PREDICTION: GRADE TABLES

GRADE Table 1: Diagnostic accuracy of PAPP-A to predict preeclampsia in the first trimester

Bibliography: Morris RK, Bilagi A, Devani P, Kilby MD. Association of serum PAPP-A levels in first trimester with small for gestational age and adverse pregnancy outcomes: systematic review and meta-analysis. Prenat Diagn. 2017 Mar;37(3):253–65.

Sensitivity	0.16 (95% CI: 0.09 to 0.28)
Specificity	0.92 (95% CI: 0.85 to 0.96)

Prevalences	10%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of10%	pre-test probability of0%	pre-test probability of0%	
True positives (patients with preeclampsia)	8 studies 132076 patients	cohort & case-control type studies	not serious	not serious	serious[a]	not serious	none	16 (9 to 28)	0 (0 to 0)	0 (0 to 0)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having preeclampsia)								84 (72 to 91)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without preeclampsia)	8 studies 132076 patients	cohort & case-control type studies	not serious	not serious	serious[a]	not serious	none	828 (765 to 864)	920 (850 to 960)	920 (850 to 960)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having preeclampsia)								72 (36 to 135)	80 (40 to 150)	80 (40 to 150)	

Explanations

a. There are concerns about inconsistency due to significant heterogeneity across the studies, I^2>50%.

GRADE TABLE 2: Diagnostic accuracy of PLGF to predict preeclampsia in the first trimester

Bibliography: Agrawal S, Shinar S, Cerdeira AS, Redman C, Vatish M. Predictive Performance of PlGF (Placental Growth Factor) for Screening Preeclampsia in Asymptomatic Women: A Systematic Review and Meta-Analysis. Hypertension [Internet]. 2019;74(5):1124–35.

Sensitivity	0.50 (95% CI: 0.36 to 0.64)
Specificity	0.89 (95% CI: 0.85 to 0.95)

Prevalences	10%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of10%	pre-test probability of0%	pre-test probability of0%	
True positives (patients with preeclampsia)	15 studies 0 patients	cohort & case-control type studies	not serious	not serious	serious[a]	not serious	none	50 (36 to 64)	0 (0 to 0)	0 (0 to 0)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having preeclampsia)								50 (36 to 64)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without preeclampsia)	15 studies 0 patients	cohort & case-control type studies	not serious	not serious	serious[a]	not serious	none	801 (765 to 855)	890 (850 to 950)	890 (850 to 950)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having preeclampsia)								99 (45 to 135)	110 (50 to 150)	110 (50 to 150)	

Explanations

a. There are concerns about inconsistency due to significant heterogeneity across the studies, I^2 =99%. The authors state that this is due to difference PlGF cutoffs used in the studies.

GRADE TABLE 3: Diagnostic accuracy of Uterine artery Doppler to predict preeclampsia in the first trimester

Bibliography: Velauthar L, Plana MN, Kalidindi M, Zamora J, Thilaganathan B, Illanes SE, et al. First-trimester uterine artery Doppler and adverse pregnancy outcome: a meta-analysis involving 55,974 women. Ultrasound in Obstetrics & Gynecology [Internet]. 2014 May;43(5):500–7.

Sensitivity	0.26 (95% CI: 0.23 to 0.31)
Specificity	0.93 (95% CI: 0.90 to 0.96)

Prevalences	10%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of10%	pre-test probability of0%	pre-test probability of0%	
True positives (patients with preeclampsia)	8 studies 37971 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious[a]	not serious	None	26 (23 to 31)	0 (0 to 0)	0 (0 to 0)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having preeclampsia)								74 (69 to 77)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without preeclampsia)	8 studies 37971 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious[a]	not serious	None	837 (810 to 864)	930 (900 to 960)	930 (900 to 960)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having preeclampsia)								63 (36 to 90)	70 (40 to 100)	70 (40 to 100)	

Explanations

a. There are concerns about inconsistency due to significant heterogeneity across the studies. The authors report that differences in information provided on the reference standard, lack of blinding and use of preventive therapy, contributed to the heterogeneity.

GRADE TABLE 4: Diagnostic accuracy of PLGF to predict preeclampsia in the second trimester

Bibliography: Agrawal S, Shinar S, Cerdeira AS, Redman C, Vatish M. Predictive Performance of PlGF (Placental Growth Factor) for Screening Preeclampsia in Asymptomatic Women: A Systematic Review and Meta-Analysis. Hypertension [Internet]. 2019;74(5):1124–35.

Sensitivity	0.72 (95% CI: 0.64 to 0.82)
Specificity	0.82 (95% CI: 0.75 to 0.87)

Prevalences	10%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of10%	pre-test probability of0%	pre-test probability of0%	
True positives (patients with preeclampsia)	18 studies 0 patients	cohort & case-control type studies	not serious	not serious	serious[a]	not serious	none	72 (64 to 82)	0 (0 to 0)	0 (0 to 0)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having preeclampsia)								28 (18 to 36)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without preeclampsia)	18 studies 0 patients	cohort & case-control type studies	not serious	not serious	serious[a]	not serious	none	738 (675 to 783)	820 (750 to 870)	820 (750 to 870)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having preeclampsia)								162 (117 to 225)	180 (130 to 250)	180 (130 to 250)	

Explanations

a. There are concerns about inconsistency due to significant heterogeneity across the studies, I^2 =99%. The authors state that this is due to the varied PlGF cutoffs used in the studies.

GRADE TABLE 5: Diagnostic accuracy of PLGF to predict preeclampsia in the second trimester in those with suspected preeclampsia

Bibliography: Chappell LC, Duckworth S, Seed PT, Griffin M, Myers J, Mackillop L, et al. Diagnostic accuracy of placental growth factor in women with suspected preeclampsia: a prospective multicenter study. Circulation. 2013 Nov 5;128(19):2121–31.

Sensitivity	0.96 (95% CI: 0.89 to 0.99)
Specificity	0.55 (95% CI: 0.48 to 0.61)

Prevalences	10%	0%	0%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of10%	pre-test probability of0%	pre-test probability of0%	
True positives (patients with preeclampsia)	1 studies 287 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	none	96 (89 to 99)	0 (0 to 0)	0 (0 to 0)	⨁⨁⨁⨁ High
False negatives (patients incorrectly classified as not having preeclampsia)								4 (1 to 11)	0 (0 to 0)	0 (0 to 0)	
True negatives (patients without preeclampsia)	1 studies 287 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	none	495 (432 to 549)	550 (480 to 610)	550 (480 to 610)	⨁⨁⨁⨁ High
False positives (patients incorrectly classified as having preeclampsia)								405 (351 to 468)	450 (390 to 520)	450 (390 to 520)	

GRADE TABLE 6: PLGF VS no PLGF for reducing time to detect preeclampsia

Bibliography: Duhig KE, Myers J, Seed PT, Sparkes J, Lowe J, Hunter RM, et al. Placental growth factor testing to assess women with suspected pre-eclampsia: a multicentre, pragmatic, stepped-wedge cluster-randomised controlled trial. Lancet [Internet]. 2019 May 4 [cited 2023 Jan 25];393(10183):1807–18. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6497988/

Certainty assessment							Summary of findings		
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Impact
							With no PlFG	With PlGF	
Time to preeclampsia diagnosis									
1023 (1 RCT)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	The median time to preeclampsia diagnosis was 4.1 days in the usual care group and was 1.9 days in the PlGF group. The time ratio was 0.36 (95% CI 0.15 to 0.87) (*high certainty evidence*), which corresponds to a 64% reduction in the time to diagnosis.		

