Annex 5. GRADE Tables

Question: Labetalol compared to hydralazine for treatment of very high blood pressure during pregnancy

Setting: hospitals in Northern Ireland, Panama (2), South Africa, United States (2)

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Maternal deaths												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/100 (0.0%)	0/100 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
Eclampsia												
2	randomized trials	serious [c]	not serious	not serious	very serious [b]	none	0/110 (0.0%)	0/110 (0.0%)	not pooled	see comment	⨁◯◯◯ VERY LOW	
Persistent high blood pressure												
4	randomized trials	serious [c]	not serious	not serious	very serious [d]	none	13/256 (5.1%)	13/254 (5.1%)	**RR 1.05** (0.32 to 3.43)	**3 more per 1,000** (from 35 fewer to 124 more)	⨁◯◯◯ VERY LOW	
Serious morbidity in women: acute renal insufficiency												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/100 (0.0%)	0/100 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
HELLP syndrome												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	2/100 (2.0%)	2/100 (2.0%)	**RR 1.00** (0.14 to 6.96)	**0 fewer per 1,000** (from 17 fewer to 119 more)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Serious morbidity in women: oliguria												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	2/100 (2.0%)	4/100 (4.0%)	**RR 0.50** (0.09 to 2.67)	**20 fewer per 1,000** (from 36 fewer to 67 more)	⨁◯◯◯ VERY LOW	
Serious morbidity in women: disseminated intravascular coagulation												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/100 (0.0%)	0/100 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
Serious morbidity in women: pulmonary oedema												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	1/100 (1.0%)	0/100 (0.0%)	**RR 3.00** (0.12 to 72.77)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	
Placental abruption												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	1/100 (1.0%)	2/100 (2.0%)	**RR 0.50** (0.05 to 5.43)	**10 fewer per 1,000** (from 19 fewer to 89 more)	⨁◯◯◯ VERY LOW	
Hypotension												
4	randomized trials	serious [c]	not serious	not serious	very serious [e]	none	0/140 (0.0%)	2/139 (1.4%)	**RR 0.20** (0.01 to 4.11)	**12 fewer per 1,000** (from 14 fewer to 45 more)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women												
3	randomized trials	serious [c]	not serious	not serious	very serious [f]	none	24/125 (19.2%)	31/125 (24.8%)	**RR 0.78** (0.49 to 1.23)	**55 fewer per 1,000** (from 57 more to 126 fewer)	⨁◯◯◯ VERY LOW	
Side-effects in women (headaches)												
1	randomized trials	serious [a]	not serious	not serious	very serious [f]	none	23/131 (17.6%)	30/130 (23.1%)	**RR 0.76** (0.47 to 1.24)	**55 fewer per 1,000** (from 55 more to 122 fewer)	⨁◯◯◯ VERY LOW	
Side-effects in women (visual symptoms)												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	11/131 (8.4%)	11/130 (8.5%)	**RR 0.99** (0.45 to 2.21)	**1 fewer per 1,000** (from 47 fewer to 102 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (epigastralgia)												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	9/131 (6.9%)	10/130 (7.7%)	**RR 0.89** (0.38 to 2.13)	**8 fewer per 1,000** (from 48 fewer to 87 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (palpitations)												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	8/131 (6.1%)	10/130 (7.7%)	**RR 0.79** (0.32 to 1.95)	**16 fewer per 1,000** (from 52 fewer to 73 more)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women (nausea)												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	6/131 (4.6%)	8/130 (6.2%)	**RR 0.74** (0.27 to 2.09)	**16 fewer per 1,000** (from 45 fewer to 67 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (flushing)												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	6/131 (4.6%)	4/130 (3.1%)	**RR 1.49** (0.43 to 5.15)	**15 more per 1,000** (from 18 fewer to 128 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (emesis)												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	2/131 (1.5%)	3/130 (2.3%)	**RR 0.66** (0.11 to 3.89)	**8 fewer per 1,000** (from 21 fewer to 67 more)	⨁◯◯◯ VERY LOW	
Fetal or neonatal deaths												
5	randomized trials	serious [c]	not serious	not serious	very serious [d]	none	3/155 (1.9%)	5/147 (3.4%)	**RR 0.63** (0.17 to 2.34)	**13 fewer per 1,000** (from 28 fewer to 46 more)	⨁◯◯◯ VERY LOW	
Apgar < 7 at 1 minute												
1	randomized trials	serious [a]	not serious	not serious	very serious [f]	none	20/103 (19.4%)	14/102 (13.7%)	**RR 1.41** (0.76 to 2.64)	**56 more per 1,000** (from 33 fewer to 225 more)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Apgar < 7 at 5 minutes												
2	randomized trials	serious [c]	serious [g]	not serious	very serious [e]	none	4/116 (3.4%)	4/108 (3.7%)	**RR 0.57** (0.03 to 10.36)	**16 fewer per 1,000** (from 36 fewer to 347 more)	⨁◯◯◯ VERY LOW	
Fetal heart rate decelerations												
4	randomized trials	serious [c]	not serious	not serious	very serious [e]	none	9/141 (6.4%)	10/133 (7.5%)	**RR 0.80** (0.13 to 4.95)	**15 fewer per 1,000** (from 65 fewer to 297 more)	⨁◯◯◯ VERY LOW	
Admission to special care baby unit												
1	randomized trials	serious [a]	not serious	not serious	very serious [f]	none	32/103 (31.1%)	32/102 (31.4%)	**RR 0.99** (0.66 to 1.49)	**3 fewer per 1,000** (from 107 fewer to 154 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (no blinding) contributing data (-1)
b. No events and small sample size (-2)
c. All studies have design limitations (-1)
d. Wide 95% CI crossing the line of no effect, low event rate (-2)
e. Wide 95% CI crossing the line of no effect, low event rate and small sample size (-2)
f. Wide 95% CI crossing the line of no effect and small sample size (-2)
g. Heterogeneity I2 = 68% (-1)

