SUPPLEMENTARY MATERIAL

Oral antihypertensives for non-severe pregnancy hypertension – systematic review, network meta- and trial sequential analyses

Bone Jeffrey N, MSc[1]

Sandhu Ash, BSc[1]

Abalos Edgardo, DPhil[2]

Khalil Asma, MD[3]

Singer Joel, PhD[4]

Prasad Sarina, BSc[1]

Omar Shazmeen, BSc[1]

Vidler Marianne, PhD[1]

von Dadelszen Peter*, DPhil[4]

Magee Laura A*, MD[4]

** Shared senior authorship*

1. Department of Obstetrics and Gynaecology, University of British Columbia, Canada;
2. Centro Rosarino de Estudios Perinatales (CREP), Rosario, Argentina;
3. Fetal Medicine Unit, Department of Obstetrics and Gynaecology, St George's University Hospitals, NHS Foundation Trust, UK;
4. School of Population and Public Health, University of British Columbia, Canada; and
5. Department of Women and Children's Health, King's College London, UK.

TABLE OF CONTENTS

Table S1: Search strategy of electronic databases*
CINAHL (The Cumulative Index to Nursing and Allied Health Literature), CENTRAL (Cochrane Central Register of Controlled Trials), ICTRP (International Clinical Trials Registry Platform), LILACS (Latin American and Caribbean Health Sciences Literature), WHO (World Health Organization)

** The search strategy was run from 01 Jan 2017 to 28 Feb 2021, without language restrictions. Study dates referred to the latest for either publication or registration, on ClinicalTrials.gov or the WHO International Clinical Trials Registry Platform (ICTRP).*

Databases	**Key words**
PubMed, Medline, Embase, CINAHL, CENTRAL, and Web of Science	
	Filter: 'Humans' {hypertension, hypertensive disorders of pregnancy, pregnancy-induced hypertension, preeclampsia, pregnancy toxemias, OR gestational hypertension} AND {antihypertensives OR antihypertensive agent} AND {Controlled trial [pt] OR controlled clinical trial [pt] OR clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR ("clinical trial" [tw]) OR ((single*[tw] OR doubl*[tw] OR trebl*[tw] OR tripl*[tw]) AND (mask*[tw] OR blind*[tw])) OR placebos[tw] OR randomi*[tw] OR research design[mh:noexp] OR comparative study[pt] OR Evaluation Studies[PT] OR Evaluation Studies as Topic[mh] OR follow-up studies[mh] OR prospective studies[mh] OR control[tw] OR control[tw] OR controls[tw] OR controll* OR prospective*[tw] OR volunteer*[tw]} AND {Pregnancy [mh] OR Pregnan* OR Gestation* OR pregnant women[mh] OR Pregnancy Complications[mh] OR "Postpartum Period"[Mesh] OR Puerperium OR postpartum OR "Peripartum Period"[Mesh] OR Peripartum* OR Perinatal Care[mh] OR perinatal}
ClinicalTrials.gov (advanced search)	
	Hypertension, pregnancy induced (in Condition) AND intervention studies
	Preeclampsia (in condition) AND intervention studies
WHO ICTRP	
	Hypertension AND pregnancy
	Preeclampsia AND pregnancy
	Preeclampsia AND pregnancy
LILACS and Cochrane Pregnancy & Childbirth Trials Register	
	{hypertension, hypertensive disorders of pregnancy, pregnancy-induced hypertension, preeclampsia, pregnancy toxemias, OR gestational hypertension} AND {antihypertensives OR antihypertensive agent}

Table S2: Outcome definitions

BP (blood pressure), HELLP (haemolysis, elevated liver enzymes, low platelet), SGA (small-for-gestational age),

** These are core outcomes in preeclampsia and defined as recommended (10). Gestational age is reported according to preterm birth, and birthweight as SGA infants.*

Outcome	**Definition**
Primary	
Severe hypertension	Whenever possible as systolic BP ≥160mmHg or diastolic BP ≥110 mmHg, but otherwise accepted as being up to 10 mmHg higher
Proteinuria/ preeclampsia	Whenever possible as new proteinuria (≥1+ by dipstick, ≥30mg/mmol protein:creatinine ratio, or ≥300 mg/24 hours
Fetal or newborn death* (including miscarriage)	Miscarriage was fetal loss before viability, usually taken as 20 or 24 weeks
	Stillbirth was fetal death at ≥22+0 weeks, birthweight ≥500g, or crown-heel length ≥25cm. If this definition could not be applied, stillbirth was defined as reported
	Neonatal death was newborn death in the first 28 days
	Perinatal deaths were stillbirths plus neonatal deaths in the first week of life
SGA infants*	Birthweight < 10th centile for gestational age, reported for all births (including stillbirths), and as assessed against a validated global, regional, or local customised growth chart. If this is not possible, alternative definitions will be accepted, including birthweight <3rd centile for gestational age, and 'low birthweight', using the definition reported
Preterm birth*	Births before 37 weeks' gestation
Neonatal unit admission*	As meeting the local, regional, or national criteria for admission to the special care baby unit or neonatal care unit
Secondary (mother)	
Need for additional antihypertensive medication	As stated for both groups if BP goals were not achieved
Maternal death*	Death of the mother during pregnancy or within 6 weeks after birth
Eclampsia*	Onset of convulsions (i.e., fits, generalised convulsatons, tonic-clonic seizure or seizure) in a woman with not attributable to other causes
HELLP syndrome*	Low platelets* is a reduction in preeclampsia the number of platelets in the blood to <100,000/mL
	Elevated liver enzymes* is an AST or ALT greater than at least twice the upper limit of normal
Severe maternal morbidity*	
Stroke	In high-income countries, acute symptoms of focal brain injury lasting >24hr, with ischaemic or haemorrhagic stroke confirmed by neuroimaging In low-income countries, acute symptoms of focal brain injury lasting >24hr
Cortical blindness	Visual impairment in presence of an intact pupillary response to light
Retinal detachment	A condition in which the retina peels away from its underlying layer of support tissue diagnosed by ophthalmological exam
Pulmonary edema	Clinical diagnosis of excess fluid in the lungs with chest x-ray confirmation or requirement of directive treatment and an oxygen saturation <95%

Outcome	Definition
Acute kidney injury	Fulfills any of the following criteria: (i) rise in serum creatinine ≥26μmol/L within 48hr (ii) >50% rise in serum creatinine within the past 7d (iii) urine output <0.5ml/kg/hr for >6hr (iv) serum creatinine >150μmol/L in absence of baseline serum creatinine
Liver capsule hematoma or rupture	Blood collection under the hepatic capsule as confirmed by ultrasound, computerised tomography, magnetic resonance imaging, or laparotomy
Admission to intensive care*	Requirement for advanced respiratory support alone or monitoring and support for ≥2 organ systems
Intubation or ventilation*	Need for continuous positive airway pressure, non-invasive positive pressure ventilation, and intubation and mechanical ventilation
Placental abruption*	In the absence of placental previa on ultrasound, vaginal bleeding in the second or third trimester with either uterine irritability or labour or clinical signs and hypovolaemic shock or coagulopathy or placental pathology with histological findings of a chronic abruption
Antenatal hospital admission	Admission to hospital before the admission for birth
Antenatal hospital length of stay (LOS) >7 days	Total days in hospital for birth > 7 days
Cesarean	Surgical incision of the uterus to allow for birth of the baby
Changed/stopped drug due to maternal side-effects	The need to discontinue the allocated treatment because of maternal side-effects
Postpartum haemorrhage*	Perceived abnormal bleeding following delivery and hypotension and/or medical or surgical interventions for postpartum haemorrhage
Secondary (baby)	
Respiratory distress syndrome (or respiratory support)* and	Need for continuous positive airway pressure, non-invasive positive pressure ventilation, and intubation and mechanical ventilation. If respiratory distress syndrome were specifically diagnosed, by clinical and/or radiological findings, this was included.
Neonatal seizures	In high-income countries, clinical recognition of neonatal seizures confirmed by electroencephalogram monitoring In low-income countries, clinical recognition of neonatal seizures

Table S3: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 checklist

Section and Topic	Item #	Checklist item	Location item is reported
TITLE			
Title	1	Identify the report as a systematic review.	1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	4
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for syntheses.	5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	5, Table S1
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	5,6
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	5,6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6

