



WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia

Evidence base

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Note: Systematic reviews identified with an asterisk have been updated during the preparation of this guideline. Hence, data used in the GRADE tables may differ from existing published version.

Box 1. Standard criteria for grading of evidence¹

Domain	Grade	Characteristic
STUDY DESIGN	0	All randomized controlled trials
	-1	All observational studies
STUDY DESIGN LIMITATIONS	0	Most of the pooled effect provided by studies, with low risk of bias ("A")
	-1	Most of the pooled effect provided by studies with moderate ("B") or high ("C") risk of bias. Studies with high risk of bias weighs <40%
	-2	Most of the pooled effect provided by studies with moderate ("B") or high ("C") risk of bias. Studies with high risk of bias weighs ≥40%
	Note:	Low risk of bias (no limitations or minor limitations) –“A” Moderate risk of bias (serious limitations or potentially very serious limitations including unclear concealment of allocation or serious limitations, excluding limitations on randomization or concealment of allocation) –“B” High risk of bias (Limitations for randomization, concealment of allocation, including small blocked randomization (<10) or other very serious, crucial methodological limitations) –“C”
INCONSISTENCY	0	No severe heterogeneity ($I^2 < 60\%$ or $\chi^2 \geq 0.05$)
	-1	Severe, non-explained, heterogeneity ($I^2 \geq 60\%$ or $\chi^2 < 0.05$) If heterogeneity could be caused by publication bias or imprecision due to small studies, downgrade only for publication bias or imprecision (i.e. the same weakness should not be downgraded twice)
INDIRECTNESS	0	No indirectness
	-1	Presence of indirect comparison, population, intervention, comparator, or outcome.

¹ Adapted from: Schünemann H, Brozek J, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. The GRADE Working Group. Available at: <<http://ims.cochrane.org/revman/grade-pro>>. (This document is contained within the “Help” section of the GRADE profiler software version v.3.2.2.)

Box 1 (continued)

Domain	Grade	Characteristic
IMPRECISION	0	<p>The confidence interval is precise according to the figure below.</p> <p>The total cumulative study population is not very small (i.e. sample size is more than 300 participants) and the total number of events is more than 30.</p>
	-1	One of the above-mentioned conditions is not fulfilled.
	-2	The two above-mentioned are not fulfilled.
	<p>Note: If the total number of events is less than 30 and the total cumulative sample size is appropriately large (e.g. above 3000 patients, consider not downgrading the evidence). If there are no events in both intervention and control groups, the quality of evidence in the specific outcome should be regarded as very low.</p>	
PUBLICATION BIAS	0	No evident asymmetry in the funnel plot or less than five studies to be plotted.
	-1	Evident asymmetry in funnel plot with at least five studies.

Table 1. Rest alone versus unrestricted activity

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Rest alone versus unrestricted activity	Control	Relative (95% CI)	Absolute		Quality
Gestational hypertension												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	1/16 (6.3%)	4/16 (25%)	RR 0.25 (0.03–2)	188 fewer per 1000 (from 243 fewer to 250 more)	VERY LOW	CRITICAL
Pre-eclampsia												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	0/16 (0%)	9/16 (56.3%)	RR 0.05 (0–0.83)	534 fewer per 1000 (from 96 fewer to 562 fewer)	LOW	CRITICAL

¹ The only study was at moderate risk of bias.

² Very small sample size and few events.

Source of evidence: Meher S, Duley L. Rest during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure. Cochrane Database of Systematic Reviews, 2006, Issue 2. Art. No.: CD005939. DOI: 10.1002/14651858.CD005939

Table 2. Rest plus nutrient supplementation versus unrestricted activity plus placebo

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Rest plus nutrient supplementation versus unrestricted activity plus placebo	Control	Relative (95% CI)	Absolute		
Gestational hypertension												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ¹	none	2/37 (5.4%)	13/37 (35.1%)	RR 0.15 (0.04–0.63)	299 fewer per 1000 (from 130 fewer to 337 fewer)	LOW	CRITICAL
Pre-eclampsia												
1	randomized trials	serious ²	no serious inconsistency	no serious indirectness	serious ¹	none	2/37 (5.4%)	16/37 (43.2%)	RR 0.12 (0.03–0.51)	381 fewer per 1000 (from 212 fewer to 419 fewer)	LOW	CRITICAL

1 Very small sample size and few events.

2 The only study was at moderate risk of bias.

Source of evidence: Meher S, Duley L. Rest during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure. Cochrane Database of Systematic Reviews, 2006, Issue 2. Art. No.: CD005939. DOI: 10.1002/14651858.CD005939.*

Table 3. Strict bedrest in hospital versus some rest in hospital for hypertension during pregnancy

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Strict bedrest in hospital versus some rest in hospital	Control	Relative (95% CI)	Absolute			
Eclampsia													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	0/53 (0%)	1/52 (1.9%)	RR 0.33 (0.01–7.85)	13 fewer per 1000 (from 19 fewer to 132 more)	LOW	CRITICAL	
Death of baby by timing of death – Perinatal death													
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	13/73 (17.8%)	12/72 (16.7%)	RR 1.07 (0.52–2.19)	12 more per 1000 (from 80 fewer to 198 more)	LOW	CRITICAL	
Admission to neonatal intensive care nursery													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	20/53 (37.7%)	26/52 (50%)	RR 0.75 (0.49–1.17)	125 fewer per 1000 (from 255 fewer to 85 more)	LOW	CRITICAL	

1 Very small sample size and few events; wide confidence interval.

Source of evidence: Meher S, Abalos E, Carroli G. Bed rest with or without hospitalisation for hypertension during pregnancy. Cochrane Database of Systematic Reviews, 2005, Issue 4. Art. No.: CD003514. DOI: 10.1002/14651858.CD003514.pub2.*

Table 4. Some rest in hospital versus routine activity at home

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Some rest in hospital versus routine activity at home	Control	Relative (95% CI)	Absolute		
Pre-eclampsia												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	69/110 (62.7%)	69/108 (63.9%)	RR 0.98 (0.8–1.2)	13 fewer per 1000 (from 128 fewer to 128 more)	MODERATE	CRITICAL
Death of baby by timing of death – Perinatal death												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	2/110 (1.8%)	1/108 (0.9%)	RR 1.96 (0.18–21.34)	9 more per 1000 (from 8 fewer to 188 more)	LOW	CRITICAL
Admission to neonatal intensive care nursery												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	10/110 (9.1%)	12/108 (11.1%)	RR 0.82 (0.37–1.81)	20 fewer per 1000 (from 70 fewer to 90 more)	LOW	

1 Very small sample size.

2 Very small sample size and few events; wide confidence interval.

Source of evidence: Meher S, Abalos E, Carroli G. Bed rest with or without hospitalisation for hypertension during pregnancy. Cochrane Database of Systematic Reviews, 2005, Issue 4. Art. No.: CD003514. DOI: 10.1002/14651858.CD003514.pub2.*

Table 5. Low versus normal salt intake in pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Low versus normal salt intake in pregnancy	Control	Relative (95% CI)	Absolute		Quality
Pre-eclampsia												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	10/294 (3.4%)	9/309 (2.9%)	RR 1.11 (0.46–2.66)	3 more per 1000 (from 16 fewer to 48 more)	MODERATE	CRITICAL
Perinatal death												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	2/206 (1%)	1/203 (0.5%)	RR 1.92 (0.18–21.03)	5 more per 1000 (from 4 fewer to 99 more)	MODERATE	CRITICAL
Admission to neonatal intensive care unit												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	47/184 (25.5%)	46/177 (26%)	RR 0.98 (0.69–1.4)	5 fewer per 1000 (from 81 fewer to 104 more)	MODERATE	CRITICAL
Apgar score <7 at 5 minutes												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	10/184 (5.4%)	7/177 (4%)	RR 1.37 (0.53–3.53)	15 more per 1000 (from 19 fewer to 100 more)	MODERATE	CRITICAL

¹ Wide confidence interval.

Source of evidence: Duley L, Henderson-Smart D, Meher S. Altered dietary salt for preventing pre-eclampsia, and its complications. Cochrane Database Syst Rev. 2005 Oct 19;(4):CD005548.*

Table 6. Routine calcium supplementation in pregnancy by hypertension risk for preventing hypertensive disorders and related problems

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Routine calcium supplementation in pregnancy by hypertension risk	Control	Relative (95% CI)	Absolute		
Pre-eclampsia												
13	randomized trials	no serious limitations	serious ¹	no serious indirectness	no serious imprecision	none	379/7851 (4.8%)	510/7879 (6.5%)	RR 0.45 (0.31–0.65)	36 fewer per 1000 (from 23 fewer to 45 fewer)	MODERATE	CRITICAL
Pre-eclampsia – Low-risk women												
8	randomized trials	no serious limitations	serious ¹	no serious indirectness	no serious imprecision	none	370/7570 (4.9%)	456/7573 (6%)	RR 0.59 (0.41–0.83)	25 fewer per 1000 (from 10 fewer to 36 fewer)	MODERATE	CRITICAL
Pre-eclampsia – High-risk women												
5	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	9/281 (3.2%)	54/306 (17.6%)	RR 0.22 (0.12–0.42)	138 fewer per 1000 (from 102 fewer to 155 fewer)	HIGH	CRITICAL
Stillbirth or death before discharge from hospital												
11	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision ²	none	183/7821 (2.3%)	205/7844 (2.6%)	RR 0.9 (0.74–1.09)	3 fewer per 1000 (from 7 fewer to 2 more)	HIGH	CRITICAL
Stillbirth or death before discharge from hospital – Low-risk women												
8	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision ²	none	183/7573 (2.4%)	204/7580 (2.7%)	RR 0.9 (0.74–1.09)	3 fewer per 1000 (from 7 fewer to 2 more)	HIGH	CRITICAL
Stillbirth or death before discharge from hospital – High-risk women												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ³	none	0/248 (0%)	1/264 (0.4%)	RR 0.39 (0.02–9.2)	2 fewer per 1000 (from 4 fewer to 31 more)	LOW	CRITICAL

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Routine calcium supplementation in pregnancy by hypertension risk	Control	Relative (95% CI)	Absolute		
Admission to neonatal intensive care unit												
4	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	530/6689 (7.9%)	507/6717 (7.5%)	RR 1.05 (0.94–1.18)	4 more per 1000 (from 5 fewer to 14 more)	HIGH	CRITICAL
Admission to neonatal intensive care unit – Low-risk women												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	529/6660 (7.9%)	503/6683 (7.5%)	RR 1.06 (0.94–1.19)	5 more per 1000 (from 5 fewer to 14 more)	HIGH	CRITICAL
Admission to neonatal intensive care unit – High-risk women												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ³	none	1/29 (3.4%)	4/34 (11.8%)	RR 0.29 (0.03–2.48)	84 fewer per 1000 (from 114 fewer to 174 more)	LOW	CRITICAL

1 Serious heterogeneity ($I^2=70\%$) possibly due to variation in baseline dietary intake of calcium.

2 The confidence interval includes results from appreciable benefit to negligible harm. However, downgrading was not performed considering the very large sample size.

3 Very small sample size and few events.

Source of evidence: Hofmeyr GJ, Lawrie TA, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database of Systematic Reviews, 2010, Issue 8. Art. No.: CD001059. DOI: 10.1002/14651858.CD001059.pub3.

Table 7. Routine calcium supplementation in pregnancy by baseline dietary calcium for preventing hypertensive disorders and related problems

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Routine calcium supplementation in pregnancy by baseline dietary calcium	Control	Relative (95% CI)	Absolute		
Pre-eclampsia												
13	randomized trials	no serious limitations	serious ¹	no serious indirectness	no serious imprecision	none ²	379/7851 (4.8%)	510/7879 (6.5%)	RR 0.45 (0.31–0.65)	36 fewer per 1000 (from 23 fewer to 45 fewer)	MODERATE	CRITICAL
Pre-eclampsia – Adequate calcium diet												
4	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ³	none	169/2505 (6.7%)	197/2517 (7.8%)	RR 0.62 (0.32–1.2)	30 fewer per 1000 (from 53 fewer to 16 more)	MODERATE	CRITICAL
Pre-eclampsia – Low calcium diet												
8	randomized trials	no serious limitations	serious ⁴	no serious indirectness	no serious imprecision	none	209/5331 (3.9%)	306/5347 (5.7%)	RR 0.36 (0.2–0.65)	37 fewer per 1000 (from 20 fewer to 46 fewer)	MODERATE	CRITICAL
Pre-eclampsia – Dietary calcium not specified												
1	randomized trials	no serious limitations	serious ⁵	no serious indirectness	very serious ⁶	none	1/15 (6.7%)	7/15 (46.7%)	RR 0.14 (0.02–1.02)	401 fewer per 1000 (from 457 fewer to 9 more)	VERY LOW	CRITICAL
Eclampsia												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ³	none	21/6719 (0.3%)	29/6706 (0.4%)	RR 0.73 (0.41–1.27)	1 fewer per 1000 (from 3 fewer to 1 more)	MODERATE	CRITICAL
Maternal death/serious morbidity												
4	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	167/4856 (3.4%)	210/4876 (4.3%)	RR 0.8 (0.65–0.97)	9 fewer per 1000 (from 1 fewer to 15 fewer)	HIGH	CRITICAL

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Routine calcium supplementation in pregnancy by baseline dietary calcium	Control	Relative (95% CI)	Absolute		
HELLP syndrome												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	16/6446 (0.2%)	6/6455 (0.1%)	RR 2.67 (1.05–6.82)	2 more per 1000 (from 0 more to 5 more)	HIGH	CRITICAL
Intensive care unit admission												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ³	none	116/4151 (2.8%)	138/4161 (3.3%)	RR 0.84 (0.66–1.07)	5 fewer per 1000 (from 11 fewer to 2 more)	MODERATE	CRITICAL
Maternal death												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ³	none	1/4151 (0%)	6/4161 (0.1%)	RR 0.17 (0.02–1.39)	1 fewer per 1000 (from 1 fewer to 1 more)	MODERATE	CRITICAL
Stillbirth or death before discharge from hospital												
11	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision ⁷	none	183/7821 (2.3%)	205/7844 (2.6%)	RR 0.9 (0.74–1.09)	3 fewer per 1000 (from 7 fewer to 2 more)	HIGH	CRITICAL
Admission to neonatal intensive care unit												
4	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	530/6689 (7.9%)	507/6717 (7.5%)	RR 1.05 (0.94–1.18)	4 more per 1000 (from 5 fewer to 14 more)	HIGH	CRITICAL

1 Serious heterogeneity ($I^2=76%$) due to variation in baseline risks of developing pre-eclampsia. All 3 studies that account for the inconsistency were conducted in women at low risk of developing pre-eclampsia.

