12.6%)	RR 0.79 (0.39 to 1.61)	26 fewer per 1000 (from 77 fewer to 77 more)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome — in babies born from singleton pregnancies												
12	randomized trials	serious[5]	serious[3]	no serious indirectness	no serious imprecision	none	187/1462 (12.8%)	309/1445 (21.4%)	RR 0.60 (0.51 to 0.70)	86 fewer per 1000 (from 64 fewer to 105 fewer)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome — in babies born from multiple pregnancies												
4	randomized trials	serious[5]	no serious inconsistency	no serious indirectness	serious[1]	none	44/167 (26.3%)	40/153 (26.1%)	RR 0.85 (0.6 to 1.2)	39 fewer per 1000 (from 105 fewer to 52 more)	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies born from singleton pregnancies												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	35/772 (4.5%)	71/789 (9.0%)	RR 0.49 (0.33 to 0.71)	46 fewer per 1000 (from 26 fewer to 60 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Cerebroventricular haemorrhage — in babies born from multiple pregnancies												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	2/77 (2.6%)	4/60 (6.7%)	RR 0.39 (0.07 to 2.06)	41 fewer per 1000 (from 62 fewer to 71 more)	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies born from singleton pregnancies (better indicated by higher values)												
6	randomized trials	serious[5]	no serious inconsistency	no serious indirectness	serious[1]	none	860	867	—	MD 16.61 lower (55.45 lower to 22.23 higher)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by singleton/ multiple pregnancy)	Relative (95% CI)	Absolute		
Mean birth weight (g) — in babies born from multiple pregnancies (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	81	69	—	MD 82.36 higher (146.23 lower to 310.95 higher)	⊕⊕OO LOW	CRITICAL

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

Table 1f. Antenatal corticosteroids (ACS) versus placebo or no treatment for accelerating fetal lung maturation for women at risk of preterm birth (preterm prelabour rupture of membranes)

Source: Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2006;(3):CD004454. (updated for the guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by intact/ruptured membranes)	Relative (95% CI)	Absolute		
Maternal death — in women with pregnancies not complicated by preterm prelabour rupture of membranes (PPROM) at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/110 (0.9%)	1/108 (0.9%)	RR 0.98 (0.06 to 15.50)	0 fewer per 1000 (from 9 fewer to 134 more)	⊕⊕OO LOW	CRITICAL
Maternal death — in women with pregnancies complicated by PPROM at 1st dose												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	0/58 (0.0%)	0/45 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women with pregnancies not complicated by PPROM at 1st dose												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	24/611 (3.9%)	30/632 (4.7%)	RR 0.83 (0.50 to 1.40)	8 fewer per 1000 (from 24 fewer to 19 more)	⊕⊕⊕O MODERATE	CRITICAL
Chorioamnionitis — in women with pregnancies complicated by PPROM at 1st dose												
7	randomized trials	serious4	no serious inconsistency	no serious indirectness	serious[3]	none	52/480 (10.8%)	53/479 (11.1%)	RR 0.98 (0.69 to 1.40)	2 fewer per 1000 (from 34 fewer to 44 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women with prolonged rupture of membranes > 24 hours												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	30/236 (12.7%)	27/247 (10.9%)	RR 1.16 (0.71 to 1.89)	17 more per 1000 (from 32 fewer to 97 more)	⊕⊕⊕O MODERATE	CRITICAL
Chorioamnionitis — in women with prolonged rupture of membranes > 48 hours												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	14/122 (11.5%)	16/114 (14.0%)	RR 0.82 (0.42 to 1.60)	25 fewer per 1000 (from 81 fewer to 84 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by intact/ruptured membranes)	Relative (95% CI)	Absolute		
Puerperal sepsis — in women with pregnancies not complicated by PPROM at 1st dose												
2	randomized trials	no serious risk of bias	serious[6]	no serious indirectness	very serious[5]	none	19/143 (13.3%)	18/146 (12.3%)	RR 1.10 (0.61 to 2.00)	12 more per 1000 (from 48 fewer to 123 more)	⊕OOO VERY LOW	CRITICAL
Puerperal sepsis — in women with pregnancies complicated by PPROM at 1st dose												
4	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	serious[3]	none	16/242 (6.6%)	14/235 (6.0%)	RR 1.11 (0.55 to 2.25)	7 more per 1000 (from 27 fewer to 74 more)	⊕⊕OO LOW	CRITICAL
Puerperal sepsis — in women with prolonged rupture of membranes > 24 hours												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	4/74 (5.4%)	6/84 (7.1%)	RR 0.76 (0.22 to 2.58)	17 fewer per 1000 (from 56 fewer to 113 more)	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies born from pregnancies not complicated by PPROM at 1st dose												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	116/659 (17.6%)	137/673 (20.4%)	RR 0.87 (0.70 to 1.08)	26 fewer per 1000 (from 61 fewer to 16 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal and neonatal deaths — in babies born from pregnancies complicated by PPROM at 1st dose												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	55/368 (14.9%)	88/365 (24.1%)	RR 0.62 (0.46 to 0.82)	92 fewer per 1000 (from 43 fewer to 130 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Fetal and neonatal deaths — in babies born following prolonged rupture of membranes > 24 hours												
2	randomized trials	no serious risk of bias	serious[6]	no serious indirectness	serious[3]	none	33/255 (12.9%)	41/253 (16.2%)	RR 0.77 (0.51 to 1.17)	37 fewer per 1000 (from 79 fewer to 28 more)	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies born following prolonged rupture of membranes > 48 hours												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	27/137 (19.7%)	25/118 (21.2%)	RR 0.93 (0.57 to 1.51)	15 fewer per 1000 (from 91 fewer to 108 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by intact/ruptured membranes)	Relative (95% CI)	Absolute		
Fetal deaths — in babies born from pregnancies not complicated by PPROM at 1st dose												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	45/659 (6.8%)	42/673 (6.2%)	RR 1.09 (0.73 to 1.64)	6 more per 1000 (from 17 fewer to 40 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths — in babies born from pregnancies complicated by PPROM at 1st dose												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	16/398 (4.0%)	19/392 (4.8%)	RR 0.86 (0.46 to 1.61)	7 fewer per 1000 (from 26 fewer to 30 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths — in babies born following prolonged rupture of membranes > 24 hours												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	17/255 (6.7%)	13/253 (5.1%)	RR 1.23 (0.62 to 2.44)	12 more per 1000 (from 20 fewer to 74 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths — in babies born following prolonged rupture of membranes > 48 hours												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	14/137 (10.2%)	11/118 (9.3%)	RR 1.10 (0.52 to 2.32)	9 more per 1000 (from 45 fewer to 123 more)	⊕⊕OO LOW	CRITICAL
Neonatal deaths — in babies born from pregnancies not complicated by PPROM at 1st dose												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	71/611 (11.6%)	95/625 (15.2%)	RR 0.77 (0.58 to 1.03)	35 fewer per 1000 (from 64 fewer to 5 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal deaths — in babies born from pregnancies complicated by PPROM at 1st dose												
8	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	54/519 (10.4%)	85/505 (16.8%)	RR 0.61 (0.46 to 0.83)	66 fewer per 1000 (from 29 fewer to 91 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal deaths — in babies born following prolonged rupture of membranes > 24 hours												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	16/238 (6.7%)	28/239 (11.7%)	RR 0.56 (0.31 to 1.01)	52 fewer per 1000 (from 81 fewer to 1 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by intact/ruptured membranes)	Relative (95% CI)	Absolute		
Neonatal deaths — in babies born following prolonged rupture of membranes > 48 hours												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	13/123 (10.6%)	14/107 (13.1%)	RR 0.81 (0.40 to 1.64)	25 fewer per 1000 (from 79 fewer to 84 more)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome — in babies born from pregnancies not complicated by PPROM at 1st dose												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	125/752 (16.6%)	211/775 (27.2%)	RR 0.62 (0.51 to 0.74)	103 fewer per 1000 (from 71 fewer to 133 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Respiratory distress syndrome — in babies born from pregnancies complicated by PPROM at 1st dose												
12	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	126/577 (21.8%)	176/552 (31.9%)	RR 0.68 (0.57 to 0.83)	102 fewer per 1000 (from 54 fewer to 137 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome — in babies born following prolonged rupture of membranes > 24 hours												
6	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	55/311 (17.7%)	82/315 (26.0%)	RR 0.68 (0.51 to 0.90)	83 fewer per 1000 (from 26 fewer to 128 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Respiratory distress syndrome — in babies born following prolonged rupture of membranes > 48 hours												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	13/128 (10.2%)	18/119 (15.1%)	RR 0.71 (0.36 to 1.41)	44 fewer per 1000 (from 97 fewer to 62 more)	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies born from pregnancies not complicated by PPROM at 1st dose												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	36/597 (6.0%)	74/603 (12.3%)	RR 0.50 (0.35 to 0.72)	61 fewer per 1000 (from 34 fewer to 80 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Cerebroventricular haemorrhage — in babies born from pregnancies complicated by PPROM at 1st dose												
5	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	19/454 (4.2%)	38/441 (8.6%)	RR 0.47 (0.28 to 0.79)	46 fewer per 1000 (from 18 fewer to 62 fewer)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by intact/ruptured membranes)	Relative (95% CI)	Absolute		
Cerebroventricular haemorrhage — in babies born following prolonged rupture of membranes > 48 hours												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	3/123 (2.4%)	3/107 (2.8%)	RR 0.87 (0.18 to 4.22)	4 fewer per 1000 (from 23 fewer to 90 more)	⊕⊕OO LOW	CRITICAL
Cerebroventricular haemorrhage — in babies born following prolonged rupture of membranes > 24 hours												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	4/238 (1.7%)	7/239 (2.9%)	RR 0.55 (0.16 to 1.84)	13 fewer per 1000 (from 25 fewer to 25 more)	⊕⊕OO LOW	CRITICAL
Systemic infection in the first 48 hours of life — in babies born from pregnancies not complicated by PPROM at 1st dose												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[8]	none	13/100 (13.0%)	28/100 (28.0%)	RR 0.46 (0.26 to 0.84)	151 fewer per 1000 (from 45 fewer to 207 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Systemic infection in the first 48 hours of life — in babies born from pregnancies complicated by PPROM at 1st dose												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	12/148 (8.1%)	12/143 (8.4%)	RR 0.97 (0.45 to 2.06)	3 fewer per 1000 (from 46 fewer to 89 more)	⊕⊕OO LOW	CRITICAL
Systemic infection in the first 48 hours of life — in babies born following prolonged rupture of membranes > 24 hours												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	8/75 (10.7%)	9/82 (11.0%)	RR 0.97 (0.40 to 2.39)	3 fewer per 1000 (from 66 fewer to 153 more)	⊕⊕OO LOW	CRITICAL
Proven infection while in the neonatal intensive care unit (NICU) — in babies born from pregnancies not complicated by PPROM at 1st dose												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	55/520 (10.6%)	81/537 (15.1%)	RR 0.69 (0.51 to 0.95)	47 fewer per 1000 (from 8 fewer to 74 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Proven infection while in the NICU — in babies born from pregnancies complicated by PPROM at 1st dose												
7	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	51/406 (12.6%)	39/390 (10.0%)	RR 1.26 (0.86 to 1.85)	26 more per 1000 (from 14 fewer to 85 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by intact/ruptured membranes)	Relative (95% CI)	Absolute		
Proven infection while in the NICU — in babies born following prolonged rupture of membranes > 24 hours												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	31/182 (17.0%)	23/181 (12.7%)	RR 1.34 (0.82 to 2.21)	43 more per 1000 (from 23 fewer to 154 more)	⊕⊕⊕O MODERATE	CRITICAL
Proven infection while in the NICU — in babies born following prolonged rupture of membranes > 48 hours												
2	randomized trials	no serious risk of bias	serious[6]	no serious indirectness	very serious[5]	none	24/133 (18.0%)	20/125 (16.0%)	RR 1.15 (0.68 to 1.95)	24 more per 1000 (from 51 fewer to 152 more)	⊕OOO VERY LOW	CRITICAL
Necrotizing enterocolitis — in babies born from pregnancies not complicated by PPROM at 1st dose												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	3/128 (2.3%)	5/129 (3.9%)	RR 0.61 (0.15 to 2.48)	15 fewer per 1000 (from 33 fewer to 57 more)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis — in babies born from pregnancies complicated by PPROM at 1st dose												
4	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	serious[9]	none	8/300 (2.7%)	20/283 (7.1%)	RR 0.39 (0.18 to 0.86)	43 fewer per 1000 (from 10 fewer to 58 fewer)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis — in babies born following prolonged rupture of membranes > 24 hours												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	4/75 (5.3%)	8/82 (9.8%)	RR 0.55 (0.17 to 1.74)	44 fewer per 1000 (from 81 fewer to 72 more)	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies born from pregnancies not complicated by PPROM at 1st dose (better indicated by higher values)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	545	562	—	MD 59.09 lower (157.84 lower to 39.67 higher)	⊕⊕⊕O MODERATE	CRITICAL
Mean birth weight (g) — in babies born from pregnancies complicated by PPROM at 1st dose (better indicated by higher values)												
5	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	serious[3]	none	420	415	—	MD 42.68 lower (108.91 lower to 23.55 higher)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (subgroups by intact/ruptured membranes)	Relative (95% CI)	Absolute		
Mean birth weight (g) — in babies born following prolonged rupture of membranes > 24 hours (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	180	169	—	MD 196.46 lower (335.19 to 57.73 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Mean birth weight (g) — in babies born following prolonged rupture of membranes > 48 hours (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[8]	none	137	118	—	MD 201.79 lower (363.3 to 40.28 lower)	⊕⊕⊕O MODERATE	CRITICAL
Mean duration of mechanical ventilation/continuous positive airway pressure (days) — in babies born from pregnancies not complicated by PPROM at 1st dose (better indicated by lower values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	14	19	—	MD 3.8 higher (20.79 lower to 28.39 higher)	⊕⊕OO LOW	CRITICAL
Mean duration of mechanical ventilation/continuous positive airway pressure (days) — in babies born from pregnancies complicated by PPROM at 1st dose (better indicated by lower values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[8]	none	87	78	—	MD 3.5 lower (5.12 to 1.88 lower)	⊕⊕⊕O MODERATE	CRITICAL
Chronic lung disease — in babies born from pregnancies not complicated by PPROM at 1st dose												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	16/218 (7.3%)	15/216 (6.9%)	RR 1.16 (0.61 to 2.24)	11 more per 1000 (from 27 fewer to 86 more)	⊕⊕⊕O MODERATE	CRITICAL
Chronic lung disease — in babies born from pregnancies complicated by PPROM at 1st dose												
1	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	serious[8]	none	23/87 (26.4%)	41/78 (52.6%)	RR 0.50 (0.33 to 0.76)	263 fewer per 1000 (from 126 fewer to 352 fewer)	⊕⊕OO LOW	CRITICAL

1 Wide confidence interval crossing the line of no effect, few events and small sample size.
2 No events.
3 Wide confidence interval crossing the line of no effect.
4 Most studies contributing data had design limitations.
5 Wide confidence interval crossing the line of no effect and small sample size.
6 Statistical heterogeneity ($I^2 > 60\%$).
7 Wide confidence interval crossing the line of no effect and few events.
8 Estimate based on small sample size.
9 Few events.

Table 1g: Antenatal corticosteroids (ACS) versus placebo or no treatment for accelerating fetal lung maturation for women at risk of preterm birth (women with chorioamnionitis)

Source: Amiya RM, Mlunde LB, Ota E, Mori R, Oladapo OT. Antenatal corticosteroid therapy for reducing adverse maternal and child outcomes in special populations of women at risk of imminent preterm birth: a systematic review. Plos One. 2015 (review in progress).

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	No ACS	Relative (95% CI)	Absolute (95% CI)		
Neonatal death — histological chorioamnionitis (HC) and/or clinical chorioamnionitis (CC)												
7	observational studies	serious[1]	not serious	not serious	serious[2]	not serious	81/787 (10.3%)	104/616 (16.9%)	OR 0.54 (0.38 to 0.76)	70 fewer per 1000 (from 35 fewer to 97 fewer)	⊕OOO VERY LOW	CRITICAL
Neonatal death — HC only												
6	observational studies	serious[1]	not serious	not serious	serious[2]	not serious	64/638 (10.0%)	89/518 (17.2%)	OR 0.49 (0.34 to 0.73)	80 fewer per 1000 (from 40 fewer to 106 fewer)	⊕OOO VERY LOW	CRITICAL
Neonatal death — CC only												
3	observational studies	serious[1]	not serious	not serious	very serious[3]	not serious	17/149 (11.4%)	15/98 (15.3%)	OR 0.77 (0.36 to 1.65)	31 fewer per 1000 (from 77 more to 92 fewer)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome — HC and/or CC												
7	observational studies	serious[1]	not serious	not serious	serious[2]	not serious	378/789 (47.9%)	384/712 (53.9%)	OR 0.62 (0.49 to 0.78)	119 fewer per 1000 (from 62 fewer to 175 fewer)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome — HC only												
5	observational studies	serious[1]	not serious	not serious	serious[2]	not serious	279/580 (48.1%)	285/504 (56.5%)	OR 0.58 (0.44 to 0.76)	135 fewer per 1000 (from 68 fewer to 201 fewer)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome — CC only												
4	observational studies	not serious	not serious	not serious	serious[2]	not serious	99/209 (47.4%)	99/208 (47.6%)	OR 0.73 (0.48 to 1.12)	77 fewer per 1000 (from 28 more to 172 fewer)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	No ACS	Relative (95% CI)	Absolute (95% CI)		
Surfactant use (HC only)												
3	observational studies	serious[1]	not serious	not serious	serious[2]	not serious	187/316 (59.2%)	244/404 (60.4%)	OR 0.93 (0.67 to 1.30)	17 fewer per 1000 (from 61 more to 99 fewer)	⊕OOO VERY LOW	CRITICAL
Intraventricular haemorrhage — HC and/or CC												
6	observational studies	not serious	not serious	not serious	serious[2]	strong association	66/626 (10.5%)	52/313 (16.6%)	OR 0.39 (0.25 to 0.61)	94 fewer per 1000 (from 58 fewer to 119 fewer)	⊕⊕OO LOW	CRITICAL
Intraventricular haemorrhage — HC only												
5	observational studies	not serious	not serious	not serious	serious[2]	strong association	53/463 (11.4%)	32/158 (20.3%)	OR 0.41 (0.24 to 0.69)	108 fewer per 1000 (from 53 fewer to 145 fewer)	⊕⊕OO LOW	CRITICAL
Intraventricular haemorrhage — CC only												
3	observational studies	not serious	not serious	not serious	serious[2]	strong association	13/163 (8.0%)	20/155 (12.9%)	OR 0.36 (0.16 to 0.82)	78 fewer per 1000 (from 21 fewer to 106 fewer)	⊕⊕OO LOW	CRITICAL
Severe intraventricular haemorrhage — HC and/or CC												
5	observational studies	not serious	not serious	not serious	serious[2]	strong association	33/538 (6.1%)	30/271 (11.1%)	OR 0.36 (0.20 to 0.65)	68 fewer per 1000 (from 36 fewer to 86 fewer)	⊕⊕OO LOW	CRITICAL
Severe intraventricular haemorrhage — HC only												
4	observational studies	not serious	not serious	not serious	serious[2]	strong association	28/375 (7.5%)	16/116 (13.8%)	OR 0.40 (0.20 to 0.79)	78 fewer per 1000 (from 26 fewer to 107 fewer)	⊕⊕OO LOW	CRITICAL
Severe intraventricular haemorrhage — CC only												
3	observational studies	not serious	not serious	not serious	very serious[3]	strong association	5/163 (3.1%)	14/155 (9.0%)	OR 0.29 (0.10 to 0.89)	62 fewer per 1000 (from 9 fewer to 80 fewer)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	No ACS	Relative (95% CI)	Absolute (95% CI)		
Periventricular leukomalacia — HC and/or CC												
4	observational studies	not serious	not serious	not serious	serious[2]	strong association	21/480 (4.4%)	30/257 (11.7%)	OR 0.47 (0.24 to 0.90)	58 fewer per 1000 (from 10 fewer to 86 fewer)	⊕OOO VERY LOW	CRITICAL
Periventricular leukomalacia — HC only												
3	observational studies	not serious	not serious	not serious	very serious[3]	not serious	13/317 (4.1%)	6/102 (5.9%)	OR 0.74 (0.26 to 2.09)	15 fewer per 1000 (from 43 fewer to 57 more)	⊕OOO VERY LOW	CRITICAL
Periventricular leukomalacia — CC only												
3	observational studies	not serious	not serious	not serious	serious[2]	strong association	8/163 (4.9%)	24/155 (15.5%)	OR 0.35 (0.14 to 0.85)	95 fewer per 1000 (from 20 fewer to 130 fewer)	⊕OOO VERY LOW	CRITICAL
Neonatal sepsis — HC and/or CC												
5	observational studies	not serious	not serious	not serious	serious[2]	not serious	113/684 (16.5%)	92/550 (16.7%)	OR 1.02 (0.73 to 1.42)	3 more per 1000 (from 39 fewer to 55 more)	⊕OOO VERY LOW	CRITICAL
Neonatal sepsis — HC only												
5	observational studies	not serious	not serious	not serious	serious[2]	not serious	87/580 (15.0%)	80/504 (15.9%)	OR 1.03 (0.72 to 1.48)	4 more per 1000 (from 39 fewer to 60 more)	⊕OOO VERY LOW	CRITICAL
Neonatal sepsis — CC only												
2	observational studies	not serious	not serious	not serious	very serious[3]	not serious	26/104 (25.0%)	12/46 (26.1%)	OR 0.94 (0.40 to 2.18)	12 fewer per 1000 (from 137 fewer to 174 more)	⊕OOO VERY LOW	CRITICAL
Necrotizing enterocolitis — HC and/or CC												
5	observational studies	serious[1]	not serious	not serious	serious[2]	not serious	76/684 (11.1%)	33/550 (6.0%)	OR 1.49 (0.91 to 2.53)	27 more per 1000 (from 5 fewer to 79 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	No ACS	Relative (95% CI)	Absolute (95% CI)		
Necrotizing enterocolitis — HC only												
5	observational studies	serious[1]	not serious	not serious	serious[2]	not serious	60/580 (10.3%)	30/504 (5.9%)	OR 1.33 (0.78 to 2.26)	18 more per 1000 (from 12 fewer to 66 more)	⊕OOO VERY LOW	CRITICAL
Necrotizing enterocolitis — CC only												
2	observational studies	serious[1]	not serious	not serious	very serious[3]	not serious	16/104 (15.4%)	3/46 (6.5%)	OR 2.63 (0.72 to 9.68)	90 more per 1000 (from 17 fewer to 338 more)	⊕OOO VERY LOW	CRITICAL
Duration of mechanical ventilation, days — HC only												
1	observational studies	not serious	not serious	not serious	very serious[3]	not serious	52	36	—	MD 2 lower (4.23 lower to 0.23 higher)	⊕OOO VERY LOW	CRITICAL
Use of mechanical ventilation — HC and/or CC												
1	observational studies	not serious	not serious	not serious	very serious[3]	strong association	115/153 (75.2%)	58/61 (95.1%)	OR 0.18 (0.06 to 0.57)	174 fewer per 1000 (from 34 fewer to 414 fewer)	⊕OOO VERY LOW	CRITICAL
Use of mechanical ventilation — HC only												
1	observational studies	not serious	not serious	not serious	very serious[3]	not serious	66/89 (74.2%)	29/32 (90.6%)	OR 0.30 (0.08 to 1.07)	163 fewer per 1000 (from 6 more to 470 fewer)	⊕OOO VERY LOW	CRITICAL
Use of mechanical ventilation — CC only												
1	observational studies	not serious	not serious	not serious	serious[4]	not serious	49/64 (76.6%)	29/29 (100%)	OR 0.05 (0.00 to 0.94)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕OOO VERY LOW	CRITICAL
Chronic lung disease/bronchopulmonary dysplasia — HC and/or CC												
4	observational studies	not serious	not serious	not serious	serious[2]	not serious	80/465 (17.2%)	42/194 (21.6%)	OR 0.74 (0.48 to 1.15)	47 fewer per 1000 (from 25 more to 99 fewer)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	No ACS	Relative (95% CI)	Absolute (95% CI)		
Chronic lung disease/bronchopulmonary dysplasia — HC only												
3	observational studies	not serious	not serious	not serious	serious[2]	not serious	55/323 (17.0%)	26/104 (25.0%)	OR 0.66 (0.38 to 1.14)	83 fewer per 1000 (from 25 more to 138 fewer)	⊕OOO VERY LOW	CRITICAL
Chronic lung disease/bronchopulmonary dysplasia — CC only												
3	observational studies	serious[1]	not serious	not serious	very serious[3]	not serious	25/142 (17.6%)	16/90 (17.8%)	OR 0.91 (0.44 to 1.86)	13 fewer per 1000 (from 91 fewer to 109 more)	⊕OOO VERY LOW	CRITICAL
Cerebral palsy (at 1 and 3 years follow-up) — HC only												
1	observational studies	serious[1]	not serious	not serious	very serious[3]	not serious	5/58 (8.6%)	3/14 (21.4%)	OR 0.35 (0.07 to 1.67)	127 fewer per 1000 (from 99 more to 196 fewer)	⊕OOO VERY LOW	CRITICAL
General development quotient at 1 years follow-up — HC only												
1	observational studies	serious[1]	not serious	not serious	very serious[3]	not serious	58	14	—	MD 6 higher (9.94 lower to 20.94 higher)	⊕OOO VERY LOW	CRITICAL
General development quotient at 3 years follow-up — HC only												
1	observational studies	serious[1]	not serious	not serious	very serious[3]	not serious	58	14	—	MD 13 higher (3.75 lower to 29.75 higher)	⊕OOO VERY LOW	CRITICAL

HC: histological chorioamnionitis; CC: clinical chorioamnionitis.
1 Evidence heavily based on studies with design limitations including lack of adjustment for potential confounding factors.
2 Estimate based on wide confidence interval crossing the line of no effect.
3 Estimate based on small sample size; wide confidence interval crossing the line of no effect.
4 Estimate based on small sample size.

Table 1h. Antenatal corticosteroids (ACS) versus placebo or no treatment for accelerating fetal lung maturation for women undergoing elective caesarean section at late preterm (34—36^{+6} weeks)

Source: Sotiriadis A, Makrydimas G, Papatheodorou S, Ioannidis JP. Corticosteroids for preventing neonatal respiratory morbidity after elective caesarean section at term. Cochrane Database Syst Rev. 2009;(4):CD006614.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	No ACS	Relative (95% CI)	Absolute (95% CI)		
Perinatal death												
1	randomized trials	not serious	not serious	very serious[1]	very serious[2]	not serious	0/467 (0.0%)	0/475 (0.0%)	not estimable	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕OOO VERY LOW	CRITICAL
Neonatal sepsis												
1	randomized trials	not serious	not serious	very serious[1]	very serious[2]	not serious	0/467 (0.0%)	0/475 (0.0%)	not estimable	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome												
1	randomized trials	not serious	not serious	very serious[1]	very serious[3]	not serious	1/467 (0.2%)	5/471 (1.1%)	RR 0.32 (0.07 to 1.58)	7 fewer per 1000 (from 6 more to 10 fewer)	⊕OOO VERY LOW	CRITICAL
Tachypnoea of the neonate												
1	randomized trials	not serious	not serious	very serious[1]	very serious[3]	not serious	10/467 (2.1%)	19/475 (4.0%)	RR 0.52 (0.25 to 1.11)	19 fewer per 1000 (from 4 more to 30 fewer)	⊕OOO VERY LOW	CRITICAL
Length of stay in neonatal intensive care unit (NICU)												
1	randomized trials	serious[4]	not serious	very serious[1]	very serious[5]	not serious	2	14	—	MD 2.14 lower (5.58 lower to 1.3 higher)	⊕OOO VERY LOW	CRITICAL
Admission to NICU for respiratory complications												
1	randomized trials	serious[4]	not serious	very serious[1]	serious[6]	strong association	2/467 (0.4%)	14/475 (2.9%)	RR 0.15 (0.03 to 0.64)	25 fewer per 1000 (from 11 fewer to 29 fewer)	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	No ACS	Relative (95% CI)	Absolute (95% CI)		
Admission to neonatal special care (all levels) for respiratory complications												
1	randomized trials	serious[4]	not serious	very serious[1]	not serious	strong association	11/467 (2.4%)	24/475 (5.1%)	RR 0.45 (0.22 to 0.90)	28 fewer per 1000 (from 5 fewer to 39 fewer)	⊕OOO VERY LOW	IMPORTANT
Admission to neonatal special care (all levels) for any indication												
1	randomized trials	serious[4]	not serious	very serious[1]	serious[7]	not serious	26/467 (5.6%)	32/475 (6.7%)	RR 0.81 (0.49 to 1.33)	13 fewer per 1000 (from 22 more to 34 fewer)	⊕OOO VERY LOW	IMPORTANT
Use of mechanical ventilation												
1	randomized trials	serious[4]	not serious	very serious[1]	very serious[3]	not serious	4/467 (0.9%)	1/475 (0.2%)	RR 4.07 (0.46 to 36.27)	6 more per 1000 (from 1 fewer to 74 more)	⊕OOO VERY LOW	CRITICAL
Lower quarter of academic ability at childhood follow-up												
1	randomized trials	serious[8]	not serious	very serious[1]	not serious	strong association	33/186 (17.7%)	14/164 (8.5%)	RR 2.08 (1.15 to 3.74)	92 more per 1000 (from 13 more to 234 more)	⊕OOO VERY LOW	CRITICAL
Reported learning difficulty at childhood follow-up												
1	randomized trials	serious[8]	not serious	very serious[1]	not serious	not serious	25/217 (11.5%)	27/190 (14.2%)	RR 0.81 (0.49 to 1.35)	27 fewer per 1000 (from 50 more to 72 fewer)	⊕OOO VERY LOW	CRITICAL

1 Evidence was derived from a population that does not correspond to the population of interest (i.e. women undergoing elective caesarean section at term rather than in late preterm).
2 No events reported for outcome.
3 Wide confidence interval crossing the line of no effect and few events.
4 For this outcome, the study was at moderate risk of bias due to non-blinded design, with the potential for performance and detection bias.
5 Wide confidence interval crossing line of no effect and small sample size.
6 Few events.
7 Wide confidence interval crossing the line of no effect.
8 Study at risk of attrition bias.