CI: confidence interval

PREVENTION: GRADE TABLES

GRADE Table 1: ASA supplementation VS placebo/no intervention for prevention of HDP

Bibliography: Duley L, Meher S, Hunter KE, Seidler AL, Askie LM. Antiplatelet agents for preventing pre-eclampsia and its complications. The Cochrane database of systematic reviews [Internet]. 2019;2019(10). Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD004659.pub3/full

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo	With aspirin		Risk with placebo	Risk difference with aspirin
Preeclampsia											
32217 (31 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	1370/16007 (8.6%)	1229/16210 (7.6%)	**RR 0.89** (0.82 to 0.95)	86 per 1,000	**9 fewer per 1,000** (from 15 fewer to 4 fewer)
Preeclampsia (low risk population)											
20583 (25 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	456/10235 (4.5%)	406/10348 (3.9%)	**RR 0.88** (0.77 to 1.00)	45 per 1,000	**5 fewer per 1,000** (from 10 fewer to 0 fewer)
Preeclampsia (high risk population)											
11076 (26 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	872/5488 (15.9%)	792/5588 (14.2%)	**RR 0.90** (0.82 to 0.98)	159 per 1,000	**16 fewer per 1,000** (from 29 fewer to 3 fewer)
Preeclampsia (dose <75mg)											

Certainty assessment							Summary of findings				
22618 (11 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	1040/11273 (9.2%)	957/11345 (8.4%)	**RR 0.92** (0.85 to 1.00)	92 per 1,000	**7 fewer per 1,000** (from 14 fewer to 0 fewer)

Preeclampsia (dose >75mg)

9107 (16 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	305/4537 (6.7%)	241/4570 (5.3%)	**RR 0.78** (0.66 to 0.92)	67 per 1,000	**15 fewer per 1,000** (from 23 fewer to 5 fewer)

PPH

23769 (19 RCTs)	not serious	serious[a]	not serious	not serious	none	⨁⨁⨁◯ Moderate	1691/11876 (14.2%)	1794/11893 (15.1%)	**RR 1.06** (1.00 to 1.12)	142 per 1,000	**9 more per 1,000** (from 0 fewer to 17 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Imprecision was downgraded to concerns about clinical heterogeneity between trials in methods for measuring blood loss.

GRADE Table 2: ASA supplementation VS placebo/ no intervention for prevention of HDP by time of initiation

Bibliography: Roberge S, Nicolaides K, Demers S, Hyett J, Chaillet N, Bujold E. The role of aspirin dose on the prevention of preeclampsia and fetal growth restriction: systematic review and meta-analysis. Am J Obstet Gynecol [Internet]. 2017 Feb [cited 2023 Jan 25];216(2):110-120.e6. Available from: https://www.ajog.org/article/S0002-9378(16)30783-9/fulltext

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo	With aspirin		Risk with placebo	Risk difference with aspirin
Preeclampsia (Initiation of aspirin <16 weeks)											
5113 (19 RCTs)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	⨁⨁⨁◯ Moderate	354/2549 (13.9%)	221/2564 (8.6%)	**RR 0.57** (0.43 to 0.75)	139 per 1,000	**60 fewer per 1,000** (from 79 fewer to 35 fewer)
Preeclampsia (Initiation of aspirin >16 weeks)											
15370 (21 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	586/7669 (7.6%)	517/7701 (6.7%)	**RR 0.81** (0.66 to 0.99)	76 per 1,000	**15 fewer per 1,000** (from 26 fewer to 1 fewer)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Funnel plot indicates that publication bias is suspected. The small studies had the most positive results, suggesting small study effects

GRADE Table 3: Calcium supplementation VS placebo for prevention of HDP

Bibliography: Hofmeyr GJ, Lawrie TA, Atallah ÁN, Torloni MR. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. Cochrane Database Syst Rev [Internet]. 2018 Jun 1;10:CD001059. Available from: http://dx.doi.org/10.1002/14651858.CD001059.pub5

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo	With calcium supplementation		Risk with placebo	Risk difference with calcium supplementation
Preeclampsia											
15730 (13 RCTs)	not serious	serious[a]	not serious	not serious	publication bias strongly suspected[b]	⨁⨁◯◯ Low	510/7879 (6.5%)	379/7851 (4.8%)	**RR 0.45** (0.31 to 0.65)	65 per 1,000	**36 fewer per 1,000** (from 45 fewer to 23 fewer)
Preeclampsia (in those with a low calcium diet)											
10678 (8 RCTs)	not serious	serious[c]	not serious	not serious	publication bias strongly suspected[b]	⨁⨁◯◯ Low	306/5347 (5.7%)	209/5331 (3.9%)	**RR 0.36** (0.20 to 0.65)	57 per 1,000	**37 fewer per 1,000** (from 46 fewer to 20 fewer)
Preeclampsia (in those with an adequate calcium diet)											
5022 (4 RCTs)	not serious	serious[d]	not serious	not serious	publication bias strongly suspected[b]	⨁⨁◯◯ Low	197/2517 (7.8%)	169/2505 (6.7%)	**RR 0.62** (0.32 to 1.20)	78 per 1,000	**30 fewer per 1,000** (from 53 fewer to 16 more)
Preeclampsia (in a low risk population)											
15143 (8 RCTs)	not serious	serious[a]	not serious	not serious	publication bias strongly suspected[b]	⨁⨁◯◯ Low	456/7573 (6.0%)	370/7570 (4.9%)	**RR 0.59** (0.41 to 0.83)	60 per 1,000	**25 fewer per 1,000** (from 36 fewer to 10 fewer)
Preeclampsia (in a high risk population)											

