MAY 2023

SYSTEMATIC REVIEW AND META-ANALYSIS

Management of Postpartum Hypertensive Disorders of Pregnancy

In Partnership with

Comparative Effectiveness Review

Number 263

Management of Postpartum Hypertensive Disorders of Pregnancy

Prepared for:
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Contract No. 75Q80120D00001

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AHRQ Publication No. 23-EHC012 **PCORI® Publication No. 2023-SR-02**
May 2023

This report is based on research conducted by the Brown Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. 75Q80120D00001). The Patient-Centered Outcomes Research Institute® (PCORI®) funded the report (PCORI Publication No. 2023-SR-02). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ or PCORI, its Board of Governors or Methodology Committee. Therefore, no statement in this report should be construed as an official position of PCORI, AHRQ, or the U.S. Department of Health and Human Services.

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

The information in this report is intended to help healthcare decision makers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of healthcare services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

A representative from AHRQ served as a Contracting Officer's Representative and reviewed the contract deliverables for adherence to contract requirements and quality. AHRQ did not directly participate in the literature search, determination of study eligibility criteria, data analysis, interpretation of data, or preparation or drafting of this report.

AHRQ and PCORI appreciate appropriate acknowledgment and citation of their work. Suggested language for acknowledgment: This work was based on an evidence report, Management of Postpartum Hypertensive Disorders of Pregnancy, by the Evidence-based Practice Center Program at the Agency for Healthcare Research and Quality (AHRQ) and funded by the Patient-Centered Outcomes Research Institute (PCORI).

Suggested citation: Steele DW, Adam GP, Saldanha IJ, Kanaan G, Zahradnik ML, Danilack VA, Stuebe AM, Peahl AF, Chen KK, Balk EM. Management of Postpartum Hypertensive Disorders of Pregnancy. Comparative Effectiveness Review No. 263. (Prepared by the Brown Evidence-based Practice Center under Contract No. 75Q80120D00001.) AHRQ Publication No. 23-EHC012. PCORI Publication No. 2023-SR-02. Rockville, MD: Agency for Healthcare Research and Quality; May 2023. DOI: https://doi.org/10.23970/AHRQEPCCER263.
Posted final reports are located on the Effective Health Care Program search page.

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new healthcare technologies and strategies.

The Patient-Centered Outcomes Research Institute® (PCORI®) was established to fund research that helps patients and caregivers make better informed healthcare choices. To fulfill its authorizing mandate, PCORI partners with AHRQ to generate evidence synthesis products and make comparative effectiveness research more available to patients and providers.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see https://effectivehealthcare.ahrq.gov/about/epc/evidence-synthesis.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the healthcare system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the website (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Acknowledgments

The authors gratefully acknowledge Associate Editor Meera Viswanathan, Ph.D., M.A., from the RTI International–University of North Carolina Evidence-based Practice Center (RTI–UNC EPC), Chapel Hill, NC, for her contributions to this report.

Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

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Technical Expert Panel

In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Peer Reviewers

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report do not necessarily represent the views of individual reviewers. AHRQ may also seek comments from other Federal agencies when appropriate.

Peer Reviewers must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential nonfinancial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

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Management of Postpartum Hypertensive Disorders of Pregnancy

Structured Abstract

Background. Hypertensive disorders of pregnancy (HDP) are increasingly common and have important implications for maternal health, healthcare utilization, and health disparities. There is limited evidence to support best management of postpartum individuals with HDP, including home blood pressure (BP) monitoring (HBPM) and choice of antihypertensive agents. For patients experiencing preeclampsia with severe features, there is robust evidence supporting delivery of the infant and treatment with magnesium sulfate ($MgSO_4$). However, $MgSO_4$ may cause unpleasant side effects and, less commonly, toxicity. Patients receiving $MgSO_4$ require additional monitoring (e.g., urinary catheterization) and often have activity restrictions, which impact their postpartum experience. Evidence regarding the optimal (lowest effective) dose and (shortest effective) duration of $MgSO_4$ treatment is needed.

Methods. We searched Medline®, Cochrane, Embase®, CINAHL®, and ClinicalTrials.gov from inception to December 1, 2022. After double screening, we extracted study data and risk of bias assessments into the Systematic Review Data Repository Plus (SRDR+; https://srdrplus.ahrq.gov). We evaluated the strength of evidence (SoE) using standard methods. The protocol was registered in PROSPERO (registration number CRD42022313075).

Results. We found 13 eligible studies (3 randomized controlled trials [RCTs], 2 nonrandomized comparative studies [NRCSs], 8 single-arm studies) evaluating postpartum HBPM, 17 RCTs evaluating pharmacological treatment of postpartum HDP, and 43 studies (41 RCTs and 2 NRCSs) that compared alternative $MgSO_4$ regimens. HBPM programs probably increase submission of any BP measurements during recommended time intervals (moderate SoE) and may increase the number of BP measurements obtained overall (low SoE). Studies have not found that HBPM affects the rate of BP treatment initiation (low SoE), but HBPM may reduce unplanned hypertension-related hospital admissions (low SoE). Most patients were satisfied with management related to HBPM (low SoE), and HBPM probably compensates for racial disparities in office-based follow-up (moderate SoE). In patients with preeclampsia or gestational hypertension (HTN), oral furosemide may shorten the duration of postpartum hypertension (low SoE). There was insufficient evidence regarding the comparative benefits and harms of other antihypertensive medications. Compared with 24-hour treatments, shorter duration $MgSO_4$ regimens shorten the urinary catheterization time (high SoE), time to ambulation (high SoE), and time to breastfeeding (moderate SoE); and may shorten time from delivery to contact with the infant and decrease toxicity as manifested by lost deep tendon reflexes (both low SoE). Loading dose only regimens increase the risk of a recurrent seizure in patients with eclampsia (moderate SoE). Lower dose $MgSO_4$ regimens, compared to standard dose regimens, reduce early signs of magnesium toxicity (high SoE), may approximately double the risk of recurrent seizure in patients with eclampsia (low SoE), but may not affect 5-minute Apgar scores in infants of patients with preeclampsia with severe features (low SoE). There is insufficient evidence regarding potential harms of concomitant use of nifedipine or other antihypertensive medications.

Conclusion. HBPM probably improves ascertainment of BP, allowing early recognition of hypertension in postpartum patients, and probably compensates for racial disparities in office based follow-up. The evidence suggests furosemide may shorten the duration of postpartum HTN. However, further evidence is needed regarding the comparative benefits and harms of the antihypertensive medications used to treat postpartum HTN. Large pragmatic trials, augmented by analysis of real-world data, are needed to evaluate the effect of postpartum HBPM on clinical event outcomes (not only process outcomes) and on the comparative effectiveness of alternative antihypertensive treatments. Given that lower dose $MgSO_4$ regimens reduce Mg toxicity, and shorter regimens decrease urinary catheterization time, time to ambulation, time to breastfeeding, and time from delivery to contact with the infant, evidence is needed to identify $MgSO_4$ regimens with the lowest effective dose and shortest effective duration that minimize side effects and toxicity but still prevent seizures among patients with preeclampsia with severe features.

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Executive Summary

Main Points

- **Home Blood Pressure Monitoring (HBPM)**
  - Probably increases the likelihood of obtaining blood pressure (BP) measurements during recommended time intervals (63% met reporting recommendations) (moderate strength of evidence [SoE]) and may increase the number of BP measurements obtained overall (low SoE).
  - Most patients may be satisfied with care related to HBPM (≥87%) (low SoE)
  - HBPM may not affect initiation of BP treatment (low SoE, no evidence of difference)
  - HBPM may reduce unplanned hypertension (HTN)-related readmissions (low SoE)
  - HBPM probably decreases disparities between non-Black and Black patients in adherence to recommended BP surveillance (moderate SoE)
- **Pharmacological Treatment of Postpartum Hypertension**
  - Oral furosemide may shorten the duration of HTN in postpartum patients with preeclampsia (or gestational HTN) (low SoE)
  - There is insufficient evidence regarding comparative benefits and harms of other antihypertensive medications to treat postpartum HTN
- **Magnesium Sulfate Regimens**
  - *Shorter-duration* magnesium sulfate ($MgSO_4$) regimens (<24 hour), compared with standard (>24 hour) regimens:
    - Reduce the duration of urinary catheterization (high SoE), the time to ambulation (High SoE), and probably the time to start breastfeeding (moderate SoE)
    - May shorten time from delivery to contact with infant (low SoE)
    - May lower rates of absent deep tendon reflexes, a sign of magnesium toxicity (low SoE)
    - Loading dose only regimens, compared with standard 24-hour regimens, probably increase the risk of recurrent seizures in patients with eclampsia (moderate SoE)
    - There is insufficient evidence regarding the risk of maternal mortality, and infant morbidities with different durations of $MgSO_4$ regimens
  - *Lower-dose* $MgSO_4$ regimens, compared with standard dose regimens:
    - May increase the risk of recurrent seizures among patients with eclampsia (low SoE)
    - May not affect mortality among patients with eclampsia (low SoE, no evidence of difference)
    - May not affect 5-minute Apgar scores among infants of patients with preeclampsia with severe features (low SoE, no evidence of difference)
    - Lowers the rate of absent deep tendon reflexes (a sign of magnesium toxicity) (high SoE)
  - There is insufficient evidence regarding whether nifedipine or other antihypertensive medications affect the rate of adverse events when administered with $MgSO_4$

Background and Purpose

Hypertensive disorders of pregnancy (HDP) affect up to 10 percent of pregnancies, and encompass a spectrum of disorders that include preexisting chronic HTN, gestational HTN, preeclampsia with and without severe features, eclampsia (seizure), and HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. Rates of HDP are rising in the United States,[1, 2] likely due to increased prevalence of pre-existing HTN, obesity, diabetes, older age at delivery, and use of artificial reproductive technologies.[3] Historically, it was believed that HDP was cured by delivery of the placenta, but it is now understood that HDP can persist, worsen, or develop *de novo* after delivery, and may result in severe morbidity or mortality due to eclampsia and stroke. Recent innovations in healthcare delivery—specifically, remote monitoring—show promise in improving early detection of postpartum HTN while also improving the patient experience by increasing the convenience of care and decreasing the need for clinical encounters.

HDP and its sequelae disproportionately affect minority and marginalized communities.[4, 5] There are substantial disparities across income and racial/ethnic minority groups in terms of who is affected and their outcomes. The prevalence of HDP is highest in non-Hispanic Black, American Indian, and Alaska Native individuals.[2] Overall, Black individuals are three times more likely than non-Hispanic White individuals to die of pregnancy-related conditions, both around the time of delivery and up to 1 year postpartum.[5] A higher percentage of these deaths are attributable to HDP (8.2% in Black individuals versus 6.7% in non-Hispanic White individuals).[5]

Some individuals require multiple antihypertensive agents, or large doses of antihypertensives, to control their BP postpartum. More evidence is needed regarding which medication(s) are most effective for outpatient postpartum BP management and have the fewest side effects, while not interfering with breastfeeding.

Individuals who develop preeclampsia with severe features are given $MgSO_4$ to prevent eclamptic seizures. However, there is uncertainty regarding optimal $MgSO_4$ regimens, particularly regarding the necessary treatment duration and dose.

This systematic review aims to inform clinical practice guideline developers, policymakers, and obstetricians/gynecologists, midwives, maternal fetal medicine specialists, family medicine clinicians, primary care physicians, nurse practitioners, nurses, other providers of care for peripartum and postpartum individuals and patients. The systematic review addresses three Key Questions (KQs) and a Contextual Question (CQ):

KQ 1: What are the effectiveness, comparative effectiveness, and harms of **home blood pressure monitoring/telemonitoring** in postpartum individuals?

KQ 2: What are the effectiveness, comparative effectiveness, and harms of **pharmacological treatments** for hypertensive disorders of pregnancy in postpartum individuals?

KQ 3: What are the comparative effectiveness and harms of alternative **$MgSO_4$ treatment regimens** to treat preeclampsia with severe features during the peripartum period?

CQ: How are race, ethnicity, and social determinants of health related to disparities associated with incidence and detection of HDP, as well as access to care, management, follow-up care, and clinical outcomes in individuals with postpartum hypertensive disorders of pregnancy?

Methods

In this systematic review, we used methods consistent with those outlined in the Agency for Healthcare Research and Quality Evidence-based Practice Center Program Methods Guidance (https://effectivehealthcare.ahrq.gov/topics/cer-methods-guide/overview). Our searches targeted comparative studies (i.e., randomized controlled trials [RCTs] and nonrandomized comparative studies [NRCSs]) for all three KQs from database inception to December 9, 2021. For KQ 1, we included single-arm studies. We extracted study data into the Systematic Review Data Repository Plus (SRDR+). With input from technical experts and key informants, we identified ten prioritized outcomes for each KQ. Where there was sufficient evidence without an unacceptable amount of heterogeneity, we conducted pairwise meta-analyses. We assessed the risk of bias and evaluated the SoE using standard methods. The PROSPERO protocol registration number is CRD42022313075.

Results

We found 73 primary studies that enrolled 13,532 participants combined. Twenty-three studies were conducted in the United States, 2 in the United Kingdom, and 48 in a variety of other low- and middle-income countries. Summary conclusions are displayed in Tables A and B.

Postpartum home blood pressure monitoring: We found 13 studies (3 RCTs, 2 NRCSs, and 8 single-arm studies). Based on one RCT and one NRCS, there is moderate-strength evidence that HBPM probably doubles adherence to recommended BP surveillance, from about 44 to 60 percent to about 92 to 94 percent. Evidence from 5 single-arm studies indicates that most patients submit BP measures when given HBPM devices (e.g., 63% meet American College of Gynecologist [ACOG] recommendation for BP reporting). Two of three RCTs that reported on BP management provided low-strength evidence of no difference in the rate of initiation of antihypertensive medications (reported adjusted odds ratio [OR] and relative risk [RR] = 1.0; other measures of BP management were sparsely reported). Three single-group studies provided low-strength evidence that most patients with postpartum HDP (≥87%) were at least very satisfied with remote monitoring (no studies compared satisfaction with care with versus without HBPM). One RCT and one NRCS provided low-strength evidence that HBPM may reduce HTN-related hospital admissions (risk difference −3.5%, 95% confidence interval [CI] −6.9 to −0.1; adjusted RR 0.12, 95% CI 0.01 to 0.96; respectively). One RCT, supported by a single arm study and a NRCS, provided moderate strength evidence that use of HBPM may reduce racial disparities in BP ascertainment (in the RCT, the relative RR was 0.51, 95% CI 0.33 to 0.78, implying a halving of the disparity between Blacks and non-Blacks; in the NRCS, the gap in adherence to a postpartum BP check decreased from 24.6% to 0.4%; in the single arm study, both Blacks and non-Blacks reported BP measurements with HBPM). There was insufficient evidence regarding the effect of HBPM on whether patients felt "in control" of managing their HDP. There was no evidence regarding the effect of HBPM on other prioritized outcomes, including maternal morbidity or mortality, quality of life, anxiety or depression, or length of postpartum hospital stay.

Pharmacological treatment of postpartum HDP: We found 17 RCTs that compared various pharmacological treatments for postpartum HTN. Five RCTs evaluated postpartum hospitalized patients with acute, severe HTN. Five RCTs evaluated oral diuretics for early postpartum HTN. Five RCTs compared oral antihypertensive treatments for persistent postpartum HTN. Two RCTs specifically evaluated end-organ protective effects of two

antihypertensive drugs in patients with postpartum HDP. Because the studies evaluated a large variety of specific drugs and evaluated disparate outcomes, we had sufficient evidence to make only two conclusions. One RCT found that treatment with the diuretic furosemide (compared to placebo) in postpartum patients may reduce the likelihood of persistent HTN by more than half (adjusted RR 0.40, 95% CI 0.20 to 0.81, and RR 0.31, 95% CI 0.11 to 0.88). There was insufficient evidence regarding the comparative benefits and harms of other parenteral or oral antihypertensive medications to treat postpartum HTN (due to inconsistent findings or the existence of only single trials). There was also insufficient evidence related to maternal morbidity and mortality (among two small studies that evaluated different drugs), length of postpartum hospital stay (reported in only one study), and adverse events (due to sparseness of data per drug). There were no eligible studies that evaluated satisfaction with care, quality of life, anxiety or depression, reduction in health disparities, or severe infant morbidities.

Comparative effects of $MgSO_4$ regimens: Twenty-one RCTs compared shorter-duration (<24 hour) $MgSO_4$ regimens with standard (24 hour) treatment, 15 RCTs compared different doses of $MgSO_4$, 2 RCTs compared intramuscular with intravenous administration, 1 RCT evaluated the effect on uterine bleeding of interrupted versus continuous $MgSO_4$ administration during cesarean section, and 1 RCT evaluated the addition of nifedipine to the $MgSO_4$ regimen.

Shorter duration $MgSO_4$ regimens decrease urinary catheterization time (4 RCTs, high SoE), time to ambulation (2 RCTs, high SoE), time to breastfeeding (2 RCTs, moderate SoE), and time from delivery to contact with the infant (1 RCT, low SoE). For morbidity and mortality outcomes, despite numerous RCTs with thousands of patients (and infants), poor clinical outcomes were sufficiently rare that summary effect estimates were highly imprecise; thus, there is insufficient evidence regarding the effect of using shorter duration $MgSO_4$, regimens on seizure in patients with preeclampsia with severe features (16 RCTs, summary OR 1.09, 95% CI 0.49 to 2.39). However, in patients with eclampsia, loading dose only regimens probably increase the odds of recurrent seizure (4 RCTs, summary OR 2.04, 95% CI 1.21 to 3.46). Shorter duration regimens may result in fewer instances of magnesium-related toxicities (as manifested by loss of deep tendon reflexes; summary OR 0.52, 95% CI 0.32 to 0.84; low SoE due to inconsistency) (4 RCTs). Due to sparse or inconsistent reporting across studies, there was also insufficient evidence related to satisfaction with care. There were no eligible studies that addressed quality of life, psychosocial distress, reduction in health disparities, or adverse drug reactions.

In six RCTs that enrolled patients with preeclampsia with severe features and *compared lower versus higher dose regimens*, no seizures were reported, regardless of $MgSO_4$ dose. In the two RCTs reporting maternal mortality, there were no maternal deaths (insufficient evidence). In the seven RCTs that enrolled patients with eclampsia, the odds of experiencing a recurrent seizure with lower dose regimens were 2-fold higher (OR 2.06, 95% CI 0.99 to 4.31, low SoE). There was no evidence of a difference in mortality (6 RCTs, summary OR 0.60, 95% CI 0.26 to 1.35; low SoE). Patients treated with lower dose $MgSO_4$, regimens have lower rates loss of deep tendon reflexes, an early indicator of magnesium toxicity (5 RCTs, summary OR 0.16, 95% CI 0.09 to 0.28; high SoE). There is no evidence of a difference in 5-minute Apgar scores (mean difference [MD] 0.15, 95% CI –0.21, 0.51) in infants of patients with preeclampsia with severe features treated with lower dose MgSO4 regimens. Due to imprecision related to rare events, evidence was insufficient for other infant morbidities. No eligible studies reported on breastfeeding outcomes, satisfaction with care, quality of life, postpartum recovery (e.g., urinary

catheterization and time to ambulation), maternal-neonatal bonding, psychosocial distress, reduction in health disparities, or adverse drug reactions.

Four studies evaluated other different $MgSO_4$ regimens (one with concomitant oral nifedipine) with disparate reported outcomes. The studies provided insufficient evidence to allow conclusions.

Limitations

Although we found a sizable evidence base overall (73 primary studies), we were able to make only a limited number of conclusions, largely because the studies were generally small and reported a heterogeneous collection of intermediate outcomes. Few studies reported subgroup data or statistically evaluated whether the effect of the intervention differed among subgroups (i.e., heterogeneity of treatment effects). Many of the prioritized outcomes were either not reported in any included study for specific comparisons or were reported in an insufficient number of studies to allow meta-analyses or merit conclusions (i.e., they provided insufficient evidence).

Implications and Conclusions

HBPM probably improves overall BP ascertainment in the early postpartum period, largely through greater adherence with reporting of BP measures (Moderate SoE) and probably decreases disparities (between Blacks and non-Blacks) in achieving recommended BP surveillance standards (Moderate SoE). HBPM may reduce unplanned hypertension related readmissions (low SoE) but may not affect the likelihood of initiating treatment for hypertension (Low SoE). There is insufficient evidence regarding the effect of HBPM on clinical outcomes.

Postpartum treatment with the diuretic oral furosemide (vs. no furosemide) may reduce the duration of postpartum HTN (Low SoE). Evidence is insufficient or lacking regarding the comparative benefits and harms of other antihypertensive medications.

The evidence regarding the effect of different $MgSO_4$ regimens on serious clinical outcomes (seizures, death) remains mostly insufficient primarily, due to the rarity of these events with any $MgSO_4$ treatment. Nevertheless, although more evidence is needed to confirm this finding, for patients with eclampsia, loading dose-only $MgSO_4$ regimens probably increase the risk of recurrent seizures (Moderate SoE) but not the risk of death (Low SoE). Loss of deep tendon reflexes (a clinical sign of Magnesium toxicity) may be reduced with shorter duration regimens (Low SoE) and is reduced with lower dose regimens (High SoE). There is no evidence of a difference in 5-minute Apgar scores in infants of patients with preeclampsia with severe features treated with lower dose MgSO4 regimens (low SoE). Shorter duration $MgSO_4$ regimens reduce the duration of urinary catheterization (High SoE), time to ambulation (High SoE), time to breastfeeding (Moderate SoE), and time from delivery to contact with the infant (Low SoE). There is insufficient evidence regarding whether nifedipine or other antihypertensive medications affect the rate of adverse events when administered with $MgSO_4$.

Overall, the evidence base remains incomplete regarding the indications for and implementation of HBPM. Further evidence is needed to determine whether HBPM can reduce the occurrence of adverse clinical outcomes, such as eclamptic seizures, stroke, and pregnancy related deaths. In some settings, hospital readmissions might reflect improved ascertainment of HDP.

The evidence for comparative benefits and harms of available antihypertensive medication is scant. Trials are needed for the numerous antihypertensive drugs commonly used in practice to

allow better decision making in choice of treatment. Both successful control of hypertension and effect on clinical event outcomes are important outcomes to be further studied.

Evidence from large pragmatic trials, augmented by analysis of real-world data, is needed to the optimal (i.e., lowest effective dose to minimize unpleasant side effects and toxicity, and shortest effective duration) $MgSO_4$ regimen(s) for individuals with preeclampsia with severe features.

Table A. Overall summary of evidence identified regarding Key Questions 1 (home monitoring) and 2 (hypertension treatment)

Outcome Category	Outcome	HBPM in PP Individuals	Pharmacological Treatments for HDP in PP Individuals
BP reporting (adherence)	BP measurements obtained during recommended time intervals	✓✓ HBPM probably improves BP reporting	N/A
	Number of BP measurements obtained	✓ May increase the number of BP measurements obtained overall	N/A
Antihypertensive treatment	Treatment initiation, adjustment, or discontinuation	✓ No evidence of difference in initiation	N/A
mBP control	Persistent HTN on PP Day 7	No eviden	✓ Oral furosemide for 5 days PP may reduce the rate of persistent HTN on PP Day 7: No conclusions for other medications
	Need for rescue medication	No evidence	No conclusions
	Days to resolution of HTN	No evidence	No conclusions
Severe maternal outcomes	Maternal morbidity and mortality	No conclusions	No evidence
Patient-reported outcomes	Satisfaction with PP care	✓ Most patients may be satisfied with care related to HBPM	No evidence
	Quality of life	No evidence	No evidence
	Anxiety/depression	No evidence	No evidence
Healthcare utilization	Length of PP hospital stay	No evidence	No evidence
	Unplanned readmission	✓ HBPM may reduce unplanned hypertension related readmissions	No evidence
	Unplanned obstetrical triage area, clinic visits or emergency department visits	No conclusions	No evidence
Infant-related outcomes	Breastfeeding	N/A	No evidence
	Severe infant morbidities	N/A	No evidence
Adverse events	Severe adverse events	N/A	No evidence
Reduction (or generation) of health disparities	Reduction of disparities in BP surveillance	✓✓ HBPM probably reduces disparities (non-Black vs. Black) in adherence to BP surveillance	No evidence

Abbreviations: BP = blood pressure, HBPM = home blood pressure monitoring, HDP = hypertensive disorders of pregnancy, HTN = hypertension, N/A = not applicable, PP = postpartum, SoE = strength of evidence, XR = extended release

✓ = Low SoE, ✓✓ = Moderate SoE, ✓✓✓ = High SoE (no instances in this table)

Color legend: High strength of evidence (green) (no instances in this table), Moderate strength of evidence (blue), Low strength of evidence (orange), Insufficient strength of evidence/no conclusions (unshaded/white), No evidence or not applicable (N/A) (gray). The colors do not provide unique information compared with the text and symbols.

Table B. Overall summary of evidence identified for Key Question 3 (alternative MgSO4 regimens)

Outcome Category	Outcome (Population)	Shorter Versus Standard Duration $MgSO_4$ Regimens for Preeclampsia With Severe Features During Peripartum	Lower Versus Higher Dose $MgSO_4$ Regimens for Preeclampsia With Severe Features During Peripartum
Severe maternal outcomes	Maternal morbidity and mortality	No conclusions (rare event)	No conclusions (rare event) for patients without prior seizure ✓ No evidence of a difference in mortality among patients with prior eclamptic seizure
	Seizure (preeclampsia with severe features)	No conclusions (rare event)	No conclusions (rare event)
	Recurrent seizure (eclampsia)	✓✓ Loading dose only $MgSO_4$ regimens probably result in increased risk of recurrent seizure	✓ Lower dose $MgSO_4$ regimen may result in increased risk of recurrent seizure
Infant-related outcomes	Breastfeeding	✓✓ Shorter duration $MgSO_4$ regimen probably yields shorter time to start breastfeeding	No evidence
	Infant morbidity	No conclusions (rare event)	✓ No evidence of a difference in 5-minute Apgar score in infants of patients with preeclampsia with severe features
Patient-reported outcomes	Satisfaction with PP care	No conclusions	No evidence
	Quality of life	No evidence	No evidence
	Anxiety/depression	No evidence	No evidence
Postpartum recovery time	Duration of urinary catheter placement	✓✓✓ Shorter duration $MgSO_4$ regimen yields shorter duration of urinary catheterization	No evidence
	Time to ambulation	✓✓✓ Shorter duration $MgSO_4$ regimen yields shorter time to ambulation	No evidence
Maternal-neonatal bonding	Time from delivery to contact with infant	✓ Shorter duration $MgSO_4$ regimen may yield shorter time from delivery to contact with infant	No evidence

Outcome Category	Outcome (Population)	Shorter Versus Standard Duration $MgSO_4$ Regimens for Preeclampsia With Severe Features During Peripartum	Lower Versus Higher Dose $MgSO_4$ Regimens for Preeclampsia With Severe Features During Peripartum
Reduction (or generation) of health disparities	Reduction of disparities in BP surveillance	No evidence	No evidence
Harms	Magnesium-related toxicity	✓ Shorter duration $MgSO_4$ regimen may lower risk of magnesium toxicity	✓✓✓ Lower dose $MgSO_4$ regimen lowers the risk of magnesium toxicity
	Other clinically important adverse events	No conclusions	No conclusions

Abbreviations: PP = postpartum, BP = blood pressure, $MgSO_4$ = magnesium sulfate, SoE = strength of evidence.

✓ = Low SoE, ✓✓ = Moderate SoE, ✓✓✓ = High SoE

Color legend: High strength of evidence (green), Moderate strength of evidence (blue), Low strength of evidence (orange), Insufficient strength of evidence/no conclusions (unshaded/white), No evidence (gray). The colors do not provide unique information compared with the text and symbols.

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1. Introduction

1.1 Background

Hypertensive disorders of pregnancy (HDP) affect up to 10 percent of pregnancies, and encompass a spectrum of disorders that include preexisting chronic hypertension (HTN), gestational HTN, preeclampsia with and without severe features, eclampsia (seizures), and HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome.[1] Severe features of preeclampsia are defined by the American College of Obstetricians and Gynecologists (ACOG) as persistent systolic blood pressure [BP] ≥160 mm Hg or diastolic BP ≥110 mm Hg, low platelet count, abnormal liver function, acute abnormal kidney function, pulmonary edema, new-onset headache, visual disturbance, and seizures (eclampsia).[2, 3] Rates of HDP are rising in the United States,[4, 5] likely due to increased prevalence of pre-existing HTN, obesity, diabetes, older age at delivery, and use of artificial reproductive technologies.[6] Historically, it was believed that HDP was cured by delivery of the placenta, but it is now understood that HDP can persist, worsen, or develop *de novo* after delivery, and may result in severe morbidity or mortality due to eclampsia and stroke.[7, 8]

Diagnoses of HDP have important implications for healthcare utilization, long-term health outcomes, patient experience, and health disparities in pregnant and postpartum individuals and their children. Over the past 30 years, pregnancy-related deaths have increased in the United States, from 7.2 deaths per 100,000 live births in 1987 to 20.1 deaths per 100,000 live births in 2019.[9, 10] More than half of pregnancy-related deaths occur in the postpartum period.[11] The Centers for Disease Control and Prevention (CDC) reports that 6.6 percent of the pregnancy-related deaths between 2014 and 2017 were attributable to HDP.[12] Beyond the postpartum period, data suggest that individuals with pregnancies complicated by HDP have a higher risk of chronic HTN and a higher lifelong risk of cardiovascular complications.[13-15]

Patients with HDP require increased monitoring during and after pregnancy and may require prolonged hospitalization at delivery for BP control and management of acute sequelae. In addition to the increased risks of death and serious complications, postpartum HDP can have important implications for the mother's wellbeing. For example, hospital readmission and medicalization of the postpartum period due to HDP may complicate the family's adjustment to parenting. Postpartum HDP may impact breastfeeding practice and experience,[16] and adversely affect postpartum mental health.[17]

HDP and its sequelae disproportionately affect minority and marginalized communities.[11, 18] There are substantial disparities across income and racial/ethnic minority groups in terms of who is affected and their outcomes. The prevalence of HDP is highest in non-Hispanic Black, American Indian, and Alaska Native individuals.[5] Overall, Black individuals are three times more likely than non-Hispanic White individuals to die of pregnancy-related conditions, both around the time of delivery and up to 1 year postpartum.[18] A higher percentage of these deaths are attributable to HDP in non-Hispanic Black individuals (9.9 %) versus 4.8 % in non-Hispanic White individuals).[19]

The mainstays of treatment for HDP include delivery of the infant, use of BP monitoring, initiation and titration of antihypertensive medications, and administration of magnesium sulfate ($MgSO_4$) to prevent seizures among individuals with preeclampsia with severe features.[3]

Recent innovations in healthcare delivery—specifically, remote BP monitoring—show promise in improving early detection of postpartum HTN, while also improving the patient experience by increasing the convenience of care and decreasing the frequency of clinical

encounters. While early data are promising, key missing information includes whether BP home- or tele-monitoring is effective, whether the chosen form of home monitoring (e.g., monitoring regimen, communication method) impacts effectiveness, and whether home monitoring may impact observed disparities in outcomes.