Question: Calcium channel blockers compared to hydralazine for treatment of very high blood pressure during pregnancy

Setting: hospitals in Brazil (2), India, Iran (2), Mexico, South Africa (2)

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Calcium channel blockers**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Maternal death												
1	randomized trials	not serious	not serious	not serious	very serious [a]	none	0/30 (0.0%)	0/30 (0.0%)	not estimable		⨁⨁◯◯ LOW	
Persistent high blood pressure												
6	randomized trials	serious [b]	not serious	not serious	not serious	none	13/160 (8.1%)	34/153 (22.2%)	**RR 0.37** (0.21 to 0.66)	**140 fewer per 1,000** (from 76 fewer to 176 fewer)	⨁⨁⨁◯ MODERATE	
Further episode/s of very high blood pressure												
2	randomized trials	serious [c]	not serious	not serious	very serious [d]	none	39/85 (45.9%)	43/78 (55.1%)	**RR 0.85** (0.65 to 1.11)	**83 fewer per 1,000** (from 61 more to 193 fewer)	⨁◯◯◯ VERY LOW	
Hypotension												
6	randomized trials	serious [b]	not serious	not serious	very serious [e]	none	3/167 (1.8%)	2/158 (1.3%)	**RR 1.12** (0.29 to 4.28)	**2 more per 1,000** (from 9 fewer to 42 more)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Calcium channel blockers**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women												
5	randomized trials	serious [b]	not serious	not serious	very serious [d]	none	25/147 (17.0%)	28/139 (20.1%)	**RR 0.81** (0.52 to 1.25)	**38 fewer per 1,000** (from 50 more to 97 fewer)	⨁◯◯◯ VERY LOW	
Side-effects in women (headache)												
5	randomized trials	serious [b]	not serious	not serious	very serious [f]	none	14/152 (9.2%)	11/144 (7.6%)	**RR 1.16** (0.56 to 2.42)	**12 more per 1,000** (from 34 fewer to 108 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (nausea and/or vomiting)												
5	randomized trials	serious [b]	not serious [g]	not serious	very serious [f]	none	12/117 (10.3%)	12/113 (10.6%)	**RR 0.97** (0.18 to 5.11)	**3 fewer per 1,000** (from 87 fewer to 436 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (palpitations)												
2	randomized trials	serious [c]	not serious	not serious	very serious [f]	none	8/45 (17.8%)	12/42 (28.6%)	**RR 0.63** (0.29 to 1.39)	**106 fewer per 1,000** (from 111 more to 203 fewer)	⨁◯◯◯ VERY LOW	
Side-effects in women (flushing)												
4	randomized trials	serious [b]	not serious	not serious	very serious [f]	none	11/87 (12.6%)	5/83 (6.0%)	**RR 1.04** (0.15 to 7.51)	**2 more per 1,000** (from 51 fewer to 392 more)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Calcium channel blockers**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women (nausea)												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	6/131 (4.6%)	8/130 (6.2%)	**RR 0.74** (0.27 to 2.09)	**16 fewer per 1,000** (from 45 fewer to 67 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (flushing)												
1	randomized trials	serious [a]	not serious	not serious	very serious [e]	none	6/131 (4.6%)	4/130 (3.1%)	**RR 1.49** (0.43 to 5.15)	**15 more per 1,000** (from 18 fewer to 128 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (dyspnoea)												
1	randomized trials	not serious	not serious	not serious	very serious [f]	none	1/20 (5.0%)	1/17 (5.9%)	**RR 0.85** (0.06 to 12.59)	**9 fewer per 1,000** (from 55 fewer to 682 more)	⨁⨁◯◯ LOW	
Side-effects in women (tachycardia)												
1	randomized trials	not serious	not serious	not serious	very serious [f]	none	2/30 (6.7%)	0/30 (0.0%)	**RR 5.00** (0.25 to 99.95)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁⨁◯◯ LOW	
Fetal or neonatal death												
5	randomized trials	serious [b]	not serious	not serious	very serious [f]	none	6/113 (5.3%)	4/108 (3.7%)	**RR 1.36** (0.42 to 4.41)	**13 more per 1,000** (from 21 fewer to 126 more)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Calcium channel blockers**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Apgar < 7 at 5 minutes												
2	randomized trials	not serious	not serious	not serious	very serious [f]	none	2/55 (3.6%)	1/55 (1.8%)	**RR 2.00** (0.19 to 20.90)	**18 more per 1,000** (from 15 fewer to 362 more)	⨁⨁◯◯ LOW	
Fetal heart rate decelerations												
4	randomized trials	serious [b]	not serious	not serious	very serious [f]	none	3/130 (2.3%)	8/123 (6.5%)	**RR 0.38** (0.11 to 1.31)	**40 fewer per 1,000** (from 20 more to 58 fewer)	⨁◯◯◯ VERY LOW	
Admission to NICU												
1	randomized trials	not serious	not serious	not serious	very serious [f]	none	2/30 (6.7%)	1/30 (3.3%)	**RR 2.00** (0.19 to 20.90)	**33 more per 1,000** (from 27 fewer to 663 more)	⨁⨁◯◯ LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. No events and small sample size (-2)
b. Most studies contributing data had design limitations (-1)
c. Most of the pooled effect provided by a study with design limitations (-1)
d. Wide 95% CI crossing the line of no effect, and small sample size (-2)
e. Wide 95% CI crossing the line of no effect and few events (-2)
f. Wide 95% CI crossing the line of no effect, small sample size and few events (-2)
g. Heterogeneity I2=58% (not downgraded)