Table 1i. Antenatal corticosteroids (ACS) versus placebo or no treatment for accelerating fetal lung maturation for women at risk of preterm birth (women with hypertension in pregnancy)

Source: Roberts D, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2006;(3):CD004454. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (women with hypertension)	Relative (95% CI)	Absolute		
Maternal death — in women with pregnancies complicated by hypertension syndromes												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/110 (0.9%)	1/108 (0.9%)	RR 0.98 (0.06 to 15.50)	0 fewer per 1000 (from 9 fewer to 134 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis — in women with pregnancies complicated by hypertension syndromes												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	3/155 (1.9%)	1/156 (0.6%)	RR 2.36 (0.36 to 15.73)	9 more per 1000 (from 4 fewer to 94 more)	⊕⊕OO LOW	CRITICAL
Puerperal sepsis — in women with pregnancies complicated by hypertension syndromes												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	9/110 (8.2%)	13/108 (12.0%)	RR 0.68 (0.30 to 1.52)	39 fewer per 1000 (from 84 fewer to 63 more)	⊕⊕OO LOW	CRITICAL
Admission into adult intensive care unit — in women with pregnancies complicated by hypertension syndromes												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	6/110 (5.5%)	8/108 (7.4%)	RR 0.74 (0.26 to 2.05)	19 fewer per 1000 (from 55 fewer to 78 more)	⊕⊕OO LOW	CRITICAL
Fetal and neonatal deaths — in babies born from pregnancies complicated by hypertension syndromes												
2	randomized trials	no serious risk of bias	serious[3]	no serious indirectness	serious[4]	none	38/156 (24.4%)	46/157 (29.3%)	RR 0.83 (0.57 to 1.20)	50 fewer per 1000 (from 126 fewer to 59 more)	⊕⊕OO LOW	CRITICAL
Fetal deaths — in babies born from pregnancies complicated by hypertension syndromes												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	22/168 (13.1%)	13/163 (8.0%)	RR 1.73 (0.91 to 3.28)	58 more per 1000 (from 7 fewer to 182 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (women with hypertension)	Relative (95% CI)	Absolute		
Neonatal deaths — in babies born from pregnancies complicated by hypertension syndromes												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[5]	none	16/134 (11.9%)	33/144 (22.9%)	RR 0.50 (0.29 to 0.87)	115 fewer per 1000 (from 30 fewer to 163 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome — in babies born from pregnancies complicated by hypertension syndromes												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	33/191 (17.3%)	68/191 (35.6%)	RR 0.50 (0.35 to 0.72)	178 fewer per 1000 (from 100 fewer to 231 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Cerebroventricular haemorrhage — in babies born from pregnancies complicated by hypertension syndromes												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	7/134 (5.2%)	19/144 (13.2%)	RR 0.38 (0.17 to 0.87)	82 fewer per 1000 (from 17 fewer to 110 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Systemic infection in the first 48 hours of life — in babies born from pregnancies complicated by hypertension syndromes												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[5]	none	13/100 (13.0%)	28/100 (28.0%)	RR 0.46 (0.26 to 0.84)	151 fewer per 1000 (from 45 fewer to 207 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Proven infection while in the neonatal intensive care unit — in babies born from pregnancies complicated by hypertension syndromes												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[5]	none	21/134 (15.7%)	40/144 (27.8%)	RR 0.55 (0.34 to 0.87)	125 fewer per 1000 (from 36 fewer to 183 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Necrotizing enterocolitis — in babies born from pregnancies complicated by hypertension syndromes												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	2/100 (2.0%)	4/100 (4.0%)	RR 0.50 (0.09 to 2.67)	20 fewer per 1000 (from 36 fewer to 67 more)	⊕⊕OO LOW	CRITICAL
Mean birth weight (g) — in babies born from pregnancies complicated by hypertension syndromes (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	46	49	—	MD 131.72 lower (319.68 lower to 56.24 higher)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	Placebo or no treatment (women with hypertension)	Relative (95% CI)	Absolute		
Chronic lung disease — in babies born from pregnancies complicated by hypertension syndromes												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/100 (1.0%)	5/100 (5.0%)	RR 0.20 (0.02 to 1.68)	40 fewer per 1000 (from 49 fewer to 34 more)	⨁⨁OO LOW	CRITICAL

1 Wide confidence interval crossing the line of no effect, few events and small sample size.
2 Wide confidence interval crossing the line of no effect and few events.
3 Statistical Heterogeneity ($I^2 > 60\%$).
4 Wide confidence interval crossing the line of no effect.
5 Estimate based on small sample size.
6 Estimate based on small sample size and few events.
7 Wide confidence interval crossing the line of no effect and small sample size.

Table 1j. Antenatal corticosteroids (ACS) versus placebo or no treatment for accelerating fetal lung maturation for women at risk of preterm birth (women with growth-restricted fetuses)

Source: Amiya RM, Mlunde LB, Ota E, Mori R, Oladapo OT. Antenatal corticosteroid therapy for reducing adverse maternal and child outcomes in special populations of women at risk of imminent preterm birth: a systematic review and meta-analysis. 2014 (unpublished).

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	No ACS	Relative (95% CI)	Absolute (95% CI)		
Mode of delivery — caesarean section (small for gestational age or SGA)												
1	observational studies	not serious	not serious	not serious	very serious[1]	not serious	139/146 (95.2%)	19/19 (100.0%)	OR 0.48 (0.03 to 8.68)	0 fewer per 1000 (from 0 fewer to 0 fewer)	⊕OOO VERY LOW	IMPORTANT
Chorioamnionitis — histological and/or clinical (SGA)												
1	observational studies	serious[2]	not serious	not serious	very serious[1]	not serious	11/63 (17.5%)	34/157 (21.7%)	OR 0.77 (0.36 to 1.63)	41 fewer per 1000 (from 94 more to 126 fewer)	⊕OOO VERY LOW	CRITICAL
Perinatal death — fetal death or neonatal death (intrauterine growth-restricted or IUGR)												
4	observational studies	not serious	not serious	not serious	serious[3]	not serious	41/324 (12.7%)	33/179 (18.4%)	OR 0.81 (0.58 to 1.04)	30 fewer per 1000 (from 6 more to 68 fewer)	⊕OOO VERY LOW	CRITICAL
Perinatal death — fetal death or neonatal death (SGA)												
6	observational studies	not serious	not serious	not serious	serious[3]	not serious	— [4]	— [4]	OR 0.78 (0.58 to 1.04)	1 fewer per 1000 (from 0 fewer to 0 fewer)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome (IUGR)												
4	observational studies	serious[2]	not serious	not serious	serious[3]	not serious	142/324 (43.8%)	88/179 (49.2%)	OR 0.81 (0.59 to 1.11)	52 fewer per 1000 (from 26 more to 128 fewer)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome (SGA)												
8	observational studies	serious[2]	not serious	not serious	serious[3]	not serious	— [4]	— [4]	OR 0.83 (0.66 to 1.05)	1 fewer per 1000 (from 0 fewer to 0 fewer)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	No ACS	Relative (95% CI)	Absolute (95% CI)		
Surfactant use (IUGR)												
1	observational studies	serious[2]	not serious	not serious	very serious[1]	not serious	19/53 (35.8%)	13/34 (38.2%)	OR 0.90 (0.37 to 2.20)	25 fewer per 1000 (from 121 more to 132 fewer)	⊕OOO VERY LOW	CRITICAL
Surfactant use (SGA)												
3	observational studies	serious[2]	not serious	not serious	serious[3]	not serious	81/262 (30.9%)	47/210 (22.4%)	OR 1.39 (0.85 to 2.28)	44 more per 1000 (from 27 fewer to 173 more)	⊕OOO VERY LOW	CRITICAL
Major brain lesion — intraventricular haemorrhage (IVH), intracranial haemorrhage (ICH), periventricular haemorrhage (PVH) or periventricular leukomalacia (PVL) (IUGR)												
2	observational studies	not serious	not serious	not serious	very serious[1]	not serious	12/116 (10.3%)	10/96 (10.4%)	OR 0.86 (0.35 to 2.10)	13 fewer per 1000 (from 65 fewer to 92 more)	⊕OOO VERY LOW	CRITICAL
Major brain lesion (IVH, ICH, PVH or PVL) (SGA)												
5	observational studies	not serious	not serious	not serious	serious[3]	serious[5]	— [4]	— [4]	OR 0.57 (0.41 to 0.78)	1 fewer per 1000 (from 0 fewer to 0 fewer)	⊕OOO VERY LOW	CRITICAL
Neonatal sepsis (IUGR)												
2	observational studies	serious[2]	not serious	not serious	very serious[1]	not serious	45/115 (39.1%)	36/96 (37.5%)	OR 0.83 (0.44 to 1.58)	43 fewer per 1000 (from 112 more to 166 fewer)	⊕OOO VERY LOW	CRITICAL
Neonatal sepsis (SGA)												
3	observational studies	serious[2]	not serious	not serious	serious[3]	not serious	51/178 (28.7%)	45/253 (17.8%)	OR 1.00 (0.58 to 1.73)	0 fewer per 1000 (from 66 fewer to 94 more)	⊕OOO VERY LOW	CRITICAL
Necrotizing enterocolitis (IUGR)												
1	observational studies	serious[2]	not serious	not serious	very serious[1]	not serious	3/53 (5.7%)	2/34 (5.9%)	OR 0.96 (0.15 to 6.07)	2 fewer per 1000 (from 50 fewer to 216 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	No ACS	Relative (95% CI)	Absolute (95% CI)		
Necrotizing enterocolitis (SGA)												
3	observational studies	serious[2]	not serious	not serious	very serious[1]	not serious	4/116 (3.4%)	5/191 (2.6%)	OR 0.90 (0.22 to 3.76)	3 fewer per 1000 (from 20 fewer to 66 more)	⊕OOO VERY LOW	CRITICAL
Chronic lung disease/bronchopulmonary dysplasia (IUGR)												
3	observational studies	serious[2]	not serious	not serious	serious[3]	not serious	47/211 (22.3%)	44/151 (29.1%)	OR 0.69 (0.43 to 1.13)	70 fewer per 1000 (from 14 more to 138 fewer)	⊕OOO VERY LOW	CRITICAL
Chronic lung disease/bronchopulmonary dysplasia (SGA)												
4	observational studies	serious[2]	not serious	not serious	serious[3]	not serious	81/357 (22.7%)	50/170 (29.4%)	OR 0.69 (0.44 to 1.07)	71 fewer per 1000 (from 14 more to 139 fewer)	⊕OOO VERY LOW	CRITICAL
Patent ductus arteriosus (IUGR)												
1	observational studies	serious[2]	not serious	not serious	very serious[1]	not serious	10/53 (18.9%)	6/34 (17.6%)	OR 1.09 (0.35 to 3.32)	13 more per 1000 (from 27 fewer to 255 more)	⊕OOO VERY LOW	CRITICAL
Patent ductus arteriosus (SGA)												
2	observational studies	serious[2]	not serious	not serious	serious[3]	not serious	19/116 (16.4%)	16/191 (8.4%)	OR 1.70 (0.82 to 3.54)	51 more per 1000 (from 14 fewer to 161 more)	⊕OOO VERY LOW	CRITICAL
Low birth weight < 3rd percentile for gestational age (SGA)												
1	observational studies	not serious	not serious	not serious	very serious[1]	not serious	63/146 (43.2%)	12/19 (63.2%)	OR 0.44 (0.16 to 1.19)	202 fewer per 1000 (from 39 more to 416 fewer)	⊕OOO VERY LOW	CRITICAL
Duration of mechanical ventilation, days (IUGR)												
2	observational studies	not serious	not serious	not serious	very serious[1]	not serious	115	96	—	MD 1.09 higher (from 0.86 lower to 3.05 higher)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ACS	No ACS	Relative (95% CI)	Absolute (95% CI)		
Use of mechanical ventilation (IUGR)												
2	observational studies	not serious	not serious	not serious	very serious[1]	not serious	61/115 (53.0%)	45/96 (46.9%)	OR 1.24 (0.72 to 2.14)	54 more per 1000 (from 80 fewer to 185 more)	⊕OOO VERY LOW	CRITICAL
Use of mechanical ventilation (SGA)												
3	observational studies	not serious	not serious	not serious	serious[3]	not serious	127/261 (48.7%)	56/115 (48.7%)	OR 1.04 (0.65 to 1.66)	10 more per 1000 (from 105 fewer to 125 more)	⊕OOO VERY LOW	CRITICAL
Survival without handicap at 2 years corrected age (IUGR)												
1	observational studies	not serious	not serious	not serious	serious[6]	not serious	51/62 (82.3%)	40/62 (64.5%)	OR 2.55 (1.11 to 5.87)	177 more per 1000 (from 24 more to 269 more)	⊕OOO VERY LOW	CRITICAL
Growth <10th percentile in early childhood (follow up to school age) (IUGR)												
1	observational studies	not serious	not serious	not serious	very serious[6]	strong association	14/49 (28.6%)	3/42 (7.1%)	OR 5.20 (1.38 to 19.62)	214 more per 1000 (from 25 more to 530 more)	⊕OOO VERY LOW	CRITICAL

1 Wide confidence interval crossing the line of no effect and small sample size.
2 Evidence based heavily or entirely on studies with design limitations including lack of adjustment for potential confounding factors.
3 Wide confidence interval crossing the line of no effect.
4 Raw data unavailable for one of the included studies (only ORs and 95% CIs reported); generic inverse variance method used for meta-analysis.
5 Funnel plot suggests the presence of some degree of publication bias.
6 Wide confidence interval crossing the line of no effect, small sample size, and few events.

Table 1k. Different corticosteroids and regimens for accelerating fetal lung maturation for women at risk of preterm birth (any regimen of dexamethasone and betamethasone)

Source: Brownfoot FC, Gagliardi DI, Bain E, Middleton P, Crowther CA. Different corticosteroids and regimens for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev. 2013;(8):CD006764.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dexamethasone (any regimen)	Betamethasone (any regimen)	Relative (95% CI)	Absolute		
Interval between admission and birth (days) (better indicated by higher values)												
1	randomized trials	serious[1]	serious[2]	no serious indirectness	very serious[3]	none	120	120	—	MD 3.48 higher (3.38 lower to 10.34 higher)	⊕OOO VERY LOW	CRITICAL
Interval between admission and birth (days) — dexamethasone vs betamethasone; ruptured membranes (better indicated by higher values)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	60	60	—	MD 0 higher (0.99 lower to 0.99 higher)	⊕⊕OO LOW	CRITICAL
Interval between admission and birth (days) — dexamethasone vs betamethasone (intact membranes) (better indicated by higher values)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	60	60	—	MD 7 higher (5.56 to 8.44 higher)	⊕⊕OO LOW	CRITICAL
Neonatal death												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[5]	none	8/278 (2.9%)	6/318 (1.9%)	RR 1.41 (0.54 to 3.67)	8 more per 1000 (from 9 fewer to 50 more)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome												
5	randomized trials	serious[6]	no serious inconsistency	no serious indirectness	serious[5]	none	122/354 (34.5%)	121/399 (30.3%)	RR 1.06 (0.88 to 1.27)	18 more per 1000 (from 36 fewer to 82 more)	⊕⊕OO LOW	CRITICAL
Severe intraventricular haemorrhage												
4	randomized trials	serious6	no serious inconsistency	no serious indirectness	serious[7]	none	4/257 (1.6%)	10/292 (3.4%)	RR 0.40 (0.13 to 1.24)	21 fewer per 1000 (from 30 fewer to 8 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dexamethasone (any regimen)	Betamethasone (any regimen)	Relative (95% CI)	Absolute		
Intraventricular haemorrhage (all grades)												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	9/257 (3.5%)	21/292 (7.2%)	RR 0.44 (0.21 to 0.92)	40 fewer per 1000 (from 6 fewer to 57 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal sepsis												
2	randomized trials	serious[8]	no serious inconsistency	no serious indirectness	serious[5]	none	29/254 (11.4%)	23/262 (8.8%)	RR 1.30 (0.78 to 2.19)	26 more per 1000 (from 19 fewer to 104 more)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis												
3	randomized trials	very serious[9]	no serious inconsistency	no serious indirectness	very serious[7]	none	5/294 (1.7%)	4/304 (1.3%)	RR 1.29 (0.38 to 4.40)	4 more per 1000 (from 8 fewer to 45 more)	⊕OOO VERY LOW	CRITICAL
Retinopathy of prematurity												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[5]	none	31/254 (12.2%)	34/262 (13.0%)	RR 0.93 (0.59 to 1.47)	9 fewer per 1000 (from 53 fewer to 61 more)	⊕⊕⊕O MODERATE	CRITICAL
Low birth weight												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	21/36 (58.3%)	45/69 (65.2%)	RR 0.89 (0.65 to 1.24)	72 fewer per 1000 (from 228 fewer to 157 more)	⊕OOO VERY LOW	CRITICAL
Birth weight (kg) (better indicated by higher values)												
5	randomized trials	serious[6]	no serious inconsistency	no serious indirectness	no serious imprecision	none	348	386	—	MD 0.01 higher (0.11 lower to 0.12 higher)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal intensive care unit admission												
2	randomized trials	serious[6]	serious[2]	no serious indirectness	serious[5]	none	42/156 (26.9%)	40/189 (21.2%)	RR 1.72 (0.44 to 6.72)	152 more per 1000 (from 119 fewer to 1000 more)	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Dexamethasone (any regimen)	Betamethasone (any regimen)	Relative (95% CI)	Absolute		
Neonatal intensive care unit stay (days) (better indicated by lower values)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	34	36	—	MD 0.91 lower (1.77 to 0.05 lower)	⨁⨁◯◯ LOW	CRITICAL
Neurosensory disability as a child (18 months)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[10]	none	1/8 (12.5%)	0/4 (0.0%)	RR 1.67 (0.08 to 33.75)	—	⨁◯◯◯ VERY LOW	CRITICAL
Periventricular leukomalacia												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	4/330 (1.2%)	5/373 (1.3%)	RR 0.83 (0.23 to 3.03)	2 fewer per 1000 (from 10 fewer to 27 more)	⨁⨁◯◯ LOW	CRITICAL
Bronchopulmonary dysplasia												
2	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	serious[5]	none	22/214 (10.3%)	27/250 (10.8%)	RR 2.50 (0.10 to 61.34)	162 more per 1000 (from 97 fewer to 1000 more)	⨁⨁◯◯ LOW	CRITICAL

1 One study with design limitations.
2 Statistical heterogeneity ($I^2 > 60\%$).
3 Wide confidence interval crossing the line of no effect and small sample size.
4 Estimate based on small sample size.
5 Wide confidence interval crossing the line of no effect.
6 Most studies contributing data had design limitations.
7 Wide confidence interval crossing the line of no effect and few events.
8 One of the studies contributing data had serious design limitations.
9 Most studies contributing data had design limitations, with more than 40% of weight from a study with serious design limitations.
10 Wide confidence interval crossing the line of no effect, few events and small sample size.

Table 1l. Repeat course(s) versus single course of antenatal corticosteroids (ACS) for accelerating fetal lung maturation for women at risk of preterm birth

Source: Crowther CA, McKinlay CJ, Middleton P, Harding JE. Repeat doses of prenatal corticosteroids for women at risk of preterm birth for improving neonatal health outcomes. Cochrane Database Syst Rev. 2011;(6):CD003935. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Repeat course(s) of ACS	Single course of ACS	Relative (95% CI)	Absolute		
Birth < 28 weeks of gestation												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	106/818 (13.0%)	99/814 (12.2%)	RR 1.07 (0.83 to 1.38)	9 more per 1000 (from 21 fewer to 46 more)	⊕⊕⊕O MODERATE	CRITICAL
Birth < 34 weeks												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	717/1058 (67.8%)	728/1082 (67.3%)	RR 1.01 (0.95 to 1.07)	7 more per 1000 (from 34 fewer to 47 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Preterm birth < 37 weeks												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	475/585 (81.2%)	501/596 (84.1%)	RR 0.97 (0.92 to 1.02)	25 fewer per 1000 (from 67 fewer to 17 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Mean gestational age at birth (weeks) (better indicated by higher values)												
8	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	1586	1593	—	MD 0.09 lower (0.33 lower to 0.15 higher)	⊕⊕⊕O MODERATE	CRITICAL
Puerperal sepsis												
5	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	72/1565 (4.6%)	61/1526 (4.0%)	RR 1.15 (0.83 to 1.60)	6 more per 1000 (from 7 fewer to 24 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis												
6	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	140/2152 (6.5%)	118/2109 (5.6%)	RR 1.16 (0.92 to 1.46)	9 more per 1000 (from 4 fewer to 26 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Repeat course(s) of ACS	Single course of ACS	Relative (95% CI)	Absolute		
Fetal and neonatal mortality												
9	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	96/2791 (3.4%)	102/2763 (3.7%)	RR 0.94 (0.71 to 1.23)	2 fewer per 1000 (from 11 fewer to 8 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal death												
7	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	4/1375 (0.3%)	5/1380 (0.4%)	RR 0.82 (0.24 to 2.84)	1 fewer per 1000 (from 3 fewer to 7 more)	⊕OOO VERY LOW	CRITICAL
Neonatal death												
7	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	47/1352 (3.5%)	52/1361 (3.8%)	RR 0.91 (0.62 to 1.34)	3 fewer per 1000 (from 15 fewer to 13 more)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome												
8	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	463/1603 (28.9%)	565/1603 (35.2%)	RR 0.83 (0.75 to 0.91)	60 fewer per 1000 (from 32 fewer to 88 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Intraventricular haemorrhage												
6	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	129/1533 (8.4%)	137/1532 (8.9%)	RR 0.94 (0.75 to 1.18)	5 fewer per 1000 (from 22 fewer to 16 more)	⊕⊕⊕O MODERATE	CRITICAL
Intraventricular haemorrhage — grade 3 or 4												
6	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	32/2419 (1.3%)	28/2400 (1.2%)	RR 1.13 (0.69 to 1.86)	2 more per 1000 (from 4 fewer to 10 more)	⊕⊕⊕O MODERATE	CRITICAL
Necrotizing enterocolitis												
8	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	45/2709 (1.7%)	60/2685 (2.2%)	RR 0.74 (0.51 to 1.08)	6 fewer per 1000 (from 11 fewer to 2 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Repeat course(s) of ACS	Single course of ACS	Relative (95% CI)	Absolute		
Retinopathy of prematurity												
7	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	140/2446 (5.7%)	137/2437 (5.6%)	RR 1.02 (0.81 to 1.28)	1 more per 1000 (from 11 fewer to 16 more)	⊕⊕⊕O MODERATE	CRITICAL
Use of surfactant												
9	randomized trials	no serious risk of bias	serious[4]	no serious indirectness	no serious imprecision	none	514/2772 (18.5%)	643/2753 (23.4%)	RR 0.78 (0.65 to 0.95)	51 fewer per 1000 (from 12 fewer to 82 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Early systemic neonatal infection (variously defined)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	177/763 (23.2%)	193/781 (24.7%)	RR 0.93 (0.79 to 1.11)	17 fewer per 1000 (from 52 fewer to 27 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Small for gestational age at birth												
7	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	191/1996 (9.6%)	163/1979 (8.2%)	RR 1.18 (0.97 to 1.43)	15 more per 1000 (from 2 fewer to 35 more)	⊕⊕⊕O MODERATE	CRITICAL
Mean birth weight (g) (better indicated by higher values)												
9	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	2820	2806	—	MD 75.79 lower (117.63 to 33.96 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Admission to the neonatal intensive care unit												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	872/1731 (50.4%)	863/1717 (50.3%)	RR 1.01 (0.95 to 1.07)	5 more per 1000 (from 25 fewer to 35 more)	⊕⊕⊕⊕ HIGH	IMPORTANT
Chronic lung disease												
8	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	181/2709 (6.7%)	170/2684 (6.3%)	RR 1.06 (0.87 to 1.30)	4 more per 1000 (from 8 fewer to 19 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Repeat course(s) of ACS	Single course of ACS	Relative (95% CI)	Absolute		
Periventricular leukomalacia												
7	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	20/2453 (0.8%)	26/2435 (1.1%)	RR 0.77 (0.43 to 1.37)	2 fewer per 1000 (from 6 fewer to 4 more)	⊕⊕⊕O MODERATE	CRITICAL
Survival free of any disability to early childhood follow-up												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1241/1584 (78.3%)	1215/1571 (77.3%)	RR 1.01 (0.97 to 1.05)	8 more per 1000 (from 23 fewer to 39 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Survival free of major neurosensory disability to early childhood follow-up												
2	randomized trials	serious[2]	serious[4]	no serious indirectness	no serious imprecision	none	557/642 (86.8%)	572/675 (84.7%)	RR 1.01 (0.92 to 1.11)	8 more per 1000 (from 68 fewer to 93 more)	⊕⊕OO LOW	CRITICAL
Disability at early childhood follow-up												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	175/495 (35.4%)	182/504 (36.1%)	RR 0.98 (0.83 to 1.16)	7 fewer per 1000 (from 61 fewer to 58 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Developmental delay at early childhood follow-up												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	260/1603 (16.2%)	269/1599 (16.8%)	RR 0.97 (0.84 to 1.13)	5 fewer per 1000 (from 27 fewer to 22 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Blindness at early childhood follow-up												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	24/1590 (1.5%)	20/1561 (1.3%)	RR 1.17 (0.65 to 2.10)	2 more per 1000 (from 4 fewer to 14 more)	⊕⊕⊕O MODERATE	CRITICAL
Deafness at early childhood follow-up												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	6/1710 (0.4%)	7/1695 (0.4%)	RR 0.85 (0.29 to 2.52)	1 fewer per 1000 (from 3 fewer to 6 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Repeat course(s) of ACS	Single course of ACS	Relative (95% CI)	Absolute		
Cerebral palsy at early childhood follow-up												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	56/1948 (2.9%)	54/1935 (2.8%)	RR 1.03 (0.71 to 1.49)	1 more per 1000 (from 8 fewer to 14 more)	⊕⊕⊕O MODERATE	CRITICAL
Any maternal side-effects of therapy												
2	randomized trials	serious[2]	serious[4]	no serious indirectness	serious[1]	none	115/739 (15.6%)	159/735 (21.6%)	RR 0.97 (0.24 to 3.90)	6 fewer per 1000 (from 164 fewer to 627 more)	⊕OOO VERY LOW	IMPORTANT

1 Wide confidence interval crossing the line of no effect.
2 Most studies contributing data had design limitations.
3 Wide confidence interval crossing the line of no effect and few events.
4 Statistical heterogeneity ($I^2 > 60\%$).