Some individuals with HDP are discharged from their postpartum hospitalization with antihypertensive medications. Others may develop HTN after discharge and require treatment. In the postpartum period, BP can change rapidly and unpredictably (due to labile postpartum physiology) before returning to normal, and this can result in shifting medication requirements. In the context of outpatient postpartum BP management, more evidence is needed regarding which medications are most effective and have the fewest side effects, as well as dosing intervals that favor adherence and are compatible with breastfeeding. Evidence is also emerging regarding the use of home BP monitoring accompanied by self-titration of antihypertensive medications.[20, 21]

There is robust evidence supporting use of $MgSO_4$ to prevent eclamptic seizures for individuals with peripartum preeclampsia with severe features.[22] However, there is uncertainty regarding optimal $MgSO_4$ regimen(s) in terms of treatment duration and dose (loading and total).[23] There is also limited evidence regarding the indications for and duration of use of $MgSO_4$ for preeclampsia with severe features arising or worsening after delivery.[7, 24]

Treatment with $MgSO_4$ is associated with a broad range of common side effects and potential toxicities. Some side effects are unpleasant (e.g., nausea), others represent early signs of magnesium toxicity (e.g., loss of deep tendon reflexes), and some are life-threatening but rare (e.g., respiratory arrest). By protocol, many centers mandate urinary catheterization and enforce bed rest during $MgSO_4$ treatment. This can increase separation between mother and newborn, delaying initiation of breastfeeding, or require additional staffing resources to support safe rooming-in, both of which are generally greatly disliked by patients.[25]

Despite some evidence to the contrary,[26] concerns persist regarding the potential for adverse interactions, such as hypotension, neuromuscular blockade, and pulmonary edema, when $MgSO_4$ is used with specific antihypertensive agents (e.g., nifedipine or other calcium channel blockers).[27] Increased maternal $MgSO_4$ concentrations at the time of delivery have been associated with infant harms, including lower 1-minute, and 5-minute Apgar scores, intubation in the delivery room, admission to a special care nursery, and hypotonia.[28]

A thorough review of the literature is critical to improve both the early detection and management of postpartum HDP and $MgSO_4$ use for peripartum preeclampsia with severe features.

1.2 Purpose of the Review

ACOG nominated this topic to the Patient-Centered Outcomes Research Institute (PCORI), which contracted with the Agency for Healthcare Research and Quality (AHRQ) to support and conduct the review.

Specifically, the systematic review summarizes the findings from (1) studies of home BP monitoring in the postpartum period, (2) studies of pharmacological treatment of HDP in the postpartum period, and (3) studies comparing the effectiveness and harms of different $MgSO_4$ regimens in patients with preeclampsia with severe features to prevent eclampsia during the peripartum period. For the third topic, the peripartum period is operationally defined as the time interval prior to, during, and after delivery when individuals may be diagnosed with preeclampsia with severe features. For all topics, the review summarizes findings related to the

comparative effectiveness (and comparative harms) of these interventions, with an emphasis, as feasible, on factors related to healthcare disparities and pregnancy-related risk factors.

The intended audience includes guideline developers, clinicians, other providers of peripartum and postpartum care, healthcare policy makers, and patients.

2. Methods

2.1 Review Approach

For all Key Questions (KQs), the systematic review (SR) followed Agency for Healthcare Research and Quality (AHRQ) Evidence-based Practice Center Program methodology, as laid out in its Methods Guide, particularly as it pertains to reviews of comparative effectiveness, and meta-analyses.[29, 30] We registered the protocol for this SR in PROSPERO (registration number CRD42022313075). The Contextual Question is addressed as a narrative review and integrated in the discussion.

2.2 Key Questions and Contextual Question

Key Question 1: What are the effectiveness, comparative effectiveness, and harms of **home blood pressure monitoring/telemonitoring** in postpartum individuals?

Key Question 2: What are the effectiveness, comparative effectiveness, and harms of **pharmacological treatments** for hypertensive disorders of pregnancy in postpartum individuals?

Key Question 3: What are the comparative effectiveness and harms of alternative **magnesium sulfate ($MgSO_4$) treatment regimens** to treat preeclampsia with severe features during the peripartum period?

> **3.a**: Are there harms associated with the concomitant use of particular antihypertensive medications during treatment with $MgSO_4$?

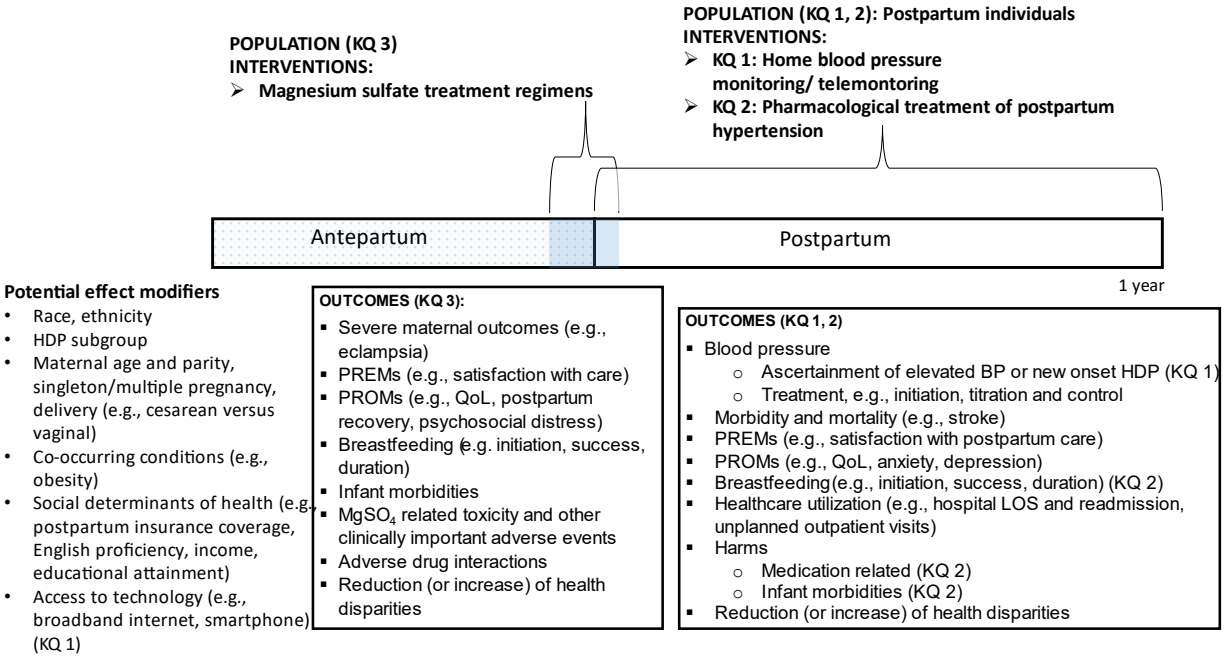
For **all Key Questions**, how do the findings vary by race, ethnicity, hypertensive disorders of pregnancy (HDP) subgroup, maternal age, parity, singleton/multiple pregnancies, mode of delivery, co-occurring conditions (e.g., obesity), and social determinants of health (e.g., postpartum insurance coverage, English proficiency, income, educational attainment)?

Contextual Question: How are race, ethnicity, and social determinants of health related to disparities in incidence and detection of HDP, as well as access to care, management, follow-up care, and clinical outcomes in individuals with postpartum hypertensive disorders of pregnancy?

2.3 Analytic Framework

Based on discussions with Key Informants and Technical Expert Panel members, we developed an analytic framework for the three KQs (Figure 2.1).

Figure 2.1. Analytic framework



Abbreviations: BP = blood pressure, ED = Emergency Department, HDP = hypertensive disorders of pregnancy, HTN = hypertension, KQ = Key Question, LOS = length of stay, $MgSO_4$ = magnesium sulfate, PREM = patient-reported experience measure, PROM = patient-reported outcome measure, QoL = quality of life

2.4 Study Selection

Appendix A provides full details for the search strategies, study eligibility criteria, and screening processes. In brief, for KQ 1 we included randomized controlled trials (RCTs) and nonrandomized comparative studies (NRCSs) that compared home blood pressure (BP) monitoring during the postpartum period (up to 1 year after delivery) with clinic-based BP monitoring, other non-clinic approaches (e.g., kiosks, pharmacy-based), or alternative home BP monitoring interventions (including alternative training, education, or alert-triggering protocols). Given the current pandemic-related interest in remote monitoring and telehealth, and the paucity of comparative trials, for KQ 1 only, we included single arm studies that offered home blood pressure monitoring to 50 or more participants, to provide additional context regarding intervention components and implementation strategies. We used the American College of Obstetrics and Gynecology (ACOG) definitions and diagnostic criteria to categorize HDP.[3] We evaluated outcomes as listed in the *Study Eligibility Criteria* section, focusing on the prioritized outcomes related to BP management, severe maternal health outcomes, patient-reported outcome measures (PROMs),[31] patient-reported experience measures (PREMs),[32] healthcare utilization, health disparities, and harms.

For KQ 2, we included comparative studies of postpartum pharmacological treatments for HDP (specifically, antihypertensive medications and diuretics). We evaluated outcomes as listed in the *Study Eligibility Criteria* section, focusing on listed prioritized outcomes related to BP management, severe maternal health outcomes, PROMs, PREMs, healthcare utilization, infant outcomes, disparities, and harms.

For KQ 3 we evaluated the comparative effectiveness of alternative $MgSO_4$ treatment regimens in individuals diagnosed with preeclampsia with severe features or eclampsia. We

evaluated studies that directly compared alternative regimens. To determine whether network meta-analyses were feasible, we graphically evaluated the network of potential comparisons including effectiveness RCTs (e.g., placebo controlled or $MgSO_4$ versus antiseizure or antihypertensive medication) to include indirect comparisons of alternative $MgSO_4$ regimens. We found that the studies were insufficient to support a complete network meta-analysis. We extracted seizure (and recurrent seizure) event rates from the $MgSO_4$ arms in effectiveness RCTs and performed a meta-analysis of risk of seizures by population (i.e., preeclampsia with severe features and eclampsia). We evaluated outcomes as listed in the *Study Eligibility Criteria* section, focusing on the prioritized outcomes related to severe maternal health outcomes, newborn/child outcomes, patient-reported outcomes and experience measures, disparities, and harms.

For all KQs, we attempted to describe differential effects of interventions in different subgroups, including by race/ethnicity, maternal and pregnancy characteristics, co-occurring conditions, and potential indicators of social determinants of health. For KQ 3, we evaluated timing with respect to delivery and subgroups with obesity or reduced kidney function.

2.5 Data Extraction and Data Management

We extracted data into the Systematic Review Data Repository Plus (SRDR+) database (https://srdrplus.ahrq.gov). Each eligible study was extracted and assessed for risk of bias/quality by one researcher. Extracted data, including risk of bias assessment, were confirmed by a second, independent researcher.

2.6 Assessment of Risk of Bias and Methodologic Quality

We evaluated each comparative study (RCT and NRCS) for risk of bias and each single arm study for methodological quality.

For RCTs, we used all the items from the Cochrane Risk of Bias tool,[33] which addresses issues related to randomization and allocation concealment methodology; blinding of participants, study personnel/care providers, and outcome assessors; completeness of outcome data; selective outcome reporting; and other issues that could be related to bias.

For NRCSs, we used the specific sections of the Risk Of Bias in Nonrandomized Studies of Interventions (ROBINS-I) tool[34] that pertain to confounding and selection bias. ROBINS-I requires the identification of specific confounders of interest for the SR. To assess the presence of potential confounding in studies, we considered age and race/ethnicity as potential confounders for all KQs. Because NRCSs, like RCTs, can be impacted by the lack of blinding and by participant loss to follow up, we also used the items from the Cochrane Risk of Bias tool that focus on issues related to blinding of participants, study personnel or care providers, objective outcome assessors, and subjective outcome assessors; incomplete outcome data; selective outcome reporting; and other issues that could lead to bias.

For single arm studies, we assessed methodological quality using items from the Cochrane Risk of Bias Tool[33] that pertain to participant loss to follow up, incomplete outcome data, and selective outcome reporting, and items from the National Heart, Lung, and Blood Institute (NHLBI) Tool[35] that focus on the adequacy of descriptions of eligibility criteria, interventions, and outcomes.

2.7 Data Synthesis

Each study included in the SR is described in summary and evidence tables that present study design features, study participant characteristics, descriptions of interventions, outcome results, and risk of bias.

For each KQ, when appropriate and feasible, we calculated the between-intervention effect sizes using the following effect measures: relative risk for common dichotomous outcomes (e.g., discharged from hospital on antihypertensive medication), Peto odds ratio for rare dichotomous outcomes (e.g., risk of seizure in preeclampsia with severe features),[36] mean difference (between group change) for continuous outcomes (e.g., duration of urinary catheterization). When a study had no events (outcomes) in one group, we calculated risk differences. Adjusted analyses were preferentially extracted over unadjusted (crude) data.

Where there were at least three studies reporting results for sufficiently similar outcomes, we conducted meta-analyses using random-effects models. For rare outcomes (e.g., occurrence of eclamptic seizure), we used fixed-effect models. We initially planned network meta-analyses, but the evidence base was insufficient to support this analysis.

2.8 Grading the Strength of Evidence for Major Comparisons and Outcomes

We graded the strength of the body of evidence (SoE) provided by RCTs and NRCSs as per the AHRQ Methods Guide on assessing SoE. For each analysis, we evaluated SoE for each prioritized outcome, which were deemed to be of greatest importance prior to compiling the evidence. We included single-arm studies in our SoE tables (evidence profiles), but did not assign a SoE rating (since these studies did not assess comparative effectiveness).

We determined the relative importance of the outcomes with input from Key Informants and the Technical Expert Panel. For each KQ, the prioritized outcomes included:

Key Question 1**:**

- Surveillance/reporting (to ascertain or track) of BP measurements, elevated BP, or new onset HDP
- Treatment initiation/discontinuation/adjustment
- BP control
- Maternal morbidity and mortality
- Satisfaction with postpartum care
- Quality of life
- Psychosocial distress (anxiety, depression)
- Length of postpartum hospital stay
- Unplanned healthcare utilization (re-hospitalization, obstetrical triage area or clinic visits, emergency department visits)
- Reduction (or generation) of health disparities

Key Question 2:

- Blood pressure control
- Maternal morbidity and mortality
- Satisfaction with care
- Quality of life
- Psychosocial distress (anxiety, depression)

- Length of postpartum hospital stay
- Unplanned healthcare utilization (re-hospitalization, obstetrical triage area or clinic visits, emergency department visits)
- Breastfeeding
- Reduction (or generation) of health disparities
- Severe adverse events
- Severe infant morbidities

Key Question 3:

- Maternal morbidity and mortality
- Infant morbidities
- Breastfeeding
- Satisfaction with care
- Quality of life
- Postpartum recovery
- Maternal-neonatal bonding
- Psychosocial distress (anxiety, depression)
- Reduction (or generation) of health disparities
- Magnesium-related toxicity
- Other clinically important adverse events
- Adverse drug interactions

For each SoE assessment, we considered the number of studies, their designs, limitations (i.e., risk of bias and overall methodological quality), the directness of the evidence to the KQs, the consistency of study results, the precision of any estimates of effect, the likelihood of reporting bias, other limitations, and the overall findings across studies. Based on these assessments, we assigned a SoE rating as being high, moderate, low, or insufficient to estimate an effect.

Outcomes with highly imprecise estimates (with 95% confidence intervals that extend beyond both 0.5 and 2.0 for categorical outcomes), highly inconsistent findings across studies (in terms of directions of effect), or with data from only one study were deemed to have insufficient evidence to allow for a conclusion (with the exception that a single particularly large, well-conducted, and generalizable single study could provide low SoE). This approach is consistent with the concept that for imprecise evidence "any estimate of effect is very uncertain," which is the definition of Very Low quality evidence per the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach.[37]

We summarize the data sources, study characteristics, and each SoE dimensional rating in evidence profile tables. These tables detail our reasoning for arriving at the overall SoE rating.

In accordance with AHRQ guidance for describing treatment effects,[38, 39] we have incorporated qualifying language regarding SoE when communicating conclusions (e.g., in Key Points sections of the text) as follows: "probably" for conclusion statements with Moderate SoE and "may" for conclusion statements with Low SoE. Conclusions with High SoE do not include any qualifiers.

3. Results

3.1 Literature Search Results

The literature search yielded 16,105 records after deduplication. Detailed search strategies, inclusion and exclusion criteria and a list of excluded studies (with reasons for their exclusion) are in Appendixes A and B. Appendix C Figure C-1 summarizes the results of the search and screening processes.

We retrieved and screened the full-text publications for 380 citations. Of these, 73 studies (reported in 80 articles or records) met our full inclusion criteria. The studies were published between 1982 and 2022 and included a total of 13,542 participants. Of these studies, 61 were randomized controlled trials (RCTs), 4 were nonrandomized comparative studies (NRCSs), and 8 (all pertaining to Key Question [KQ] 1) were single-arm studies.

For all 73 included studies, Appendix Tables C-1.1 to C-3.3.2 summarize the design, arm, and patient characteristics for each KQ. Appendix D Tables D-1.1 to D-1.3 summarize the risk of bias (RoB) for comparative studies for RCTs and NRCSs, and methodological quality for single arm studies. Detailed results are in Appendix E Tables E–1.2 to E–3.1. References for all appendixes are in Appendix F.

3.2 Description of Included Evidence

Tables describing study designs, groups, and sample characteristics; risk of bias; and details of outcome data are in the Appendix C, Results. We call attention to specific appendix table numbers in the relevant subsections.

3.3 KQ 1: What are the effectiveness, comparative effectiveness, and harms of home blood pressure monitoring/telemonitoring in postpartum individuals?

3.3.1 Key Points

- Home blood pressure (BP) monitoring (HBPM) of postpartum individuals with a prior hypertensive disorders of pregnancy (HDP) diagnosis:
    - Probably increases the likelihood of obtaining BP measurements during recommended time intervals (63% met reporting recommendations) (Moderate strength of evidence [SoE])
    - May increase the number of BP measurements obtained overall (Low SoE)
    - May not affect likelihood of initiation of BP treatment (Low SoE, no evidence of difference)
    - May reduce unplanned hypertension [HTN]-related hospital readmissions (Low SoE)
    - Probably decreases disparities between non-Blacks and Blacks in adherence to recommended BP surveillance (Moderate SoE)
    - Patients may be satisfied with care related to HBPM (Low SoE)

3.3.2 Evidence Identified

The evidence for KQ 1 includes 13 studies (in 18 articles) published between 2017 and 2022, that reported data from 3,3867 participants.[40-57] Eleven studies were conducted in the U.S., one was conducted in the U.K., and one in India. Of these, 3 were RCTs with a total of 510 participants, 2 were NRCSs (901 participants), and 8 were single-arm studies (2456 participants). The proportion of Black participants enrolled in the U.S studies ranged from 21 to 68 percent.

Table 3.1 provides the evidence profile for KQ 1. None of the studies reported on the prioritized outcome categories of quality of life and psychosocial distress. Risk of bias assessments for RCTs and NRCSs are in Appendix Tables D–1.1 and D–1.2, respectively. Methodologic quality assessment for single arm studies are in Appendix Table D–1.3. Results are in Appendix Tables E–1.2 and E–3.1

3.3.3 Detailed Findings for Key Question 1

3.3.3.1 HBPM Versus Usual Care

We found three studies (2 RCTs and 1 NRCS) that compared HBPM to usual care.

The Cairns 2018 RCT[41, 42] (moderate RoB) randomized 91 participants to HPBM with supervised self-management of antihypertensive medication versus usual care. The experimental group transmitted home BP readings via a smartphone app or text message. Patients were automatically sent instructions about medication titration that incorporated an individualized medication reduction schedule. Those allocated to usual care had their BP monitored by their community midwife and their antihypertensive medication adjusted by their general practitioner. ***BP treatment initiation, adjustment, discontinuation*** — Median treatment duration (the time until patients were able to cease antihypertensive medication treatment) was 29 days (interquartile range [IQR] 17 to 49) in the intervention group and 41 days (IQR 23 to 58) in the control group (adjusted mean difference [aMD] −12 days, 95% confidence interval [CI] −39 to 6). ***BP control*** — Participants who self-managed had significantly lower mean diastolic BP at 4 weeks (aMD −3.0 mm Hg, 95% CI −5.8 to −0.1), 6 weeks (aMD −5.8 mm Hg, 95% CI −9.1 to −2.5), 12 weeks (−4.3 mm Hg, 95% CI −7.7 to −0.8), and 26 weeks (aMD −4.5 mm Hg, 95% CI −8.1 to −0.8). The reductions in DBP persisted despite progressively fewer participants remaining on antihypertensive medications. ***Patient experience*** — Participants in the experimental group were significantly more likely to report higher scores (Likert scale 1 to 5) when asked "How much in control do you feel of managing your condition?" The intervention group mean at 6 months was 4.8 versus a mean of 3.9 in usual-care group (aMD 0.7, 95% CI 0.3 to 1.2).[42]

A follow-up study, Kitt 2021[43], included 63 (69%) participants from the original trial who were evaluated with 24-hour BP measurements. The follow-up study occurred 3 to 4 years postpartum. Those who had self-managed their BP continued to have significantly lower DBP than those in the usual-care group (aMD −7.4 mm Hg, 95% CI −10.7 to −4.2). This multicenter, UK-based RCT concluded that HBPM with self-titration of antihypertensive medications resulted in shorter total treatment duration. Notably, they found reductions in DBP persisted for 6 weeks during the trial and 3 to 4 years after the trial ended.

The Hirshberg 2018 RCT[47] (moderate RoB) randomized 206 individuals (68% Black) with pregnancy related HTN to HBPM via bidirectional Short Messaging Service (SMS) text messaging, or to office based follow up 4 to 6 days postpartum. Participants in the intervention group were automatically reminded to text their BP measurements twice daily for 2 weeks

postpartum. ***Surveillance/BP reporting*** — During the first 10 days postpartum, significantly more participants in the texting group than the usual-care group had a least one BP measurement: 95/103 (92.2%) versus 45/103 (43.7%); after adjusting for age, race, insurance, body mass index, parity, disease severity, mode of delivery and chronic HTN, the adjusted odds ratio (aOR) was higher for the texting group (58.2, 95% CI 6.2 to 208.1). ***BP treatment initiation*** — Outpatient antihypertensive medication(s) (hydrochlorothiazide, amlodipine or both, using a standardized algorithm) was initiated in 17/103 (16.5%) of the intervention group and 10 of the 45 (22.2%) of individuals in the office visit group (aOR 1.0, 95% CI 0.3 to 3.1). ***Unplanned healthcare utilization*** — There were no HTN-related readmissions (0/103) in the HBPM group and 4/103 (3.9%) in the usual-care group (risk difference [RD] −3.9%, 95% CI −7.6, − 0.15). ***Patient experience*** — Patients assigned to HBPM rated the importance of face-to-face communication significantly lower (on a 0 to 5 Likert scale) than those in the office visit group (P=0.02). ***Reduction of health disparities*** — Overall, 141/206 (68.4%) of study participants were Black. In the usual-care arm, 21/30 (70.0%) of non-Black participants returned for a BP visit compared to 24/73 (32.9%) of Black participants (RR 2.13; 95% CI 1.42 to 3.19). In the HBPM arm, 32/35 (91.4%) of non-Black participants reported at least one BP, compared to 63/68 (92.6%) of Black participants (RR 0.99, 95% CI 0.87 to 1.11). The ratio of relative rates (RRR) in the two arms (i.e., 0.99 in the HBPM arm divided by 2.13 in the office-based follow-up arm) was 0.46 (95% CI 0.30 to 0.71), which can be interpreted as an approximately 50 percent reduction in racial disparity due to the HBPM intervention.[48]

Hoppe 2020[49] performed a single center, prospective NRCS (high RoB, due to lack of random assignment and potential for confounding resulting from inclusion of 93/214 [43.4%] participants in the standard care arm who had declined to participate in the HBPM intervention). They allocated 428 patients (race not reported) matched by similar HDP diagnosis to remote BP monitoring or standard care, with clinic visits at 7 to 10 days and at 6 weeks postpartum. Participants in the HBPM arm were asked to submit BP readings for 6 weeks using a Bluetooth-enabled BP monitor. ***Surveillance/BP reporting*** — Significantly more participants in the telehealth arm, had BP measurements within 10 days of delivery, 202/214 (94.4%) compared to 129/214 (60.3%) in the usual-care arm (adjusted relative risk [aRR] 1.59, 95% CI 1.36 to 1.77). ***BP treatment*** — In the unadjusted analysis, significantly more participants in the telehealth arm, 57/214 (26.6%) versus 37/214 (17.3%), received antihypertensive medications (extended release [XR] nifedipine or labetalol or both), based on a standardized algorithm. (RR 1.54, 95% CI 1.06 to 2.23). However, after adjusting for delivery mode, insurance status, antihypertensive medication use at time of discharge, and duration of postpartum admission, this effect was no longer statistically significant (aRR 1.03, 95% CI 0.74 to 1.44). ***Unplanned healthcare utilization*** — The telehealth arm had significantly fewer HTN-related hospital readmissions, (aRR 0.12, 95% CI 0.01 to 0.96).

Based on these studies, there is moderate SoE that HBPM improves reporting of BP measurements (see Table 3.1). Two studies found a reduced likelihood of HTN-related hospital admissions with HBPM compared to usual care (low SoE). In the Hirshberg study, the proportion of Black individuals in the HBPM arm reporting BPs was similar to that in the non-Black participants. However, in the Black participants assigned to office based follow up were less likely than non-Black participants to attend scheduled follow up appointments. This study helped to support a low SoE that HBPM reduced racial health disparities.

3.3.3.2 Comparisons of HBPM Regimens

We found two studies (1 RCT and 1 retrospective pre-post NRCS) that provided a BP monitor at discharge and compared remote patient monitoring and audio-only telehealth respectively.

3.3.3.2.1 HBPM With Bluetooth-Enabled BP Monitor Versus HBPM With a Paper Log

A single center RCT[56] (NCT03728790) with partial results reported on ClinicalTrials.gov randomized 213 participants (moderate RoB, due to lack of blinding in participants and personnel and incomplete reporting). The remote patient monitoring group was given a Bluetooth-enabled BP cuff that transmitted BP measures from the monitor to a tablet. The usual-care group received a prescription for a BP cuff and were asked to keep a paper log. Participants were asked to monitor their BP twice a day for 14 days after discharge. ***Surveillance/BP reporting*** — Adherence with BP reporting (the percentage of the 28 requested BP measurements reported) was substantially higher in the intervention group (with a Bluetooth-enabled BP cuff) with a median of 61.1 percent adherence (range 0 to 92.3) compared with a median of 0 percent (range 0 to 100) in the usual-care group. In other words, more than half the usual-care group did not report any home BP measurements. ***BP treatment initiation, adjustment, discontinuation*** — Among patients discharged without antihypertensive therapy, patients in the intervention group were significantly more likely to have HTN diagnosed with subsequent prescription of antihypertensive medication, 24/60 (40%) in intervention versus 10/65 (15%) in usual-care group (RR 2.60, 95% CI 1.36 to 4.98). Patients in the intervention group were more likely to be referred to a primary care physician for continued BP management, 38/101 (37.6%) versus 31/112 (27.7%) (RR 1.36, 95% CI 0.92 to 2.01). ***Unplanned healthcare utilization*** — More patients in the intervention group (25/101; 24.8%) had an emergency department visit than controls (17/112; 15.2%) (RR 1.63, 95% CI 0.94 to 2.84). Patients in the intervention group were readmitted at higher rates: 13/101 (12.9%) versus 7/112 (6.3%) (RR 2.06, 95% 0.86 to 4.96). ***Maternal morbidity and mortality*** — A larger percentage of preeclampsia related complications were detected in the intervention group: 9/101 (8.9%) versus 4/112 (3.6%) (RR 2.50, 95% CI 0.79 to 7.85). There were no maternal deaths in either group.

A single center retrospective NRCS (Khosla 2022[54]) evaluated 473 patients (moderate RoB) with HDP discharged during two time periods (76.3% non-Hispanic Black). All patients were managed according to the Systematic Treatment And Management of PostPartum Hypertension (STAMPP HTN) quality improvement bundle, given home BP cuffs at discharge and instructed to take their BP daily and record BP readings on a paper log. During the period from December 2019 to February 2020, telehealth was not used for postpartum HTN (PPHTN) follow-up visits (scheduled 7 to 10 days post discharge). From March 2020 to June 2020, 98.0 percent of PPHTN follow up was done via audio-only telehealth. ***Surveillance/BP reporting*** — During the pre-telehealth period, adherence with at least one PPHTN visit was 48.5% for non-Hispanic Black patients and 73.1% for non-Hispanic White patients (racial gap 24.6%). In the post-telehealth period, PPHTN visit adherence for non-Hispanic Black patients was 76.3%, and 76.7% for non-Hispanic White patients (racial gap 0.4%). In the multivariable model, the overall improvement in adherence with PPHTN visits associated with telehealth ($P < 0.0001$) was explained by increased adherence in non-Hispanic Black patients. ***Unplanned healthcare utilization*** — postpartum readmission rates within 6 weeks of delivery were similar between the pre- and post-telehealth periods overall (17.7% versus 17.4% respectively) and when stratified by race.

Both studies evaluated patients discharged with a home BP monitor. Participants who automatically transmitted their home BP readings versus those who were asked to keep a paper log had higher adherence to BP surveillance and were diagnosed and treated for HTN at higher rates. A transition to audio-only telehealth (after discharge with a home BP monitor) during COVID-19 pandemic reduced racial disparities in postpartum follow up among non-Hispanic Black patients, supporting the low SoE conclusion that remote HBPM via text or an audio-only telehealth encounter may reduce racial disparities in follow up.

3.3.3.3 HBPM—Single Arm Studies

Eight studies offered HBPM to all individuals who met specific inclusion criteria.[40, 44-46, 52, 53, 55, 57] Four of the studies were self-described as feasibility studies that assessed the practicality of HBPM in a small group of participants.[40, 44, 52, 55] Three of the studies evaluated outcomes in patients after implementation of HBPM in routine clinical practice.[46, 53, 57] The eighth study was a quality improvement study attempted to contact all postpartum patients by phone (most of whom had been provided with a home BP cuff) to obtain a BP measurement 1 week after discharge.[45]

3.3.3.3.1 Feasibility Studies

Rhoads 2017[55] reported an early feasibility study (52.1% participation rate) enrolled 50 participants who had been diagnosed with preeclampsia and offered Bluetooth enabled m-health devices that included a BP cuff, scale, and pulse oximeter. These devices transmitted results to a cloud-based portal that was monitored by a nurse call center. Only 25 individuals chose to use the devices. Users and nonusers completed a baseline survey (each item was scored on a Likert scale from 1=strongly disagree to 7=strongly agree, then summed). Nonusers expressed less agreement (18.5) versus users (19.9; P=0.002) when asked to respond to the following questions regarding facilitating conditions 1) "I have the resources at home necessary to use the m-health system", 2) "I have the knowledge necessary to use the m-health system at home", and 3) "there is a specific person or people available at home to assist me if I have difficulties with the m-health system". Nonusers reported a significantly higher perceived barriers score (10.2 vs. 6.9, P=0.005), when asked to reflect on the following questions: 1) "Using the m-health system would take too much time", 2) "I don't know how to go about using the m-health system", 3) "Using the m-health system would compromise my health privacy", and 4) "Using the m-health system daily would be hard for me to do". Reported barriers to using the m-health devices included difficulty connecting to the wireless gateway, particularly for rural users, and limited number of available minutes on their cellular phones.

The Hoppe 2019 feasibility study[52] (45% participation rate) enrolled 55 individuals with any HTN-related diagnosis during pregnancy. Participants received a tablet that synced results from a BP cuff, weight scale and oximeter via Bluetooth at discharge, and were asked to transmit their measurements each day beginning on postpartum Day 1 and continuing for 6 weeks. ***Surveillance/BP reporting*** — Participants transmitted a mean of 33.4 BP measurements over a 6-week study period. ***Patient experience*** — Overall, 39/45 (87%) of participants reported they were "very" or "extremely" satisfied with remote monitoring.

The Burgess 2021 feasibility study[40] (unclear participation rate) followed 54 women who were provided with a BP cuff and agreed to upload BP readings twice daily for the first postpartum week to an electronic health record portal (EPIC MyChart) via a smartphone app. ***Surveillance/BP reporting*** — Among participants, 37/54 (69%) submitted at least one BP measurement.