Question: Prostacyclin compared to hydralazine for treatment of very high blood pressure during pregnancy

Setting: hospital in South Africa

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Prostacyclin**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Persistent high blood pressure												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/22 (0.0%)	2/25 (8.0%)	**RR 0.23** (0.01 to 4.47)	**62 fewer per 1,000** (from 79 fewer to 278 more)	⨁◯◯◯ VERY LOW	
Side-effects in women												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	1/22 (4.5%)	1/25 (4.0%)	**RR 1.14** (0.08 to 17.11)	**6 more per 1,000** (from 37 fewer to 644 more)	⨁◯◯◯ VERY LOW	
Neonatal death												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	1/22 (4.5%)	1/25 (4.0%)	**RR 1.14** (0.08 to 17.11)	**6 more per 1,000** (from 37 fewer to 644 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)

b. Wide 95% CI crossing the line of no effect, few events, and small sample size (-2)

Question: Ketanserin compared to hydralazine for treatment of very high blood pressure during pregnancy

Setting: hospitals in Netherlands (3), and South Africa (2)

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Ketanserin**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Maternal deaths												
2	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/64 (0.0%)	2/60 (3.3%)	**RR 0.32** (0.03 to 2.96)	**23 fewer per 1,000** (from 32 fewer to 65 more)	⨁◯◯◯ VERY LOW	
Eclampsia												
2	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	1/32 (3.1%)	2/32 (6.3%)	**RR 0.60** (0.08 to 4.24)	**25 fewer per 1,000** (from 58 fewer to 203 more)	⨁◯◯◯ VERY LOW	
Persistent high blood pressure												
4	randomized trials	serious [a]	not serious	not serious	serious [c]	none	37/111 (33.3%)	7/99 (7.1%)	**RR 4.99** (2.37 to 10.48)	**282 more per 1,000** (from 97 more to 670 more)	⨁⨁◯◯ LOW	
Severe maternal morbidity												
1	randomized trials	serious [d]	not serious	not serious	very serious [b]	none	3/32 (9.4%)	7/24 (29.2%)	**RR 0.32** (0.09 to 1.12)	**198 fewer per 1,000** (from 35 more to 265 fewer)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Ketanserin**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
HELLP syndrome												
2	randomized trials	serious [a]	not serious [e]	not serious	very serious [b]	none	3/37 (8.1%)	10/37 (27.0%)	**RR 0.53** (0.04 to 6.86)	**127 fewer per 1,000** (from 259 fewer to 1,000 more)	⨁◯◯◯ VERY LOW	
Serious morbidity in women: disseminated intravascular coagulation												
1	randomized trials	serious [d]	not serious	not serious	very serious [b]	none	1/22 (4.5%)	0/22 (0.0%)	**RR 3.00** (0.13 to 69.87)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	
Pulmonary oedema												
1	randomized trials	serious [d]	not serious	not serious	very serious [b]	none	0/22 (0.0%)	4/22 (18.2%)	**RR 0.11** (0.01 to 1.95)	**162 fewer per 1,000** (from 173 more to 180 fewer)	⨁◯◯◯ VERY LOW	
Hypotension												
3	randomized trials	serious [d]	not serious	not serious	serious [f]	none	4/57 (7.0%)	11/49 (22.4%)	**RR 0.34** (0.12 to 0.93)	**148 fewer per 1,000** (from 16 fewer to 198 fewer)	⨁⨁◯◯ LOW	
Placental abruption												
2	randomized trials	serious [d]	not serious	not serious	very serious [b]	none	0/32 (0.0%)	6/32 (18.8%)	**RR 0.14** (0.02 to 1.10)	**161 fewer per 1,000** (from 19 more to 184 fewer)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Ketanserin**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women												
3	randomized trials	serious [a]	not serious	not serious	serious [c]	none	13/64 (20.3%)	36/56 (64.3%)	**RR 0.32** (0.19 to 0.53)	**437 fewer per 1,000** (from 302 fewer to 521 fewer)	⨁⨁◯◯ LOW	
Side-effects in women (headache)												
1	randomized trials	not serious	not serious	not serious	very serious [b]	none	4/15 (26.7%)	6/15 (40.0%)	**RR 0.67** (0.23 to 1.89)	**132 fewer per 1,000** (from 308 fewer to 356 more)	⨁⨁◯◯ LOW	
Side-effects in women (nausea and/or vomiting)												
1	randomized trials	not serious	not serious	not serious	very serious [b]	none	0/15 (0.0%)	6/15 (40.0%)	**RR 0.08** (0.00 to 1.25)	**368 fewer per 1,000** (from -- to 100 more)	⨁⨁◯◯ LOW	
Side-effects in women (palpitations)												
1	randomized trials	not serious	not serious	not serious	very serious [b]	none	4/15 (26.7%)	5/15 (33.3%)	**RR 0.80** (0.27 to 2.41)	**67 fewer per 1,000** (from 243 fewer to 470 more)	⨁⨁◯◯ LOW	
Side-effects in women (tachycardia)												
1	randomized trials	not serious	not serious	not serious	very serious [b]	none	1/15 (6.7%)	6/15 (40.0%)	**RR 0.17** (0.02 to 1.22)	**332 fewer per 1,000** (from 88 more to 392 fewer)	⨁⨁◯◯ LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Ketanserin**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women (diarrhoea)												
1	randomized trials	not serious	not serious	not serious	very serious [b]	none	1/15 (6.7%)	2/15 (13.3%)	**RR 0.50** (0.05 to 4.94)	**67 fewer per 1,000** (from 127 fewer to 525 more)	⨁⨁◯◯ LOW	
Side-effects in women (tiredness)												
1	randomized trials	not serious	not serious	not serious	very serious [b]	none	6/15 (40.0%)	8/15 (53.3%)	**RR 0.75** (0.34 to 1.64)	**133 fewer per 1,000** (from 341 more to 352 fewer)	⨁⨁◯◯ LOW	
Side-effects in women (sleepiness)												
1	randomized trials	not serious	not serious	not serious	very serious [b]	none	7/15 (46.7%)	9/15 (60.0%)	**RR 0.78** (0.39 to 1.54)	**132 fewer per 1,000** (from 324 more to 366 fewer)	⨁⨁◯◯ LOW	
Side-effects in women (dry mouth)												
1	randomized trials	not serious	not serious	not serious	very serious [b]	none	9/15 (60.0%)	5/15 (33.3%)	**RR 1.80** (0.79 to 4.11)	**267 more per 1,000** (from 70 fewer to 1,000 more)	⨁⨁◯◯ LOW	
Side-effects in women (stuffy nose)												
1	randomized trials	not serious	not serious	not serious	very serious [b]	none	9/15 (60.0%)	7/15 (46.7%)	**RR 1.29** (0.65 to 2.54)	**135 more per 1,000** (from 163 fewer to 719 more)	⨁⨁◯◯ LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Ketanserin**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Perinatal death												
3	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	5/74 (6.8%)	5/72 (6.9%)	**RR 0.84** (0.09 to 8.19)	**11 fewer per 1,000** (from 63 fewer to 499 more)	⨁◯◯◯ VERY LOW	
Side effects - neonatal hypotension												
1	randomized trials	not serious	not serious	not serious	very serious [b]	none	4/12 (33.3%)	1/15 (6.7%)	**RR 5.00** (0.64 to 39.06)	**267 more per 1,000** (from 24 fewer to 1,000 more)	⨁⨁◯◯ LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Studies contributing data have design limitations (-1)
b. Wide 95% CI crossing the line of no effect, few events, and small sample size (-2)
c. Small sample size (-1)
d. Single study with design limitations (-1)
e. Heterogeneity I2 = 59% (not downgraded)
f. Few events and small sample size (-1)