Certainty assessment							Summary of findings				
587 (5 RCTs)	not serious	not serious	not serious	not serious	publication bias strongly suspected[b]	⨁⨁⨁◯ Moderate	54/306 (17.6%)	9/281 (3.2%)	**RR 0.22** (0.12 to 0.42)	176 per 1,000	**138 fewer per 1,000** (from 155 fewer to 102 fewer)
High blood pressure											
15470 (12 RCTs)	not serious	serious[e]	not serious	not serious	publication bias strongly suspected[b]	⨁⨁◯◯ Low	1472/7744 (19.0%)	1260/7726 (16.3%)	**RR 0.65** (0.53 to 0.81)	190 per 1,000	**67 fewer per 1,000** (from 89 fewer to 36 fewer)
High blood pressure (in those with a low calcium diet)											
10418 (7 RCTs)	not serious	serious[f]	not serious	not serious	publication bias strongly suspected[b]	⨁⨁◯◯ Low	847/5212 (16.3%)	703/5206 (13.5%)	**RR 0.44** (0.28 to 0.70)	163 per 1,000	**91 fewer per 1,000** (from 117 fewer to 49 fewer)
High blood pressure (in those with an adequate calcium diet)											
5022 (4 RCTs)	not serious	not serious	not serious	not serious	publication bias strongly suspected[b]	⨁⨁⨁◯ Moderate	614/2517 (24.4%)	547/2505 (21.8%)	**RR 0.90** (0.81 to 0.99)	244 per 1,000	**24 fewer per 1,000** (from 46 fewer to 2 fewer)
High blood pressure (in a low risk population)											
15143 (8 RCTs)	not serious	serious[c]	not serious	not serious	publication bias strongly suspected[b]	⨁⨁◯◯ Low	1407/7573 (18.6%)	1235/7570 (16.3%)	**RR 0.71** (0.57 to 0.89)	186 per 1,000	**54 fewer per 1,000** (from 80 fewer to 20 fewer)
High blood pressure (in a high risk population)											
327 (4 RCTs)	not serious	serious[g]	not serious	not serious	publication bias strongly suspected[b]	⨁⨁◯◯ Low	65/171 (38.0%)	25/156 (16.0%)	**RR 0.47** (0.22 to 0.97)	380 per 1,000	**201 fewer per 1,000** (from 296 fewer to 11 fewer)
Preterm birth											

Certainty assessment							Summary of findings				
15275 (11 RCTs)	not serious	serious[h]	not serious	not serious	publication bias strongly suspected[b]	⨁⨁◯◯ Low	795/7655 (10.4%)	722/7620 (9.5%)	**RR 0.76** (0.60 to 0.97)	104 per 1,000	**25 fewer per 1,000** (from 42 fewer to 3 fewer)

HELLP syndrome

12901 (2 RCTs)	not serious	not serious	not serious	not serious	serious[i]	none	⨁⨁⨁◯ Moderate	6/6455 (0.1%)	16/6446 (0.2%)	**RR 2.67** (1.05 to 6.82)	1 per 1,000	**2 more per 1,000** (from 0 fewer to 5 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. The results from these studies are inconsistent; I^2 = 70%
b. Funnel plot indicates that publication bias is suspected. The small studies had the most positive results, suggesting small study effects.
c. The results from these studies are inconsistent; I^2 = 76%
d. The results from these studies are inconsistent; I^2 = 52%, and the confidence interval crosses the null.
e. The results from theses studies are inconsistent; I^2 = 74%
f. The results from theses studies are inconsistent; I^2 = 84%
g. The results from theses studies are inconsistent; I^2 = 73%
h. The results from theses studies are inconsistent; I^2 = 60%
i. Imprecision was rated serious due to low event numbers.

GRADE Table 4: Vitamin C/E supplementation VS placebo/ no intervention for prevention of HDP

Bibliography: Rumbold A, Ota E, Nagata C, Shahrook S, Crowther CA. Vitamin C supplementation in pregnancy. Cochrane Database of Systematic Reviews [Internet]. 2015;(9). Available from: http://dx.doi.org/10.1002/14651858.CD004072.pub3

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo	With vitamin C/E	Relative effect (95% CI)	Risk with placebo	Risk difference with vitamin C/E
Preeclampsia											
20765 (13 RCTs)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	⨁⨁⨁◯ Moderate	996/10388 (9.6%)	967/10377 (9.3%)	**RR 0.91** (0.78 to 1.06)	96 per 1,000	**9 fewer per 1,000** (from 21 fewer to 6 more)
Term PROM											
3060 (2 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	86/1544 (5.6%)	146/1516 (9.6%)	**RR 1.73** (1.34 to 2.23)	56 per 1,000	**41 more per 1,000** (from 19 more to 69 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Funnel plot indicates that publication bias is suspected. Small studies reporting negative results may be missing, which could indicate reporting bias.

GRADE Table 5: Folic acid VS placebo/ no intervention for prevention of HDP

Bibliography: Liu C, Liu C, Wang Q, Zhang Z. Supplementation of folic acid in pregnancy and the risk of preeclampsia and gestational hypertension: a meta-analysis. Archives of Gynecology & Obstetrics [Internet]. 2018 Oct;298(4):697–704. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6153594/

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo/no intervention	With folic acid		Risk with placebo/no intervention	Risk difference with folic acid
Preeclampsia (supplementation with a multivitamin containing folic acid)											
51479 (7 observational studies)	not serious	Serious[b]	not serious	not serious	publication bias strongly suspected[a]	⨁◯◯◯ Very low	419/16037 (2.6%)	857/35442 (2.4%)	**RR 0.70** (0.53 to 0.93)	26 per 1,000	**8 fewer per 1,000** (from 12 fewer to 2 fewer)
Preeclampsia (supplementation with folic acid alone)											
210896 (5 observational studies)	not serious	not serious	not serious	not serious	publication bias strongly suspected[a]	⨁◯◯◯ Very low	2745/114034 (2.4%)	2425/96862 (2.5%)	**RR 0.97** (0.80 to 1.17)	24 per 1,000	**1 fewer per 1,000** (from 5 fewer to 4 more)
Gestational hypertension (supplementation with folic acid alone)											
247186 (5 observational studies)	not serious	Serious[c]	not serious	Serious[d]	none	⨁◯◯◯ Very low	9958/125746 (7.9%)	9794/121440 (8.1%)	**RR 1.19** (0.92 to 1.54)	79 per 1,000	**15 more per 1,000** (from 6 fewer to 43 more)

CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio

Explanations

a. Funnel plot indicates that publication bias is suspected. The small studies had the most positive results, suggesting small study effects.
b. The results from these studies are inconsistent; I^2 =60%
c. The results from these studies are inconsistent; I^2= 89%
d. Imprecision was rated serious due a large confidence interval that crosses the null.