The Deshpande 2022[44] feasibility study (unclear participation rate) approached 156 individuals with HDP, of whom 63 patients and their birth companion agreed to participate. Prior to discharge on postpartum day 5, the birth companion received training 90 minutes of training on use of the digital BP apparatus, including supervised BP measurement in 5 women, and were instructed to obtain BPs on days 10, 15, 30, 45 and 60 or earlier for any warning signs or symptoms. BP measurements were sent to the obstetrician via the WhatsApp messaging service. BP measurements were used to titrate and discontinue antihypertensive medications. ***Surveillance/BP reporting*** — Most participants (60/63, 95.2%) obtained BPs through day 60. ***Patient experience*** — Overall, 50/60 (83.3%) reported that they were very satisfied or satisfied with HBPM by teleconsultation. None reported that they were either very unsatisfied or unsatisfied.

The feasibility studies had relatively low (or unclear) participation rates and used varied HBPM implementations. They provide supporting evidence that HBPM improves reporting of BP measurements (see Table 3.1). At least 83.3 to 87 percent of patients who received HBPM were satisfied with their postpartum care (Table 3.1).

3.3.3.3.2 Implementation Studies

Hauspurg 2019[46] (unclear participation rate) reported implementation of a quality improvement project that designed nursing call center–driven BP management and treatment algorithms. The study enrolled 409 participants with HDP in HBPM, using a text messaging-enabled smartphone program until 6 weeks postpartum**.** ***Surveillance/BP reporting*** — based on the protocol, 177/409 (43%) did not require an in-office BP check at 1-week. **Treatment initiation and adjustment** — 168/409 (41%) of participants had antihypertensive medications initiated or titrated via the program. **Program engagement and retention** — Most patients continued with the HBPM program through the study: 94.9% at 2 weeks, 83.1% at 3 weeks, 73.8% at 4 weeks and 67.5 for ≥5 weeks. ***Patient experience*** — 235/250 (94% of survey respondents) reported they were satisfied with the program.

Two studies evaluated implementation of the *Heart Safe Motherhood* texting program platform.

Triebwasser 2020[57] (unclear participation rate) implemented the *Heart Safe Motherhood* program in a clinical cohort of 333 (40.8% Black) patients who had an HDP diagnosis at the time of their delivery admission. Patients received a validated BP cuff and were instructed on proper use prior to discharge. When elevated BPs were reported via text, patients were managed based on a clinical algorithm for escalation and initiation of antihypertensive medications that included amlodipine or extended release nifedipine and hydrochlorothiazide, without additional outpatient visits, if deemed appropriate by their provider. ***Surveillance/BP reporting*** — 318/333 (95.5%) women texted at least one BP measurement during the 10-day monitoring period. ***Reduction of health disparities*** — BP ascertainment was similar by race (96.5% Black vs. 94.1% non-Black; P = 0.31). Participants texted a mean of 15 BP measurements over a 10-day period. The American College of Gynecologists (ACOG) recommendation for a BP measurement on postpartum day 3 or 4 and again between days 7 to10 was achieved by 282/333 (84.7%) of all participants.

Janssen 2021[53] (unclear participation rate) described implementation of the *Heart Safe Motherhood* platform in 199 patients enrolled in three U.S. academic medical centers. ***Surveillance/BP reporting*** — Almost all participants 192/199 (96.5%) submitted at least one BP measurement via text message during the 10 days after hospital discharge. For individuals with

HDP, ACOG recommends evaluation of BP no later than 7 to 10 days postpartum and that those with severe hypertension should be seen within 72 hours.[58] The ACOG recommendation to submit BP measures during the 3 to 4 day and the 7 to 10 day timeframes was met by 126/199 (63.3%) of participants. Based on the protocol, 177 (43%) of participants did not require a previously scheduled in-office BP check at 1-week postpartum. ***Treatment initiation and adjustment*** — Antihypertensive treatment was initiated or titrated based on the home monitoring in 168 of 409 (41.1%) participants. ***Patient experience*** — Survey responses of 4 or 5 on a Likert scale were considered to be a positive experience. Of the 99 participants who responded to a patient experience survey, 91/99 (91.9%) would recommend the program to others, 92/99 (92.9%) felt text messages were easy to receive, and 92/99 (92.9%) felt that the program helped them pay attention to their BP.

Single-group implementation studies had unclear participation rates, but found high levels of adherence to BP surveillance, successful initiation of antihypertensive treatment, satisfaction with HBPM by patients, and, in one study, no disparity between Blacks and non-Blacks in postpartum BP ascertainment.[57] These studies provide supporting evidence for the conclusion that HBPM improves reporting of BP measurements, and that HBPM may help reduce racial disparities in BP surveillance (Table 3.1).

3.3.3.3.3 Quality Improvement Studies

Hacker 2022[45] (high nonresponse/refusal rate) reported a quality improvement initiative that contacted individuals who had received some portion of their prenatal care virtually and were provided an automatic BP cuff for home monitoring. All patients discharged between July 2020 and June 2021 (during the COVID-19 pandemic) were contacted 1 week after discharge by a nurse or patient educator. After excluding those with previously diagnosed HDP, 1192 individuals (15% Black) had access to a BP cuff and were willing to provide at least one BP measurement. ***Surveillance/BP reporting*** — Among enrolled participants, 222 (19%) had an initial elevated BP based on home monitoring. Seventeen participants (7.7% of those with HTN, 1.4% of total sample) were referred to the emergency department for evaluation of a severe range BP (≥160/110 mmHg or ≥140/90 mmHg with symptoms, including headache, vision changes, right upper quadrant pain, shortness of breath, or chest pain). Eight participants (3.6% of those with HTN, 0.7% of total sample without a prior diagnosis of preeclampsia) were diagnosed with *de novo* severe postpartum preeclampsia. ***Health disparities*** — Patients with newly elevated BP were more likely to be non-Hispanic Black and were more likely to have a higher early pregnancy body mass index. This single-group study conducted during the COVID-19 pandemic described successful diagnosis of *de novo* postpartum HDP based on HBPM. It did not provide sufficient evidence for a graded conclusion.

3. Results

Table 3.1. Evidence profile for postpartum home blood pressure measurement versus usual care (clinic monitoring) (Key Question 1)[a]

Outcome	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall SoE	Conclusion Statements
Surveillance/BP reporting	1 RCT[47], 1 NRCS[49] (624)	Moderate	Consistent	Precise	Direct	None	Moderate	*HBPM improves reporting of BP measurements* **RR 2.11 (1.68, 2.65)[b] aRR 1.59 (1.36, 1.77)**
	5 single-arm[40, 44, 52, 53, 57] (807)	N/A	Consistent	Precise	Indirect[c]	Noncomparative	N/A	*Most patients report BP measurements with HBPM* (e.g., 63% to 85% met ACOG recommendations for BP reporting)
Treatment initiation / discontinuation / adjustment and BP control	3 RCTs[41, 43, 47, 49] (713)	Moderate	Consistent	Precise	Direct	None	Low	*No evidence of difference in initiation* aOR 1.0 (0.3, 3.1) aRR 1.03 (0.74, 1.44) Other outcomes sparse (insufficient)
Maternal morbidity and mortality	0	.	.	.	.	.	.	No evidence
Satisfaction with postpartum care	2 RCTs[42, 47] (274)	Moderate	N/A	Precise	Indirect[d]	Disparate measures	Insufficient	No conclusion
	4 single arm[44, 46, 52, 53] (719)	N/A	Consistent	Precise	Direct	Noncomparative	N/A	87% very/extremely satisfied 94% satisfied 92% would recommend 83% satisfied/very satisfied
Quality of life	0	.	.	.	.	.	.	No evidence
Psychosocial distress (anxiety, depression)	0	.	.	.	.	.	.	No evidence
Length of postpartum hospital stay	0	.	.	.	.	.	.	No evidence
Unplanned healthcare utilization	1 RCT[47], 1 NRCS[49] (634)	Moderate	Consistent	Precise	Direct	Few events	Low	*HBPM reduced HTN-related admissions* **RD −3.5% (−6.9, −0.1) aRR 0.12 (0.01, 0.96)**

3. Results

Outcome	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall SoE	Conclusion Statements
Health disparities	1 RCT[47] (206) 1 NRCS (473)[54]	Moderate	Consistent	Precise	Direct	Sparse, but large effects	Moderate	*HBPM reduced racial disparity* RCT: Postpartum BP follow up of HBPM via text (Black vs. non-Black): **RRR[e] 0.51 (0.33, 0.78)** NRCS: Reduction of racial gap from 25% pre-audio-only-telehealth to 0.4% in post-implementation period
	1 Single arm[57] (333)	N/A	N/A	Precise	Direct	Noncomparative	N/A	*BP ascertainment similar by race (~95%)*

Abbreviations: . = no information, aRR = adjusted relative risk, ACOG = American College of Obstetricians and Gynecologists, aOR = adjusted odds ratio, aRR = adjusted relative risk, BP = blood pressure, ED = emergency department, HBPM = home blood pressure monitoring, HTN = hypertension, N/A = not applicable (single study), NRCS = nonrandomized comparative study, RCT = randomized controlled trial, RD = risk difference, RR = relative risk, RRR = ratio of relative risks, SoE = strength of evidence. Statistically significant results are in bold font.

[a] Evidence profile omits the one unpublished study (NCT03728790) that compared different HBPM methods (Bluetooth vs. paper log).
[b] Study reported OR 15.31 (95% CI 6.74 to 34.75) and adjusted OR 58.2 (95% CI 6.2 to 208). Converted to risk ratio to make more comparable to other study and to provide a value that is more consistent with the doubling of percent adherence from 44% to 92%.
[c] No comparison with usual care (clinic measurement).
[d] Unvalidated, study-specific measures
[e] Reduction in racial disparity due to the intervention.

3.4 KQ 2: What are the effectiveness, comparative effectiveness, and harms of pharmacological treatments for hypertensive disorders of pregnancy in postpartum individuals?

3.4.1 Key Points

- Treatment of postpartum patients with preclampsia (or gestational HTN) with or without severe features with the oral diuretic furosemide (compared with placebo) may shorten the duration of persistent postpartum HTN (low SoE)
- There was insufficient, or no, comparative evidence for the benefits and harms other antihypertensive medications

3.4.2 Evidence Identified

Seventeen RCTs (reported in 18 articles), published between 1982 and 2021, evaluated the effects and comparative effects of various pharmacological treatments in 1,765 participants with postpartum HTN. [59-76] Eight studies were conducted in the U.S., one in the U.K., two in Mexico and one study each in Brazil, India, Iran, Pakistan, Panama, and Turkey. Risk of bias in RCTs was rated as low in four, moderate in eight, and high in four studies.

Among the 17 studies, five RCTs evaluated treatment of acute, severe HTN in hospitalized individuals with intravenous (IV) or oral medications.[60, 62, 65-67, 73] Five RCTs evaluated the effectiveness of oral diuretics for treatment of early postpartum HTN.[61, 63, 69, 72, 74] Five RCTs compared oral medications used for outpatient treatment of persistent postpartum HTN.[59, 64, 70, 71, 76] Two RCTs reported evidence regarding potential end-organ protective effects of losartan, an angiotensin II receptor blocker (renal protection), and enalapril, an angiotensin II converting enzyme inhibitor (cardioprotection).[68, 75]

Table 3.2 provides the evidence profile for KQ 2. None of the studies reported the outcomes pertinent to the following prioritized outcome categories: satisfaction with care, quality of life, psychosocial distress (anxiety or depression), reduction (or generation) of health disparities. See Appendix Table E–2.1 to E–2.2 for detailed results.

3.4.3 Detailed Findings for Key Question 2

3.4.3.1 Early Inpatient Treatment of Acute Severe Postpartum Hypertension

Five RCTs compared IV or oral regimens for treatment of acute severe HTN during postpartum hospitalization.

3.4.3.1.1 Parenteral Medications for Acute Severe Postpartum Hypertension

Two studies evaluated parenteral medications. The Griffis 1989 RCT[65] (moderate RoB, due to lack of blinding and unclear reporting) enrolled 26 patients with preeclampsia and compared IV methyldopa with intramuscular (IM) hydralazine enrolled in the first postpartum day. ***BP control*** — By 6 hours after beginning treatment, mean arterial pressure (MAP) was significantly lower in the IM hydralazine (mean difference [MD] −8.0 mmHg, P=0.006) group and remained lower at 12 hours (MD −8.1 mmHg, P=0.07).

The Vigil-De Gracia 2007 RCT[73] (low RoB) randomized 82 individuals with systolic BP (SBP) ≥160 mmHg or DBP ≥100 mmHg to treatment with IV hydralazine or IV labetalol. ***BP control*** — Effective BP control with one to two doses was similar in both groups: 35/42 (83.3%) of patients in the hydralazine arm and 35/40 (87.5%) patients who received labetalol (RR 0.95, 95% CI 0.80 to 1.14).

A small study comparing IM hydralazine with IV methyldopa found larger decreases in MAP in the hydralazine arm.[65] A single study comparing IV hydralazine with IV labetalol found similar proportions of patients who achieved BP control.[73] The single studies for each medication comparison did not provide sufficient evidence for a graded conclusions.

3.4.3.1.2 Oral Medications for Acute Severe Postpartum Hypertension

Three studies evaluated oral medications.

The Barton 1990 RCT[62] (high RoB, due unclear reporting of most items) compared immediate release nifedipine versus placebo in 31 participants with preeclampsia with severe features. ***BP control*** — The nifedipine group had significantly lower MAP than the control group 24 hours following delivery (MD −6.3 mmHg, 95% CI −12.2 to −0.3).

The Arias-Hernández 2022 RCT[60] (low RoB) randomized 42 patients with preeclampsia with severe features during the first 24 hours after delivery to immediate release diltiazem or immediate release nifedipine. ***BP control*** — After 6 hours of treatment, patients in the diltiazem group had significantly lower SBP (MD −14.5, 95% CI −20.5 to −8.5). A repeated measures analysis of variance (ANOVA) showed that both drugs resulted in lower BP, with greater reductions in the diltiazem arm that were sustained for 48 hours (P<0.001). No patients in the diltiazem arm 0/21 versus 7/21 (33%) in the nifedipine arm experienced hypertensive episodes requiring rescue therapy with hydralazine (RD −33%, 95% CI −53 to −13; RR 0.07, 95% CI 0.004 to 1.10, P=0.06). ***Adverse events*** — Patients' heart rates were higher in the nifedipine arm from 12 to 48 hours (P<0.001). Hypotensive episodes were less common in the diltiazem arm 3/21 (14.3%) compared to 15/21 (71.4%) in the nifedipine arm (RR 0.20, 95% CI 0.07 to 0.59).

The Noronha Neto 2017 RCT[66] (low RoB) enrolled 90 postpartum individuals with SBP ≥180 or DBP ≥110 who had required magnesium sulfate ($MgSO_4$)and were admitted to an obstetrical intensive care unit. Patients were randomized to treatment with oral clonidine or captopril. ***BP control*** — Repeated measures ANOVA showed no significant differences between treatment groups with respect to mean daily SBP (P=0.20) or DBP (P=0.67). ***Adverse events*** — Adverse reactions (e.g., cough, rash, fever, nausea) occurred in 8/43 (18.6%) individuals in the clonidine arm and 13/45 (28.8%) in the captopril arm (RR 0.64, 95% CI 0.29 to 1.40).

Across three RCTs of postpartum patients with acute severe HTN, immediate-release nifedipine lowered BP more than placebo, and diltiazem was more effective than immediate-release nifedipine to lower BP with fewer adverse events. Blood pressure and adverse events were similar in oral clonidine and captopril arms. However, the single studies for each medication comparison did not provide sufficient evidence for graded conclusions.

3.4.3.2 Oral Diuretics for Treatment of Postpartum Hypertension

Five RCTs, two with low RoB, two with moderate RoB, and one with high RoB, evaluated the effect of oral diuretics.

The Dabaghi 2019 RCT[63] (high RoB, due to lack of blinding and unclear reporting) enrolled 90 patients with preeclampsia with severe features. Participants were randomized to daily oral furosemide for 5 days versus no furosemide. Participants received unspecified antihypertensive

medications for SBP ≥160 mmHg or DBP ≥110 mmHg. ***BP control*** — On postpartum day 3, mean SBP was 127.9 mmHg in the treatment group and 130.1 mmHg in the control group (P=0.36). Mean DBP in the treatment group was 82.8 with furosemide versus 82.6 mmHg in the control group (P=0.86). Overall, 26.7 percent of participants in the intervention arm required treatment with antihypertensive medications prior to discharge compared to 33.3 percent in the control arm (P=0.64). ***Length of postpartum hospital stay*** — Hospital length of stay was similar (5.04 vs. 5.07 days, P=0.93).

The Lopes Perdigao 2021 RCT[69] (low RoB) enrolled 384 postpartum participants with preeclampsia (or gestational HTN) with or without severe features. All participants were enrolled the *HeartSafe Motherhood* HBPM program. Patients were randomized to receive oral furosemide 20 mg daily for 5 days or placebo. Overall, 32 percent had preeclampsia with severe features and 68 percent had non-severe HDP. ***BP control*** — Adjusted for delivery mode (i.e., cesarean vs. vaginal), fewer individuals had persistent HTN by postpartum day 7 in the furosemide arm, 10/192 (5.2%) versus 23/192 (12%) in the placebo arm (aRR 0.40, 95% CI 0.20 to 0.81). ***Heterogeneity of effectiveness by HDP severity*** — When stratified by HDP severity, the aRR of persistent HTN was significantly lower in the non-severe subgroup (aRR 0.26, 95% CI 0.10 to 0.67). In the severe HDP subgroup, the aRR estimate was nonsignificant (aRR 0.86, 95% CI 0.27 to 2.79). However, by our calculation, there was no significant difference between the aRRs (relative aRR 0.59, 95% CI 0.31 to 1.14). The adjusted hazard ratios (aHR) for days to resolution of HTN were not significantly different between treatment groups (aHR >1 represents faster time to resolution) overall (aHR 1.20, 95% CI 0.95 to 1.51). In the non-severe group, HTN resolved significantly more quickly in the furosemide arm (aHR 1.62, 95% CI 1.22 to 2.15), but not in the severe group (aHR 0.77, 95% CI 0.52 to 1.15). By our calculation, there was a significant difference between groups (relative aHR 1.38, 95% CI 1.12 to 1.71). Postpartum BP trajectories peaked earlier (days 3 to 4) in the severe HDP group compared to the non-severe group (days 6 to 8). Overall, 63/192 (33%) in the furosemide arm and 62/192 (32%) in the placebo arm required medication for HTN, either prior to or after discharge (RR 1.02, 95% CI 0.76 to 1.36). ***Unplanned healthcare utilization*** — HTN-related emergency department visits and/or readmissions occurred in similar percentages in both groups: 9/192 (5%) in the furosemide arm and 16/192 (8%) in the placebo arm (aRR 0.55, 95% CI 0.25 to 1.21). ***Breastfeeding outcomes*** — Self reported breastfeeding issues including decreased breast milk production were reported in 4/133 (3%) of breastfeeding mothers in the furosemide arm and 9/150 (6%) in the placebo arm (RR 0.46, 95% CI 0.15 to 1.47).

The Ascarelli 2005 RCT[61] (moderate RoB, due to lack of blinding) enrolled 264 individuals with preeclampsia, of whom 70 (26.5%) had preeclampsia with severe features. The experimental group received once daily furosemide with oral potassium supplementation for 5 days, and the control group received no furosemide (or potassium). Analyses were reported by subgroup. ***BP control*** — On postpartum day 2, the participants with preeclampsia with severe features treated with furosemide had lower mean SBP (142 mmHg) compared to (153 mmHg) in the control group (P <0.004). At discharge, significantly fewer patients with severe preeclampsia in the furosemide group (2/35, 6%) required additional antihypertensive medication than in the control group (9/35, 26%; RR 0.22, 95% CI 0.05 to 0.96).

The Veena 2017 RCT[72] (low RoB) enrolled 108 participants with preeclampsia with severe features (defined in this study as BP ≥150/100 mm/Hg or DBP ≥100 mmHg). All patients were treated with immediate release nifedipine. Participants were randomly allocated to receive daily furosemide 20 mg for 3 days, versus no routine diuretic. ***BP control*** — There were no between-

group differences (P values only were reported) in the mean SBP (P=0.46), DBP (P=0.64) or MAP (P=0.38). Significantly fewer participants in the furosemide group (4/50, 8%) than the control group (13/50, 26%) were treated with atenolol for persistent HTN (RR 0.31, 95% CI 0.11 to 0.88). By discharge, 13/50 (26%) in the furosemide group and 7/50 (14%) in the control group were receiving antihypertensive medication, which was nonsignificant (RR 1.86, 95% CI 0.81 to 4.25).

The Viteri 2018 RCT[74] (moderate RoB, due to incomplete outcome data) enrolled 118 participants with preeclampsia. Overall, 30/118 (48%) had preeclampsia with severe features. Patients were randomized to receive once daily oral torsemide or placebo for 5 days. Overall, 69/118 (58.5%) participants missed a follow up visit scheduled 7 to 10 days postpartum. ***BP control*** — Persistent HTN was similar by 7 to 10 days in the two groups: 13/34 (38%) in the torsemide group and 10/28 (36%) in the placebo group (RR 1.1, 95% CI 0.6 to 2.1).

In individuals with preeclampsia, treatment with furosemide may reduce the risk of persistent HTN by postpartum day 7 (low SoE, see Table 3.2). One study suggested that severity of preeclampsia may be an effect modifier, with greater effects in individuals with preeclampsia *without* severe features. The five studies reported heterogeneous outcomes, precluding meta-analysis.

3.4.3.3 Antihypertensive (Nondiuretic) Medications for Treatment of Postpartum Hypertension

Five RCTs evaluated the comparative effectiveness of other (nondiuretic) medications for persistent postpartum hypertension. Of these, three had moderate RoB and two had high RoB.

The Fidler 1982 RCT[64] (high RoB, due to highly unclear reporting) enrolled 80 participants with postpartum diastolic HTN (DBP between 95 and 104 mmHg). Patients received either oral timolol or methyldopa 3 times a day. Doses of each agent were escalated to a target DBP of ≤95 mmHg. ***BP control*** — The comparison of treatment failure (failure to achieve target DBP) was imprecise. It occurred in 3/40 (7.5%) in the timolol arm and 1/40 (2.5%) of patients in the methyldopa arm (RR 3.0, 95% CI 0.33 to 27.63).

The Sayin 2005 RCT[70] (high RoB, due to unclear reporting) enrolled 83 participants with HDP with persistent HTN (BP >160/110 mmHg after the first postpartum day). The study randomized participants to immediate release nifedipine versus oral alpha-methyldopa. ***BP control*** — In the nifedipine arm, 13/42 (30.9%) required additional antihypertensive medication versus 20/41 (48.8%) in the alpha-methyldopa arm (RR 0.63, 95% CI 0.36 to 1.10).

Three studies evaluated the effects of treatment with labetalol compared to long acting nifedipine.

The Ainuddin 2019 RCT[59] (moderate RoB, due to unclear reporting) randomized 123 patients with persistent postpartum HTN (defined as SBP ≥150 mmHg or DBP ≥100 mmHg). ***BP control*** — Participants assigned to the labetalol arm required a mean of 35.6 hours for BP control versus 30.4 hours in the nifedipine arm (MD −5.2 hours, P=0.041). Significantly fewer individuals in the labetalol arm 38/62 (61%) versus 54/62 (87%) in the long-acting nifedipine arm achieved sustained BP control after 72 hours (RR 0.70, 95% CI 0.56 to 0.88). ***Adverse events*** — One person in the labetalol group had bronchospasm. The potential side effects of headache and palpitations were less frequently reported in the labetalol versus the nifedipine group: headache 6.4% versus 12.9% and palpitations 1.6% versus 9.6%.

The Sharma 2017[8] RCT (moderate RoB, due to lack of blinding) randomized 50 individuals to oral labetalol or extended release nifedipine. ***BP control*** — The mean time to achieve BP

control was 37.6 hours in the labetalol arm versus 38.2 hours in the nifedipine arm (P=0.51). A larger proportion of participants in the labetalol arm (16/21, 76.2%) achieved BP control with the starting dose than in the nifedipine arm (10/22, 45.4%; RR 1.68, 95% CI 1.00 to 2.81). ***Adverse events*** — Headache was the most commonly reported side effect and occurred in 6/25 (24%) of patients in the nifedipine arm versus 0/25 in the labetalol arm (RD −24.0%, 95% CI −40.7 to −7.3).

A single center RCT (moderate RoB)[77] with partial results reported on ClinicalTrials.gov (NCT04236258) randomized 94 postpartum patients with HTN to enalapril or ER nifedipine as their starting antihypertensive medication. ***BP control*** — The time to sustained BP control (defined as no need for changes to antihypertensive regimen for at least 24 hours) was 1.9 days in the enalapril group versus 0.7 days in the nifedipine group (MD 1.2 days, 95% CI 0.2 to 2.2). In the enalapril group, significantly more patients, 16/47 (34%), needed an additional antihypertensive medication(s) compared to 6/47 (12.8%) in the nifedipine group (RR 2.67, 95% CI 1.14 to 6.22). ***Length of postpartum hospital stay*** — in the enalapril group 17/47 (36.2%) had a postpartum hospitalization "beyond the normal length of stay" versus 13/47 (27.7%) in the nifedipine group (RR 1.31, 95% CI 0.72 to 2.38). ***Unplanned healthcare utilization: rehospitalization*** — in the enalapril group 4/47 (8.5%) were readmitted versus 3/47 (6.4%) in the nifedipine group (RR 1.33, 95% CI 0.32 to 5.64). ***Unplanned healthcare utilization: obstetrical triage area or clinic visits*** — in the enalapril group 34/47 (72.3%) had at least one unscheduled visit to the obstetrical triage are or clinic versus 32/47 (68.1%) in the nifedipine group (RR 1.06, 95% CI 0.82 to 1.38).

The comparisons between timolol or nifedipine and methyldopa/alpha-methyldopa are highly imprecise. Two studies suggested that nifedipine with dose escalation might more effectively achieve sustained BP control than labetalol, albeit with a higher proportion patients reporting headache. One study concluded that patients treated with enalapril versus nifedipine were more likely to require at least one additional antihypertensive medication.

3.4.3.4 Treatments Targeting End Organ Protection

Two RCTs, one with low RoB and the other with moderate RoB, enrolled patients at higher risk for end organ injury (due to preterm eclampsia or requiring intensive care unit treatment and multiple antihypertensive medications).

The Ormesher 2020 RCT[68] (low RoB) randomized 60 postpartum individuals diagnosed with preterm preeclampsia and evaluated potential cardioprotective effect of enalapril in addition to treatments recommended by the UK National Institute for Health and Care Excellence (NICE) for postpartum HTN. The intervention group received titrated enalapril (5 mg once daily for 1 week, then 10 mg for 2 weeks, then 20 mg maintenance dose). The control group received placebo. ***End-organ protection*** (heart) — At baseline, a large proportion of participants had abnormal echocardiographic findings: 52 of 59 (88%) had diastolic dysfunction, 14 of 59 (24%) had systolic dysfunction, and 47 of 59 (68%) had concentric remodeling or hypertrophy (relative wall thickness >0.42). After 6 months of treatment, participants treated with enalapril had improvement in some echocardiographic measurements at 6 months compared to placebo, consistent with improved diastolic function: Doppler E/E‘ aMD −1.07 (95% CI −2.08 to −0.06); left ventricular remodeling (relative wall thickness >0.42; aOR 0.26 (95% CI 0.07 to 1.01, P=0.01); left ventricular mass index aMD −9.23 (95% CI −17.75 to −0.71, P=0.03). ***BP control*** — At 6 months, BPs were generally lower in the enalapril group: SBP MD −5.8 (95% CI −14 to

2.4), DBP MD −7.3 (95% CI −14.2 to −0.4 calculated, P=0.04 reported), and MAP MD –6.8 (95% CI −13.9 to 0.4).

The Vázquez Rodríguez 2020 RCT[75] (moderate RoB, due to lack of blinding and unclear reporting) enrolled 49 postpartum individuals under treatment in the intensive care unit for preeclampsia with severe features who were treated with a three-drug regimen of methyldopa, hydralazine, and metoprolol. The experimental group also received losartan. As HTN resolved, medications were gradually suspended in the following order, first methyldopa, then hydralazine, then metoprolol. In the experimental group, losartan was continued at 40 mg per day for 3 months. ***End-organ protection*** (kidney) — In the experimental group, the final (postpartum day 90) 24-hour urine protein excretion was significantly lower (benefit) in the losartan group than in the experimental group (MD −0.5 g/24 h, 95% CI −0.56 to −0.44).

These studies found that early treatment of postpartum HTN with renin angiotensin system inhibitors improved longer-term BP control and end organ function. However, the single studies for each medication comparison and outcome did not provide sufficient evidence for graded conclusions.

3. Results

Table 3.2. Evidence profile for pharmaceutical treatment of postpartum hypertensive disorders of pregnancy[a]

Outcome	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall Strength of Evidence	Conclusion Statements
Blood pressure control: Various in patients with acute severe hypertension	5[41, 43, 47, 49] (26-90)	Low (3), Moderate (1), High (1)	N/A	Precise	Direct	Sparse per drug and comparison	Insufficient (per drug or comparison)	*No conclusions*
Blood pressure control: Diuretics in patients with preeclampsia (or gestational HTN) with or without severe features	5[61, 63, 69, 72, 74] (964)	Low (2) Moderate (2) High (1)	Inconsistent	Precise	Direct	Variable comparisons	Low	*BP control: (variable) Furosemide may reduce persistent HTN* **aRR 0.40 (0.20, 0.81) RR 0.31 (0.11, 0.88)**
Blood pressure control: Oral labetalol vs. XR nifedipine	2[59, 71] (173)	Moderate	Inconsistent	Precise	Direct	None	Insufficient	*Time to BP control: Unclear (variable) Sustained BP control: Unclear (inconsistent)*
Blood pressure control: Oral, other drugs	3[64, 68, 70] (80-84)	Low (1), Moderate (1), High (1)	N/A	Precise	Direct	Sparse per drug and comparison	Insufficient (per drug or comparison)	*No conclusions*
Maternal morbidity and mortality	2 (49-84)	Low (1), Moderate (1)	N/A	Precise	Indirect[b]	Sparse per drug	Insufficient (per drug)	*No conclusions*
Satisfaction with care	0	.	.	.	.	.	.	*No evidence*
Quality of life	0	.	.	.	.	.	.	*No evidence*
Psychosocial distress	0	.	.	.	.	.	.	*No evidence*
Length of postpartum hospital stay	1[63] (90)[c]	High	N/A	Precise	Direct	Sparse	Insufficient	*No conclusion*
Unplanned healthcare utilization	1[69] (384)[d]	Low	N/A	Precise	Direct	Sparse	Insufficient	*No conclusion*
Breastfeeding	1[69] (384)	Low	N/A	Imprecise	Direct	Sparse	Insufficient	*No conclusion*
Reduction of health disparities	0	.	.	.	.	.	.	*No evidence*
Adverse events	4 (42-384)	Low (3), High (1)	N/A	Precise	Indirect[e]	Sparse per drug and comparison	Insufficient (per drug or comparison)	*No conclusions*
Severe infant morbidities	0	.	.	.	.	.	.	*No evidence*

Abbreviations: . = no information, aRR = adjusted risk ratio, BP = blood pressure, N/A = not applicable, RR = risk ratio, XR = extended release.

Text in some cells is in bold font to emphasize statistically significant estimates, as indicated by the 95% CI excluding the effect.