Question: Urapidil compared to hydralazine for treatment of very high blood pressure during pregnancy

Setting: hospitals in Germany (2), and South Africa

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Urapidil**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Eclampsia												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/13 (0.0%)	0/13 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
Persistent high blood pressure												
3	randomized trials	serious c	not serious	not serious	very serious d	none	1/56 (1.8%)	1/45 (2.2%)	**RR 0.69** (0.08 to 5.66)	**7 fewer per 1,000** (from 20 fewer to 104 more)	⨁◯◯◯ VERY LOW	
Hypotension												
3	randomized trials	serious [c]	not serious	not serious	very serious [d]	none	3/56 (5.4%)	8/45 (17.8%)	**RR 0.32** (0.09 to 1.19)	**121 fewer per 1,000** (from 34 more to 162 fewer)	⨁◯◯◯ VERY LOW	
Side-effects in women												
3	randomized trials	serious [c]	not serious	not serious	very serious [d]	none	3/56 (5.4%)	8/45 (17.8%)	**RR 0.32** (0.09 to 1.19)	**121 fewer per 1,000** (from 34 more to 162 fewer)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Urapidil**	**Hydralazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Placental abruption												
1	randomized trials	serious [a]	not serious	not serious	very serious [d]	none	0/23 (0.0%)	1/10 (10.0%)	**RR 0.15** (0.01 to 3.46)	**85 fewer per 1,000** (from 99 fewer to 246 more)	⨁◯◯◯ VERY LOW	
Stillbirth												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/13 (0.0%)	0/13 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
Neonatal death												
3	randomized trials	serious [c]	not serious	not serious	very serious [d]	none	1/56 (1.8%)	2/45 (4.4%)	**RR 0.54** (0.10 to 3.03)	**20 fewer per 1,000** (from 40 fewer to 90 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)
b. No events, and small sample size (-2)
c. Most of the pooled effect provided by studies with design limitations (-1)
d. Wide confidence intervals crossing the line of no effect, few events, and small sample size (-2)

Question: Labetalol compared to calcium channel blockers for treatment of very high blood pressure during pregnancy