2 No downgrading in spite of the evident asymmetry in the funnel plot because the studies are already downgraded for significant heterogeneity.

3 Wide confidence interval.

4 Serious heterogeneity ($I^2=76%$) due to variation in baseline risks of developing pre-eclampsia. All studies showing no effect of intervention involved women at low risk of developing pre-eclampsia.

5 The only study was at moderate risk of bias.

6 Very small sample size and few events; wide confidence interval.

7 The confidence interval includes results from appreciable benefit to negligible harm. However, downgrading was not performed considering the very large sample size.

Source of evidence: Hofmeyr GJ, Lawrie TA, Atallah ÁN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database of Systematic Reviews, 2010, Issue 8. Art. No.: CD001059. DOI: 10.1002/14651858.CD001059.pub3.

Table 8. Vitamin D supplementation

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Vitamin D + calcium versus no treatment/placebo no vitamin or minerals)	Control	Relative (95% CI)	Absolute		
Pre-eclampsia (ALL)												
1	randomized trials	serious ¹	serious ²	no serious indirectness	serious ^{1,3}	none	12/200 (6%)	18/200 (9%)	RR 0.67 (0.33–1.35)	30 fewer per 1000 (from 60 fewer to 32 more)	VERY LOW	CRITICAL

1 Wide confidence intervals.

2 Only one study reported on this outcome.

3 The study is unclear about lack of blinding or large or differential loss to follow-up in the compared groups as only data on biochemical was done for those who developed pre-eclampsia and some of those with no pre-eclampsia and a group of non pregnant controls.

Source of evidence: De-Regil LM, Palacios C, Ansary A, Kulier R, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. Cochrane Database of Systematic Reviews, 2011 (in press)

Table 9. Any antioxidants versus control or placebo for preventing pre-eclampsia

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Any antioxidants versus control or placebo	Control	Relative (95% CI)	Absolute			
Gestational hypertension													
10	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	652/5344 (12.2%)	574/4940 (11.6%)	RR 1.02 (0.85–1.23)	2 more per 1000 (from 17 fewer to 27 more)	HIGH	CRITICAL	
Severe hypertension													
4	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	124/3979 (3.1%)	123/4011 (3.1%)	RR 1.02 (0.8–1.31)	1 more per 1000 (from 6 fewer–10 more)	HIGH	CRITICAL	
Use of antihypertensives – Intravenous antihypertensives													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	31/1196 (2.6%)	16/1199 (1.3%)	RR 1.94 (1.07–3.53)	13 more per 1000 (from 1 more to 34 more)	HIGH	CRITICAL	
Pre-eclampsia													
15	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	983/10349 (9.5%)	1011/10399 (9.7%)	RR 0.94 (0.82–1.07)	6 fewer per 1000 (from 17 fewer to 7 more)	HIGH	CRITICAL	
Severe pre-eclampsia													
6	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	264/8162 (3.2%)	262/8179 (3.2%)	RR 1.01 (0.85–1.19)	0 more per 1000 (from 5 fewer to 6 more)	HIGH	CRITICAL	
Serious maternal morbidity (including eclampsia, liver and renal failure, DIC, stroke)													
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	6/2247 (0.3%)	5/2276 (0.2%)	RR 1.22 (0.39–3.81)	0 more per 1000 (from 1 fewer to 6 more)	Moderate	CRITICAL	

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Any antioxidants versus control or placebo	Control	Relative (95% CI)	Absolute		
Maternal death												
8	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	2/9783 (0%)	4/9803 (0%)	RR 0.6 (0.14–2.51)	0 fewer per 1000 (from 0 fewer to 1 more)	HIGH	CRITICAL
Any baby death												
8	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	285/9914 (2.9%)	288/9868 (2.9%)	RR 0.97 (0.82–1.13)	1 fewer per 1000 (from 5 fewer to 4 more)	HIGH	CRITICAL
Admission to special care nursery/intensive care nursery												
4	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1118/7459 (15%)	1097/7467 (14.7%)	RR 1.02 (0.95–1.1)	3 more per 1000 (from 7 fewer to 15 more)	HIGH	CRITICAL
Apgar score at 5 minutes – Low (<7)												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	39/1749 (2.2%)	31/1743 (1.8%)	RR 1.25 (0.79–2)	4 more per 1000 (from 4 fewer to 18 more)	MODERATE	

1 Very few events; wide confidence interval.

Source of evidence: Rumbold A, Duley L, Crowther CA, Haslam RR. Antioxidants for preventing pre-eclampsia. Cochrane Database of Systematic Reviews, 2008, Issue 1. Art. No.: CD004227. DOI: 10.1002/14651858.CD004227.pub3.*

Table 10. Antiplatelet agents versus placebo/no antiplatelet for primary prevention (subgrouped by maternal risk) for preventing pre-eclampsia and its complications

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Antiplatelet agents versus placebo/ no antiplatelet for primary prevention (subgrouped by maternal risk)	Control	Relative (95% CI)	Absolute		
Gestational hypertension												
33	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	1077/10424 (10.3%)	1103/10277 (10.7%)	RR 0.95 (0.88–1.03)	5 fewer per 1000 (from 13 fewer to 3 more)	MODERATE	CRITICAL
Gestational hypertension – Moderate-risk women												
22	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	1014/10008 (10.1%)	982/9855 (10%)	RR 1 (0.92–1.08)	0 fewer per 1000 (from 8 fewer to 8 more)	MODERATE	CRITICAL
Gestational hypertension – High-risk women												
12	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	63/416 (15.1%)	121/422 (28.7%)	RR 0.54 (0.41–0.7)	132 fewer per 1000 (from 86 fewer to 169 fewer)	MODERATE	CRITICAL
Pre-eclampsia												
44	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1085/16478 (6.6%)	1302/16272 (8%)	RR 0.82 (0.76–0.89)	14 fewer per 1000 (from 9 fewer to 19 fewer)	HIGH	CRITICAL
Pre-eclampsia – Moderate-risk women												
26	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	762/14408 (5.3%)	877/14221 (6.2%)	RR 0.86 (0.78–0.94)	9 fewer per 1000 (from 4 fewer to 14 fewer)	HIGH	CRITICAL
Pre-eclampsia – High-risk women												
18	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	323/2070 (15.6%)	425/2051 (20.7%)	RR 0.75 (0.66–0.85)	52 fewer per 1000 (from 31 fewer to 70 fewer)	HIGH	CRITICAL

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Antiplatelet agents versus placebo/ no antiplatelet for primary prevention (subgrouped by maternal risk)	Control	Relative (95% CI)	Absolute		
Eclampsia												
9	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	33/11259 (0.3%)	36/11325 (0.3%)	RR 0.94 (0.59–1.48)	0 fewer per 1000 (from 1 fewer to 2 more)	LOW	CRITICAL
Placental abruption												
16	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	172/12567 (1.4%)	150/12415 (1.2%)	RR 1.1 (0.89–1.37)	1 more per 1000 (from 1 fewer to 4 more)	MODERATE	CRITICAL
Maternal death												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	3/6349 (0%)	1/6360 (0%)	RR 2.57 (0.39–17.06)	0 more per 1000 (from 0 fewer to 3 more)	MODERATE	CRITICAL
Fetal, neonatal, infant and childhood deaths (subgroups by time of death) – Perinatal deaths												
15	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	190/8294 (2.3%)	212/8256 (2.6%)	RR 0.89 (0.74–1.08)	3 fewer per 1000 (from 7 fewer to 2 more)	MODERATE	CRITICAL
Admission to a special care baby unit												
15	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	2025/14168 (14.3%)	2101/14130 (14.9%)	RR 0.95 (0.9–1.01)	7 fewer per 1000 (from 15 fewer to 1 more)	HIGH	CRITICAL

1 Most studies were at moderate risk of bias.

2 Wide confidence interval.

Source of evidence: Duley L, Henderson-Smith DJ, Meher S, King JF. Antiplatelet agents for preventing pre-eclampsia and its complications. Cochrane Database of Systematic Reviews, 2007, Issue 2. Art. No.: CD004659.

DOI: 10.1002/14651858.CD004659.pub2.*

Table 11. Antiplatelet agents versus placebo/no antiplatelet for primary prevention (subgrouped by gestation at entry) for preventing pre-eclampsia and its complications

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Antiplatelet agents versus placebo/ no antiplatelet for primary prevention (subgrouped by gestation at entry)	Control	Relative (95% CI)	Absolute		
Fetal, neonatal or infant death – Entered into the study <20 weeks												
19	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	224/8853 (2.5%)	270/8813 (3.1%)	RR 0.82 (0.69–0.98)	6 fewer per 1000 (from 1 fewer to 9 fewer)	MODERATE	CRITICAL
Fetal, neonatal or infant death – Entered into the study >20 weeks												
19	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	146/5519 (2.6%)	163/5538 (2.9%)	RR 0.91 (0.73–1.13)	3 fewer per 1000 (from 8 fewer to 4 more)	LOW	CRITICAL
Fetal, neonatal or infant death – Unclassified												
6	randomized trials	serious ³	no serious inconsistency	no serious indirectness	serious ²	none	44/2209 (2%)	36/2114 (1.7%)	RR 1.11 (0.72–1.7)	2 more per 1000 (from 5 fewer to 12 more)	LOW	CRITICAL

1 Most studies were at high risk of bias.

2 Wide confidence interval.

3 All studies were at moderate risk of bias.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S, King JF. Antiplatelet agents for preventing pre-eclampsia and its complications. Cochrane Database of Systematic Reviews, 2007, Issue 2. Art. No.: CD004659.

DOI: 10.1002/14651858.CD004659.pub2.*

Table 12. Antiplatelet agents versus placebo/no treatment for primary prevention (subgrouped by dose) for preventing pre-eclampsia and its complications

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Antiplatelet agents versus placebo/ no treatment for primary prevention (subgrouped by dose)	Control	Relative (95% CI)	Absolute		
Gestational hypertension – 75 mg or less aspirin												
19	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	803/8057 (10%)	817/8038 (10.2%)	RR 0.98 (0.9–1.08)	2 fewer per 1000 (from 10 fewer to 8 more)	MODERATE	CRITICAL
Gestational hypertension – >75 mg aspirin												
9	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	58/428 (13.6%)	73/372 (19.6%)	RR 0.67 (0.49–0.92)	65 fewer per 1000 (from 16 fewer to 100 fewer)	MODERATE	CRITICAL
Gestational hypertension – Aspirin >75 mg + dipyridamole												
3	randomized trials	very serious ²	no serious inconsistency	no serious indirectness	no serious imprecision	none	58/250 (23.2%)	54/163 (33.1%)	RR 0.7 (0.51–0.95)	99 fewer per 1000 (from 17 fewer to 162 fewer)	LOW	
Pre-eclampsia – 75 mg or less aspirin												
21	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	958/13514 (7.1%)	1089/13470 (8.1%)	RR 0.88 (0.81–0.95)	10 fewer per 1000 (from 4 fewer to 15 fewer)	HIGH	CRITICAL
Pre-eclampsia – >75 mg aspirin												
17	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	108/2560 (4.2%)	164/2501 (6.6%)	RR 0.64 (0.51–0.8)	24 fewer per 1000 (from 13 fewer to 32 fewer)	HIGH	CRITICAL
1 Pre-eclampsia – Aspirin >75 mg + dipyridamole												
5	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	10/296 (3.4%)	25/210 (11.9%)	RR 0.3 (0.15–0.6)	83 fewer per 1000 (from 48 fewer to 101 fewer)	MODERATE	CRITICAL

1 Most studies were at moderate risk of bias.

2 Studies were at high risk of bias.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S, King JF. Antiplatelet agents for preventing pre-eclampsia and its complications. Cochrane Database of Systematic Reviews, 2007, Issue 2. Art. No.: CD004659. DOI: 10.1002/14651858.CD004659.pub2.*

Table 13. Antiplatelet agents versus placebo/no antiplatelet for women with gestational hypertension for preventing pre-eclampsia and its complications

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Antiplatelet agents versus placebo/no antiplatelet for women with gestational hypertension	Control	Relative (95% CI)	Absolute		
Pre-eclampsia												
5	randomized trials	serious ¹	serious ²	no serious indirectness	no serious imprecision	none	71/818 (8.7%)	122/825 (14.8%)	RR 0.6 (0.45–0.78)	59 fewer per 1000 (from 33 fewer to 81 fewer)	LOW	CRITICAL
Severe pre-eclampsia												
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ⁴	none	6/46 (13%)	19/48 (39.6%)	RR 0.33 (0.14–0.75)	265 fewer per 1000 (from 99 fewer to 340 fewer)	VERY LOW	CRITICAL
Eclampsia												
3	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ⁴	none	0/175 (0%)	3/179 (1.7%)	RR 0.25 (0.03–2.24)	13 fewer per 1000 (from 16 fewer to 21 more)	VERY LOW	CRITICAL
Placental abruption												
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ⁴	none	0/46 (0%)	1/48 (2.1%)	RR 0.35 (0.01–8.32)	14 fewer per 1000 (from 21 fewer to 152 more)	VERY LOW	CRITICAL
Fetal, neonatal or infant death												
4	randomized trials	no serious limitations	serious ²	no serious indirectness	serious ⁵	none	58/862 (6.7%)	57/866 (6.6%)	RR 1.02 (0.72–1.45)	1 more per 1000 (from 18 fewer to 30 more)	LOW	CRITICAL
Admission to a special care baby unit												
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ⁴	none	1/46 (2.2%)	2/48 (4.2%)	RR 0.52 (0.05–5.56)	20 fewer per 1000 (from 40 fewer to 190 more)	VERY LOW	CRITICAL

1 Most of the studies were at moderate risk of bias.

4 Very small sample size and few events; wide confidence interval.

2 Severe heterogeneity

5 Wide confidence interval.

3 Study was at moderate risk of bias.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S, King JF. Antiplatelet agents for preventing pre-eclampsia and its complications. Cochrane Database of Systematic Reviews, 2007, Issue 2. Art. No.: CD004659. DOI: 10.1002/14651858.CD004659.pub2.*