[a] The evidence profile includes only outcomes prioritized by stakeholders.
[b] Outcomes are organ function, not patient morbidity
[c] Furosemide vs. no furosemide
[d] Furosemide vs. placebo: hypertension-related emergency department visits or readmissions
[e] Studies did not report (or experience) severe adverse events

3.5 KQ 3: What are the comparative effectiveness and harms of alternative magnesium sulfate treatment regimens to treat preeclampsia with severe features during the peripartum period?

3.5.1 Key Points

- In individuals with preeclampsia with severe features, **shorter-duration $MgSO_4$ regimens** (<24 hour, compared with standard 24-hour regimens:
  - Reduce duration of urinary catheterization (High SoE)
  - Reduce time to ambulation (High SoE)
  - Probably reduce time to breastfeeding initiation (Moderate SoE)
  - May reduce time from delivery to contact with infant (Low SoE)
  - May reduce the risk of loss of deep tendon reflexes, a sign of magnesium toxicity (Low SoE)
  - There is insufficient evidence regarding the risk of seizures, maternal mortality, and infant morbidities with different durations of $MgSO_4$ regimens
- In individuals with eclampsia, **loading dose only $MgSO_4$ regimens**
  - Probably increase the risk of recurrent seizures (Moderate SoE)
- **Lower dose $MgSO_4$ regimens**, compared with standard regimens:
  - May increase the risk of recurrent seizures among patients with eclampsia (Low SoE)
  - May not affect likelihood of mortality among patients with eclampsia (Low SoE, no evidence of difference)
  - May not affect 5-minute Apgar scores among infants of patients with preeclampsia with severe features (Low SoE, no evidence of difference)
  - May reduce rates of loss of deep tendon reflexes, a sign of magnesium toxicity, among patients with preeclampsia with severe features and eclampsia (High SoE)
- Among patients with preeclampsia with severe features, there is insufficient evidence regarding risk of seizures and maternal mortality.
- Regardless of population (preeclampsia with severe features or eclampsia), there is insufficient evidence regarding risk of infant morbidities with different dose $MgSO_4$ regimens
- There is insufficient evidence regarding whether nifedipine or other antihypertensive medications affect the rate of adverse events when administered with $MgSO_4$

3.5.2 Evidence Identified

Forty-one RCTs (reported in 42 articles) and two NRCSs compared alternative $MgSO_4$ regimens. [78-121] These studies were published between 1996 and 2022 and reported data from 7,910 participants. The overall RoB was low in 10 studies, moderate in 16 studies, and high in 14 studies.

Of these, 25 RCTs enrolled patients with **preeclampsia with severe features** as defined by ACOG. Another 18 RCTs enrolled patients with **eclampsia** (i.e., patients who experienced an eclamptic seizure during the current pregnancy) prior to allocation to a $MgSO_4$ regimen.

Four studies were conducted in the U.S., and the remaining were conducted in a low- and middle-income countries: 14 in India; 4 in Thailand; 3 in Nigeria; 5 in Pakistan; 2 each in Bangladesh, Brazil, and Egypt and Nepal; and 1 each in China, Ghana, Iran, and Panama. A multicenter trial enrolled participants treated in the Dominican Republic, Ecuador, El Salvador, Panama, and Peru.

Twenty-two RCTs and one NRCS compared shorter-duration $MgSO_4$ regimes with 24-hour regimens (total duration or for 24 hours after delivery or last seizure). Sixteen RCTs compared different doses of $MgSO_4$.

Two RCTs compared the intramuscular (Pritchard) regimen with the intravenous (Zuspan) regimen.[104, 105] See Table 3.3 for details of the commonly used regimens. One NRCS evaluated blood loss when $MgSO_4$ infusion was paused versus continued during caesarean delivery.[107]

One RCT evaluated a standard dose of nifedipine added to the $MgSO_4$ regimen compared with no nifedipine.

No study reported any of the following prioritized outcome categories: quality of life, psychosocial distress (anxiety, depression), breastfeeding success, reduction (or generation) of health disparities. See Appendix Table E-3.1 for detailed outcomes.

The most commonly used regimens are detailed in Table 3.3. Tables 3.4 and 3.5 provide the evidence profiles for KQ 3. Results are in Appendix Table E–3.1.

Table 3.3. Commonly used $MgSO_4$ regimens

Citation	Regimen Details
Pritchard 1955[122]	Loading dose: 4 g IV over 10 minutes followed by 5 g IM in each buttock Maintenance dose: 5 g IM every 4 hours in alternate buttock for 24 hours
Zuspan 1978[123]	Loading dose: 4 g IV over 20 minutes Maintenance dose: 1 to 2 g/hour via continuous IV infusion
2020 ACOG Practice Bulletin[3] [a]	Loading dose: 4 to 6 gm over 20 to 30 minutes Maintenance dose: 1 to 2 g/hour via continuous IV infusion

Abbreviations: ACOG = American College of Obstetrics and Gynecology, IM = intramuscular, IV = intravenous, $MgSO_4$ = magnesium sulfate.

[a]The regimen generally preferred in the United States.

3.5.3 Detailed Findings for Key Question 3

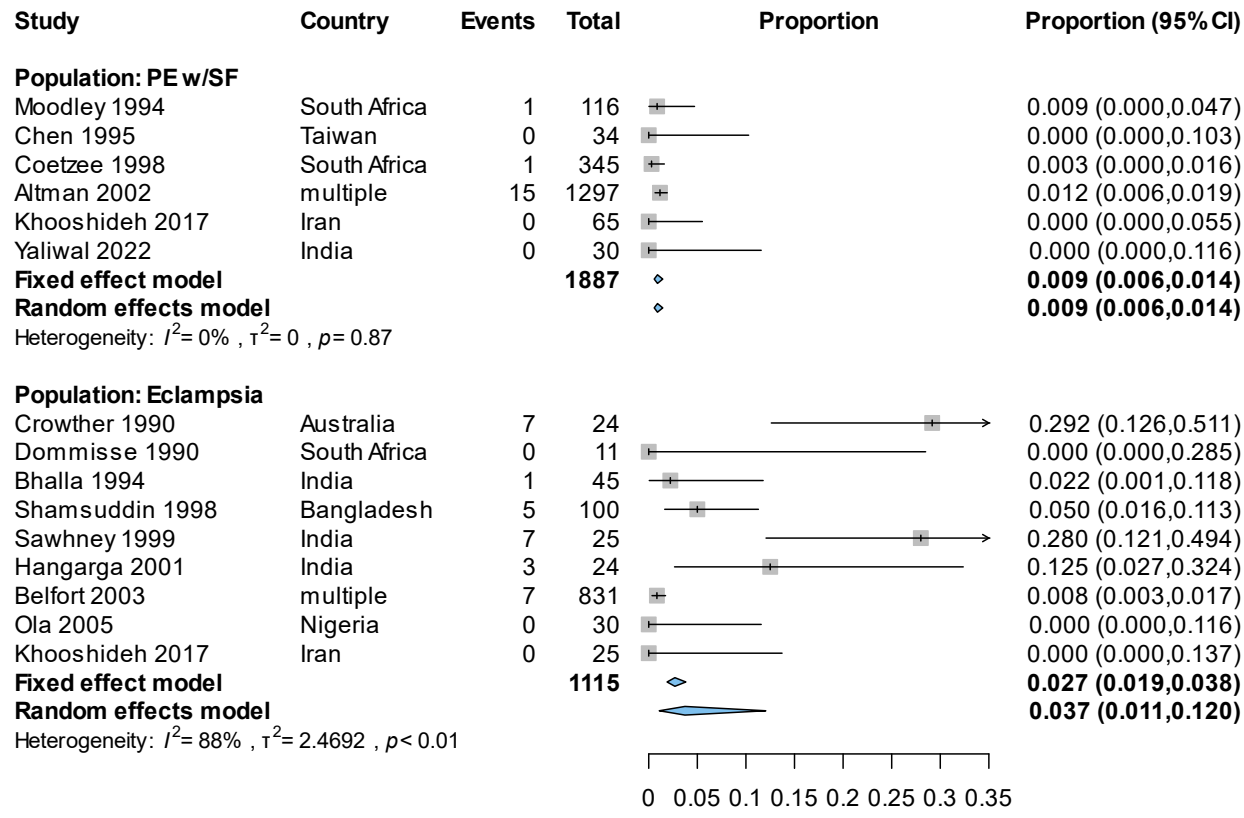
3.5.3.1 Risk of Seizure After Treatment With $MgSO_4$

To estimate baseline risks of seizure in individuals with preeclampsia with severe features and risk of a subsequent seizure in individuals with eclampsia, we extracted the risk of seizure from the $MgSO_4$ arms of an additional 14 RCTs that compared the effectiveness of treatment with $MgSO_4$ versus other treatments (placebo, antiseizure medications, and antihypertensive medications).[22, 124-135]

Six trials reported seizure outcomes in 1,887 patients with preeclampsia with severe features. Nine trials reported recurrent seizures in 1,115 patients with eclampsia (i.e., who had a seizure prior to $MgSO_4$ treatment). One trial, Khooshideh 2017[131], reported two subgroups: 65 patients with preeclampsia with severe features and 25 patients with eclampsia. By meta-analysis (Figure

3.1), the summary risk of seizure among 1,887 patients with preeclampsia with severe features treated with $MgSO_4$ was 0.9% (95% CI 0.6% to 1.4%, I^2=0%). In the 1,115 patients with eclampsia, the risks were higher, and with much more variability between studies. The pooled random effect estimate for the risk of recurrent seizure was 3.7% (95% CI 1.1% to 12%).

Figure 3.1. Meta-analysis of seizure risk for patients assigned to $MgSO_4$ treatment arms of efficacy trials



Abbreviations: CI = confidence interval, I^2 = measure of statistical heterogeneity (% of total variability that is due to between-study variability), $MgSO_4$ = magnesium sulfate, PE w/SF = pre-eclampsia with severe features.

3.5.3.2 $MgSO_4$ Regimens With Shortened Treatment Durations

We found 22 studies [81-86, 89, 91, 92, 94-96, 98-100, 102, 109-111, 113, 118-120] that compared shorter (<24 hours) with 24-hour $MgSO_4$ regimens.

3.5.3.2.1 $MgSO_4$ Toxicity: Absent Deep Tendon Reflexes

Two RCTs that compared shorter versus standard 24-hour regimens reported on absent deep tendon reflexes (DTRs), a sign of $MgSO_4$ toxicity. Rimal 2017 (moderate RoB),[111] from Nepal, included 60 patients with preeclampsia with severe features and evaluated a loading dose only regimen (versus a 24 hour regimen). Rao 2015 (moderate RoB),[109] from Pakistan, included 120 patients with eclampsia and evaluated a 12-hour (vs. 24-hour) regimen. In both trials, no patient in the shorter duration regimen groups lo st their DTRs, in contrast with 16/30 (53%) of participants with preeclampsia with severe features in Rimal 2017 (Peto OR 0.07, 95% CI 0.02 to 0.21) and 5/60 (8.3%) of participants with eclampsia in Rao 2015 (Peto OR 0.13, 95% CI 0.02 to 0.75).

Two additional RCTs, conducted in individuals with preeclampsia with severe features, reported combined loss of DTRs with hyporeflexia (reduced DTRs), which may be considered an early sign of toxicity. Both Unwaha 2020 (moderate RoB),[118] from Nigeria, and Beyuo 2022 (moderate RoB),[85] from Ghana, found no significant difference in hyporeflexia in individuals with preeclampsia with severe features (OR 0.74, 95% CI 0.31 to 1.78; OR 1.12, 95% CI 0.56 to 2.26; respectively).

Given that there were only two small trials, which each evaluated a different short-duration regimen in a different population, we conclude that there is low SoE that shorter duration $MgSO_4$ regimens may result in less $MgSO_4$ toxicity as manifested by lower odds of absent DTRs.

3.5.3.2.2 Seizures in Patients With Preeclampsia With Severe Features

Sixteen RCTs evaluated shorter $MgSO_4$ treatment durations (i.e., <24 hours) in individuals with preeclampsia with severe features. Figure 3.2 summarizes the seizure rates and comparative effects to prevent seizure for these studies. In nine of the RCTs, no seizures occurred in either treatment arm among a total of 1,291 participants. The summary OR comparing shorter versus standard duration (based on the 7 RCTs in which at least one seizure occurred) was imprecise (summary OR 1.1, 95% CI 0.5 to 2.4). Three of the RCTs used only a $MgSO_4$ loading dose (compared with standard regimen). There was no evidence of a difference between those studies that used only a loading dose and those that treated for up to 12 hours (P=0.32).

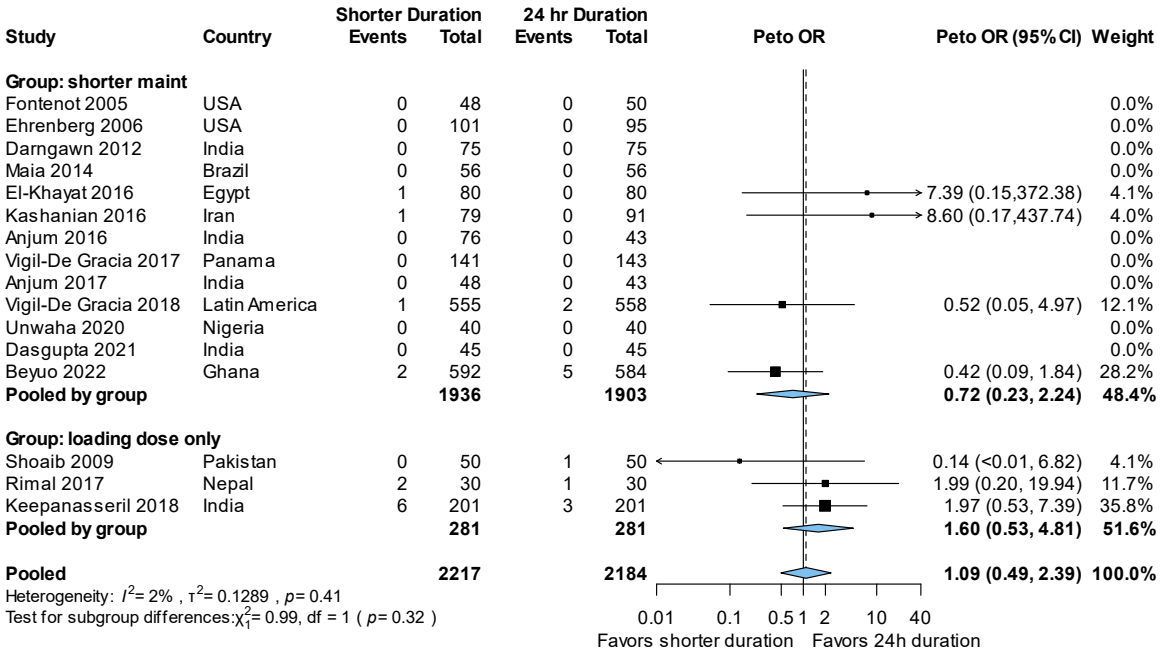
The $MgSO_4$ treatment regimens were heterogeneous with respect to route of administration (IV versus IV plus IM) and treatment duration (12 hours versus 8 hours versus loading dose only). Some studies defined treatment duration from delivery, while others reported total treatment duration, irrespective of when delivery occurred. A U.S.-based RCT (Fontenot 2005[96]) compared a conditional shorter treatment duration ($MgSO_4$ infusion was stopped in the experimental arm when urine output exceeded 100 mL/h for 2 hours) with treatment for 24 hours after delivery.

Three studies contributed most of the information to the summary estimate of comparative effects. The Vigil-De Gracia 2017 RCT[119] (moderate RoB) enrolled 1,113 women with preeclampsia with severe features who had received the Zuspan regimen for at least 8 hours prior to delivery. In the experimental group, the $MgSO_4$ was stopped immediately after delivery. In the control group, the $MgSO_4$ infusion was continued for 24 hours after delivery.

Beyuo 2022[85] (low RoB) enrolled 1,176 participants. The majority of participants (90.1 percent) had preeclampsia with severe features and 9.9 percent had eclampsia. The experimental group were treated for IM for 12 hours (5g IM every 4 hours for 3 doses) versus treatment for 24 hours (5g IM every 4 hours for 6 doses) in the standard treatment arm.

Keepanasseril 2018[99] randomized 402 patients (low RoB). Their experimental group received a loading dose only (4 g IV then 6 g IM) and was compared to the usual treatment group that received a maintenance injection of 2.5 g IM every 4 hours for a total duration of 24 hours postpartum.

Figure 3.2 Seizures with shorter duration (or loading dose only) versus standard 24 hour $MgSO_4$ treatment regimens



Abbreviations: CI = confidence interval, I^2 = measure of statistical heterogeneity (% of total variability that is due to between-study variability), maint = maintenance, $MgSO_4$ = magnesium sulfate, OR = Odds ratio

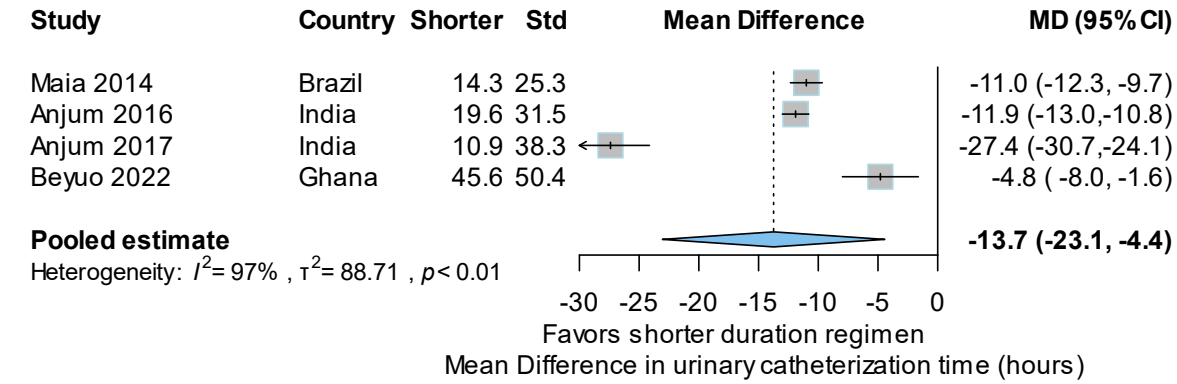
The summary estimate was highly imprecise; thus, we are unable to come to a graded conclusion.

In section 3.3.4.1 we estimated a seizure risk of 9 per 1000 for patients receiving a standard 24-hour $MgSO_4$ regimen. The upper (97.5^{th} percentile) bound of the pooled odds ratio (OR) implies a 2.24-fold increase in the odds of a seizure with shorter duration therapy. The calculated risk of seizure under this conservative 97.5 percentile scenario, would be approximately 20 seizures per 1000 patients receiving shorter-duration therapy. Thus, 92 patients (the number needed to treat) would need to receive standard duration therapy to prevent one additional seizure.

3.5.3.2.3 Functional Outcomes in Patients With Preeclampsia With Severe Features

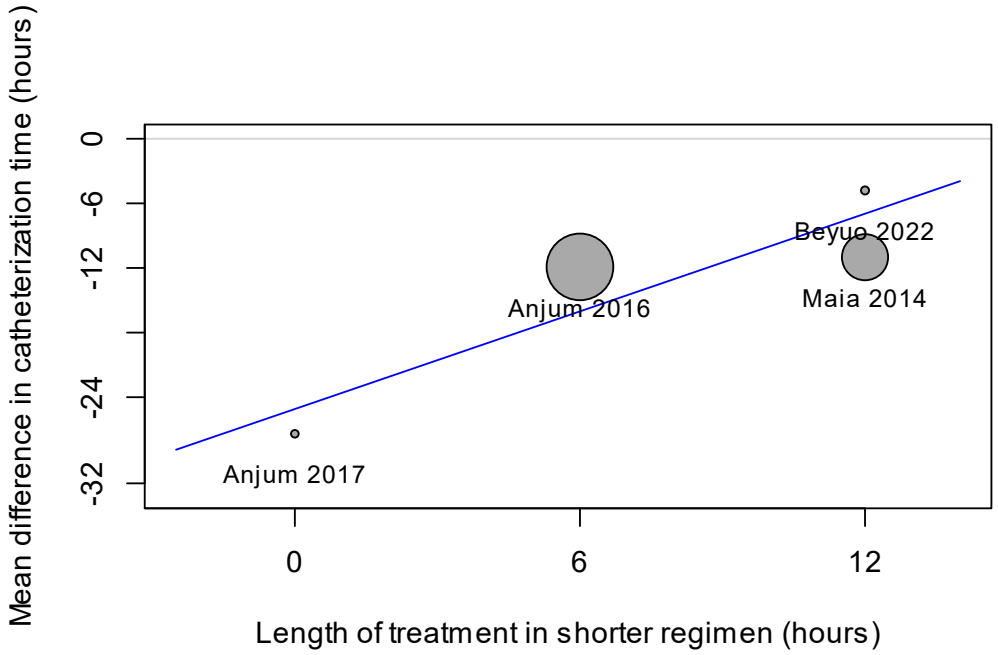
Urinary catheterization — The duration of urinary catheter use was the most commonly reported functional outcome (4 studies) with a shorter mean difference in hours of catheterization among patients receiving shorter duration treatment (Figure 3.3). A bubble plot (Figure 3.4) illustrates association (meta-regression) between the duration of urinary catheter use and the length of $MgSO_4$ treatment in the shorter regimen.

Figure 3.3. Duration of urinary catheterization with shorter versus standard duration $MgSO_4$ treatment regimens



Abbreviations: CI = confidence interval, MD = mean duration shorter minus mean duration Std, Shorter = shorter regimen, Std = standard regimen

Figure 3.4. Bubble plot for meta regression of catheterization time by length of $MgSO_4$ treatment in shorter regimens



Dasgupta 2021(low RoB)[92] reported duration of catheterization categorically. In the experimental group (8-hour post-delivery regimen), 44/45 (97.8%) of were catheterized for ≤8 hours versus the control group (24-hours post-delivery regimen), where all patients were catheterized for >8 hours.

Vigil-De Gracia 2017[119] (moderate RoB) enrolled 155 participants. The experimental arm (shorter duration) arm received $MgSO_4$ for 6 hours after delivery, compared to 24-hour $MgSO_4$ infusion post-delivery in the control arm. ***Time to start ambulation*** was significantly shorter; 10.9 hours in the experimental group and 24.9 hours in the control arm (MD –14 hours, 95% CI –15.1 to –12.9). ***Time to start breastfeeding*** was also significantly shorter in the short duration arm: 25.7 versus 36.5 hours (MD –10.8 hours, 95% CI: –15.1 to –6.5).

A second, larger RCT by the same group, Vigil-De Gracia 2018[120] (moderate RoB) enrolled 1,113 participants. In the experimental (short duration) arm, $MgSO_4$ was stopped immediately after delivery. In the standard treatment arm, the $MgSO_4$ infusion was continued for 24 hours postpartum. ***Time to start ambulation*** was significantly shorter: 11.8 hours in the experimental group and 18.1 hours in the control arm (MD –6.3 hours, 95% CI –7.6 to –5.1). ***Time to start breastfeeding*** was also significantly shorter in the short duration arm: 17.1 versus 24.1 hours (MD –7.0 hours, 95% CI −9.0 to –5.0)

There is high SoE of a decrease in the duration of urinary catheterization and time to ambulation, and a moderate SoE of shorter time to start breastfeeding among those treated with shorter duration $MgSO_4$ regimens (see Table 3.4).

3.5.3.2.4 Maternal Mortality in Patients With Preeclampsia With Severe Features

There were no maternal deaths in either treatment arm of five studies that reported maternal mortality.[92, 111, 118-120] In patients with preeclampsia with severe features, maternal mortality is rare in all active treatment arms, but we cannot make a conclusion about the comparative risk of mortality with different duration therapies.

3.5.3.2.5 Infant Morbidities

Four studies (in 5 publications) reported on infant morbidity outcomes.[85, 86, 89, 99, 111] Three RCTs evaluated Apgar scores at delivery.[85, 99, 111] The three trials reported inconsistent findings related to low Apgar scores (defined as <7 at 5 minutes). In Beyuo 2022, significantly fewer infants born to individuals allocated to the 12-hour regimen (69/619, 11.1%), had low Apgar scores (defined as <7) compared with 90/599 (17.5%) infants in 24-hour regimen (RR 0.74, 95% CI: 0.55 to 0.99). Keepanasseril 2018 found no significant difference (favoring standard duration treatment): 14/201 (7.0%) of infants in the loading dose only arm had a 5-minute Apgar score <7, compared to 9/201(4.5%) in the standard duration arm (RR 1.56, 95% CI: 0.69 to 3.51). Rimal 2017 reported no infants with a 5-minute Apgar <7 in either arm; thus, precluding meta-analysis across the three trials.

Chama 2013 reported birth asphyxia (undefined) in 10/48 (20.8%) of infants in the 8-hour regimen, compared with 12/50 (24%) in the standard duration arm (RR 0.87, 95% CI: 0.41 to 1.82).[89]

Overall, the comparative effect of $MgSO_4$ on infant morbidity were heterogeneous and imprecise for low Apgar scores. Based on one study that did not define asphyxia, it is difficult to interpret the findings. Thus, the evidence is insufficient to allow conclusions regarding infant morbidities related to duration of therapy.

3.5.3.2.6 Satisfaction With Care in Patients With Preeclampsia With Severe Features

Satisfaction with care was reported by Maia 2014.[102] The trial reported that 41 of 56 (73.2%) of patients assigned to the 12-hour regimen were very satisfied or satisfied with treatment, compared with 36/56 (64.3%) of patients who received standard 24-hour therapy, which yielded a nonsignificant effect size (RR 1.14, 95% CI 0.89 to 1.46). The single study did not provide sufficient evidence for a graded conclusion.

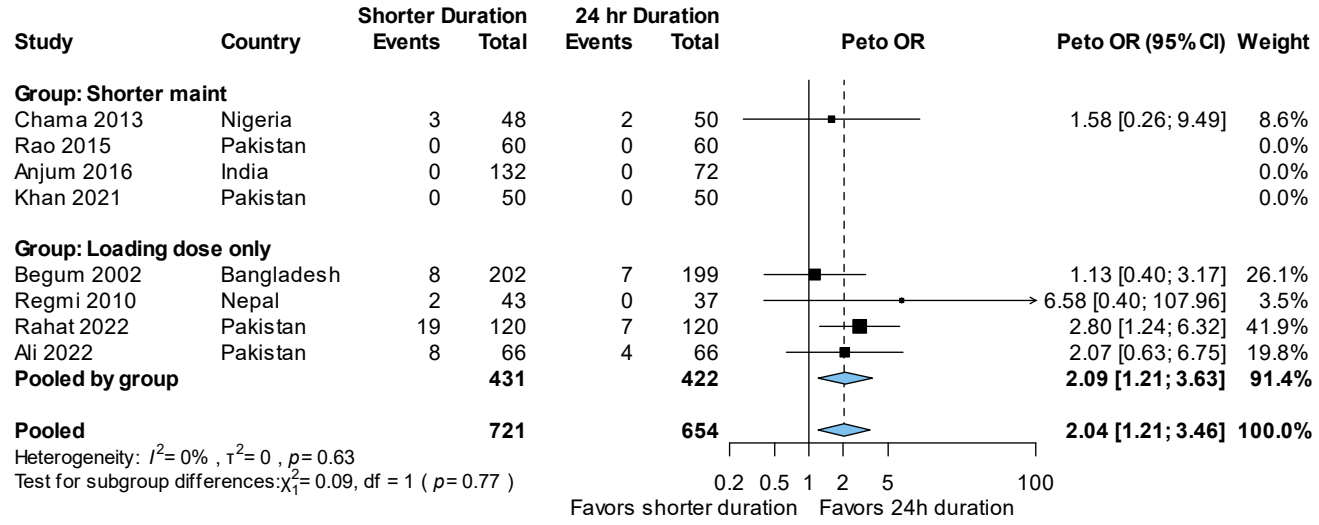
3.5.3.2.7 Maternal-Neonatal Bonding in Patients With Preeclampsia With Severe Features

The Maia 2014 RCT (moderate RoB) also reported ***time from delivery to contact with infant***.[102] The mean time from delivery to contact with the newborn was statistically significantly shorter, 29.6 hours for the 12-hour regimen, compared with 35.0 hours in the standard 24-hour regimen (MD –5.4 hours, 95% CI: –10.0 to –0.80). Although only a single study, given the size of the effect we concluded there is low SoE that shorter duration $MgSO_4$ therapy may yield shorter time from delivery to maternal contact with their infant (see Table 3.4).

3.5.3.2.8 Recurrent Seizures in Patients With Eclampsia

Eight studies (N=1,375) compared $MgSO_4$ regimens of different durations in patients with eclampsia (i.e., who had had a seizure prior to $MgSO_4$ treatment). In this population, the baseline risk for a recurrent seizure after treatment with $MgSO_4$ was higher. In three studies, no participant experienced a recurrent seizure, leaving five studies that could be included in meta-analysis (Figure 3.5). Overall, the odds of recurrent seizure was significantly greater (OR 2.04, 95% CI 1.21 to 3.46) for shorter versus standard duration regimens. In four of the five studies that contributed to the summary estimate, patients received a loading dose only. In this subgroup, the odds of recurrent seizure was significantly greater (OR 2.09, 95% CI 1.21 to 3.63).

Figure 3.5. Recurrent seizure with shorter versus standard duration $MgSO_4$ treatment regimens in patients with eclampsia



Abbreviations: CI = confidence interval, I^2 = measure of statistical heterogeneity (% of total variability that is due to between-study variability), maint = maintenance, $MgSO_4$ = magnesium sulfate, OR = odds ratio.

The largest study (Begum 2002[84]) enrolled 401 participants. Both groups received a lower dose adapted for treatment of the lower average weight of Bangladeshi women. The loading dose only group received the loading dose of 4 g IV and 6 g IM. The standard, 24-hour duration group received the same loading dose, followed by 2.5g IM every 4 hours for 24 hours. The rate of recurrent seizures after treatment completion was similar between groups, 3.7% overall. A smaller (n=80) study, Regmi 2010,[110] compared a loading dose consisting of 4 g IV followed by 10 g IM, compared with the same loading dose followed by then 5 g IM every 4 hours for 24 hours after delivery or the last seizure. A third study, Chama 2013,[89] enrolled 98 participants and

compared the Pritchard regimen (see Table 3.3) with an 8-hour maintenance period with the standard 24-hour maintenance period. Ali 2022[80], enrolled 132 patients and compared the Pritchard regimen given for up to 24 hours after last seizure to a group given the loading dose only. Rahat 2022[108], enrolled 240 patients and compared the Pritchard regimen given for 24 hours (after the last seizure or delivery, whichever comes later) with loading dose only.

Evidence is insufficient regarding the risk of recurrent seizure in patients with shorter duration $MgSO_4$ regimens. However, there is probably an increased risk of recurrent seizure in patients with eclampsia treated with a loading dose only (moderate SoE), compared to a standard 24-hour $MgSO_4$ regimen (see Table 3.4).

3.5.3.2.9 Functional Outcomes in Patients With Eclampsia

Two studies reported on ***duration of urinary catheterization***. Anjum 2016[81] found significantly shorter duration of urinary catheterization: 19.6 hours with a 12-hour regimen versus 31.5 hours in the 24-hour regimen (MD –11.9 hours, 95% CI –12.8 to –11.0).