Setting: hospitals in China (2), India (2), Malaysia, and Tunisia

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Calcium channel blockers**	**Relative (95% CI)**	**Absolute (95% CI)**		
Maternal death												
1	randomized trials	not serious	not serious	not serious	very serious [a]	none	0/50 (0.0%)	0/50 (0.0%)	not estimable		⨁⨁◯◯ LOW	
Eclampsia												
3	randomized trials	serious [b]	not serious	not serious	very serious [c]	none	4/85 (4.7%)	3/85 (3.5%)	**RR 1.25** (0.35 to 4.52)	**9 more per 1,000** (from 23 fewer to 124 more)	⨁◯◯◯ VERY LOW	
Stroke												
1	randomized trials	not serious	not serious	not serious	very serious [c]	none	2/50 (4.0%)	1/50 (2.0%)	**RR 2.00** (0.19 to 21.36)	**20 more per 1,000** (from 16 fewer to 407 more)	⨁⨁◯◯ LOW	
Persistent high blood pressure												
3	randomized trials	serious [b]	not serious	not serious	very serious [c]	none	21/85 (24.7%)	15/85 (17.6%)	**RR 1.29** (0.72 to 2.31)	**51 more per 1,000** (from 49 fewer to 231 more)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Calcium channel blockers**	**Relative (95% CI)**	**Absolute (95% CI)**		
Any serious morbidity: heart failure												
1	randomized trials	not serious	not serious	not serious	very serious [c]	none	1/50 (2.0%)	1/50 (2.0%)	**RR 1.00** (0.06 to 15.55)	**0 fewer per 1,000** (from 19 fewer to 291 more)	⨁⨁◯◯ LOW	
Hypotension												
5	randomized trials	serious [d]	not serious	not serious	very serious [e]	none	0/168 (0.0%)	0/169 (0.0%)	not pooled	see comment	⨁◯◯◯ VERY LOW	
Side-effects in women												
2	randomized trials	serious [b]	not serious	not serious	very serious [f]	none	27/98 (27.6%)	17/99 (17.2%)	**RR 1.60** (0.94 to 2.72)	**103 more per 1,000** (from 10 fewer to 295 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (headache - mild)												
1	randomized trials	serious [g]	not serious	not serious	very serious [c]	none	2/73 (2.7%)	4/74 (5.4%)	**RR 0.51** (0.10 to 2.68)	**26 fewer per 1,000** (from 49 fewer to 91 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (nausea and/or vomiting)												
2	randomized trials	serious [d]	not serious	not serious	very serious [c]	none	4/103 (3.9%)	2/104 (1.9%)	**RR 2.02** (0.38 to 10.77)	**20 more per 1,000** (from 12 fewer to 188 more)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Calcium channel blockers**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women (palpitations)												
1	randomized trials	serious [g]	not serious	not serious	very serious [a]	none	0/30 (0.0%)	0/30 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
Side-effects in women (moderate tachycardia)												
1	randomized trials	serious [g]	not serious	not serious	very serious [c]	none	0/10 (0.0%)	1/10 (10.0%)	**RR 0.33** (0.02 to 7.32)	**67 fewer per 1,000** (from 98 fewer to 632 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (tachycardia)												
1	randomized trials	serious [g]	not serious	not serious	very serious [c]	none	4/73 (5.5%)	3/74 (4.1%)	**RR 1.35** (0.31 to 5.83)	**14 more per 1,000** (from 28 fewer to 196 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (dizziness)												
1	randomized trials	serious [g]	not serious	not serious	very serious [c]	none	3/73 (4.1%)	2/74 (2.7%)	**RR 1.52** (0.26 to 8.84)	**14 more per 1,000** (from 20 fewer to 212 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (chest pain)												
1	randomized trials	serious [g]	not serious	not serious	very serious [a]	none	0/73 (0.0%)	0/74 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Calcium channel blockers**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women (shortness of breath)												
1	randomized trials	serious [g]	not serious	not serious	very serious [a]	none	0/73 (0.0%)	0/74 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
Postpartum haemorrhage: defined as blood loss of 500ml or more												
1	randomized trials	serious [g]	not serious	not serious	serious [h]	none	2/60 (3.3%)	15/60 (25.0%)	**RR 0.13** (0.03 to 0.56)	**218 fewer per 1,000** (from 110 fewer to 243 fewer)	⨁⨁◯◯ LOW	
Admission to intensive care												
1	randomized trials	not serious	not serious	not serious	very serious [c]	none	2/25 (8.0%)	0/25 (0.0%)	**RR 5.00** (0.25 to 99.16)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁⨁◯◯ LOW	
Perinatal death												
1	randomized trials	not serious	not serious	not serious	very serious [c]	none	2/30 (6.7%)	0/30 (0.0%)	**RR 5.00** (0.25 to 99.95)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁⨁◯◯ LOW	
Apgar score <7 at five minutes												
4	randomized trials	serious [b]	not serious	not serious	serious [i]	none	24/213 (11.3%)	25/214 (11.7%)	**RR 1.02** (0.40 to 2.62)	**2 more per 1,000** (from 70 fewer to 189 more)	⨁⨁◯◯ LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Calcium channel blockers**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects associated with drug - FHR abnormality												
1	randomized trials	not serious	not serious	not serious	very serious [c]	none	3/50 (6.0%)	6/50 (12.0%)	**RR 0.50** (0.13 to 1.89)	**60 fewer per 1,000** (from 104 fewer to 107 more)	⨁⨁◯◯ LOW	
Admission to special care baby unit												
3	randomized trials	not serious	not serious	not serious	very serious [c]	none	11/105 (10.5%)	6/105 (5.7%)	**RR 1.83** (0.71 to 4.75)	**47 more per 1,000** (from 17 fewer to 214 more)	⨁⨁◯◯ LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. No events and small sample size (-2)
b. Substantial proportion of pooled effect (>50%) from study with design limitations (-1)
c. Wide confidence interval crossing the line of no effect, small sample size and few events (-2)
d. Contributing studies have design limitations (-1)
e. No events (-2)
f. Wide confidence interval crossing the line of no effect, and small sample size (-2)
g. Single study with design limitations (-1)
h. Small sample size and few events (-1)
i. Wide 95% CI crossing line of no effect (-1)

Question: Labetalol compared to methyldopa for treatment of very high blood pressure during pregnancy

Setting: hospital in the United Kingdom.