Table 2a. Betamimetics for inhibiting preterm labour

Source: Neilson JP, West HM, Dowswell T. Betamimetics for inhibiting preterm labour. Cochrane Database Syst Rev. 2014;(2):CD004352.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	All betamimetics	Placebo	Relative (95% CI)	Absolute		
Delivery < 37 weeks of gestation												
10	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	404/654 (61.8%)	383/558 (68.6%)	RR 0.95 (0.88 to 1.03)	34 fewer per 1000 (from 82 fewer to 21 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Maternal death												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	0/502 (0.0%)	0/405 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Cessation of treatment due to adverse drug reaction												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	77/590 (13.1%)	5/491 (1.0%)	RR 11.38 (5.21 to 24.86)	106 more per 1000 (from 43 more to 243 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth within 48 hours of treatment												
10	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	151/652 (23.2%)	218/557 (39.1%)	RR 0.68 (0.53 to 0.88)	125 fewer per 1000 (from 47 fewer to 184 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Delivery within 7 days												
5	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	184/454 (40.5%)	238/457 (52.1%)	RR 0.80 (0.65 to 0.98)	104 fewer per 1000 (from 10 fewer to 182 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Perinatal death (7 days)												
11	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	16/712 (2.2%)	20/620 (3.2%)	RR 0.84 (0.46 to 1.55)	5 fewer per 1000 (from 17 fewer to 18 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal death												
6	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	19/629 (3.0%)	12/545 (2.2%)	RR 0.90 (0.27 to 3.00)	2 fewer per 1000 (from 16 fewer to 44 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	All betamimetics	Placebo	Relative (95% CI)	Absolute		
Infant death												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	1/370 (0.3%)	2/380 (0.5%)	RR 0.51 (0.05 to 5.64)	3 fewer per 1000 (from 5 fewer to 24 more)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome												
8	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	123/664 (18.5%)	136/575 (23.7%)	RR 0.87 (0.71 to 1.08)	31 fewer per 1000 (from 69 fewer to 19 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Cerebral palsy												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	1/125 (0.8%)	5/121 (4.1%)	RR 0.19 (0.02 to 1.63)	33 fewer per 1000 (from 40 fewer to 26 more)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/75 (1.3%)	3/74 (4.1%)	RR 0.42 (0.06 to 2.78)	24 fewer per 1000 (from 38 fewer to 72 more)	⊕OOO VERY LOW	CRITICAL
Neonatal sepsis or infection												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	45/399 (11.3%)	40/410 (9.8%)	RR 2.72 (0.19 to 39.63)	168 more per 1000 (from 79 fewer to 1000 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal tachycardia												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	12/15 (80.0%)	5/15 (33.3%)	RR 2.40 (1.12 to 5.13)	467 more per 1000 (from 40 more to 1000 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal hypoglycaemia												
3	randomized trials	serious[2]	serious[7]	no serious indirectness	serious[3]	none	143/427 (33.5%)	29/430 (6.7%)	RR 1.89 (0.35 to 10.04)	60 more per 1000 (from 44 fewer to 610 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	All betamimetics	Placebo	Relative (95% CI)	Absolute		
Maternal pulmonary oedema												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[4]	none	1/425 (0.2%)	0/427 (0.0%)	RR 3.03 (0.12 to 74.23)	—	⊕⊕⊕O MODERATE	CRITICAL
Myocardial ischaemia												
1	randomized trials	serious[8]	no serious inconsistency	no serious indirectness	very serious[5]	none	6/54 (11.1%)	0/52 (0.0%)	RR 12.53 (0.72 to 216.91)	—	⊕OOO VERY LOW	CRITICAL
Palpitation												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	214/592 (36.1%)	19/497 (3.8%)	RR 9.91 (6.46 to 15.20)	341 more per 1000 (from 209 more to 543 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Tachycardia												
2	randomized trials	no serious risk of bias	serious[7]	no serious indirectness	very serious[9]	none	65/165 (39.4%)	19/64 (29.7%)	RR 2.01 (0.02 to 252.89)	300 more per 1000 (from 291 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Cardiac arrhythmias												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	7/352 (2.0%)	2/356 (0.6%)	RR 3.54 (0.74 to 16.92)	14 more per 1000 (from 1 fewer to 89 more)	⊕⊕OO LOW	CRITICAL
Chest pain												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	39/406 (9.6%)	3/408 (0.7%)	RR 11.29 (3.81 to 33.46)	76 more per 1000 (from 21 more to 239 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Headaches												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	98/516 (19.0%)	22/420 (5.2%)	RR 4.07 (2.60 to 6.35)	161 more per 1000 (from 84 more to 280 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Hypotension												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	4/69 (5.8%)	2/67 (3.0%)	RR 1.56 (0.12 to 20.86)	17 more per 1000 (from 26 fewer to 593 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	All betamimetics	Placebo	Relative (95% CI)	Absolute		
Hyperglycaemia												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	106/352 (30.1%)	37/356 (10.4%)	RR 2.9 (2.05 to 4.09)	197 more per 1000 (from 109 more to 321 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Hypokalaemia												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	138/352 (39.2%)	23/356 (6.5%)	RR 6.07 (4.00 to 9.2)	328 more per 1000 (from 194 more to 530 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Dyspnoea												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	55/406 (13.5%)	14/408 (3.4%)	RR 3.86 (2.21 to 6.77)	98 more per 1000 (from 42 more to 198 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Tremor												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	138/352 (39.2%)	13/356 (3.7%)	RR 10.74 (6.20 to 18.59)	356 more per 1000 (from 190 more to 642 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Infant long-term neurological development (Bayley score: psychomotor development) (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	125	121	—	MD 1.30 higher (2.74 lower to 5.34 higher)	⊕⊕⊕O MODERATE	CRITICAL
Infant long-term neurological development (Bayley score: mental development) (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	125	121	—	MD 5.20 higher (0.56 to 9.84 higher)	⊕⊕⊕O MODERATE	CRITICAL

1 No events.
2 Most studies contributing data had design limitations.
3 Wide confidence interval crossing the line of no effect.
4 Wide confidence interval crossing the line of no effect and few events.
5 Wide confidence interval crossing the line of no effect, few events and small sample size.
6 Estimate based on small sample size.
7 Statistical heterogeneity ($I^2 > 60\%$).
8 One study with design limitations.
9 Wide confidence interval crossing the line of no effect and small sample size.

Table 2b. Calcium channel blockers for inhibiting preterm labour

Source: Flenady V, Wojcieszek AM, Papatsonis DNM, Stock OM, Murray L, Jardine LA, Carbonne B. Calcium channel blockers for inhibiting preterm labour and birth. Cochrane Database Syst Rev. 2014;(6):CD002255.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any calcium channel blocker	Placebo	Relative (95% CI)	Absolute		
Preterm birth (< 37 weeks of gestation)												
2	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	very serious[2]	none	65/101 (64.4%)	69/72 (95.8%)	RR 0.65 (0.18 to 2.43)	335 fewer per 1000 (from 786 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Birth < 48 hours after trial entry												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	27/101 (26.7%)	62/72 (86.1%)	RR 0.30 (0.21 to 0.43)	603 fewer per 1000 (from 491 fewer to 680 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Maternal adverse drug reaction												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	25/45 (55.6%)	0/44 (0%)	RR 49.89 (3.13 to 795.02)	—	⊕⊕⊕O MODERATE	CRITICAL

1 Statistical heterogeneity ($I^2 > 60\%$).
2 Wide confidence interval crossing the line of no effect and small sample size.
3 Estimate based on small sample size.

Table 2c. Cyclo-oxygenase (COX) inhibitors for inhibiting preterm labour

Source: King JF, Flenady V, Cole S, Thornton S. Cyclo-oxygenase (COX) inhibitors for treating preterm labour. Cochrane Database Syst Rev. 2005;(2):CD001992. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any Cox inhibitors	Placebo	Relative (95% CI)	Absolute		
Preterm birth < 37 weeks of gestation												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	3/18 (16.7%)	14/18 (77.8%)	RR 0.21 (0.07 to 0.62)	614 fewer per 1000 (from 296 fewer to 723 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Delivery within 48 hours of initiation of treatment												
2	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	very serious[3]	none	4/34 (11.8%)	22/36 (61.1%)	RR 0.20 (0.03 to 1.28)	489 fewer per 1000 (from 593 fewer to 171 more)	⊕OOO VERY LOW	CRITICAL
Delivery within 7 days of initiation of treatment												
2	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	very serious[4]	none	11/34 (32.4%)	27/36 (75.0%)	RR 0.41 (0.10 to 1.66)	442 fewer per 1000 (from 675 fewer to 495 more)	⊕OOO VERY LOW	CRITICAL
Gestation at birth (weeks) (better indicated by higher values)												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	34	33	—	MD 3.53 higher (1.13 to 5.92 higher)	⊕⊕⊕O MODERATE	CRITICAL
Maternal adverse drug reaction												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	9/50 (18.0%)	6/51 (11.8%)	RR 1.58 (0.66 to 3.78)	68 more per 1000 (from 40 fewer to 327 more)	⊕⊕OO LOW	CRITICAL
Chorioamnionitis or endometritis												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	4/31 (12.9%)	2/33 (6.1%)	RR 1.94 (0.44 to 8.60)	57 more per 1000 (from 34 fewer to 461 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any Cox inhibitors	Placebo	Relative (95% CI)	Absolute		
Postpartum haemorrhage												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	7/16 (43.8%)	2/18 (11.1%)	RR 3.94 (0.95 to 16.29)	327 more per 1000 (from 6 fewer to 1000 more)	⊕⊕OO LOW	CRITICAL
Perinatal mortality												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	4/53 (7.5%)	5/53 (9.4%)	RR 0.80 (0.25 to 2.58)	19 fewer per 1000 (from 71 fewer to 149 more)	⊕⊕OO LOW	CRITICAL
Intraventricular haemorrhage — grade 3 or 4												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	1/19 (5.3%)	0/20 (0.0%)	RR 3.15 (0.14 to 72.88)	—	⊕⊕OO LOW	CRITICAL
Neonatal sepsis												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	0/35 (0.0%)	1/35 (2.9%)	RR 0.31 (0.01 to 7.15)	20 fewer per 1000 (from 28 fewer to 176 more)	⊕⊕OO LOW	CRITICAL
Patent ductus arteriosus												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	4/19 (21.1%)	3/20 (15.0%)	RR 1.40 (0.36 to 5.46)	60 more per 1000 (from 96 fewer to 669 more)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	3/35 (8.6%)	3/35 (8.6%)	RR 0.97 (0.21 to 4.43)	3 fewer per 1000 (from 68 fewer to 294 more)	⊕⊕OO LOW	CRITICAL
Respiratory distress syndrome												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	8/53 (15.1%)	8/53 (15.1%)	RR 1.00 (0.40 to 2.49)	0 fewer per 1000 (from 91 fewer to 225 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any Cox inhibitors	Placebo	Relative (95% CI)	Absolute		
Chronic neonatal lung disease												
2	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	very serious[3]	none	5/35 (14.3%)	4/35 (11.4%)	RR 0.96 (0.07 to 12.37)	5 fewer per 1000 (from 106 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Premature closure of the ductus arteriosus												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	0/53 (0.0%)	0/53 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Persistent pulmonary hypertension of the newborn												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	0/53 (0.0%)	0/53 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Birth weight (better indicated by higher values)												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	34	33	—	MD 716.34 higher (425.52 to 1007.16 higher)	⊕⊕⊕O MODERATE	CRITICAL
Admission to neonatal intensive care nursery												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	13/19 (68.4%)	17/20 (85.0%)	RR 0.80 (0.56 to 1.15)	170 fewer per 1000 (from 374 fewer to 127 more)	⊕⊕OO LOW	CRITICAL

1 Estimate based on small sample size.
2 Statistical heterogeneity ($I^2 > 60\%$).
3 Wide confidence interval crossing the line of no effect, few events and small sample size.
4 Wide confidence interval crossing the line of no effect and small sample size.
5 No events.

Table 2d. Magnesium sulfate for inhibiting preterm labour

Source: Crowther CA, Hiller JE, Doyle LW. Magnesium sulphate for preventing preterm birth in threatened preterm labour. Cochrane Database Syst Rev. 2002;(4):CD001060. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No tocolytic treatment	Relative (95% CI)	Absolute		
Preterm birth (< 37 weeks of gestation)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	seriousv	none	18/30 (60.0%)	34/35 (97.1%)	RR 0.62 (0.46 to 0.83)	369 fewer per 1000 (from 165 fewer to 525 fewer)	⊕⊕OO LOW	CRITICAL
Serious maternal outcome												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/45 (0.0%)	0/45 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL
Maternal adverse effects leading to discontinuation of treatment												
4	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[5]	none	8/151 (5.3%)	5/159 (3.1%)	RR 1.31 (0.01 to 221.68)	10 more per 1000 (from 31 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Birth < 48 hours after trial entry												
3	randomized trials	serious[4]	serious[6]	no serious indirectness	very serious[7]	none	36/91 (39.6%)	73/99 (73.7%)	RR 0.57 (0.28 to 1.15)	317 fewer per 1000 (from 531 fewer to 111 more)	⊕OOO VERY LOW	CRITICAL
Birth < 24 hours after trial entry												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	22/76 (28.9%)	22/80 (27.5%)	RR 1.05 (0.64 to 1.74)	14 more per 1000 (from 99 fewer to 204 more)	⊕⊕OO LOW	CRITICAL
Interval between trial entry and birth (days) (better indicated by higher values)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[8]	none	137	144	—	MD 0.08 higher (4.08 lower to 4.24 higher)	⊕⊕⊕O MODERATE	CRITICAL
Gestational age at birth (better indicated by higher values)												
3	randomized trials	serious[9]	serious[6]	no serious indirectness	serious[2]	none	137	144	—	MD 0.78 lower (1.4 to 0.17 lower)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No tocolytic treatment	Relative (95% CI)	Absolute		
Total deaths (fetal, neonatal and infant)												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	8/123 (6.5%)	2/134 (1.5%)	RR 4.56 (1.00 to 20.86)	53 more per 1000 (from 0 more to 296 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal deaths												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[10]	none	2/123 (1.6%)	0/134 (0.0%)	RR 5.70 (0.28 to 116.87)	—	⊕⊕OO LOW	CRITICAL
Neonatal/infant deaths												
3	randomized trials	no serious risk of bias	very serious[11]	no serious indirectness	very serious[10]	none	7/137 (5.1%)	6/153 (3.9%)	RR 1.37 (0.48 to 3.97)	15 more per 1000 (from 20 fewer to 116 more)	⊕OOO VERY LOW	CRITICAL
Serious infant outcome												
3	randomized trials	no serious risk of bias	very serious[11]	no serious indirectness	very serious[10]	none	9/139 (6.5%)	6/153 (3.9%)	RR 1.74 (0.63 to 4.77)	29 more per 1000 (from 15 fewer to 148 more)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	80/136 (58.8%)	86/153 (56.2%)	RR 1.09 (0.98 to 1.22)	51 more per 1000 (from 11 fewer to 124 more)	⊕⊕⊕O MODERATE	CRITICAL
Proven neonatal infection (variously defined)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[10]	none	2/15 (13.3%)	0/19 (0.0%)	RR 6.25 (0.32 to 121.14)	—	⊕⊕OO LOW	CRITICAL
Severe intraventricular haemorrhage (IVH) (grade 3 or 4) or periventricular leukomalacia (PVL)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/45 (0.0%)	0/45 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL
IVH (any)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[10]	none	5/136 (3.7%)	7/153 (4.6%)	RR 0.86 (0.28 to 2.62)	6 fewer per 1000 (from 33 fewer to 74 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No tocolytic treatment	Relative (95% CI)	Absolute		
Necrotizing enterocolitis												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[10]	none	4/136 (2.9%)	4/153 (2.6%)	RR 1.19 (0.33 to 4.29)	5 more per 1000 (from 18 fewer to 86 more)	⊕⊕OO LOW	CRITICAL
Respiratory arrest												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[10]	none	1/76 (1.3%)	0/80 (0.0%)	RR 3.16 (0.13 to 76.3)	—	⊕⊕OO LOW	CRITICAL
Admission to neonatal intensive care unit												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[10]	none	5/76 (6.6%)	12/89 (13.5%)	RR 0.49 (0.18 to 1.32)	69 fewer per 1000 (from 111 fewer to 43 more)	⊕⊕OO LOW	CRITICAL
Need for assisted ventilation												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	15/76 (19.7%)	15/89 (16.9%)	RR 1.17 (0.61 to 2.24)	29 more per 1000 (from 66 fewer to 209 more)	⊕⊕OO LOW	CRITICAL
Caesarean section												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	22/136 (16.2%)	22/144 (15.3%)	RR 1.08 (0.63 to 1.85)	12 more per 1000 (from 57 fewer to 130 more)	⊕⊕OO LOW	CRITICAL
Hypotension (variously defined)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[10]	none	1/76 (1.3%)	0/80 (0.0%)	RR 3.16 (0.13 to 76.3)	—	⊕⊕OO LOW	CRITICAL
Tachycardia (variously defined)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	0/16 (0.0%)	0/19 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL

1 One study with design limitations.
2 Estimate based on small sample size.
3 No events.
4 Two of the studies contributing data had design limitations.
5 Wide confidence interval crossing the line of no effect and few events.
6 Statistical heterogeneity ($I^2 > 60\%$). Variation in size of effect.
7 Wide confidence interval crossing the line of no effect and small sample size.
8 Wide confidence interval crossing the line of no effect.
9 More than 40% of weight from a study with design limitations.
10 Wide confidence interval crossing the line of no effect, few events and small sample size.
11 Statistical heterogeneity ($I^2 > 60\%$). Variation in size and direction of effect.

Table 2e. Oxytocin receptor antagonists for inhibiting preterm labour

Source: Flenady V, Reinebrant HE, Liley HG, Tambimuttu EG, Papatsonis DNM. Oxytocin receptor antagonists for inhibiting preterm labour. Cochrane Database Syst Rev. 2014;(6):CD004452.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oxytocin receptor antagonist (atosiban)	Placebo	Relative (95% CI)	Absolute		
Extremely preterm birth (< 28 weeks of gestation)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	12/246 (4.9%)	4/255 (1.6%)	RR 3.11 (1.02 to 9.51)	33 more per 1000 (from 0 more to 133 more)	⊕⊕⊕O MODERATE	CRITICAL
Preterm birth (< 37 weeks)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	144/246 (58.5%)	128/255 (50.2%)	RR 1.17 (0.99 to 1.37)	85 more per 1000 (from 5 fewer to 186 more)	⊕⊕OO LOW	CRITICAL
Maternal death												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/246 (0.0%)	0/255 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL
Maternal adverse drug reaction requiring cessation of treatment												
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	40/306 (13.1%)	10/307 (3.3%)	RR 4.02 (2.05 to 7.85)	98 more per 1000 (from 34 more to 223 more)	⊕⊕⊕O MODERATE	CRITICAL
Birth within 48 hours of initiation of treatment												
2	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[5]	none	6/76 (7.9%)	5/76 (6.6%)	RR 1.05 (0.15 to 7.43)	3 more per 1000 (from 56 fewer to 423 more)	⊕OOO VERY LOW	CRITICAL
Gestational age (weeks) (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	57	57	—	MD 0.5 lower (1.56 lower to 0.56 higher)	⊕⊕⊕O MODERATE	CRITICAL
Perinatal mortality												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[7]	none	11/288 (3.8%)	5/295 (1.7%)	RR 2.25 (0.79 to 6.40)	21 more per 1000 (from 4 fewer to 92 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oxytocin receptor antagonist (atosiban)	Placebo	Relative (95% CI)	Absolute		
Stillbirth												
3	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[7]	none	5/365 (1.4%)	8/372 (2.2%)	RR 0.63 (0.22 to 1.84)	8 fewer per 1000 (from 17 fewer to 18 more)	⊕OOO VERY LOW	CRITICAL
Neonatal death												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[7]	none	8/288 (2.8%)	2/295 (0.7%)	RR 4.10 (0.88 to 19.13)	21 more per 1000 (from 1 fewer to 123 more)	⊕OOO VERY LOW	CRITICAL
Infant death (up to 12 months)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	12/288 (4.2%)	2/295 (0.7%)	RR 6.15 (1.39 to 27.22)	35 more per 1000 (from 3 more to 178 more)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome												
2	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	serious[2]	none	67/340 (19.7%)	54/349 (15.5%)	RR 1.28 (0.93 to 1.76)	43 more per 1000 (from 11 fewer to 118 more)	⊕⊕OO LOW	CRITICAL
Intraventricular haemorrhage												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	16/243 (6.6%)	19/246 (7.7%)	RR 0.85 (0.45 to 1.62)	12 fewer per 1000 (from 42 fewer to 48 more)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[7]	none	1/283 (0.4%)	5/292 (1.7%)	RR 0.21 (0.02 to 1.76)	14 fewer per 1000 (from 17 fewer to 13 more)	⊕OOO VERY LOW	CRITICAL
Birth weight (g) (better indicated by higher values)												
2	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	343	349	—	MD 138.31 lower (248.76 to 27.86 lower)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Oxytocin receptor antagonist (atosiban)	Placebo	Relative (95% CI)	Absolute		
Admission to neonatal intensive care												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	115/274 (42.0%)	110/286 (38.5%)	RR 1.09 (0.89 to 1.34)	35 more per 1000 (from 42 fewer to 131 more)	⊕⊕OO LOW	CRITICAL
Caesarean section												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	13/56 (23.2%)	8/56 (14.3%)	RR 1.62 (0.73 to 3.61)	89 more per 1000 (from 39 fewer to 373 more)	⊕⊕OO LOW	CRITICAL
Maternal drug reaction												
2	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	no serious imprecision	none	49/306 (16.0%)	32/307 (10.4%)	RR 1.54 (1.02 to 2.32)	56 more per 1000 (from 2 more to 138 more)	⊕⊕⊕O MODERATE	CRITICAL

1 One study with design limitations.
2 Wide confidence interval crossing the line of no effect.
3 No events.
4 Most studies contributing data had design limitations.
5 Wide confidence interval crossing the line of no effect, few events and small sample size.
6 Estimate based on small sample size.
7 Wide confidence interval crossing the line of no effect and few events.

Table 2f. Nitric oxide donors for inhibiting preterm labour

Source: Duckitt K, Thornton S, O'Donovan OP, Dowswell T. Nitric oxide donors for treating preterm labour. Cochrane Database Syst Rev. 2014;(5):CD002860.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Nitric oxide donors	Placebo or no treatment	Relative (95% CI)	Absolute		
Delivery < 28 completed weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	8/74 (10.8%)	16/79 (20.3%)	RR 0.53 (0.24 to 1.17)	95 fewer per 1000 (from 154 fewer to 34 more)	⊕⊕OO LOW	CRITICAL
Delivery < 34 completed weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	26/74 (35.1%)	30/79 (38%)	RR 0.93 (0.61 to 1.41)	27 fewer per 1000 (from 148 fewer to 156 more)	⊕⊕OO LOW	CRITICAL
Delivery < 37 completed weeks												
2	randomized trials	no serious risk of bias[2]	serious[3]	no serious indirectness	serious[4]	none	44/149 (29.5%)	65/154 (42.2%)	RR 0.57 (0.16 to 2.01)	181 fewer per 1000 (from 355 fewer to 426 more)	⊕⊕OO LOW	CRITICAL
Prolongation of pregnancy > 48 hours												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[5]	none	67/91 (73.6%)	64/95 (67.4%)	RR 1.19 (0.74 to 1.90)	128 more per 1000 (from 175 fewer to 606 more)	⊕⊕⊕O MODERATE	CRITICAL
Death in utero unrelated to congenital abnormalities												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	0/74 (0.0%)	1/79 (1.3%)	RR 0.36 (0.01 to 8.59)	8 fewer per 1000 (from 13 fewer to 96 more)	⊕⊕OO LOW	CRITICAL
Death in first 28 days of life unrelated to congenital abnormalities												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/91 (1.1%)	3/95 (3.2%)	RR 0.43 (0.06 to 2.89)	18 fewer per 1000 (from 30 fewer to 60 more)	⊕⊕OO LOW	CRITICAL
Birth weight (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	17	16	—	MD 327 higher (272.13 lower to 926.13 higher)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Nitric oxide donors	Placebo or no treatment	Relative (95% CI)	Absolute		
Respiratory distress syndrome												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	3/17 (17.6%)	6/16 (37.5%)	RR 0.47 (0.14 to 1.57)	199 fewer per 1000 (from 322 fewer to 214 more)	⊕⊕OO LOW	CRITICAL
Intraventricular haemorrhage												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	2/74 (2.7%)	1/79 (1.3%)	RR 2.14 (0.20 to 23.06)	14 more per 1000 (from 10 fewer to 279 more)	⊕⊕OO LOW	CRITICAL
Chronic lung disease												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/74 (1.4%)	7/79 (8.9%)	RR 0.15 (0.02 to 1.21)	75 fewer per 1000 (from 87 fewer to 19 more)	⊕⊕OO LOW	CRITICAL
Adverse drug reactions												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	61/91 (67.0%)	43/95 (45.3%)	RR 1.49 (1.14 to 1.94)	222 more per 1000 (from 63 more to 425 more)	⊕⊕⊕O MODERATE	CRITICAL
Headache												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[6]	none	42/74 (56.8%)	23/79 (29.1%)	RR 1.95 (1.31 to 2.90)	277 more per 1000 (from 90 more to 553 more)	⊕⊕⊕O MODERATE	CRITICAL
Dizziness												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	9/74 (12.2%)	6/79 (7.6%)	RR 1.60 (0.60 to 4.28)	46 more per 1000 (from 30 fewer to 249 more)	⊕⊕OO LOW	CRITICAL
Flushing												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	11/74 (14.9%)	13/79 (16.5%)	RR 0.90 (0.43 to 1.89)	16 fewer per 1000 (from 94 fewer to 146 more)	⊕⊕OO LOW	IMPORTANT

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Nitric oxide donors	Placebo or no treatment	Relative (95% CI)	Absolute		
Hypotension												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	9/74 (12.2%)	8/79 (10.1%)	RR 1.20 (0.49 to 2.95)	20 more per 1000 (from 52 fewer to 197 more)	⊕⊕OO LOW	CRITICAL
Completion of course of maternal steroids												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	74/91 (81.3%)	74/95 (77.9%)	RR 1.04 (0.90 to 1.20)	31 more per 1000 (from 78 fewer to 156 more)	⊕⊕OO LOW	IMPORTANT

1 Wide confidence interval crossing the line of no effect, few events and small sample size.
2 Most of the pooled effect provided by studies with low risk of bias.
3 Statistical heterogeneity (I^2 = 90%).
4 Wide confidence interval crossing the line of no effect.
5 Wide confidence interval crossing the line of no effect and small sample size.
6 Estimate based on small sample size.

Table 2g. Progestational agents for inhibiting preterm labour

Source: Su LL, Samuel M, Chong YS. Progestational agents for treating threatened or established preterm labour. Cochrane Database Syst Rev. 2014;(1):CD006770.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Progestational agents	Placebo	Relative (95% CI)	Absolute		
Preterm birth < 34 weeks of gestation												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	8/31 (25.8%)	13/31 (41.9%)	RR 0.62 (0.30 to 1.27)	159 fewer per 1000 (from 294 fewer to 113 more)	⊕OOO VERY LOW	CRITICAL
Preterm delivery < 35 weeks												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/30 (10%)	7/30 (23.3%)	RR 0.43 (0.12 to 1.50)	133 fewer per 1000 (from 205 fewer to 117 more)	⊕OOO VERY LOW	CRITICAL
Preterm delivery < 37 weeks												
4	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	51/147 (34.7%)	77/146 (52.7%)	RR 0.62 (0.39 to 0.98)	200 fewer per 1000 (from 11 fewer to 322 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Delivery within 48 hours of intervention												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	11/54 (20.4%)	15/56 (26.8%)	RR 0.76 (0.38 to 1.50)	64 fewer per 1000 (from 166 fewer to 134 more)	⊕OOO VERY LOW	CRITICAL
Perinatal mortality												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	0/43 (0.0%)	1/40 (2.5%)	RR 0.31 (0.01 to 7.41)	17 fewer per 1000 (from 25 fewer to 160 more)	⊕OOO VERY LOW	CRITICAL
Intraventricular haemorrhage												
1	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	very serious[2]	none	1/51 (2.0%)	0/53 (0.0%)	RR 3.12 (0.13 to 74.76)	—	⊕OOO VERY LOW	CRITICAL
Necrotizing enterocolitis												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/51 (2.0%)	1/53 (1.9%)	RR 1.04 (0.07 to 16.18)	1 more per 1000 (from 18 fewer to 286 more)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/43 (2.3%)	1/40 (2.5%)	RR 0.93 (0.06 to 14.38)	2 fewer per 1000 (from 24 fewer to 335 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Progestational agents	Placebo	Relative (95% CI)	Absolute		
Low birth weight (< 2.5 kg)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	19/51 (37.3%)	20/54 (37%)	RR 1.01 (0.61 to 1.65)	4 more per 1000 (from 144 fewer to 241 more)	⊕OOO VERY LOW	CRITICAL
Birth weight (g) (better indicated by higher values)												
2	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	serious[4]	none	73	70	—	MD 324.7 higher (155.05 to 494.34 higher)	⊕⊕OO LOW	CRITICAL
Admission to neonatal intensive care unit												
2	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[5]	none	17/94 (18.1%)	16/93 (17.2%)	RR 1.08 (0.59 to 1.97)	14 more per 1000 (from 71 fewer to 167 more)	⊕OOO VERY LOW	CRITICAL
Mechanical ventilation												
2	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	7/94 (7.4%)	6/93 (6.5%)	RR 1.18 (0.41 to 3.37)	12 more per 1000 (from 38 fewer to 153 more)	⊕OOO VERY LOW	CRITICAL
Oxygen requirement on day 7 of life												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/51 (7.8%)	6/53 (11.3%)	RR 0.69 (0.21 to 2.31)	35 fewer per 1000 (from 89 fewer to 148 more)	⊕OOO VERY LOW	CRITICAL
Oxygen requirement on day 28 of life												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	2/51 (3.9%)	5/53 (9.4%)	RR 0.42 (0.08 to 2.05)	55 fewer per 1000 (from 87 fewer to 99 more)	⊕OOO VERY LOW	CRITICAL

1 One study with design limitations.
2 Wide confidence interval crossing the line of no effect, few events and small sample size.
3 Most studies contributing data had design limitations.
4 Estimate based on small sample size.
5 Wide confidence interval crossing the line of no effect and small sample size.