Section and Topic	Item #	Checklist item	Location item is reported
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	6,7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	6,7
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	6,7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	6,7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	6,7
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	7
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	7
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	8
Study characteristics	17	Cite each included study and present its characteristics.	8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 2, Fig 2 & S3, Table S4 & S5
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	8
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the	8-10

Section and Topic	Item #	Checklist item	Location item is reported
		summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	9
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	10
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	9 (Fig S2)
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	9,10
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	11,12
	23b	Discuss any limitations of the evidence included in the review.	12,13
	23c	Discuss any limitations of the review processes used.	12,13
	23d	Discuss implications of the results for practice, policy, and future research.	13
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	5
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	13
Competing interests	26	Declare any competing interests of review authors.	13
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	14

Table S4: PRISMA checklist for abstracts

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

Table S5: Characteristics of 61 included trials contributing data to the network meta-analysis

A (low risk of bias), B (risk of bias unclear), antiHTN (antihypertensive), BP (blood pressure), C (high risk of bias), cHTN (chronic hypertension), dBP (diastolic BP), gov (government), HDP (hypertensive disorder of pregnancy), LT control ('less tight' BP control), NA (not applicable), None (no antihypertensive therapy), NS (not specified), PET (pre-ecampsia/eclampsia), PIH (pregnancy-induced hypertension), reg (registration), sBP (systolic BP), T control ('tight' BP control), T1 (first trimester), T2 (second trimester), T3 (third trimester)

** These were trials of differential BP control.*

				BP				Control arm			Treatment arm								BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
Argentina (Voto) 1985	1985	No	60	≥160	≥100	NS	NS	No	Yes	2	Atenolol	Methyldopa	-	-	T3	Full paper	No	NS	NS	dBP ≥100	NA	NS	B	NS	NS	Open label	No	No	Published only
Argentina (Voto) 1987	1987	No	20	≥160	≥100	NS	NS	No	Yes	2	Ketanserin	Methyldopa	-	-	T3	Full paper	No	NS	NS	dBP ≥100	NA	NS	B	NS	NS	Open label	No	No	Published only
Argentina (Casavilla) 1988	1988	No	36	≥140	≥90	cHTN	NS	No	Yes	2	Mepindolol	Methyldopa	-	-	T1	Abstract	No	NS	NS	≥140/90	NA	Optimal response	B	NS	NS	Open label	No	No	Published only
Australia (Livingstone) 1983	1983	Yes	28	≥140	≥90	PIH	NS	No	Yes	2	Propran-olol	Methyldopa	-	-	T2 - T3	Full paper	No	NS	NS	≥140/ 90	NA	NS	B	NS	NS	Open label	No	No	Published only

				BP				Control arm			Treatment arm									BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
Australia (Gallery) 1985a	1985	Yes	183	NS	≥90	NS	IV	No	Yes	2	Oxpren-olol	Methyldopa	-	-	T3	Full paper	No	NS	NS	dBP ≥90	NA	dBP <80	B	Series random numbers	NS	Open label	No	No	Published only
Australia (Davis) 2001	2001	Yes	16	NS	NS	PIH	NS	Yes	No	2	GTN patches	-	-	Placebo	T2 - T3	Letter	Yes	NS	NS	NS	NS	NS	B	Central telephone	Telephone	Single blind	No	No	Published only
Brazil (Kahhale) 1985	1985	No	100	≥140	≥90	cHTN	NS	Yes	No	2	Pindolol	-	-	None	T2	Full paper	No	NS	NS	≥140/90	NS	BP stabili-sation	B	NS	NS	Open label	No	No	Published only
Brazil (Freire) 1988	1988	No	40	NS	≥95	cHTN	NS	No	Yes	2	Pindolol	Methyldopa	-	-	T3	Full paper	Yes	NS	NS	dBP ≥85	NA	Lack of satisfactory	B	NS	Consecutive boxes	Open label	No	No	Published and
Brazil (Nascime) 2000a	2000	No	199	NS	≥90	cHTN	V	Yes	No	2	Verapamil	-	-	Placebo	T2	Full thesis	Yes	NS	NS	≥140/90	NS	"BP control"	A	NS	Consecutive boxes	Double blind	Yes	7.5%	Published only

				BP				Control arm			Treatment arm									BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
Brazil (Trapini) 2016	2016	No	100	≥140	≥90	PET	IV	Yes	No	2	Sildenafil	-	-	Placebo	T2 - T3	Full paper	No	NS	Non commercial.	≥140/90	NS	NS	A	NS (but blocked)	Sealed envelopes	Double blind	Yes	7.0%	Published only
Caribbean Is (Plouin) 1990	1990	No	155	NS	≥85	PIH	IV	Yes	No	2	Oxprenolol + Dihydralazine	-	-	Placebo	T3	Full paper	Yes	NS	Industry.	dBP ≥85	dBP >105	dBP <86	A	NS (but blocked)	Consecutive boxes	Double blind	Yes	0.6%	Published and
France (Plouin) 1987	1987	Yes	188	NS	≥90	cHTN	IV	No	Yes	2	Labetalol	Methyldopa	-	-	T2 - T3	Full paper	No	NS	Industry.	dBP ≥90	NA	DBP <86mmHg	B	NS (but blocked)	Sealed envelopes	Open label	No	6.4%	Published only
France (Lardoux) 1988a	1988	Yes	63	NS	≥90	NS	NS	No	Yes	3	Labetalol	Methyldopa	Acebutolol	-	T2	Full paper	No	NS	NS	dBP ≥90	NA	NS	B	NS	NS	Open label	No	No	Published only
France (Jannet) 1994	1994	Yes	100	≥140	≥90	NS	NS	No	Yes	2	Nicardipine	Metoprolol	-	-	T2 - T3	Full paper	No	NS	NS	≥140/90	NA	NS	B	Computer generated	Sealed envelopes	Open label	No	No	Published only

				BP				Control arm			Treatment arm									BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
Hong Kong (Li) 1990	1990	Yes	41	≥140	≥90	PET	NS	Yes	No	2	Labetalol	-	-	Placebo	NS	Abstract	No	NS	NS	≥140/90	BP>165/105	NS	B	NS	NS	Double blind	Yes	No	Published only
India (Oumachigui) 1992	1992	No	30	≥140	≥90	PIH	NS	No	Yes	2	Metoprolol	Methyldopa	-	-	T3	Full paper	No	NS	Industry.	≥140/90	NA	dBP <86	B	NS	NS	Open label	No	No	Published only
India (Banerjee) 2002	2002	No	111	≥140	≥90	PIH/ PET	NS	No	Yes	2	Nimodipine	Methyldopa	-	-	T2 - T3	Full paper	No	NS	NS	≥140/90	NA	NS	B	NS	NS	Open label	No	6%	Published only
India (Molvi) 2012	2012	No	150	≥140	≥90	PIH	V	Yes	Yes	3	Labetalol	Methyldopa	=	None	T2 - T3	Full paper	No	NS	University	≥140/90	dBP >105	>110/ 70 & <140/ 90	**C**	Manually shuffled	Sealed envelopes	Open label	No	0.6 %	Published only
India (Aparna) 2013b	2013	No	100	≥150	≥100	PIH	V	No	Yes	2	Nifedipine	Methyldopa	-	-	T3	Full paper	No	NS	NS	≥150/ 100	NA	dBP 80-100	B	Random numbers	NS	Open label	No	8%	Published only
India (Babbar) 2015a	2015	No	240	≥140	≥90	PIH	IV	No	Yes	3	Labetalol	Methyldopa	Nifedipine	-	T2 - T3	Full paper	No	NS	NS	≥140/90	NA	"BP control"	B	NS	NS	Open label	No	No	Published only

				BP				Control arm			Treatment arm									BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
Ireland (Blake) 1991	1991	Yes	36	≥140	≥90	NS	V	Yes	No	2	Atenolol and/or Methyldopa			None	NS	Full paper	Yes	NS	NS	≥140/90	140/90	"Average normal" BP	**C**	Manually shuffled	Sealed envelopes	Open label	No	No	Published only
Israel (Ellenbogen) 1986a	1986	Yes	32	NS	≥90	PIH	NS	No	Yes	2	Pindolol	Methyldopa		-	T3	Full paper	No	NS	NS	dBP ≥90	NA	NS	B	NS	NS	Open label	No	No	Published only
Israel (Rosenfeld) 1986b	1986	Yes	44	≥150	≥90	NS	NS	No	Yes	2	Pindolol + Hydralazine	Hydralazine	-	-	T2 - T3	Full paper	No	NS	NS	≥150/90	NA	BdP ≤90	B	NS	NS	Open label	No	No	Published only
Israel (Bott-Kanner) 1992a	1992	Yes	60	NS	≥85	NS	IV	Yes	No	2	Pindolol	-	-	Placebo	T2 - T3	Full paper	No	NS	NS	DBP 85-99	dBP 100-109	dBP < 85	A	Random numbers	Consecutive boxes	Double blind	Yes	No	Published only
Israel (Paran) 1995	1995	Yes	51	≥140	≥95	NS	V	No	Yes	3	Propranolol + Hydralazine	Pindolol + hydralazine	Hydralazine	-	T3	Full paper	No	NS	NS	140-160/95-11	NS	≤140/90	B	NS	NS	Open label	No	No	Published only