GRADE Table 6: Vitamin D supplementation VS placebo/ no intervention for prevention of HDP

Bibliography: Palacios C, Kostiuk LK, Peña-Rosas JP. Vitamin D supplementation for women during pregnancy. Cochrane Database of Systematic Reviews [Internet]. 2019;(7). Available from: http://dx.doi.org/10.1002/14651858.CD008873.pub

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo/ no intervention	With vitamin D		Risk with placebo/ no intervention	Risk difference with vitamin D
Preeclampsia											
499 (4 RCTs)	serious[a]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	38/226 (16.8%)	21/273 (7.7%)	**RR 0.48** (0.30 to 0.79)	168 per 1,000	**87 fewer per 1,000** (from 118 fewer to 35 fewer)
Gestational hypertension											
1130 (2 RCTs)	serious[c]	not serious	not serious	serious[d]	none	⨁⨁◯◯ Low	19/543 (3.5%)	17/587 (2.9%)	**RR 0.78** (0.41 to 1.49)	35 per 1,000	**8 fewer per 1,000** (from 21 fewer to 17 more)
Preterm birth											
1640 (7 RCTs)	serious[e]	not serious	not serious	serious[d]	none	⨁⨁◯◯ Low	47/784 (6.0%)	34/856 (4.0%)	**RR 0.66** (0.34 to 1.30)	60 per 1,000	**20 fewer per 1,000** (from 40 fewer to 18 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias assessments from the Cochrane review "Vitamin D supplementation for women during pregnancy" (2019) have been used. In these assessments, concerns about allocation concealment were identified.
b. Imprecision was rated serious due to a low number of events and a small sample size.

c. Risk of bias assessments from the Cochrane review "Vitamin D supplementation for women during pregnancy" (2019) have been used. In these assessments, concerns about allocation concealment, blinding, and attrition bias were identified.
d. Imprecision was rated serious due to a low number of events and a large confidence interval that crosses the null.
e. Risk of bias assessments from the Cochrane review "Vitamin D supplementation for women during pregnancy" (2019) have been used. In these assessments, concerns about selection bias were identified.

GRADE Table 7: Selenium supplementation VS placebo for prevention of HDP

Bibliography: Xu M, Guo D, Gu H, Zhang L, Lv S. Selenium and Preeclampsia: a Systematic Review and Meta-analysis. Biological trace element research [Internet]. 2016;171(2):283–92. Available from: https://link.springer.com/article/10.1007/s12011-015-0545-7

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo/no intervention	With other micronutrient supplementation		Risk with placebo/no intervention	Risk difference with other micronutrient supplementation
Preeclampsia											
439 (3 RCTs)	serious[a]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	15/221 (6.8%)	3/218 (1.4%)	**RR 0.28** (0.09 to 0.84)	68 per 1,000	**49 fewer per 1,000** (from 62 fewer to 11 fewer)

CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio

Explanations

a. Risk of bias was rated serious due to concerns about randomization.

b. Imprecision was rated serious due to a small sample size, low number of events, and a wide confidence interval.

GRADE Table 8: L-arginine supplementation VS placebo for prevention of HDP

Bibliography: Vadillo-Ortega F, Perichart-Perera O, Espino S, Avila-Vergara MA, Ibarra I, Ahued R, et al. Effect of supplementation during pregnancy with L-arginine and antioxidant vitamins in medical food on pre-eclampsia in high risk population: randomised controlled trial. BMJ: British Medical Journal (Overseas & Retired Doctors Edition) [Internet]. 2011 May 28;342(7808):1193.
Camarena Pulido EE, García Benavides L, Panduro Barón JG, Pascoe Gonzalez S, Madrigal Saray AJ, García Padilla FE, et al. Efficacy of L-arginine for preventing preeclampsia in high-risk pregnancies: A double-blind, randomized, clinical trial. Hypertension in pregnancy. 2016 May;35(2).

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo/no intervention	With other micronutrient supplementation		Risk with placebo/no intervention	Risk difference with other micronutrient supplementation
Preeclampsia											
546 (2 RCTs)	not serious	not serious	not serious	serious[a]	none	⨁⨁⨁◯ Moderate	78/269 (29.0%)	32/277 (11.6%)	**RR 0.40** (0.28 to 0.59)	290 per 1,000	**174 fewer per 1,000** (from 209 fewer to 119 fewer)

CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio

Explanations

a. Imprecision was rated serious due to a small sample size and low event number.

GRADE Table 9: Probiotics VS no intervention for prevention of HDP

Bibliography: Brantsæter AL, Myhre R, Haugen M, Myking S, Sengpiel V, Magnus P, et al. Intake of Probiotic Food and Risk of Preeclampsia in Primiparous Women. American Journal of Epidemiology [Internet]. 2011 Oct;174(7):807–15. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3203379/

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo/no intervention	With other micronutrient supplementation	Relative effect (95% CI)	Risk with placebo/no intervention	Risk difference with other micronutrient supplementation
Preeclampsia											
23412 (1 observational study)	not serious	not serious	not serious	not serious	none	⨁⨁◯◯ Low	1129/20104 (5.6%)	136/3308 (4.1%)	**OR 0.80** (0.66 to 0.96)	56 per 1,000	**11 fewer per 1,000** (from 18 fewer to 2 fewer)

CI: confidence interval; **OR:** odds ratio

GRADE Table 10: Probiotics VS placebo for prevention of GDM

Bibliography: Davidson SJ, Barrett HL, Price SA, Callaway LK, Dekker Nitert M. Probiotics for preventing gestational diabetes. Cochrane Database Syst Rev. 2021;4:CD009951. Probiotics for preventing gestational diabetes - Davidson, SJ - 2021 | Cochrane Library

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo/no intervention	With other micronutrient supplementation		Risk with placebo/no intervention	Risk difference with other micronutrient supplementation
Preeclampsia											
955 (4 RCTs)	not serious	not serious	serious[b]	serious[a]	none	⨁⨁◯◯ Low	17/483 (3.5%)	31/472 (6.6%)	**RR 1.85** (1.04 to 3.29)	35 per 1,000	**30 more per 1,000** (from 1 more to 81 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Imprecision was rated serious due to a small sample size and low event number.

b. These studies only included pregnant people with higher BMIs (overweight and obesity). Research has shown that birthing parents with a BMI > 30 kg/m2 are at increased risk of pre-eclampsia, RR 2.81 (95% CI 2.56 to 3.09). (2) The results of the Cochrane review may have been impacted by this variable. Furthermore, these results may not be generalizable to all populations.

GRADE Table 11: Omega 3 fatty acid supplementation VS placebo/no intervention for prevention of HDP

Bibliography: Middleton P, Gomersall JC, Gould JF, Shepherd E, Olsen SF, Makrides M. Omega-3 fatty acid addition during pregnancy. Cochrane Database of Systematic Reviews [Internet]. 2018;(11). Available from: http://dx.doi.org/10.1002/14651858.CD003402.pub3

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo/no intervention	With Omega 3 fatty acid supplementation		Risk with placebo/no intervention	Risk difference with Omega 3 fatty acid supplementation
Preeclampsia											
5825 (13 RCTs)	serious[a]	not serious	not serious	not serious	none	⨁⨁⨁◯ Moderate	146/2849 (5.1%)	143/2976 (4.8%)	**RR 0.95** (0.76 to 1.19)	51 per 1,000	**3 fewer per 1,000** (from 12 fewer to 10 more)
High blood pressure											
4431 (6 RCTs)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	268/2228 (12.0%)	276/2203 (12.5%)	**RR 1.05** (0.90 to 1.22)	120 per 1,000	**6 more per 1,000** (from 12 fewer to 26 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias was rated serious due to concerns about attrition bias and selective reporting.