Khan 2021[100] compared a 12-hour regimen with a 24-hour regimen. Participants in the 12-hour arm had a urinary catheter inserted for a mean of 19.6 hours. This was significantly shorter than in the mean 32.1 hours with the 24-hour regimen (MD –12.5 hours, 95% CI: –13.8 to –11.2)

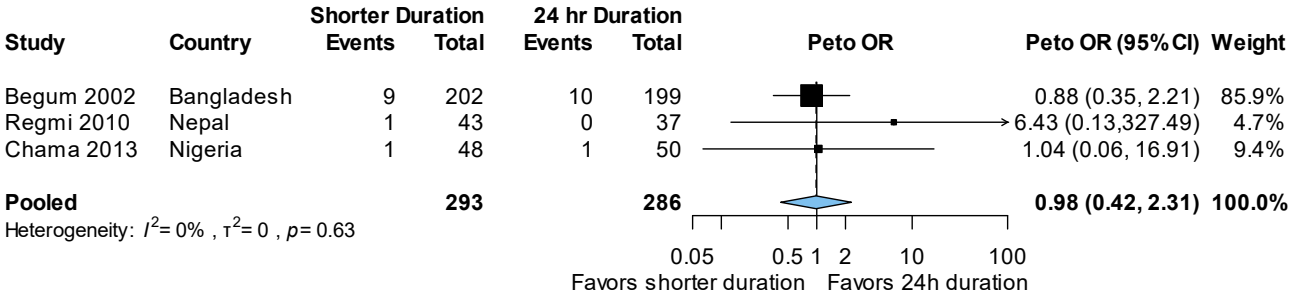
Supporting the high SoE conclusion regarding duration of urinary catheterization (Table 3.4), shorter duration $MgSO_4$ treatments similarly shorten the duration of urinary catheterization in women with eclampsia. This was also the case for studies evaluating patients with preeclampsia with severe features (but without seizures).

3.5.3.2.10 Maternal Mortality in Patients With Eclampsia

Three studies reported maternal mortality among patients who had experienced an eclamptic seizure.[84, 89, 110] As shown in Figure 3.6, the trials were underpowered for the low frequency of the outcome (1% to 5% of patients with eclampsia prior to treatment died); thus, all effect estimates were highly imprecise. By meta-analysis, the summary OR for maternal mortality for shorter versus standard duration regimens was also imprecise (Peto OR 0.98, 95% CI 0.42 to 2.31).

In patients with eclampsia, maternal mortality is appreciable, but occurs in similar, albeit imprecisely estimated proportions of participants in standard and reduced duration treatment arms. Thus, we were unable to come to a graded conclusion.

Figure 3.6. Maternal mortality with shorter versus standard 24 hour $MgSO_4$ treatment regimens in patients with eclampsia



Abbreviations: CI = confidence interval, I^2 = measure of statistical heterogeneity (% of total variability that is due to between-study variability), OR = Peto odds ratio.

3.5.3.3 $MgSO_4$ Regimens With Varying Doses

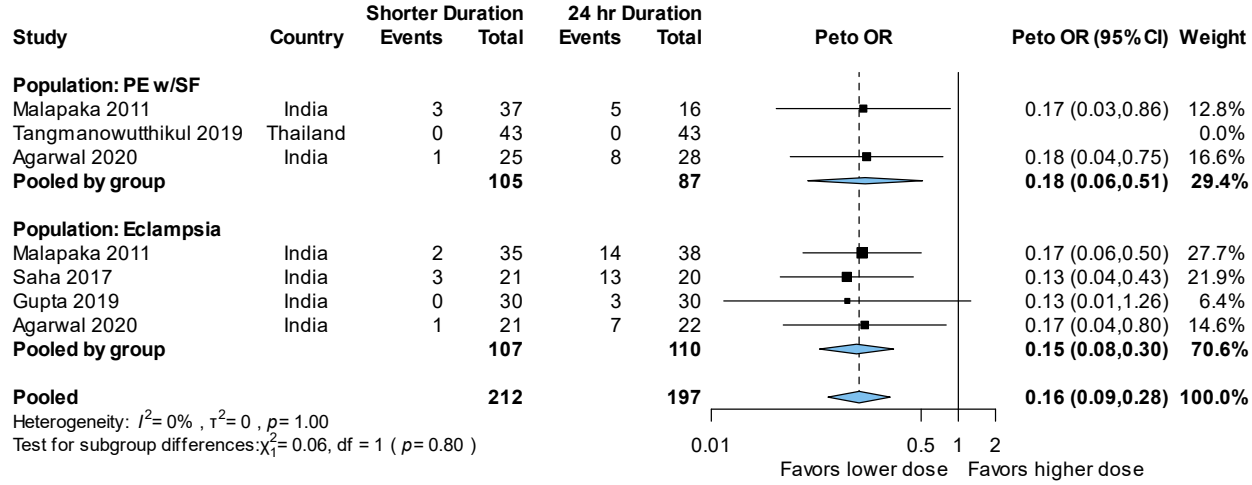
Fifteen studies compared regimens containing different $MgSO_4$ doses.[78, 79, 87, 88, 90, 93, 97, 101, 103, 106, 112, 114-117]

3.5.3.3.1 $MgSO_4$ Toxicity: Absent Deep Tendon Reflexes

Five RCTs reported the number of patients with absent (or loss of) DTRs, a clinical sign of magnesium toxicity (Figure 3.7).[79, 97, 103, 112, 117] The trials consistently found that loss of DTRs during $MgSO_4$ treatment was more than five times as likely in patients receiving higher dose $MgSO_4$ regimens (OR of low vs. high dose <0.2). By meta-analysis, the summary OR of lower versus standard dose $MgSO_4$ regimens was 0.16 (95% CI 0.09 to 0.28).

Thus, there is high SoE that lower dose $MgSO_4$ regimens are considerably less likely to result in $MgSO_4$ toxicity as manifested by loss of DTRs (see Figure 3.7.

Figure 3.7. Absent deep tendon reflexes with lower versus higher dose $MgSO_4$ treatment regimens, grouped by population



Abbreviations: CI = confidence interval, I^2 = measure of statistical heterogeneity (% of total variability that is due to between-study variability), OR = Peto odds ratio, PE w/SF = preeclampsia with severe features.

3.5.3.3.2 Maternal Seizures

3.5.3.3.2.1 Patients With Preeclampsia With Severe Features

Six studies (N=351) enrolled patients with preeclampsia with severe features and compared $MgSO_4$ regimens that differed by dose. There were no eclamptic seizures in either treatment group in any study, precluding meta-analysis. One of these studies (Malapaka 2011(moderate RoB[103]) reported outcomes in two subgroups. The first subgroup an "imminent eclampsia" subgroup (categorized as preeclampsia with severe features) with 53 patients, none of whom had a seizure. The other subgroup included 73 patients with eclampsia. The only study comparing alternative dosing done in the United States (Brookfield 2020, low RoB[88]) enrolled individuals with body mass index ≥35. They defined a "therapeutic" Mg concentration target of 4.8 mg/dL. A significantly higher proportion of participants who received a higher dose (loading dose of 6 g IV followed by 2 g/h) had therapeutic Mg levels at 4 hours of therapy and at delivery (P <0.01).

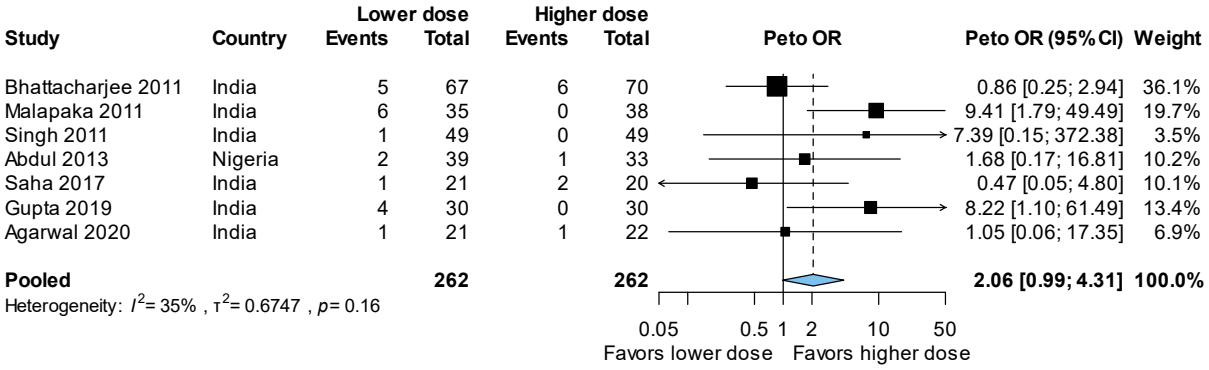
None of these studies reported a seizure in either treatment arm, precluding a graded conclusion. The U.S. study (Brookfield 2020[88]) suggests that dosing adjustments might be required in high BMI individuals.

3.5.3.3.2.2 Recurrent Seizures in Patients With Eclampsia

Eight studies enrolled individuals with eclampsia (who had a prior seizure) and compared lower dose regimens with higher dose regimens.[78, 79, 87, 97, 103, 112, 114, 116] Of these, seven studies administered $MgSO_4$ for 24 hours. One study, Sultana 2013 (high RoB) compared an IV loading dose of 8 g (low dose) with a 10 g loading dose (4g IV then 6 g IM) without a maintenance infusion in either group.[116] This study was excluded from the meta-analysis. As shown in Figure 3.8, the pooled odds of a recurrent seizure are approximately 2-folder higher in low dose compared with higher dose regimens (OR 2.06, 95% CI 0.99 to 4.31).

Patients with eclampsia treated with lower dose $MgSO_4$ may be at higher risk for subsequent seizures than those treated with higher dose $MgSO_4$ regimens (low SoE, see Figure 3.8. The comparative effect for lower versus higher dose regimens is imprecise.

Figure 3.8. Recurrent seizure with lower versus higher dose $MgSO_4$ treatment in patients with eclampsia



Abbreviations: CI = confidence interval, I^2 = measure of statistical heterogeneity (% of total variability that is due to between-study variability), $MgSO_4$ = magnesium sulfate, OR = odds ratio.

3.5.3.3.3 Maternal Mortality

3.5.3.3.3.1 Patients With Preeclampsia With Severe Features

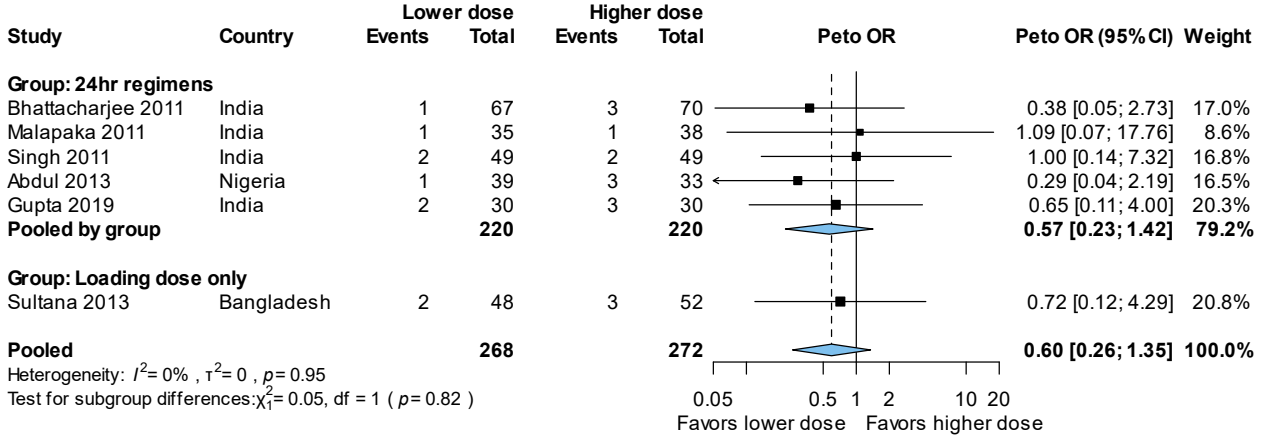
Both studies (N = 253) that reported the outcome reported no maternal deaths in either treatment arm.[93, 103] Thus, no conclusion could be made about the comparative effectiveness of different dose $MgSO_4$ regimens to prevent maternal mortality.

3.5.3.3.3.2 Patients With Eclampsia

Six studies enrolled individuals with prior eclampsia and compared lower dose with higher dose regimens.[78, 87, 97, 103, 114, 116] Of these, five studies administered $MgSO_4$ for 24 hours and one (Sultana 2013) used only a loading dose, comparing a lower and a higher loading dose. The trials were all small; thus, each trial yielded an imprecise estimate of maternal mortality. As shown in Figure 3.9, there was no significant difference in mortality between higher and lower dose regimens (summary OR 0.60, 95% CI 0.26 to 1.35). The effect estimate was unchanged with or without the study that compared different dose loading doses (Sultana 2013).

With a nonsignificant summary effect estimate, with a wide confidence interval, we conclude that, with low SoE, there is no evidence of a difference in risk of death in patients with eclampsia.

Figure 3.9. Maternal mortality with lower versus higher dose $MgSO_4$ treatment regimens in patients with eclampsia

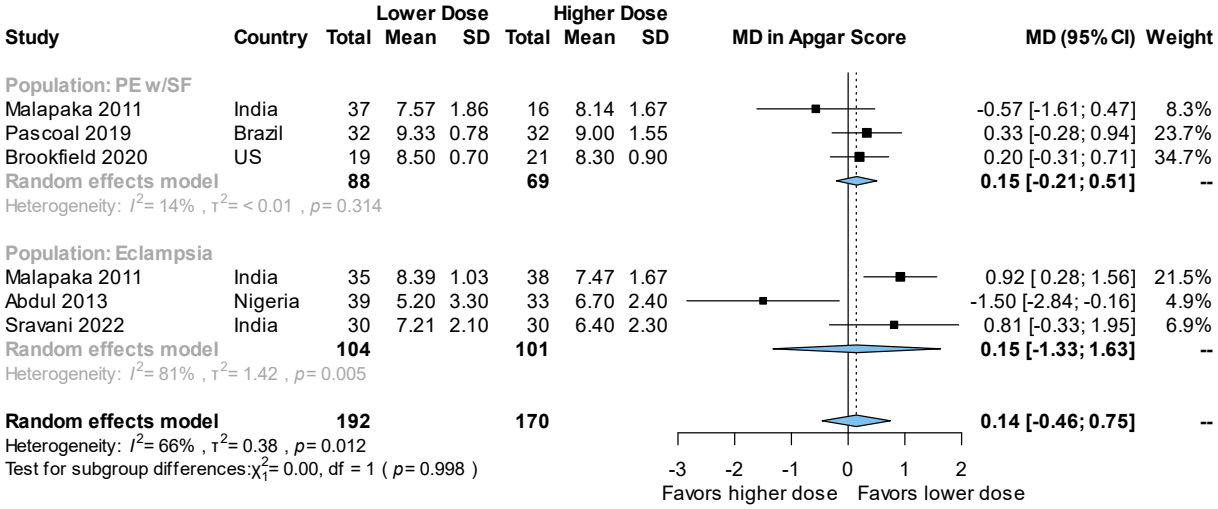


Abbreviations: CI = confidence interval, I^2 = measure of statistical heterogeneity (% of total variability that is due to between-study variability), $MgSO_4$ = magnesium sulfate, OR = odds ratio.

3.5.3.3.4 Infant Morbidities: 5-Minute Apgar Score

Five RCTs[78, 88, 103, 106, 115] reported mean or median 5-minute Apgar scores (where higher scores are better). Two RCTs enrolled individuals with preeclampsia, two RCTs enrolled individuals with eclampsia and one RCT[103] separately reported outcomes in both populations. Figure 3.10 summarizes a meta-analysis, by population, of the mean difference in 5-minute Apgar scores between lower dose and higher dose $MgSO_4$ regimens.

Figure 3.10. Mean difference in Apgar score with lower versus higher dose $MgSO_4$ treatment regimens



Abbreviations: CI = confidence interval, I^2 = measure of statistical heterogeneity (% of total variability that is due to between-study variability), $MgSO_4$ = magnesium sulfate, MD = mean difference, PE w/SF = preeclampsia with severe features

Two studies enrolled infants born to mothers with preeclampsia with severe features and reported Apgar score categorically or proportion with birth asphyxia. The Charoenvidhya 2013[90] RCT (moderate RoB) enrolled 60 individuals who were given a 4 g loading dose of $MgSO_4$ and randomized to a lower dose regimen (1g/h) or a higher dose regimen (2g/h). They reported that

only that Apgar score was similar between the two groups (P >0.05). The Kitiyodom 2016[101] RCT (moderate RoB) enrolled 38 mothers with a body mass index (BMI) ≥25. In the lower dose arm, 10.5% (10.5%) of infants had birth asphyxia (undefined) versus 15.8% (3/19) in the higher dose arm (RR 0.67, 95% CI: 0.13 to 3.55).

Two studies enrolled infants born to mothers with eclampsia. The Saha 2017[112] RCT (moderate RoB) reported 9.5% (2/21) infants with a 5-minute Apgar score <7 in the low dose arm versus 25% (5/20) infants born to mothers who received the Zuspan regimen arm (RR 0.38, 95% CI 0.08 to 1.74). The Gupta 2018[97] RCT (high RoB) reported a 5-minute Apgar of <6 in 10% (3/30) of infants in the low dose arm and 6.7% (2/30) of infants in the standard dose arm (RR 1.50, 95% CI 0.27 to 8.34).

Overall, for infants of patients with preeclampsia with severe features, the mean difference in 5-minute Apgar score was small (MD 0.15, 95% CI –0.21, 0.51), consistent with no difference (low SoE). For infants whose mothers with eclampsia, the overall mean difference in 5-minute Apgar score between regimens is imprecise and heterogeneous, precluding a graded conclusion.

3.5.3.4 Comparisons of Alternative $MgSO_4$ Delivery Strategies

Three studies evaluated different $MgSO_4$ delivery strategies.[104, 105, 107]

The Manorot 1996 RCT (moderate RoB)[104] compared the Zuspan regimen (4 g IV then 1 g/h) with the Pritchard regimen (4 g IV then 10 g IM, followed by 5 g IM every 4 hours) and reported significantly higher serum Mg levels in participants assigned to the Pritchard regimen, at 60 minutes (MD –3.1 mEq/L, 95% CI –4.2 to –2.1); 240 minutes (MD –1.6 mEq/L, 95% CI –2.1 to –1.0).

Mundle 2012 RCT (moderate RoB)[105] compared the Zuspan regimen—administered via an inexpensive, spring-loaded pump that does not require electricity—with the IM Pritchard regimen. They reported significantly less flushing (94/147 [63.9%] vs. 115/153 [75.2%]; RR 0.85, 95% CI 0.73 to 0.99) and less nausea (27/147 [18.4%] vs. 50/153 [32.7%]; (RR 0.56, 95% CI 0.37 to 0.85) in the experimental arm versus the control arm. The magnesium levels achieved with the IM Pritchard regimen were higher at 60 and 120 minutes than those obtained in patients who received the IV Zuspan regimen.

In these two RCTs, the IV Zuspan regimen resulted in lower serum Mg levels than the IM Pritchard regimen and a lower rate flushing and nausea than in those who received the IM Pritchard regimen.

The Pippen 2020 NRCS (moderate RoB)[107] evaluated blood loss at cesarean delivery when $MgSO_4$ infusion was paused versus continued during cesarean delivery. Postpartum hemorrhage occurred in 9.9% of participants in the interrupted $MgSO_4$ infusion group and 10.2% in the continued infusion group (RR 0.97, 95% CI 0.44 to 2.15).

3.5.3.5 Concomitant Use of Antihypertensive Medications During Treatment With $MgSO_4$

The Wang 2019 RCT (high RoB) [121] compared two $MgSO_4$ regimens, with and without the addition of oral nifedipine 10 mg every 8 hours. In the $MgSO_4$ plus nifedipine arm, treatment was significantly more effective (based on the composite outcome of absence or improved clinical symptoms, decreases in urinary protein and reduction in BP) in 111/120 (92.5%) of patients and in 85/120 (70.8%) patients in the $MgSO_4$ only arm (RR 1.31, 95% CI 1.15 to 1.48). The number of adverse reactions (nausea, vomiting and dizziness) were similar in both arms. In

the combined treatment arm, 7/120 participants (5.8%) had at least one adverse event compared with 8/120 (6.7%) participants in the $MgSO_4$ only arm (RR 0.88, 95% CI 0.33 to 2.34).

Overall, the study found that addition of nifedipine to the $MgSO_4$ regimen improved clinical outcomes without a difference in adverse events. The study was small and there were no severe adverse events reported in either group, precluding a graded conclusion.

Table 3.4. Evidence profile for shorter versus longer duration $MgSO_4$ regimens (Key Question 3)

Outcome (Population)	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall Strength of Evidence	Conclusion Statements
Maternal morbidity: Seizure(preeclampsia with severe features)	16[82, 83, 85, 86, 91, 92, 94-96, 98, 99, 102, 111, 113, 118-120] (4,481)	Moderate	Consistent	Highly imprecise	Direct	None	Insufficient	*No conclusion (imprecise)* Sum OR 1.09 (0.49, 2.39)
Maternal morbidity: Recurrent seizure (eclampsia)	4[80, 84, 108, 110, 136] (853)	Moderate	Consistent	Precise	Direct	None	Moderate	*Greater risk of recurrent seizure after loading dose only regimen* **Sum *OR 2.09 (1.21, 3.63)***
Maternal mortality (preeclampsia with severe features)	5 [92, 111, 118-120] (1627)	Moderate	Consistent	Imprecise	Direct	No deaths across studies	Insufficient	*No conclusion (imprecise)*
Maternal mortality (eclampsia)	3[84, 89, 110] (579)	Moderate	Consistent	Imprecise	Direct	None	Insufficient	*No conclusion (imprecise)*
Infant morbidities (5-minute Apgar score)	9[78, 88, 90, 97, 101, 103, 106, 112, 115] (561)	Moderate	Inconsistent	Imprecise	Direct	None	Insufficient	*No conclusion (inconsistent and imprecise)*
Breastfeeding	2[119, 120] (1,397)	Moderate	Consistent	Precise	Direct	Variable comparisons	Moderate	*Shorter $MgSO_4$ duration yielded shorter time to start breastfeeding*
Satisfaction with care	1[102] (112)	Moderate	N/A	Imprecise	Direct	Sparse	Insufficient	*No conclusion (sparse)*
Quality of life	0	.	.	.	.	.	.	*No evidence*
Postpartum recovery: Urinary catheterization	4[81-83, 100] (518)	Low	Consistent	Precise	Direct	None	High	*Shorter $MgSO_4$ duration yielded shorter catheterization duration*

3. Results

Outcome (Population)	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall Strength of Evidence	Conclusion Statements
Postpartum recovery: Ambulation	2[119, 120] (1,397)	Low	Consistent	Precise	Direct	None	High	*Shorter $MgSO_4$ duration yielded shorter time to ambulation*
Maternal-neonatal bonding: Time from delivery to contact with infant	1[102] (112)	Moderate	N/A	Precise	Direct	Sparse, but large effect	Low	*Shorter $MgSO_4$ duration yielded shorter time from delivery to contact with infant* ***MD −5.4 hr (−10.0, −0.8)***
Psychosocial distress	0	.	.	.	.	.	.	*No evidence*
Reduction of health disparities	0	.	.	.	.	.	.	*No evidence*
Magnesium-related toxicity and other adverse events (Absent DTR)	4[109, 111] (180)	Moderate	Consistent	Precise	Direct	Single study each for different short-duration regimens each in a different population	Low SoE	*Lower risk of decreased DTR with shorter $MgSO_4$ duration ORs 0.07 and 0.13*
Adverse drug interactions	0	.	.	.	.	.	.	*No evidence*

Abbreviations: . = no information, DTR = deep tendon reflexes, hr = hours, $MgSO_4$ = magnesium sulfate, Sum OR = summary odds ratio.

Text in some cells is in bold font to emphasize statistically significant estimates, as indicated by the 95% CI excluding the effect.

Table 3.5. Evidence profile for lower versus higher dose $MgSO_4$ regimens (Key Question 3)

Outcome (Population)	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall Strength of Evidence	Conclusion Statements
Maternal morbidity: Seizure (preeclampsia with severe features)	6[81, 84, 89, 100, 109, 110] (351)	Moderate	Consistent	Imprecise	Direct	No seizures across studies	Insufficient	*No conclusion (no events)*
Maternal morbidity: Recurrent seizure (eclampsia)	7 [78, 79, 87, 97, 103, 112, 114] (524)	Moderate	Consistent	Precise	Direct	Large, but nonsignificant effect	Low	*Lower dose resulted in higher risk of recurrent seizure Sum OR 2.06 (95% CI 0.99 to 4.31)[a]*
Maternal mortality (preeclampsia with severe features)	2[93, 103] (253)	Moderate	Consistent	Imprecise	Direct	No seizures across studies	Insufficient	*No conclusion (imprecise)*
Maternal mortality (eclampsia)	6 [78, 87, 97, 103, 114, 116] (540)	Moderate	Consistent	Imprecise	Direct	None	Low	*No evidence of a difference Sum OR 0.60 (0.26, 1.35)*
Infant morbidity: 5-minute Apgar score (preeclampsia with severe features)	3[88, 103, 106] (157)	Moderate	Consistent	Precise	Direct	Sparse	Low	*No evidence of a difference MD 0.15 (−0.21, 0.51)*
Infant Morbidity: 5-minute Apgar score (eclampsia)	5[78, 97, 103, 112, 115] (306)	High	Inconsistent	Imprecise	Direct	None	Insufficient	*No conclusion (imprecise)*
Breastfeeding	0	.	.	.	.	.	.	*No evidence*
Satisfaction with care	0	.	.	.	.	.	.	*No evidence*
Quality of life	0	.	.	.	.	.	.	*No evidence*
Postpartum recovery	0	.	.	.	.	.	.	*No evidence*
Urinary catheterization	0	.	.	.	.	.	.	*No evidence*
Ambulation	0	.	.	.	.	.	.	*No evidence*
Maternal-neonatal bonding	0	.	.	.	.	.	.	*No evidence*
Psychosocial distress	0	.	.	.	.	.	.	*No evidence*

3. Results

Outcome (Population)	No. Studies (Subjects)	Risk of Bias	Consistency	Precision	Directness	Other	Overall Strength of Evidence	Conclusion Statements
Reduction of health disparities	0	.	.	.	.	.	.	*No evidence*
Magnesium-related toxicity or other adverse events (decreased deep tendon reflexes)	5 [79, 97, 103, 112, 117] (409)	Moderate	Consistent	Precise	Direct	Large effect size	High	*Lower odds of magnesium toxicity in lower dose regimens) Sum OR 0.16 (0.09, 0.28)*
Adverse drug interactions	0	.	.	.	.	.	.	*No evidence*

Abbreviations: . = no information, $MgSO_4$ = magnesium sulfate, Sum OR = summary odds ratio.

Text in some cells is in bold font to emphasize statistically significant estimates, as indicated by the 95% CI excluding the effect..

[a] Lower versus higher dose regimens, excluding one study that used only a loading dose.

4. Discussion

4.1 Contextual Question

How are race, ethnicity, and social determinants of health related to disparities in incidence and detection of hypertensive disorders of pregnancy (HDP), as well as access to care, management, follow-up care, and clinical outcomes in individuals with postpartum hypertensive disorders of pregnancy?

Disparities in healthcare access, delivery, and outcomes are ubiquitous across multiple fields of medicine and clinical domains. The situation is particularly egregious in maternal healthcare. HDP and its sequelae disproportionately affect minority and marginalized communities.[11, 18]

Maternal morbidity and mortality — Data suggest that **HDP is more common and more severe** in Black women. An analysis of data from the Healthcare Cost and Utilization Project (HCUP) found that Black women are more likely than non-Hispanic White women to develop preeclampsia. In 2014, the rate of preeclampsia/eclampsia was 69.8 per 1,000 deliveries in Black women, compared with 43.3 per 1,000 in White women. Black women were more likely than women of other races to have a more severe diagnosis and were more likely to have preexisting hypertension (HTN).[137]

In a cohort of pregnant patients diagnosed with HDP, Black patients had higher odds of development of preeclampsia with severe features, preterm birth, small for gestational age neonates, cesarean delivery, and severe maternal morbidity.[138] In a study of individuals with preeclampsia, 9.8% of non-Hispanic Black women had severe maternal morbidity (9.8%), compared with 6.1% of non-Hispanic White women. For stroke, the rate was 17.1 per 10,000 deliveries for Black women compared with 6.5 per 10,000 deliveries for non-Hispanic White women.[12] Black individuals are three times more likely than non-Hispanic White individuals to die of pregnancy-related conditions, both around the time of delivery and up to 1 year postpartum.[18] A higher percentage of deaths are attributable to HDP (8.2% in Black individuals versus 6.7% in non-Hispanic White individuals).[18] Similar disparities in exist in Hispanic, American Indian, Alaska Native, Native Hawaiian, and Other Pacific Islander birthing people.[11]

Disparities in the postpartum period—A study of insurance claims concluded that 14 percent of severe maternal morbidity events occurred after the delivery hospitalization, most within the first 2 weeks after discharge. The adjusted odds of having a *de novo* severe maternal morbidity event were 1.69-fold higher in non-Hispanic Black women than in all other women.[139]

In a Pittsburgh cohort, Black women had slower decreases in blood pressure (BP) than White women, with higher BP at 6 weeks and higher rates of persistent HTN at 6 weeks (68.1% in Black women vs. 51.4% in White women).[140] In a Philadelphia cohort, body mass index and race were identified as determinants of postpartum BP trends and HTN resolution. Among those with body mass index <35, 81% of non-Black women had normal BPs at 16 days compared with 49% of Black women.[141]

Racism, whether structural, institutional, or individual, is understood to be the root cause of the disparities in incidence, severity, and outcome, mediated by multiple levels of influence that impact structural and social determinants of health.[142-144]

Some of the hypothesized reasons for disparities in postpartum outcomes relate to differential incidence of **risk factors** (e.g., diabetes and obesity) and **social determinants of health** (e.g.,

income, access to healthy food, education, social stressors, rural location). An analysis of a California birth cohort found that White women are at lower risk for preeclampsia, and that higher socioeconomic status (SES) further reduced risk. For Black women, higher SES did not attenuate risk to the same extent.[145] These differences are believed to reflect the effects of internalized, interpersonal, institutional, and structural racism, which manifests in poorer healthcare and adverse social determinants of health.[146]

Provider-level factors may include implicit bias and lack of racial, cultural, and language concordance, which can hamper communication between providers and patients, affecting both patients' adherence to provider recommendations and providers' understanding of the patients' concerns and medical issues.[147] **Health system-level factors** may include gaps in health coverage, lower access to care or quality care (e.g., differences in preconception insurance coverage and duration of postpartum insurance coverage), unequal treatment of different subgroups of pregnant individuals by providers and the healthcare system, ineffective follow up plans, and lack of a unified medical home.[148]

Social issues may include structural consequences of policies, such as redlining[149], which produces disparities in housing security and intergenerational wealth and differential ability to take time off from work or differential access to transportation and social support systems.[150]

Historic and present-day **racism** creates chronic social, structural, and environmental stressors. Allostatic load, or the cumulative physiological effects of racism and stress over the life-course, may explain the paradoxical lack of improvement in pregnancy outcomes despite increasing education and socioeconomic status among some pregnant Black individuals.[151]

Race-based practice may worsen health inequities—Recent editorials argue that race is a poor proxy for human variation and such racially tailored care may worsen health inequities if effective therapies are withheld based on providers' perception of patients' race.[22, 151-153] Several relatively recent hypertension management guidelines endorse race-based practice recommendations for the treatment of hypertension in Black patients,[154, 155] and a recent study concludes that providers seem to be following race-based guidelines.[156] For example, a statement indicates that thiazide diuretics or calcium channel blockers are more effective than renin angiotensin system inhibitors in lowering BP in Black patients.[157] Although contraindicated during pregnancy, renin angiotensin system inhibitors may be used in postpartum individuals with hypertension. While guidelines may change, prior race-based beliefs and practices may persist, and limit use of an effective class of medications, thereby perpetuating disparities in hypertension treatment.