Table 2h. Relaxin for inhibiting preterm labour

Source: Bain E, Heatley E, Hsu K, Crowther CA. Relaxin for preventing preterm birth. Cochrane Database Syst Rev. 2013;(8):CD010073.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relaxin	No relaxin	Relative (95% CI)	Absolute		
Preterm birth												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	33/37 (89.2%)	31/32 (96.9%)	RR 0.92 (0.81 to 1.05)	77 fewer per 1000 (from 184 fewer to 48 more)	⊕OOO VERY LOW	CRITICAL
Birth within 7 days of treatment												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	serious[3]	none	7/15 (46.7%)	14/15 (93.3%)	RR 0.50 (0.29 to 0.87)	467 fewer per 1000 (from 121 fewer to 663 fewer)	⊕OOO VERY LOW	CRITICAL
Birth within 7 days of treatment (subgroups) — premature rupture of membranes												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/7 (57.1%)	11/11 (100.0%)	RR 0.59 (0.31 to 1.09)	410 fewer per 1000 (from 690 fewer to 90 more)	⊕OOO VERY LOW	CRITICAL
Birth within 7 days of treatment (subgroups) — placental pathology												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/3 (100.0%)	3/3 (100.0%)	RR 1.00 (0.59 to 1.69)	0 fewer per 1000 (from 410 fewer to 690 more)	⊕OOO VERY LOW	CRITICAL
Birth within 7 days of treatment (subgroups) — maternal complications												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	2/5 (40.0%)	2/3 (66.7%)	RR 0.60 (0.16 to 2.29)	267 fewer per 1000 (from 560 fewer to 860 more)	⊕OOO VERY LOW	CRITICAL
Birth within 7 days of treatment (subgroups) — uncomplicated premature labour												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/5 (0.0%)	1/1 (100.0%)	RR 0.11 (0.01 to 1.78)	890 fewer per 1000 (from 990 fewer to 780 more)	⊕OOO VERY LOW	CRITICAL
Perinatal mortality												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	5/15 (33.3%)	6/15 (40.0%)	RR 0.83 (0.32 to 2.15)	68 fewer per 1000 (from 272 fewer to 460 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relaxin	No relaxin	Relative (95% CI)	Absolute		
Perinatal mortality (subgroups) — premature rupture of membranes												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/7 (42.9%)	4/11 (36.4%)	RR 1.18 (0.37 to 3.76)	65 more per 1000 (from 229 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Perinatal mortality (subgroups) — placental pathology												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/3 (33.3%)	2/3 (66.7%)	RR 0.50 (0.08 to 2.99)	333 fewer per 1000 (from 613 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Perinatal mortality (subgroups) — maternal complications												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/5 (80.0%)	2/3 (66.7%)	RR 1.20 (0.48 to 2.99)	133 more per 1000 (from 347 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Perinatal mortality (subgroups) — uncomplicated premature labour												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/5 (0.0%)	1/1 (100.0%)	RR 0.11 (0.01 to 1.78)	890 fewer per 1000 (from 990 fewer to 780 more)	⊕OOO VERY LOW	CRITICAL
Neonatal death												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/15 (26.7%)	5/15 (33.3%)	RR 0.80 (0.27 to 2.41)	67 fewer per 1000 (from 243 fewer to 470 more)	⊕OOO VERY LOW	CRITICAL
Fetal death												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/15 (6.7%)	1/15 (6.7%)	RR 1.00 (0.07 to 14.55)	0 fewer per 1000 (from 62 fewer to 903 more)	⊕OOO VERY LOW	CRITICAL
Intrapartum fever												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	2/7 (28.6%)	0/11 (0.0%)	RR 7.50 (0.41 to 136.52)	—	⊕OOO VERY LOW	CRITICAL
Labour stopped												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	17/25 (68.0%)	18/25 (72.0%)	RR 0.94 (0.66 to 1.36)	43 fewer per 1000 (from 245 fewer to 259 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Relaxin	No relaxin	Relative (95% CI)	Absolute		
Birth weight < 2500 g												
1	randomized trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	4/15 (26.7%)	2/15 (13.3%)	RR 2.00 (0.43 to 9.32)	133 more per 1000 (from 76 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL

1 One study with serious design limitations.
2 Wide confidence interval crossing the line of no effect and small sample size.
3 Few events and small sample size.
4 Wide confidence interval crossing the line of no effect, few events and small sample size.

Table 2i. Hydration for inhibiting preterm labour

Source: Stan CM, Boulvain M, Pfister R, Hirsbrunner-Almagbaly P. Hydration for treatment of preterm labour. Cochrane Database Syst Rev. 2013;(11):CD003096.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Hydration (all women)	No treatment/ bed rest alone	Relative (95% CI)	Absolute		
Delivery < 32 weeks of gestation												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	9/73 (12.3%)	6/37 (16.2%)	RR 0.76 (0.29 to 1.97)	39 fewer per 1000 (from 115 fewer to 157 more)	⊕OOO VERY LOW	CRITICAL
Delivery < 34 weeks												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/62 (6.5%)	5/56 (8.9%)	RR 0.72 (0.20 to 2.56)	25 fewer per 1000 (from 71 fewer to 139 more)	⊕OOO VERY LOW	CRITICAL
Delivery < 37 weeks												
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	38/135 (28.1%)	24/93 (25.8%)	RR 1.09 (0.71 to 1.68)	23 more per 1000 (from 75 fewer to 175 more)	⊕OOO VERY LOW	CRITICAL
Time to delivery (days) (better indicated by lower values)												
2	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[3]	none	135	93	—	MD 0.99 lower (7.85 lower to 5.87 higher)	⊕OOO VERY LOW	CRITICAL
Admission to neonatal intensive care unit												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	11/62 (17.7%)	10/56 (17.9%)	RR 0.99 (0.46 to 2.16)	2 fewer per 1000 (from 96 fewer to 207 more)	⊕OOO VERY LOW	CRITICAL
Use of tocolytic drugs												
2	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[3]	none	41/138 (29.7%)	30/96 (31.3%)	RR 0.83 (0.57 to 1.20)	53 fewer per 1000 (from 134 fewer to 63 more)	⊕OOO VERY LOW	IMPORTANT
Cost of treatment (first 24 hours, in US$) (better indicated by lower values)												
1	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	54	49	—	MD 39 higher (26.11 lower to 104.11 higher)	⊕OOO VERY LOW	IMPORTANT

1 One study with design limitations.
2 Wide confidence interval crossing the line of no effect, few events and small sample size.
3 Wide confidence interval crossing the line of no effect and small sample size.
4 All studies contributing data had design limitations.

Table 2j. Maintenance betamimetic therapy for inhibiting preterm labour

Source: Dodd JM, Crowther CA, Middleton P. Oral betamimetics for maintenance therapy after threatened preterm labour. Cochrane Database Syst Rev. 2012;(12):CD003927. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any betamimetic	Placebo/no treatment	Relative (95% CI)	Absolute		
Very preterm birth (< 34 weeks of gestation)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	3/62 (4.8%)	1/58 (1.7%)	RR 2.81 (0.30 to 26.22)	31 more per 1000 (from 12 fewer to 435 more)	⊕⊕OO LOW	CRITICAL
Preterm birth (< 37 weeks)												
6	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	111/336 (33.0%)	98/308 (31.8%)	RR 1.11 (0.91 to 1.35)	35 more per 1000 (from 29 fewer to 111 more)	⊕⊕OO LOW	CRITICAL
Preterm birth within 24 hours of therapy												
1	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[1]	none	2/23 (8.7%)	3/23 (13.0%)	RR 0.67 (0.12 to 3.62)	43 fewer per 1000 (from 115 fewer to 342 more)	⊕OOO VERY LOW	CRITICAL
Preterm birth within 48 hours of therapy												
1	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[1]	none	7/100 (7.0%)	9/100 (9.0%)	RR 0.78 (0.30 to 2.01)	20 fewer per 1000 (from 63 fewer to 91 more)	⊕OOO VERY LOW	CRITICAL
Preterm birth within 1 week of therapy												
2	randomized trials	serious[5]	no serious inconsistency	no serious indirectness	serious[3]	none	19/150 (12.7%)	28/145 (19.3%)	RR 0.67 (0.40 to 1.13)	64 fewer per 1000 (from 116 fewer to 25 more)	⊕⊕OO LOW	CRITICAL
Side-effects sufficient to stop therapy												
2	randomized trials	no serious risk of bias[6]	no serious inconsistency	no serious indirectness	very serious[1]	none	1/73 (1.4%)	0/68 (0.0%)	RR 2.71 (0.11 to 64.79)	—	⊕⊕OO LOW	CRITICAL
Perinatal mortality												
6	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[7]	none	11/349 (3.2%)	4/332 (1.2%)	RR 2.41 (0.86 to 6.74)	17 more per 1000 (from 2 fewer to 69 more)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome												
6	randomized trials	serious[8]	no serious inconsistency	no serious indirectness	serious[3]	none	20/388 (5.2%)	19/382 (5.0%)	RR 1.10 (0.61 to 1.98)	5 more per 1000 (from 19 fewer to 49 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any betamimetic	Placebo/no treatment	Relative (95% CI)	Absolute		
Necrotizing enterocolitis												
2	randomized trials	serious[8]	no serious inconsistency	no serious indirectness	very serious[7]	none	3/212 (1.4%)	3/204 (1.5%)	RR 0.98 (0.22 to 4.28)	0 fewer per 1000 (from 11 fewer to 48 more)	⊕OOO VERY LOW	CRITICAL
Intraventricular haemorrhage												
3	randomized trials	serious[8]	no serious inconsistency	no serious indirectness	very serious[7]	none	4/237 (1.7%)	4/229 (1.7%)	RR 0.97 (0.27 to 3.58)	1 fewer per 1000 (from 13 fewer to 45 more)	⊕OOO VERY LOW	CRITICAL
Low birth weight (< 2500 g)												
1	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[1]	none	1/80 (1.3%)	5/60 (8.3%)	RR 0.15 (0.02 to 1.25)	71 fewer per 1000 (from 82 fewer to 21 more)	⊕OOO VERY LOW	CRITICAL
Birth weight (better indicated by higher values)												
7	randomized trials	serious[8]	no serious inconsistency	no serious indirectness	serious[3]	none	395	385	—	MD 4.13 higher (91.89 lower to 100.16 higher)	⊕⊕OO LOW	CRITICAL
Neonatal intensive care unit admission												
2	randomized trials	serious[5]	no serious inconsistency	no serious indirectness	very serious[9]	none	19/134 (14.2%)	14/126 (11.1%)	RR 1.28 (0.68 to 2.41)	31 more per 1000 (from 36 fewer to 157 more)	⊕OOO VERY LOW	CRITICAL
Tachycardia												
4	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	no serious imprecision	none	68/210 (32.4%)	31/204 (15.2%)	RR 2.13 (1.52 to 2.98)	172 more per 1000 (from 79 more to 301 more)	⊕⊕⊕O MODERATE	CRITICAL
Tachypnoea												
2	randomized trials	no serious risk of bias[10]	no serious inconsistency	no serious indirectness	serious[11]	none	15/134 (11.2%)	4/126 (3.2%)	RR 3.52 (1.20 to 10.33)	80 more per 1000 (from 6 more to 296 more)	⊕⊕⊕O MODERATE	CRITICAL
Hypotension												
2	randomized trials	serious[5]	no serious inconsistency	no serious indirectness	serious[11]	none	21/85 (24.7%)	11/81 (13.6%)	RR 1.89 (1.13 to 3.19)	121 more per 1000 (from 18 more to 297 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any betamimetic	Placebo/no treatment	Relative (95% CI)	Absolute		
Palpitations												
1	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	serious[11]	none	12/72 (16.7%)	2/68 (2.9%)	RR 5.67 (1.32 to 24.40)	137 more per 1000 (from 9 more to 688 more)	⊕⊕OO LOW	CRITICAL
Headache												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/50 (2.0%)	0/45 (0.0%)	RR 2.71 (0.11 to 64.79)	—	⊕⊕OO LOW	CRITICAL
Maternal antenatal readmission to hospital												
4	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[3]	none	40/167 (24.0%)	36/168 (21.4%)	RR 1.11 (0.76 to 1.62)	24 more per 1000 (from 51 fewer to 133 more)	⊕⊕OO LOW	CRITICAL
Need for mechanical ventilation												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/62 (1.6%)	1/58 (1.7%)	RR 0.94 (0.06 to 14.61)	1 fewer per 1000 (from 16 fewer to 235 more)	⊕⊕OO LOW	CRITICAL
Neonatal jaundice												
1	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[9]	none	10/25 (40.0%)	6/25 (24.0%)	RR 1.67 (0.71 to 3.89)	161 more per 1000 (from 70 fewer to 694 more)	⊕OOO VERY LOW	CRITICAL

1 Wide confidence interval crossing the line of no effect, few events and small sample size.
2 Most studies contributing data had design limitations.
3 Wide confidence interval crossing the line of no effect.
4 One study with design limitations.
5 More than 40% of weight from a study with design limitations.
6 One study contributing data rated low risk of bias.
7 Wide confidence interval crossing the line of no effect and few events.
8 All studies contributing data had design limitations.
9 Wide confidence interval crossing the line of no effect and small sample size.
10 More than 50% of weight from studies at low risk of bias.
11 Estimate based on small sample size.

Table 2k. Magnesium maintenance therapy inhibiting preterm labour

Source: Han S, Crowther CA, Moore V. Magnesium maintenance therapy for preventing preterm birth after threatened preterm labour. Cochrane Database Syst Rev. 2013;(5):CD000940.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium	Placebo or no treatment	Relative (95% CI)	Absolute		
Birth < 37 weeks of gestation												
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	31/50 (62.0%)	30/49 (61.2%)	RR 1.05 (0.80 to 1.40)	31 more per 1000 (from 122 fewer to 245 more)	⊕OOO VERY LOW	CRITICAL
Gestational age at delivery (weeks) (better indicated by higher values)												
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	90	93	—	MD 0.55 lower (1.34 lower to 0.25 higher)	⊕OOO VERY LOW	CRITICAL
Perinatal mortality (death before discharge among live-born infants)												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	2/25 (8.0%)	0/25 (0.0%)	RR 5 (0.25 to 99.16)	—	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/25 (4.0%)	0/25 (0.0%)	RR 3.00 (0.13 to 70.30)	—	⊕OOO VERY LOW	CRITICAL
Periventricular haemorrhage												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/25 (4.0%)	0/25 (0.0%)	RR 3.00 (0.13 to 70.3)	—	⊕OOO VERY LOW	CRITICAL
Neonatal length of stay (days) (better indicated by lower values)												
2	randomized trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	87	93	—	MD 1.18 higher (0.46 lower to 2.82 higher)	⊕OOO VERY LOW	CRITICAL
Neonatal intensive care unit admissions												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	15/65 (23.1%)	10/68 (14.7%)	RR 1.57 (0.76 to 3.24)	84 more per 1000 (from 35 fewer to 329 more)	⊕OOO VERY LOW	CRITICAL
Maternal readmission for threatened preterm labour												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[2]	none	11/25 (44.0%)	14/25 (56.0%)	RR 0.79 (0.45 to 1.38)	118 fewer per 1000 (from 308 fewer to 213 more)	⊕OOO VERY LOW	CRITICAL

1 Both studies contributing data had design limitations.
2 Wide confidence interval crossing the line of no effect and small sample size.
3 One study with design limitations.
4 Wide confidence interval crossing the line of no effect, few events and small sample size.

Table 2l. Maintenance therapy with calcium channel blockers for inhibiting preterm labour

Source: Naik Gaunekar N, Raman P, Bain E, Crowther CA. Maintenance therapy with calcium channel blockers for preventing preterm birth after threatened preterm labour. Cochrane Database Syst Rev. 2013;(10):CD004071.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Calcium channel blockers	Control	Relative (95% CI)	Absolute		
Birth < 28 weeks of gestation												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	3/29 (10.3%)	1/31 (3.2%)	RR 3.21 (0.35 to 29.11)	71 more per 1000 (from 21 fewer to 907 more)	⊕⊕OO LOW	CRITICAL
Birth < 34 weeks												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	116/267 (43.4%)	111/273 (40.7%)	RR 1.07 (0.88 to 1.30)	28 more per 1000 (from 49 fewer to 122 more)	⊕⊕⊕O MODERATE	CRITICAL
Birth < 37 weeks												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	208/337 (61.7%)	218/344 (63.4%)	RR 0.97 (0.87 to 1.09)	19 fewer per 1000 (from 82 fewer to 57 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Gestation at birth (better indicated by higher values)												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	337	344	—	MD 0.32 higher (0.61 lower to 1.25 higher)	⊕⊕⊕O MODERATE	CRITICAL
Birth within 48 hours of treatment												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/62 (1.6%)	3/66 (4.5%)	RR 0.46 (0.07 to 3.00)	25 fewer per 1000 (from 42 fewer to 91 more)	⊕⊕OO LOW	CRITICAL
Birth within 7 days of treatment												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	7/62 (11.3%)	7/66 (10.6%)	RR 1.07 (0.40 to 2.87)	7 more per 1000 (from 64 fewer to 198 more)	⊕⊕OO LOW	CRITICAL
Pregnancy prolongation (days) (better indicated by higher values)												
4	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	no serious imprecision	none	136	139	—	MD 5.35 higher (0.49 to 10.21 higher)	⊕⊕⊕O MODERATE	CRITICAL
Maternal death												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	0/230 (0.0%)	0/236 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Calcium channel blockers	Control	Relative (95% CI)	Absolute		
Maternal intrauterine infection												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	13/201 (6.5%)	15/205 (7.3%)	RR 0.88 (0.43 to 1.81)	9 fewer per 1000 (from 42 fewer to 59 more)	⊕⊕OO LOW	CRITICAL
Maternal admission to intensive care unit												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	1/230 (0.4%)	1/236 (0.4%)	RR 1.02 (0.06 to 16.19)	0 more per 1000 (from 4 fewer to 64 more)	⊕⊕OO LOW	CRITICAL
Maternal adverse drug reaction causing treatment cessation												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	0/33 (0.0%)	0/35 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Perinatal mortality												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	6/230 (2.6%)	4/236 (1.7%)	RR 1.48 (0.45 to 4.86)	8 more per 1000 (from 9 fewer to 65 more)	⊕⊕OO LOW	CRITICAL
Stillbirth												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	0/29 (0.0%)	0/31 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Neonatal death												
2	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[1]	none	1/66 (1.5%)	2/67 (3%)	RR 0.75 (0.05 to 11.76)	7 fewer per 1000 (from 28 fewer to 321 more)	⊕OOO VERY LOW	CRITICAL
Composite neonatal morbidity												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	40/249 (16.1%)	38/248 (15.3%)	RR 1.03 (0.69 to 1.54)	5 more per 1000 (from 47 fewer to 83 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal sepsis												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	18/238 (7.6%)	19/241 (7.9%)	RR 0.96 (0.52 to 1.79)	3 fewer per 1000 (from 38 fewer to 62 more)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome												
3	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	serious[2]	none	19/275 (6.9%)	23/279 (8.2%)	RR 0.84 (0.47 to 1.50)	13 fewer per 1000 (from 44 fewer to 41 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Calcium channel blockers	Control	Relative (95% CI)	Absolute		
Intraventricular haemorrhage												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	3/275 (1.1%)	8/278 (2.9%)	RR 0.41 (0.12 to 1.42)	17 fewer per 1000 (from 25 fewer to 12 more)	⊕⊕OO LOW	CRITICAL
Intraventricular haemorrhage — any												
2	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[1]	none	1/74 (1.4%)	3/73 (4.1%)	RR 0.42 (0.06 to 2.78)	24 fewer per 1000 (from 39 fewer to 73 more)	⊕OOO VERY LOW	CRITICAL
Intraventricular haemorrhage — grade 3 or 4												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	2/201 (1.0%)	5/205 (2.4%)	RR 0.41 (0.08 to 2.08)	14 fewer per 1000 (from 22 fewer to 26 more)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	7/275 (2.5%)	4/278 (1.4%)	RR 1.68 (0.53 to 5.35)	10 more per 1000 (from 7 fewer to 63 more)	⊕⊕OO LOW	CRITICAL
Small for gestational age												
1	randomized trials	serious[6]	no serious inconsistency	no serious indirectness	very serious[1]	none	3/37 (8.1%)	2/37 (5.4%)	RR 1.50 (0.27 to 8.46)	27 more per 1000 (from 39 fewer to 403 more)	⊕OOO VERY LOW	CRITICAL
Low birth weight												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	25/48 (52.1%)	25/43 (58.1%)	RR 0.90 (0.62 to 1.3)	58 fewer per 1000 (from 221 fewer to 174 more)	⊕⊕OO LOW	CRITICAL
Neonatal intensive care unit admission												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	130/348 (37.4%)	128/361 (35.5%)	RR 1.06 (0.87 to 1.28)	21 more per 1000 (from 46 fewer to 99 more)	⊕⊕⊕O MODERATE	CRITICAL
Length of neonatal intensive care unit stay (days) (better indicated by lower values)												
3	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[7]	none	70	62	—	MD 0.14 lower (3.25 lower to 2.96 higher)	⊕OOO VERY LOW	CRITICAL
Length of neonatal hospital stay (days) (better indicated by lower values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[8]	none	29	31	—	MD 14 higher (4.21 to 23.79 higher)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Calcium channel blockers	Control	Relative (95% CI)	Absolute		
Chronic lung disease												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	5/238 (2.1%)	7/241 (2.9%)	RR 0.74 (0.25 to 2.20)	8 fewer per 1000 (from 22 fewer to 35 more)	⊕⊕OO LOW	CRITICAL
Periventricular leukomalacia												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	0/238 (0.0%)	0/241 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Mechanical ventilation												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	38/282 (13.5%)	37/294 (12.6%)	RR 1.07 (0.70 to 1.64)	9 more per 1000 (from 38 fewer to 81 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal jaundice												
1	randomized trials	serious[6]	no serious inconsistency	no serious indirectness	very serious[7]	none	19/37 (51.4%)	19/37 (51.4%)	RR 1.00 (0.64 to 1.56)	0 fewer per 1000 (from 185 fewer to 288 more)	⊕OOO VERY LOW	CRITICAL

1 Wide confidence interval crossing the line of not effect, few events and small sample size.
2 Wide confidence interval crossing the line of no effect.
3 Most studies contributing data had design limitations.
4 No events.
5 Wide confidence interval crossing the line of no effect and few events.
6 One study with design limitations.
7 Wide confidence interval crossing the line of no effect and small sample size.
8 Estimate based on small sample size.

Table 2m. Maintenance therapy with oxytocin antagonists for inhibiting preterm labour

Source: Papatsonis DN, Flenady V, Liley HG. Maintenance therapy with oxytocin antagonists for inhibiting preterm birth after threatened preterm labour. Cochrane Database Syst Rev. 2013;(10):CD005938.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Atosiban	Placebo	Relative (95% CI)	Absolute		
Birth < 28 weeks of gestation												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	7/45 (15.6%)	6/29 (20.7%)	RR 0.75 (0.28 to 2.01)	52 fewer per 1000 (from 149 fewer to 209 more)	⊕⊕OO LOW	CRITICAL
Birth < 32 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	19/158 (12.0%)	18/127 (14.2%)	RR 0.85 (0.47 to 1.55)	21 fewer per 1000 (from 75 fewer to 78 more)	⊕⊕OO LOW	CRITICAL
Birth < 37 weeks												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	90/267 (33.7%)	92/243 (37.9%)	RR 0.89 (0.71 to 1.12)	42 fewer per 1000 (from 110 fewer to 45 more)	⊕⊕⊕O MODERATE	CRITICAL
Maternal death												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	0/261 (0.0%)	0/251 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Perinatal death												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	4/261 (1.5%)	5/251 (2.0%)	RR 0.77 (0.21 to 2.83)	5 fewer per 1000 (from 16 fewer to 36 more)	⊕⊕OO LOW	CRITICAL
Fetal death												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	1/261 (0.4%)	0/251 (0.0%)	RR 2.89 (0.12 to 70.50)	—	⊕⊕OO LOW	CRITICAL
Neonatal death												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	3/261 (1.1%)	5/251 (2.0%)	RR 0.58 (0.14 to 2.39)	8 fewer per 1000 (from 17 fewer to 28 more)	⊕⊕OO LOW	CRITICAL
Infant death (up to 12 months)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	4/289 (1.4%)	5/269 (1.9%)	RR 0.74 (0.20 to 2.74)	5 fewer per 1000 (from 15 fewer to 32 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Atosiban	Placebo	Relative (95% CI)	Absolute		
Respiratory distress syndrome												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	33/288 (11.5%)	29/269 (10.8%)	RR 1.06 (0.66 to 1.70)	6 more per 1000 (from 37 fewer to 75 more)	⊕⊕⊕O MODERATE	CRITICAL
Necrotizing enterocolitis												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	5/288 (1.7%)	2/269 (0.7%)	RR 2.34 (0.46 to 11.93)	10 more per 1000 (from 4 fewer to 81 more)	⊕⊕OO LOW	CRITICAL
Birth weight (g) (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	289	269	—	MD 0.10 higher (131.78 lower to 131.98 higher)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal intensive care unit admission												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	61/284 (21.5%)	68/266 (25.6%)	RR 0.84 (0.62 to 1.14)	41 fewer per 1000 (from 97 fewer to 36 more)	⊕⊕⊕O MODERATE	CRITICAL

1 Wide confidence interval crossing the line of no effect, few events and small sample size.
2 Wide confidence interval crossing the line of no effect and small sample size.
3 Wide confidence interval crossing the line of no effect.
4 No events.
5 Wide confidence interval crossing the line of no effect and few events.