GRADE Table 12: Magnesium supplement VS placebo/no intervention for prevention of HDP

Bibliography: Makrides M, Crosby DD, Shepherd E, Crowther CA. Magnesium supplementation in pregnancy. Cochrane Database of Systematic Reviews [Internet]. 2014;(4). Available from: http://dx.doi.org/10.1002/14651858.CD000937.pub2

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo/ no intervention	With magnesium		Risk with placebo/ no intervention	Risk difference with magnesium
Preeclampsia											
1042 (3 RCTs)	serious [a]	not serious	not serious	serious [b]	none	⨁⨁◯◯ Low	42/529 (7.9%)	36/513 (7.0%)	**RR 0.87** (0.58 to 1.32)	79 per 1,000	**10 fewer per 1,000** (from 33 fewer to 25 more)
Preterm birth											
5981 (7 RCTs)	serious [a]	not serious	not serious	serious [b]	none	⨁⨁◯◯ Low	329/3032 (10.9%)	302/2949 (10.2%)	**RR 0.89** (0.69 to 1.14)	109 per 1,000	**12 fewer per 1,000** (from 34 fewer to 15 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias assessments from the Cochrane review "Magnesium supplementation in pregnancy" (2014) have been used. In these assessments, concerns about allocation concealment and attrition bias were identified.
b. Inconsistency was rated serious due to a wide confidence interval that crosses the null.

GRADE Table 13: Vitamin B6 supplementation VS placebo/no intervention for prevention of HDP

Bibliography: Salam RA, Zuberi NF, Bhutta ZA. Pyridoxine (vitamin B6) supplementation during pregnancy or labour for maternal and neonatal outcomes. Cochrane Database of Systematic Reviews [Internet]. 2015;(6). Available from: http://dx.doi.org/10.1002/14651858.CD000179.pub3

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo/no intervention	With vitamin B6	Relative effect (95% CI)	Risk with placebo/no intervention	Risk difference with vitamin B6
Preeclampsia											
1197 (2 RCTs)	serious[a]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	12/593 (2.0%)	21/604 (3.5%)	**RR 1.71** (0.85 to 3.45)	20 per 1,000	**14 more per 1,000** (from 3 fewer to 50 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias assessments from the Cochrane review "Pyridoxine (vitamin B6) supplementation during pregnancy or labour for maternal and neonatal outcomes" (2015) have been used. In these assessments concerns about randomization, allocation concealment and selective reporting were identified.
b. Imprecision was rated serious due to low event numbers and a wide confidence interval that crosses the null.

GRADE Table 14: Zinc supplementation VS placebo/no intervention for prevention of HDP

Bibliography: Carducci B, Keats EC, Bhutta ZA. Zinc supplementation for improving pregnancy and infant outcome. The Cochrane database of systematic reviews. 2021;3:CD000230.

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo/ no intervention	With zinc		Risk with placebo/ no intervention	Risk difference with zinc
Preeclampsia											
2568 (6 RCTs)	serious[a]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	45/1303 (3.5%)	41/1265 (3.2%)	**RR 0.93** (0.62 to 1.42)	35 per 1,000	**2 fewer per 1,000** (from 13 fewer to 15 more)
Preterm birth											
9833 (21 RCTs)	serious[c]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	620/4879 (12.7%)	559/4954 (11.3%)	**RR 0.87** (0.74 to 1.03)	127 per 1,000	**17 fewer per 1,000** (from 33 fewer to 4 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias was rated serious due to concerns about attrition bias and reporting bias.
b. Imprecision was rated serious due to a wide confidence interval that crosses the null.
c. Risk of bias assessments from the Cochrane review "Zinc supplementation for improving pregnancy and infant outcome" (2021) have been used. In these assessments, concerns about randomization, attrition bias and reporting bias were identified.

GRADE Table 15: Garlic supplementation VS placebo/no intervention for prevention of HDP

Bibliography: Meher S, Duley L. Garlic for preventing pre-eclampsia and its complications. The Cochrane database of systematic reviews. 2006 Jul 19;(3):CD006065.

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With placebo/ no intervention	With garlic		Risk with placebo/ no intervention	Risk difference with garlic
Preeclampsia											
100 (1 RCT)	serious[a]	not serious	not serious	serious[b]	none	⨁⨁◯◯ Low	9/50 (18.0%)	7/50 (14.0%)	**RR 0.78** (0.31 to 1.93)	180 per 1,000	**40 fewer per 1,000** (from 124 fewer to 167 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias was rated serious due to a lack of information about randomization and allocation concealment.
b. Imprecision was rated very serious due to a small sample size, low number of events, and a wide confidence interval.

GRADE Table 16: Rest VS no intervention for prevention of HDP

Bibliography: Meher S, Duley L. Rest during pregnancy for preventing pre-eclampsia and its complications in women with normal blood pressure. The Cochrane database of systematic reviews. 2006 Apr 19;(2):CD005939.

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With no intervention	With exercise		Risk with no intervention	Risk difference with exercise
Preeclampsia											
32 (1 RCT)	serious[a]	not serious	not serious	very serious[b]	none	⨁◯◯◯ Very low	9/16 (56.3%)	0/16 (0.0%)	**RR 0.05** (0.00 to 0.83)	563 per 1,000	**534 fewer per 1,000** (from 96 fewer to --)
Gestational hypertension											
32 (1 RCT)	serious[a]	not serious	not serious	very serious[b]	none	⨁◯◯◯ Very low	4/16 (25.0%)	1/16 (6.3%)	**RR 0.25** (0.03 to 2.00)	250 per 1,000	**188 fewer per 1,000** (from 243 fewer to 250 more)

CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio

Explanations

a. Risk of bias was rated serious due to lack of information about allocation concealment and selective reporting.
b. Imprecision was rated very serious due to the small sample size, low number of events and wide confidence interval.

ANTEPARTUM CONSIDERATIONS: GRADE TABLES

GRADE Table 1: Home blood pressure monitoring VS standard care for detection of HDP

Bibliography: Tucker KL, Mort S, Yu LM, Campbell H, Rivero-Arias O, Wilson HM, et al. Effect of Self-monitoring of Blood Pressure on Diagnosis of Hypertension During Higher-Risk Pregnancy: The BUMP 1 Randomized Clinical Trial. JAMA. 2022;327(17):1656–65.