Table 14. Any antihypertensive drug versus none for mild to moderate hypertension during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Any antihypertensive drug versus none (subgrouped by class of drug)	Control	Relative (95% CI)	Absolute		
Proteinuria/pre-eclampsia												
22	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	239/1377 (17.4%)	241/1325 (18.2%)	RR 0.97 (0.83–1.13)	5 fewer per 1000 (from 31 fewer to 24 more)	MODERATE	CRITICAL
Severe pre-eclampsia												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	7/132 (5.3%)	12/135 (8.9%)	RR 0.61 (0.25–1.48)	35 fewer per 1000 (from 67 fewer to 43 more)	VERY LOW	CRITICAL
Eclampsia												
5	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	0/298 (0%)	1/280 (0.4%)	RR 0.34 (0.01–8.15)	2 fewer per 1000 (from 4 fewer to 26 more)	VERY LOW	CRITICAL
HELLP syndrome												
1	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	very serious ²	none	4/98 (4.1%)	2/99 (2%)	RR 2.02 (0.38–10.78)	21 more per 1000 (from 13 fewer to 198 more)	VERY LOW	CRITICAL
Pulmonary oedema												
1	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	very serious ²	none	2/86 (2.3%)	0/90 (0%)	RR 5.23 (0.25–107.39)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL
Maternal death												
4	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ⁵	none	2/190 (1.1%)	0/186 (0%)	RR 2.85 (0.3–27)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Any antihypertensive drug versus none (subgrouped by class of drug)	Control	Relative (95% CI)	Absolute		
Fetal or neonatal death (subgrouped by time of death) – Perinatal death												
20	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ³	none	30/1243 (2.4%)	31/1139 (2.7%)	RR 0.96 (0.6–1.54)	1 fewer per 1000 (from 11 fewer to 15 more)	LOW	CRITICAL
Admission to special care baby unit												
8	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ³	none	178/647 (27.5%)	168/674 (24.9%)	RR 1.11 (0.93–1.32)	27 more per 1000 (from 17 fewer to 80 more)	LOW	CRITICAL
Changed/stopped drugs due to maternal side-effects												
15	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ⁵	none	24/704 (3.4%)	7/699 (1%)	RR 2.59 (1.33–5.04)	16 more per 1000 (from 3 more to 40 more)	LOW	CRITICAL

1 Studies were at moderate high risk of bias.

2 Very small sample size and few events; wide confidence interval.

3 Wide confidence interval.

4 Only study at moderate risk of bias.

5 Few events; wide confidence interval.

Source of evidence: Abalos E, Duley L, Steyn DW. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database of Systematic Reviews, 2007, Issue 1. Art. No.: CD002252. DOI: 10.1002/14651858.CD002252.pub2.*

Table 15. Any antihypertensive drug versus none (subgrouped by gestation at trial entry) for mild to moderate hypertension during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Any antihypertensive drug versus none (subgrouped by gestation at trial entry)	Control	Relative (95% CI)	Absolute		
Proteinuria/pre-eclampsia – Entry <32 weeks												
8	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ⁴	none	103/609 (16.9%)	86/538 (16%)	RR 1.05 (0.81–1.36)	8 more per 1000 (from 30 fewer to 58 more)	LOW	CRITICAL
Proteinuria/pre-eclampsia – Entry >32 weeks												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ⁵	none	4/58 (6.9%)	13/62 (21%)	RR 0.34 (0.12–0.96)	138 fewer per 1000 (from 8 fewer to 185 fewer)	LOW	CRITICAL
Total reported fetal or neonatal death (including miscarriage) – Entry <32 weeks												
10	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ⁴	none	19/689 (2.8%)	30/587 (5.1%)	RR 0.66 (0.39–1.14)	17 fewer per 1000 (from 31 fewer to 7 more)	LOW	CRITICAL
Total reported fetal or neonatal death (including miscarriage) – Entry >32 weeks												
1	randomized trials	serious ²	no serious inconsistency	no serious indirectness	very serious ³	none	1/60 (1.7%)	2/60 (3.3%)	RR 0.5 (0.05–5.37)	17 fewer per 1000 (from 32 fewer to 146 more)	VERY LOW	CRITICAL

1 Studies were at moderate risk of bias.

2 Only study at moderate risk of bias.

3 Very small sample size and few events; wide confidence interval.

4 Wide confidence interval.

5 Very small sample size and few events.

Source of evidence: Abalos E, Duley L, Steyn DW. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database of Systematic Reviews, 2007, Issue 1. Art. No.: CD002252. DOI: 10.1002/14651858.CD002252.pub2.*

Table 16. Any antihypertensive versus methyldopa for mild to moderate hypertension during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Any antihypertensive versus methyldopa (subgrouped by class of drug)	Control	Relative (95% CI)	Absolute		
Proteinuria/pre-eclampsia												
9	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	49/420 (11.7%)	55/384 (14.3%)	RR 0.81 (0.57–1.16)	27 fewer per 1000 (from 62 fewer to 23 more)	LOW	CRITICAL
Total reported fetal or neonatal death (including miscarriage)												
17	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	17/585 (2.9%)	24/545 (4.4%)	RR 0.67 (0.37–1.21)	15 fewer per 1000 (from 28 fewer to 9 more)	LOW	CRITICAL
Admission to special care baby unit												
3	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	52/197 (26.4%)	51/182 (28%)	RR 0.94 (0.68–1.29)	17 fewer per 1000 (from 90 fewer to 81 more)	LOW	CRITICAL
Maternal side-effects												
4	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ³	none	1/62 (1.6%)	18/60 (30%)	RR 0.07 (0.02–0.37)	279 fewer per 1000 (from 189 fewer to 294 fewer)	LOW	CRITICAL
Changed/stopped drugs due to maternal side-effects												
4	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ⁴	none	1/139 (0.7%)	0/133 (0%)	RR 2.8 (0.12–67.91)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL

1 Studies were at moderate risk of bias.

2 Wide confidence interval.

3 Very small sample size and few events.

4 Very small sample size and few events; wide confidence interval.

Source of evidence: Abalos E, Duley L, Steyn DW. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database of Systematic Reviews, 2007, Issue 1. Art. No.: CD002252.

DOI: 10.1002/14651858.CD002252.pub2.*

Table 17. Any antihypertensive versus calcium channel blocker (subgrouped by class of drug) for mild to moderate hypertension during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Any antihypertensive versus calcium channel blocker (subgrouped by class of drug)	Control	Relative (95% CI)	Absolute		
Proteinuria/pre-eclampsia												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	10/70 (14.3%)	4/58 (6.9%)	RR 2.15 (0.73–6.38)	79 more per 1000 (from 19 fewer to 371 more)	VERY LOW	CRITICAL
HELLP syndrome												
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ²	none	3/50 (6%)	2/50 (4%)	RR 1.5 (0.26–8.6)	20 more per 1000 (from 30 fewer to 304 more)	VERY LOW	CRITICAL
Total reported fetal or neonatal death (including miscarriage)												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	1/74 (1.4%)	1/62 (1.6%)	RR 1 (0.06–15.55)	0 fewer per 1000 (from 15 fewer to 235 more)	VERY LOW	CRITICAL
Admission to special care baby unit												
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ²	none	6/50 (12%)	4/49 (8.2%)	RR 1.47 (0.44–4.89)	38 more per 1000 (from 46 fewer to 318 more)	VERY LOW	CRITICAL
Changed/stopped drug due to side-effects												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	2/74 (2.7%)	0/62 (0%)	RR 2.6 (0.13–50.25)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL

1 Studies were at moderate risk of bias.

2 Very small sample size and few events; wide confidence interval.

3 Only study was at moderate risk of bias.

Source of evidence: Abalos E, Duley L, Steyn DW. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database of Systematic Reviews, 2007, Issue 1. Art. No.: CD002252.

DOI: 10.1002/14651858.CD002252.pub2.*

Table 18. Labetalol versus hydralazine for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Labetalol versus hydralazine	Control	Relative (95% CI)	Absolute		
Eclampsia												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/108 (0%)	0/109 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Persistent high blood pressure												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	11/108 (10.2%)	7/109 (6.4%)	RR 1.58 (0.66–3.77)	37 more per 1000 (from 22 fewer to 178 more)	VERY LOW	CRITICAL
Maternal pulmonary oedema												
1	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	very serious ³	none	1/98 (1%)	0/99 (0%)	RR 3.03 (0.12–73.49)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL
HELLP syndrome												
1	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	very serious ³	none	2/98 (2%)	2/99 (2%)	RR 1.01 (0.15–7.03)	0 more per 1000 (from 17 fewer to 122 more)	VERY LOW	CRITICAL
Disseminated intravascular coagulation												
1	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	very serious ²	none	0/98 (0%)	0/99 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Oliguria												
1	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	very serious ³	none	2/98 (2%)	4/99 (4%)	RR 0.51 (0.09–2.69)	20 fewer per 1000 (from 37 fewer to 68 more)	VERY LOW	CRITICAL
Maternal death												
1	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	very serious ²	none	0/98 (0%)	0/99 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Fetal or neonatal deaths												
4	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	3/141 (2.1%)	4/133 (3%)	RR 0.75 (0.17–3.21)	8 fewer per 1000 (from 25 fewer to 66 more)	VERY LOW	CRITICAL

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Labetalol versus hydralazine	Control	Relative (95% CI)	Absolute		Quality
Apgar <7 at 5 minutes												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	4/116 (3.4%)	4/108 (3.7%)	RR 0.81 (0.25–2.61)	7 fewer per 1000 (from 28 fewer to 60 more)	VERY LOW	CRITICAL
Hypotension												
3	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	0/123 (0%)	2/124 (1.6%)	RR 0.2 (0.01–4.15)	13 fewer per 1000 (from 16 fewer to 51 more)	VERY LOW	CRITICAL

1 Studies were at moderate risk of bias.

2 Very small sample size and no events.

3 Very small sample size and few events; wide confidence interval.

4 The only study was at moderate risk of bias.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449.

DOI: 10.1002/14651858.CD001449.pub2.*

Table 19. Calcium channel blockers versus hydralazine for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Calcium channel blockers versus hydralazine	Control	Relative (95% CI)	Absolute		
Persistent high blood pressure												
5	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	8/135 (5.9%)	23/128 (18%)	RR 0.33 (0.15–0.7)	120 fewer per 1000 (from 54 fewer to 153 fewer)	VERY LOW	CRITICAL
Further episode/s of very high blood pressure												
2	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	39/85 (45.9%)	43/78 (55.1%)	RR 0.85 (0.65–1.11)	83 fewer per 1000 (from 193 fewer to 61 more)	VERY LOW	CRITICAL
Fetal or neonatal death												
4	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	very serious ⁵	none	6/83 (7.2%)	4/78 (5.1%)	RR 1.36 (0.42–4.41)	18 more per 1000 (from 30 fewer to 175 more)	VERY LOW	CRITICAL
Low blood pressure for the woman												
3	randomized trials	serious ⁶	no serious inconsistency	no serious indirectness	very serious ⁵	none	1/102 (1%)	0/97 (0%)	RR 2.83 (0.12–64.89)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL
Side-effects for the woman												
4	randomized trials	serious ⁷	no serious inconsistency	no serious indirectness	very serious ⁵	none	22/122 (18%)	25/114 (21.9%)	RR 0.79 (0.5–1.24)	46 fewer per 1000 (from 110 fewer to 53 more)	VERY LOW	CRITICAL

1 The study that contributed most of the effect size was at high risk of bias.

2 Very small sample size.

3 Very small sample size; wide confidence interval.

4 Studies were at moderate risk of bias.

5 Very small sample size and few events; wide confidence interval.

6 The only study that contributed the effect size was at moderate risk of bias.

7 Most studies were at moderate risk of bias.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub2.*

Table 20. Prostacyclin versus hydralazine for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Prostacyclin versus hydralazine	Control	Relative (95% CI)	Absolute		
Persistent high blood pressure												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/22 (0%)	2/25 (8%)	RR 0.23 (0.01–4.47)	62 fewer per 1000 (from 79 fewer to 278 more)	VERY LOW	CRITICAL
Neonatal death												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	1/22 (4.5%)	1/25 (4%)	RR 1.14 (0.08–17.11)	6 more per 1000 (from 37 fewer to 644 more)	VERY LOW	CRITICAL
Side-effects for the woman												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	1/22 (4.5%)	1/25 (4%)	RR 1.14 (0.08–17.11)	6 more per 1000 (from 37 fewer to 644 more)	VERY LOW	CRITICAL

1 The only study was at moderate risk of bias.

2 Very small sample size and few events; wide confidence interval.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub2.*

Table 21. Ketanserin versus hydralazine for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Ketanserin versus hydralazine	Control	Relative (95% CI)	Absolute		
Eclampsia												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	1/32 (3.1%)	2/32 (6.3%)	RR 0.6 (0.08–4.24)	25 fewer per 1000 (from 58 fewer to 202 more)	VERY LOW	CRITICAL
Persistent high blood pressure												
3	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ³	none	26/96 (27.1%)	5/84 (6%)	RR 4.79 (1.95–11.73)	226 more per 1000 (from 57 more to 639 more)	LOW	CRITICAL
Severe maternal morbidity												
1	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	very serious ²	none	3/32 (9.4%)	7/24 (29.2%)	RR 0.32 (0.09–1.12)	198 fewer per 1000 (from 265 fewer to 35 more)	VERY LOW	CRITICAL
Maternal death												
2	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	very serious ²	none	0/64 (0%)	2/60 (3.3%)	RR 0.32 (0.03–2.96)	23 fewer per 1000 (from 32 fewer to 65 more)	VERY LOW	CRITICAL
Perinatal death												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	1/59 (1.7%)	5/57 (8.8%)	RR 0.27 (0.05–1.64)	64 fewer per 1000 (from 83 fewer to 56 more)	VERY LOW	CRITICAL
Hypotension												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	2/42 (4.8%)	7/34 (20.6%)	RR 0.26 (0.07–1.03)	152 fewer per 1000 (from 191 fewer to 6 more)	VERY LOW	CRITICAL
Side-effects for the women												
3	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	serious ³	none	13/64 (20.3%)	36/56 (64.3%)	RR 0.32 (0.19–0.53)	437 fewer per 1000 (from 302 fewer to 521 fewer)	LOW	CRITICAL

1 Studies were at moderate risk of bias.

2 Very small sample size and few events; wide confidence interval.

3 Very small sample size.

4 The only study was at moderate risk of bias.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub2.*

Table 22. Urapidil versus hydralazine for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Urapidil versus hydralazine	Control	Relative (95% CI)	Absolute		
Eclampsia												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/13 (0%)	0/13 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Persistent high blood pressure												
2	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ⁴	none	1/36 (2.8%)	0/23 (0%)	RR 1.38 (0.06–31.14)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL
Stillbirth												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/13 (0%)	0/13 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Neonatal death												
2	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ⁴	none	1/36 (2.8%)	1/23 (4.3%)	RR 0.66 (0.08–5.25)	15 fewer per 1000 (from 40 fewer to 185 more)	VERY LOW	CRITICAL
Hypotension												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ⁴	none	1/23 (4.3%)	2/10 (20%)	RR 0.22 (0.02–2.13)	156 fewer per 1000 (from 196 fewer to 226 more)	VERY LOW	CRITICAL
Side-effects for the woman												
2	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ⁴	none	2/36 (5.6%)	2/23 (8.7%)	RR 0.59 (0.1–3.58)	36 fewer per 1000 (from 78 fewer to 224 more)	VERY LOW	CRITICAL