Table 3a. Magnesium sulfate for fetal neuroprotection in women at risk of preterm birth (all women and babies)

Source: Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev. 2009;(1):CD004661. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Maternal mortality												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	10/2682 (0.4%)	8/2729 (0.3%)	RR 1.25 (0.51 to 3.07)	1 more per 1000 (from 1 fewer to 6 more)	⊕⊕OO LOW	CRITICAL
Maternal cardiac arrest												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/2682 (0.0%)	3/2729 (0.1%)	RR 0.34 (0.04 to 3.26)	1 fewer per 1000 (from 1 fewer to 2 more)	⊕⊕OO LOW	CRITICAL
Maternal respiratory arrest												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/2682 (0.0%)	1/2729 (0.0%)	RR 1.02 (0.06 to 16.25)	0 more per 1000 (from 0 fewer to 6 more)	⊕⊕OO LOW	CRITICAL
Mother admitted to intensive care unit												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	28/1300 (2.2%)	32/1306 (2.5%)	RR 0.89 (0.54 to 1.47)	3 fewer per 1000 (from 11 fewer to 12 more)	⊕⊕⊕O MODERATE	CRITICAL
Cessation of maternal therapy												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	192/2396 (8.0%)	60/2451 (2.4%)	RR 3.26 (2.46 to 4.31)	55 more per 1000 (from 36 more to 81 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Paediatric mortality (fetal mortality and mortality occurring later)												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	435/2997 (14.5%)	430/3042 (14.1%)	RR 1.02 (0.90 to 1.15)	3 more per 1000 (from 14 fewer to 21 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Fetal death												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	128/2997 (4.3%)	133/3042 (4.4%)	RR 0.96 (0.77 to 1.21)	2 fewer per 1000 (from 10 fewer to 9 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Deaths among live-borns (during primary hospitalization)												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	267/2967 (9.0%)	258/3013 (8.6%)	RR 1.04 (0.84 to 1.29)	3 more per 1000 (from 14 fewer to 25 more)	⊕⊕⊕O MODERATE	CRITICAL
Deaths among live-borns (to latest age of follow-up)												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	307/2997 (10.2%)	297/3042 (9.8%)	RR 1.03 (0.84 to 1.27)	3 more per 1000 (from 16 fewer to 26 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Death or cerebral palsy												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	539/2997 (18.0%)	580/3042 (19.1%)	RR 0.92 (0.78 to 1.09)	15 fewer per 1000 (from 42 fewer to 17 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or any neurological impairment												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	499/1427 (35.0%)	495/1421 (34.8%)	RR 1.00 (0.91 to 1.11)	0 fewer per 1000 (from 31 fewer to 38 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or substantial gross motor dysfunction												
4	randomized trials	no serious risk of bias	serious[3]	no serious indirectness	no serious imprecision	none	490/2967 (16.5%)	523/3013 (17.4%)	RR 0.92 (0.75 to 1.12)	14 fewer per 1000 (from 43 fewer to 21 more)	⊕⊕⊕O MODERATE	CRITICAL
Death or major neurological disability												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	394/1427 (27.6%)	386/1421 (27.2%)	RR 1.02 (0.90 to 1.15)	5 more per 1000 (from 27 fewer to 41 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Intraventricular haemorrhage												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	454/2169 (20.9%)	482/2218 (21.7%)	RR 0.96 (0.86 to 1.08)	9 fewer per 1000 (from 30 fewer to 17 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Intraventricular haemorrhage — grade 3 or 4												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	72/1817 (4.0%)	88/1882 (4.7%)	RR 0.83 (0.62 to 1.13)	8 fewer per 1000 (from 18 fewer to 6 more)	⊕⊕⊕O MODERATE	CRITICAL
Periventricular leukomalacia												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	70/2169 (3.2%)	76/2218 (3.4%)	RR 0.92 (0.67 to 1.26)	3 fewer per 1000 (from 11 fewer to 9 more)	⊕⊕⊕O MODERATE	CRITICAL
Major neurological disability												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	98/1427 (6.9%)	91/1421 (6.4%)	RR 1.07 (0.82 to 1.40)	4 more per 1000 (from 12 fewer to 26 more)	⊕⊕⊕O MODERATE	CRITICAL
Any neurological impairment												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	203/1427 (14.2%)	200/1421 (14.1%)	RR 1.01 (0.86 to 1.19)	1 more per 1000 (from 20 fewer to 27 more)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Substantial gross motor dysfunction												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	57/2967 (1.9%)	94/3013 (3.1%)	RR 0.61 (0.44 to 0.85)	12 fewer per 1000 (from 5 fewer to 17 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Blindness												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	3/1779 (0.2%)	4/1757 (0.2%)	RR 0.74 (0.17 to 3.3)	1 fewer per 1000 (from 2 fewer to 5 more)	⊕⊕⊕O MODERATE	CRITICAL
Deafness												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	9/1779 (0.5%)	12/1757 (0.7%)	RR 0.79 (0.24 to 2.56)	1 fewer per 1000 (from 5 fewer to 11 more)	⊕⊕⊕O MODERATE	CRITICAL
Developmental delay or intellectual impairment												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	647/2967 (21.8%)	670/3013 (22.2%)	RR 0.99 (0.91 to 1.09)	2 fewer per 1000 (from 20 fewer to 20 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Cerebral palsy												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	104/2997 (3.5%)	151/3042 (5.0%)	RR 0.70 (0.55 to 0.89)	15 fewer per 1000 (from 5 fewer to 22 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Chronic lung disease (infant requires oxygen at age 28 days)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	280/629 (44.5%)	260/626 (41.5%)	RR 1.07 (0.94 to 1.22)	29 more per 1000 (from 25 fewer to 91 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Chronic lung disease (infant requires oxygen at 36 weeks of age)												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	220/981 (22.4%)	195/962 (20.3%)	RR 1.12 (0.95 to 1.32)	24 more per 1000 (from 10 fewer to 65 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal convulsions												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	55/2169 (2.5%)	70/2218 (3.2%)	RR 0.80 (0.56 to 1.13)	6 fewer per 1000 (from 14 fewer to 4 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal hypotonia												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	85/1188 (7.2%)	88/1256 (7.0%)	RR 1.02 (0.77 to 1.36)	1 more per 1000 (from 16 fewer to 25 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Duration of primary hospital stay for newborns (days) (better indicated by lower values)												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	1418	1410	—	MD 0.52 lower (4.15 lower to 3.11 higher)	⊕⊕⊕O MODERATE	CRITICAL
Ongoing respiratory support												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	980/2169 (45.2%)	1069/2218 (48.2%)	RR 0.94 (0.89 to 1.00)	29 fewer per 1000 (from 53 fewer to 0 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Maternal respiratory depression												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	41/1631 (2.5%)	31/1672 (1.9%)	RR 1.31 (0.83 to 2.07)	6 more per 1000 (from 3 fewer to 20 more)	⊕⊕⊕O MODERATE	CRITICAL
Maternal hypotension												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	80/821 (9.7%)	52/805 (6.5%)	RR 1.51 (1.09 to 2.09)	33 more per 1000 (from 6 more to 70 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Maternal tachycardia												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	56/535 (10.5%)	36/527 (6.8%)	RR 1.53 (1.03 to 2.29)	36 more per 1000 (from 2 more to 88 more)	⊕⊕⊕⊕ HIGH	CRITICAL

1 Wide confidence interval crossing the line of no effect and few events.
2 Wide confidence interval crossing the line of no effect.
3 Statistical heterogeneity ($I^2 > 60\%$).

Table 3b. Magnesium sulfate for fetal neuroprotection in women at risk of preterm birth (singleton and multiple pregnancy subgroups)

Source: Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev. 2009;(1):CD004661. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Paediatric mortality (fetal mortality and mortality occurring later) — both singleton and multiple pregnancies												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	395/2468 (16.0%)	388/2516 (15.4%)	RR 1.04 (0.85 to 1.26)	6 more per 1000 (from 23 fewer to 40 more)	⊕⊕⊕O MODERATE	CRITICAL
Paediatric mortality (fetal mortality and mortality occurring later) — singleton pregnancy subgroup												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	329/2113 (15.6%)	327/2143 (15.3%)	RR 1.01 (0.85 to 1.20)	2 more per 1000 (from 23 fewer to 31 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Paediatric mortality (fetal mortality and mortality occurring later) — multiple pregnancy subgroup												
3	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	serious[1]	none	66/355 (18.6%)	61/373 (16.4%)	RR 1.22 (0.68 to 2.18)	36 more per 1000 (from 52 fewer to 193 more)	⊕⊕OO LOW	CRITICAL
Death or cerebral palsy — both singleton and multiple pregnancies												
2	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	no serious imprecision	none	334/1427 (23.4%)	344/1421 (24.2%)	RR 0.97 (0.76 to 1.24)	7 fewer per 1000 (from 58 fewer to 58 more)	⊕⊕⊕O MODERATE	CRITICAL
Death or cerebral palsy — singleton pregnancy subgroup												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	277/1163 (23.8%)	285/1158 (24.6%)	RR 0.97 (0.82 to 1.14)	7 fewer per 1000 (from 44 fewer to 34 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or cerebral palsy — multiple pregnancy subgroup												
2	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	serious[1]	none	57/264 (21.6%)	59/263 (22.4%)	RR 1.14 (0.45 to 2.92)	31 more per 1000 (from 123 fewer to 431 more)	⊕⊕OO LOW	CRITICAL
Death or neurological impairment — both singleton and multiple pregnancies												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	499/1427 (35.0%)	495/1421 (34.8%)	RR 1.00 (0.86 to 1.16)	0 fewer per 1000 (from 49 fewer to 56 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or neurological impairment — singleton pregnancy subgroup												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	405/1163 (34.8%)	399/1158 (34.5%)	RR 1.00 (0.90 to 1.12)	0 fewer per 1000 (from 34 fewer to 41 more)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Death or neurological impairment — multiple pregnancy subgroup												
2	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	serious[1]	none	94/264 (35.6%)	96/263 (36.5%)	RR 1.21 (0.56 to 2.65)	77 more per 1000 (from 161 fewer to 602 more)	⊕⊕OO LOW	CRITICAL
Death or major neurological disability — both singleton and multiple pregnancies												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	394/1427 (27.6%)	386/1421 (27.2%)	RR 1.02 (0.85 to 1.22)	5 more per 1000 (from 41 fewer to 60 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or major neurological disability — singleton pregnancy												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	326/1163 (28.0%)	319/1158 (27.5%)	RR 1.02 (0.89 to 1.16)	6 more per 1000 (from 30 fewer to 44 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or major neurological disability — multiple pregnancy subgroup												
2	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	serious[1]	none	68/264 (25.8%)	67/263 (25.5%)	RR 1.20 (0.53 to 2.71)	51 more per 1000 (from 120 fewer to 436 more)	⊕⊕OO LOW	CRITICAL
Cerebral palsy — both singleton and multiple pregnancies												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	38/1427 (2.7%)	47/1421 (3.3%)	RR 0.80 (0.53 to 1.22)	7 fewer per 1000 (from 16 fewer to 7 more)	⊕⊕⊕O MODERATE	CRITICAL
Cerebral palsy — singleton pregnancy subgroup												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	31/1163 (2.7%)	33/1158 (2.8%)	RR 0.92 (0.57 to 1.49)	2 fewer per 1000 (from 12 fewer to 14 more)	⊕⊕⊕O MODERATE	CRITICAL
Cerebral palsy — multiple pregnancy subgroup												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	7/264 (2.7%)	14/263 (5.3%)	RR 0.52 (0.21 to 1.25)	26 fewer per 1000 (from 42 fewer to 13 more)	⊕⊕OO LOW	CRITICAL
Neurological impairment — both singleton and multiple pregnancies												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	203/1427 (14.2%)	200/1421 (14.1%)	RR 1.01 (0.85 to 1.19)	1 more per 1000 (from 21 fewer to 27 more)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Neurological impairment — singleton pregnancy subgroup												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	159/1163 (13.7%)	147/1158 (12.7%)	RR 1.06 (0.88 to 1.28)	8 more per 1000 (from 15 fewer to 36 more)	⊕⊕⊕O MODERATE	CRITICAL
Neurological impairment — multiple pregnancy subgroup												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	44/264 (16.7%)	53/263 (20.2%)	RR 0.86 (0.61 to 1.21)	28 fewer per 1000 (from 79 fewer to 42 more)	⊕⊕⊕O MODERATE	CRITICAL
Major neurological disability — both singleton and multiple pregnancies												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	98/1427 (6.9%)	91/1421 (6.4%)	RR 1.07 (0.82 to 1.40)	4 more per 1000 (from 12 fewer to 26 more)	⊕⊕⊕O MODERATE	CRITICAL
Major neurological disability — singleton pregnancy subgroup												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	80/1163 (6.9%)	67/1158 (5.8%)	RR 1.17 (0.87 to 1.59)	10 more per 1000 (from 8 fewer to 34 more)	⊕⊕⊕O MODERATE	CRITICAL
Major neurological disability — multiple pregnancy subgroup												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	18/264 (6.8%)	24/263 (9.1%)	RR 0.77 (0.44 to 1.37)	21 fewer per 1000 (from 51 fewer to 34 more)	⊕⊕⊕O MODERATE	CRITICAL

1 Wide confidence interval crossing the line of no effect.
2 Statistical heterogeneity ($I^2 > 60\%$).
3 Wide confidence interval crossing the line of no effect and few events.

Table 3c. Magnesium sulfate for fetal neuroprotection in women at risk of preterm birth (gestational age at administration)

Source: Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev. 2009;(1):CD004661. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Paediatric mortality (fetal mortality and mortality occurring later) — < 34 weeks of gestation at randomization												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	391/2573 (15.2%)	399/2619 (15.2%)	RR 0.98 (0.84 to 1.14)	3 fewer per 1000 (from 24 fewer to 21 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Paediatric mortality (fetal mortality and mortality occurring later) — < 30 weeks at randomization												
2	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	serious[2]	none	187/769 (24.3%)	196/768 (25.5%)	RR 0.97 (0.67 to 1.41)	8 fewer per 1000 (from 84 fewer to 105 more)	⊕⊕OO LOW	CRITICAL
Death or cerebral palsy — < 34 weeks at randomization												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	492/2573 (19.1%)	547/2619 (20.9%)	RR 0.91 (0.80 to 1.03)	19 fewer per 1000 (from 42 fewer to 6 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or cerebral palsy — < 30 weeks at randomization												
2	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	serious[2]	none	224/769 (29.1%)	239/768 (31.1%)	RR 0.97 (0.69 to 1.38)	9 fewer per 1000 (from 96 fewer to 118 more)	⊕⊕OO LOW	CRITICAL
Death or neurological impairment — < 34 weeks at randomization												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	452/1033 (43.8%)	459/1027 (44.7%)	RR 0.98 (0.89 to 1.08)	9 fewer per 1000 (from 49 fewer to 36 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or neurological impairment — < 30 weeks at randomization												
2	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	no serious imprecision	none	383/769 (49.8%)	386/768 (50.3%)	RR 1.03 (0.86 to 1.24)	15 more per 1000 (from 70 fewer to 121 more)	⊕⊕⊕O MODERATE	CRITICAL
Death or major neurological disability — < 34 weeks at randomization												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	347/1033 (33.6%)	350/1027 (34.1%)	RR 0.99 (0.88 to 1.11)	3 fewer per 1000 (from 41 fewer to 37 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or major neurological disability — < 30 weeks at randomization												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	278/769 (36.2%)	277/768 (36.1%)	RR 1.04 (0.86 to 1.24)	14 more per 1000 (from 50 fewer to 87 more)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Cerebral palsy — < 34 weeks at randomization												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	101/2573 (3.9%)	149/2619 (5.7%)	RR 0.69 (0.54 to 0.88)	18 fewer per 1000 (from 7 fewer to 26 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Cerebral palsy — < 30 weeks at randomization												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	37/769 (4.8%)	43/768 (5.6%)	RR 0.86 (0.56 to 1.31)	8 fewer per 1000 (from 25 fewer to 17 more)	⊕⊕⊕O MODERATE	CRITICAL
Neurological impairment — < 34 weeks at randomization												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	198/1033 (19.2%)	194/1027 (18.9%)	RR 1.02 (0.86 to 1.20)	4 more per 1000 (from 26 fewer to 38 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Neurological impairment — < 30 weeks at randomization												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	196/769 (25.5%)	190/768 (24.7%)	RR 1.03 (0.87 to 1.21)	7 more per 1000 (from 32 fewer to 52 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Major neurological disability — < 34 weeks at randomization												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	93/1033 (9.0%)	85/1027 (8.3%)	RR 1.09 (0.83 to 1.43)	7 more per 1000 (from 14 fewer to 36 more)	⊕⊕⊕O MODERATE	CRITICAL
Major neurological disability — < 30 weeks at randomization												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	91/769 (11.8%)	81/768 (10.5%)	RR 1.12 (0.85 to 1.48)	13 more per 1000 (from 16 fewer to 51 more)	⊕⊕⊕O MODERATE	CRITICAL

1 Statistical heterogeneity ($I^2 > 60\%$).
2 Wide confidence interval crossing the line of no effect.

Table 3d. Magnesium sulfate for fetal neuroprotection in women at risk of preterm birth (intention to prevent preterm-birth related neurological complications

Source: Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev. 2009;(1):CD004661. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Paediatric mortality (fetal mortality and mortality occurring later) — neuroprotective intent												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	226/2199 (10.3%)	242/2247 (10.8%)	RR 0.95 (0.80 to 1.12)	5 fewer per 1000 (from 22 fewer to 13 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Paediatric mortality (fetal mortality and mortality occurring later) — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	209/798 (26.2%)	188/795 (23.6%)	RR 1.11 (0.93 to 1.31)	26 more per 1000 (from 17 fewer to 73 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal death — neuroprotective intent												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	17/2199 (0.8%)	22/2247 (1.0%)	RR 0.78 (0.42 to 1.46)	2 fewer per 1000 (from 6 fewer to 5 more)	⊕⊕⊕O MODERATE	CRITICAL
Fetal death — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	111/798 (13.9%)	111/795 (14.0%)	RR 1.00 (0.78 to 1.27)	0 fewer per 1000 (from 31 fewer to 38 more)	⊕⊕⊕O MODERATE	CRITICAL
Deaths among live-borns — to latest age of follow-up — neuroprotective intent												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	209/2199 (9.5%)	220/2247 (9.8%)	RR 0.96 (0.77 to 1.18)	4 fewer per 1000 (from 23 fewer to 18 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Deaths among live-borns — to latest age of follow-up — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	98/798 (12.3%)	77/795 (9.7%)	RR 1.27 (0.96 to 1.68)	26 more per 1000 (from 4 fewer to 66 more)	⊕⊕⊕O MODERATE	CRITICAL
Deaths among live-borns — during primary hospitalization — neuroprotective intent												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	187/2169 (8.6%)	195/2218 (8.8%)	RR 0.97 (0.76 to 1.23)	3 fewer per 1000 (from 21 fewer to 20 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Deaths among live-borns — during primary hospitalization — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	80/798 (10.0%)	63/795 (7.9%)	RR 1.27 (0.92 to 1.73)	21 more per 1000 (from 6 fewer to 58 more)	⊕⊕⊕O MODERATE	CRITICAL
Death or cerebral palsy — neuroprotective intent												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	328/2199 (14.9%)	387/2247 (17.2%)	RR 0.85 (0.74 to 0.98)	26 fewer per 1000 (from 3 fewer to 45 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or cerebral palsy — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	211/798 (26.4%)	193/795 (24.3%)	RR 1.09 (0.92 to 1.29)	22 more per 1000 (from 19 fewer to 70 more)	⊕⊕⊕O MODERATE	CRITICAL
Death or any neurological impairment — neuroprotective intent												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	280/629 (44.5%)	294/626 (47.0%)	RR 0.95 (0.84 to 1.07)	23 fewer per 1000 (from 75 fewer to 33 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or any neurological impairment — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	219/798 (27.4%)	201/795 (25.3%)	RR 1.09 (0.92 to 1.28)	23 more per 1000 (from 20 fewer to 71 more)	⊕⊕⊕O MODERATE	CRITICAL
Death or substantial gross motor dysfunction — neuroprotective intent												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	280/2169 (12.9%)	335/2218 (15.1%)	RR 0.84 (0.71 to 1.00)	24 fewer per 1000 (from 44 fewer to 0 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or substantial gross motor dysfunction — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	210/798 (26.3%)	188/795 (23.6%)	RR 1.11 (0.94 to 1.32)	26 more per 1000 (from 14 fewer to 76 more)	⊕⊕⊕O MODERATE	CRITICAL
Death or major neurological disability — neuroprotective intent												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	176/629 (28.0%)	185/626 (29.6%)	RR 0.95 (0.80 to 1.13)	15 fewer per 1000 (from 59 fewer to 38 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or major neurological disability — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	218/798 (27.3%)	201/795 (25.3%)	RR 1.08 (0.92 to 1.27)	20 more per 1000 (from 20 fewer to 68 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Developmental delay or intellectual impairment — neuroprotective intent												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	639/2169 (29.5%)	660/2218 (29.8%)	RR 1.00 (0.91 to 1.09)	0 fewer per 1000 (from 27 fewer to 27 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Developmental delay or intellectual impairment — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	8/798 (1.0%)	10/795 (1.3%)	RR 0.80 (0.32 to 2.01)	3 fewer per 1000 (from 9 fewer to 13 more)	⊕⊕OO LOW	CRITICAL
Major neurological disability — neuroprotective intent												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	89/629 (14.1%)	78/626 (12.5%)	RR 1.14 (0.86 to 1.51)	17 more per 1000 (from 17 fewer to 64 more)	⊕⊕⊕O MODERATE	CRITICAL
Major neurological disability — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	9/798 (1.1%)	13/795 (1.6%)	RR 0.69 (0.30 to 1.6)	5 fewer per 1000 (from 11 fewer to 10 more)	⊕⊕OO LOW	CRITICAL
Cerebral palsy — neuroprotective intent: mild cerebral palsy												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	54/2169 (2.5%)	74/2218 (3.3%)	RR 0.74 (0.52 to 1.04)	9 fewer per 1000 (from 16 fewer to 1 more)	⊕⊕⊕O MODERATE	CRITICAL
Cerebral palsy — neuroprotective intent: moderate cerebral palsy												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	14/981 (1.4%)	21/962 (2.2%)	RR 0.66 (0.34 to 1.28)	7 fewer per 1000 (from 14 fewer to 6 more)	⊕⊕⊕O MODERATE	CRITICAL
Cerebral palsy — neuroprotective intent: moderate/severe cerebral palsy												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	45/2169 (2.1%)	72/2218 (3.2%)	RR 0.64 (0.44 to 0.92)	12 fewer per 1000 (from 3 fewer to 18 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Cerebral palsy — neuroprotective intent: severe cerebral palsy												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	11/981 (1.1%)	13/962 (1.4%)	RR 0.82 (0.37 to 1.82)	2 fewer per 1000 (from 9 fewer to 11 more)	⊕⊕OO LOW	CRITICAL
Cerebral palsy — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	2/798 (0.3%)	5/795 (0.6%)	RR 0.40 (0.08 to 2.05)	4 fewer per 1000 (from 6 fewer to 7 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate	No active treatment	Relative (95% CI)	Absolute		
Any neurological impairment — neuroprotective intent												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	193/629 (30.7%)	187/626 (29.9%)	RR 1.03 (0.87 to 1.21)	9 more per 1000 (from 39 fewer to 63 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Any neurological impairment — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	10/798 (1.3%)	13/795 (1.6%)	RR 0.77 (0.34 to 1.74)	4 fewer per 1000 (from 11 fewer to 12 more)	⊕⊕OO LOW	CRITICAL
Substantial gross motor dysfunction — neuroprotective intent												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	56/2169 (2.6%)	94/2218 (4.2%)	RR 0.60 (0.43 to 0.83)	17 fewer per 1000 (from 7 fewer to 24 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Substantial gross motor dysfunction — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	1/798 (0.1%)	0/795 (0.0%)	RR 2.99 (0.12 to 73.26)	—	⊕⊕OO LOW	CRITICAL
Deafness — neuroprotective intent												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	8/981 (0.8%)	11/962 (1.1%)	RR 0.51 (0.05 to 4.96)	6 fewer per 1000 (from 11 fewer to 45 more)	⊕⊕OO LOW	CRITICAL
Deafness — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	1/798 (0.1%)	1/795 (0.1%)	RR 1.00 (0.06 to 15.90)	0 fewer per 1000 (from 1 fewer to 19 more)	⊕⊕OO LOW	CRITICAL
Blindness — neuroprotective intent												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	2/981 (0.2%)	2/962 (0.2%)	RR 0.97 (0.14 to 6.9)	0 fewer per 1000 (from 2 fewer to 12 more)	⊕⊕OO LOW	CRITICAL
Blindness — other intent (maternal neuroprotective — pre-eclampsia)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	1/798 (0.1%)	2/795 (0.3%)	RR 0.50 (0.05 to 5.48)	1 fewer per 1000 (from 2 fewer to 11 more)	⊕⊕OO LOW	CRITICAL

1 Wide confidence interval crossing the line of no effect.
2 Wide confidence interval crossing the line of no effect and few events.

Table 3e. Magnesium sulfate for fetal neuroprotection in women at risk of preterm birth (retreatment)

Source: Doyle LW, Crowther CA, Middleton P, Marret S, Rouse D. Magnesium sulphate for women at risk of preterm birth for neuroprotection of the fetus. Cochrane Database Syst Rev. 2009;(1):CD004661. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Retreatment	No retreatment	Relative (95% CI)	Absolute		
Paediatric mortality (fetal mortality and mortality occurring later)												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	433/2967 (14.6%)	429/3013 (14.2%)	RR 1.00 (0.84 to 1.18)	0 fewer per 1000 (from 23 fewer to 26 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Paediatric mortality (fetal mortality and mortality occurring later) — retreatment permitted												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	103/1188 (8.7%)	96/1256 (7.6%)	RR 1.13 (0.87 to 1.48)	10 more per 1000 (from 10 fewer to 37 more)	⊕⊕⊕O MODERATE	CRITICAL
Paediatric mortality (fetal mortality and mortality occurring later) — retreatment not permitted												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	330/1779 (18.5%)	333/1757 (19.0%)	RR 0.95 (0.75 to 1.19)	9 fewer per 1000 (from 47 fewer to 36 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or cerebral palsy												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	534/2967 (18.0%)	579/3013 (19.2%)	RR 0.92 (0.79 to 1.06)	15 fewer per 1000 (from 40 fewer to 12 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or cerebral palsy — retreatment permitted												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	144/1188 (12.1%)	170/1256 (13.5%)	RR 0.90 (0.73 to 1.10)	14 fewer per 1000 (from 37 fewer to 14 more)	⊕⊕⊕O MODERATE	CRITICAL
Death or cerebral palsy — retreatment not permitted												
3	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	serious[1]	none	390/1779 (21.9%)	409/1757 (23.3%)	RR 0.91 (0.74 to 1.13)	21 fewer per 1000 (from 61 fewer to 30 more)	⊕⊕OO LOW	CRITICAL
Death or neurological impairment												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	499/1427 (35.0%)	495/1421 (34.8%)	RR 1.00 (0.91 to 1.11)	0 fewer per 1000 (from 31 fewer to 38 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or neurological impairment — retreatment not permitted												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	499/1427 (35.0%)	495/1421 (34.8%)	RR 1.00 (0.91 to 1.11)	0 fewer per 1000 (from 31 fewer to 38 more)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Retreatment	No retreatment	Relative (95% CI)	Absolute		
Death or major neurological disability												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	394/1427 (27.6%)	386/1421 (27.2%)	RR 1.02 (0.90 to 1.15)	5 more per 1000 (from 27 fewer to 41 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Death or major neurological disability — retreatment not permitted												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	394/1427 (27.6%)	386/1421 (27.2%)	RR 1.02 (0.90 to 1.15)	5 more per 1000 (from 27 fewer to 41 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Major neurological disability												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	98/1427 (6.9%)	91/1421 (6.4%)	RR 1.07 (0.82 to 1.40)	4 more per 1000 (from 12 fewer to 26 more)	⊕⊕⊕O MODERATE	CRITICAL
Major neurological disability — retreatment not permitted												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	98/1427 (6.9%)	91/1421 (6.4%)	RR 1.07 (0.82 to 1.40)	4 more per 1000 (from 12 fewer to 26 more)	⊕⊕⊕O MODERATE	CRITICAL
Neurologic impairment												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	203/1427 (14.2%)	200/1421 (14.1%)	RR 1.01 (0.86 to 1.19)	1 more per 1000 (from 20 fewer to 27 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Neurologic impairment — retreatment not permitted												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	203/1427 (14.2%)	200/1421 (14.1%)	RR 1.01 (0.86 to 1.19)	1 more per 1000 (from 20 fewer to 27 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Cerebral palsy												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	101/2967 (3.4%)	151/3013 (5.0%)	RR 0.68 (0.53 to 0.87)	16 fewer per 1000 (from 7 fewer to 24 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Cerebral palsy — retreatment permitted												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	41/1188 (3.5%)	74/1256 (5.9%)	RR 0.59 (0.40 to 0.85)	24 fewer per 1000 (from 9 fewer to 35 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Retreatment	No retreatment	Relative (95% CI)	Absolute		
Cerebral palsy — retreatment not permitted												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	60/1779 (3.4%)	77/1757 (4.4%)	RR 0.76 (0.55 to 1.06)	11 fewer per 1000 (from 20 fewer to 3 more)	⨁⨁⨁◯ MODERATE	CRITICAL

1 Wide confidence interval crossing the line of no effect.
2 Statistical heterogeneity ($I^2 > 60\%$).

Table 4a. Antibiotic prophylaxis for women at risk of preterm birth and with intact membranes (any antibiotics)