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With standard care	With HBPM		Risk with standard care	Risk difference with HBPM
Time to clinical hypertension											
2346 (1 RCT)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	1175	1171	-	The mean time to clinical hypertension was **104.3** days	MD **1.6 days lower** (8.1 lower to 4.9 higher)

CI: confidence interval; **MD:** mean difference

GRADE Table 2: Diagnostic accuracy of dipstick test with a threshold of 1+ to diagnose proteinuria in those with hypertension in pregnancy

Bibliography: Teeuw HM, Amoakoh HB, Ellis CA, Lindsley K, Browne JL. Diagnostic accuracy of urine dipstick tests for proteinuria in pregnant women suspected of preeclampsia: A systematic review and meta-analysis. Pregnancy Hypertens. 2022 Mar;27:123–30.

Sensitivity	0.63 (95% CI: 0.53 to 0.73)
Specificity	0.84 (95% CI: 0.68 to 0.93)

Prevalences	10%	90%	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested		Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 10%	pre-test probability of 90%	
True positives (patients with proteinuria)	13 studies 2156 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	very serious[a]	not serious	none	63 (53 to 73)	567 (477 to 657)	⨁⨁◯◯ Low
False negatives (patients incorrectly classified as not having proteinuria)								37 (27 to 47)	333 (243 to 423)	
True negatives (patients without proteinuria)	13 studies 2156 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	very serious[a]	not serious	none	756 (612 to 837)	84 (68 to 93)	⨁⨁◯◯ Low
False positives (patients incorrectly classified as having proteinuria)								144 (63 to 288)	16 (7 to 32)	

Explanations

a. There are concerns about inconsistency due to significant heterogeneity across the studies; sensitivity I^2 = 76%, specificity= I^2 = 95

GRADE Table 3: Diagnostic accuracy of PCR with a threshold of 30mg/mmol to diagnose proteinuria in those with hypertension in pregnancy

Bibliography: Geneen LJ, Webster KE, Reeves T, Eadon H, Maresh M, Fishburn S, et al. Protein-creatinine ratio and albumin-creatinine ratio for the diagnosis of significant proteinuria in pregnant women with hypertension: Systematic review and meta-analysis of diagnostic test accuracy. Pregnancy Hypertens. 2021 Aug;25:196–203.

Sensitivity	0.91 (95% CI: 0.85 to 0.94)
Specificity	0.89 (95% CI: 0.77 to 0.95)

Prevalences	10%	90%	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested		Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 10%	pre-test probability of 90%	
True positives (patients with proteinuria)	13 studies 3577 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	very serious[a]	not serious	none	91 (85 to 94)	819 (765 to 846)	⨁⨁◯◯ Low
False negatives (patients incorrectly classified as not having proteinuria)								9 (6 to 15)	81 (54 to 135)	
True negatives (patients without proteinuria)	13 studies 3577 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	very serious[a]	not serious	none	801 (693 to 855)	89 (77 to 95)	⨁⨁◯◯ Low
False positives (patients incorrectly classified as having proteinuria)								99 (45 to 207)	11 (5 to 23)	

Explanations

a. There are concerns about inconsistency due to significant heterogeneity across the studies; sensitivity $I^2 = 94\%$, specificity= $I^2 = 97\%$

GRADE Table 4: Diagnostic accuracy of ACR with a threshold of 2mg/mmol to diagnose proteinuria in those with hypertension in pregnancy

Bibliography: Geneen LJ, Webster KE, Reeves T, Eadon H, Maresh M, Fishburn S, et al. Protein-creatinine ratio and albumin-creatinine ratio for the diagnosis of significant proteinuria in pregnant women with hypertension: Systematic review and meta-analysis of diagnostic test accuracy. Pregnancy Hypertens. 2021 Aug;25:196–203.

Sensitivity	0.98 (95% CI: 0.94 to 0.99)
Specificity	0.69 (95% CI: 0.38 to 0.89)

Prevalences	10%	90%	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested		Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 10%	pre-test probability of 90%	
True positives (patients with proteinuria)	4 studies 1412 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	very serious[a]	not serious	none	98 (94 to 99)	882 (846 to 891)	⨁⨁◯◯ Low
False negatives (patients incorrectly classified as not having proteinuria)								2 (1 to 6)	18 (9 to 54)	
True negatives (patients without proteinuria)	4 studies 1412 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	very serious[a]	serious[b]	none	621 (342 to 801)	69 (38 to 89)	⨁◯◯◯ Very low
False positives (patients incorrectly classified as having proteinuria)								279 (99 to 558)	31 (11 to 62)	

Explanations

a. There are concerns about inconsistency due to significant heterogeneity across the studies; sensitivity I^2 =96%, specificity I^2 =99%

b. Imprecision was rated serious due to the wide confidence interval for this estimate of effect.

GRADE Table 5: Diagnostic accuracy of ACR with a threshold of 8mg/mmol to diagnose proteinuria in those with hypertension in pregnancy

Bibliography: Geneen LJ, Webster KE, Reeves T, Eadon H, Maresh M, Fishburn S, et al. Protein-creatinine ratio and albumin-creatinine ratio for the diagnosis of significant proteinuria in pregnant women with hypertension: Systematic review and meta-analysis of diagnostic test accuracy. Pregnancy Hypertens. 2021 Aug;25:196–203.

Sensitivity	1.00 (95% CI: 0.75 to 1.00)
Specificity	0.96 (95% CI: 0.92 to 0.99)

Prevalences	10%	90%	

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested		Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of 10%	pre-test probability of 90%	
True positives (patients with proteinuria)	1 studies 150 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	serious[a]	none	100 (75 to 100)	900 (675 to 900)	⨁⨁⨁◯ Moderate
False negatives (patients incorrectly classified as not having proteinuria)								0 (0 to 25)	0 (0 to 225)	
True negatives (patients without proteinuria)	1 studies 150 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	serious[a]	none	864 (828 to 891)	96 (92 to 99)	⨁⨁⨁◯ Moderate
False positives (patients incorrectly classified as having proteinuria)								36 (9 to 72)	4 (1 to 8)	

Explanations

a. Imprecision was rated serious because there is only one study with a small sample size.