1 The only study was at moderate risk of bias.

2 Very small sample size and no events.

3 Studies were at moderate risk of bias.

4 Very small sample size and few events; wide confidence interval.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub2.*

Table 23. Labetolol versus calcium channel blockers for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Labetolol versus calcium channel blockers	Control	Relative (95% CI)	Absolute		
Eclampsia												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/10 (0%)	2/10 (20%)	RR 0.2 (0.01–3.7)	160 fewer per 1000 (from 198 fewer to 540 more)	VERY LOW	CRITICAL
Persistent high blood pressure												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	11/30 (36.7%)	9/30 (30%)	RR 1.22 (0.59–2.51)	66 more per 1000 (from 123 fewer to 453 more)	LOW	
Hypotension												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ³	none	0/40 (0%)	0/40 (0%)	not pooled	not pooled	LOW	CRITICAL
Side-effects for the woman (specific effects) – Palpitations												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	0/30 (0%)	3/30 (10%)	RR 0.14 (0.01–2.65)	86 fewer per 1000 (from 99 fewer to 165 more)	LOW	

1 The only study was at moderate risk of bias.

2 Very small sample size and few events; wide confidence interval.

3 Very small sample size and no events.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub2.*

Table 24. Labetolol versus methyldopa for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Labetolol versus methyldopa	Control	Relative (95% CI)	Absolute		
Persistent high blood pressure												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	20/38 (52.6%)	15/34 (44.1%)	RR 1.19 (0.74–1.94)	84 more per 1000 (from 115 fewer to 415 more)	VERY LOW	CRITICAL
Fetal or neonatal death – total stillbirths and neonatal deaths												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	2/38 (5.3%)	0/34 (0%)	RR 4.49 (0.22–90.3)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL
Admission to special care baby unit												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	19/38 (50%)	16/34 (47.1%)	RR 1.06 (0.66–1.71)	28 more per 1000 (from 160 fewer to 334 more)	VERY LOW	CRITICAL
Changed drugs due to side-effects												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	4/38 (10.5%)	0/34 (0%)	RR 8.08 (0.45–144.73)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	

1 The only study was at moderate risk of bias.

2 Very small sample size; wide confidence interval.

3 Very small sample size and few events; wide confidence interval.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub2.*

Table 25. Labetolol versus diazoxide for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Labetolol versus diazoxide	Control	Relative (95% CI)	Absolute		
Persistent high blood pressure												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	3/45 (6.7%)	6/45 (13.3%)	RR 0.5 (0.13–1.88)	67 fewer per 1000 (from 116 fewer to 117 more)	VERY LOW	CRITICAL
Perinatal deaths												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/45 (0%)	3/45 (6.7%)	RR 0.14 (0.01–2.69)	57 fewer per 1000 (from 66 fewer to 113 more)	VERY LOW	CRITICAL
Low blood pressure, requiring treatment												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/45 (0%)	8/45 (17.8%)	RR 0.06 (0–0.99)	167 fewer per 1000 (from 2 fewer to 178 fewer)	VERY LOW	CRITICAL

1 The only study was at moderate risk of bias.

2 Very small sample size and few events; wide confidence interval.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub2.*

Table 26. Nitrates versus magnesium sulfate for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Nitrates versus magnesium sulfate	Control	Relative (95% CI)	Absolute		Quality
Eclampsia												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/18 (0%)	0/18 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Persistent high blood pressure												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	0/18 (0%)	3/18 (16.7%)	RR 0.14 (0.01–2.58)	143 fewer per 1000 (from 165 fewer to 263 more)	VERY LOW	CRITICAL

1 The only study was at moderate risk of bias.

2 Very small sample size and no events.

3 Very small sample size and few events; wide confidence interval.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449.

DOI: 10.1002/14651858.CD001449.pub2.*

Table 27. Nimodipine versus magnesium sulfate for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Nimodipine versus magnesium sulfate	Control	Relative (95% CI)	Absolute		Quality
Eclampsia												
2	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	serious ³	none	21/837 (2.5%)	9/846 (1.1%)	RR 2.24 (1.06–4.73)	13 more per 1000 (from 1 more to 40 more)	VERY LOW	CRITICAL
Persistent high blood pressure												
1	randomized trials	very serious ²	no serious inconsistency	no serious indirectness	no serious imprecision	none	374/819 (45.7%)	451/831 (54.3%)	RR 0.84 (0.76–0.93)	87 fewer per 1000 (from 38 fewer to 130 fewer)	LOW	CRITICAL
Stroke												
1	randomized trials	very serious ²	no serious inconsistency	no serious indirectness	very serious ³	none	0/819 (0%)	0/831 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Coagulopathy for the woman												
1	randomized trials	very serious ²	no serious inconsistency	no serious indirectness	very serious ⁴	none	5/819 (0.6%)	3/831 (0.4%)	RR 1.69 (0.41–7.05)	2 more per 1000 (from 2 fewer to 22 more)	VERY LOW	CRITICAL
Oliguria												
1	randomized trials	very serious ²	no serious inconsistency	no serious indirectness	very serious ⁴	none	47/819 (5.7%)	55/831 (6.6%)	RR 0.87 (0.59–1.26)	9 fewer per 1000 (from 27 fewer to 17 more)	VERY LOW	CRITICAL
Side-effects for the woman (specific effects) – Flushing												
1	randomized trials	very serious ²	no serious inconsistency	no serious indirectness	no serious imprecision	none	13/819 (1.6%)	59/831 (7.1%)	RR 0.22 (0.12–0.4)	55 fewer per 1000 (from 43 fewer to 62 fewer)	LOW	CRITICAL
Hypotension												
1	randomized trials	very serious ²	no serious inconsistency	no serious indirectness	very serious ⁴	none	5/819 (0.6%)	7/831 (0.8%)	RR 0.72 (0.23–2.27)	2 fewer per 1000 (from 6 fewer to 11 more)	VERY LOW	CRITICAL

1 The study contributing most of the effect size was at high risk of bias.

2 The only study was at high risk of bias.

3 No events.

4 Wide confidence interval and/or very few events.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub2.*

Table 28. Nifedipine versus chlorpromazine for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Nifedipine versus chlorpromazine	Control	Relative (95% CI)	Absolute		Quality
Eclampsia												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	1/30 (3.3%)	0/25 (0%)	RR 2.52 (0.11–59.18)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL
Persistent high blood pressure												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/30 (0%)	5/30 (16.7%)	RR 0.09 (0.01–1.57)	152 fewer per 1000 (from 165 fewer to 95 more)	VERY LOW	CRITICAL

1 The only study was at moderate risk of bias.

2 Very small sample size and few events; wide confidence interval.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub2.*

Table 29. Nifedipine versus prazosin for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Nifedipine versus prazosin	Control	Relative (95% CI)	Absolute		
Eclampsia												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/74 (0%)	0/71 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
HELLP syndrome												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	6/74 (8.1%)	5/71 (7%)	RR 1.15 (0.37–3.6)	11 more per 1000 (from 44 fewer to 183 more)	VERY LOW	CRITICAL
Renal failure												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	1/74 (1.4%)	2/71 (2.8%)	RR 0.48 (0.04–5.17)	15 fewer per 1000 (from 27 fewer to 117 more)	VERY LOW	CRITICAL
Pulmonary oedema												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	1/74 (1.4%)	5/71 (7%)	RR 0.19 (0.02–1.6)	57 fewer per 1000 (from 69 fewer to 42 more)	VERY LOW	CRITICAL
Admission to intensive care												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	0/74 (0%)	1/71 (1.4%)	RR 0.32 (0.01–7.73)	10 fewer per 1000 (from 14 fewer to 95 more)	VERY LOW	CRITICAL
Maternal death												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	0/74 (0%)	1/71 (1.4%)	RR 0.32 (0.01–7.73)	10 fewer per 1000 (from 14 fewer to 95 more)	VERY LOW	CRITICAL
Stillbirth												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	6/75 (8%)	13/74 (17.6%)	RR 0.46 (0.18–1.13)	95 fewer per 1000 (from 144 fewer to 23 more)	VERY LOW	CRITICAL
Admission to special care baby unit												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	22/69 (31.9%)	25/61 (41%)	RR 0.78 (0.49–1.23)	90 fewer per 1000 (from 209 fewer to 94 more)	VERY LOW	CRITICAL

1 The only study was at moderate risk of bias.

2 Very small sample size and no events.

3 Very small sample size and few events; wide confidence interval.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub2.*

Table 30. Nitroglycerine versus nifedipine for treatment of very high blood pressure during pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Nitroglycerine versus Nifedipine	Control	Relative (95% CI)	Absolute		Quality
Maternal death												
1	randomized trials	no serious limitations		no serious indirectness	very serious ¹	none	0/16 (0%)	0/16 (0%)	not pooled	not pooled	LOW	CRITICAL
Perinatal death												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	0/16 (0%)	0/16 (0%)	not pooled	not pooled	LOW	CRITICAL
Apgar <8 at 5 min												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	1/16 (6.3%)	0/16 (0%)	RR 3 (0.13–68.57)	0 more per 1000 (from 0 fewer to 0 more)	LOW	CRITICAL
Side-effects for the mother – Headache												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	3/16 (18.8%)	2/16 (12.5%)	RR 1.5 (0.29–7.81)	62 more per 1000 (from 89 fewer to 851 more)	LOW	CRITICAL
Side-effects for the mother – Palpitations												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	3/16 (18.8%)	2/16 (12.5%)	RR 1.5 (0.29–7.81)	62 more per 1000 (from 89 fewer to 851 more)	LOW	CRITICAL
Side-effects for the mother – Flushing												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	4/16 (25%)	6/16 (37.5%)	RR 0.67 (0.23–1.92)	124 fewer per 1000 (from 289 fewer to 345 more)	LOW	CRITICAL

1 Very small sample size and no events.

2 Very small sample size and few events; wide confidence interval.

Source of evidence: Duley L, Henderson-Smart DJ, Meher S. Drugs for treatment of very high blood pressure during pregnancy. Cochrane Database of Systematic Reviews, 2006, Issue 3. Art. No.: CD001449. DOI: 10.1002/14651858.CD001449.pub2.*

Table 31. Diuretic versus placebo or no treatment for preventing pre-eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Diuretic versus placebo or no treatment	Control	Relative (95% CI)	Absolute		
Hypertension (new or worsening)												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	107/841 (12.7%)	121/634 (19.1%)	RR 0.85 (0.68–1.08)	29 fewer per 1000 (from 61 fewer to 15 more)	LOW	CRITICAL
Pre-eclampsia												
4	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	34/681 (5%)	53/710 (7.5%)	RR 0.68 (0.45–1.03)	24 fewer per 1000 (from 41 fewer to 2 more)	VERY LOW	CRITICAL
Severe pre-eclampsia												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	3/637 (0.5%)	2/660 (0.3%)	RR 1.56 (0.26–9.17)	2 more per 1000 (from 2 fewer to 25 more)	VERY LOW	CRITICAL
Eclampsia												
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ⁵	none	0/506 (0%)	0/524 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Use of antihypertensive drugs												
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ²	none	2/10 (20%)	1/10 (10%)	RR 2 (0.21–18.69)	100 more per 1000 (from 79 fewer to 1769 more)	VERY LOW	CRITICAL
Perinatal death												
5	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	22/1016 (2.2%)	26/820 (3.2%)	RR 0.72 (0.4–1.27)	9 fewer per 1000 (from 19 fewer to 9 more)	LOW	
Apgar score at 5 minutes <7												
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ⁴	none	1/10 (10%)	0/10 (0%)	RR 3 (0.14–65.9)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL
Intervention stopped due to side-effects												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	15/606 (2.5%)	8/611 (1.3%)	RR 1.85 (0.81–4.22)	11 more per 1000 (from 2 fewer to 42 more)	LOW	CRITICAL

1 Studies are at moderate risk of bias.

2 Wide confidence interval.

3 Only study at moderate risk of bias.

4 Very small sample size and few events; wide confidence interval.

5 No events.

Source of evidence: Churchill D, Beevers GDG, Meher S, Rhodes C. Diuretics for preventing pre-eclampsia. Cochrane Database of Systematic Reviews, 2007, Issue 1. Art. No.: CD004451.

DOI: 10.1002/14651858.CD004451.pub2.*

Table 32. Magnesium sulfate versus none/placebo (subgroups by severity of pre-eclampsia) for women with pre-eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus none/placebo (subgroups by severity of pre-eclampsia)	Control	Relative (95% CI)	Absolute		
Maternal death												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	11/5400 (0.2%)	21/5395 (0.4%)	RR 0.54 (0.26–1.1)	2 fewer per 1000 (from 3 fewer to 0 more)	HIGH	CRITICAL
Eclampsia												
6	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	43/5722 (0.8%)	107/5722 (1.9%)	RR 0.41 (0.29–0.58)	11 fewer per 1000 (from 8 fewer to 13 fewer)	HIGH	CRITICAL
Serious maternal morbidity												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	196/5164 (3.8%)	183/5168 (3.5%)	RR 1.08 (0.89 to 1.32)	3 more per 1000 (from 4 fewer to 11 more)	HIGH	CRITICAL
Respiratory arrest												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	5/5055 (0.1%)	2/5055 (0%)	RR 2.5 (0.49–12.88)	1 more per 1000 (from 0 fewer to 5 more)	MODERATE	CRITICAL
Toxicity – Absent or reduced tendon reflexes												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	60/5344 (1.1%)	60/5333 (1.1%)	RR 1 (0.7–1.42)	0 fewer per 1000 (from 3 fewer to 5 more)	MODERATE	CRITICAL
Toxicity – Respiratory depression, or other respiratory problem												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	52/5344 (1%)	26/5333 (0.5%)	RR 1.98 (1.24–3.15)	5 more per 1000 (from 1 more to 10 more)	HIGH	CRITICAL
Toxicity – Respiratory depression and absent tendon reflexes												
3	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	5/5453 (0.1%)	0/5446 (0%)	RR 5.96 (0.72–49.4)	0 more per 1000 (from 0 fewer to 0 more)	LOW	CRITICAL
Given calcium gluconate												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	15/5400 (0.3%)	11/5395 (0.2%)	RR 1.35 (0.63–2.88)	1 more per 1000 (from 1 fewer to 4 more)	MODERATE	

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus none/placebo (subgroups by severity of pre-eclampsia)	Control	Relative (95% CI)	Absolute		Quality
Side-effects – Any reported side-effects												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1201/4999 (24%)	228/4993 (4.6%)	RR 5.26 (4.59–6.03)	195 more per 1000 (from 164 more to 230 more)	HIGH	CRITICAL
Stillbirths and neonatal deaths												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	634/5003 (12.7%)	611/4958 (12.3%)	RR 1.04 (0.93–1.15)	5 more per 1000 (from 9 fewer to 18 more)	HIGH	CRITICAL
Admission to special care baby unit												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	1629/4162 (39.1%)	1591/4098 (38.8%)	RR 1.01 (0.96–1.06)	4 more per 1000 (from 16 fewer to 23 more)	HIGH	CRITICAL
Apgar score <7 at 5 minutes												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	235/4162 (5.6%)	227/4098 (5.5%)	RR 1.02 (0.85–1.22)	1 more per 1000 (from 8 fewer to 12 more)	HIGH	CRITICAL

1 Study contributing to more than half of effect size at moderate risk of bias.

2 Wide confidence interval.

Source of evidence: Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulfate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 11. Art. No.: CD000025. DOI: 10.1002/14651858.CD000025.pub2.