Source: Flenady V, Hawley G, Stock OM, Kenyon S, Badawi N. Prophylactic antibiotics for inhibiting preterm labour with intact membranes. Cochrane Database Syst Rev. 2013;(12):CD000246.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any antibiotic	No antibiotics	Relative (95% CI)	Absolute		
Birth < 36 or < 37 weeks of gestation												
10	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1973/5251 (37.6%)	871/2136 (40.8%)	RR 0.98 (0.92 to 1.05)	8 fewer per 1000 (from 33 fewer to 20 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth within 48 hours of randomization												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	509/4959 (10.3%)	183/1841 (9.9%)	RR 1.04 (0.89 to 1.23)	4 more per 1000 (from 11 fewer to 23 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth within 7 days of randomization												
8	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	817/5091 (16.0%)	342/1962 (17.4%)	RR 0.98 (0.87 to 1.10)	3 fewer per 1000 (from 23 fewer to 17 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Interval between randomization and birth (days) (better indicated by higher values)												
6	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	1773	726	—	MD 5.59 higher (0.31 to 10.87 higher)	⊕⊕⊕O MODERATE	CRITICAL
Gestational age at birth (better indicated by higher values)												
10	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	495	491	—	MD 0.53 higher (0 to 1.06 higher)	⊕⊕⊕O MODERATE	CRITICAL
Maternal infection												
10	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	458/5246 (8.7%)	236/2125 (11.1%)	RR 0.74 (0.63 to 0.86)	29 fewer per 1000 (from 16 fewer to 41 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Maternal adverse drug reaction requiring cessation of treatment												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	54/313 (17.3%)	41/313 (13.1%)	RR 1.32 (0.92 to 1.89)	42 more per 1000 (from 10 fewer to 117 more)	⊕⊕⊕O MODERATE	CRITICAL
Perinatal mortality												
10	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	141/5213 (2.7%)	43/2091 (2.1%)	RR 1.22 (0.88 to 1.69)	5 more per 1000 (from 2 fewer to 14 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any antibiotic	No antibiotics	Relative (95% CI)	Absolute		
Stillbirth												
8	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	39/5105 (0.8%)	19/1975 (1.0%)	RR 0.73 (0.43 to 1.26)	3 fewer per 1000 (from 5 fewer to 3 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal death												
9	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	101/5183 (1.9%)	24/2065 (1.2%)	RR 1.57 (1.03 to 2.40)	7 more per 1000 (from 0 more to 16 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Infant death (> 28 days)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	78/3508 (2.2%)	24/1146 (2.1%)	RR 1.06 (0.68 to 1.67)	1 more per 1000 (from 7 fewer to 14 more)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome												
9	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	463/5159 (9%)	197/2041 (9.7%)	RR 0.99 (0.84 to 1.16)	1 fewer per 1000 (from 15 fewer to 15 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Necrotizing enterocolitis												
6	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	62/5004 (1.2%)	25/1876 (1.3%)	RR 1.06 (0.64 to 1.73)	1 more per 1000 (from 5 fewer to 10 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal sepsis												
10	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	127/5252 (2.4%)	76/2134 (3.6%)	RR 0.86 (0.64 to 1.16)	5 fewer per 1000 (from 13 fewer to 6 more)	⊕⊕⊕O MODERATE	CRITICAL
Intraventricular haemorrhage												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	59/4968 (1.2%)	30/1845 (1.6%)	RR 0.76 (0.48 to 1.19)	4 fewer per 1000 (from 8 fewer to 3 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal mechanical ventilation												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	371/4685 (7.9%)	121/1556 (7.8%)	RR 1.02 (0.84 to 1.24)	2 more per 1000 (from 12 fewer to 19 more)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any antibiotic	No antibiotics	Relative (95% CI)	Absolute		
Birth weight < 2500 g												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1438/4882 (29.5%)	524/1746 (30.0%)	RR 0.97 (0.81 to 1.15)	9 fewer per 1000 (from 57 fewer to 45 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth weight (better indicated by higher values)												
12	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	5327	2204	—	MD 58.38 higher (26.24 lower to 143 higher)	⊕⊕⊕O MODERATE	CRITICAL
Admission to neonatal intensive or special care nursery												
5	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	serious[1]	none	1301/4992 (26.1%)	493/1883 (26.2%)	RR 0.82 (0.62 to 1.10)	47 fewer per 1000 (from 99 fewer to 26 more)	⊕⊕OO LOW	CRITICAL
Moderate/severe functional impairment at 7 years of age												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	417/2317 (18.0%)	124/735 (16.9%)	RR 1.07 (0.89 to 1.28)	12 more per 1000 (from 19 fewer to 47 more)	⊕⊕⊕O MODERATE	CRITICAL
Chronic neonatal lung disease												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	102/4685 (2.2%)	29/1556 (1.9%)	RR 1.17 (0.78 to 1.76)	3 more per 1000 (from 4 fewer to 14 more)	⊕⊕⊕O MODERATE	CRITICAL
Cerebral palsy at 7 years of age												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	68/2403 (2.8%)	12/770 (1.6%)	RR 1.82 (0.99 to 3.34)	13 more per 1000 (from 0 fewer to 36 more)	⊕⊕⊕O MODERATE	CRITICAL
Any functional impairment at 7 years of age												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	957/2317 (41.3%)	275/735 (37.4%)	RR 1.10 (0.99 to 1.23)	37 more per 1000 (from 4 fewer to 86 more)	⊕⊕⊕⊕ HIGH	CRITICAL

1 Wide confidence interval crossing the line of no effect.
2 Statistical heterogeneity ($I^2 > 60\%$).

Table 4b. Antibiotic prophylaxis for women at risk of preterm birth and with intact membranes (antibiotic regimen)

Source: Flenady V, Hawley G, Stock OM, Kenyon S, Badawi N. Prophylactic antibiotics for inhibiting preterm labour with intact membranes. Cochrane Database Syst Rev. 2013;(12):CD000246.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A particular type of antibiotic	Placebo or no treatment	Relative (95% CI)	Absolute		
Birth < 36 or < 37 weeks of gestation — betalactam antibiotics alone												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	643/1721 (37.4%)	288/709 (40.6%)	RR 0.99 (0.89 to 1.10)	4 fewer per 1000 (from 45 fewer to 41 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth < 36 or < 37 weeks — macrolide antibiotics alone												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	622/1658 (37.5%)	223/577 (38.6%)	RR 1.02 (0.91 to 1.15)	8 more per 1000 (from 35 fewer to 58 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth < 36 or < 37 weeks — macrolide and betalactam antibiotics												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	683/1813 (37.7%)	326/800 (40.8%)	RR 0.99 (0.89 to 1.10)	4 fewer per 1000 (from 45 fewer to 41 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth < 36 or < 37 weeks — antibiotics active against anaerobic bacteria												
2	randomized trials	no serious risk of bias	serious[1]	no serious indirectness	serious[2]	none	63/117 (53.8%)	70/109 (64.2%)	RR 0.83 (0.53 to 1.30)	109 fewer per 1000 (from 302 fewer to 193 more)	⊕⊕OO LOW	CRITICAL
Birth within 48 hours of randomization — betalactam antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	152/1534 (9.9%)	51/519 (9.8%)	RR 1.01 (0.75 to 1.36)	1 more per 1000 (from 25 fewer to 35 more)	⊕⊕⊕O MODERATE	CRITICAL
Birth within 48 hours of randomization — macrolide antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	166/1600 (10.4%)	51/519 (9.8%)	RR 1.06 (0.78 to 1.42)	6 more per 1000 (from 22 fewer to 41 more)	⊕⊕⊕O MODERATE	CRITICAL
Birth within 48 hours of randomization — macrolide and betalactam antibiotics												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	192/1767 (10.9%)	74/753 (9.8%)	RR 1.12 (0.86 to 1.45)	12 more per 1000 (from 14 fewer to 44 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A particular type of antibiotic	Placebo or no treatment	Relative (95% CI)	Absolute		
Birth within 48 hours of randomization — antibiotics active against anaerobic bacteria												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	5/58 (8.6%)	8/51 (15.7%)	RR 0.55 (0.19 to 1.57)	71 fewer per 1000 (from 127 fewer to 89 more)	⊕⊕OO LOW	CRITICAL
Interval between randomization and birth (days) — betalactam antibiotics alone (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	1534	519	—	MD 0.09 lower (2.96 lower to 2.78 higher)	⊕⊕⊕O MODERATE	CRITICAL
Interval between randomization and birth (days) — macrolide antibiotics alone (better indicated by higher values)												
3	randomized trials	no serious risk of bias	very serious[4]	no serious indirectness	serious[2]	none	1691	611	—	MD 4.26 higher (2.88 lower to 11.41 higher)	⊕OOO VERY LOW	CRITICAL
Interval between randomization and birth (days) — macrolide and betalactam antibiotics (better indicated by higher values)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	1629	592	—	MD 0.27 lower (2.95 lower to 2.41 higher)	⊕⊕⊕O MODERATE	CRITICAL
Interval between randomization and birth (days) — antibiotics active against anaerobic bacteria (better indicated by higher values)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	154	139	—	MD 10.5 higher (4.95 to 16.06 higher)	⊕⊕⊕⊕ HIGH	CRITICAL
Maternal infection — betalactam antibiotics alone												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	146/1696 (8.6%)	76/689 (11.0%)	RR 0.74 (0.56 to 0.97)	29 fewer per 1000 (from 3 fewer to 49 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Maternal infection — macrolide antibiotics alone												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	157/1653 (9.5%)	64/569 (11.2%)	RR 0.82 (0.62 to 1.08)	20 fewer per 1000 (from 43 fewer to 9 more)	⊕⊕⊕O MODERATE	CRITICAL
Maternal infection — macrolide and betalactam antibiotics												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	165/1790 (9.2%)	97/773 (12.5%)	RR 0.79 (0.64 to 0.98)	26 fewer per 1000 (from 3 fewer to 45 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A particular type of antibiotic	Placebo or no treatment	Relative (95% CI)	Absolute		
Maternal infection — antibiotics active against anaerobic bacteria												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	5/155 (3.2%)	6/139 (4.3%)	RR 0.66 (0.11 to 3.92)	15 fewer per 1000 (from 38 fewer to 126 more)	⊕⊕OO LOW	CRITICAL
Maternal adverse drug reaction requiring cessation of treatment — betalactam antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	1/40 (2.5%)	0/42 (0.0%)	RR 3.15 (0.13 to 75.05)	—	⊕⊕OO LOW	CRITICAL
Maternal adverse drug reaction requiring cessation of treatment — macrolide antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[5]	none	15/53 (28.3%)	16/50 (32.0%)	RR 0.88 (0.49 to 1.59)	38 fewer per 1000 (from 163 fewer to 189 more)	⊕⊕OO LOW	CRITICAL
Maternal adverse drug reaction requiring cessation of treatment — macrolide and betalactam antibiotics												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	34/161 (21.1%)	24/170 (14.1%)	RR 1.49 (0.93 to 2.40)	69 more per 1000 (from 10 fewer to 198 more)	⊕⊕⊕O MODERATE	CRITICAL
Maternal adverse drug reaction requiring cessation of treatment — antibiotics active against anaerobic bacteria												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	19/112 (17.0%)	17/101 (16.8%)	RR 1.04 (0.59 to 1.83)	7 more per 1000 (from 69 fewer to 140 more)	⊕⊕⊕O MODERATE	CRITICAL
Perinatal mortality — betalactam antibiotics alone												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	42/1668 (2.5%)	14/655 (2.1%)	RR 1.13 (0.64 to 2.01)	3 more per 1000 (from 8 fewer to 22 more)	⊕⊕⊕O MODERATE	CRITICAL
Perinatal mortality — macrolide antibiotics alone												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	45/1653 (2.7%)	13/569 (2.3%)	RR 1.17 (0.64 to 2.11)	4 more per 1000 (from 8 fewer to 25 more)	⊕⊕⊕O MODERATE	CRITICAL
Perinatal mortality — macrolide and betalactam antibiotics												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	52/1790 (2.9%)	14/779 (1.8%)	RR 1.39 (0.79 to 2.43)	7 more per 1000 (from 4 fewer to 26 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A particular type of antibiotic	Placebo or no treatment	Relative (95% CI)	Absolute		
Perinatal mortality — antibiotics active against anaerobic bacteria												
3	randomized trials	serious[6]	no serious inconsistency	no serious indirectness	very serious	none	4/155 (2.6%)	2/139 (1.4%)	RR 1.63 (0.36 to 7.39)	9 more per 1000 (from 9 fewer to 92 more)	⊕OOO VERY LOW	CRITICAL
Stillbirth — betalactam antibiotics alone												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	16/1668 (1.0%)	7/655 (1.1%)	RR 0.91 (0.39 to 2.14)	1 fewer per 1000 (from 7 fewer to 12 more)	⊕⊕OO LOW	CRITICAL
Stillbirth — macrolide antibiotics alone												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	10/1653 (0.6%)	6/569 (1.1%)	RR 0.54 (0.20 to 1.48)	5 fewer per 1000 (from 8 fewer to 5 more)	⊕⊕OO LOW	CRITICAL
Stillbirth — macrolide and betalactam antibiotics												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[7]	none	13/1684 (0.8%)	6/663 (0.9%)	RR 0.73 (0.28 to 1.90)	2 fewer per 1000 (from 7 fewer to 8 more)	⊕⊕OO LOW	CRITICAL
Stillbirth — antibiotics active against anaerobic bacteria												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[8]	none	0/155 (0.0%)	0/139 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Neonatal death — betalactam antibiotics alone												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	26/1668 (1.6%)	7/655 (1.1%)	RR 1.32 (0.61 to 2.86)	3 more per 1000 (from 4 fewer to 20 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal death — macrolide antibiotics alone												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	35/1653 (2.1%)	7/569 (1.2%)	RR 1.68 (0.77 to 3.64)	8 more per 1000 (from 3 fewer to 32 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal death — macrolide and betalactam antibiotics												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	38/1760 (2.2%)	8/753 (1.1%)	RR 1.83 (0.88 to 3.82)	9 more per 1000 (from 1 fewer to 30 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal death — antibiotics active against anaerobic bacteria												
3	randomized trials	serious[6]	no serious inconsistency	no serious indirectness	very serious[3]	none	4/155 (2.6%)	2/139 (1.4%)	RR 1.63 (0.36 to 7.39)	9 more per 1000 (from 9 fewer to 92 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A particular type of antibiotic	Placebo or no treatment	Relative (95% CI)	Absolute		
Infant death (>28 days) — betalactam antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	17/1133 (1.5%)	8/382 (2.1%)	RR 0.72 (0.31 to 1.65)	6 fewer per 1000 (from 14 fewer to 14 more)	⊕⊕⊕O MODERATE	CRITICAL
Infant death (>28 days) — macrolide antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	29/1204 (2.4%)	8/382 (2.1%)	RR 1.15 (0.53 to 2.49)	3 more per 1000 (from 10 fewer to 31 more)	⊕⊕⊕O MODERATE	CRITICAL
Infant death (>28 days) — macrolide and betalactam antibiotics												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	32/1171 (2.7%)	8/382 (2.1%)	RR 1.30 (0.61 to 2.81)	6 more per 1000 (from 8 fewer to 38 more)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome — betalactam antibiotics alone												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	142/1628 (8.7%)	154/1650 (9.3%)	RR 0.93 (0.75 to 1.16)	7 fewer per 1000 (from 23 fewer to 15 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Respiratory distress syndrome — macrolide antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	133/1600 (8.3%)	138/1556 (8.9%)	RR 0.94 (0.75 to 1.18)	5 fewer per 1000 (from 22 fewer to 16 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Respiratory distress syndrome — macrolide and betalactam antibiotics												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	153/1682 (9.1%)	149/1700 (8.8%)	RR 1.04 (0.84 to 1.29)	4 more per 1000 (from 14 fewer to 25 more)	⊕⊕⊕O MODERATE	CRITICAL
Respiratory distress syndrome — antibiotics active against anaerobic bacteria												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	2/58 (3.4%)	3/51 (5.9%)	RR 0.59 (0.10 to 3.37)	24 fewer per 1000 (from 53 fewer to 139 more)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis — betalactam antibiotics alone												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	20/1621 (1.2%)	6/606 (1.0%)	RR 1.31 (0.52 to 3.32)	3 more per 1000 (from 5 fewer to 23 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A particular type of antibiotic	Placebo or no treatment	Relative (95% CI)	Absolute		
Necrotizing enterocolitis — macrolide antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	16/1600 (1.0%)	4/519 (0.8%)	RR 1.30 (0.44 to 3.86)	2 more per 1000 (from 4 fewer to 22 more)	⊕⊕⊕O MODERATE	CRITICAL
Necrotizing enterocolitis — macrolide and betalactam antibiotics												
2	randomized trials	serious[9]	no serious inconsistency	no serious indirectness	serious[2]	none	26/1682 (1.5%)	9/663 (1.4%)	RR 1.36 (0.60 to 3.11)	5 more per 1000 (from 5 fewer to 29 more)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis — antibiotics active against anaerobic bacteria												
2	randomized trials	serious[9]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/101 (0.0%)	6/89 (6.7%)	RR 0.13 (0.02 to 1.01)	59 fewer per 1000 (from 66 fewer to 1 more)	⊕OOO VERY LOW	CRITICAL
Intraventricular haemorrhage — betalactam antibiotics alone												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	19/1628 (1.2%)	9/613 (1.5%)	RR 0.84 (0.38 to 1.87)	2 fewer per 1000 (from 9 fewer to 13 more)	⊕⊕⊕O MODERATE	CRITICAL
Intraventricular haemorrhage — macrolide antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	18/1600 (1.1%)	7/519 (1.3%)	RR 0.83 (0.35 to 1.99)	2 fewer per 1000 (from 9 fewer to 13 more)	⊕⊕⊕O MODERATE	CRITICAL
Intraventricular haemorrhage — macrolide and betalactam antibiotics												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	21/1682 (1.2%)	8/663 (1.2%)	RR 0.97 (0.43 to 2.19)	0 fewer per 1000 (from 7 fewer to 14 more)	⊕⊕⊕O MODERATE	CRITICAL
Intraventricular haemorrhage — antibiotics active against anaerobic bacteria												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[3]	none	1/58 (1.7%)	5/51 (9.8%)	RR 0.18 (0.02 to 1.46)	80 fewer per 1000 (from 96 fewer to 45 more)	⊕⊕OO LOW	CRITICAL
Moderate/severe functional impairment at 7 years of age — betalactam antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	131/763 (17.2%)	41/245 (16.7%)	RR 1.03 (0.75 to 1.41)	5 more per 1000 (from 42 fewer to 69 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A particular type of antibiotic	Placebo or no treatment	Relative (95% CI)	Absolute		
Moderate/severe functional impairment at 7 years of age — macrolide antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	142/785 (18.1%)	41/245 (16.7%)	RR 1.08 (0.79 to 1.48)	13 more per 1000 (from 35 fewer to 80 more)	⊕⊕⊕O MODERATE	CRITICAL
Moderate/severe functional impairment at 7 years of age. — macrolide and betalactam antibiotics												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	144/769 (18.7%)	41/245 (16.7%)	RR 1.12 (0.82 to 1.53)	20 more per 1000 (from 30 fewer to 89 more)	⊕⊕⊕O MODERATE	CRITICAL
Cerebral palsy at 7 years of age — betalactam antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	15/792 (1.9%)	4/257 (1.6%)	RR 1.22 (0.41 to 3.63)	3 more per 1000 (from 9 fewer to 41 more)	⊕⊕⊕O MODERATE	CRITICAL
Cerebral palsy at 7 years of age — macrolide antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	18/816 (2.2%)	4/257 (1.6%)	RR 1.42 (0.48 to 4.15)	7 more per 1000 (from 8 fewer to 49 more)	⊕⊕⊕O MODERATE	CRITICAL
Cerebral palsy at 7 years of age — macrolide and betalactam antibiotics												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	35/795 (4.4%)	4/257 (1.6%)	RR 2.83 (1.02 to 7.88)	28 more per 1000 (from 0 more to 107 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Any functional impairment at 7 years of age — betalactam antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	299/763 (39.2%)	92/245 (37.6%)	RR 1.04 (0.87 to 1.25)	15 more per 1000 (from 49 fewer to 94 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Any functional impairment at 7 years of age — macrolide antibiotics alone												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	333/785 (42.4%)	92/245 (37.6%)	RR 1.13 (0.94 to 1.35)	49 more per 1000 (from 23 fewer to 131 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	A particular type of antibiotic	Placebo or no treatment	Relative (95% CI)	Absolute		
Any functional impairment at 7 years of age — macrolide and betalactam antibiotics												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	325/769 (42.3%)	92/245 (37.6%)	RR 1.13 (0.94 to 1.35)	49 more per 1000 (from 23 fewer to 131 more)	⊕⊕⊕O MODERATE	CRITICAL

1 Statistical heterogeneity ($I^2 > 60\%$).
2 Wide confidence interval crossing the line of no effect.
3 Wide confidence interval crossing the line of no effect, few events and small sample size.
4 Statistical heterogeneity ($I^2 > 60\%$). Variation in size and direction of effect.
5 Wide confidence interval crossing the line of no effect and small sample size.
6 One study with design limitations contributed 80% of the weight.
7 Wide confidence interval crossing the line of no effect and few events.
8 No events.
9 One study with design limitations contributed > 40% of the weight.

Table 5a. Antibiotic prophylaxis for women at risk of preterm birth and ruptured membranes

Source: Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. Cochrane Database Syst Rev. 2013;(12):CD001058.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any antibiotic	Placebo	Relative (95% CI)	Absolute		
Birth < 37 weeks of gestation												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	3104/3642 (85.2%)	1102/1289 (85.5%)	RR 1.00 (0.98 to 1.03)	0 fewer per 1000 (from 17 fewer to 26 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Maternal death												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	0/369 (0.0%)	0/394 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Chorioamnionitis												
11	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	126/767 (16.4%)	196/792 (24.7%)	RR 0.66 (0.46 to 0.96)	84 fewer per 1000 (from 10 fewer to 134 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Major adverse drug reaction												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	0/3913 (0.0%)	0/1574 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Birth within 48 hours of randomization												
7	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1296/4128 (31.4%)	717/1799 (39.9%)	RR 0.71 (0.58 to 0.87)	116 fewer per 1000 (from 52 fewer to 167 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth within 7 days of randomization												
7	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	no serious imprecision	none	2388/4145 (57.6%)	1221/1820 (67.1%)	RR 0.79 (0.71 to 0.89)	141 fewer per 1000 (from 74 fewer to 195 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Perinatal death/death before discharge (all studies: placebo and no treatment)												
18	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	299/4604 (6.5%)	172/2268 (7.6%)	RR 0.89 (0.74 to 1.08)	8 fewer per 1000 (from 20 fewer to 6 more)	⊕⊕⊕O MODERATE	CRITICAL
Perinatal death/death before discharge (sensitivity analysis: placebo-controlled trials only)												
12	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	276/4315 (6.4%)	138/1986 (6.9%)	RR 0.93 (0.76 to 1.14)	5 fewer per 1000 (from 17 fewer to 10 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any antibiotic	Placebo	Relative (95% CI)	Absolute		
Neonatal necrotizing enterocolitis												
11	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	100/4273 (2.3%)	58/1956 (3.0%)	RR 1.09 (0.65 to 1.83)	3 more per 1000 (from 10 fewer to 25 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal respiratory distress syndrome												
12	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	965/4303 (22.4%)	551/1984 (27.8%)	RR 0.95 (0.83 to 1.09)	14 fewer per 1000 (from 47 fewer to 25 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Treatment with surfactant												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	526/3584 (14.7%)	217/1225 (17.7%)	RR 0.83 (0.72 to 0.96)	30 fewer per 1000 (from 7 fewer to 50 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal encephalopathy												
1	randomized trials	serious[4]	no serious inconsistency	no serious indirectness	very serious[1]	none	0/30 (0.0%)	0/30 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL
Positive neonatal blood culture												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	234/3654 (6.4%)	104/1307 (8.0%)	RR 0.79 (0.63 to 0.99)	17 fewer per 1000 (from 1 fewer to 29 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal infection including pneumonia												
12	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	85/823 (10.3%)	141/857 (16.5%)	RR 0.67 (0.52 to 0.85)	54 fewer per 1000 (from 25 fewer to 79 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Major cerebral abnormality on ultrasound before discharge												
12	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	240/4303 (5.6%)	184/1986 (9.3%)	RR 0.81 (0.68 to 0.98)	18 fewer per 1000 (from 2 fewer to 30 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth weight < 2500 g												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	2605/3614 (72.1%)	911/1262 (72.2%)	RR 1.00 (0.96 to 1.04)	0 fewer per 1000 (from 29 fewer to 29 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth weight (better indicated by higher values)												
12	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	4355	2019	—	MD 53.83 higher (7.06 to 100.6 higher)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any antibiotic	Placebo	Relative (95% CI)	Absolute		
Serious childhood disability at 7 years of age												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	938/2375 (39.5%)	311/796 (39.1%)	RR 1.01 (0.91 to 1.12)	4 more per 1000 (from 35 fewer to 47 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Days in neonatal intensive care unit (NICU) (better indicated by lower values)												
3	randomized trials	serious[5]	no serious inconsistency	no serious indirectness	serious[6]	none	110	115	—	MD 5.05 lower (9.77 to 0.33 lower)	⊕⊕OO LOW	CRITICAL
Admission to NICU												
4	randomized trials	no serious risk of bias	serious[2]	no serious indirectness	no serious imprecision	none	2583/3687 (70.1%)	975/1336 (73%)	RR 0.98 (0.84 to 1.13)	15 fewer per 1000 (from 117 fewer to 95 more)	⊕⊕⊕O MODERATE	CRITICAL
Number of newborns requiring ventilation												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	757/3641 (20.8%)	292/1283 (22.8%)	RR 0.90 (0.80 to 1.02)	23 fewer per 1000 (from 46 fewer to 5 more)	⊕⊕⊕⊕ HIGH	CRITICAL

1 No events.
2 Statistical heterogeneity ($I^2 > 60\%$).
3 Wide confidence interval crossing the line of no effect.
4 One study with design limitations.
5 Half the weight from a study with design limitations.
6 Estimate based on small sample size.

Table 5b. Antibiotic prophylaxis for women at risk of preterm birth and ruptured membranes (antibiotic regimens)

Source: Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. Cochrane Database Syst Rev. 2013;(12):CD001058.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antibiotic prophylaxis	Placebo	Relative (95% CI)	Absolute		
Maternal death: subgroup analysis by type of antibiotic — all penicillin (excluding co-amoxiclav)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious	none	0/40 (0.0%)	0/45 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Maternal death: subgroup analysis by type of antibiotic — other antibiotic												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	0/329 (0.0%)	0/349 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Perinatal death/death before discharge: subgroup analysis by type of antibiotic (placebo-controlled trials only) — all penicillin (excluding co-amoxiclav)												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	7/165 (4.2%)	10/167 (6.0%)	RR 0.73 (0.30 to 1.80)	16 fewer per 1000 (from 42 fewer to 48 more)	⊕⊕OO LOW	CRITICAL
Perinatal death/death before discharge: subgroup analysis by type of antibiotic (placebo-controlled trials only) — betalactam (including co-amoxiclav)												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	80/1236 (6.5%)	46/644 (7.1%)	RR 0.91 (0.64 to 1.30)	6 fewer per 1000 (from 26 fewer to 21 more)	⊕⊕⊕O MODERATE	CRITICAL
Perinatal death/death before discharge: subgroup analysis by type of antibiotic (placebo-controlled trials only) — macrolide (including erythromycin)												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	84/1354 (6.2%)	56/784 (7.1%)	RR 0.90 (0.65 to 1.25)	7 fewer per 1000 (from 25 fewer to 18 more)	⊕⊕⊕O MODERATE	CRITICAL
Perinatal death/death before discharge: subgroup analysis by type of antibiotic (placebo-controlled trials only) — other antibiotic												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	28/371 (7.5%)	26/391 (6.6%)	RR 1.13 (0.68 to 1.88)	9 more per 1000 (from 21 fewer to 59 more)	⊕⊕⊕O MODERATE	CRITICAL
Necrotizing enterocolitis: subgroup analysis by type of antibiotic — all penicillin (excluding co-amoxiclav)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	5/124 (4.0%)	6/138 (4.3%)	RR 0.85 (0.25 to 2.97)	7 fewer per 1000 (from 33 fewer to 86 more)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis: subgroup analysis by type of antibiotic — betalactam (including co-amoxiclav)												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	29/1236 (2.3%)	3/644 (0.5%)	RR 4.72 (1.57 to 14.23)	17 more per 1000 (from 3 more to 62 more)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antibiotic prophylaxis	Placebo	Relative (95% CI)	Absolute		
Necrotizing enterocolitis: subgroup analysis by type of antibiotic — macrolide (including erythromycin)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	21/1322 (1.6%)	19/754 (2.5%)	RR 0.88 (0.45 to 1.69)	3 fewer per 1000 (from 14 fewer to 17 more)	⊕⊕⊕O MODERATE	CRITICAL
Necrotizing enterocolitis: subgroup analysis by type of antibiotic — other antibiotic												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	25/402 (6.2%)	30/421 (7.1%)	RR 0.89 (0.54 to 1.47)	8 fewer per 1000 (from 33 fewer to 33 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal infection including pneumonia: subgroup analysis by type of antibiotic — all penicillin (excluding co-amoxiclav)												
5	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/258 (2.3%)	25/263 (9.5%)	RR 0.30 (0.13 to 0.68)	67 fewer per 1000 (from 30 fewer to 83 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal infection including pneumonia: subgroup analysis by type of antibiotic — betalactam (including co-amoxiclav)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	0/31 (0.0%)	1/31 (3.2%)	RR 0.33 (0.01 to 7.88)	22 fewer per 1000 (from 32 fewer to 222 more)	⊕⊕OO LOW	CRITICAL
Neonatal infection including pneumonia: subgroup analysis by type of antibiotic — macrolide (including erythromycin)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	19/163 (11.7%)	25/171 (14.6%)	RR 0.79 (0.45 to 1.37)	31 fewer per 1000 (from 80 fewer to 54 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal infection including pneumonia: subgroup analysis by type of antibiotic — other antibiotic												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	60/371 (16.2%)	90/392 (23.0%)	RR 0.71 (0.53 to 0.95)	67 fewer per 1000 (from 11 fewer to 108 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Major cerebral abnormality on ultrasound before discharge: subgroup analysis by type of antibiotic — all penicillin (excluding co-amoxiclav)												
3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	10/124 (8.1%)	23/138 (16.7%)	RR 0.49 (0.25 to 0.96)	85 fewer per 1000 (from 7 fewer to 125 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Major cerebral abnormality on ultrasound before discharge: subgroup analysis by type of antibiotic — betalactam (including co-amoxiclav)												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	53/1236 (4.3%)	39/644 (6.1%)	RR 0.78 (0.52 to 1.16)	13 fewer per 1000 (from 29 fewer to 10 more)	⊕⊕⊕O MODERATE	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antibiotic prophylaxis	Placebo	Relative (95% CI)	Absolute		
Major cerebral abnormality on ultrasound before discharge: subgroup analysis by type of antibiotic — macrolide (including erythromycin)												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	68/1352 (5.0%)	47/784 (6.0%)	RR 0.93 (0.60 to 1.44)	4 fewer per 1000 (from 24 fewer to 26 more)	⊕⊕⊕O MODERATE	CRITICAL
Major cerebral abnormality on ultrasound before discharge: subgroup analysis by type of antibiotic — other antibiotic												
4	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	63/402 (15.7%)	76/421 (18.1%)	RR 0.85 (0.45 to 1.64)	27 fewer per 1000 (from 99 fewer to 116 more)	⊕⊕⊕O MODERATE	CRITICAL

1 No events.
2 Wide confidence interval crossing the line of no effect and few events.
3 Wide confidence interval crossing the line of no effect.
4 Wide confidence interval crossing the line of no effect, few events and small sample size.