ANTEPARTUM MANAGEMENT: GRADE TABLES

GRADE Table 1: Home blood pressure monitoring VS clinic monitoring for management of HDP

Bibliography: Kalafat E, Benlioglu C, Thilaganathan B, Khalil A. Home blood pressure monitoring in the antenatal and postpartum period: A systematic review meta-analysis. Pregnancy Hypertens [Internet]. 2020 Jan [cited 2023 Jan 25];19:44–51. Available from: https://www.sciencedirect.com/science/article/abs/pii/S2210778919304738?via%3Dihub

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With standard care	With home blood pressure monitoring	Relative effect (95% CI)	Risk with standard care	Risk difference with home blood pressure monitoring
NICU admission											
444 (2 observational studies)	not serious	not serious	not serious	not serious	none	⨁⨁◯◯ Low	41/278 (14.7%)	12/166 (7.2%)	**OR 0.53** (0.27 to 1.07)	147 per 1,000	**63 fewer per 1,000** (from 103 fewer to 9 more)
Antenatal visits											
738 (5 observational studies)	not serious	serious[a]	not serious	not serious	none	⨁◯◯◯ Very low	400	338	-	-	SMD **0.49 lower** (0.82 lower to 0.16 lower)
Labor induction											
444 (2 observational studies)	not serious	not serious	not serious	not serious	none	⨁⨁◯◯ Low	139/278 (50.0%)	65/166 (39.2%)	**OR 0.55** (0.36 to 0.82)	500 per 1,000	**145 fewer per 1,000** (from 235 fewer to 49 fewer)
Prenatal admissions											

Certainty assessment							Summary of findings				
416 (3 observational studies)	not serious	not serious	not serious	not serious	none	⨁⨁◯◯ Low	147/273 (53.8%)	36/143 (25.2%)	**OR 0.31** (0.19 to 0.49)	538 per 1,000	**273 fewer per 1,000** (from 357 fewer to 175 fewer)

CI: confidence interval; **OR:** odds ratio; **SMD:** standardised mean difference

Explanations

a. The results from these studies are inconsistent; $I^2 = 75\%$

GRADE Table 2: Antihypertensive therapy VS placebo/no intervention for management of mild to moderate HDP

Bibliography: Abalos E, Duley L, Steyn DW, Gialdini C. Antihypertensive drug therapy for mild to moderate hypertension during pregnancy. Cochrane Database Syst Rev [Internet]. 2018 Feb 1 [cited 2023 Jan 25];10:CD002252. Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002252.pub4/full

Certainty assessment							Summary of findings				
							Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo/no intervention	With antihypertensive therapy		Risk with placebo/no intervention	Risk difference with antihypertensive therapy
Severe hypertension											
2558 (20 RCTs)	serious[a]	not serious	not serious	not serious	none	⨁⨁⨁◯ Moderate	242/1222 (19.8%)	125/1336 (9.4%)	**RR 0.49** (0.40 to 0.60)	198 per 1,000	**101 fewer per 1,000** (from 119 fewer to 79 fewer)
Preeclampsia											
2851 (23 RCTs)	serious[a]	not serious	not serious	not serious	publication bias strongly suspected[b]	⨁⨁◯◯ Low	256/1375 (18.6%)	251/1476 (17.0%)	**RR 0.92** (0.74 to 1.14)	186 per 1,000	**15 fewer per 1,000** (from 48 fewer to 26 more)
Preterm birth (<37 weeks)											
2141 (15 RCTs)	serious[a]	not serious	not serious	not serious	none	⨁⨁⨁◯ Moderate	279/1006 (27.7%)	289/1135 (25.5%)	**RR 0.96** (0.83 to 1.12)	277 per 1,000	**11 fewer per 1,000** (from 47 fewer to 33 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias assessments from the Cochrane review "Antihypertensive drug therapy for mild to moderate hypertension during pregnancy" (2018) have been used. In these assessments, concerns about blinding and selective reporting were identified.
b. Funnel plot indicates that publication bias is suspected. The small studies had the most positive results, suggesting small study effects.

GRADE Table 3: Induction after 37 weeks gestation VS expectant management in those with gestational hypertension or mild preeclampsia

Bibliography: Koopmans CM, Bijlenga D, Groen H, Vijgen SM, Aarnoudse JG, Bekedam DJ, et al. Induction of labour versus expectant monitoring for gestational hypertension or mild pre-eclampsia after 36 weeks' gestation (HYPITAT): a multicentre, open-label randomised controlled trial. Lancet. 2009 Sep 19;374(9694):979–88.

Certainty assessment							Summary of findings				
							Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With expectant management	With induction		Risk with expectant management	Risk difference with induction
Adverse birthing parent outcome											
756 (1 RCT)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	166/379 (43.8%)	117/377 (31.0%)	**RR 0.71** (0.59 to 0.86)	44 per 100	**13 fewer per 100** (from 18 fewer to 6 fewer)
Adverse neonatal outcome											
756 (1 RCT)	not serious	not serious	not serious	serious[a]	none	⨁⨁⨁◯ Moderate	32/379 (8.4%)	24/377 (6.4%)	**RR 0.75** (0.45 to 1.26)	8 per 100	**2 fewer per 100** (from 5 fewer to 2 more)
C-section											
756 (1 RCT)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	72/379 (19.0%)	54/377 (14.3%)	**RR 0.75** (0.55 to 1.04)	19 per 100	**5 fewer per 100** (from 9 fewer to 1 more)

CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio

Explanations

a. Imprecision was rated serious due to a large confidence interval that cross the null, a low number of events, and small sample size.

GRADE Table 4: Induction between 34-37 weeks gestation VS expectant management for those with HDP

Bibliography: Broekhuijsen K, van Baaren GJ, van Pampus MG, Ganzevoort W, Sikkema JM, Woiski MD, et al. Immediate delivery versus expectant monitoring for hypertensive disorders of pregnancy between 34 and 37 weeks of gestation (HYPITAT-II): an open-label, randomised controlled trial. Lancet [Internet]. 2015 Jun 20 [cited 2023 Jan 25];385(9986):2492–501. Available from: https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(14)61998-X/fulltext

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With expectant management	With induction		Risk with expectant management	Risk difference with induction
Adverse birthing parent outcome											
703 (1 RCT)	not serious	not serious	not serious	serious[a]	none	⨁⨁⨁◯ Moderate	11/351 (3.1%)	4/352 (1.1%)	**RR 0.36** (0.12 to 1.13)	3 per 100	**2 fewer per 100** (from 3 fewer to 0 fewer)
RDS											
703 (1 RCT)	not serious	not serious	not serious	serious[b]	none	⨁⨁⨁◯ Moderate	6/351 (1.7%)	20/352 (5.7%)	**RR 3.32** (1.35 to 8.18)	2 per 100	**4 more per 100** (from 1 more to 12 more)
NICU admission											
702 (1 RCT)	not serious	not serious	not serious	serious[b]	none	⨁⨁⨁◯ Moderate	13/350 (3.7%)	26/352 (7.4%)	**RR 1.99** (1.04 to 3.81)	4 per 100	**4 more per 100** (from 0 fewer to 10 more)
Any neonatal morbidity											

Certainty assessment							Summary of findings				
512 (1 RCT)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	89/245 (36.3%)	131/267 (49.1%)	**RR 1.35** (1.10 to 1.66)	36 per 100	**13 more per 100** (from 4 more to 24 more)

C-section

703 (1 RCT)	not serious	not serious	not serious	not serious	none	⨁⨁⨁⨁ High	114/351 (32.5%)	107/352 (30.4%)	**RR 0.94** (0.75 to 1.16)	32 per 100	**2 fewer per 100** (from 8 fewer to 5 more)

CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio

Explanations

a. Imprecision was rated serious due to a large confidence interval that cross the null, a low number of events, and small sample size.
b. Imprecision was rated serious due to a low number of events.