Table 33. Magnesium sulfate versus none/placebo (subgroups by whether delivered at trial entry) for women with pre-eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus none/placebo (subgroups by whether delivered at trial entry)	Control	Relative (95% CI)	Absolute		
Eclampsia – Antepartum at trial entry												
6	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	39/5083 (0.8%)	99/5026 (2%)	RR 0.4 (0.27–0.57)	12 fewer per 1000 (from 8 fewer to 14 fewer)	HIGH	CRITICAL
Eclampsia – Postpartum at trial entry												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	4/639 (0.6%)	8/696 (1.1%)	RR 0.54 (0.16–1.8)	5 fewer per 1000 (from 10 fewer to 9 more)	LOW	CRITICAL

¹ Few events, wide confidence interval.

Source of evidence: Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulfate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 11. Art. No.: CD000025. DOI: 10.1002/14651858.CD000025.pub2.

Table 34. Magnesium sulfate versus none/placebo (subgroups by gestation at trial entry) for women with pre-eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus none/placebo (subgroups by gestation at trial entry)	Control	Relative (95% CI)	Absolute		
Eclampsia – <34 weeks												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	13/1206 (1.1%)	24/1206 (2%)	RR 0.54 (0.28–1.06)	9 fewer per 1000 (from 14 fewer to 1 more)	HIGH	CRITICAL
Eclampsia – ≥34 weeks												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	24/3277 (0.7%)	64/3221 (2%)	RR 0.37 (0.24–0.59)	13 fewer per 1000 (from 8 fewer to 15 fewer)	HIGH	CRITICAL
Eclampsia – Gestation not specified												
4	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	2/600 (0.3%)	11/599 (1.8%)	RR 0.22 (0.06–0.84)	14 fewer per 1000 (from 3 fewer to 17 fewer)	LOW	CRITICAL

1 Most studies at moderate risk of bias.

2 Few events.

Source of evidence: Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulfate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 11. Art. No.: CD000025. DOI: 10.1002/14651858.CD000025.pub2.

Table 35. Magnesium sulfate versus none/placebo (subgroups by whether anticonvulsant before trial entry) for women with pre-eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus none/placebo (subgroups by whether anticonvulsant before trial entry)	Control	Relative (95% CI)	Absolute		
Eclampsia – Anticonvulsant before trial entry												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	10/439 (2.3%)	8/435 (1.8%)	RR 1.24 (0.49–3.11)	4 more per 1000 (from 9 fewer to 39 more)	MODERATE	CRITICAL
Eclampsia – No anticonvulsant before trial entry												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	32/5047 (0.6%)	99/5039 (2%)	RR 0.33 (0.22–0.48)	13 fewer per 1000 (from 10 fewer to 15 fewer)	HIGH	CRITICAL
Eclampsia – Unclear whether anticonvulsant before trial entry												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	1/210 (0.5%)	0/211 (0%)	RR 3.04 (0.13–73.42)	0 more per 1000 (from 0 fewer to 0 more)	MODERATE	

¹ Wide confidence interval.

Source of evidence: Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulfate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 11. Art. No.: CD000025. DOI: 10.1002/14651858.CD000025.pub2.

Table 36. Magnesium sulfate versus none/placebo (subgroups by dose and route of administration for maintenance therapy) for women with pre-eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus none/placebo (subgroups by dose and route of administration for maintenance therapy)	Control	Relative (95% CI)	Absolute		
Eclampsia – Intramuscular maintenance regimen												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	21/2413 (0.9%)	54/2408 (2.2%)	RR 0.39 (0.24–0.65)	14 fewer per 1000 (from 8 fewer to 17 fewer)	HIGH	CRITICAL
Eclampsia – Intravenous maintenance regimen – 1 g/hour												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	21/3133 (0.7%)	53/3133 (1.7%)	RR 0.4 (0.24–0.66)	10 fewer per 1000 (from 6 fewer to 13 fewer)	HIGH	
Eclampsia – Intravenous maintenance regimen – 2 g/hour												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	Very serious ¹	none	1/176 (0.6%)	0/181 (0%)	RR 3.04 (0.13–73.42)	0 more per 1000 (from 0 fewer to 0 more)	LOW	CRITICAL

1 Very few events and wide confidence interval.

Source of evidence: Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulfate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 11. Art. No.: CD000025. DOI: 10.1002/14651858.CD000025.pub2.

Table 37. Magnesium sulfate versus phenytoin for women with pre-eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus phenytoin	Control	Relative (95% CI)	Absolute		
Eclampsia												
3	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/1134 (0%)	12/1157 (1%)	RR 0.08 (0.01–0.6)	10 fewer per 1000 (from 4 fewer to 10 fewer)	MODERATE	CRITICAL

¹ All studies were at moderate risk of bias.

Source of evidence: Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulfate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 11. Art. No.: CD000025. DOI: 10.1002/14651858.CD000025.pub2.

Table 38. Magnesium sulfate versus diazepam for women with pre-eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus diazepam	Control	Relative (95% CI)	Absolute		Quality
Eclampsia												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	1/29 (3.4%)	0/37 (0%)	RR 3 (0.13–69.31)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL

1 Both studies were at moderate risk of bias.

2 Very small sample size and few events, wide confidence interval.

Source of evidence: Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulfate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 11. Art. No.: CD000025. DOI: 10.1002/14651858.CD000025.pub2.

Table 39. Magnesium sulfate versus nimodipine for women with pre-eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus nimodipine	Control	Relative (95% CI)	Absolute		
Eclampsia												
1	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	7/831 (0.8%)	21/819 (2.6%)	RR 0.33 (0.14–0.77)	17 fewer per 1000 (from 6 fewer to 22 fewer)	LOW	CRITICAL

1 High risk of bias.

Source of evidence: Duley L, Gülmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulfate and other anticonvulsants for women with pre-eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 11. Art. No.: CD000025. DOI: 10.1002/14651858.CD000025.pub2.

Table 40. Magnesium sulfate versus diazepam for eclampsia

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus diazepam	Control	Relative (95% CI)	Absolute			
Maternal death													
7	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	29/707 (4.1%)	47/689 (6.8%)	RR 0.59 (0.38–0.92)	28 fewer per 1000 (from 5 fewer to 42 fewer)	MODERATE	CRITICAL	
Recurrence of seizures													
7	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	74/706 (10.5%)	176/684 (25.7%)	RR 0.42 (0.33–0.54)	149 fewer per 1000 (from 118 fewer to 172 fewer)	HIGH	CRITICAL	
Any serious morbidity (stroke, renal failure, HELLP, DIC, pulmonary oedema, cardiac arrest, or as reported)													
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	63/477 (13.2%)	73/479 (15.2%)	RR 0.88 (0.64–1.19)	18 fewer per 1000 (from 55 fewer to 29 more)	MODERATE	CRITICAL	
Respiratory depression													
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	38/512 (7.4%)	44/513 (8.6%)	RR 0.86 (0.57–1.3)	12 fewer per 1000 (from 37 fewer to 26 more)	MODERATE	CRITICAL	
Pulmonary oedema													
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ^{2,3}	none	8/504 (1.6%)	10/509 (2%)	RR 0.86 (0.35–2.07)	3 fewer per 1000 (from 13 fewer to 21 more)	LOW	CRITICAL	
Woman admitted to intensive care unit													
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	67/518 (12.9%)	84/516 (16.3%)	RR 0.8 (0.59–1.07)	33 fewer per 1000 (from 67 fewer to 11 more)	MODERATE	CRITICAL	
Death of the fetus or infant – Perinatal death													
4	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	97/400 (24.3%)	90/388 (23.2%)	RR 1.04 (0.81–1.34)	9 more per 1000 (from 44 fewer to 79 more)	MODERATE	CRITICAL	
Admitted to special care baby unit (SCBU) – Admission to SCBU													
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	166/329 (50.5%)	167/305 (54.8%)	RR 0.92 (0.79–1.06)	44 fewer per 1000 (from 115 fewer to 33 more)	HIGH	CRITICAL	

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus diazepam	Control	Relative (95% CI)	Absolute		
Apgar scores – Apgar <7 at 5 minutes												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	76/330 (23%)	104/313 (33.2%)	RR 0.7 (0.54–0.9)	100 fewer per 1000 (from 33 fewer to 153 fewer)	HIGH	CRITICAL

1 Most of the studies have moderate risk of bias.

2 Wide confidence interval.

3 Few events.

Source of evidence: Duley L, Henderson-Smart DJ, Walker GJA, Chou D. Magnesium sulfate versus diazepam for eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 12. Art. No.: CD000127.

DOI: 10.1002/14651858.CD000127.pub2.

Table 41. Magnesium sulfate versus diazepam (subgroups by route of magnesium sulfate maintenance) for eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus diazepam (subgroups by route of magnesium maintenance)	Control	Relative (95% CI)	Absolute		Quality
Maternal cardiac arrest – IM magnesium sulfate maintenance												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	1/59 (1.7%)	3/61 (4.9%)	RR 0.52 (0.1–2.66)	24 fewer per 1000 (from 44 fewer to 82 more)	LOW	CRITICAL
Maternal respiratory depression – IM magnesium sulfate maintenance												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	3/59 (5.1%)	11/61 (18%)	RR 0.3 (0.1–0.93)	126 fewer per 1000 (from 13 fewer to 162 fewer)	MODERATE	CRITICAL
Maternal ventilation – IM magnesium sulfate maintenance												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ²	none	2/59 (3.4%)	10/61 (16.4%)	RR 0.2 (0.05–0.88)	131 fewer per 1000 (from 20 fewer to 156 fewer)	MODERATE	CRITICAL

1 Very small sample size and few events; wide confidence interval.

2 Very small sample size and few events.

Source of evidence: Duley L, Henderson-Smart DJ, Walker GJA, Chou D. Magnesium sulfate versus diazepam for eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 12. Art. No.: CD000127. DOI: 10.1002/14651858.CD000127.pub2.

Table 42. Magnesium sulfate versus phenytoin for eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus phenytoin	Control	Relative (95% CI)	Absolute		
Maternal death												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	10/424 (2.4%)	20/423 (4.7%)	RR 0.5 (0.24–1.05)	24 fewer per 1000 (from 36 fewer to 2 more)	MODERATE	CRITICAL
Recurrence of convulsions												
6	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	33/489 (6.7%)	96/483 (19.9%)	RR 0.34 (0.24–0.49)	131 fewer per 1000 (from 101 fewer to 151 fewer)	HIGH	CRITICAL
Respiratory depression												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	32/388 (8.2%)	45/387 (11.6%)	RR 0.71 (0.46–1.09)	34 fewer per 1000 (from 63 fewer to 10 more)	MODERATE	CRITICAL
Pulmonary oedema												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ^{1,2}	none	13/454 (2.9%)	14/448 (3.1%)	RR 0.92 (0.45–1.89)	2 fewer per 1000 (from 17 fewer to 28 more)	LOW	CRITICAL
Admission to intensive care unit												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	No serious imprecision	none	65/388 (16.8%)	97/387 (25.1%)	RR 0.67 (0.5–0.89)	83 fewer per 1000 (from 28 fewer to 125 fewer)	HIGH	CRITICAL
Mortality for the fetus or infant – Perinatal death												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	84/325 (25.8%)	103/340 (30.3%)	RR 0.85 (0.67–1.09)	45 fewer per 1000 (from 100 fewer to 27 more)	MODERATE	CRITICAL
Apgar scores – Apgar <7 at 5 minutes												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ¹	none	25/259 (9.7%)	29/259 (11.2%)	RR 0.86 (0.52–1.43)	16 fewer per 1000 (from 54 fewer to 48 more)	MODERATE	

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus phenytoin	Control	Relative (95% CI)	Absolute		
Utilization of special care baby unit (SCBU) – Admission to SCBU												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	82/259 (31.7%)	113/259 (43.6%)	RR 0.73 (0.58–0.91)	118 fewer per 1000 (from 39 fewer to 183 fewer)	HIGH	CRITICAL

1 Wide confidence interval.

2 Few events.

Source of evidence: Duley L, Henderson-Smart DJ, Chou D. Magnesium sulfate versus phenytoin for eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 10. Art. No.: CD000128.

DOI: 10.1002/14651858.CD000128.pub2.

Table 43. Magnesium sulfate versus lytic cocktail for eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Magnesium sulfate versus lytic cocktail	Control	Relative (95% CI)	Absolute		
Maternal death												
3	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ³	none	1/197 (0.5%)	14/200 (7%)	RR 0.14 (0.03–0.59)	60 fewer per 1000 (from 29 fewer to 68 fewer)	LOW	CRITICAL
Recurrence of convulsions												
3	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	no serious imprecision	none	6/197 (3%)	110/200 (55%)	RR 0.06 (0.03–0.12)	517 fewer per 1000 (from 484 fewer to 534 fewer)	MODERATE	CRITICAL
Coma >24 hours												
1	randomized trials	serious ²	no serious inconsistency	no serious indirectness	no serious imprecision	none	0/51 (0%)	12/57 (21.1%)	RR 0.04 (0–0.74)	202 fewer per 1000 (from 55 fewer to 211 fewer)	MODERATE	CRITICAL
Respiratory depression												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	serious ³	none	0/96 (0%)	8/102 (7.8%)	RR 0.12 (0.02–0.91)	69 fewer per 1000 (from 7 fewer to 77 fewer)	LOW	CRITICAL
Death of the fetus or infant (subgroups by stillbirth, perinatal and neonatal death) – Stillbirth												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ⁴	none	9/89 (10.1%)	16/88 (18.2%)	RR 0.33 (0.01–7.16)	122 fewer per 1000 (from 180 fewer to 1120 more)	VERY LOW	CRITICAL
Death of the fetus or infant (subgroups by stillbirth, perinatal and neonatal death) – Neonatal death												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ⁴	none	5/80 (6.3%)	13/73 (17.8%)	RR 0.37 (0.14 to 1)	112 fewer per 1000 (from 153 fewer to 0 more)	VERY LOW	CRITICAL

1 All studies were at moderate risk of bias.

2 The only study was at moderate risk of bias.

3 Very small sample size and few events.

4 Very small sample size and few events; wide confidence interval.

Source of evidence: Duley L, Gülmezoglu AM, Chou D. Magnesium sulfate versus lytic cocktail for eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 9. Art. No.: CD002960.