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Methyldopa**	**Relative (95% CI)**	**Absolute (95% CI)**		
Persistent high blood pressure												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	20/38 (52.6%)	15/34 (44.1%)	**RR 1.19** (0.74 to 1.94)	**84 more per 1,000** (from 115 fewer to 415 more)	⨁◯◯◯ VERY LOW	
Changed drugs due to side-effects												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	4/38 (10.5%)	0/34 (0.0%)	**RR 8.08** (0.45 to 144.73)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	
Fetal or neonatal death - Stillbirth												
1	randomized trials	serious [a]	not serious	not serious	very serious [d]	none	0/38 (0.0%)	0/34 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
Fetal or neonatal death - Neonatal death												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	2/38 (5.3%)	0/34 (0.0%)	**RR 4.49** (0.22 to 90.30)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Methyldopa**	**Relative (95% CI)**	**Absolute (95% CI)**		
Admission to special care baby unit												
1	randomized trials	serious a	not serious	not serious	very serious b	none	19/38 (50.0%)	16/34 (47.1%)	**RR 1.06** (0.66 to 1.71)	**28 more per 1,000** (from 160 fewer to 334 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)
b. Wide 95% CI crossing the line of no effect, and small sample size (-2)
c. Wide 95% CI crossing the line of no effect, few events and small sample size (-2)
d. No events and small sample size (-2)

Question: Labetalol compared to diazoxide for treatment of very high blood pressure during pregnancy

Setting: hospital in Australia.

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Labetalol**	**Diazoxide**	**Relative (95% CI)**	**Absolute (95% CI)**		
Persistent high blood pressure												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	3/45 (6.7%)	6/45 (13.3%)	**RR 0.50** (0.13 to 1.88)	**67 fewer per 1,000** (from 116 fewer to 117 more)	⨁◯◯◯ VERY LOW	
Hypotension												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	0/45 (0.0%)	8/45 (17.8%)	**RR 0.06** (0.00 to 0.99)	**167 fewer per 1,000** (from -- to 2 fewer)	⨁◯◯◯ VERY LOW	
Perinatal deaths												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/45 (0.0%)	3/45 (6.7%)	**RR 0.14** (0.01 to 2.69)	**57 fewer per 1,000** (from 66 fewer to 113 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)
b. Wide 95% CI crossing the line of no effect, few events and small sample size (-2)
c. Small sample size and few events (-1)

Question: Nitrates compared to magnesium sulfate for treatment of very high blood pressure during pregnancy

Setting: hospital in Mexico

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Nitrates**	**Magnesium sulfate**	**Relative (95% CI)**	**Absolute (95% CI)**		
Eclampsia												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/18 (0.0%)	0/18 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
Persistent high blood pressure												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	0/18 (0.0%)	3/18 (16.7%)	**RR 0.14** (0.01 to 2.58)	**143 fewer per 1,000** (from 165 fewer to 263 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)
b. No events and small sample size (-2)
c. Wide 95% confidence interval crossing the line of no effect, small sample size and few events (-2)

Question: Nimodipine compared to magnesium sulfate for treatment of very high blood pressure during pregnancy

Setting: hospitals in Turkey, and eight countries in a multicentre trial.