				BP				Control arm			Treatment arm									BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
Italy (Catalano) 1997	1997	Yes	100	≥140	≥90	PET	NS	Yes	No	2	Nifedipine			None	T3	Full paper	No	NS	NS	≥140/90	NS	≤140/90	B	NS	NS	Open label	No	No	Published only
Italy (Fruppo di Studio) 1998	1998	Yes	283	NS	≥90	PIH/ PET	NS	Yes	No	2	Nifedipine			None	T2 - T3	Full paper	No	YES	University	06≤ dBp	dBP >110	NS	B	Computer generated	Telephone	Open label	No	7.8 0%	Published only
Italy (Neri) 1999	1999	Yes	36	≥140	≥90	PIH/ PET	IV	No	Yes	3	GTN	Nifedipine	-	-	T3	Full paper	Yes	NS	NS	≥140/90	NA	NS	B	NS	sealed envelopes	Open label	No	16.6%	Published & unpublished
Italy (Borghi) 2000	2000	Yes	20	NS	NS	PET	NS	No	Yes	2	Nifedipine	Methyldopa	-	-	NS	Full paper	Yes	NS	NS	NS	NA	NS	B	NS	Consecutive boxes	Single blind	No	No	Published & unpublished
Pakistan (Sharif) 2016	2016	No	314	≥140	≥100	PIH	NS	No	Yes	2	Labetalol	Methyldopa	-	-	T3	Full paper	No	NS	NS	≥140/90	NA	dBP <90	B	Lottery method	NS	Open label	No	1.3%	Published only
Panama (Vigil-De Gracia) 2014	2014	No	63	≥140	≥90	cHTN	NS	No	Yes	3	Amlodipine	Furosemide	-	ASA 75mg/d	T2	Full paper	No	NS	NS	≥140/90	NA	NS	B	Computer generated	Sealed envelopes	Open label	No	5.0%	Published only

				BP				Control arm			Treatment arm									BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
South Africa (Odendaal), 1991a	1991	No	32	≥140	≥90	PIH	NS	Yes	No	2	Prazosin	-	-	Placebo	T2 - T3	Full report	No	NS	NS	≥140/90	>160/110	130/80 to 140/90	B	NS	Sealed envelopes	NS	NS	No	Published only
South Africa (Eloff) 1993	1993	No	29	NS	≥90	NS	NS	No	Yes	2	Nifedipine	Methyldopa	-	-	T3	Abstract	No	NS	NS	dBP ≥90	NA	"To control BP"	B	NS	NS	Open label	No	10.3%	Published only
Sudan (Hassan) 2002	2002	No	70	NS	≥90	PET	IV	Yes	No	2	Methyldopa	-	-	None	T3	Full paper	No	NS	NS	dBP ≥90	dBP >110	dBP <90	B	NS	NS	Open label	No	No	Published only
Sweden (Wichman) 1984	1984	Yes	52	≥140	≥90	NS	V	Yes	No	2	Metoprolol	-	-	Placebo	T3	Full paper	Yes	NS	Charity	≥140/90	140/90	<140/90	A	NS	Telephone	Double blind	Yes	No	Published & unpublished
Sweden (Högstedt) 1985	1985	Yes	168	NS	≥90	PIH	V	Yes	No	2	Metoprolol + Hydralazine	-	-	None	T2 - T3	Full paper	Yes	NS	NS	dBP ≥90	dBP >110	dBP < 90	B	NS	Envelopes (no details)	Open label	No	4.0%	Published only
Sweden (Swensson) 1995	1995	Yes	118	NS	≥95	NS	IV	Yes	No	2	Isradipine	-	-	Placebo	T3	Full paper	No	NS	NS	dBP 95 -110	dBP >110	NS	B	NS	NS	Double blind	Yes	6.0%	Published only

				BP				Control arm			Treatment arm								BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
UK (Leather) 1968	1968	Yes	100	NS	≥90	NS	NS	Yes	No	2	Methyldopa + benfluorazide	-	-	None	NS	Full paper	No	NS	Non commercial	dBP ≥90	NS	NS	B	NS	NS	Open label	No	No	Published only
UK (Redman) 1976	1976	Yes	247	≥140	≥90	NS	IV	Yes	No	2	Methyldopa	-	-	None	T2 - T3	Full paper	No	NS	Industry.	≥140/90 to 28w, ≥ 150/95 after 28w	>170/110	"To achieve good BP control"	B	NS	NS	Open label	No	2.00%	Published only
UK (Lamming) 1980	1980	Yes	26	NS	NS	PIH	IV	No	Yes	2	Labetalol	Methyldopa	-	-	T3	Full paper	No	NS	Industry.	not reported	NA	MAP < 103.3	B	Random numbers	NS	Open label	No	No	Published only
UK (Walker) 1982	1982	Yes	126	NS	≥95	PIH/ PET/ cHTN	NS	Yes	No	2	Labetalol	-	-	None	T2 - T3	Full report	Yes	NS	Industry.	dBP ≥95	NS	"BP control"	B	NS	Envelopes (no details)	Open label	No	No	Published & unpublished
UK (Rubin) 1983a	1983	Yes	120	≥140	>/=90	PIH/ PET	IV	Yes	No	2	Atenolol	-	-	Placebo	T3	Full paper	No	NHS	Industry.	≥140/90	>170/110	dBP <90	B	NS	NS	Double blind	Yes	No	Published only

				BP				Control arm			Treatment arm								BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
UK (Fidler) 1983b	1983	Yes	100	NS	≥95	PIH/ PET/ cHTN	IV	No	Yes	2	Oxprenolol	Methyldopa	-	-	T3	Full paper	No	NS	Industry.	dBP ≥95	NA	dBP < 95	B	NS	NS	Open label	No	4.00%	Published only
UK (Thorley) 1984	1984	Yes	60	NS	NS	NS	V	No	Yes	2	Atenolol	Methyldopa	-	-	T2 - T3	Full paper	No	NS	NS	NS	NS	NS	B	NS	NS	Open label	No	4.0%	Published only
UK (Pickles) 1989	1989	Yes	152	≥140	≥90	PIH	IV	Yes	No	2	Labetalol	-	-	Placebo	T2 - T3	Full paper	No	NS	Industry.	≥140/90	Inadequate BP control	"BP control"	A	Random numbers	Consecutive boxes	Double blind	Yes	5.3%	Published only
UK (Butter) 1990	1990	Yes	33	≥140	≥90	cHTN	V	Yes	No	2	Atenolol	-	-	Placebo	T2	Full paper	Yes	NHS	Industry.	≥140/90	NS	<140/90 or 200mg atenolo	B	NS	NS	Double blind	Yes	12.1%	Published & unpublished
UK (Cruickshank) 1992	1992	Yes	114	NS	≥90	PIH	IV	Yes	No	2	Labetalol	-	-	None	T3	Full paper	Yes	NS	Industry.	dBP ≥90	NS	DBP < 90mm Hg	B	NS	Sealed envelopes	Open label	No	No	Published & unpublished
UK (Samangaya) 2009	2009	Yes	30	NS	≥90	PIH/ PET/ cHTN	NS	Yes	No	2	Sildenafil	-	-	Placebo	T2 - T3	Full paper	No	Yes	Industry.	dBP ≥90	At clinician discretion	NS	B	Computer generated	Telephone	Double blind	Yes	10.3%	Published only