Further understanding of the effects of race, ethnicity, and social determinants of health on healthcare disparities is hampered by numerous factors. Race and ethnicity are social constructs that do not have standard definitions and are not based on biological differences. It is standard in the United States for studies to report race (at least Black/White) and ethnicity (usually just Hispanic/Non-Hispanic), primarily based on the Office of Management and Budget (OMB) categorizations for race and ethnicity.[158] There have been calls for more granular descriptions of race and ethnicity.[159]

Two studies addressed differential outcomes between Black and non-Black women. In these studies, non-Black women were more likely than Black women to return for a BP visit, but home blood pressure monitoring (HBPM) intervention reduced the disparity between races.[69] More such analyses are needed. This would require that studies not only tabulate race but enroll sufficient non-White participants to allow for meaningful analyses by race (and other factors pertinent to social determinants of health, such as access to transportation and childcare).

4.2 Findings in Relation to the Decisional Dilemmas

In regard to home BP monitoring, there is sufficient evidence to support home BP monitoring (as opposed to usual, clinic-based BP monitoring) to increase rates of BP ascertainment (moderate strength of evidence [SoE]). One multicenter randomized controlled trial (RCT) and several implementation studies have found that, while patients successfully used HBPM and adhered to reporting BP measures (moderate SoE), published trials failed to show a significant effect of HBPM on whether patients initiate antihypertensive medications (low SoE).

The available RCTs provide an incomplete assessment of the numerous pharmacological treatment options for postpartum patients with HDP.

Five RCTs enrolled hospitalized patients with acute severe HTN and compared multiple parenteral and or oral medications — intramuscular (IM) hydralazine versus intravenous (IV) methyldopa, IV hydralazine versus IV labetalol, immediate-release oral nifedipine versus placebo, immediate release nifedipine versus diltiazem and oral clonidine versus captopril.

Among the five RCTs that investigated the effect of oral diuretics, two reported comparative benefits. In particular, one relatively large (n = 384, low risk of bias [RoB]) trial recruited postpartum patients with preeclampsia (or gestational HTN) who were discharged with a 5-day course of oral furosemide, or placebo.[69] From this trial, we conclude that furosemide may shorten the duration of postpartum HTN and allow fewer days of antihypertensive treatment (low SoE). A second trial randomized participants to daily furosemide for 5 days (versus no diuretic), and found that participants had lower mean systolic blood pressure on postpartum day 2 and required additional antihypertensive medications at discharge.[61] However, evidence regarding potential effect modifiers, e.g., severity of preeclampsia, presence of edema on physical exam, is insufficient.

Four RCTs evaluated the comparative effectiveness of other (nondiuretic) oral medications for persistent postpartum HTN — timolol versus methyldopa, immediate release nifedipine versus oral alpha-methyldopa, labetalol versus long acting nifedipine, and extended release (XR) nifedipine versus labetalol. Three included studies evaluated the comparative effects of nifedipine and labetalol. In one study, patients treated with long acting nifedipine, versus labetalol, were more likely to achieve BP control and did so more quickly.[71] A second study found that a larger proportion of subjects achieved BP control with the starting dose of labetalol, and experienced fewer headaches than those treated with XR nifedipine.[71] Overall, evidence regarding comparative effectiveness, side-effect profiles, optimal dosage, and relative need for dose escalation is insufficient.

A study of supervised self-titration of antihypertensive medications found persistent small, but possibly important, decreases in diastolic BP (DBP) at 6 months and up to 3 to 4 years, well after participants had stopped antihypertensive medications (insufficient SoE). Two studies have suggested that treatment with a renin angiotensin system inhibitor, in addition to standard treatments for postpartum HTN, may have renal or cardioprotective effects (insufficient SoE).[68, 75] If confirmed, these observations suggest that more stringent blood pressure control and/or prolonged treatment might be useful to decrease the known increased cardiovascular risks subsequent to preeclampsia.

Despite numerous studies, there is sparse evidence to support any particular magnesium sulfate ($MgSO_4$)regimen. Shorter duration treatment regimens (<24 hours) reduce the duration of urinary catheterization and time to ambulation (high SoE), time to breastfeeding (moderate SoE), and time to contact with infant (low SoE) compared with 24-hour regimens (total duration or from delivery). Shorter duration $MgSO_4$ regimens may result in a lower risk of magnesium-

related toxicity (as least as manifested by loss of deep tendon reflexes in patients with preeclampsia with severe features) (low SoE). There is insufficient evidence regarding the effect (or harm) of shorter duration therapy on other outcomes. However, given the low seizure event rate (~ 9/1000), a conservative analysis suggests when given the opportunity for shared decision-making, some patients might trade a somewhat higher odds of seizure for a reduced period of bed rest with shorter duration $MgSO_4$.

4.3 Strengths and Limitations

4.3.1 Strengths and Limitations of the Evidence Base

4.3.1.1 Key Question (KQ) 1: Home BP monitoring

Strengths – One HBPM program (*Heart Safe Motherhood*) has been evaluated in both a randomized clinical trial and in single- and multi-center cohorts. Other similar programs have been evaluated in a nonrandomized comparative study (NRCS) and in large cohorts. A single (not yet published) comparative effectiveness trial supports use of remote communication of results over simple availability of a BP cuff.

Limitations – Comparative studies have enrolled small samples and were not powered to detect differences in patient outcomes. With one exception, studies enrolled participants with an antepartum HDP diagnosis, and enrolled individuals treated in urban, academic medical centers. Results may not be generalizable to all communities and settings. Some of the single-group studies have relatively low enrollment rates that may reflect implementation challenges.

4.3.1.2 KQ 2: Pharmacological Treatment of Postpartum Hypertension

Strengths – Seventeen RCTs have provided limited evidence regarding the comparative effects and harms of antihypertensive medications used in the postpartum period, with some promising findings.

Limitations – With the exception of one study[69] that used HBPM to obtain BP measurements after discharge, most studies report only short-term (while hospitalized) outcomes or are at high risk of attrition bias due to dropouts after hospital discharge. None of the RCTs are powered to detect treatment effect heterogeneity by subgroup (e.g., non-severe vs. preeclampsia with severe features) or to estimate the risk of side-effects. Studies vary regarding choice of medication, initial dose, and dose escalation strategies, resulting in sparse evidence for specific treatment regimens.

4.3.1.3 KQ 3: $MgSO_4$ Treatment Regimens

Strengths – There are a relatively large number of trials that compare alternative regimens, and a small number of traditional regimens (i.e., the Zuspan and Pritchard regimens).

Limitations – We adopted the American College of Obstetricians and Gynecologists (ACOG) criteria[3] defining preeclampsia with severe features, however current international guidelines vary in how they classify the severity of preeclampsia severity and have changed over time.[160] We have excluded studies that include individuals with "mild" preeclampsia, however, the severity of participants in included studies is likely to be somewhat heterogeneous.

There are no well accepted proxies for the outcome of interest (i.e., prevention of seizure in preeclampsia with severe features or recurrent seizure in eclampsia). Given the low observed event rate for seizures, most studies have been small and underpowered, commonly reported no

events in either treatment arm. With a baseline rate of 9 per 1000, a sample size of at least 4768 patients would be needed to have 95% power to reject the null hypothesis that the shorter-duration treatment arm was non-inferior (for differences in favor of standard regimen of up to 0.9 percent) at a significance level of 0.05.[161] Duration of treatment is inconsistently reported; it is sometimes expressed as total duration and sometimes as duration of treatment from delivery. None of the studies describe patient reported outcomes (e.g., overall postpartum experience, breastfeeding success, or opportunity to bond with infant). The majority of studies were performed in non-U.S. settings, severely limiting applicability of our conclusions.

4.3.2 Strengths and Limitations of the Systematic Review Process

Opportunities for meta-analysis were limited by heterogeneous reporting of outcomes. For KQ 3, we hoped to implement a network meta-analysis that would have included data from prior effectiveness studies ($MgSO_4$ versus other treatments). However, the available comparisons were linked in a star-shaped network, such that pairwise comparisons linked alternative regimens with a reference treatment, but not with each other. Estimation of effects for comparisons between non-reference treatments rely on indirect evidence only, and the consistency assumption cannot be checked by comparison with direct evidence, limiting the reliability of results.[162] Given the star topology, low event rates, and population heterogeneity (preeclampsia with severe features versus eclampsia), we were unable to conduct a meaningful network meta-analysis. In lieu of this, we briefly extracted the risk of seizures in effectiveness studies that enrolled individuals with preeclampsia, and the risk of recurrent seizures in studies that enrolled individuals with eclampsia.

We followed contemporary standards for conducting systematic reviews, including engaging multiple stakeholders in KQ development and refinement and careful adherence to recommended methods for literature searching, screening, data extraction, risk of bias assessment, qualitative synthesis, quantitative synthesis, and SoE assessment. During protocol development, we prioritized interventions in consultation with panels of Key Informants. However, due to the varied outcomes reported across studies and the short duration of follow-up for most studies, many of the outcomes were reported in an insufficient number of studies to allow conclusions (or to support meta-analysis), particularly for long-term clinical outcomes.

4.4 Applicability

KQ 1 – The self-titration studies were conducted in England. Given the differences in healthcare systems between the United States and the United Kingdom, the feasibility of self-titration of antihypertensive medications is unclear. In rural areas of the United States with limited internet access[163] and few specialist providers,[164] implementation of home BP monitoring may be particularly helpful, albeit challenging.

KQ 2 – The antihypertensive medications studied in available RCTs may not reflect current practice. Within a given drug class (e.g., calcium channel blockers, diuretics) clinicians may choose different medications (e.g., amlodipine, hydrochlorothiazide) whose effectiveness and comparative effectiveness have not been evaluated in trials performed in the postpartum setting.

KQ 3 –The majority of comparative studies were done in low- and middle-income countries, motivated by resource limitations (e.g., cost, availability of intravenous infusion devices), often enrolling very high risk patients with eclampsia. In the United States, intramuscular administration of $MgSO_4$, which was used in many of the included studies, is used only when IV access cannot be obtained.

4.5 Implications for Clinical Practice

The current pandemic has greatly increased the use of telemedicine during and after pregnancy. Clinicians and health systems providing care to postpartum individuals will need to create care pathways and quality improvement initiatives that incorporate HBPM, identification of severe range postpartum HTN, treatment, and coordination of care for these individuals at risk from worsening or newly elevated BPs.[54]

Care of patients with preeclampsia with severe features at risk for seizures and other serious sequelae should incorporate the best currently available evidence (albeit mostly insufficient and of uncertain applicability to clinical practice in the United States). There may be opportunities for shared decision making between providers and patients, particularly regarding duration of $MgSO_4$ treatment. Given that shorter duration regimens allow patients to ambulate and facilitate earlier contact with their infants, some patients and clinicians may be willing to accept a possible incremental increase in seizure risk with shorter duration regimens.

4.6 Implications for Research

Given the very large disparities in healthcare and health outcomes related to HDP that adversely affect Black and other minority and marginalized individuals in the United States, future research evaluating all topics addressed by this review should focus on reducing these disparities. It is important, though, to recognize that race is a social construct[165] and is, thus, an imprecise and potentially harmful surrogate for genetic variation, and critically challenge race-based beliefs and practices. In addition to requiring inclusion of sufficient numbers of participants from various marginalized groups, research (incorporating both qualitative and quantitative methods) will require community partnerships and diverse multidisciplinary research teams to identify and address the particular needs of marginalized individuals and communities.[166]

KQ 1 – There is a need for large pragmatic trials of postpartum home BP monitoring (such as the Blood Pressure Monitoring in High Risk Pregnancy to Improve the Detection and Monitoring of Hypertension (BUMP) 1 and 2 trials that evaluated use of home BP monitoring during pregnancy for detection of HTN[167] and BP control[168]) that are powered to detect clinical outcomes in the early postpartum period. Effectiveness research is needed to answer the questions – For whom? How often? For how long? Since home BP monitoring involves multiple intervention components, including those related to education and technology (remote monitoring of BP only versus comprehensive telehealth, inclusive of treatment/titration), comparative effectiveness trials are also needed.

With one exception,[45] studies enrolled individuals with an antepartum HDP diagnosis. We agree with the draft recommendation of the related Agency for Healthcare Research and Quality review, "Screening for Hypertensive Disorders in Pregnancy: An Evidence Update for the U.S. Preventive Services Task Force",[169] that research is needed regarding the comparative benefits and harms of universal home BP screening to detect new onset (*de novo*) postpartum preeclampsia in individuals without an HDP diagnosis.

Research is currently in progress (e.g., Physician Optimized Postpartum Hypertension Treatment Trial [POP-HT]; NCT04273854)[170] designed to replicate the finding of the Cairnes 2018 study that suggested supervised self-titration of antihypertensive medication may result in long term improvement in diastolic BP for up to 3 years.

KQ 2 – There is need for comparative trials of other antihypertensive medications (e.g., amlodipine, hydrochlorothiazide) in postpartum individuals. There is a need to identify clinical factors (e.g., heart rate, edema, biomarkers and comorbidities) that predict a favorable response to a particular medication, to compare side effect profiles (e.g., headaches, effects on mood, and impact on breastfeeding) and to consistently report a core outcome set of adverse events.[171] A recent retrospective NRCS, Do 2022[172], that analyzed claims data (and was therefore excluded from our evidence synthesis) reported that readmission for HTN between 5 days and 6 weeks postpartum differed between patients discharged on oral nifedipine or labetalol. The adjusted odds of readmission were significantly higher (adjusted odds ratio 1.63, 95% confidence interval 1.43 to 1.85) for patients discharged on labetalol compared with nifedipine. Future pragmatic RCTs or NRCSs should evaluate whether comparative effectiveness is mediated by improved adherence to medications with longer dosing intervals.

Further study is needed to confirm possible end-organ protective effects of angiotensin II receptor blockers and angiotensin II converting enzyme inhibitors.

KQ 3 – Alternatives to current standard dosing regimens should investigate pharmacokinetic approaches to tailored dosing, particularly for individuals who are lower weight/underweight or overweight/obese. The patient reported impact of $MgSO_4$ treatment should be assessed. Future studies should evaluate whether prognostic models that include clinical features, novel clinical measurements or biomarkers associated with occurrence of seizures may allow for shorter duration $MgSO_4$ therapy.

4.7 Conclusions

HBPM probably improves overall BP ascertainment (determination of BP measures) in the early postpartum period. HBPM may also reduce HTN-related hospital admissions and probably reduces disparities in BP ascertainment between Blacks and non-Blacks. Patients appear to be generally satisfied with HBPM management. The rate of antihypertensive medication initiation is not significantly different in the published comparative studies among those using HBPM. There is insufficient evidence to conclude that HBPM reduces severe maternal morbidity or mortality or reduces racial disparities in clinical outcomes.

Treatment with oral diuretic furosemide may shorten the duration of persistent postpartum HTN in patients with preeclampsia or gestational HTN. Overall, there is insufficient evidence comparing most antihypertensive treatments in patients with postpartum HDP.

Shorter $MgSO_4$ regimens improve several functional outcomes (duration of urinary catheterization, time to ambulation, time to breastfeeding and time to contact with infant). Lower dose, and possibly shorter duration $MgSO_4$ regimens, may lower the risk magnesium toxicity. In patients with eclampsia, lower dose regimens may increase the risk of recurrent seizures, and loading dose only regimens probably increase the risk of recurrent seizures. Evidence from large pragmatic trials, augmented by analysis of real-world data, will be needed to develop MgSO4 regimen(s) that are optimal (i.e., lowest effective dose to minimize unpleasant side effects and potential toxicity, for the shortest effective duration).

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6. Abbreviations and Acronyms

ACOG	American College of Obstetrics and Gynecology
AHRQ	Agency for Healthcare Research and Quality
ANOVA	analysis of variance
BP	Blood pressure
BUMP	Blood Pressure Monitoring in High Risk Pregnancy to Improve the Detection and Monitoring of Hypertension
CDC	Centers for Disease Control and Prevention
CI	confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
COI	conflicts of interest
DTR	deep tendon reflexes
E/E‘	the ratio of the peak early mitral inflow velocity (E) over the early diastolic mitral annular velocity (E′)
EPC	Evidence-based Practice Center
GRADE	Grading of Recommendations, Assessment, Development, and Evaluations
HCUP	Healthcare Cost and Utilization Project
HDP	Hypertensive disorders of pregnancy
HELLP	Hemolysis, elevated liver enzymes, and low platelets syndrome
HBPM	Home blood pressure monitoring
HTN	Hypertension
IM	intramuscular
IV	intravenous
KI	Key Informant
KQ	Key Question
MD	mean difference
Mg	magnesium
N	number of subjects
N/A	not applicable
MD	mean difference
aMD	adjusted mean difference
MAP	mean arterial pressure
$MgSO_4$	Magnesium sulfate
NR	not reported
NRCS	nonrandomized comparative study
OMB	Office of Management and Budget
OR	odds ratio
aOR	adjusted odds ratio
PCORI	Patient-Centered Outcomes Research Institute
PE w/SF	preeclampsia with severe features
POP-HT	Physician Optimized Postpartum Hypertension Treatment Trial
PPHTN	postpartum hypertension
PP	postpartum
PREM	patient-reported experience measure

PROM	patient-reported outcome measure
PROSPERO	International prospective register of systematic reviews
QoL	quality of life
RCT	randomized controlled trial
RD	risk difference
RoB	risk of bias
ROBINS-I	Risk of Bias in Nonrandomized Studies of Interventions
RR	relative risk
aRR	adjusted relative risk
RRR	ratio of relative risks
SBP	systolic blood pressure
SoE	strength of evidence
SR	systematic review
SRDR+	Systematic Review Data Repository Plus
STAMPP HTN	Systematic Treatment And Management of PostPartum Hypertension
TEP	Technical Expert Panel
TOO	Task Order Officer
U.S.	United States
U.K.	United Kingdom
XR	extended release

Appendix Contents

Tables

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Appendix A. Methods

A.1 Details of Study Selection

A.1.1 Search Strategy (Details)

We searched for studies and existing systematic reviews in MEDLINE (via PubMed), the Cochrane Register of Clinical Trials, the Cochrane Database of Systematic Reviews, Embase, and CINAHL. Duplicate citations were removed, when identified, prior to screening. We did not apply language, date, or country restrictions. Search strategies included filters to remove nonhuman studies and articles that are not primary studies, systematic reviews, or clinical practice guidelines.

The searches include MeSH or Emtree terms, along with free-text words, for concepts related to postpartum and peripartum care crossed with terms for hypertension, high blood pressure, preeclampsia, and eclampsia. The PubMed, Embase, Cochrane and CINAHL search strategies are detailed in Appendix A.

During screening of abstracts, we flagged articles that might pertain to the Contextual Question. These may include single group (including registry) studies, qualitative and mixed-methods studies, and narrative reviews that specifically evaluate how race, ethnicity, and social determinants of health influence health disparities in individuals with HDP.

Additional searches were conducted in the ClinicalTrials.gov registry for unpublished study protocols, unpublished study results, and ongoing studies. The reference lists of relevant existing systematic reviews and guidelines were screened for additional eligible studies.

As per our EPC's standard processes to conduct systematic reviews, we took advantage of the machine learning capacities of Abstrackr (http://abstrackr.cebm.brown.edu/) to limit resources spent on abstract screening. We trained the machine learning algorithm as follows: (1) We reviewed the reference lists from known existing systematic reviews and clinical practice guidelines to identify potentially relevant studies for each KQ. (2) We confirmed that this set of potentially relevant citations were successfully captured by our PubMed search. (3) Based on recently published work by Sampson et. al.,[1] we selected the top 500 articles from our search using PubMed's best-match algorithm. (4) The articles from steps (1) and (3) were entered into Abstrackr and screened by all team members, with resolution of all conflicts in conference. (5) Subsequently, citations found by the full literature searches will be added to the already-screened citations in Abstrackr, and abstract screening will continue in duplicate, with conflicts adjudicated in conference or by a third screener. (6) As screening progressed, the pretrained Abstrackr machine learning algorithm will continue to adapt and will sort the list of unscreened abstracts such that the most potentially relevant articles are presented first. This process will make screening more efficient and will enable us to capture the preponderance of relevant articles relatively early in the abstract screening process. (7) We will stop double screening when the predicted likelihood of the remaining unscreened papers being relevant is very low. We typically use a threshold for the prediction score of the unscreened citations of 0.40 (this threshold is based on experience with several dozen screening projects and an analysis in preparation for publication but may be lowered depending on whether we continue to find eligible abstracts near the threshold). To confirm that the selected prediction score threshold is appropriate for this literature base, when the maximum prediction score is <0.40, we will screen at least 400 additional consecutive citations (this sample size is chosen because the upper 97.5%

confidence interval bound for a proportion of 0/400 is less than 1%). If any of the 400 citations are screened in (at the abstract level), we will repeat the process (restart counting an additional 400 citations) until we have rejected at least 400 consecutive citations.

A Supplemental Evidence And Data for Systematic review (SEADS) portal will be available for this review. Additional articles suggested to us from any source, including peer and public review, will be screened applying identical eligibility criteria.

Potentially relevant citations will be retrieved in full text. Non-English language articles will be screened, and data extracted from full text, either by readers of the relevant languages or after translation via Google Translate (https://translate.google.com/) if possible. Searches were updated on December 1st, 2022 during the draft report's public posting period.

We also ran a search of the ClinicalTrials.gov registry for records describing planned, ongoing, or completed studies. Unpublished conference abstracts were cross-checked for records with results in ClinicalTrials.gov.

Additional articles suggested to us in any language from any source, during peer and public review, will be screened applying identical eligibility criteria.

A.1.1.1 PubMed Search

(((((postpartum OR post-partum OR postnatal OR post-natal OR puerperal OR puerperium OR postdelivery OR post-delivery OR "post delivery" OR Peripartum OR Peri-partum OR "Perinatal Care"[Mesh] OR "Postnatal Care"[Mesh] OR "Peripartum Period"[Mesh] OR breastfeeding OR "breast feeding" OR lactation OR "Breast Feeding"[Mesh] OR "Lactation"[Mesh]) AND (Hyperten* OR "Hypertension"[Mesh] OR "high blood pressure" OR pre-eclampsia OR eclampsia OR "Pre-Eclampsia"[Mesh] OR "Eclampsia"[Mesh] OR HELLP syndrome OR "HELLP Syndrome"[Mesh] OR "Antihypertensive Agents"[Mesh] OR Antihypertensive* OR Anti-hypertensive* OR "Anti hypertensive*"))) OR (((postpartum OR post-partum OR postnatal OR post-natal OR puerperal OR puerperium OR postdelivery OR post-delivery OR "post delivery" OR Peripartum OR Peri-partum OR "Perinatal Care"[Mesh] OR "Postnatal Care"[Mesh] OR "Peripartum Period"[Mesh] OR "Prenatal Care"[Mesh] OR "Pregnancy"[Mesh] OR "Pregnant Women"[Mesh] OR "Pregnancy Trimesters"[Mesh] OR pregnancy OR pregnant OR antenatal OR ante-natal OR pregnancies OR prenatal OR pre-natal OR obstetrics OR gestation OR breastfeeding OR "breast feeding" OR lactation OR "Breast Feeding"[Mesh] OR "Lactation"[Mesh]) AND (Hyperten* OR "Hypertension"[Mesh] OR "high blood pressure" OR pre-eclampsia OR eclampsia OR HELLP syndrome OR "Hypertension, Pregnancy-Induced/physiopathology"[MeSH]) AND (Magnesium OR "Magnesium Sulfate"[Mesh]))))) OR (((eclampsia OR "Eclampsia"[Mesh] OR HELLP syndrome OR "HELLP Syndrome"[Mesh]) AND ((home) AND ("blood pressure" OR "blood-pressure") AND monitoring)))) NOT (("address"[pt] OR "autobiography"[pt] OR "bibliography"[pt] OR "biography"[pt] OR "congress"[pt] OR "dictionary"[pt] OR "directory"[pt] OR "festschrift"[pt] OR "government publication"[pt] OR "historical article"[pt] OR "interview"[pt] OR "case reports"[pt] OR "Cross-Sectional Studies"[Mesh] OR "Focus Groups"[Mesh] OR ("Review"[pt] NOT ("Systematic Review" OR "scoping review" OR "clinical trial" OR "Randomized Controlled Trial")) OR "lecture"[pt] OR "legal case"[pt] OR "legislation"[pt] OR "news"[pt] OR "newspaper article"[pt] OR "patient education handout"[pt] OR "periodical index"[pt] OR "in vitro techniques"[mh] OR "introductory journal article"[pt] OR "Editorial"[pt] OR ("Animals"[Mesh] NOT "Humans"[Mesh]) OR rats[tw] OR rat[tw] OR cow[tw] OR cows[tw] OR chicken*[tw] OR

horse[tw] OR horses[tw] OR mice[tw] OR mouse[tw] OR bovine[tw] OR sheep[tw] OR ovine[tw] OR murinae[tw] OR cats[tw] OR cat[tw] OR dog[tw] OR dogs[tw] OR rodent[tw]))

A.1.1.2 Embase Search

No.	Query
#88.	#75 AND #87
#87.	#85 NOT #86
#86.	(book OR conference) AND paper OR editorial OR letter OR review OR survey OR qualitative
#85.	#84 NOT #83
#84.	#76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82
#83.	animal NOT human
#82.	random OR placebo OR 'single blind' OR 'double blind' OR 'triple blind'
#81.	'randomized controlled trial'
#80.	'follow up'
#79.	'retrospective study'
#78.	'prospective study'
#77.	'longitudinal study'
#76.	'cohort analysis'
#75.	#74 AND ('Article'/it OR 'Conference Abstract'/it OR 'Letter'/it)
#74.	#63 OR #73
#73.	#62 AND #71 AND #72
#72.	#53 OR #64 OR #65 OR #66 OR #67 OR #68
#71.	#69 OR #70
#70.	'magnesium sulfate'
#69.	'magnesium'
#68.	gestation
#67.	'obstetrics'
#66.	prenatal
#65.	antenatal
#64.	'pregnant woman'
#63.	#53 AND #62
#62.	OR/#54-61
#61.	'antihypertensive agent'
#60.	'hellp syndrome'
#59.	'eclampsia'
#58.	'pre-eclampsia'
#57.	'preeclampsia'
#56.	'high blood pressure'
#55.	hypertensive
#54.	'hypertension'
#53.	OR/#45-52
#52.	'lactation'
#51.	'breast feeding'
#50.	'breastfeeding'
#49.	'perinatal period'

#48. peripartum
#47. 'puerperium'
#46. 'postnatal care'
#45. 'postpartum'/exp OR postpartum

A.1.1.3 Cochrane Search

#1 ((address:pt OR autobiography:pt OR bibliography:pt OR biography:pt OR congress:pt OR dictionary:pt OR directory:pt OR festschrift:pt OR "government publication":pt OR "historical article":pt OR interview:pt OR "case reports":pt OR [mh "Cross-Sectional Studies"] OR [mh "Focus Groups"] OR (Review:pt NOT ("Systematic Review" OR "scoping review" OR "clinical trial" OR "Randomized Controlled Trial")) OR lecture:pt OR "legal case":pt OR legislation:pt OR news:pt OR "newspaper article":pt OR "patient education handout":pt OR "periodical index":pt OR [mh "in vitro techniques"] OR "introductory journal article":pt OR Editorial:pt OR ([mh Animals] NOT [mh Humans]) OR rats:ti,ab,kw OR rat:ti,ab,kw OR cow:ti,ab,kw OR cows:ti,ab,kw OR chicken*:ti,ab,kw OR horse:ti,ab,kw OR horses:ti,ab,kw OR mice:ti,ab,kw OR mouse:ti,ab,kw OR bovine:ti,ab,kw OR sheep:ti,ab,kw OR ovine:ti,ab,kw OR murinae:ti,ab,kw OR cats:ti,ab,kw OR cat:ti,ab,kw OR dog:ti,ab,kw OR dogs:ti,ab,kw OR rodent:ti,ab,kw)) 33182

#2 (postpartum OR post-partum OR postnatal OR post-natal OR puerperal OR puerperium OR postdelivery OR post-delivery OR "post delivery" OR Peripartum OR Peri-partum OR [mh "Perinatal Care"] OR [mh "Postnatal Care"] OR [mh "Peripartum Period"] OR breastfeeding OR "breast feeding" OR lactation OR [mh "Breast Feeding"] OR [mh Lactation]) 25616

#3 Hypertension OR [mh Hypertension] OR "high blood pressure" OR pre-eclampsia OR eclampsia OR "HELLP syndrome" OR [mh "HELLP Syndrome"] OR [mh "Antihypertensive Agents"] OR Antihypertensive OR Anti-hypertensive 75500

#4 #2 AND #3 1819

#5 postpartum OR post-partum OR postnatal OR post-natal OR puerperal OR puerperium OR postdelivery OR post-delivery OR "post delivery" OR Peripartum OR Peri-partum OR [mh "Perinatal Care"] OR [mh "Postnatal Care"] OR [mh "Peripartum Period"] OR [mh "Prenatal Care"] OR [mh Pregnancy] OR [mh "Pregnant Women"] OR [mh "Pregnancy Trimesters"] OR pregnancy OR pregnant OR antenatal OR ante-natal OR pregnancies OR prenatal OR pre-natal OR obstetrics OR gestation OR breastfeeding OR "breast feeding" OR lactation OR [mh "Breast Feeding"] OR [mh Lactation] 103532

#6 Hypertension OR [mh Hypertension] OR "high blood pressure" OR pre-eclampsia OR eclampsia OR "HELLP syndrome" 71183

#7 (Magnesium OR [mh "Magnesium Sulfate"]) 8480

#8 #5 AND #6 AND #7 498

#9 (eclampsia OR [mh Eclampsia] OR "HELLP syndrome" OR [mh "HELLP Syndrome"]) AND ((home) AND ("blood pressure" OR blood-pressure) AND monitoring) 60

#10 #4 OR #8 OR #9 2141

#11 #10 NOT #1 2106

A.1.1.4 CINAHL Search

(((((postpartum OR post-partum OR postnatal OR post-natal OR puerperal OR puerperium OR postdelivery OR post-delivery OR "post delivery" OR Peripartum OR Peri-partum OR (MH "Perinatal Care"+) OR (MH "Postnatal Care"+) OR (MH "Peripartum Period"+) OR

breastfeeding OR "breast feeding" OR lactation OR (MH "Breast Feeding"+) OR (MH Lactation+)) AND (Hyperten* OR (MH Hypertension+) OR "high blood pressure" OR pre-eclampsia OR eclampsia OR (MH Pre-Eclampsia+) OR (MH Eclampsia+) OR "HELLP syndrome" OR (MH "HELLP Syndrome"+) OR (MH "Antihypertensive Agents"+) OR Antihypertensive* OR Anti-hypertensive* OR "Anti hypertensive*"))) OR (((postpartum OR post-partum OR postnatal OR post-natal OR puerperal OR puerperium OR postdelivery OR post-delivery OR "post delivery" OR Peripartum OR Peri-partum OR (MH "Perinatal Care"+) OR (MH "Postnatal Care"+) OR (MH "Peripartum Period"+) OR (MH "Prenatal Care"+) OR (MH Pregnancy+) OR (MH "Pregnant Women"+) OR (MH "Pregnancy Trimesters"+) OR pregnancy OR pregnant OR antenatal OR ante-natal OR pregnancies OR prenatal OR pre-natal OR obstetrics OR gestation OR breastfeeding OR "breast feeding" OR lactation OR (MH "Breast Feeding"+) OR (MH Lactation+)) AND (Hyperten* OR (MH Hypertension+) OR "high blood pressure" OR pre-eclampsia OR eclampsia OR "HELLP syndrome" OR (MH "Hypertension, Pregnancy-Induced/physiopathology"+)) AND (Magnesium OR (MH "Magnesium Sulfate"+))))) OR (((eclampsia OR (MH Eclampsia+) OR "HELLP syndrome" OR (MH "HELLP Syndrome"+)) AND ((home) AND ("blood pressure" OR blood-pressure) AND monitoring)))) NOT ((PT address OR PT autobiography OR PT bibliography OR PT biography OR PT congress OR PT dictionary OR PT directory OR PT festschrift OR PT "government publication" OR PT "historical article" OR PT interview OR PT "case reports" OR (MH "Cross-Sectional Studies"+) OR (MH "Focus Groups"+) OR (PT Review NOT ("Systematic Review" OR "scoping review" OR "clinical trial" OR "Randomized Controlled Trial")) OR PT lecture OR PT "legal case" OR PT legislation OR PT news OR PT "newspaper article" OR PT "patient education handout" OR PT "periodical index" OR (MH "in vitro techniques"+) OR PT "introductory journal article" OR PT Editorial OR ((MH Animals+) NOT (MH Humans+)) OR rats OR rat OR cow OR cows OR chicken* OR horse OR horses OR mice OR mouse OR bovine OR sheep OR ovine OR murinae OR cats OR cat OR dog OR dogs OR rodent))

A.1.1.5 ClinicalTrials.gov Search

(postpartum OR post-partum OR postnatal OR post-natal OR puerperal OR puerperium OR postdelivery OR post-delivery OR Peripartum OR Peri-partum) AND (Hypertension OR high blood pressure OR pre-eclampsia OR eclampsia OR HELLP OR Antihypertensive)

A.1.2 Inclusion and Exclusion Criteria (Details)

The specific eligibility criteria provided below have been refined based on discussions with a panel of Key Informants (KIs) and a Technical Expert Panel (TEP).