Table 5c. Antibiotic prophylaxis for women at risk of preterm birth and ruptured membranes (erythromycin versus co-amoxiclav)

Source: Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. Cochrane Database Syst Rev. 2013;(12):CD001058.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Erythromycin	Co-amoxiclav	Relative (95% CI)	Absolute		
Birth < 37 weeks of gestation												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	1006/1190 (84.5%)	1025/1205 (85.1%)	RR 0.99 (0.96 to 1.03)	9 fewer per 1000 (from 34 fewer to 26 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Major adverse drug reaction												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	0/1190 (0.0%)	0/1205 (0.0%)	not pooled	not pooled	⊕⊕OO LOW	CRITICAL
Birth within 48 hours of randomization												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	414/1190 (34.8%)	367/1205 (30.5%)	RR 1.14 (1.02 to 1.28)	43 more per 1000 (from 6 more to 85 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth within 7 days of randomization												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	725/1190 (60.9%)	695/1205 (57.7%)	RR 1.06 (0.99 to 1.13)	35 more per 1000 (from 6 fewer to 75 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Perinatal death/death before discharge												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	70/1190 (5.9%)	79/1205 (6.6%)	RR 0.90 (0.66 to 1.23)	7 fewer per 1000 (from 22 fewer to 15 more)	⊕⊕⊕O MODERATE	CRITICAL
Neonatal necrotizing enterocolitis												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	11/1190 (0.9%)	24/1205 (2.0%)	RR 0.46 (0.23 to 0.94)	11 fewer per 1000 (from 1 fewer to 15 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal respiratory distress syndrome												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	236/1190 (19.8%)	241/1205 (20.0%)	RR 0.99 (0.84 to 1.16)	2 fewer per 1000 (from 32 fewer to 32 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Treatment with surfactant												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	176/1190 (14.8%)	182/1205 (15.1%)	RR 0.98 (0.81 to 1.19)	3 fewer per 1000 (from 29 fewer to 29 more)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Erythromycin	Co-amoxiclav	Relative (95% CI)	Absolute		
Positive neonatal blood culture												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	68/1190 (5.7%)	82/1205 (6.8%)	RR 0.84 (0.62 to 1.15)	11 fewer per 1000 (from 26 fewer to 10 more)	⊕⊕⊕O MODERATE	CRITICAL
Major cerebral abnormality on ultrasound before discharge												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	50/1190 (4.2%)	46/1205 (3.8%)	RR 1.10 (0.74 to 1.63)	4 more per 1000 (from 10 fewer to 24 more)	⊕⊕⊕O MODERATE	CRITICAL
Birth weight < 2500 g												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	863/1190 (72.5%)	877/1205 (72.8%)	RR 1.00 (0.95 to 1.05)	0 fewer per 1000 (from 36 fewer to 36 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Birth weight (better indicated by higher values)												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[2]	none	1190	1205	—	MD 19 higher (41.92 lower to 79.92 higher)	⊕⊕⊕O MODERATE	CRITICAL
Serious childhood disability at 7 years of age												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	293/788 (37.2%)	344/824 (41.7%)	RR 0.89 (0.79 to 1.01)	46 fewer per 1000 (from 88 fewer to 4 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Neonatal intensive care												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	836/1190 (70.3%)	848/1205 (70.4%)	RR 1.00 (0.95 to 1.05)	0 fewer per 1000 (from 35 fewer to 35 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Number of newborns requiring ventilation												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	251/1190 (21.1%)	254/1205 (21.1%)	RR 1 .00 (0.86 to 1.17)	0 fewer per 1000 (from 30 fewer to 36 more)	⊕⊕⊕⊕ HIGH	CRITICAL

1 No events.
2 Wide confidence interval crossing the line of no effect.

Table 5d. Antibiotic prophylaxis for women at risk of preterm birth and ruptured membranes (3-day versus 7-day ampicillin regimens)

Source: Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. Cochrane Database Syst Rev. 2013;(12):CD001058.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	3-day ampicillin regimen	7-day ampicillin regimen	Relative (95% CI)	Absolute		
Chorioamnionitis												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	8/42 (19.0%)	11/42 (26.2%)	RR 0.73 (0.33 to 1.63)	71 fewer per 1000 (from 175 fewer to 165 more)	⊕⊕OO LOW	CRITICAL
Birth within 48 hours of randomization												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	8/42 (19.0%)	7/42 (16.7%)	RR 1.14 (0.46 to 2.87)	23 more per 1000 (from 90 fewer to 312 more)	⊕⊕OO LOW	CRITICAL
Birth within 7 days of randomization												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	25/42 (59.5%)	25/42 (59.5%)	RR 1.00 (0.7 to 1.42)	0 fewer per 1000 (from 179 fewer to 250 more)	⊕⊕OO LOW	CRITICAL
Perinatal death/death before discharge												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/65 (1.5%)	4/65 (6.2%)	RR 0.40 (0.05 to 2.94)	37 fewer per 1000 (from 58 fewer to 119 more)	⊕⊕OO LOW	CRITICAL
Neonatal necrotizing enterocolitis												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	1/65 (1.5%)	3/65 (4.6%)	RR 0.43 (0.07 to 2.86)	26 fewer per 1000 (from 43 fewer to 86 more)	⊕⊕OO LOW	CRITICAL
Neonatal respiratory distress syndrome												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[2]	none	24/65 (36.9%)	25/65 (38.5%)	RR 0.96 (0.62 to 1.49)	15 fewer per 1000 (from 146 fewer to 188 more)	⊕⊕OO LOW	CRITICAL
Neonatal intraventricular haemorrhage												
2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[1]	none	0/65 (0.0%)	2/65 (3.1%)	RR 0.33 (0.04 to 3.12)	21 fewer per 1000 (from 30 fewer to 65 more)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	3-day ampicillin regimen	7-day ampicillin regimen	Relative (95% CI)	Absolute		
Neonatal intensive care												
1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[3]	none	36/42 (85.7%)	36/42 (85.7%)	RR 1.00 (0.84 to 1.19)	0 fewer per 1000 (from 137 fewer to 163 more)	⊕⊕⊕O MODERATE	CRITICAL

1 Wide confidence interval crossing the line of no effect, few events and small sample size.
2 Wide confidence interval crossing the line of no effect and small sample size.
3 Estimate based on small sample size.

Table 6a. Mode of delivery for women at risk of preterm birth

Source: Alfirevic Z, Milan SJ, Livio S. Caesarean section versus vaginal delivery for preterm birth in singletons. Cochrane Database Syst Rev. 2013;(9):CD000078.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Caesarean section	Vaginal delivery	Relative (95% CI)	Absolute		
Major maternal postpartum complications												
4	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	7/58 (12.1%)	0/58 (0.0%)	RR 7.21 (1.37 to 38.08)	—	⊕⊕OO LOW	CRITICAL
Major maternal postpartum complications — breech												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	7/35 (20.0%)	0/43 (0.0%)	RR 7.21 (1.37 to 38.08)	—	⊕⊕OO LOW	CRITICAL
Major maternal postpartum complications — cephalic												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/23 (0.0%)	0/15 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL
Maternal puerperal pyrexia												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	11/46 (23.9%)	4/43 (9.3%)	RR 2.98 (1.18 to 7.53)	184 more per 1000 (from 17 more to 607 more)	⊕⊕OO LOW	CRITICAL
Maternal puerperal pyrexia — breech												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	11/23 (47.8%)	4/28 (14.3%)	RR 2.98 (1.18 to 7.53)	283 more per 1000 (from 26 more to 933 more)	⊕⊕OO LOW	CRITICAL
Maternal puerperal pyrexia — cephalic												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/23 (0.0%)	0/15 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL
Maternal wound infection												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/53 (1.9%)	1/50 (2.0%)	RR 1.16 (0.18 to 7.70)	3 more per 1000 (from 16 fewer to 134 more)	⊕OOO VERY LOW	CRITICAL
Maternal wound infection — breech												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/30 (3.3%)	1/35 (2.9%)	RR 1.16 (0.18 to 7.70)	5 more per 1000 (from 23 fewer to 191 more)	⊕OOO VERY LOW	CRITICAL
Maternal wound infection — cephalic												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/23 (0.0%)	0/15 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Caesarean section	Vaginal delivery	Relative (95% CI)	Absolute		
Other maternal infection												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	10/53 (18.9%)	4/50 (8.0%)	RR 2.63 (1.02 to 6.78)	130 more per 1000 (from 2 more to 462 more)	⊕⊕OO LOW	CRITICAL
Other maternal infection — breech												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	10/30 (33.3%)	4/35 (11.4%)	RR 2.63 (1.02 to 6.78)	186 more per 1000 (from 2 more to 661 more)	⊕⊕OO LOW	CRITICAL
Other maternal infection — cephalic												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/23 (0.0%)	0/15 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL
Cord prolapse												
4	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	0/58 (0.0%)	4/58 (6.9%)	RR 0.25 (0.03 to 1.92)	52 fewer per 1000 (from 67 fewer to 63 more)	⊕OOO VERY LOW	CRITICAL
Cord prolapse — breech												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	0/35 (0.0%)	4/43 (9.3%)	RR 0.25 (0.03 to 1.92)	70 fewer per 1000 (from 90 fewer to 86 more)	⊕OOO VERY LOW	CRITICAL
Cord prolapse — cephalic												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/23 (0.0%)	0/15 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL
Head entrapment												
4	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/58 (0.0%)	0/58 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL
Head entrapment — breech												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/35 (0.0%)	0/43 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL
Head entrapment — cephalic												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[4]	none	0/23 (0.0%)	0/15 (0.0%)	not pooled	not pooled	⊕OOO VERY LOW	CRITICAL
Delivery < 7 days after entry — breech												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[6]	none	22/23 (95.7%)	28/28 (100.0%)	RR 0.95 (0.73 to 1.24)	50 fewer per 1000 (from 270 fewer to 240 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Caesarean section	Vaginal delivery	Relative (95% CI)	Absolute		
Perinatal death												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	2/46 (4.3%)	8/43 (18.6%)	RR 0.29 (0.07 to 1.14)	132 fewer per 1000 (from 173 fewer to 26 more)	⊕OOO VERY LOW	CRITICAL
Perinatal death — breech												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/23 (4.3%)	6/28 (21.4%)	RR 0.28 (0.05 to 1.49)	154 fewer per 1000 (from 204 fewer to 105 more)	⊕OOO VERY LOW	CRITICAL
Perinatal death — cephalic												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/23 (4.3%)	2/15 (13.3%)	RR 0.33 (0.03 to 3.29)	89 fewer per 1000 (from 129 fewer to 305 more)	⊕OOO VERY LOW	CRITICAL
Birth asphyxia — breech												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[6]	none	5/5 (100.0%)	4/7 (57.1%)	RR 1.63 (0.84 to 3.14)	360 more per 1000 (from 91 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Neonatal fitting/seizures — breech												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	0/35 (0.0%)	2/42 (4.8%)	RR 0.22 (0.01 to 4.32)	37 fewer per 1000 (from 47 fewer to 158 more)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[6]	none	9/53 (17.0%)	16/50 (32.0%)	RR 0.55 (0.27 to 1.10)	144 fewer per 1000 (from 234 fewer to 32 more)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome — breech												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[6]	none	6/30 (20.0%)	12/35 (34.3%)	RR 0.57 (0.25 to 1.30)	147 fewer per 1000 (from 257 fewer to 103 more)	⊕OOO VERY LOW	CRITICAL
Respiratory distress syndrome — cephalic												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[6]	none	3/23 (13.0%)	4/15 (26.7%)	RR 0.49 (0.13 to 1.88)	136 fewer per 1000 (from 232 fewer to 235 more)	⊕OOO VERY LOW	CRITICAL
Hypoxic ischaemic encephalopathy — breech												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/5 (20.0%)	0/7 (0.0%)	RR 4.00 (0.20 to 82.01)	—	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Caesarean section	Vaginal delivery	Relative (95% CI)	Absolute		
Intracranial pathology												
4	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	4/56 (7.1%)	4/54 (7.4%)	RR 0.92 (0.27 to 3.14)	6 fewer per 1000 (from 54 fewer to 159 more)	⊕OOO VERY LOW	CRITICAL
Birth injury to baby — breech												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/18 (5.6%)	2/20 (10.0%)	RR 0.56 (0.05 to 5.62)	44 fewer per 1000 (from 95 fewer to 462 more)	⊕OOO VERY LOW	CRITICAL
Intracranial pathology — breech												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	1/33 (3.0%)	3/39 (7.7%)	RR 0.58 (0.12 to 2.86)	32 fewer per 1000 (from 68 fewer to 143 more)	⊕OOO VERY LOW	CRITICAL
Intracranial pathology — cephalic												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[5]	none	3/23 (13.0%)	1/15 (6.7%)	RR 1.96 (0.22 to 17.1)	64 more per 1000 (from 52 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Necrotizing enterocolitis — breech												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[5]	none	2/5 (40.0%)	0/7 (0.0%)	RR 6.67 (0.39 to 114.78)	—	⊕OOO VERY LOW	CRITICAL
Neonatal infection (proven)												
3	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[6]	none	4/53 (7.5%)	5/50 (10.0%)	RR 0.76 (0.12 to 4.66)	24 fewer per 1000 (from 88 fewer to 366 more)	⊕OOO VERY LOW	CRITICAL
Neonatal infection (proven) — breech												
2	randomized trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[5]	none	3/30 (10.0%)	3/35 (8.6%)	RR 1.10 (0.07 to 17.74)	9 more per 1000 (from 80 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Neonatal infection (proven) — cephalic												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[6]	none	1/23 (4.3%)	2/15 (13.3%)	RR 0.33 (0.03 to 3.29)	89 fewer per 1000 (from 129 fewer to 305 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Caesarean section	Vaginal delivery	Relative (95% CI)	Absolute		
Ventilation (days) — breech (better indicated by lower values)												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[6]	none	5	7	—	MD 18.26 higher (19.9 lower to 56.42 higher)	⊕OOO VERY LOW	CRITICAL
Need for mechanical ventilation — breech												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[6]	none	4/5 (80.0%)	3/7 (42.9%)	RR 1.87 (0.71 to 4.88)	373 more per 1000 (from 124 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Supplemental oxygen (days) — breech (better indicated by lower values)												
1	randomized trials	serious[3]	no serious inconsistency	no serious indirectness	very serious[6]	none	5	7	—	MD 3.71 higher (20.85 lower to 28.27 higher)	⊕OOO VERY LOW	CRITICAL

1 Estimate based on small sample size.
2 All studies contributing data had design limitations.
3 One study with design limitations.
4 No events.
5 Wide confidence interval crossing the line of no effect, few events and small sample size.
6 Wide confidence interval crossing the line of no effect and small sample size.

Table 7a. Kangaroo mother care (KMC) versus conventional care for preterm newborns

Source: Conde-Agudelo A, Belizan JM, Diaz-Rossello J. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. Cochrane Database Syst Rev. 2011;(3):CD002771.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	KMC	Conventional care	Relative (95% CI)	Absolute (95% CI)		
Overall mortality at discharge or at 40—41 weeks postmenstrual age												
8	randomized trials	not serious	not serious	not serious	not serious	none	28/888 (3.2%)	45/848 (5.3%)	RR 0.60 (0.39 to 0.92)	21 fewer per 1000 (from 4 fewer to 32 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Mortality at discharge or at 40—41 weeks postmenstrual age for studies in low- and middle-income countries												
7	randomized trials	not serious	not serious	not serious	not serious	none	26/855 (3.0%)	44/821 (5.4%)	RR 0.57 (0.37 to 0.89)	23 fewer per 1000 (from 6 fewer to 34 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Mortality at discharge or at 40—41 weeks postmenstrual age for studies in high-income countries												
1	randomized trial	not serious	serious[1]	not serious	serious[2]	none	2/33 (6.1%)	1/27 (3.7%)	RR 1.64 (0.16 to 17.09)	24 more per 1000 (from 31 fewer to 596 more)	⊕⊕OO LOW	CRITICAL
Overall mortality at latest follow-up												
11	randomized trials	not serious	not serious	not serious	not serious	none	46/1088 (4.2%)	69/1079 (6.4%)	RR 0.67 (0.48 to 0.95)	21 fewer per 1000 (from 3 fewer to 33 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Overall mortality at last follow-up for studies in low- and middle-income countries												
9	randomized trials	not serious	not serious	not serious	not serious	none	42/1020 (4.1%)	66/1016 (6.5%)	RR 0.65 (0.45 to 0.93)	23 fewer per 1000 (from 5 fewer to 36 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Overall mortality at last follow-up for studies in high-income countries												
2	randomized trials	not serious	not serious	not serious	very serious[3]	none	4/68 (5.9%)	3/63 (4.8%)	RR 1.25 (0.29 to 5.42)	12 more per 1000 (from 34 fewer to 210 more)	⊕⊕OO LOW	CRITICAL
Severe infection at last follow-up												
7	randomized trials	not serious	not serious	not serious	not serious	none	47/685 (6.9%)	80/658 (12.2%)	RR 0.56 (0.40 to 0.78)	53 fewer per 1000 (from 27 fewer to 73 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Nosocomial infection at discharge or at 40—41 weeks postmenstrual age												
3	randomized trials	not serious	not serious	not serious	not serious	none	19/469 (4.1%)	40/444 (9.0%)	RR 0.45 (0.27 to 0.76)	50 fewer per 1000 (from 22 fewer to 66 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	KMC	Conventional care	Relative (95% CI)	Absolute (95% CI)		
Hypothermia												
6	randomized trials	not serious	not serious	not serious	not serious	none	32/354 (9.0%)	95/344 (27.6%)	RR 0.34 (0.17 to 0.67)	182 fewer per 1000 (from 91 fewer to 229 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Hyperthermia												
4	randomized trials	not serious	not serious	not serious	serious[1]	none	52/228 (22.8%)	64/220 (29.1%)	RR 0.79 (0.59 to 1.05)	61 fewer per 1000 (from 15 more to 119 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Readmission to hospital at latest follow-up												
2	randomized trials	not serious	not serious	not serious	serious[1]	none	18/474 (3.8%)	30/472 (6.4%)	RR 0.60 (0.34 to 1.06)	25 fewer per 1000 (from 4 more to 42 fewer)	⊕⊕⊕O MODERATE	CRITICAL

1 Only one study conducted, hence consistency could not be assessed.
2 Wide confidence intervals for the outcome.
3 Very wide confidence intervals because of very few events.

Table 7b. Continuous Kangaroo mother care (KMC) versus conventional care for preterm newborns

Source: Conde-Agudelo A, Belizan JM, Diaz-Rossello J. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. Cochrane Database Syst Rev. 2011;(3):CD002771.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Continuous KMC	Conventional care	Relative (95% CI)	Absolute (95% CI)		
Overall mortality at discharge or at 40—41 weeks postmenstrual age												
3	randomized trials	not serious	not serious	not serious	not serious	none	23/575 (4.0%)	37/542 (6.8%)	RR 0.60 (0.38 to 0.96)	27 fewer per 1000 (from 3 fewer to 42 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Overall mortality at latest follow-up												
4	randomized trials	not serious	not serious	not serious	not serious	none	39/692 (5.6%)	59/692 (8.5%)	RR 0.67 (0.46 to 0.98)	28 fewer per 1000 (from 2 fewer to 46 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Severe infection at latest follow-up												
1	randomized trials	not serious	serious[1]	not serious	serious[2]	none	26/343 (7.6%)	35/320 (10.9%)	RR 0.69 (0.43 to 1.12)	34 fewer per 1000 (from 13 more to 62 fewer)	⊕⊕OO LOW	CRITICAL
Nosocomial infection at discharge or at 40—41 weeks postmenstrual age												
1	randomized trials	not serious	serious[1]	not serious	not serious	none	13/343 (3.8%)	25/320 (7.8%)	RR 0.49 (0.25 to 0.93)	40 fewer per 1000 (from 5 fewer to 59 fewer)	⊕⊕⊕O MODERATE	CRITICAL

1 Only one trial, hence consistency could not be assessed.
2 Wide confidence intervals crossing the line of no effect.

Table 7c. Intermittent Kangaroo mother care (KMC) versus conventional care for preterm newborns

Source: Conde-Agudelo A, Belizan JM, Diaz-Rossello J. Kangaroo mother care to reduce morbidity and mortality in low birthweight infants. Cochrane Database Syst Rev. 2011;(3):CD002771.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Intermittent KMC	Conventional care	Relative (95% CI)	Absolute (95% CI)		
Overall mortality at discharge or at 40—41 weeks postmenstrual age												
5	randomized trials	not serious	not serious	not serious	serious[1]	none	5/313 (1.6%)	8/306 (2.6%)	RR 0.59 (0.19 to 1.81)	11 fewer per 1000 (from 21 fewer to 21 more)	⊕⊕⊕O MODERATE	CRITICAL
Overall mortality at latest follow-up												
7	randomized trials	not serious	not serious	not serious	serious[1]	none	7/396 (1.8%)	10/387 (2.6%)	RR 0.68 (0.26 to 1.77)	8 fewer per 1000 (from 19 fewer to 20 more)	⊕⊕⊕O MODERATE	CRITICAL
Severe infection												
6	randomized trials	not serious	not serious	not serious	not serious	none	21/342 (6.1%)	45/338 (13.3%)	RR 0.45 (0.28 to 0.73)	73 fewer per 1000 (from 36 fewer to 96 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Nosocomial infection at discharge or at 40—41 weeks postmenstrual age												
2	randomized trials	not serious	not serious	not serious	not serious	none	6/124 (4.8%)	15/124 (12.1%)	RR 0.39 (0.16 to 0.96)	74 fewer per 1000 (from 5 fewer to 102 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Hypothermia												
6	randomized trials	not serious	not serious	not serious	not serious	none	320/354 (90.4%)	95/344 (27.6%)	RR 0.34 (0.17 to 0.67)	182 fewer per 1000 (from 91 fewer to 229 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Hyperthermia												
4	randomized trials	not serious	not serious	not serious	serious[1]	none	52/228 (22.8%)	64/220 (29.1%)	RR 0.79 (0.59 to 1.05)	61 fewer per 1000 (from 15 more to 119 fewer)	⊕⊕⊕O MODERATE	CRITICAL

1 Wide confidence intervals crossing the line of no effect and few events.

Table 7d. Radiant warmers versus incubators for care of unstable or sick preterm newborns

Source: Flenady VJ, Woodgate PG. Radiant warmers versus incubators for regulating body temperature in newborn infants. Cochrane Database Syst Rev. 2003;(4):CD000435. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiant warmer	Incubator	Relative (95% CI)	Absolute		
Neonatal mortality												
2	randomized trials	no serious risk of bias[1]	no serious inconsistency	serious[2]	very serious[3,4]	none	1/47 (2.1%)	5/47 (10.6%)	RR 0.27 (0.05 to 1.59)	78 fewer per 1000 (from 101 fewer to 63 more)	⊕OOO VERY LOW	CRITICAL
Culture positive sepsis (assessed with positive blood culture)												
1	randomized trials	serious[5]	serious[6]	serious[7]	serious[3]	none	3/30 (10.0%)	5/30 (16.7%)	RR 0.60 (0.16 to 2.29)	67 fewer per 1000 (from 140 fewer to 215 more)	⊕OOO VERY LOW	CRITICAL
Bronchopulmonary dysplasia												
1	randomized trials	very serious[5,8]	serious6	serious[7]	serious[3]	none	0/30 (0.0%)	2/30 (6.7%)	RR 0.20 (0.01 to 4.00)	53 fewer per 1000 (from 66 fewer to 200 more)	⊕OOO VERY LOW	CRITICAL
Severe intraventricular haemorrhage (IVH) (grade 3 or 4) (assessed by ultrasound)												
2	randomized trials	very serious[9,10]	no serious inconsistency	serious[2]	very serious[3,4]	none	0/45 (0.0%)	1/45 (2.2%)	RR 0.33 (0.01 to 7.87)	15 fewer per 1000 (from 22 fewer to 153 more)	⊕OOO VERY LOW	CRITICAL
Weight gain (better indicated by higher values)												
2	randomized trials	very serious[5,8]	no serious inconsistency	serious[2]	serious[3]	none	43	43	—	MD 1.06 higher (0.94 lower to 3.06 higher)	⊕OOO VERY LOW	IMPORTANT
Time to regain birth weight (better indicated by lower values)												
2	randomized trials	very serious[11,12]	no serious inconsistency	serious[2]	serious[3]	none	45	45	—	MD 0.86 higher (1.49 lower to 3.21 higher)	⊕OOO VERY LOW	IMPORTANT

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Radiant warmer	Incubator	Relative (95% CI)	Absolute		
Insensible water losses (better indicated by lower values)												
3	randomized trials	very serious[8,13]	no serious inconsistency	serious[2]	no serious imprecision	none	26	27	—	MD 0.94 higher (0.47 to 1.41 higher)	⊕OOO VERY LOW	IMPORTANT

1 Majority of evidence from the study with no blinding but the outcome is objective.
2 All the studies were from high-income countries.
3 95% CI around the pooled estimate includes both: (1) no effect and (2) appreciable benefit or appreciable harm.
4 Event rate very low.
5 Post-randomization exclusions.
6 Single study.
7 Study from high-income country.
8 No blinding of outcome assessment.
9 All the evidence from the study with post-randomization exclusions.
10 All the evidence from the study with no blinding of outcome assessment.
11 Majority of evidence from the study with post-randomization exclusions (one infant excluded because of refusal of consent following randomization).
12 Majority of evidence from the study with no blinding of outcome assessment.
13 Unclear allocation concealment in all the studies.

Table 7e. Plastic bags or wraps versus conventional care immediately after birth in preterm (and some term) newborns

Source: Oatley H, Blencowe H, Lawn JE. Systematic review of the effect of coverings including plastic bags and wraps on mortality and morbidity in preterm and term neonates. 2014 (unpublished).