				BP				Control arm			Treatment arm									BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
UK (Webster) 2017	2017	Yes	114	≥140	≥90	cHTN	NS	No	Yes	2	Labetalol	Nifedipine	-	None	T2 - T3	Full paper	No	Yes	Nonncommercial	≥140/90	NA	dBP < 85	B	Computer generated	Computer system	Open label	NS	1.8%	Published only
USA (Arias) 1979	1979	Yes	58	≥140	≥90	cHTN	NS	Yes	No	2	Methyldopa and/or hydral and/or HCTZ	-	-	None	T2	Full paper	No	NS	NS	≥140/90	NS	dBP <90		NS	NS	Open label	No	No	Published only
USA (Sibai) 1987a	1987	Yes	200	≥140	≥90	PET	NS	Yes	No	2	Labetalol	-	-	None	T3	Full paper	No	NS	NS	≥140/90	Clinician discretion	dBP <90	B	Computer generated	Sealed envelopes	Open label	No	0.1%	Published only
USA (Weitz) 1987b	1987	Yes	25	≥140	≥90	cHTN	NS	Yes	No	2	Methyldopa	-	-	Placebo	NS	Full paper	No	NS	Industry.	≥140/90	NS	BP ≤140/90	B	NS	NS	Double blind	Yes	No	Published only
USA (Sibai) 1990a	1990	Yes	300	NS	NS	cHTN	NS	Yes	Yes	3	Labetalol	Methyldopa	-	None	T1	Full paper	Yes	NS	NS	NS	>160/110	NS	B	Computer generted	Sealed envelopes	Open label	No	12.0%	published and unpublished

				BP				Control arm			Treatment arm									BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
USA (Sibai) 1992	1992	Yes	200	≥140	≥9	pet	NS	Yes	No	2	Nifedipine	-	-	None	T3	Full paper	No	NS	NS	≥140/90	Clinician discretion	<140/90	B	Computer generated	Sealed envelopes	Open label	No	1.5%	Published only
Venezuela (Faneite) 1988	1988	No	31	≥140	≥90	PIH/ cHTN	NS	No	Yes	2	Mepindolol	Methyldopa	-	-	T2 - T3	Full paper	No	NS	Industry.	≥140/90	NA	<140/90	B	Random numbers	NS	Open label	No	No	Published only
Australia (Horvath) 1985b	1985	Yes	100	>130	>85	PIH/ cHTN	NS	No	Yes	2	Clonidine hydrochloride	Methyldopa	-	-	T2 - T3	Full paper	No	NS	Industry & gov	>135/85	NA	NS	B	NS	NS	Double blind	Yes	5.0%	Published only
Finland (Tuimala) 1988b	1988	Yes	51	≥150	≥95	NS	NS	No	Yes	2	Pindolol	Atenolol		-	T2 - T3	Full paper	No	NS	NS	≥150/95	NA	NS	B	Random number table	NS	Open label	NS	no	Published only
Sweden (Montan) 1992	1992	Yes	29	≥140	≥90	PIH/ PET/ cHTN	V	No	Yes	2	Atenolol	Pindolol	-	-	T3	Full paper	No	NS	Non commercial	≥140/90	NA	NS	B	NS	Sealed envelopes	Double blind	Yes	9.4%	Published only

				BP				Control arm			Treatment arm									BP (mmHg)			Risk of bias						
Study (1st author)	**Publicatinon year**	**Developed country**	**N women**	sBP	dBP	**HDP**	**Korotkoff for dBP**	Placebo/no therapy	Drug	**N trial arms**	1	2	3	**Placebo/no therapy**	**GA at entry**	**Publication type**	**Unpublished data**	**Prospective reg**	**Funding**	Threshold (Treatment arm)	Threshold (placebo/ no therapy arm) for additional antiHTN	Target	OVERALL	Random sequence generation	Concealment	Blinding	Blinding outcome	Incomplete data	Selective reporting
Egypt (El-Guindy) 2008*	2008	No	120	140-159	90-99	PIH/ cHTN	V	No	Yes	2	Methyldopa (very tight <130/80)	Methyldopa (tight 130-139/80-89)	-	-	T3	Full paper	No	NS	NS	≥140/90	NA	<130/80 vs. 130-139/80-89	A	Computer generated	Sealed opaque envelopes	Double blind	Yes	4.0%	Published only
Canada (Magee) 2007*	2007	Yes	132	<170	90-109	PIH/chronic	V	Yes	No	2	T control (most often labetalol)	-	LT control	-	T2 - T3	Full paper	No	NS	Non commercial	dBP 90-109	dBP >105 but could consider at 101-105	T: dBP 85 LT: dBP 100	A	Computer generated	Telephone	Open label	Yes	0.8%	Published only
Canada (Magee) 2015*	2015	Yes	987	<160	dBP 85-105 if on meds, 90-105 if not	PIH/chronic	V	Yes	No	2	T control (most often labetalol)	-	-	LT control	T2 - T3	Full paper	No	Yes	Non commercial	dBP 90-105	dBP ≥105 or sBP ≥160 regardless of dBP	LT: dBP 100 T: dBP 85	A	Computer generated	Telephone	Open label	Yes	4.2%	Published only

Table S6: Characteristics of included trials by main outcomes for primary analysis

SGA (small-for-gestational age)

** Treatments considered were placebo/no therapy, and the antihypertensives labetalol, methyldopa, calcium channel blockers, beta-blockers, and multi-drug.*

ł Two three-arm trials informed both drug vs. placebo/no therapy and drug vs. drug comparisons.

	Severe hypertension	**Proteinuria/ preeclampsia**	**Perinatal death**	**SGA**	**Preterm birth**	**Admission to neonatal care unit**
N studies reporting outcome	32	32	44	26	27	16
Two-arm trials	30	29	40	24	25	15
Three-arm trials	2	3	4	2	2	1
N participants	3811	4662	5051	3848	4283	2909
N treatments considered*	6	6	6	6	6	6
N possible pairwise comparisons	15	15	15	15	15	15
N with direct data	13	15	9	13	12	12
N drug vs. placebo/no therapy	9ł	7	5	7	6	6
N drug vs drug	6ł	8	10	6	6	6
N events	599 (15.7%)	688 (14.8%)	226 (4.5%)	482 (12.5%)	842 (19.6%)	557 (19.1%)
Median event rate (IQR)	13% (7%, 22%)	14% (8%, 21%)	3% (0%, 6%)	12% (7%, 17%)	16% (11%, 26%)	18% (12%, 24%)
N studies by N events in each arm						
≥1 event in each arm	27/32	30/32	23/44	21/26	25/27	15/16
≥1 arm with no events	5/30	2/34	21/23	5/26	2/24	1/16
No event in any arm	0	0	12/23	1/26	0	0
Median N events (IQR)	6 (2,11)	7 (4,14)	1 (0,3)	6 (4,12)	9 (5,17)	13 (7,20)

Table S7: Sensitivity analyses of main outcomes for antihypertensives vs. placebo/no therapy, in comparison with results from the primary analysis (OR and 95% CI)

CI (credible interval), OR (odds ratio)

** Sensitivity analysis 1 includes all data in the primary analysis, plus three additional trials of differential BP control.*

*** Sensitivity analysis 2 includes all data in the primary analysis, plus all other trials of additional drugs that were not of primary interest in the network. Only results for drugs of interest are presented, as additional estimates were not informative.*

**** Sensitivity analysis 3 excludes two trials at high risk of bias (Molvi et al 2012 [PMID: 22249781] and Blake et al 1991 [PMID: 2021561])*