DOI: 10.1002/14651858.CD002960.pub2.

Table 44. Treatment of eclampsia: loading dose alone versus loading dose + maintenance regimen for women with pre-eclampsia and eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment of eclampsia: loading dose alone versus loading dose + maintenance regimen	Control	Relative (95% CI)	Absolute		
Recurrence of convulsions												
1	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ^{2,3}	none	8/202 (4%)	7/199 (3.5%)	RR 1.13 (0.42– 3.05)	5 more per 1000 (from 20 fewer to 72 more)	VERY LOW	CRITICAL
Maternal death												
1	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ^{2,3}	none	9/202 (4.5%)	10/199 (5%)	RR 0.89 (0.37–2.14)	6 fewer per 1000 (from 32 fewer to 57 more)	VERY LOW	CRITICAL
Stillbirth												
1	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	serious ²	none	25/171 (14.6%)	22/170 (12.9%)	RR 1.13 (0.66–1.92)	17 more per 1000 (from 44 fewer to 119 more)	VERY LOW	CRITICAL

1 The only study was at high risk of bias.

2 Wide confidence interval.

3 Few events

Source of evidence: Duley L, Matar HE, Almerie MQ, Hall DR. Alternative magnesium sulfate regimens for women with pre-eclampsia and eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 8. Art. No.: CD007388. DOI: 10.1002/14651858.CD007388.pub2.

Table 45. Treatment of eclampsia: lower dose regimens versus standard dose regimens for women with eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Treatment of eclampsia: lower dose regimens versus standard dose regimens	Control	Relative (95% CI)	Absolute		
Recurrence of convulsions												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	1/25 (4%)	0/25 (0%)	RR 3 (0.13–70.3)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL
Oliguria												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	1/25 (4%)	5/25 (20%)	RR 0.2 (0.03–1.59)	160 fewer per 1000 (from 194 fewer to 118 more)	VERY LOW	CRITICAL
Any baby death												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	8/25 (32%)	9/25 (36%)	RR 0.89 (0.41–1.93)	40 fewer per 1000 (from 212 fewer to 335 more)	VERY LOW	CRITICAL
Admission to special care baby unit												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	5/18 (27.8%)	2/17 (11.8%)	RR 2.36 (0.53–10.58)	160 more per 1000 (from 55 fewer to 1127 more)	VERY LOW	

1 The only study was at moderate risk of bias.

2 Very small sample size and few events; wide confidence interval.

Source of evidence: Duley L, Matar HE, Almerie MQ, Hall DR. Alternative magnesium sulfate regimens for women with pre-eclampsia and eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 8. Art. No.: CD007388. DOI: 10.1002/14651858.CD007388.pub2.

Table 46. Prevention of eclampsia: IV maintenance versus standard IM maintenance regimen (subgroups by dose of regimen) for women with pre-eclampsia and eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Prevention of eclampsia: IV maintenance versus standard IM maintenance regimen (subgroups by dose of regimen)	Control	Relative (95% CI)	Absolute		
Eclampsia												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/8 (0%)	0/9 (0%)	not pooled	0 fewer per 1000 (from 0 fewer to 0 fewer)	VERY LOW	CRITICAL
Renal failure												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	1/8 (12.5%)	0/9 (0%)	RR 3.33 (0.15–71.9)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL
Stillbirth												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	1/8 (12.5%)	1/10 (10%)	RR 1.25 (0.09–17.02)	25 more per 1000 (from 91 fewer to 1602 more)	VERY LOW	CRITICAL
Magnesium sulfate toxicity												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ³	none	1/8 (12.5%)	0/9 (0%)	RR 3.33 (0.15–71.9)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL

1 The only study was at moderate risk of bias.

2 Very small sample size and no events .

3 Very small sample size and few events; wide confidence interval.

Source of evidence: Duley L, Matar HE, Almerie MQ, Hall DR. Alternative magnesium sulfate regimens for women with pre-eclampsia and eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 8. Art. No.: CD007388. DOI: 10.1002/14651858.CD007388.pub2.

Table 47. Duration of postpartum maintenance regimen: short versus for 24 hours after delivery (subgroups by severity of pre-eclampsia) for women with pre-eclampsia and eclampsia

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Duration of postpartum maintenance regimen: short versus for 24 hours after delivery (subgroups by severity of pre-eclampsia)	Control	Relative (95% CI)	Absolute		
Eclampsia												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	0/199 (0%)	0/195 (0%)	not pooled	0 fewer per 1000 (from 0 fewer to 0 fewer)	VERY LOW	CRITICAL
Magnesium sulfate toxicity												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	0/101 (0%)	0/95 (0%)	not pooled	0 fewer per 1000 (from 0 fewer to 0 fewer)	VERY LOW	CRITICAL

1 No events in both intervention and control arms.

Source of evidence: Duley L, Matar HE, Almerie MQ, Hall DR. Alternative magnesium sulfate regimens for women with pre-eclampsia and eclampsia. Cochrane Database of Systematic Reviews, 2010, Issue 8. Art. No.: CD007388. DOI: 10.1002/14651858.CD007388.pub2.

Table 48. Any corticosteroid versus placebo or control for HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome in pregnancy

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Any corticosteroid versus placebo or control	Control	Relative (95% CI)	Absolute		
Eclampsia												
1	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	8/66 (12.1%)	10/66 (15.2%)	RR 0.8 (0.34–1.9)	30 fewer per 1000 (from 100 fewer to 136 more)	VERY LOW	CRITICAL
Maternal death or severe morbidity												
1	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	1/15 (6.7%)	4/16 (25%)	RR 0.27 (0.03–2.12)	183 fewer per 1000 (from 243 fewer to 280 more)	VERY LOW	CRITICAL
Maternal liver hematoma, rupture or failure												
2	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/45 (0%)	4/46 (8.7%)	RR 0.22 (0.03–1.83)	68 fewer per 1000 (from 84 fewer to 72 more)	VERY LOW	CRITICAL
Maternal pulmonary oedema												
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	6/152 (3.9%)	7/145 (4.8%)	RR 0.77 (0.24–2.48)	11 fewer per 1000 (from 37 fewer to 71 more)	LOW	CRITICAL
Maternal pulmonary oedema – Treatment commenced antenatally												
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ²	none	1/30 (3.3%)	1/30 (3.3%)	RR 1 (0.07–15.26)	0 fewer per 1000 (from 31 fewer to 475 more)	VERY LOW	CRITICAL
Maternal pulmonary oedema – Treatment commenced postnatally												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	2/56 (3.6%)	5/49 (10.2%)	RR 0.35 (0.07–1.72)	66 fewer per 1000 (from 95 fewer to 73 more)	LOW	CRITICAL
Maternal pulmonary oedema – Treatment commencement mixed or uncertain												
1	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	3/66 (4.5%)	1/66 (1.5%)	RR 3 (0.32–28.1)	30 more per 1000 (from 10 fewer to 411 more)	VERY LOW	CRITICAL
Need for dialysis												
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ²	none	1/30 (3.3%)	0/30 (0%)	RR 3 (0.13–70.83)	0 more per 1000 (from 0 fewer to 0 more)	VERY LOW	CRITICAL

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Any corticosteroid versus placebo or control	Control	Relative (95% CI)	Absolute			
Maternal renal failure													
3	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	17/152 (11.2%)	23/145 (15.9%)	RR 0.69 (0.39–1.22)	49 fewer per 1000 (from 97 fewer to 35 more)	LOW	CRITICAL	
Maternal renal failure – Treatment commenced antenatally													
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ²	none	2/30 (6.7%)	3/30 (10%)	RR 0.67 (0.12–3.71)	33 fewer per 1000 (from 88 fewer to 271 more)	VERY LOW	CRITICAL	
Maternal renal failure – Treatment commenced postnatally													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	9/56 (16.1%)	12/49 (24.5%)	RR 0.66 (0.3–1.42)	83 fewer per 1000 (from 171 fewer to 103 more)	LOW	CRITICAL	
Maternal renal failure – Treatment commencement mixed or uncertain													
1	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	6/66 (9.1%)	8/66 (12.1%)	RR 0.75 (0.28–2.04)	30 fewer per 1000 (from 87 fewer to 126 more)	VERY LOW		
Maternal death													
5	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	serious ⁴	none	5/184 (2.7%)	5/178 (2.8%)	RR 0.95 (0.28–3.21)	1 fewer per 1000 (from 20 fewer to 62 more)	VERY LOW	CRITICAL	
Maternal death – Treatment commenced antenatally													
2	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/45 (0%)	1/46 (2.2%)	RR 0.35 (0.02–8.08)	14 fewer per 1000 (from 21 fewer to 154 more)	VERY LOW	CRITICAL	
Maternal death – Treatment commenced postnatally													
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	2/73 (2.7%)	3/66 (4.5%)	RR 0.67 (0.13–3.46)	15 fewer per 1000 (from 40 fewer to 112 more)	LOW	CRITICAL	
Maternal death – Treatment commencement mixed or uncertain													
1	randomized trials	no serious limitations	very serious ¹	no serious indirectness	very serious ²	none	3/66 (4.5%)	1/66 (1.5%)	RR 3 (0.32–28.1)	30 more per 1000 (from 10 fewer to 411 more)	VERY LOW	CRITICAL	

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Any corticosteroid versus placebo or control	Control	Relative (95% CI)	Absolute		Quality
Perinatal/infant death												
2	randomized trials	very serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	4/28 (14.3%)	7/30 (23.3%)	RR 0.64 (0.21–1.97)	84 fewer per 1000 (from 184 fewer to 226 more)	VERY LOW	
Apgar score at 5 minutes <7												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	4/28 (14.3%)	5/30 (16.7%)	RR 0.89 (0.27–2.95)	18 fewer per 1000 (from 122 fewer to 325 more)	LOW	CRITICAL

1 The only study has a high risk of bias.

2 Very small sample size and few events; wide confidence interval.

3 Only study has a moderate risk of bias.

4 Wide confidence interval.

Source of evidence: Woudstra DM, Chandra S, Hofmeyr GJ, Dowswell T. Corticosteroids for HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome in pregnancy. Cochrane Database of Systematic Reviews, 2010, Issue 9. Art. No.: CD008148. DOI: 10.1002/14651858.CD008148.pub2.

Table 49. Dexamethasone versus bethamethasone for HELLP syndrome

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Dexamethasone versus betamethasone	Control	Relative (95% CI)	Absolute		
Perinatal/infant death												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	2/22 (9.1%)	2/21 (9.5%)	RR 0.95 (0.15–6.17)	5 fewer per 1000 (from 81 fewer to 492 more)	LOW	CRITICAL
Apgar score at 5 minutes <7												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	3/22 (13.6%)	3/21 (14.3%)	RR 0.95 (0.22–4.21)	7 fewer per 1000 (from 111 fewer to 459 more)	LOW	CRITICAL

1 Very small sample size and few events; wide confidence interval.

Source of evidence: Woudstra DM, Chandra S, Hofmeyr GJ, Dowswell T. Corticosteroids for HELLP (hemolysis, elevated liver enzymes, low platelets) syndrome in pregnancy. Cochrane Database of Systematic Reviews, 2010, Issue 9. Art. No.: CD008148. DOI: 10.1002/14651858.CD008148.pub2.

Table 50. Interventionist care versus expectant (delayed delivery) care for severe pre-eclampsia for severe pre-eclampsia before term

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Interventionist care versus expectant (delayed delivery) care for severe pre-eclampsia	Control	Relative (95% CI)	Absolute		
Eclampsia												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	0/46 (0%)	0/49 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Renal failure												
2	randomized trials	serious ²	no serious inconsistency	no serious indirectness	very serious ³	none	0/66 (0%)	1/67 (1.5%)	RR 0.3 (0.01–6.97)	10 fewer per 1000 (from 15 fewer to 89 more)	VERY LOW	CRITICAL
Pulmonary oedema												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	0/46 (0%)	0/49 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
HELLP syndrome												
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ³	none	1/46 (2.2%)	2/49 (4.1%)	RR 0.53 (0.05–5.68)	19 fewer per 1000 (from 39 fewer to 191 more)	LOW	CRITICAL
Death of the baby (subgrouped by time of death) – Perinatal death												
2	randomized trials	serious ⁴	no serious inconsistency	no serious indirectness	very serious ³	none	7/35 (20%)	6/33 (18.2%)	RR 1.14 (0.45–2.89)	25 more per 1000 (from 100 fewer to 344 more)	VERY LOW	CRITICAL
Admission to neonatal intensive care unit												
2	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	serious ⁵	none	61/61 (100%)	47/64 (73.4%)	RR 1.35 (1.16–1.58)	257 more per 1000 (from 117 more to 426 more)	MODERATE	CRITICAL

1 Very small sample size and no events.

2 Study that determine effect size at moderate risk of bias.

3 Very small sample size and few events; wide confidence interval.

4 Both studies were at moderate risk of bias.

5 Very small sample size

Source of evidence: Churchill D, Duley L. Interventionist versus expectant care for severe pre-eclampsia before term. Cochrane Database of Systematic Reviews, 2002, Issue 3. Art. No.: CD003106.