A.1.2.1 Key Question 1 (Home BP Monitoring)

Population

- Postpartum individuals (with or without a prior HDP diagnosis)

Modifiers/Subgroups of interest

- Subgroups defined by ACOG HDP classification (some of which may arise *de novo* in the postpartum period)
    - chronic HTN
    - gestational HTN

    - preeclampsia (may be superimposed on chronic HTN)
    - preeclampsia with severe features (as defined by study authors)
    - *de novo* HTN postpartum
- Subgroups defined by BP diagnostic threshold(s)
- Race, ethnicity
- Maternal age, parity, singleton/multiple pregnancy, delivery (e.g., cesarean versus vaginal delivery, preterm versus term)
- Co-occurring disorders (e.g., obesity, diabetes)
- Subgroups defined by potential indicators of social determinants of health (e.g., insurance coverage, English proficiency, income, educational attainment)
- Access to technology (e.g., broadband internet, smartphone)

Interventions and Intervention Components

- Postpartum home BP monitoring interventions
    - Electronic, digital monitors, any
    - With or without web-based connectivity and communication
    - With or without education or training in use of monitor
    - With or without validation of accuracy of patient's monitor
- *Exclude: Ambulatory BP monitoring (e.g.,24- or 48-hour continuous monitoring)*
- *Exclude: Monitors with manual inflation and auscultation*
- *Exclude: BP monitoring only by third parties, such as home health aides, visiting nurses*
- *Exclude: Very limited use of monitoring (e.g., single reading or single day)*
- *Exclude: Use of device only in laboratory or clinic setting*

Comparators

- No home BP monitoring (e.g., usual care with clinic-only BP monitoring)
- Alternative non-clinic-based BP monitoring approaches (e.g., kiosks, pharmacy-based BP monitoring, home health aide visits)
- Alternative education modalities about self-monitoring BP (e.g., demonstration of correct use, confirmation of appropriate cuff size)
- Alternative home BP monitor characteristics (e.g., direct transmission of results, prompts for communication of symptoms)
- Alternative home BP monitoring regimen (e.g., BP measurement frequency, duration)
- Alternative instructions for when to communicate results immediately (e.g., different BP threshold alerts)
- Alternative mode of communicating results (e.g., during clinic visit, automatic web-based, via text/email/portal/phone)
- Alternative clinician feedback processes
- No use of validation of accuracy of patient's monitor

Outcomes (prioritized outcomes are indicated with an asterisk and are in bold font)

- Blood pressure
    - **Ascertainment of elevated BP or new onset HDP***
        - Time to clinical recognition of elevated BP
    - **Treatment***

        - Initiation or discontinuation of antihypertensive medications
        - Increase or decrease in dose (or number) of antihypertensive medications
        - BP control (e.g., BP normalization)
    - Documentation of BP after discharge
    - Recognition of white coat HTN
- Severe maternal outcomes
    - **Maternal mortality, including pregnancy-related mortality***
    - **Severe maternal morbidity*** (e.g., **stroke***, eclampsia, pulmonary edema)
- Patient reported outcomes
    - Patient reported experience measures (PREMs) for example
        - **Satisfaction with postpartum care***
        - Ease of access to care
        - Quality of communication
        - Support to manage HTN
        - Patient Reported Experience Measure of Obstetric racism (PREM-OB Scale)
    - Patient reported outcome measures (PROMs), for example
        - **Global Quality of life***, e.g., SF-36
        - Psychosocial distress
            - **Anxiety***, e.g., State-Trait Anxiety Inventory (STAI)
            - **Depression***, e.g., Edinburgh Postnatal Depression Score (EPDS)
- Healthcare utilization
    - **Length of postpartum hospital stay***
    - **Unplanned obstetrical triage area or clinic visits***
    - **Emergency department visits***
    - **Re-hospitalization after discharge***
- **Reduction of health disparities*** (increase in disparities included under *Harms*)
- Other Harms
    - **Generation or exacerbation of health disparities***
    - Anxiety associated with use of monitoring technology

Study Design

- Comparative studies (comparisons of different interventions or regimens)
    - Randomized controlled trials (N ≥10 per group)
    - Nonrandomized comparative studies (prospective or retrospective) that use statistical techniques (e.g., regression adjustment, propensity score matching, inverse probability weighting) to reduce bias due to confounding)
    - Single-group (noncomparative) studies (N ≥ 50 participants offered home blood pressure monitoring)
- Any publication language (unless cannot be translated)
- <u>*Exclude*</u>
    - Case-control studies
    - Claims database analyses
    - Feasibility studies (N < 50 participants offered home blood pressure monitoring)
    - Device validation studies (not including validation of patients' monitors in the clinic)

- Qualitative studies
- Conference abstracts prior to 2020 (without subsequent, eligible peer-reviewed publication)

Timing

- Intervention: Day of birth through 1 year postpartum
  - Self-monitoring may start antenatal, in hospital, or postpartum, but must continue postpartum
- Outcomes: Any duration of postpartum follow up.

Setting

- Outpatient postpartum management (although training and initiation may start in hospital or at clinic)
- Any publication date
- Any country

A.1.2.2 Key Question 2 (Treatment of HDP)

Population

- Postpartum individuals with diagnosed HDP (whether diagnosed antenatal, peripartum, or postpartum)

Modifiers/Subgroups of interest

- Subgroups defined by ACOG HDP classification (these may arise *de novo* in the postpartum period)
  - chronic HTN
  - gestational HTN
  - preeclampsia (may be superimposed on chronic HTN)
  - preeclampsia with severe features (as defined by study authors)
  - *de novo* HTN postpartum
- Subgroups defined by BP thresholds/categories
- Race, ethnicity
- Maternal age, parity, singleton/multiple pregnancy, mode of delivery (e.g., cesarean versus vaginal delivery, preterm versus term)
- Co-occurring disorders (e.g., obesity, diabetes)
- Subgroups defined by potential indicators of social determinants of health (e.g., insurance coverage, English proficiency, income, educational attainment)
- Use of home monitoring

Interventions

- Pharmacological treatments for HTN or HDP administered postpartum
  - Antihypertensive medications (single or combination therapies)
  - Loop diuretics (alone or in combination with antihypertensive medications)
- *Exclude:*
  - *Medication not available for use in the U.S.*
  - *Nonpharmacological treatments (e.g., uterine curettage)*

- *Corticosteroids (e.g., for HELLP)*
- *Interventions to prevent preeclampsia (e.g., low-dose aspirin)*
- *Treatments not used to treat HDP (e.g., NSAIDs)*
- *Behavioral modification (e.g., diet, exercise)*
- *Non-medical interventions (e.g., traditional medicine, complementary and alternative medicine, meditation, mindfulness)*

Comparators

- Alternative specific treatments (e.g., alternative antihypertensive medication(s) or combinations of medications, alternative diuretic)
- Alternative treatment regimen (e.g., alternative dose, duration of treatment)
- Alternative blood pressure targets
- No treatment (or placebo)
- *Exclude: Excluded interventions*

Outcomes (prioritized outcomes are indicated with an asterisk and are in bold font)

- Intermediate outcomes
  - **Blood pressure control***
  - Measures of end-organ function
    - Cardiovascular measures (e.g., echocardiographic measurements of diastolic function and hypertrophy)
    - Kidney function (e.g., estimated glomerular filtration rate)
- Severe maternal outcomes
  - **Maternal mortality, including pregnancy-related mortality***
  - **Severe maternal morbidity*** (e.g., **stroke*,** eclampsia, pulmonary edema)
- Patient reported outcomes
  - Patient reported experience measures (PREMs), for example
    - **Satisfaction with postpartum care***
    - Ease of access to care
    - Quality of communication
    - Support to manage HTN
  - Patient reported outcome measures (PROMs), for example
    - **Global Quality of life***, e.g., SF-36
    - Maternal-neonatal bonding, e.g., Postpartum Bonding Questionnaire
    - Psychosocial distress
      - **Anxiety***, e.g., State-Trait Anxiety Inventory (STAI)
      - **Depression***, e.g., Edinburgh Postnatal Depression Score (EPDS)
- Healthcare utilization
  - **Length of postpartum hospital stay***
  - **Unplanned obstetrical triage area or clinic visits***
  - **Emergency department visits***
  - **Re-hospitalization after discharge***
- Infant health outcomes
  - **Breastfeeding outcomes (e.g., initiation, success, duration)***
- **Reduction of health disparities*** (increase in disparities included under *Harms*)

- Harms
    - **Severe adverse events*** (e.g., electrolyte abnormalities, severe hypotension)
    - **Infant morbidities*** (e.g., hypotension, other symptoms attributed to medication exposure via breast milk)
    - **Generation or exacerbation of health disparities***
    - Adverse interactions with other medications

Study Design

- Comparative studies (comparisons of different interventions or regimens)
    - Randomized controlled trials (N ≥10 per group)
    - Nonrandomized comparative studies (prospective or retrospective) that use statistical techniques (e.g., regression adjustment, propensity score matching, inverse probability weighting) to reduce bias due to confounding
- Any publication language (unless cannot be translated)
- *Exclude*
    - Single group (noncomparative) studies
    - Case-control studies
    - Claims database analyses
    - Feasibility studies
    - Qualitative studies
    - Conference abstracts

Timing

- Intervention: Day of birth up to 1 year postpartum
    - Intervention may start antenatal, in hospital, or postpartum, but must continue postpartum
- Outcomes: Any (postpartum)

Setting

- Outpatient, non-acute management (treatment may start inpatient)
- Any publication date
- Any country

A.1.2.3 Key Question 3 ($MgSO_4$ for Preeclampsia With Severe Features)

Population

- Individuals who have preeclampsia with severe features (as defined by study authors) during the peripartum period (prior to and/or after delivery)
- *Exclude: Pregnant patients who are treated with $MgSO_4$ with the goal of suppressing premature labor, for fetal neuroprotection, or for other reasons*

Modifiers/Subgroups of interest

- Race, ethnicity
- Maternal age, parity, singleton/multiple pregnancy, mode of delivery (e.g., cesarean versus vaginal delivery, preterm versus term)

- Co-occurring disorders (e.g., obesity, diabetes)
- Subgroups defined by potential indicators of social determinants of health (e.g., insurance coverage, English proficiency, income, educational attainment)
- Timing of $MgSO_4$ administration or onset of preeclampsia with severe features with respect to delivery
    - Antepartum
    - Intrapartum
    - Postpartum
- Individuals with reduced kidney function

Interventions

- Peripartum $MgSO_4$ administration
    - Any dose, route (except oral), timing, duration of treatment, concomitant treatment, or regimen
- *Exclude:* Oral magnesium supplementation

Comparators

- Alternative $MgSO_4$ regimens
    - Different criteria for initiation of treatment
    - Different criteria for stopping (or continuing) treatment
    - Different criteria for altering dosing during treatment
    - Different loading dose
    - Different planned total dose
    - Different route
    - Different planned duration of treatment
    - Tailored interventions based on pharmacokinetic monitoring (i.e., based on serum Mg levels)
    - Combined treatment with antihypertensive medications (including regimens with alternative antihypertensive medications)
    - Other variations in regimens
- Exclude: No $MgSO_4$ treatment (either placebo, no treatment, or non-$MgSO_4$ comparators)
    - Except retain RCTs with placebo, no treatment, or non-$MgSO_4$ comparators and NRCSs comparing $MgSO_4$ with no $MgSO_4$ for postpartum preeclampsia with severe features
      These may be included in network meta-analyses to indirectly compare alternative $MgSO_4$ regimens.

Outcomes (prioritized outcomes are indicated with an asterisk and are in bold font)

- Severe maternal health outcomes
    - **Maternal mortality, including pregnancy-related mortality***
    - **Severe maternal morbidity* (e.g., eclampsia***, stroke**)**
- Newborn/child outcomes
    - **Infant morbidities*** (e.g., respiratory depression, Apgar score)
    - **Breastfeeding outcomes* (e.g., initiation, success, duration)**
    - Fetal/neonatal mortality

    - Cognitive function
- Healthcare utilization and functional status
    - Length of postpartum hospital stay
    - Time to ambulation
- Patient reported outcomes
    - Patient reported experience measures (PREMs) , for example
        - **Satisfaction with care***
        - Quality of communication
        - Support to manage preeclampsia treatment
    - Patient reported outcome measures (PROMs), for example
        - **Global Quality of life*,** e.g., SF-36
        - **Specific to postpartum population***, e.g., Mother-Generated Index, Functional Status After Childbirth scales
        - Psychosocial distress
            - **Anxiety***, e.g., State-Trait Anxiety Inventory (STAI)
            - **Depression***, e.g., Edinburgh Postnatal Depression Score (EPDS)
            - **Stress***, e.g., Impact of Event Scale
        - **Maternal-neonatal bonding*,** e.g., Postpartum Bonding Questionnaire
- **Reduction of health disparities*** (increase in disparities included under *Harms*)
- Maternal harms/adverse events
    - **Magnesium-related toxicity*** (respiratory depression, loss of reflexes, reduced urine output, need for calcium infusion)*
    - **Other clinically important adverse events*** (e.g., hypotension, neuromuscular blockade)
    - **Adverse drug interactions*** (e.g., with antihypertensive medications)
    - **Generation or exacerbation of health disparities***
    - Other serious (e.g., severe flushing)

Study Design

- Comparative studies (comparisons of different interventions)
    - Randomized controlled trials N ≥10 per group
        - Comparisons between $MgSO_4$ and placebo/no treatment or non-$MgSO_4$ treatments must be randomized (for potential network meta-analyses)
    - Nonrandomized comparative studies (prospective or retrospective) that use statistical techniques (e.g., regression adjustment, propensity score matching, inverse probability weighting) to reduce bias due to confounding
- Any publication language (unless cannot be translated)
- <u>*Exclude*</u>
    - Single group (noncomparative) studies
    - Case-control studies
    - Claims database analyses
    - Feasibility studies
    - Qualitative studies
    - Conference abstracts

Timing

- Intervention: Peripartum (antenatal, during delivery hospitalization, postpartum)
- Outcomes: Any

Setting

- Inpatient management
- Any publication date
- Any country

A.1.2.4. Contextual Question

The Contextual Question will not be addressed by a formal systematic review. However, articles meeting the following criteria will be reviewed for potential inclusion.

Population

- Same as for KQs 1, 2, and 3

Interventions/Comparators

- Same as for KQs 1, 2, and 3

Outcomes

- Health disparities across populations defined by race, ethnicity, or social determinants of health (as discussed or described by authors)

Study Design

- Any, including comparative, noncomparative (single group), qualitative studies, surveys, claims or other database analyses, narrative reviews

A.2 Data Extraction and Data Management (Details)

We extracted data from eligible primary studies into the Systematic Review Data Repository-Plus (https://srdrplus.ahrq.gov). For each study, one researcher extracted and entered data, which were confirmed by a second, independent researcher. Each individual study that was reported in multiple articles was extracted as a single record. In the instance where two studies were reported within a single article, each study was extracted separately.

For each study, we extracted article-identifying information, study design features, funding source, population characteristics and sample sizes, intervention and comparator names and descriptions, and relevant outcomes and their definitions.

A.3 Assessing Applicability

For each KQ, we assessed the applicability of the included studies primarily based on the studies' eligibility criteria and their included participants, specifically related to such factors as age, race/ethnicity, and risk factors for postpartum complications. These were qualitatively compared with typical distributions of these factors among postpartum individuals in the United States.

A.4 Peer Review and Public Commentary

Experts in obstetrics and gynecology, maternal and fetal medicine, family medicine, social work, health services research, clinical practice guidelines, and individuals representing other stakeholder and user communities are being invited to provide external peer review of this SR. The Agency for Healthcare Research and Quality (AHRQ) and an Associate Editor from a fellow Evidence-based Practice Center were also invited to provide comments. The draft report was posted on the AHRQ Website to elicit public comment for a period of 45 days. We have addressed all reviewer and public comments, revising the text as appropriate. A summary of peer review comments and a disposition of public comments table will be posted on the Effective Health Care website (https://effectivehealthcare.ahrq.gov).

A.5 Abbreviations

ACOG	American College of Obstetrics and Gynecology
AHRQ	Agency for Healthcare Research and Quality
BP	blood pressure
BMI	body mass index
CI	confidence interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
COI	conflicts of interest
E	eclampsia
EPDS	Edinburgh Postnatal Depression Score
EPC	Evidence-based Practice Center
HBPM	home blood pressure monitoring
HDP	hypertensive disorders of pregnancy
HELLP	hemolysis, elevated liver enzymes, low platelet count
HTN	hypertension
ICTR	International Clinical Trials Registry Platform
IQR	interquartile range
IM	intramuscular
IV	intravenous
KI	Key Informant
KQ	Key Question
MgSO4	Magnesium sulfate
MD	mean difference
MeSH	Medical Subject Headings
Mg	magnesium
N	sample size
N/A	not applicable
NCT	ClinicalTrials.gov identifier prefix
NR	not reported
NRCS	nonrandomized comparative study
NSAID	non-steroidal anti-inflammatory drug
OB/GYN	obstetrics/gynecology (specialty)
aOR	adjusted odds ratio
OR	odds ratio

PACTR	Pan African Clinical Trials Registry
PE	preeclampsia
PMID	PubMed identifier
PO	*per os* (administered orally)
PP	postpartum
PREM	Patient Reported Experience Measures
PREM-OB	Patient Reported Experience Measure of Obstetric racism
PROM	Patient Reported Outcome Measures
q(dosing interval)h	every (dosing interval) hours
RCT	randomized controlled trial
RoB	risk of bias
ROBINS-I	Risk of Bias in Nonrandomized Studies of Interventions
aRR	adjusted relative risk
RR	relative risk
SD	standard deviation
SF-36	36-item Short form Survey (Rand Corporation)
SEADS	Supplemental Evidence And Data for Systematic review portal
SoE	strength of evidence
sPE	severe preeclampsia
SR	systematic review
SRDR+	Systematic Review Data Repository Plus
STAI	State-Trait Anxiety Inventory
TOO	Task Order Officer
U.S.	United States

Appendix B. List of Excluded Studies

The 286 excluded articles and records, along with reasons for exclusion, are summarized in Appendix Table B–1. Details on exclusion reasons and numbers are given in Figure C–1, Flow diagram for studies.

Table B–1. Excluded articles and records with reasons for exclusion

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
1	Abbade	2006	CN-00582363 (cochrane)	Zuspan's scheme versus alternative scheme of magnesium sulphate to prevent or to treat eclampsia: comparison of magnesium serum concentrations	*Hypertension in pregnancy*	Abstract, subsequently published
2	Abbade	2010	20132023	Zuspan's scheme versus an alternative magnesium sulfate scheme: Randomized clinical trial of magnesium serum concentrations	*Hypertens Pregnancy*	No outcomes of interest
3	Abbate	2021	148435156 (cinahl)	911 Readmission for hypertension among women in a postpartum remote blood pressure monitoring program	*American Journal of Obstetrics & Gynecology*	Abstract, 2020 or later, not yet published
4	Agarwal	2019	L628473806 (embase)	Modification of Pritchard regimen of magnesium sulphate for the conditions of a developing country	*BJOG: An International Journal of Obstetrics and Gynaecology*	Abstract prior to 2020, unpublished
5	Alkan	2006	16761542	Effects of postpartum uterine curettage on maternal well-being in severe preeclamptic patients	*Clin Exp Obstet Gynecol*	Not an intervention of interest
6	Amorim	2015	L72206003 (embase)	Clonidine compared with captopril for severe postpartum hypertension	*Obstetrics and Gynecology*	Abstract, subsequently published
7	Añez-Aguayo	2020	29804488	Dexamethasone in HELLP syndrome: experience in Bolivia	*Journal of Maternal-Fetal & Neonatal Medicine*	Not an intervention of interest
8	Appleton	1991	1951552	Magnesium sulfate versus phenytoin for seizure prophylaxis in pregnancy-induced hypertension	*Am J Obstet Gynecol*	Not population of interest
9	Arkerson	2022	CN-02421802 (cochrane)	Pregnancy-Related Hypertension: adherence to a New Type of Monitoring (PHANTOM)	*Obstetrics and gynecology*	Abstract, 2020 or later, not yet published

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
10	Ascarelli	1998	9790377	Individually determined postpartum magnesium sulfate therapy with clinical parameters to safely and cost-effectively shorten treatment for pre-eclampsia.	*American journal of obstetrics and gynecology*	Not a comparison of interest
11	Atkinson	1995	7485324	Does magnesium sulfate affect the length of labor induction in women with pregnancy-associated hypertension?	*Am J Obstet Gynecol*	No outcomes of interest
12	Bank	2021	148435255 (cinahl)	1010 Reduction of racial disparities in readmission associated with a standardized postpartum hypertension management protocol	*American Journal of Obstetrics & Gynecology*	Abstract, 2020 or later, not yet published
13	Barrilleaux	2005	15802415	Postpartum intravenous dexamethasone for severely preeclamptic patients without hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome: a randomized trial	*Obstet Gynecol*	Not an intervention of interest
14	Beatty	2018	L622555614 (embase)	Timely discharge: Oral nifedipine is superior to labetalol for postpartum bp control in patients with preeclampsia	*Obstetrics and Gynecology*	Abstract prior to 2020, unpublished
15	Begum	2000	10996685	Reducing maternal mortality from eclampsia, using magnesium sulphate	*Eur J Obstet Gynecol Reprod Biol*	NRCS (no adjustment)
16	Begum	2002	12466730	Management of hypertensive emergencies of pregnancy by hydralazine bolus injection vs continuous drip--a comparative study	*Medscape Womens Health*	Not population of interest
17	Begum	2002	CN-00370384 (cochrane)	Loading dose vs standard regime of magnesium sulphate in the management of eclampsia - a randomized trial	*XVI FIGO world congress of obstetrics & gynecology (book 2); 2000 sept 3-8; washington dc, USA*	Duplicate
18	Belfort	1992	1542820	Nisoldipine--a new orally administered calcium antagonist used in the treatment of severe postpartum pregnancy-induced hypertension. Preliminary results	*S Afr Med J*	Not a comparative study
19	Belfort	1999	10454691	Change in estimated cerebral perfusion pressure after treatment with nimodipine or magnesium sulfate in patients with preeclampsia	*Am J Obstet Gynecol*	Less than 10 participants per group
20	Boatin	2021	33579213	Wireless versus routine physiologic monitoring after cesarean delivery to reduce maternal morbidity and mortality in a resource-limited setting: protocol of type 2 hybrid effectiveness-implementation study	*BMC Pregnancy Childbirth*	Not population of interest

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
21	Boggess	2020	140990221 (cinahl)	720: Home blood pressure (BP) monitoring in postpartum women with hypertensive disorders of pregnancy	*American Journal of Obstetrics & Gynecology*	Abstract, subsequently published
22	Bolte	2001	11234612	Ketanserin for the treatment of preeclampsia	*J Perinat Med*	Not an intervention of interest
23	Borekci	2008	CN-00707589 (embase)	Effects of postpartum corticosteroids in patients with HELLP syndrome	*Journal of the turkish german gynecology association*	Not an intervention of interest
24	Bramham	2013	23440270	Postpartum management of hypertension	*Bmj*	Not a primary study
25	Bricker	2000	CN-00355018 (cochrane)	The Magpie Trial: magnesium sulphate versus placebo for women with pre-eclampsia	*XVI FIGO world congress of obstetrics & gynecology; 2000 sept 3-8; washington dc, USA*	Abstract, subsequently published
26	Brookfield	2020	CN-02075396 (cochrane)	19: a randomized trial of an alternate dosing protocol of magnesium sulfate in obese preeclamptic women	*American journal of obstetrics and gynecology*	Abstract, subsequently published
27	Bump	2022	L633633927 (embase)	Characteristics of postpartum patients readmitted for management of hypertensive disorders of pregnancy	*Obstetrics and Gynecology*	Abstract, 2020 or later, not yet published
28	Burgess	2020	146809718 (cinahl)	Remote Monitoring of Blood Pressure After Preeclampsia	*JOGNN: Journal of Obstetric, Gynecologic & Neonatal Nursing*	Abstract, subsequently published
29	Cairns	2017	L621236193 (embase)	A novel self-management intervention for adjustment of postnatal antihypertensive treatment	*European Heart Journal*	Abstract, subsequently published
30	Cairns	2017	L615337678 (embase)	Self-management of postnatal antihypertensive treatment: A pilot randomised controlled trial	*BJOG Int. J. Obstet. Gynaecol.*	Abstract, subsequently published
31	Cairns	2017	124609877 (cinahl)	OP 32 Hypertension self-management postpartum – The SNAP-HT pilot study – Can women do it better?	*Pregnancy Hypertension*	Abstract, subsequently published
32	Cairns		29187414	Postpartum management of hypertensive disorders of pregnancy: a systematic review	*BMJ Open*	Not a primary study
33	Chandran	2014	L71135629 (embase)	Labetalol versus magnesium sulfate in prevention of eclampsia trial (LAMPET trial)	*BJOG: An International Journal of Obstetrics and Gynaecology*	Abstract prior to 2020, unpublished

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
34	Chissell	1994	7839282	Intravenous and intramuscular magnesium sulphate regimens in severe pre-eclampsia	*S Afr Med J*	Less than 10 participants per group
35	Chowdhury	2009	19215558	Comparison of intramuscular magnesium sulfate with low dose intravenous magnesium sulfate regimen for treatment of eclampsia	*J Obstet Gynaecol Res*	NRCS (no adjustment)
36	Collins	2021	148435128 (cinahl)	883 Racial disparities in utilization of oral anti-hypertensives in the postpartum period	*American Journal of Obstetrics & Gynecology*	Abstract, 2020 or later, not yet published
37	Costas	2022	157762094 (cinahl)	Effects of Intensive Blood Pressure Monitoring in Pregnant and Postpartum Women With Severe Hypertension...Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN) Convention, 25-29 June, 2022, Aurora, Colorado	*JOGNN: Journal of Obstetric, Gynecologic & Neonatal Nursing*	Abstract, 2020 or later, not yet published
38	Crousillat	2022	155841144 (cinahl)	FEASIBILITY OF A VIRTUAL BLOOD PRESSURE MONITORING PROGRAM TITRATED TO ACC/AHA GUIDELINES AMONG OUTPATIENT POSTPARTUM WOMEN WITH HYPERTENSION: A PILOT STUDY	*Journal of the American College of Cardiology (JACC)*	Abstract, 2020 or later, not yet published
39	CTRI		CN-02377532 (cochrane)	Randomized controlled trial comparing the effectiveness and safety of 12 hours duration with the 24 hours duration of magnesium sulphate in maintenance therapy in patients of severe preeclampsia	*https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2022/01/039776*	CTRI record only
40	CTRI		CN-02328408 (cochrane)	Low dose magnesium sulphate for treatment of seizures in pregnancy	*https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2021/08/035456*	CTRI record only
41	CTRI		CN-02281798 (cochrane)	STUDY COMPARISON OF EFFICACY OF LEVETIRACETAM AND MAGNESIUM SULPHATE IN THE MANAGEMENT OF ANTEPARTUM, INTRAPARTUM AND POSTPARTUM CONVULSIONS	*https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2021/04/032963*	CTRI record only
42	CTRI		CN-02280062 (cochrane)	To study the effects of two different drugs for blood pressure control in women immediately after delivery	*https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2021/04/033252*	CTRI record only
43	CTRI		CN-02472925 (cochrane)	Comparative study of 2 different doses of magnesium sulfate treatment as a drug to prevent fits in patients of eclampsia	*https://trialsearch.who.int/Trial2.aspx?TrialID=CTRI/2022/08/045003*	CTRI record only

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
44	Cursino	2015	26242730	Diuretics vs. placebo for postpartum blood pressure control in preeclampsia (DIUPRE): a randomized clinical trial	*Reprod Health*	Protocol, no published study data
45	Dayicioglu	2003	14572362	The use of standard dose of magnesium sulphate in prophylaxis of eclamptic seizures: do body mass index alterations have any effect on success?	*Hypertens Pregnancy*	Not a comparison of interest
46	De Zoysa	2022	L2016042390 (embase)	The effect of magnesium sulfate loading dose and body mass index in achieving therapeutic levels	*American Journal of Obstetrics and Gynecology*	Abstract, 2020 or later, not yet published
47	DeNicola	2019	L633843799 (embase)	Evaluation of Antepartum and Postpartum Remote Blood Pressure Monitoring in Low-Risk Pregnancy	*Obstetrics and Gynecology*	Abstract prior to 2020, unpublished
48	Deshmukh	1985	3834084	Preliminary report on the use of magnesium sulfate in cases of severe pre-eclampsia and eclampsia	*J Postgrad Med*	NRCS (no adjustment)
49	Dewan	2011	CN-00774337 (cochrane)	Different anticonvulsant regimen of magnesium sulphate and feto-maternal outcome in treatment of eclampsia	*54th all india congress of obstetrics and gynaecology; 2011 january 5-9; hyderabad, andhra pradesh, india*	Abstract prior to 2020, unpublished
50	DeYoung	2020	L633633855 (embase)	Effects of selective early magnesium cessation protocol on preeclampsia with severe features	*Obstetrics and Gynecology*	NRCS (no adjustment)
51	Dianrong	2000	10699198	A comparison of phentolamine and magnesium sulfate therapy in pre-eclampsia	*Int J Gynaecol Obstet*	No outcomes of interest
52	Diao	2021	L2015474621 (embase)	Efficacy of normodyne-magnesium sulfate combination treatment on pregnancy-induced hypertension, and its effect on VEGF and Flt-1 levels	*Tropical Journal of Pharmaceutical Research*	Not population of interest
53	Do	2022	36075068	Postpartum Readmission for Hypertension After Discharge on Labetalol or Nifedipine	*Obstet Gynecol*	Analysis of claims database
54	Du	2019	30422321	Population Pharmacokinetic Modeling to Evaluate Standard Magnesium Sulfate Treatments and Alternative Dosing Regimens for Women With Preeclampsia	*Journal of Clinical Pharmacology*	Not a comparative study
55	Du	2019	31157410	Alternative Magnesium Sulfate Dosing Regimens for Women With Preeclampsia: A Population Pharmacokinetic Exposure-Response Modeling and Simulation Study	*J Clin Pharmacol*	Not a primary study