Drug	Severe hypertension				Proteinuria				Perinatal death				Small for gestational age				Preterm birth				Admission to NICU			
	Pri-mary	Sensitivity 1*	Sensitivity 2**	Sensitivity 3***	Pri-mary	Sensitivity 1*	Sensitivity 2**	Sensitivity 3***	Pri-mary	Sensitivity 1*	Sensitivity 2**	Sensitivity 3***	Pri-mary	Sensitivity 1*	Sensitivity 2**	Sensitivity 3***	Primary	Sensitivity 1*	Sensitivity 2**	Sensitivity 3***	Primary	Sensitivity 1*	Sensitivity 2**	Sensitivity 3***
Placebo	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)		1.00 (ref)	1.00 (ref)	1.00 (ref)	
Labetalol	0.31 (0.17, 0.52)	0.31 (0.17, 0.53)	0.31 (0.17, 0.52)	0.35 (0.19, 0.65)	0.73 (0.54, 0.99)	0.74 (0.55, 1.00)	0.73 (0.55, 1.02)	0.87 (0.64,1.20)	0.54 (0.27, 1.01)	0.55 (0.28, 1.05)	0.56 (0.28, 1.03)	0.51 (0.24, 1.29)	1.01 (0.72, 1.46)	1.00 (0.70, 1.44)	1.00 (0.70, 1.45)	1.20 (0.81,1.80)	0.85 (0.62, 1.15)	0.86 (0.63, 1.16)	0.84 (0.63, 1.14)	1.01 (0.74,1.41)	0.96 (0.64, 1.41)	0.97 (0.65, 1.42)	0.96 (0.65, 1.38)	1.19 (0.79,1.84)
Methyldopa	0.60 (0.40, 0.91)	0.60 (0.40, 0.92)	0.60 (0.40, 0.91)	0.59 (0.39, 1.02)	1.12 (0.77, 1.62)	1.13 (0.80, 1.57)	1.11 (0.78, 1.57)	1.24 (0.86,1.83)	0.65 (0.34, 1.17)	0.65 (0.35, 1.16)	0.65 (0.37, 1.17)	0.66 (0.36, 1.38)	0.99 (0.65, 1.55)	1.01 (0.64, 1.55)	1.01 (0.67, 1.53)	1.21 (0.67,2.15)	0.99 (0.71, 1.42)	1.01 (0.73, 1.43)	1.00 (0.70, 1.42)	1.28 (0.84,1.95)	1.24 (0.84, 2.13)	1.26 (0.82, 1.96)	1.23 (0.82, 1.89)	1.53 (0.92,2.70)
BB	0.53 (0.34, 0.79)	0.52 (0.34, 0.81)	0.52 (0.34, 0.79)	0.51 (0.31, 0.83)	0.88 (0.54, 1.43)	0.89 (0.55, 1.42)	0.88 (0.56, 1.35)	0.92 (0.59,1.51)	0.76 (0.35, 1.82)	0.74 (0.30, 1.76)	0.78 (0.34, 1.62)	0.77 (0.33, 1.89)	1.27 (0.63, 2.60)	1.25 (0.64, 2.58)	1.25 (0.66, 2.53)	1.33 (0.67,2.66)	0.88 (0.51, 1.59)	0.90 (0.51, 1.56)	0.94 (0.52, 1.63)	1.02 (0.55,2.08)	1.04 (0.45, 2.48)	1.05 (0.45, 2.54)	1.01 (0.44, 2.40)	1.23 (0.54,3.01)
CCB	0.59 (0.37, 0.89)	0.59 (0.36, 0.90)	0.59 (0.37, 0.87)	0.57 (0.33, 0.89)	1.18 (0.84, 1.64)	1.17 (0.85, 1.64)	1.14 (0.85, 1.57)	1.22 (0.87,1.67)	0.73 (0.35, 1.40)	0.71 (0.40, 1.56)	0.71 (0.35, 1.43)	0.71 (0.34, 1.78)	0.85 (0.56, 1.29)	0.84 (0.55, 1.31)	0.86 (0.56, 1.29)	0.88 (0.58,1.36)	1.17 (0.63, 2.16)	1.05 (0.78, 1.38)	1.03 (0.80, 1.36)	1.07 (0.82,1.42)	1.04 (0.63, 1.60)	1.04 (0.65, 1.60)	1.04 (0.65, 1.59)	1.13 (0.70,1.75)
Multi drug	0.31 (0.11, 0.79)	0.60 (0.34, 0.88)	0.60 (0.36, 0.87)	0.31 (0.10, 0.82)	0.83 (0.47, 1.45)	0.91 (0.68, 1.21)	0.92 (0.69, 1.22)	0.97 (0.56,1.66)	1.01 (0.41, 2.40)	0.96 (0.51, 1.76)	0.95 (0.49, 1.75)	0.88 (0.35, 2.38)	0.93 (0.41, 2.12)	1.35 (0.81, 2.03)	1.37 (0.84, 1.99)	0.91 (0.41,2.12)	0.94 (0.53, 1.70)	0.92 (0.71, 1.24)	0.93 (0.71, 1.22)	0.95 (0.55,1.67)	0.65 (0.26, 1.59)	0.98 (0.64, 1.51)	0.99 (0.65, 1.49)	0.66 (0.266,1.57)

Table S8: Trial sequential analyses sample sizes per arm for detection of a relative risk reduction of 20%*

CCB (calcium channel blocker)

** These calculations assume the median event rates observed across trials, 90% power, and a superiority hypothesis, and are based on at least one direct comparison of one antihypertensive vs. another. For similar calculations for the outcome of severe hypertension, see Figure 3.*

Ł Median event rates were taken from Table S3.

Drug comparison	**Severe hypertension**	**Proteinuria/ preeclampsia**	**Perinatal death**	**Small-for-gestational age**	**Preterm birth**	**Admission to neonatal care unit**
Median event rate in trialsł	13% (7%, 22%)	14% (8%, 21%)	3% (0%, 6%)	12% (7%, 17%)	16% (11%, 26%)	18% (12%, 24%)
Labetalol vs. methyldopa	5120	6893	2952	3420	2530	2202
Labetalol vs. other beta-blocker	(No trial)	2952	15,336	3515	2530	2202
Labetalol vs. CCB	(No trial)	2952	15,336	3515	2530	2202
Beta blocker vs. CCB	9780	2952	15,336	(No trial)	(No trial)	2202
Beta blocker vs. methyldopa	9780	2952	15,336	(No trial)	2595	(No trial)
Methyldopa vs CCB	3212	(No trial)	15,336	3515	2530	6665

Figure S1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram*

** For references of key publications excluded and all those included, see Supplementary References 1 and 2, respectively.*

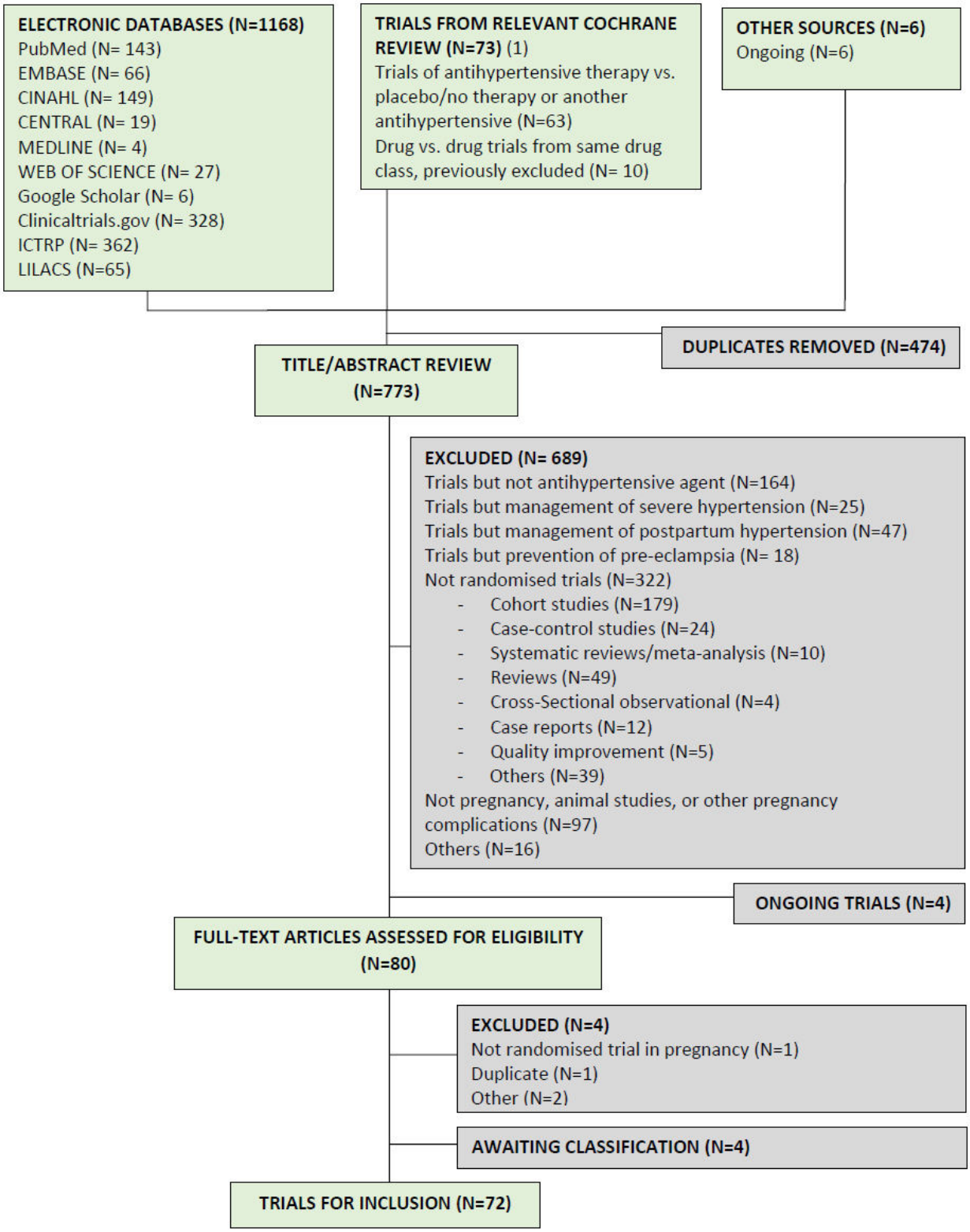


Figure S2: Network plots for main outcomes, primary analysis)

Outcomes are (from top left to bottom right): severe hypertension (Figure S2a), proteinuria (Figure S2b), perinatal death (Figure S2c), small-for-gestational age infants (Figure S2d), preterm birth (Figure S2e), and neonatal care unit admission (Figure S2f).