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Nimodipine**	**Magnesium sulfate**	**Relative (95% CI)**	**Absolute (95% CI)**		
Eclampsia												
2	randomized trials	serious [a]	not serious	not serious	serious [b]	none	21/837 (2.5%)	9/846 (1.1%)	**RR 1.03** (0.07 to 16.03)	**0 fewer per 1,000** (from 10 fewer to 160 more)	⨁⨁◯◯ LOW	
Stroke												
1	randomized trials	serious [c]	not serious	not serious	serious [d]	none	0/819 (0.0%)	0/831 (0.0%)	not estimable		⨁⨁◯◯ LOW	
Persistent high blood pressure												
1	randomized trials	serious [c]	not serious	not serious	not serious	none	374/819 (45.7%)	451/831 (54.3%)	**RR 0.84** (0.76 to 0.93)	**87 fewer per 1,000** (from 38 fewer to 130 fewer)	⨁⨁⨁◯ MODERATE	
Coagulopathy in women												
1	randomized trials	serious [c]	not serious	not serious	very serious [e]	none	5/819 (0.6%)	3/831 (0.4%)	**RR 1.69** (0.41 to 7.05)	**2 more per 1,000** (from 2 fewer to 22 more)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Nimodipine**	**Magnesium sulfate**	**Relative (95% CI)**	**Absolute (95% CI)**		
Serious morbidity in women: Oliguria												
1	randomized trials	serious [c]	not serious	not serious	serious [b]	none	47/819 (5.7%)	55/831 (6.6%)	**RR 0.87** (0.59 to 1.26)	**9 fewer per 1,000** (from 17 more to 27 fewer)	⨁⨁◯◯ LOW	
Hypotension												
1	randomized trials	serious [c]	not serious	not serious	very serious [e]	none	5/819 (0.6%)	7/831 (0.8%)	**RR 0.72** (0.23 to 2.27)	**2 fewer per 1,000** (from 6 fewer to 11 more)	⨁◯◯◯ VERY LOW	
Postpartum haemorrhage												
1	randomized trials	serious [c]	not serious	not serious	serious [f]	none	8/819 (1.0%)	20/831 (2.4%)	**RR 0.41** (0.18 to 0.92)	**14 fewer per 1,000** (from 2 fewer to 20 fewer)	⨁⨁◯◯ LOW	
Placental abruption												
1	randomized trials	serious [c]	not serious	not serious	very serious [e]	none	6/819 (0.7%)	8/831 (1.0%)	**RR 0.76** (0.27 to 2.18)	**2 fewer per 1,000** (from 7 fewer to 11 more)	⨁◯◯◯ VERY LOW	
Respiratory difficulty in women												
1	randomized trials	serious [c]	not serious	not serious	serious [f]	none	3/819 (0.4%)	11/831 (1.3%)	**RR 0.28** (0.08 to 0.99)	**10 fewer per 1,000** (from 0 fewer to 12 fewer)	⨁⨁◯◯ LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Nimodipine**	**Magnesium sulfate**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women (all side-effects)												
1	randomized trials	serious [c]	not serious	not serious	not serious	none	109/819 (13.3%)	162/831 (19.5%)	**RR 0.68** (0.55 to 0.85)	**62 fewer per 1,000** (from 29 fewer to 88 fewer)	⨁⨁⨁◯ MODERATE	
Side-effects in women (headache)												
1	randomized trials	serious [c]	not serious	not serious	very serious [b]	none	47/819 (5.7%)	45/831 (5.4%)	**RR 1.06** (0.71 to 1.58)	**3 more per 1,000** (from 16 fewer to 31 more)	⨁◯◯◯ VERY LOW	
Side-effects in women (nausea and/or vomiting)												
1	randomized trials	serious [c]	not serious	not serious	serious [b]	none	49/819 (6.0%)	58/831 (7.0%)	**RR 0.86** (0.59 to 1.24)	**10 fewer per 1,000** (from 17 more to 29 fewer)	⨁⨁◯◯ LOW	
Side-effects in women (flushing)												
1	randomized trials	serious [c]	not serious	not serious	not serious	none	13/819 (1.6%)	59/831 (7.1%)	**RR 0.22** (0.12 to 0.40)	**55 fewer per 1,000** (from 43 fewer to 62 fewer)	⨁⨁⨁◯ MODERATE	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Nimodipine**	**Magnesium sulfate**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects: Low blood pressure in babies												
1	randomized trials	serious [c]	not serious	not serious	very serious [e]	none	6/767 (0.8%)	2/797 (0.3%)	**RR 3.12** (0.63 to 15.40)	**5 more per 1,000** (from 1 fewer to 36 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Studies contributing data had design limitations (-1)
b. Wide 95% CI crossing the line of no effect (-1)
c. Single study with design limitations (-1)
d. No events (-2)
e. Wide 95% CI crossing the line of no effect, low event rate (-2)
f. Low event rate (-1)

Question: Nifedipine compared to prazosin for treatment of very high blood pressure during pregnancy

Setting: hospital in South Africa

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Nifedipine**	**Prazosin**	**Relative (95% CI)**	**Absolute (95% CI)**		
Maternal death												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/74 (0.0%)	1/71 (1.4%)	**RR 0.32** (0.01 to 7.73)	**10 fewer per 1,000** (from 14 fewer to 95 more)	⨁◯◯◯ VERY LOW	
Eclampsia												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	0/74 (0.0%)	0/71 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
HELLP syndrome												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	6/74 (8.1%)	5/71 (7.0%)	**RR 1.15** (0.37 to 3.60)	**11 more per 1,000** (from 44 fewer to 183 more)	⨁◯◯◯ VERY LOW	
Renal failure												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	1/74 (1.4%)	2/71 (2.8%)	**RR 0.48** (0.04 to 5.17)	**15 fewer per 1,000** (from 27 fewer to 117 more)	⨁◯◯◯ VERY LOW	
Pulmonary oedema												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	1/74 (1.4%)	5/71 (7.0%)	**RR 0.19** (0.02 to 1.60)	**57 fewer per 1,000** (from 42 more to 69 fewer)	⨁◯◯◯ VERY LOW	

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Nifedipine**	**Prazosin**	**Relative (95% CI)**	**Absolute (95% CI)**		
Placental abruption												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	9/74 (12.2%)	9/71 (12.7%)	**RR 0.96** (0.40 to 2.28)	**5 fewer per 1,000** (from 76 fewer to 162 more)	⨁◯◯◯ VERY LOW	
Admission to intensive care												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/74 (0.0%)	1/71 (1.4%)	**RR 0.32** (0.01 to 7.73)	**10 fewer per 1,000** (from 14 fewer to 95 more)	⨁◯◯◯ VERY LOW	
Stillbirth												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	6/75 (8.0%)	13/74 (17.6%)	**RR 0.46** (0.18 to 1.13)	**95 fewer per 1,000** (from 23 more to 144 fewer)	⨁◯◯◯ VERY LOW	
Admission to special care baby unit												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	22/69 (31.9%)	25/61 (41.0%)	**RR 0.78** (0.49 to 1.23)	**90 fewer per 1,000** (from 94 more to 209 fewer)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)
b. Wide 95% CI crossing the line of no effect, low event rate and small sample size (-2)
c. No events and small sample size (-2)

Question: Nifedipine compared to chlorpromazine for treatment of very high blood pressure during pregnancy

Setting: hospital in Mexico

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Nifedipine**	**Chlorpromazine**	**Relative (95% CI)**	**Absolute (95% CI)**		
Eclampsia												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	1/30 (3.3%)	0/25 (0.0%)	**RR 2.52** (0.11 to 59.18)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	
Persistent high blood pressure												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/30 (0.0%)	5/30 (16.7%)	**RR 0.09** (0.01 to 1.57)	**152 fewer per 1,000** (from 95 more to 165 fewer)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)
b. Wide 95% CI crossing the line of no effect, low event rate and small sample size (-2)