DOI: 10.1002/14651858.CD003106.*

Table 51. Induction of labour versus expectant management for pre-eclampsia at term

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect				
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Induction of labour versus expectant management for pre-eclampsia at term	Control	Relative (95% CI)	Absolute			
Severe systolic hypertension (systolic \geq 170 mm Hg), measured twice													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	26/377 (7%)	44/379 (12%)	0.60 (95% CI 0.38–0.95)	46 fewer per 1000 (from 6 fewer to 72 more)	HIGH	CRITICAL	
Severe diastolic hypertension (\geq 110 mm Hg), measured twice													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	no serious imprecision	none	28/377 (7%)	50/379 (13%)	0.56 (95% CI 0.36–0.87)	58 fewer per 1000 (from 17 fewer to 84 more)	HIGH	CRITICAL	
Eclampsia													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	0/377 (0%)	0/379 (0%)	not pooled	not pooled	VERY LOW	CRITICAL	
Pulmonary oedema													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	0/377 (0%)	2/379 (0.5%)	RR 0.2 (0.01–4.17)	4 fewer per 1000 (from 5 fewer to 17 more)	LOW	CRITICAL	
HELLP syndrome													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	4/377 (1.1%)	11/379 (2.9%)	RR 0.37 (0.12–1.14)	18 fewer per 1000 (from 26 fewer to 4 more)	LOW	CRITICAL	
Maternal ICU admission													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	6/377 (1.6%)	14/379 (3.7%)	RR 0.43 (0.17–1.11)	21 fewer per 1000 (from 31 fewer to 4 more)	LOW	CRITICAL	
Maternal death													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	0/377 (0%)	0/379 (0%)	not pooled	not pooled	MODERATE	CRITICAL	

Quality assessment							Summary of findings					Quality	Importance
							No. of patients		Effect		Control		
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Induction of labour versus expectant management for pre-eclampsia at term						
Perinatal death													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ¹	none	0/377 (0%)	0/379 (0%)	not pooled	not pooled	VERY LOW	CRITICAL	
Admission to neonatal intensive care unit													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	10/377 (2.7%)	8/379 (2.1%)	RR 1.26 (0.5–3.15)	5 more per 1000 (from 11 fewer to 45 more)	LOW		
Apgar score <7 at 5 minutes													
1	randomized trials	no serious limitations	no serious inconsistency	no serious indirectness	very serious ²	none	7/377 (1.9%)	9/379 (2.4%)	RR 0.78 (0.29–2.08)	5 fewer per 1000 (from 17 fewer to 26 more)	LOW		

1 No events.

2 Few events and wide confidence interval.

Source of evidence: Koopmans CM, Bijnenga D, Groen H et al. Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomized controlled trial. *Lancet*, 2009; 374: (9694): 979–88.

Table 52. Routine postnatal oral antihypertensive therapy for prevention of postpartum hypertension

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Routine postnatal oral antihypertensive therapy for prevention of postpartum hypertension	Control	Relative (95% CI)	Absolute		
Maternal death												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious	none	0/148 (0%)	0/147 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Maternal organ failure												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/132 (0%)	0/132 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Severe hypotension												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/16 (0%)	0/15 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Medication changed secondary to maternal side-effects												
1	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/16 (0%)	0/15 (0%)	not pooled	not pooled	VERY LOW	CRITICAL

1 Study at moderate risk of bias.

2 Very small sample size and no events.

Source of evidence: Magee L, Sadeghi S, von Dadelszen P. Prevention and treatment of postpartum hypertension. Cochrane Database of Systematic Reviews, 2005, Issue 1. Art. No.: CD004351.

DOI: 10.1002/14651858.CD004351.pub2.*

Table 53. Oral antihypertensive therapy for treatment of postpartum hypertension

Quality assessment							Summary of findings					Importance
							No. of patients		Effect		Quality	
No. of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Oral antihypertensive therapy for treatment of postpartum hypertension	Control	Relative (95% CI)	Absolute		Quality
Maternal death – Antihypertensive agent versus another for mild-moderate postpartum hypertension												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	0/52 (0%)	0/54 (0%)	not pooled	not pooled	VERY LOW	CRITICAL
Medication changed secondary to maternal side-effects – Antihypertensive agent versus another for mild-moderate postpartum hypertension												
2	randomized trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ⁴	none	1/52 (1.9%)	2/54 (3.7%)	RR 0.5 (0.05–5.3)	19 fewer per 1000 (from 35 fewer to 159 more)	VERY LOW	CRITICAL
Maternal hypotension – Antihypertensive agent versus another for severe postpartum hypertension												
1	randomized trials	serious ³	no serious inconsistency	no serious indirectness	very serious ²	none	0/40 (0%)	0/42	not pooled	not pooled	VERY LOW	CRITICAL

1 Both studies at moderate risk of bias.

2 Very small sample size and no events.

3 The only study was at moderate risk of bias.

4 Very small sample size and few events.

Source of evidence: Magee L, Sadeghi S, von Dadelszen P. Prevention and treatment of postpartum hypertension. Cochrane Database of Systematic Reviews, 2005, Issue 1. Art. No.: CD004351. DOI: 10.1002/14651858.CD004351.pub2.*

Table 54. Template for the summary of considerations related to the strength of recommendations with explanations for completing the template

Recommendation	1	Which recommendation?
Intervention	rest at home	What is the intervention?
Quality of the evidence	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input type="checkbox"/> Very low	<p>The higher the quality of the evidence, the stronger the recommendation.</p> <p>However, when “low” or “very-low” quality, consider more carefully the other criteria below in deciding the strength of the recommendation.</p>
Values and preferences	<input type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability	<p>This refers to values placed by health workers, policy-makers, patients and other stakeholders on the intended outcomes of interventions.</p> <p>If there is wide variability between values and preferences of various stakeholders, it is less likely to have a strong recommendation.</p>
Absolute magnitude of effect	<input type="checkbox"/> Large effect in the long term <input type="checkbox"/> Small effect for short duration	<p>This refers to the potential of the intervention to have large effects. The effects can be enhanced by combining with other interventions. Consider what are the possible associations (or “bundles”) that will enhance the effect.</p> <p>The larger the potential effects and for longer periods of time, the more likely to have a strong recommendation.</p>
Balance of benefits versus disadvantages	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<p>Benefits should consider the intended effects of the intervention.</p> <p>Disadvantages should consider the potentially negative effects of the intervention, as well as the unintended effects.</p> <p>The less potentially negative effects, the more likely to have a strong recommendation</p>
Resource use	<input type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<p>The resource needed for implementing the recommendation may comprise financial resources, human resources, and infrastructure or equipment. Ideally, the benefits of the intervention should come at reasonable, affordable and sustainable costs. One should consider that capital costs, such as for infrastructure development, even if initially high, may yield benefits in the long run.</p> <p>The higher the incremental or recurrent costs, all other things being equal, the less likely it is to have a strong recommendation.</p>
Feasibility	<input type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally	<p>All interventions require political commitment and wide stakeholder engagement as a prerequisite. In addition, “technical” feasibility requires functional organizational and institutional structures necessary to manage, follow through, and monitor the implementation of the recommendation. The elements of technical feasibility vary widely by country or context, but if these elements are likely to be functional in a wide variety of settings, the more likely is to have a strong recommendation.</p>
Overall ranking	<input type="checkbox"/> Strong recommendation <input type="checkbox"/> Weak recommendation	Strength of the recommendation.
Conclusion about recommendation direction	<input type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	

Notes with additional information, particularly where there is a mismatch between quality of evidence and the strength of the recommendations.

Table 55. Summary of considerations related to the strength of recommendations (recommendations 1–5)

Recommendation	1	2	3	4	5
Intervention	rest at home	bedrest in hospital	restricted dietary salt intake (to 20 or 50 mmol/day)	calcium supplementation (1.5–2.0 g/day)	vitamin D supplementation
Quality of the evidence	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input checked="" type="checkbox"/> Low <input type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input checked="" type="checkbox"/> Low <input type="checkbox"/> Very low	<input type="checkbox"/> High <input checked="" type="checkbox"/> Moderate <input type="checkbox"/> Low <input type="checkbox"/> Very low	<input type="checkbox"/> High <input checked="" type="checkbox"/> Moderate <input type="checkbox"/> Low <input type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input checked="" type="checkbox"/> Low <input type="checkbox"/> Very low
Values and preferences	<input type="checkbox"/> No significant variability <input checked="" type="checkbox"/> Significant variability	<input type="checkbox"/> No significant variability <input checked="" type="checkbox"/> Significant variability	<input type="checkbox"/> No significant variability <input checked="" type="checkbox"/> Significant variability	<input type="checkbox"/> No significant variability <input checked="" type="checkbox"/> Significant variability	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability
Absolute magnitude of effect	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input checked="" type="checkbox"/> Large effect in the long term <input type="checkbox"/> Small effect for short duration	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration
Balance of benefits versus disadvantages	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input checked="" type="checkbox"/> Benefits clearly outweigh disadvantages <input type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits
Resource use	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive
Feasibility	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally	<input type="checkbox"/> Yes, globally <input checked="" type="checkbox"/> Yes, conditionally	<input type="checkbox"/> Yes, globally <input checked="" type="checkbox"/> Yes, conditionally	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally
Overall ranking	<input type="checkbox"/> Strong recommendation <input checked="" type="checkbox"/> Weak recommendation	<input type="checkbox"/> Strong recommendation <input checked="" type="checkbox"/> Weak recommendation	<input type="checkbox"/> Strong recommendation <input checked="" type="checkbox"/> Weak recommendation†	<input checked="" type="checkbox"/> Strong recommendation <input type="checkbox"/> Weak recommendation	<input checked="" type="checkbox"/> Strong recommendation‡ <input type="checkbox"/> Weak recommendation
Conclusion about recommendation direction	<input type="checkbox"/> In favour of the intervention <input checked="" type="checkbox"/> Against the intervention	<input type="checkbox"/> In favour of the intervention <input checked="" type="checkbox"/> Against the intervention	<input type="checkbox"/> In favour of the intervention <input checked="" type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input type="checkbox"/> In favour of the intervention <input checked="" type="checkbox"/> Against the intervention

† This recommendation was made weak despite of moderate quality of evidence showing no statistical differences in the risk of critical outcomes. The guideline development group considered that there is significant variability on women's preferences regarding salt intake in different cultures and populations and possibly at different stages of pregnancy. It was also considered that while policy-makers in populations with normal baseline salt intake would be able to readily support unrestricted salt diet during pregnancy, they may be concerned about such advice in populations considered to have high baseline salt intake. In the end, advising women to continue salt diet according to their personal preferences would not require any special commitment of the policy-makers or stakeholder engagement as a prerequisite. However, in settings where the baseline salt intake is considered high, specific guidance may be needed

‡ This recommendation was made strong against the intervention despite of the low quality of evidence due to the fact that some participants expressed concerns about the limited evidence on safety of vitamin D supplementation during pregnancy. The guideline development group also noted that several studies were ongoing on this topic which may lead to a change in the evidence base in the future

Table 56. Summary of considerations related to the strength of recommendations (recommendations 6–10)

Recommendation	6	7	8	9	10
Intervention	vitamin C and E supplementation	low-dose acetylsalicylic acid for prevention of pre-eclampsia	initiation of low-dose acetylsalicylic acid before 20 weeks of pregnancy	antihypertensive drug treatment for women with severe hypertension	one antihypertensive drug versus another
Quality of the evidence	<input checked="" type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input type="checkbox"/> Very low	<input type="checkbox"/> High <input checked="" type="checkbox"/> Moderate <input type="checkbox"/> Low <input type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input checked="" type="checkbox"/> Low <input type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input checked="" type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input checked="" type="checkbox"/> Very low
Values and preferences	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability	<input type="checkbox"/> No significant variability <input checked="" type="checkbox"/> Significant variability
Absolute magnitude of effect	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input checked="" type="checkbox"/> Large effect in the long term <input type="checkbox"/> Small effect for short duration	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration
Balance of benefits versus disadvantages	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input checked="" type="checkbox"/> Benefits clearly outweigh disadvantages <input type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input checked="" type="checkbox"/> Benefits clearly outweigh disadvantages <input type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits
Resource use	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive
Feasibility	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally
Overall ranking	<input checked="" type="checkbox"/> Strong recommendation <input type="checkbox"/> Weak recommendation	<input checked="" type="checkbox"/> Strong recommendation [†] <input type="checkbox"/> Weak recommendation	<input type="checkbox"/> Strong recommendation <input checked="" type="checkbox"/> Weak recommendation	<input checked="" type="checkbox"/> Strong recommendation [†] <input type="checkbox"/> Weak recommendation	<input type="checkbox"/> Strong recommendation <input checked="" type="checkbox"/> Weak recommendation
Recommendation direction	<input type="checkbox"/> In favour of the intervention <input checked="" type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention

[†] This recommendation was made based on expert opinion. The group considered that there is a lack of clinical uncertainty over whether treatment of severe hypertension is beneficial. The guideline development group considered that most maternal deaths related to hypertensive disorders are associated with complications of uncontrolled severe high blood pressure. It was considered that most care providers and the women concerned would accept this intervention given the risk of morbidity and mortality associated with uncontrolled severe hypertension. Overall the benefits were considered clinically significant compared with the minor-moderate side-effects of selected antihypertensive drug. It was also noted that the treatment of severe hypertension (compared to no intervention) may increase health care resource use in the short term (in settings where it is not already in use), but it is believed that it is cost effective in terms of long term outcomes and associated costs. No major barriers to implementation of this recommendation are foreseen.