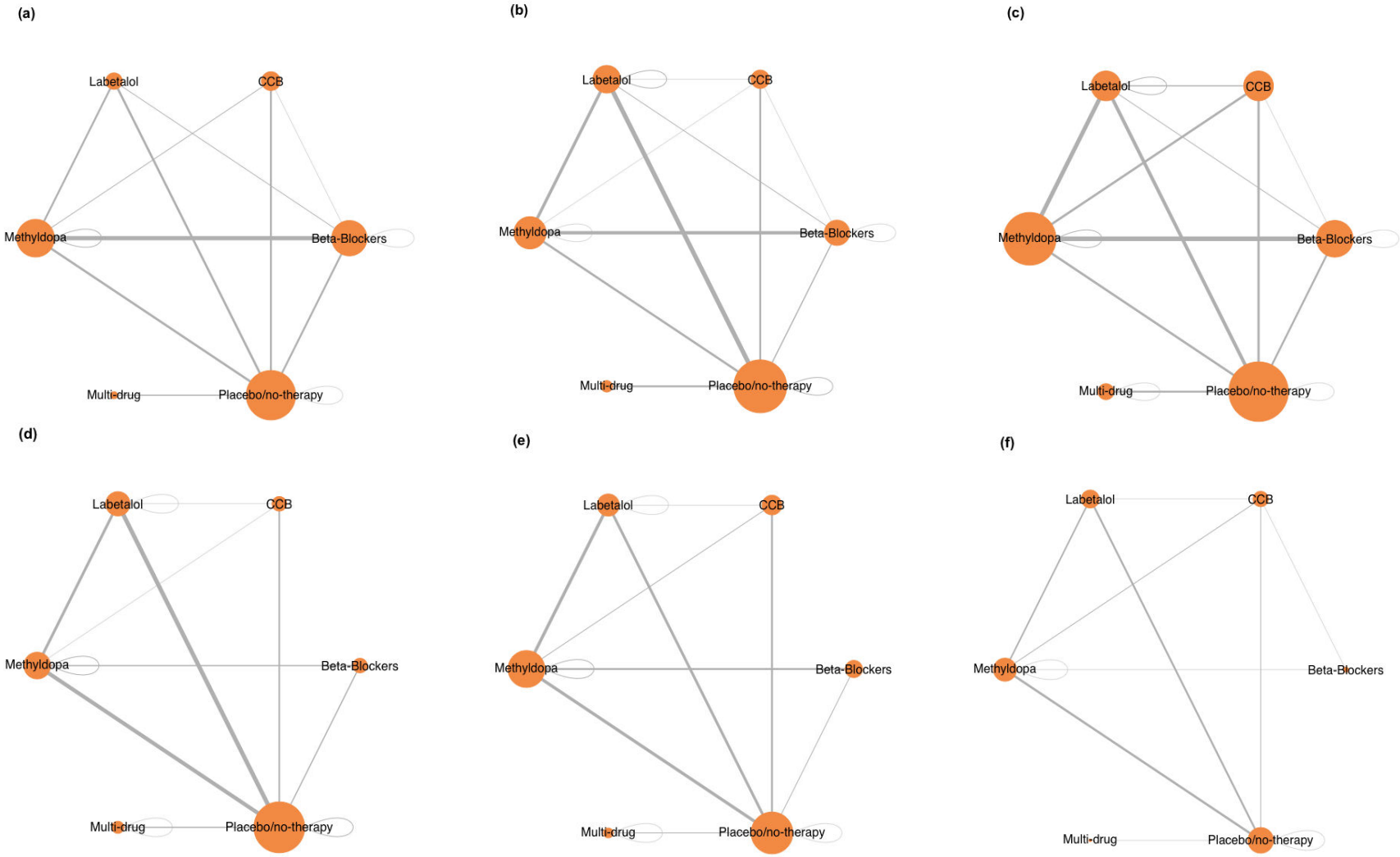


Figure S3: Funnel plots for the main outcomes.

All estimates of effect are odds ratios on a log scale. Outcomes are severe hypertension (A), proteinuria/preeclampsia (B), perinatal death (C), small for gestational age (D), preterm birth (E), and neonatal intensive care unit admission (F)

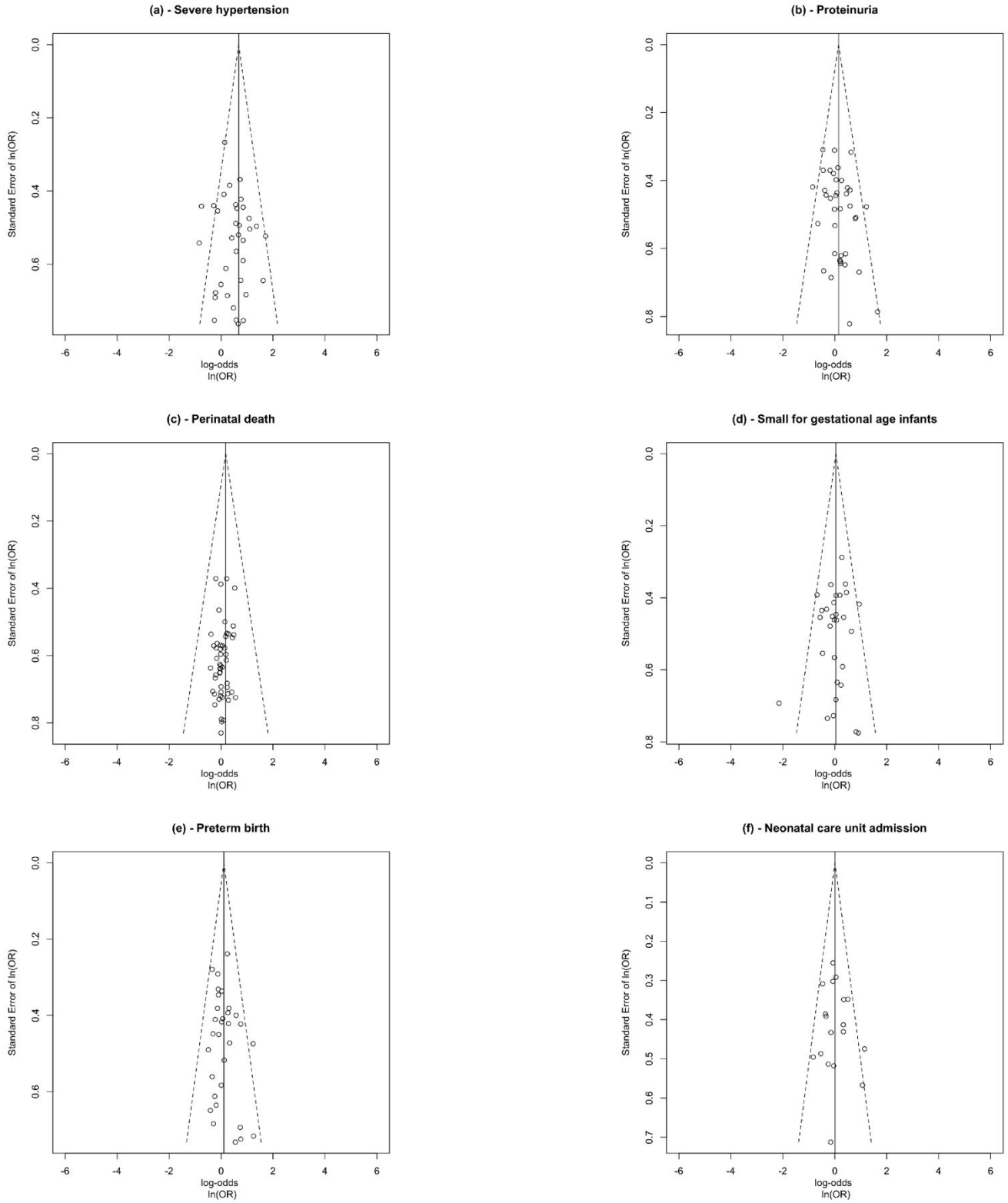


Figure S4: League tables comparing primary drugs of interest vs. placebo/no therapy and each other, for the secondary outcomes of interest.