Question: Hydralazine compared to diazoxide for treatment of very high blood pressure during pregnancy

Setting: hospital in Australia

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Hydralazine**	**Diazoxide**	**Relative (95% CI)**	**Absolute (95% CI)**		
Perinatal death												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	3/49 (6.1%)	0/52 (0.0%)	**RR 7.42** (0.39 to 140.06)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	
Stillbirth												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	2/49 (4.1%)	0/52 (0.0%)	**RR 5.30** (0.26 to 107.70)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	
Neonatal death												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/49 (0.0%)	1/52 (1.9%)	**RR 0.35** (0.01 to 8.47)	**13 fewer per 1,000** (from 19 fewer to 144 more)	⨁◯◯◯ VERY LOW	
Apgar score < 7 at 5 minutes												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	4/49 (8.2%)	4/52 (7.7%)	**RR 1.06** (0.28 to 4.01)	**5 more per 1,000** (from 55 fewer to 232 more)	⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)

b. Wide 95% CI crossing the line of no effect, low event rate and small sample size (-2)

Question: Methyldopa compared to atenolol for treatment of very high blood pressure during pregnancy

Setting: hospital in Argentina

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Methyldopa**	**Atenolol**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women (somnolence)												
1	randomized trials	serious [a]	not serious	not serious	serious [b]	none	10/30 (33.3%)	0/30 (0.0%)	**RR 21.00** (1.29 to 342.93)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁⨁◯◯ LOW	
Stillbirth												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	1/30 (3.3%)	1/30 (3.3%)	**RR 1.00** (0.07 to 15.26)	**0 fewer per 1,000** (from 31 fewer to 475 more)	⨁◯◯◯ VERY LOW	
Neonatal death												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	1/30 (3.3%)	1/30 (3.3%)	**RR 1.00** (0.07 to 15.26)	**0 fewer per 1,000** (from 31 fewer to 475 more)	⨁◯◯◯ VERY LOW	
Side-effects in babies												
1	randomized trials	serious [a]	not serious	not serious	very serious [d]	none	0/30 (0.0%)	0/30 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)
b. Low event rate and small sample size (-1)
c. Wide 95% CI crossing the line of no effect, low event rate and small sample size (-2)
d. No events and small sample size (-2)

Question: Methyldopa compared to ketanserin for treatment of very high blood pressure during pregnancy

Setting: hospital in Argentina

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Methyldopa**	**Ketanserin**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women (somnolence)												
1	randomized trials	serious [a]	not serious	not serious	serious [b]	none	10/30 (33.3%)	0/30 (0.0%)	**RR 21.00** (1.29 to 342.93)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁⨁◯◯ LOW	
Stillbirth												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	1/30 (3.3%)	0/30 (0.0%)	**RR 3.00** (0.13 to 70.83)	**0 fewer per 1,000** (from 0 fewer to 0 fewer)	⨁◯◯◯ VERY LOW	
Neonatal death												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	1/30 (3.3%)	3/30 (10.0%)	**RR 0.33** (0.04 to 3.03)	**67 fewer per 1,000** (from 96 fewer to 203 more)	⨁◯◯◯ VERY LOW	
Side-effects in babies												
1	randomized trials	serious [a]	not serious	not serious	very serious [d]	none	0/30 (0.0%)	0/30 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)
b. Low event rate and small sample size (-1)
c. Wide 95% CI crossing the line of no effect, low event rate and small sample size (-2)
d. No events and small sample size (-2)

Question: Ketanserin compared to atenolol for treatment of very high blood pressure during pregnancy

Setting: hospital in Argentina

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Ketanserin**	**Atenolol**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women (somnolence)												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/30 (0.0%)	0/30 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	
Stillbirth												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	0/30 (0.0%)	1/30 (3.3%)	**RR 0.33** (0.01 to 7.87)	**22 fewer per 1,000** (from 33 fewer to 229 more)	⨁◯◯◯ VERY LOW	
Neonatal death												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	3/30 (10.0%)	1/30 (3.3%)	**RR 3.00** (0.33 to 27.23)	**67 more per 1,000** (from 22 fewer to 874 more)	⨁◯◯◯ VERY LOW	
Side-effects in babies												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	0/30 (0.0%)	0/30 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)
b. No events and small sample size (-2)
c. Wide 95% CI crossing the line of no effect, low event rate and small sample size (-2)

Question: Urapidil compared to calcium channel blockers for treatment of very high blood pressure during pregnancy

Setting: Hospital in France

Certainty assessment							№ of women		Effect		Certainty	Importance
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Urapidil**	**Calcium channel blockers**	**Relative (95% CI)**	**Absolute (95% CI)**		
Side-effects in women												
1	randomized trials	serious [a]	not serious	not serious	very serious [b]	none	1/9 (11.1%)	6/9 (66.7%)	**RR 0.17** (0.02 to 1.12)	**553 fewer per 1,000** (from 80 more to 653 fewer)	⨁◯◯◯ VERY LOW	
Side-effects in babies												
1	randomized trials	serious [a]	not serious	not serious	very serious [c]	none	0/9 (0.0%)	0/9 (0.0%)	not estimable		⨁◯◯◯ VERY LOW	

CI: Confidence interval; **RR:** Risk ratio

Explanations

a. Single study with design limitations (-1)
b. Wide 95% CI crossing the line of no effect, low event rate and small sample size (-2)
c. No events and small sample size (-2)