INTRAPARTUM MANAGEMENT: GRADE TABLES

GRADE Table 1: Risk of hypotension after epidural in those without HDP compared to those with HDP

Bibliography: Aya AGM, Mangin R, Vialles N, Ferrer J-M, Robert C, Ripart J, et al. Patients with severe preeclampsia experience less hypotension during spinal anesthesia for elective cesarean delivery than healthy parturients: a prospective cohort comparison. Anesthesia and analgesia. 2003 Sep;97(3):867–72.

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							Risk in participants with no HDP	Risk in participants with preeclampsia		Risk with no intervention	Risk difference with Epidural
Hypotension											
60 (1 observational study)	not serious	not serious	not serious	serious[a]	none	⨁◯◯◯ Very low	16/30 (53.3%)	5/30 (16.7%)	**OR 0.17** (0.05 to 0.58)	533 per 1,000	**371 fewer per 1,000** (from 479 fewer to 135 fewer)

CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio

Explanations

a. Imprecision was rated serious due to a low number of events, and small sample size.

GRADE Table 2: Ergometrine VS oxytocin for the prevention of PPH in those with preeclampsia

Bibliography:

Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ, et al. Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database Syst Rev. 2018;12:CD011689. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011689.pub3/full

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With oxytocin	With carbetocin		Risk with oxytocin	Risk difference with carbetocin
Hypertension											
1410 (3 RCTs)	serious[a]	serious[b]	not serious	not serious	none	⨁⨁◯◯ Low	29/704 (4.1%)	195/706 (27.6%)	**RR 13.39** (2.01 to 89.44)	41 per 1,000	**510 more per 1,000** (from 42 more to 1,000 more)

CI: confidence interval; **RR:** risk ratio

Explanations

a. Risk of bias was rated serious due to concerns about randomization, allocation concealment and blinding.

b. The results from these studies are inconsistent; $I^2 = 63\%$

POSTPARTUM MANAGEMENT: GRADE TABLES

GRADE Table 1: Home blood pressure monitoring VS standard care for those with HDP postpartum

Bibliography: Kalafat E, Benlioglu C, Thilaganathan B, Khalil A. Home blood pressure monitoring in the antenatal and postpartum period: A systematic review meta-analysis. Pregnancy Hypertension [Internet]. 2020 Jan;19:44–51

Certainty assessment							Summary of findings				
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	Study event rates (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With standard care	With home blood pressure monitoring		Risk with standard care	Risk difference with home blood pressure monitoring
Postpartum readmission											
297 (2 RCTs)	not serious	serious[a]	not serious	very serious[b]	none	⨁◯◯◯ Very low	7/149 (4.7%)	5/148 (3.4%)	**OR 0.58** (0.03 to 9.58)	47 per 1,000	**19 fewer per 1,000** (from 46 fewer to 274 more)

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio; **SMD:** standardized mean difference

Explanations

a. The results from these studies are inconsistent; $I^2 = 67\%$
b. Imprecision was rated serious due to a large confidence interval that cross the null, a low number of events, and small sample size.

GRADE Table 2: NSAIDs VS placebo/no intervention for postpartum pain management in those with HDP

Bibliography: Premkumar A, Ayala NK, Miller CH, Grobman WA, Miller ES. Postpartum NSAID Use and Adverse Outcomes among Women with Hypertensive Disorders of Pregnancy: A Systematic Review and Meta-analysis. American Journal of Perinatology [Internet]. 2021 Jan;38(1):1–9.

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With placebo/no intervention	With NSAIDS	Relative effect (95% CI)	Risk with placebo/no intervention	Risk difference with NSAIDS
BP ≥150/100											
537 (3 observational studies)	not serious	serious[a]	not serious	not serious	none	⨁◯◯◯ Very low	117/187 (62.6%)	252/350 (72.0%)	**RR 1.21** (0.89 to 1.64)	626 per 1,000	**131 more per 1,000** (from 69 fewer to 400 more)
Length of hospital stay											
647 (3 observational studies)	not serious	not serious	not serious	not serious	none	⨁⨁◯◯ Low	206	441	-	The mean length of hospital stay was **0**	MD **0.21 higher** (0.04 higher to 0.38 higher)
Antihypertensives											
670 (4 observational studies)	not serious	not serious	not serious	not serious	none	⨁⨁◯◯ Low	86/289 (29.8%)	117/381 (30.7%)	**RR 1.03** (0.82 to 1.30)	298 per 1,000	**9 more per 1,000** (from 54 fewer to 89 more)

Certainty assessment							Summary of findings				
Readmission for BP control											
738 (4 observational studies)	not serious	not serious	not serious	serious[b]	none	⨁◯◯◯ Very low	7/274 (2.6%)	14/464 (3.0%)	**RR 0.83** (0.35 to 1.98)	26 per 1,000	**4 fewer per 1,000** (from 17 fewer to 25 more)

CI: confidence interval; **MD:** mean difference; **RR:** risk ratio

Explanations

a. The results from these studies are inconsistent; $I^2 = 84\%$

b. Imprecision was rated serious due to a low number of events and a large confidence interval that crosses the null.

GRADE Table 3: Chest/breast feeding VS no chest/breast feeding at the first postpartum visit

Bibliography: Burgess A, McDowell W, Ebersold S. Association Between Lactation and Postpartum Blood Pressure in Women with Preeclampsia. MCN Am J Matern Child Nurs [Internet]. 2019 Mar [cited 2023 Jan 25];44(2):86–93. Available from: https://journals.lww.com/mcnjournal/Abstract/2019/03000/Association_Between_Lactation_and_Postpartum_Blood.5.aspx

Certainty assessment							Summary of findings				
							Study event rates (%)			Anticipated absolute effects	
Participants (studies) Follow-up	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty of evidence	With [comparison]	With breastfeeding	Relative effect (95% CI)	Risk with [comparison]	Risk difference with breastfeeding
sBP											
147 (1 observational study)	not serious	not serious	not serious	not serious	none	⨁⨁◯◯ Low	69	78	-	The mean SBP was **0**	MD **5.3 lower** (10.01 lower to 0.59 lower)
dBP											
147 (1 observational study)	not serious	not serious	not serious	not serious	none	⨁⨁◯◯ Low	69	78	-	The mean DBP was **0**	MD **3.6 lower** (6.94 lower to 0.26 lower)

CI: confidence interval; **MD:** mean difference