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Covering in plastic bags or wraps	Conventional care	Relative (95% CI)	Absolute (95% CI)		
All-cause neonatal mortality including neonates born ≤ 29 weeks of gestation												
7	randomized trials	not serious	not serious	serious[1]	very serious[2]	none	27/166 (16.3%)	34/175 (19.4%)	RR 0.84 (0.54 to 1.30)	31 fewer per 1000 (from 58 more to 89 fewer)	⊕OOO VERY LOW	CRITICAL
All-cause mortality including neonates born 26—36 weeks of gestation												
2	randomized trials	not serious	serious[3]	serious[1]	very serious[3]	none	12/99 (12.1%)	13/115 (11.3%)	RR 2.62 (0.72 to 9.58)	183 more per 1000 (from 32 fewer to 970 more)	⊕OOO VERY LOW	CRITICAL
Hypothermia												
2	randomized trials	not serious	serious[4]	serious[1]	not serious[3]	none	51/112 (45.5%)	92/117 (78.6%)	RR 0.58 (0.46 to 0.72)	330 fewer per 1000 (from 220 fewer to 425 fewer)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis												
1	randomized trials[5]	serious[6]	serious[7]	serious[1]	very serious[3]	none	34/180 (18.9%)	29/203 (14.3%)	RR 5.98 (0.29 to 121.80)	711 more per 1000 (from 101 fewer to 1000 more)	⊕OOO VERY LOW	CRITICAL
Intraventricular haemorrhage												
2	randomized trials[5]	not serious	not serious	serious[1]	serious[2]	none	32/219 (14.6%)	52/241 (21.6%)	RR 0.30 (0.03 to 2.60)	151 fewer per 1000 (from 209 fewer to 345 more)	⊕⊕OO LOW	CRITICAL

1 All facility-based studies conducted in high-income settings.
2 Wide confidence intervals crossing the line of no effect.
3 Very wide confidence intervals crossing the line of no effect.
4 Some heterogeneity.
5 There were two other observational studies.
6 Methodological inconsistencies.
7 No explanation was provided.

Table 8a. Continuous positive airway pressure (CPAP) therapy for preterm newborns with respiratory distress syndrome

Source: Ho JJ, Subramaniam P, Henderson-Smart DJ, Davis PG. Continuous distending pressure for respiratory distress syndrome in preterm infants. Cochrane Database Syst Rev 2002;(2):CD002271 (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	CPAP	Oxygen by head box or cannula	Relative (95% CI)	Absolute		
In-hospital mortality (assessed with: mortality during initial hospital stay)												
6	randomized trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	16/176 (9.1%)	32/179 (17.9%)	RR 0.52 (0.32 to 0.87)	86 fewer per 1000 (from 23 fewer to 122 fewer)	⊕⊕OO LOW	CRITICAL
Bronchopulmonary dysplasia (assessed with: oxygen requirement at 28 days of age)												
3	randomized trials	serious[3]	no serious inconsistency	serious[2]	serious[4]	none	6/126 (4.8%)	6/134 (4.5%)	RR 1.22 (0.44 to 3.39)	10 more per 1000 (from 25 fewer to 107 more)	⊕OOO VERY LOW	CRITICAL
Respiratory failure warranting mechanical ventilation												
5	randomized trials	serious[3]	no serious inconsistency	serious[2]	no serious imprecision	none	56/154 (36.4%)	84/160 (52.5%)	RR 0.72 (0.56 to 0.91)	147 fewer per 1000 (from 47 fewer to 231 fewer)	⊕⊕OO LOW	CRITICAL
Need for surfactant												
1	randomized trials	serious[3]	serious[5]	serious[6]	serious[4]	none	3/26 (11.5%)	7/26 (26.9%)	RR 0.43 (0.12 to 1.48)	153 fewer per 1000 (from 237 fewer to 129 more)	⊕OOO VERY LOW	CRITICAL
Any air leak												
6	randomized trials	serious[3]	no serious inconsistency	serious[2]	no serious imprecision	none	25/172 (14.5%)	11/179 (6.1%)	RR 2.42 (1.26 to 4.65)	87 more per 1000 (from 16 more to 224 more)	⊕⊕OO LOW	CRITICAL

1 Allocation concealment unclear in two studies with combined weight of > 50%.
2 All studies are from high-income countries.
3 Neither outcome assessors nor treatment team was blinded to group allocation.
4 95% CI around the pooled estimate includes both: (1) no effect and (2) appreciable benefit or appreciable harm.
5 Single study.
6 Study from high-income country.

Table 8b. Timing of initiation (early versus late) of continuous positive airway pressure (CPAP) therapy for preterm newborns with respiratory distress syndrome

Source: Ho JJ, Henderson-Smart DJ, Davis PG. Early versus delayed initiation of continuous distending pressure for respiratory distress syndrome in preterm infants. Cochrane Database Syst Rev. 2002;(2):CD002975. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early CPAP	Late CPAP	Relative (95% CI)	Absolute		
Neonatal mortality												
2	randomized trials	serious[1]	no serious inconsistency	serious[2]	serious[3]	none	1/23 (4.3%)	2/38 (5.3%)	RR 0.93 (0.13 to 6.81)	4 fewer per 1000 (from 46 fewer to 306 more)	⊕OOO VERY LOW	CRITICAL
In-hospital mortality												
7	randomized trials	no serious risk of bias[4]	no serious inconsistency	serious[5]	serious[3]	none	15/109 (13.8%)	24/128 (18.8%)	RR 0.70 (0.40 to 1.24)	56 fewer per 1000 (from 112 fewer to 45 more)	⊕⊕OO LOW	CRITICAL
Bronchopulmonary dysplasia (assessed with: oxygen requirement at 28 days of age)												
2	randomized trials	serious[6]	no serious inconsistency	no serious indirectness[7]	very serious[3,8]	none	2/53 (3.8%)	3/55 (5.5%)	RR 0.70 (0.12 to 3.98)	16 fewer per 1000 (from 48 fewer to 163 more)	⊕OOO VERY LOW	CRITICAL
Need for mechanical ventilation												
6	randomized trials	very serious[1,6]	no serious inconsistency	serious[2]	no serious imprecision	none	13/73 (17.8%)	29/92 (31.5%)	—	142 fewer per 1000 (from 13 fewer to 214 fewer)	⊕OOO VERY LOW	CRITICAL
Need for surfactant therapy												
1	randomized trials	serious[6]	serious[9]	no serious indirectness	no serious imprecision	none	18/36 (50.0%)	28/36 (77.8%)	RR 0.64 (0.44 to 0.93)	280 fewer per 1000 (from 54 fewer to 436 fewer)	⊕⊕OO LOW	CRITICAL
Air leaks												
5	randomized trials	very serious[1,6]	no serious inconsistency	serious[2]	serious[3]	none	8/63 (12.7%)	12/81 (14.8%)	RR 0.84 (0.37 to 1.91)	24 fewer per 1000 (from 93 fewer to 135 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early CPAP	Late CPAP	Relative (95% CI)	Absolute		
Sepsis												
1	randomized trials	serious[6]	serious[9]	no serious indirectness	no serious imprecision	none	11/36 (30.6%)	24/36 (66.7%)	RR 0.46 (0.27 to 0.79)	360 fewer per 1000 (from 140 fewer to 487 fewer)	⨁⨁◯◯ LOW	CRITICAL

1 Allocation concealment unclear in most/all studies.
2 Studies from high-income countries.
3 95% CI around the pooled estimate includes both: (1) no effect and (2) appreciable benefit or appreciable harm.
4 Allocation concealment mentioned in two studies with combined weight of > 50%.
5 All studies except one with weight of evidence < 50% from high-income countries.
6 Neither treatment team nor outcome assessors were masked to group allocation.
7 > 50% weight of evidence from the study from a low- and middle-income country setting.
8 Only two and three events in the two studies (both groups combined).
9 Single study.

Table 9a. Surfactant replacement therapy with animal-derived surfactants for preterm newborns with respiratory distress syndrome

Source: Seger N, Soll R. Animal derived surfactant extract for treatment of respiratory distress syndrome. Cochrane Database Syst Rev. 2009;(2):CD007836. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Surfactant replacement therapy	No therapy or placebo	Relative (95% CI)	Absolute		
Neonatal mortality												
10	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	145/744 (19.5%)	206/725 (28.4%)	RR 0.68 (0.57 to 0.82)	9 fewer per 100 (from 5 fewer to 12 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Bronchopulmonary dysplasia (assessed with: use of supplemental oxygen at 36 weeks postmenstrual age)												
9	randomized trials	no serious risk of bias	serious[2]	serious[1]	no serious imprecision	none	278/796 (34.9%)	285/772 (36.9%)	RR 0.95 (0.84 to 1.08)	18 fewer per 1000 (from 59 fewer to 30 more)	⊕⊕OO LOW	CRITICAL
Air leaks (assessed with: any air leak syndromes such as pulmonary interstitial emphysema, pneumothorax, pneumomediastinum, etc.)												
7	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	102/694 (14.7%)	213/686 (31%)	RR 0.47 (0.39 to 0.58)	165 fewer per 1000 (from 130 fewer to 189 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Pulmonary haemorrhage												
2	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[3]	none	32/457 (7.0%)	24/441 (5.4%)	RR 1.29 (0.77 to 2.15)	16 more per 1000 (from 13 fewer to 63 more)	⊕⊕OO LOW	CRITICAL
Sepsis (assessed with: culture proven bacterial sepsis)												
4	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[3]	none	95/513 (18.5%)	82/499 (16.4%)	RR 1.14 (0.87 to 1.48)	23 more per 1000 (from 21 fewer to 79 more)	⊕⊕OO LOW	CRITICAL
Severe intraventricular haemorrhage (IVH) (assessed with: grade 3 or 4 IVH detected by ultrasound or computerized tomography [CT] scan of the head)												
10	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[3]	none	195/758 (25.7%)	206/743 (27.7%)	RR 0.93 (0.79 to 1.10)	19 fewer per 1000 (from 58 fewer to 28 more)	⊕⊕OO LOW	CRITICAL

1 All the studies were done in level-3 NICUs in high-income countries.
2 There was significant heterogeneity.
3 Confidence intervals were wide and crossed the line of no effect.

Table 9b. Surfactant replacement therapy with protein-free synthetic surfactants for preterm newborns with respiratory distress syndrome

Source: Soll R. Synthetic surfactant for respiratory distress syndrome in preterm infants. Cochrane Database Syst Rev. 2000;(2):CD001149.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Protein-free synthetic surfactant treatment or prophylaxis	Natural surfactant	Relative (95% CI)	Absolute (95% CI)		
Overall neonatal mortality												
6	randomized trials	not serious	not serious	serious[1]	not serious	non applicable	149/1176 (12.7%)	200/1176 (17.0%)	RR 0.73 (0.61 to 0.88)	43 fewer per 1000 (from 1 fewer to 1 fewer)	⊕⊕⊕O MODERATE	CRITICAL
In-hospital mortality												
6	randomized trials	not serious	not serious	serious[1]	not serious	non applicable	201/1178 (17.1%)	251/1174 (21.3%)	RR 0.79 (0.68 to 0.92)	42 fewer per 1000 (from 1 fewer to 1 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Air leaks												
5	randomized trials	not serious	not serious	serious[1]	not serious	non applicable	186/1161 (16.0%)	289/1167 (24.8%)	RR 0.64 (0.55 to 0.76)	88 fewer per 1000 (from 1 fewer to 1 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Bronchopulmonary dysplasia												
5	randomized trials	not serious	not serious	serious[1]	not serious	non applicable	123/1123 (11.0%)	162/1125 (14.4%)	RR 0.75 (0.61 to 0.92)	34 fewer per 1000 (from 1 fewer to 1 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Severe intraventricular haemorrhage												
5	randomized trials	not serious	not serious	serious[1]	serious[2]	non applicable	80/1161 (6.8%)	95/1167 (8.1%)	RR 0.84 (0.63 to 1.12)	13 fewer per 1000 (from 1 fewer to 1 fewer)	⊕⊕OO LOW	CRITICAL

1 All trials conducted in high-income countries.
2 Wide confidence intervals crossing the line of no effect.

Table 9c. Protein-free synthetic surfactant treatment or prophylaxis versus natural surfactant therapy for preterm newborns with respiratory distress syndrome

Source: Soll RF, Blanco F. Natural surfactant extract versus synthetic surfactant for neonatal respiratory distress syndrome. Cochrane Database Syst Rev. 2001;(2):CD000144.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Protein-free synthetic surfactant	Animal derived surfactant extract	Relative (95% CI)	Absolute		
Neonatal mortality												
12	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	765/2838 (27.0%)	553/2609 (21.2%)	RR 1.07 (0.99 to 1.17)	15 more per 1000 (from 2 fewer to 36 more)	⊕⊕⊕O MODERATE	CRITICAL
Bronchopulmonary dysplasia (assessed with: use of supplemental oxygen at 36 weeks postmenstrual age)												
7	randomized trials	serious[2]	no serious inconsistency	serious[1]	no serious imprecision	none	688/2123 (32.4%)	569/1883 (30.2%)	RR 1.00 (0.92 to 1.10)	0 fewer per 1000 (from 24 fewer to 30 more)	⊕⊕OO LOW	CRITICAL
Pneumothorax												
11	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	313/2804 (11.2%)	187/2577 (7.3%)	RR 1.49 (1.26 to 1.77)	36 more per 1000 (from 19 more to 56 more)	⊕⊕⊕O MODERATE	CRITICAL
Sepsis												
10	randomized trials	serious[2]	no serious inconsistency	serious[1]	no serious imprecision	none	735/2776 (26.5%)	594/2468 (24.1%)	RR 0.99 (0.90 to 1.08)	2 fewer per 1000 (from 24 fewer to 19 more)	⊕⊕OO LOW	CRITICAL
Severe intraventricular haemorrhage												
9	randomized trials	serious[2]	no serious inconsistency	serious[1]	no serious imprecision	none	349/2590 (13.5%)	316/2379 (13.3%)	RR 0.95 (0.83 to 1.09)	7 fewer per 1000 (from 23 fewer to 12 more)	⊕⊕OO LOW	CRITICAL

1 All the studies were done in level-3 NICUs in high-income countries.
2 Subjective outcome; blinding of outcome assessment not done in most studies.

Table 9d. Protein-containing synthetic surfactant treatment or prophylaxis versus natural surfactant therapy for preterm newborns with respiratory distress syndrome

Source: Pfister RH, Soll RF, Wiswell T. Protein-containing synthetic surfactant versus animal derived surfactant extract for the prevention and treatment of respiratory distress syndrome. Cochrane Database Syst Rev. 2007;(3):CD006069.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Protein-containing synthetic surfactant	Animal-derived surfactant	Relative (95% CI)	Absolute		
Neonatal mortality												
2	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	114/646 (17.6%)	81/382 (21.2%)	RR 0.79 (0.61 to 1.02)	45 fewer per 1000 (from 83 fewer to 4 more)	⊕⊕OO LOW	CRITICAL
Bronchopulmonary dysplasia at 36 weeks of gestation												
2	randomized trials	no serious risk of bias	serious[3]	serious[1]	no serious imprecision	none	235/646 (36.4%)	127/382 (33.2%)	RR 0.99 (0.84 to 1.18)	3 fewer per 1000 (from 53 fewer to 60 more)	⊕⊕OO LOW	CRITICAL
Air leaks												
2	randomized trials	no serious risk of bias	serious[3]	serious[1]	serious[2]	none	93/646 (14.4%)	51/382 (13.4%)	RR 1.00 (0.73 to 1.37)	0 fewer per 1000 (from 36 fewer to 49 more)	⊕OOO VERY LOW	CRITICAL
Pulmonary haemorrhage												
2	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	61/646 (9.4%)	46/382 (12%)	RR 0.73 (0.51 to 1.06)	33 fewer per 1000 (from 59 fewer to 7 more)	⊕⊕OO LOW	CRITICAL
Sepsis (culture proven)												
1	randomized trials	no serious risk of bias	serious[4]	serious[1]	no serious imprecision	none	232/527 (44.0%)	113/258 (43.8%)	RR 1.01 (0.85 to 1.19)	4 more per 1000 (from 66 fewer to 83 more)	⊕⊕OO LOW	CRITICAL
Necrotizing enterocolitis												
2	randomized trials	no serious risk of bias	serious[5]	serious[1]	no serious imprecision	none	50/646 (7.7%)	53/382 (13.9%)	RR 0.60 (0.42 to 0.86)	55 fewer per 1000 (from 19 fewer to 80 fewer)	⊕⊕OO LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Protein-containing synthetic surfactant	Animal-derived surfactant	Relative (95% CI)	Absolute		
Severe intraventricular haemorrhage (IVH) (assessed with: grade 3 or 4 IVH detected by ultrasound or computerized tomography [CT] scan of the head)												
1	randomized trials	no serious risk of bias	serious[4]	serious[1]	serious[2]	none	16/119 (13.4%)	11/124 (8.9%)	RR 1.52 (0.73 to 3.13)	46 more per 1000 (from 24 fewer to 189 more)	⨁◯◯◯ VERY LOW	CRITICAL

1 Both the studies were done in level-3 NICUs in high-income countries.
2 95% CI around the pooled estimate of effect includes both: (1) no effect and (2) increased risk.
3 Effect size of the two studies in different directions.
4 Single study.
5 Effect size of the two studies in same direction but $I^2 > 60\%$.

Table 9e. Prophylactic surfactant replacement therapy versus rescue surfactant therapy with or without continuous positive airway pressure (CPAP) for preterm newborns with respiratory distress syndrome

Source: Rojas-Reyes MX, Morley CJ, Soll R. Prophylactic versus selective use of surfactant in preventing morbidity and mortality in preterm infants. Cochrane Database Syst Rev. 2012;(3):CD000510.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prophylactic surfactant replacement therapy	Selective surfactant therapy	Relative (95% CI)	Absolute		
Neonatal mortality												
10	randomized trials	no serious risk of bias	serious[1]	serious[2]	no serious imprecision	none	246/2256 (10.9%)	274/2251 (12.2%)	RR 0.89 (0.76 to 1.04)	13 fewer per 1000 (from 29 fewer to 5 more)	⊕⊕OO LOW	CRITICAL
In-hospital mortality												
5	randomized trials	no serious risk of bias	serious[1]	serious[2]	serious[3]	none	101/728 (13.9%)	125/730 (17.1%)	RR 0.79 (0.63 to 10)	36 fewer per 1000 (from 63 fewer to 0 more)	⊕OOO VERY LOW	CRITICAL
Bronchopulmonary dysplasia												
10	randomized trials	no serious risk of bias	no serious inconsistency	serious[2]	no serious imprecision	none	362/1607 (22.5%)	357/1584 (22.5%)	RR 1.02 (0.91 to 1.14)	5 more per 1000 (from 20 fewer to 32 more)	⊕⊕⊕O MODERATE	CRITICAL
Air leaks												
9	randomized trials	no serious risk of bias	serious[5]	serious[2]	Serious[3]	none	165/2044 (8.1%)	189/2032 (9.3%)	RR 0.86 (0.71 to 1.04)	13 fewer per 1000 (from 27 fewer to 4 more)	⊕OOO VERY LOW	CRITICAL
Pulmonary haemorrhage												
4	randomized trials	no serious risk of bias	no serious inconsistency	serious[2]	very serious[3]	none	13/1015 (1.3%)	12/1008 (1.2%)	RR 1.05 (0.49 to 2.22)	1 more per 1000 (from 6 fewer to 15 more)	⊕OOO VERY LOW	CRITICAL
Sepsis												
6	randomized trials	no serious risk of bias	Serious[1]	serious[2]	Serious[3]	none	95/1227 (7.7%)	113/1211 (9.3%)	RR 0.83 (0.64 to 1.08)	16 fewer per 1000 (from 34 fewer to 7 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prophylactic surfactant replacement therapy	Selective surfactant therapy	Relative (95% CI)	Absolute		
Severe intraventricular haemorrhage												
10	randomized trials	no serious risk of bias	no serious inconsistency	serious[2]	Serious[3]	none	211/2170 (9.7%)	241/2177 (11.1%)	RR 0.87 (0.74 to 1.04)	14 fewer per 1000 (from 29 fewer to 4 more)	⊕⊕OO LOW	CRITICAL

1 Significant heterogeneity: $P < 0.05$; $I^2 > 50\%$.
2 All the studies were done in level-3 neonatal intensive care units in high-income countries.
3 Wide confidence interval around the pooled estimate of effect crossing the line of no effect.

Table 9f. Prophylactic surfactant replacement therapy versus rescue surfactant therapy without continuous positive airway pressure (CPAP) for preterm newborns with respiratory distress syndrome

Source: Rojas-Reyes MX, Morley CJ, Soll R. Prophylactic versus selective use of surfactant in preventing morbidity and mortality in preterm infants. Cochrane Database Syst Rev. 2012;(3):CD000510. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prophylactic surfactant replacement therapy	Rescue surfactant therapy without CPAP	Relative (95% CI)	Absolute (95% CI)		
Overall neonatal mortality												
8	randomized trials	serious[1]	not serious	serious[2]	not serious	none	122/1394 (8.8%)	172/1367 (12.6%)	RR 0.69 (0.56 to 0.85)	39 fewer per 1000 (from 19 fewer to 55 fewer)	⊕⊕OO LOW	CRITICAL
In-hospital mortality												
4	randomized trials	serious[1]	not serious	serious[2]	not serious	none	86/520 (16.5%)	116/510 (22.7%)	RR 0.72 (0.56 to 0.93)	64 fewer per 1000 (from 16 fewer to 100 fewer)	⊕⊕OO LOW	CRITICAL
Air leaks												
8	randomized trials	serious[1]	not serious	serious[2]	not serious	none	117/1391 (8.4%)	144/1369 (10.5%)	RR 0.79 (0.63 to 0.98)	22 fewer per 1000 (from 2 fewer to 39 fewer)	⊕⊕OO LOW	CRITICAL
Pulmonary haemorrhage												
3	randomized trials	serious[1]	not serious	serious[2]	serious[3]	none	7/806 (0.9%)	9/786 (1.1%)	RR 0.73 (0.28 to 1.87)	3 fewer per 1000 (from 8 fewer to 10 more)	⊕OOO VERY LOW	CRITICAL
Bronchopulmonary dysplasia												
9	randomized trials	serious[1]	not serious	serious[2]	serious[3]	none	235/1411 (16.7%)	242/1378 (17.6%)	RR 0.95 (0.81 to 1.11)	9 fewer per 1000 (from 19 more to 33 fewer)	⊕OOO VERY LOW	CRITICAL
Severe intraventricular haemorrhage												
8	randomized trials	serious[1]	not serious	serious[2]	serious[3]	none	127/1339 (9.5%)	143/1317 (10.9%)	RR 0.87 (0.70 to 1.08)	14 fewer per 1000 (from 9 more to 33 fewer)	⊕OOO VERY LOW	CRITICAL
Sepsis												
5	randomized trials	serious[1]	not serious	serious[2]	not serious	none	68/1022 (6.7%)	96/991 (9.7%)	RR 0.68 (0.51 to 0.92)	31 fewer per 1000 (from 8 fewer to 47 fewer)	⊕⊕OO LOW	CRITICAL

1 No blinding in the assessment of outcomes except one study.
2 All trials from level 3 neonatal Intensive care units in high-income countries.
3 Wide confidence intervals including no effect.

Table 9g. Prophylactic surfactant replacement therapy versus rescue surfactant therapy with continuous positive airway pressure (CPAP) for preterm newborns with respiratory distress syndrome

Source: Rojas-Reyes MX, Morley CJ, Soll R. Prophylactic versus selective use of surfactant in preventing morbidity and mortality in preterm infants. Cochrane Database Syst Rev. 2012;(3):CD000510. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prophylactic surfactant replacement therapy	Rescue surfactant therapy with CPAP	Relative (95% CI)	Absolute (95% CI)		
Overall neonatal mortality												
2	randomized trials	serious1	not serious	serious[2]	serious[3]	none	124/862 (14.4%)	172/884 (19.5%)	RR 1.24 (0.97 to 1.58)	47 more per 1000 (from 6 fewer to 113 more)	⊕OOO VERY LOW	CRITICAL
In-hospital mortality												
1	randomized trials	serious[1]	serious[4]	serious[2]	serious[3]	none	15/208 (7.2%)	9/220 (4.1%)	RR 1.76 (0.79 to 3.94)	31 more per 1000 (from 9 fewer to 120 more)	⊕OOO VERY LOW	CRITICAL
Air leaks												
1	randomized trials	serious[1]	serious[4]	serious[2]	serious[3]	none	48/653 (7.4%)	45/663 (6.8%)	RR 1.08 (0.73 to 1.60)	5 more per 1000 (from 18 fewer to 41 more)	⊕OOO VERY LOW	CRITICAL
Pulmonary haemorrhage												
1	randomized trials	serious[1]	serious[4]	serious[2]	serious[3]	none	6/209 (2.9%)	3/222 (1.4%)	RR 2.12 (0.54 to 8.39)	15 more per 1000 (from 6 fewer to 100 more)	⊕OOO VERY LOW	CRITICAL
Bronchopulmonary dysplasia												
1	randomized trials	serious[1]	serious[4]	serious[2]	serious[3]	none	127/196 (64.8%)	115/206 (55.8%)	RR 1.16 (0.99 to 1.36)	89 more per 1000 (from 6 fewer to 201 more)	⊕OOO VERY LOW	CRITICAL
Severe intraventricular haemorrhage												
2	randomized trials	serious[1]	not serious	serious[2]	serious[3]	none	12/72 (16.7%)	14/92 (15.2%)	RR 0.88 (0.67 to 1.16)	18 fewer per 1000 (from 24 more to 50 fewer)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prophylactic surfactant replacement therapy	Rescue surfactant therapy with CPAP	Relative (95% CI)	Absolute (95% CI)		
Sepsis												
1	randomized trials	serious[1]	serious[4]	serious[2]	serious[3]	none	27/205 (13.2%)	17/220 (7.7%)	RR 1.70 (0.96 to 3.03)	54 more per 1000 (from 3 fewer to 157 more)	⊕OOO VERY LOW	CRITICAL

1 No blinding in the assessment of outcomes except one study.
2 No trial from low- and middle-income countries.
3 Wide confidence intervals crossing the line of no effect.
4 Only one study, hence consistency could not be assessed.

Table 9h. Early surfactant replacement therapy (within 2—3 hours of birth) versus late rescue surfactant therapy (after waiting for symptoms to worsen) with or without continuous positive airway pressure (CPAP) for preterm newborns with respiratory distress syndrome

Source: Bahadue FL, Soll R. Early versus delayed selective surfactant treatment for neonatal respiratory distress syndrome. Cochrane Database Syst Rev. 2012;(11):CD001456. (updated for this guideline)

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early surfactant replacement therapy	Late rescue surfactant therapy	Relative (95% CI)	Absolute		
Neonatal mortality												
6	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	353/1782 (19.8%)	424/1795 (23.6%)	RR 0.84 (0.74 to 0.95)	38 fewer per 1000 (from 12 fewer to 61 fewer)	⊕⊕⊕O MODERATE	CRITICAL
In-hospital mortality												
5	randomized trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	376/1570 (23.9%)	431/1587 (27.2%)	RR 0.88 (0.78 to 0.99)	33 fewer per 1000 (from 3 fewer to 60 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Bronchopulmonary dysplasia (assessed with: use of supplemental oxygen at 36 weeks postmenstrual age)												
4	randomized trials	serious[3]	no serious inconsistency	serious[4]	no serious imprecision	none	118/1135 (10.4%)	177/1547 (11.4%)	RR 0.67 (0.54 to 0.84)	38 fewer per 1000 (from 18 fewer to 53 fewer)	⊕⊕OO LOW	CRITICAL
Air leaks (assessed with: any air leak syndromes such as pulmonary interstitial emphysema, pneumothorax, pneumomediastinum, etc.)												
2	randomized trials	no serious risk of bias	no serious inconsistency	serious[4]	no serious imprecision	none	65/233 (27.9%)	105/230 (45.7%)	RR 0.61 (0.48 to 0.78)	178 fewer per 1000 (from 100 fewer to 237 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Severe intraventricular haemorrhage												
3	randomized trials	serious[3]	no serious inconsistency	serious[4]	serious[5]	none	245/1519 (16.1%)	257/1531 (16.8%)	RR 0.96 (0.82 to 1.12)	7 fewer per 1000 (from 30 fewer to 20 more)	⊕OOO VERY LOW	CRITICAL

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Early surfactant replacement therapy	Late rescue surfactant therapy	Relative (95% CI)	Absolute		
Confirmed bacterial sepsis												
1	randomized trials	no serious risk of bias	serious[6]	no serious indirectness[7]	serious[5]	none	24/35 (68.6%)	24/40 (60%)	RR 1.14 (0.81 to 1.60)	84 more per 1000 (from 114 fewer to 360 more)	⊕⊕OO LOW	CRITICAL

1 All the studies were done in level-3 neonatal intensive care units (NICUs) in high-income countries except one.
2 We used the data from the studies with the lowest and highest risk in the control group to estimate the "low" and "high" control risk.
3 Subjective outcome; blinding of outcome assessment unclear (not mentioned) in all the studies.
4 All the studies were done in level-3 NICUs in high-income countries.
5 95% CI around the pooled estimate of effect includes both: (1) no effect and (2) increased risk.
6 Single study.
7 Conducted in a low- or middle-income country.

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