All estimates are odds ratios and 95% credible intervals. Outcomes are: need for additional antihypertensive therapy (A), changed/stopped drugs due to maternal side effects (B), maternal antenatal admission for more than 7 days (C), Cesarean birth (D), placental abruption (E), and respiratory distress syndrome (RDS, F). All grey squares represent comparisons that could not be reliably computed from the network due a lack of direct comparisons and sparse (or no) indirect pathways between comparators.

CCB (calcium channel blocker)

Figure S4A: Need for additional antihypertensive therapy

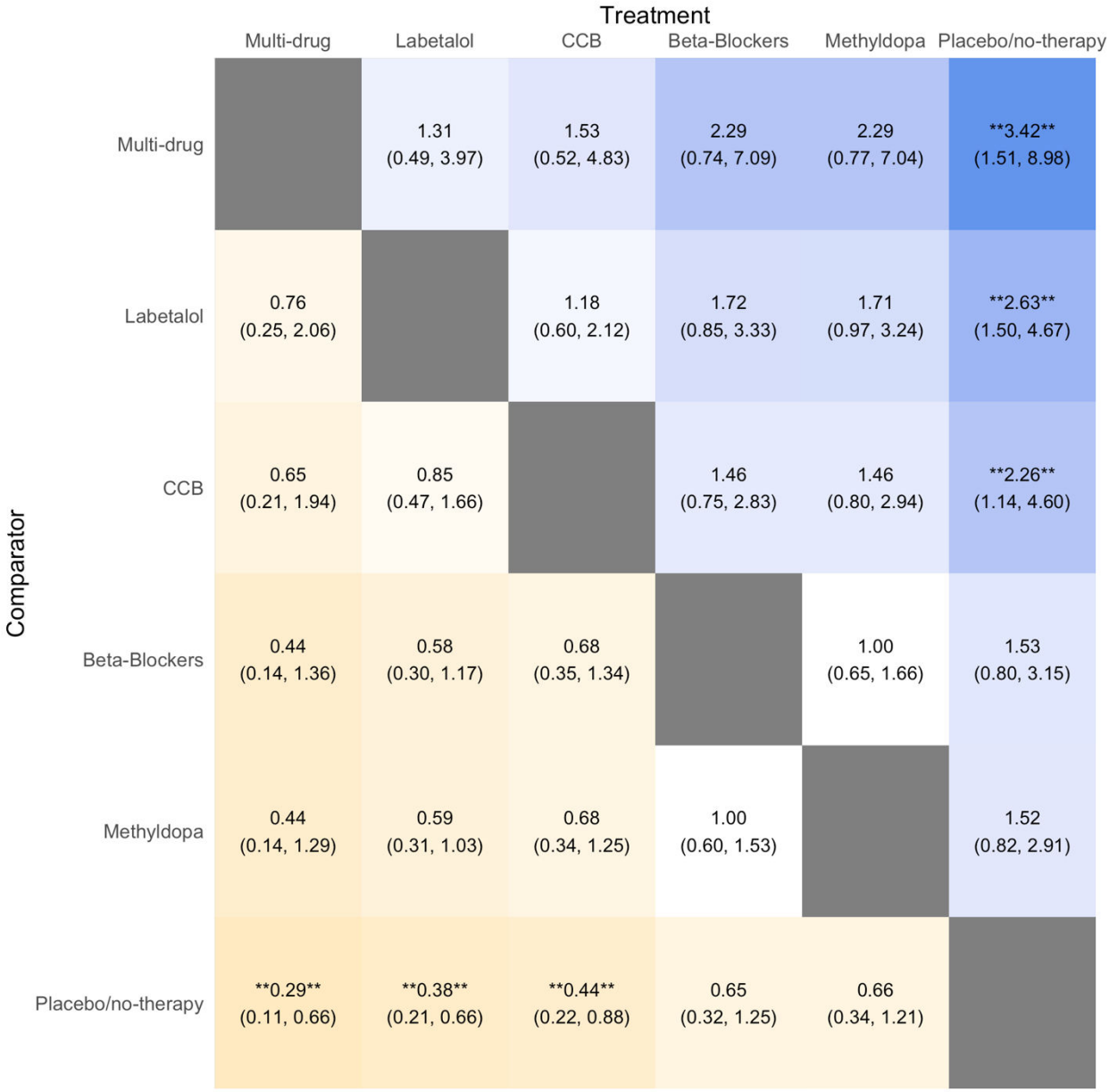
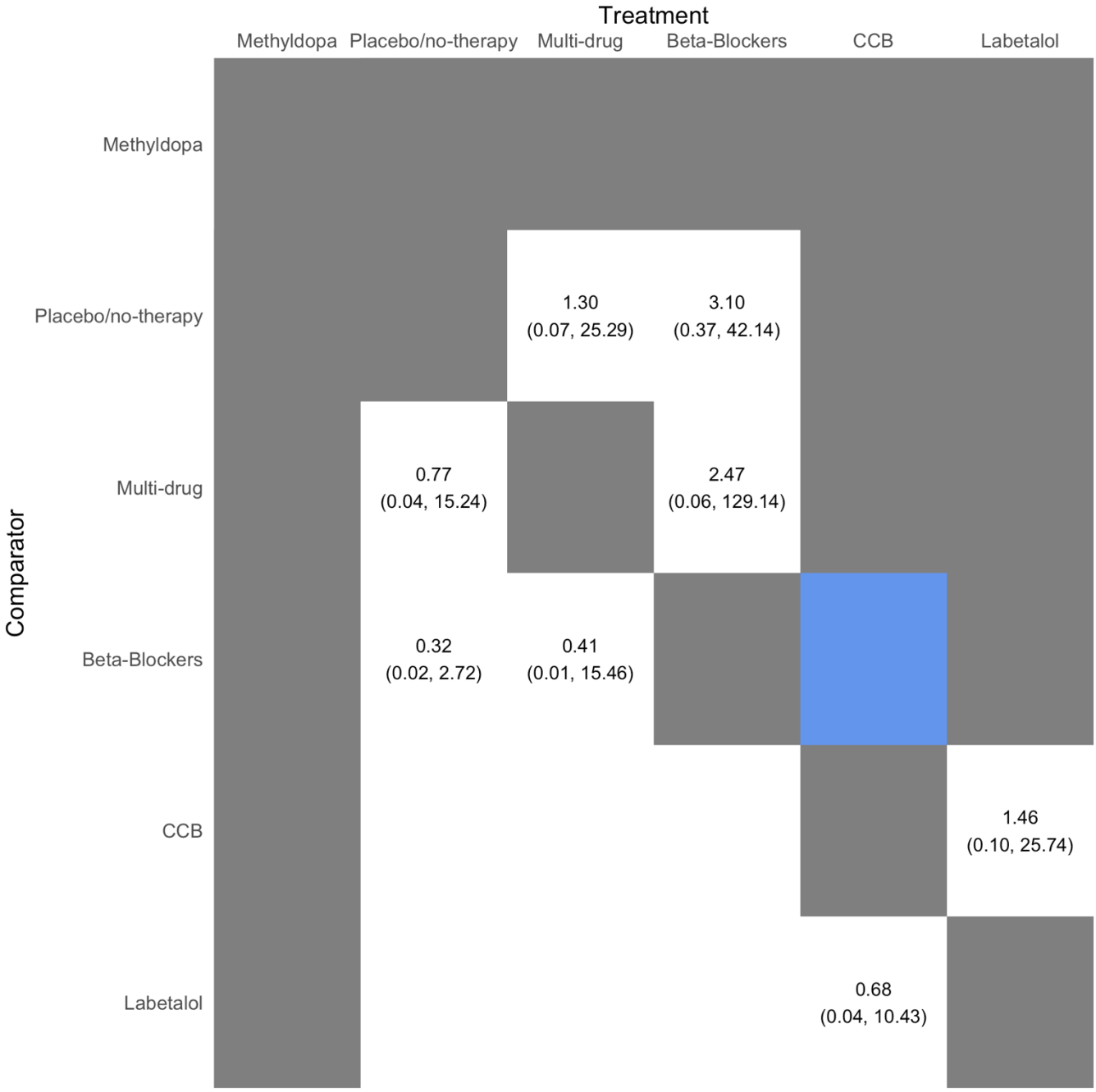