Table 57. Summary of considerations related to the strength of recommendations (recommendations 11–15)

Recommendation	11	12	13	14	15
Intervention	Thiazide diuretics for prevention of pre-eclampsia	Magnesium sulfate for prevention of eclampsia	Magnesium sulfate for treatment of eclampsia	Full intravenous or intramuscular magnesium sulfate regimens	In settings where it is not possible to administer the full magnesium sulfate regimen, loading dose only
Quality of the evidence	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input checked="" type="checkbox"/> Low <input type="checkbox"/> Very low	<input checked="" type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input type="checkbox"/> Very low	<input type="checkbox"/> High <input checked="" type="checkbox"/> Moderate <input type="checkbox"/> Low <input type="checkbox"/> Very low	<input type="checkbox"/> High <input checked="" type="checkbox"/> Moderate <input type="checkbox"/> Low <input type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input checked="" type="checkbox"/> Very low
Values and preferences	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability	<input type="checkbox"/> No significant variability <input checked="" type="checkbox"/> Significant variability	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability
Absolute magnitude of effect	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input checked="" type="checkbox"/> Large effect in the long term <input type="checkbox"/> Small effect for short duration	<input checked="" type="checkbox"/> Large effect in the long term <input type="checkbox"/> Small effect for short duration	<input checked="" type="checkbox"/> Large effect in the long term <input type="checkbox"/> Small effect for short duration	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration
Balance of benefits versus disadvantages	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input type="checkbox"/> Benefits and disadvantages are balanced <input checked="" type="checkbox"/> Disadvantages clearly outweigh benefits	<input checked="" type="checkbox"/> Benefits clearly outweigh disadvantages <input type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input checked="" type="checkbox"/> Benefits clearly outweigh disadvantages <input type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits
Resource use	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input type="checkbox"/> Less resource intensive <input checked="" type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input type="checkbox"/> Less resource intensive <input checked="" type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive
Feasibility	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally	<input type="checkbox"/> Yes, globally <input checked="" type="checkbox"/> Yes, conditionally	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally	<input type="checkbox"/> Yes, globally <input checked="" type="checkbox"/> Yes, conditionally	<input type="checkbox"/> Yes, globally <input checked="" type="checkbox"/> Yes, conditionally
Overall ranking	<input checked="" type="checkbox"/> Strong recommendation <input type="checkbox"/> Weak recommendation	<input checked="" type="checkbox"/> Strong recommendation <input type="checkbox"/> Weak recommendation	<input checked="" type="checkbox"/> Strong recommendation <input type="checkbox"/> Weak recommendation	<input checked="" type="checkbox"/> Strong recommendation <input type="checkbox"/> Weak recommendation	<input type="checkbox"/> Strong recommendation <input checked="" type="checkbox"/> Weak recommendation
Recommendation direction	<input type="checkbox"/> In favour of the intervention <input checked="" type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention

†Low quality of evidence shows that the use of thiazide diuretics is not associated with better outcomes. It was considered that most women and care providers would accept not to use thiazide diuretics for preventing pre-eclampsia given its lack of benefits, its maternal side-effects and the safety concerns regarding such treatment. Maternal side-effects include minor to severe nausea and vomiting. Potential harmful effects of thiazide diuretics in pregnancy include possible association with congenital abnormalities, neonatal thrombocytopenia and hypoglycaemia, electrolyte imbalances in fetus and mother and maternal hypovolaemia.

Table 58. Summary of considerations related to the strength of recommendations (recommendations 16–20)

Recommendation	16	17	18	19	20
Intervention	corticosteroids for HELLP syndrome treatment	induction of labour for women with severe pre-eclampsia at a gestational age where fetal viability is unlikely to be achieved with expectant care.	expectant management for women with severe pre-eclampsia, a viable fetus and before 34 weeks of gestation	expectant management for women with severe pre-eclampsia, a viable fetus, after 34 weeks of gestation but before term.	early delivery for women with severe pre-eclampsia at term.
Quality of the evidence	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input checked="" type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input checked="" type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input checked="" type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input checked="" type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input checked="" type="checkbox"/> Low <input type="checkbox"/> Very low
Values and preferences	<input type="checkbox"/> No significant variability <input checked="" type="checkbox"/> Significant variability	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability	<input type="checkbox"/> No significant variability <input checked="" type="checkbox"/> Significant variability	<input type="checkbox"/> No significant variability <input checked="" type="checkbox"/> Significant variability	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability
Absolute magnitude of effect	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input checked="" type="checkbox"/> Large effect in the long term <input type="checkbox"/> Small effect for short duration
Balance of benefits versus disadvantages	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input checked="" type="checkbox"/> Benefits clearly outweigh disadvantages <input type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input checked="" type="checkbox"/> Benefits clearly outweigh disadvantages <input type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits
Resource use	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input type="checkbox"/> Less resource intensive <input checked="" type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive
Feasibility	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally	<input type="checkbox"/> Yes, globally <input checked="" type="checkbox"/> Yes, conditionally	<input type="checkbox"/> Yes, globally <input checked="" type="checkbox"/> Yes, conditionally	<input type="checkbox"/> Yes, globally <input checked="" type="checkbox"/> Yes, conditionally	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally
Overall ranking	<input type="checkbox"/> Strong recommendation <input checked="" type="checkbox"/> Weak recommendation	<input checked="" type="checkbox"/> Strong recommendation [†] <input type="checkbox"/> Weak recommendation	<input type="checkbox"/> Strong recommendation <input checked="" type="checkbox"/> Weak recommendation	<input type="checkbox"/> Strong recommendation <input checked="" type="checkbox"/> Weak recommendation	<input checked="" type="checkbox"/> Strong recommendation <input type="checkbox"/> Weak recommendation
Recommendation direction	<input type="checkbox"/> In favour of the intervention <input checked="" type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention [‡] <input type="checkbox"/> Against the intervention

† A systematic review of observational studies compared outcomes associated with expectant versus interventionist care for women with severe pre-eclampsia. With either policy, a perinatal mortality of >80% was observed for women with pre-eclampsia at gestation <24 weeks. Most clinicians, women concerned and policy-makers would accept this intervention considering the generally poor outcomes for both mother and child. If severe pre-eclampsia is present at a gestational age where expectant management cannot lead to local fetal viability, the perinatal outcome will be very poor with both lines of action. The maternal risk will be reduced if early delivery is applied by anticipating the only definitive treatment of pre-eclampsia (i.e. delivery). In terms of benefits and disadvantages for mothers, early delivery was perceived as associated with a clinically significant risk reduction for mothers, whereas potential risks of induction of labour at this gestational age were noted, particularly in resource-poor settings. Benefits and disadvantages may be balanced for fetuses as early delivery will be associated with a poor outcome. In this context, it is noted that with early delivery or expectant management, induction of labour is a matter of time. In resource-poor settings, expectant management practically translates to watchful expectancy. In more

developed settings, the use of facilities for fetal and maternal surveillance and the neonatal support within the expectant management policy is comparatively more resource intensive. Uptake of a policy of interventionist care and early delivery by induction of labour may face social, cultural and economic barriers in many settings.

‡The guideline development group considered that there is no clinical uncertainty over whether termination of pregnancy in women with severe pre-eclampsia at term is beneficial. Evidence from the Hypitac trial (further downgraded for indirectness) is used to support this recommendation. The effect observed in the Hypitac trial is expected to be increased in this population. Most care providers and women concerned would accept this intervention given the risks of morbidity and mortality associated with severe pre-eclampsia that outweighs the downsides of interventionist care. In terms of benefits and disadvantages, early delivery is perceived as associated with a significant risk reduction for other severe maternal and perinatal morbidity and mortality, while the potential risks of induction of labour and caesarean section were noted particularly in resource poor settings. Overall and considering the resources associated with the management of complications, in women with severe pre-eclampsia at term, early delivery is considered less resource intensive as compared with expectant management. No major barriers to implementation of this recommendation are foreseen.

Table 59. Summary of considerations related to the strength of recommendations (recommendations 21–23)

Recommendation	21	22	23
Intervention	induction of labour for women with mild pre-eclampsia at term.	continuation of antihypertensive treatment post partum	antihypertensive treatment for severe post partum hypertension
Quality of the evidence	<input type="checkbox"/> High <input checked="" type="checkbox"/> Moderate <input type="checkbox"/> Low <input type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input checked="" type="checkbox"/> Very low	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input checked="" type="checkbox"/> Very low
Values and preferences	<input type="checkbox"/> No significant variability <input checked="" type="checkbox"/> Significant variability	<input type="checkbox"/> No significant variability <input checked="" type="checkbox"/> Significant variability	<input checked="" type="checkbox"/> No significant variability <input type="checkbox"/> Significant variability
Absolute magnitude of effect	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input type="checkbox"/> Large effect in the long term <input checked="" type="checkbox"/> Small effect for short duration	<input checked="" type="checkbox"/> Large effect in the long term <input type="checkbox"/> Small effect for short duration
Balance of benefits versus disadvantages	<input type="checkbox"/> Benefits clearly outweigh disadvantages <input checked="" type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input checked="" type="checkbox"/> Benefits clearly outweigh disadvantages <input type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits	<input checked="" type="checkbox"/> Benefits clearly outweigh disadvantages <input type="checkbox"/> Benefits and disadvantages are balanced <input type="checkbox"/> Disadvantages clearly outweigh benefits
Resource use	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive	<input type="checkbox"/> Less resource intensive <input checked="" type="checkbox"/> More resource intensive	<input checked="" type="checkbox"/> Less resource intensive <input type="checkbox"/> More resource intensive
Feasibility	<input type="checkbox"/> Yes, globally <input checked="" type="checkbox"/> Yes, conditionally	<input type="checkbox"/> Yes, globally <input checked="" type="checkbox"/> Yes, conditionally	<input checked="" type="checkbox"/> Yes, globally <input type="checkbox"/> Yes, conditionally
Overall ranking	<input type="checkbox"/> Strong recommendation <input checked="" type="checkbox"/> Weak recommendation [†]	<input checked="" type="checkbox"/> Strong recommendation [‡] <input type="checkbox"/> Weak recommendation	<input checked="" type="checkbox"/> Strong recommendation [§] <input type="checkbox"/> Weak recommendation
Recommendation direction	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention	<input checked="" type="checkbox"/> In favour of the intervention <input type="checkbox"/> Against the intervention

† A systematic review that included one trial with 756 women compared a policy of induction of labour with expectant management for women with mild pre-eclampsia or gestational hypertension between 36 weeks (0 days) and 41 weeks (0 days). Although no serious limitations were apparent in the conduct of the trial, the results were generally imprecise due to the small sample size and sparse data. In settings where gestational age is difficult to be determined accurately, some women and clinicians may prefer to delay the induction of labour from 37 to 38/39 weeks in order to reduced the risk of iatrogenic prematurity. In order to maximize the chance of success and spontaneous onset of labour, similar approach can be used in settings where induction of labour and caesarean section face quality/safety issues. Moderate reduction in the risk of severe hypertension. No evidence on long-term effects. As benefits, no evidence of benefits regarding critical outcomes is observed. There is a moderate reduction of the risk of severe hypertension and use of anticonvulsants. As disadvantages, potential risks of induction of labour (e.g. increased caesarean sections) in resource-poor settings. Expectant management in women with mild pre-eclampsia at term was associated with an increased risk of severe hypertension and consequently increased risk of endovenous antihypertensive use and prophylactic anticonvulsants. Overall, in resource-poor settings, early delivery may be more resource intensive as compared with expectant management. Uptake of a policy of induction of labour for “mild disease condition” may face social, cultural and economic barriers in resource-poor settings.

‡ In a Cochrane review of three randomized controlled trials comparing routine antihypertensive therapy with an approach that dictated antihypertensive treatment only for severely elevated blood pressure postpartum in women with antenatal pre-eclampsia, there were insufficient data for any conclusions about the possible benefits and harms of these management strategies. Clinical practice often depends on capacity for postpartum clinical monitoring of changes in blood pressure. Initiating antihypertensive drug treatment where follow-up is not guaranteed carries both potential benefits and harms. No events in comparison groups to determine magnitude of effect. The guideline development group put more emphasis on the frequency of postpartum deaths related to stroke and recognized that the maximum increase in blood pressure usually occurs towards the end of the first postpartum week (when, in most settings, women have been already discharged from facility care). Continued antihypertensive drug use is more resource intensive than interrupting the use of antihypertensive drugs. It is unclear whether, overall, the continued use of antihypertensive drugs will reduce adverse outcomes and, with that, reduce the use of resources. Locally available resources to follow up postpartum patients vary widely between settings.

§ This recommendation is inferred from the evidence on consequences of untreated severe postpartum hypertension e.g. stroke and maternal death. The guideline development group considered that there is little clinical uncertainty over whether treatment of severe postpartum hypertension is beneficial. This recommendation was made based on expert opinion and the guideline development group considered that most maternal deaths related to hypertensive disorders are associated with complications of uncontrolled severe high blood pressure. Based on that, the guideline development group agreed that antihypertensive treatment should be recommended in all cases of severe acute hypertension. Most clinicians and the women concerned would accept treatment for severe hypertension given its associated morbidity and mortality compared with the few downsides of antihypertensive drugs. Considering that most maternal deaths related to hypertensive disorders are associated with complications of uncontrolled severe high blood pressure, treatment of this conditions is expected to avert maternal deaths and other severe maternal complications. Benefits: the guideline development group put more emphasis on the frequency of postpartum deaths related to stroke and recognized that the maximum increase in blood pressure usually occurs towards the end of the first postpartum week (when, in most settings, women have been already discharged from facility care). Disadvantages: side-effects of the chosen antihypertensive drug. Overall, the implementation of this recommendation was considered less resource intensive compared with not treating a severe hypertension and facing the risk of a severe complication with its associated higher resource needs. No major barriers to implementation of this recommendation are foreseen.

Box 2. Priority actions for dissemination and implementation

- Prepare guideline derivatives for policy-makers, consumers, clinicians and other groups (e.g. a two-page policy brief, and a press release for engaging the public via the media. Managing Complications in Pregnancy and Childbirth update).
- Prepare the translation of WHO Executive Summary: three to five pages into six official United Nations languages.
- Seek endorsement by national and international professional societies, including International Federation of Gynecology and Obstetrics, International Confederation of Midwives, and others (e.g. American Congress of Obstetricians and Gynecologists, and Royal College of Obstetricians and Gynaecologists).
- Promote discussion, dissemination and uptake during the International Society for the Study of Hypertension in Pregnancy World Congress in Geneva, 2012.
- Foster agreement between guidelines for unified recommendations.
- Promote the development of local guidelines/protocols based on these guidelines.
- Continue working with the Norwegian Knowledge Centre for developing tools to facilitate the formulation of health policies based on evidence-based guidelines.
- Prepare health system interventions including advocacy actions, “Health Systems Taskforce” and “use of evidence in policy-making” (e.g. EVIPNet (Evidence-Informed Policy Network)).
- Further understand facility processes and develop strategies for behaviour change and guideline uptake.
- Engage local opinion leaders early in the process/explore the use of multifaceted approaches.
- Foster the implementation of near-miss criterion-based clinical audits.
- Increase the visibility and availability of WHO guidelines.
- Disseminate WHO guidelines in Health Sector Review meetings.
- Involve education institutions, develop training and pre-service curriculum.
- Disseminate these guidelines using WHO guidance community and Knowledge Gateway to virtual community.
- Prepare WHO–UNFPA Joint Statements related to the main recommendations of these guidelines.
- Maximize the dissemination of these guidelines across WHO (regional and country offices).
- Promote active engagement and dialogue rather than passive distribution and action plans.
- Develop appropriate job aids and clinical decision tools e.g. how to mix magnesium sulfate.
- Foster availability of magnesium sulfate (e.g. Beximco pharmaceuticals product).
- Promote task shifting (including independent use by all care providers skilled in magnesium sulfate use).
- Explore the development of means to capture issues related to the implementation of these guidelines (e.g. through web site or Knowledge Gateway).
- Further develop maternal and newborn outcome indicators that could better inform clinical practice.