Figure S4B: Changed/stopped drug due to maternal side effects



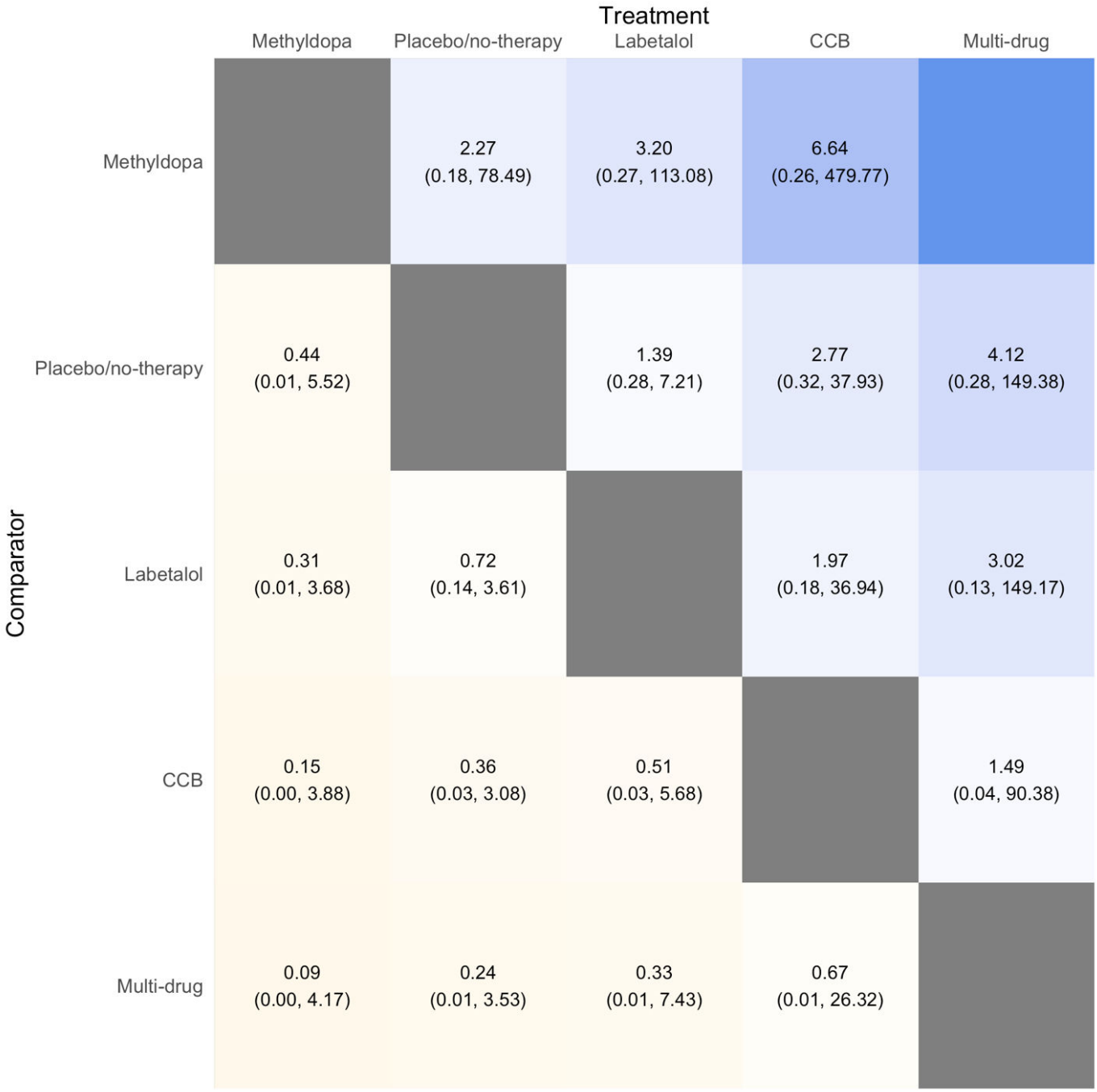


Figure S4C: Placental abruption

Figure S4D: Cesarean delivery

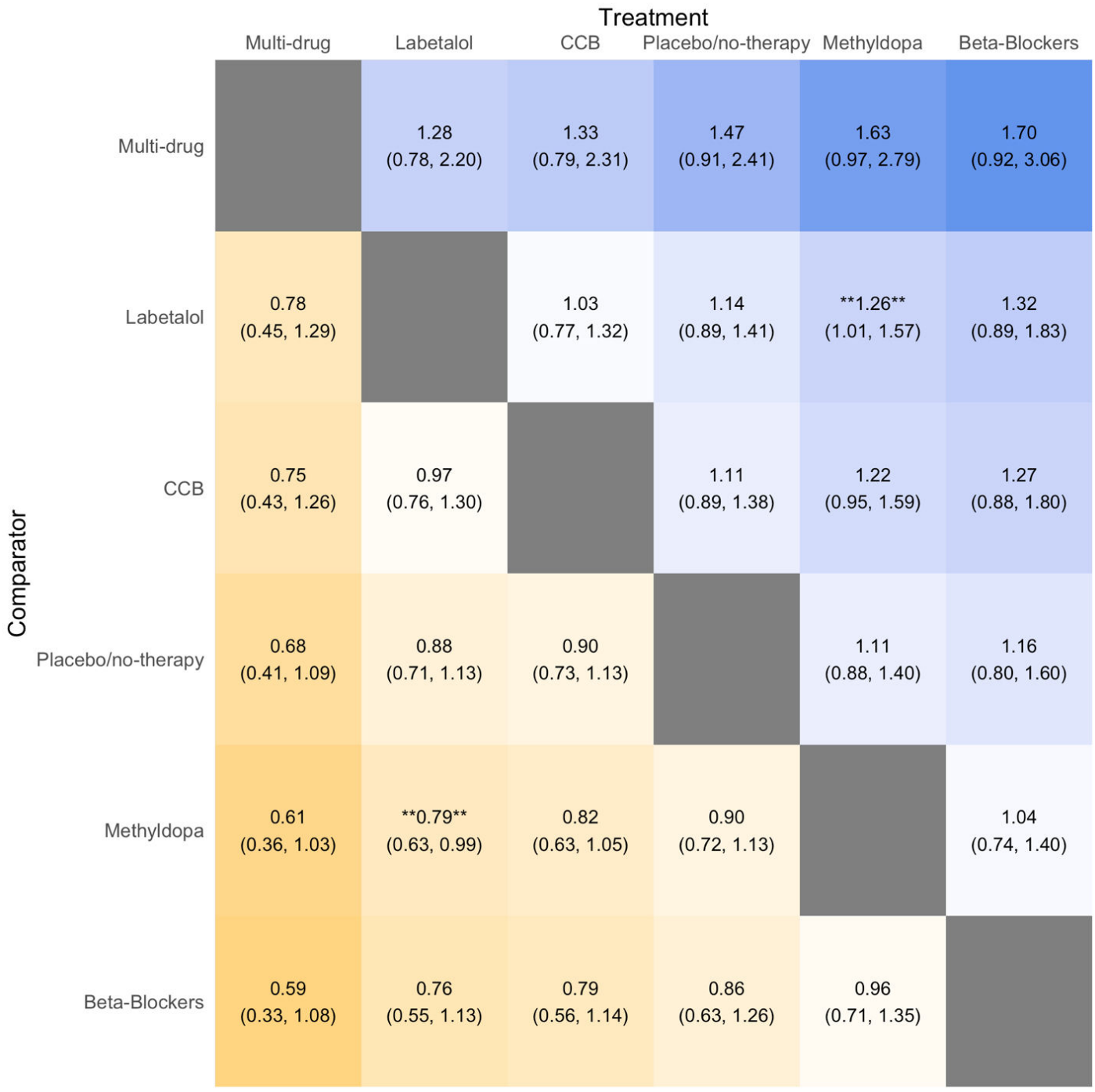


Figure S4E: Respiratory distress syndrome