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
56	Du Plessis	2010	70511184 (embase)	HELLP syndrome: does postpartum dexamethasone improve maternal outcome?	*Pregnancy hypertension*	Not an intervention of interest
57	Duley	1998	CN-01780937 (cochrane)	Magnesium sulphate for treatment of pre-eclampsia: a trial to evaluate the effects on women and their babies	*Contemporary reviews in obstetrics and gynaecology*	Not a primary study
58	Duley	2000	10796145	Magnesium sulphate versus diazepam for eclampsia	*Cochrane Database Syst Rev*	Duplicate
59	Duley	2003	14583911	Magnesium sulphate versus phenytoin for eclampsia	*Cochrane Database Syst Rev*	Duplicate
60	Duley	2007	17166220	The Magpie Trial: A randomised trial comparing magnesium sulphate with placebo for pre-eclampsia. Outcome for women at 2 years	*BJOG: An International Journal of Obstetrics and Gynaecology*	No outcomes of interest
61	Duley	2007	17166221	The Magpie Trial: A randomised trial comparing magnesium sulphate with placebo for pre-eclampsia. Outcome for children at 18 months	*BJOG: An International Journal of Obstetrics and Gynaecology*	No outcomes of interest
62	Duley	2010	21154341	Magnesium sulphate versus diazepam for eclampsia	*Cochrane Database Syst Rev*	Not a primary study
63	Duley		10796146	Magnesium sulphate versus phenytoin for eclampsia	*Cochrane Database Syst Rev*	Not a primary study
64	Duley		10796090	Anticonvulsants for women with pre-eclampsia	*Cochrane Database Syst Rev*	Not a primary study
65	Duley		21069663	Magnesium sulphate and other anticonvulsants for women with pre-eclampsia	*Cochrane Database Syst Rev*	Not a primary study
66	Easterling	2012	26105248	OS034. Magnesium sulfate for prevention of eclampsia: Are intramuscularand intravenous regimens equivalent?	*Pregnancy Hypertens*	Abstract, subsequently published
67	Ekele	2009	19691837	Magnesium sulphate therapy in eclampsia: the Sokoto (ultra short) regimen	*BMC Res Notes*	Not a comparative study
68	Eyal	2010	20145263	Atenolol pharmacokinetics and excretion in breast milk during the first 6 to 8 months postpartum	*J Clin Pharmacol*	No outcomes of interest
69	Faifan	2017	L616813338 (embase)	Maternal body weight and dosage of magnesium sulfate treatment in preeclampsia	*Journal of Obstetrics and Gynaecology Research*	Abstract prior to 2020, unpublished

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
70	Farrell	2007	17208626	Doing the undoable: Magpie Trial long-term follow-up	*Lancet*	Not a primary study
71	Fejgin	2003	12850631	Postpartum seizure prophylaxis: using maternal clinical parameters to guide therapy.	*Obstetrics and gynecology*	Not a primary study
72	Firoz	2012	26105410	PP088. Oral antihypertensive therapy for severe hypertension in pregnancy	*Pregnancy Hypertens*	Not a primary study
73	Flowers	1962	13893679	Magnesium sulfate in toxemia of pregnancy. New dosage schedule based on body weight	*Obstet Gynecol*	Full text unavailable
74	Fonseca	2005	16260197	Dexamethasone treatment does not improve the outcome of women with HELLP syndrome: a double-blind, placebo-controlled, randomized clinical trial	*Am J Obstet Gynecol*	Not an intervention of interest
75	Fox	2021	L635186620 (embase)	Short term postpartum blood pressure management and long-term blood pressure control: A randomised controlled trial	*Australian and New Zealand Journal of Obstetrics and Gynaecology*	Abstract, subsequently published
76	Fox	2021	CN-02286071 (cochrane)	Short term postpartum blood pressure management and long-term blood pressure control: a randomised controlled trial	*Australian & New Zealand journal of obstetrics & gynaecology*	Abstract, subsequently published
77	Friedman	1993	8517903	Phenytoin versus magnesium sulfate in preeclampsia: a pilot study	*Am J Perinatol*	Not population of interest
78	Friedman	1995	CN-00231733 (cochrane)	Phenytoin vs magnesium sulfate in patients with eclampsia: preliminary results from a randomized trial	*American journal of obstetrics and gynecology*	Full text unavailable
79	Gaisin	2013	L71258522 (embase)	Indapamide in the management of post-partum hypertension: A randomized, case-control study	*European Heart Journal*	Abstract prior to 2020, unpublished
80	Garg	2017	L619028531 (embase)	Low-dose magnesium sulfate regime for eclampsia in India	*Journal of SAFOG*	NRCS (no adjustment)
81	Ghahiri	2005	L40542303 (embase)	A comparison between intravenous magnesium sulfate and oral magnesium chloride in mild preeclampsia	*Journal of Research in Medical Sciences*	Not a comparison of interest
82	Griffin	2022	L638410924 (embase)	Postpartum Readmission Rates for Hypertensive Disorders of Pregnancy During the COVID-19 Pandemic	*Obstetrics and Gynecology*	Abstract, subsequently published
83	Griffin	2022	36164558	Postpartum readmissions for hypertensive disorders in pregnancy during the COVID-19 pandemic	*AJOG Glob Rep.*	Not an intervention of interest

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84	Grillo	2021	CN-02322485 (cochrane)	Y-011. Comparison 0f zuspan regime and its 12-hour modification in women with severe pre-eclampsia and eclampsia In two hospitals In Abeokuta, South Western Nigeria	*Pregnancy hypertension*	Abstract, 2020 or later, not yet published
85	Gutiérrez-Vela	2021	L2017829792 (embase)	Effectiveness of a shortened treatment with magnesium sulfate for prevention of eclampsia during puerperium	*Ginecologia y Obstetricia de Mexico*	NRCS (no adjustment)
86	Hauspurg	2020	33351087	Racial Differences in Postpartum Blood Pressure Trajectories Among Women After a Hypertensive Disorder of Pregnancy	*JAMA Netw Open*	Not a comparison of interest
87	Hauspurg	2022	154270900 (cinahl)	Feasibility of utilizing telehealth in a multi-disciplinary postpartum hypertension clinic	*American Journal of Obstetrics & Gynecology*	Abstract prior to 2020, unpublished
88	Heida	2012	22525036	Neonatal side effects of maternal labetalol treatment in severe preeclampsia	*Early Hum Dev*	Not population of interest
89	Hennessy	2007	17627681	A randomised comparison of hydralazine and mini-bolus diazoxide for hypertensive emergencies in pregnancy: the PIVOT trial	*Aust N Z J Obstet Gynaecol*	Not population of interest
90	Hirshberg	2016	L613313119 (embase)	Text message based remote monitoring in the management of postpartum hypertension	*Obstetrics and Gynecology*	Abstract, subsequently published
91	Hirshberg	2017	L614526768 (embase)	Rapid-cycle innovation testing of text-based monitoring for management of postpartum hypertension	*Journal of Clinical Outcomes Management*	Single arm study (N < 50)
92	Hirshberg	2019	CN-01757732 (cochrane)	7: text message remote blood pressure monitoring eliminated racial disparities in postpartum hypertension care	*American journal of obstetrics and gynecology*	Abstract, subsequently published
93	Hirshberg	2020	33351081	Race Differences in Blood Pressure Trajectory After Delivery-A Window Into Opportunities to Decrease Racial Disparities in Maternal Morbidity and Mortality	*JAMA Netw Open*	Not a primary study
94	Hladunewich	2006	16582128	Effect of L-arginine therapy on the glomerular injury of preeclampsia: a randomized controlled trial	*Obstet Gynecol*	Not an intervention of interest
95	Hollenberg	2003	12918532	A comparison of magnesium sulfate and nimodipine for the prevention of eclampsia	*Curr Hypertens Rep*	Not a primary study
96	Hong	1993	7968328	[Nifedipine in preeclampsia for cesarean section]	*Ma Zui Xue Za Zhi*	Not population of interest

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97	Isler	2002	12375546	Repeat postpartum magnesium sulfate administration for seizure prophylaxis: is there a patient profile predictive of need for additional therapy?	*J Matern Fetal Neonatal Med*	Not population of interest
98	Isler	2003	12628531	Dexamethasone compared with betamethasone for glucocorticoid treatment of postpartum HELLP syndrome	*Int J Gynaecol Obstet*	Not an intervention of interest
99	Isler	2003	12517647	Postpartum seizure prophylaxis: Using maternal clinical parameters to guide therapy	*Obstetrics and Gynecology*	Not a comparison of interest
100	ISRCTN		CN-02429833 (cochrane)	Simplified treatment for eclampsia prevention using magnesium sulfate	*https://trialsearch.who.int/Trial2.aspx?TrialID=ISRCTN13720473*	ISRCTN record only
101	Ivanova	1976	969298	[Comparative evaluation of diuretic effect of hypothiazide, furosemide and magnesium sulfate in the complex treatment of pregnant women with toxemia of the 2d half of pregnancy]	*Vopr Okhr Materin Det*	Not population of interest
102	Jacob	1995	CN-00232450 (cochrane)	Standardised clinical trial of magnesium sulphate regime in comparison with M.K.K. Menon's Lytic cocktail regime in the management of eclampsia	*27th british congress of obstetrics and gynaecology;1995 july 4-7; dublin, ireland*	Full text unavailable
103	Jana	2013	23587234	Experience of a low-dose magnesium sulfate regimen for the management of eclampsia over a decade	*Int J Gynaecol Obstet*	Not a comparative study
104	Kalafat	2018	29786155	Is home blood-pressure monitoring in hypertensive disorders of pregnancy consistent with clinic recordings?	*Ultrasound Obstet Gynecol*	Not a comparison of interest
105	Kamravamanesh	2018	29776432	A comprehensive postpartum follow-up health care program for women with history of preeclampsia: protocol for a mixed methods research	*Reprod Health*	Not an intervention of interest
106	Katz	2008	18194800	Postpartum dexamethasone for women with hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome: a double-blind, placebo-controlled, randomized clinical trial	*Am J Obstet Gynecol*	Not an intervention of interest
107	Katz	2013	23697398	COHELLP: collaborative randomized controlled trial on corticosteroids in HELLP syndrome	*Reprod Health*	Not an intervention of interest

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108	Katz	2015	L71809118 (embase)	Clonidine versus captopril for severe postpartum hypertension: A randomized controlled trial	*Pregnancy Hypertension*	Abstract, subsequently published
109	Katz	2016	L614983519 (embase)	Serum magnesemia during maintenance dose of 1 g/h vs. 2 g/h of magnesium sulfate infusion for the prevention of eclampsia in women with severe preeclampsia: Randomized trial	*Pregnancy Hypertension*	Abstract, subsequently published
110	Keiseb	2002	12517329	Comparison of the efficacy of continuous furosemide and low-dose dopamine infusion in preeclampsia/eclampsia related oliguria in the immediate postpartum period	*Hypertension in Pregnancy*	Not population of interest
111	Kern-Goldberger	2021	33904843	Reducing Disparities Using Telehealth Approaches for Postdelivery Preeclampsia Care.	*Clinical obstetrics and gynecology*	Not a primary study
112	Khan	1998	9692428	A randomised controlled trial of intravenous magnesium sulphate versus placebo...Br J Obstet Gynaecol. 1998 Mar;105(3):300-3	*British Journal of Obstetrics & Gynaecology*	Not a primary study
113	Kidd	2022	L2016042182 (embase)	Barriers to obstetric patient utilization of remote patient monitoring for blood pressure	*American Journal of Obstetrics and Gynecology*	Abstract, 2020 or later, not yet published
114	Kilpatrick	2016	26829504	Severe maternal morbidity in a large cohort of women with acute severe intrapartum hypertension	*American Journal of Obstetrics and Gynecology*	Not a comparison of interest
115	Kitt	2022	35197335	Postpartum blood pressure self-management following hypertensive pregnancy: protocol of the Physician Optimised Post-partum Hypertension Treatment (POP-HT) trial	*BMJ Open*	Protocol, no published study data
116	Krishna	2013	L71135794 (embase)	A randomised controlled trial of oral nifedipine and intravenous labetalol in pregnant women with severe pre eclampsia and eclampsia	*BJOG: An International Journal of Obstetrics and Gynaecology*	Not population of interest
117	Kumru	2016	L611870070 (embase)	Postpartum dexamethasone for women with hellp (hemolysis, elevated liver enzymes, and low)	*Journal of Maternal-Fetal and Neonatal Medicine*	Not an intervention of interest
118	Kyank	1973	4793614	[Treatment of eclampsia]	*Zentralbl Gynakol*	Full text unavailable
119	Laiteerapong	1999	CN-00644060 (cochrane)	Comparative study of serum magnesium levels attained from magnesium sulfate therapy for severe pre-eclamptic patients between 1 gm/hr and 2 gm/hr regimen	*Thai journal of obstetrics and gynaecology*	Full text unavailable

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120	Lan	2017	29153682	Home blood pressure measurement in women with pregnancy-related hypertensive disorders	*Pregnancy Hypertens*	Not a comparison of interest
121	Leal	2014	CN-01063671 (cochrane)	12-Hour compared with 24-hour postpartum magnesium sulfate therapy in preeclampsia: a randomized clinical trial	*Obstetrics and gynecology.*	Abstract, subsequently published
122	Lemon	2022	36244624	Neighborhood disadvantage and the racial disparity in postpartum hypertension	*Am J Obstet Gynecol MFM*	No outcomes of interest
123	Leveno	1998	9579432	Does magnesium sulfate given for prevention of eclampsia affect the outcome of labor?	*American Journal of Obstetrics & Gynecology*	Not population of interest
124	Levine	2016	27583396	Factors associated with postpartum follow-up and persistent hypertension among women with severe preeclampsia	*J Perinatol*	Not a comparison of interest
125	Liu	1982	6814850	Different doses and routes of magnesium sulfate administration in treating severe preeclamptic and eclamptic patients	*Chin Med J (Engl)*	Not a comparison of interest
126	Liu	2009	19548438	[Treatment of albuminuria in gestational hypertension puerpera in the severe preeclampeia stage by TCM therapy for stasis-removing and diuresis]	*Zhongguo Zhong Xi Yi Jie He Za Zhi*	Not an intervention of interest
127	Livingstone	1983	6872291	Propranolol in pregnancy three year prospective study	*Clin Exp Hypertens B*	Not population of interest
128	Lo	2002	12439526	Use of automated home blood pressure monitoring in pregnancy: is it safe?	*American Journal of Obstetrics & Gynecology*	Not population of interest
129	Lopes Perdigao	2020	32143061	Postpartum blood pressure trends are impacted by race and BMI	*Pregnancy Hypertens*	Not a comparison of interest
130	Lu	2002	12403646	Pharmacokinetic-pharmacodynamic modelling of magnesium plasma concentration and blood pressure in preeclamptic women	*Clin Pharmacokinet*	Not a comparative study
131	Luan	1995	7647530	[Observation on treatment of mailuoning injection for 46 pregnancy induced hypertension patients]	*Zhongguo Zhong Xi Yi Jie He Za Zhi*	Not a comparison of interest
132	Lucas	1995	7791836	A comparison of magnesium sulfate with phenytoin for the prevention of eclampsia	*N Engl J Med*	Not population of interest

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133	Ludmir	2017	CN-01304035 (cochrane)	Is magnesium sulfate use of benefit post partum? A randomized controlled trial	*American journal of obstetrics and gynecology*	Abstract, subsequently published
134	Ma	2019	30988752	Effect of the drug combination of magnesium sulfate and phentolamine on homocysteine and C-reactive protein in the serum of patients with pregnancy-induced hypertension syndrome	*Exp Ther Med*	NRCS (no adjustment)
135	Mabie	1987	3306494	A comparative trial of labetalol and hydralazine in the acute management of severe hypertension complicating pregnancy	*Obstet Gynecol*	Not population of interest
136	Magann	1993	8459956	Immediate postpartum curettage: accelerated recovery from severe preeclampsia	*Obstet Gynecol*	Not an intervention of interest
137	Magann	1994	7943089	Postpartum corticosteroids: accelerated recovery from the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP)	*Am J Obstet Gynecol*	Not an intervention of interest
138	Magann	1994	9419773	Accelerated recovery from severe preeclampsia: uterine curettage versus nifedipine	*Journal of the Society for Gynecologic Investigation*	Not a comparison of interest
139	Magee	2005	16021073	Therapy with both magnesium sulfate and nifedipine does not increase the risk of serious magnesium-related maternal side effects in women with preeclampsia	*Am J Obstet Gynecol*	NRCS (no adjustment)
140	Mahajan	2009	18824861	Padhar regime' - a low-dose magnesium sulphate treatment for eclampsia	*Gynecol Obstet Invest*	NRCS (no adjustment)
141	Martin	1997	9396884	Better maternal outcomes are achieved with dexamethasone therapy for postpartum HELLP (hemolysis, elevated liver enzymes, and thrombocytopenia) syndrome	*Am J Obstet Gynecol*	Not an intervention of interest
142	Martin	1998	CN-00478209 (cochrane)	Early puerperal hypertension management: hydralazine vs methyldopa	*6th international congress of the international society for the study of hypertension in pregnancy; 1988 may 22-26, montreal, quhydralazine vs methyldopa Qebec, canada*	Abstract, subsequently published
143	Martin	2021	33416295	Semiautonomous Treatment Algorithm for the Management of Severe Hypertension in Pregnancy	*Obstet Gynecol*	Not population of interest
144	Martin	2022	154270181 (cinahl)	Home Blood Pressure Monitoring in Women with Severe Hypertension Utilizing Audio-Only and In-Person Postpartum Encounters	*American Journal of Obstetrics & Gynecology*	Abstract, 2020 or later, not yet published

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145	Martin	2022	154271002 (cinahl)	Postpartum Audio-Only Virtual Visits Versus In-Person Follow-up in Women with Severe Hypertension	*American Journal of Obstetrics & Gynecology*	Abstract, 2020 or later, not yet published
146	Martin	2003	14526324	Maternal benefit of high-dose intravenous corticosteroid therapy for HELLP syndrome	*American Journal of Obstetrics & Gynecology*	Not an intervention of interest
147	Matsumura	2014	24131296	Placental transfer of intravenous nicardipine and disposition into breast milk during the control of hypertension in women with pre-eclampsia	*Hypertens Pregnancy*	No outcomes of interest
148	Matthews	1997	15511760	A randomised placebo controlled trial of loop diuretics in moderate/severe pre-eclampsia, following delivery	*J Obstet Gynaecol*	Less than 10 participants per group
149	Matthys	2004	15167870	Delayed postpartum preeclampsia: an experience of 151 cases	*Am J Obstet Gynecol*	Not a comparative study
150	McDonald		22703834	A systematic review of maternal and infant outcomes following magnesium sulfate for pre-eclampsia/eclampsia in real-world use	*Int J Gynaecol Obstet*	Not a primary study
151	McLaughlin	2019	137209662 (cinahl)	Remote Monitoring of Postpartum Hypertension...2019 AWHONN Annual Convention, June 8-12, 2019, Atlanta, Georgia	*JOGNN: Journal of Obstetric, Gynecologic & Neonatal Nursing*	Abstract, subsequently published
152	McManus	2016	CN-01407972 (cochrane)	The snap-HT trial: self-management of antihypertensive medication postpartum-can women do it better?	*Journal of hypertension*	Abstract, subsequently published
153	McManus	2017	CN-01407140 (cochrane)	The snap-HT trial: self-management of antihypertensive medication postpartum - Can women do it better?	*Journal of hypertension*	Abstract, subsequently published
154	Montenegro	1985	2931024	The effect of serotonergic blockade in postpartum preeclamptic patients	*Am J Obstet Gynecol*	Not an intervention of interest
155	Moodley	1999	10426656	A randomised controlled trial of intravenous magnesium sulphate versus placebo in the management of women with severe pre-eclampsia	*Br J Obstet Gynaecol*	Not a primary study
156	Mourad	2005	16238275	Maternal benefit of postpartum corticosteroid therapy in patients with HELLP (hemolysis elevated liver enzymes low platelets count) syndrome	*Tunisie Medicale*	Not an intervention of interest

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157	Muhammad	2009	CN-00726388 (cochrane)	Low dose magnesium sulfate in the control of eclamptic fits: a randomized control trial	*International journal of gynaecology and obstetrics*	Abstract prior to 2020, unpublished
158	Muijsers	2020	32131802	Blood pressure after PREeclampsia/HELLP by SELF monitoring (BP-PRESELF): rationale and design of a multicenter randomized controlled trial	*BMC Womens Health*	Not population of interest
159	Muijsers	2022	36425535	Home blood pressure monitoring detects unrevealed hypertension in women with a history of preeclampsia: Results of the BP-PRESELF study	*Am J Prev Cardiol*	Not population of interest
160	Mukhtarova	2021	33451628	Evaluation of different blood pressure assessment strategies and cutoff values to predict postpartum hypertension-related readmissions: a retrospective cohort study	*Am J Obstet Gynecol MFM*	Not a comparison of interest
161	Mukhtarova	2022	34894998	Longitudinal blood pressure patterns of women with hypertensive disorders of pregnancy: preconception through postpartum	*Journal of Maternal-Fetal & Neonatal Medicine*	No outcomes of interest
162	Naeimi	2014	23157847	Preeclampsia and benefit form magnesium sulfate. about 105 cases	*Gynecologie Obstetrique et Fertilite*	NRCS (no adjustment)
163	Nagaria	2017	28969211	Single Loading Low Dose MgSo(4) Regimen: A Simple, Safe and Effective Alternative to Pritchard's Regimen for Indian Women	*J Clin Diagn Res*	NRCS (no adjustment)
164	Naidu	1996	8616125	Randomised study assessing the effect of phenytoin and magnesium sulphate on maternal cerebral circulation in eclampsia using transcranial Doppler ultrasound	*Br J Obstet Gynaecol*	Not population of interest
165	Naito	2015	25447596	Amlodipine passage into breast milk in lactating women with pregnancy-induced hypertension and its estimation of infant risk for breastfeeding	*J Hum Lact*	Not a comparative study
166	Naz	2005	19810301	Eclampsia--management and outcome with magnesium sulphate as the anticonvulsant	*J Coll Physicians Surg Pak*	NRCS (no adjustment)
167	NCT		CN-02367669 (cochrane)	Monitoring and Testing of Blood Pressure in Postpartum Women	*https://clinicaltrials.gov/show/NCT05236725*	CT.gov record only
168	NCT		CN-02252202 (cochrane)	Effectiveness of the use of methyldopa in comparison to captopril in hypertension post partum	*https://clinicaltrials.gov/show/NCT04835233*	CT.gov record only

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169	NCT		CN-02345476 (cochrane)	Postpartum Hypertension Study	*https://clinicaltrials.gov/show/NCT05139238*	CT.gov record only
170	NCT		CN-02307217 (cochrane)	Lisinopril for Renal Protection in Postpartum Preeclamptic Women	*https://clinicaltrials.gov/show/NCT05016440*	CT.gov record only
171	NCT		CN-02392061 (cochrane)	Labetalol or Nifedipine for Control of Postpartum Hypertension: a Randomized Controlled Trial	*https://clinicaltrials.gov/show/NCT05309460*	CT.gov record only
172	NCT		CN-02253357 (cochrane)	Pregnancy-Related Hypertension: Adherence to a New Type of Monitoring	*https://clinicaltrials.gov/show/NCT04823949*	CT.gov record only
173	NCT		CN-02249766 (cochrane)	Amlodipine Versus Nifedipine ER for the Management of Postpartum Hypertension	*https://clinicaltrials.gov/show/NCT04790279*	CT.gov record only
174	NCT		CN-02423833 (cochrane)	Blood Pressure Monitoring in Postpartum Women at Risk of Hypertension	*https://clinicaltrials.gov/show/NCT05457504*	CT.gov record only
175	NCT		CN-02235140 (cochrane)	Lasix for the Prevention of De Novo Postpartum Hypertension	*https://clinicaltrials.gov/show/NCT04752475*	CT.gov record only
176	NCT		CN-02340841 (cochrane)	Oral Combined Hydrochlorothiazide/Lisinopril Versus Oral Nifedipine for Postpartum Hypertension	*https://clinicaltrials.gov/show/NCT05049616*	CT.gov record only
177	NCT		CN-02464567 (cochrane)	Safest Choice of Antihypertensive Regimen for Postpartum Hypertension	*https://clinicaltrials.gov/show/NCT05551104*	CT.gov record only
178	NCT		CN-02488120 (cochrane)	App-based Remote Blood Pressure Monitoring	*https://clinicaltrials.gov/show/NCT05595629*	CT.gov record only
179	NCT		CN-02458765 (cochrane)	Guideline-directed Management and Therapy (GDMT) for the Prevention of Postpartum Cardiac Dysfunction in Preeclamptic African American Women	*https://clinicaltrials.gov/show/NCT05534932*	CT.gov record only
180	Nuckols	2022	35671544	Postpartum ambulatory and home blood pressure monitoring in women with history of preeclampsia: Diagnostic agreement and detection of masked hypertension	*Pregnancy Hypertens*	Not population of interest

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181	Nuss	2021	148435145 (cinahl)	900 The impact of postpartum blood pressure monitoring amongst women with hypertensive disorders of pregnancy	*American Journal of Obstetrics & Gynecology*	Abstract, 2020 or later, not yet published
182	Okonkwo	2022	35271534	Duration of Postpartum Magnesium Sulphate for the Prevention of Eclampsia: A Systematic Review and Meta-analysis	*Obstetrics & Gynecology*	Not a primary study
183	Okusanya	2012	22728971	The efficacy of intramuscular loading dose of MgSO4 in severe pre-eclampsia/ eclampsia at a tertiary referral centre in Northwest Nigeria	*Niger Postgrad Med J*	Duplicate
184	Okusanya	2012	23064169	The efficacy of 10gram intramuscular loading dose of MgSO(4) in severe preeclampsia/ eclampsia at a tertiary referral centre in Northwest Nigeria	*Niger Postgrad Med J*	NRCS (no adjustment)
185	Ononge	2021	L635302025 (embase)	Magnesium sulphate for preeclampsia and eclampsia with Springfusor¬Æ pump versus intramuscular approach	*BJOG: An International Journal of Obstetrics and Gynaecology*	Abstract, 2020 or later, not yet published
186	PACTR	19303	CN-02379110 (cochrane)	The STEP-Mag Trial	*https://trialsearch.who.int/Trial2.aspx?TrialID=PACTR202112816270738*	PACTR record only
187	PACTR		CN-02379123 (cochrane)	Magnesium Sulphate Loading Dose Only versus Standard Pritchard Regimen in the Management of Eclampsia – A Multi-centre Randomized Clinical Trial	*https://trialsearch.who.int/Trial2.aspx?TrialID=PACTR202201609390328*	PACTR record only
188	PACTR		CN-02458337 (cochrane)	Comparative study of the efficacy of Dhaka-and Pritchard-regimen of magnesium sulphate in the management of eclamptic fits	*https://trialsearch.who.int/Trial2.aspx?TrialID=PACTR202208671536129*	PACTR record only
189	Payakachat	2020	32119129	Using mHealth in postpartum women with pre-eclampsia: Lessons learned from a qualitative study.	*International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*	NRCS (no adjustment)
190	Pechere-Bertschi	2022	CN-02426786 (cochrane)	TREATMENT OF PERSISTENT RENAL DYSFUNCTION AFTER PREECLAMPSIA WITH BENAZEPRIL: a RANDOMIZED, DOUBLEBLIND TRIAL	*Journal of hypertension*	Abstract, 2020 or later, not yet published
191	Pechère-Bertschi	2022	157436713 (cinahl)	TREATMENT OF PERSISTENT RENAL DYSFUNCTION AFTER PREECLAMPSIA WITH BENAZEPRIL: A RANDOMIZED, DOUBLE-BLIND TRIAL	*Journal of Hypertension*	Abstract, 2020 or later, not yet published

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
192	Pechère-Bertschi	2022	L638439528 (embase)	TREATMENT OF PERSISTENT RENAL DYSFUNCTION AFTER PREECLAMPSIA WITH BENAZEPRIL: A RANDOMIZED, DOUBLEBLIND TRIAL	*Journal of Hypertension*	Duplicate
193	Peracoli	2021	152464861 (cinahl)	O-006. Modulatory effect of two regimens of magnesium sulfate on the systemic inflammatory response in pregnant women with eclampsia or imminent eclampsia	*Pregnancy Hypertension*	No outcomes of interest
194	Peraçoli	2022	35728369	Modulatory effect of two regimens of magnesium sulfate on the systemic inflammatory response in pregnant women with imminent eclampsia	*Pregnancy Hypertension*	No outcomes of interest
195	Perdigao	2020	2004455715 (embase)	LB 4: furosemide for Accelerated Recovery of Blood Pressure Postpartum: a randomized placebo controlled trial (FoR BP)	*American journal of obstetrics and gynecology*	Abstract, subsequently published
196	Presl	1970	5444802	[Magnesium sulfate in the therapy of pre-eclampsia and eclampsia]	*Cesk Gynekol*	Abstract prior to 2020, unpublished
197	Pritchard		13238166	The use of the magnesium ion in the management of eclamptogenic toxemias	*Surg Gynecol Obstet*	Not a comparative study
198	Qi	2020	32388119	Efficacy of low-dose nicardipine for emergent treatment of severe postpartum hypertension in maternal intensive care units: An observational study	*Pregnancy Hypertens*	Not a comparative study
199	Qian	1991	1773467	[Treatment of hypertension syndrome of pregnancy with ligustrazine]	*Zhong Xi Yi Jie He Za Zhi*	Not a comparison of interest
200	Quinn	2020	146809693 (cinahl)	Engaging Postpartum Women Through Implementation of a Remote Monitoring Protocol for Hypertensive Disorders of Pregnancy	*JOGNN: Journal of Obstetric, Gynecologic & Neonatal Nursing*	Abstract, subsequently published
201	Ragab	2013	23644921	Does immediate postpartum curettage of the endometrium accelerate recovery from preeclampsia-eclampsia? A randomized controlled trial	*Arch Gynecol Obstet*	Not an intervention of interest
202	Rani	2021	L2016194344 (embase)	Comparison of Pritchard and Dhaka Regimen in Outcome of Patients with Severe Preeclampsia and Eclampsia in Eastern Part of India: A Prospective Observational Study	*Journal of Clinical and Diagnostic Research*	NRCS (no adjustment)

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
203	Redman	2019	31599846	Clinical Course, Associated Factors, and Blood Pressure Profile of Delayed-Onset Postpartum Preeclampsia	*Obstet Gynecol*	Not a comparison of interest
204	Rezk	2020	32697618	Methyldopa versus labetalol or no medication for treatment of mild and moderate chronic hypertension during pregnancy: a randomized clinical trial	*Hypertens Pregnancy*	Not population of interest
205	Rimal	2017	L611870171 (embase)	A randomized controlled trial of loading dose only versus standard dose magnesium sulfate seizure prophylaxis in severe pre-eclamptic women	*Journal of Maternal-Fetal and Neonatal Medicine*	Duplicate
206	Rivera-Alsina	1983	6577872	Intravenous vs. intramuscular magnesium sulfate for preeclampsia	*Bol Asoc Med P R*	Full text unavailable
207	Rudnicki	1991	1763608	The effect of magnesium on maternal blood pressure in pregnancy-induced hypertension. A randomized double-blind placebo-controlled trial	*Acta Obstet Gynecol Scand*	Not an intervention of interest
208	Rudnicki	2000	10828704	Comparison of magnesium and methyldopa for the control of blood pressure in pregnancies complicated with hypertension	*Gynecol Obstet Invest*	Not an intervention of interest
209	Sabol	2021	148435170 (cinahl)	925 Implementation of postpartum home blood pressure monitoring to reduce readmissions for hypertensive disorders of pregnancy	*American Journal of Obstetrics & Gynecology*	Abstract, 2020 or later, not yet published
210	Salinger	2013	23530757	Magnesium sulphate for prevention of eclampsia: are intramuscular and intravenous regimens equivalent? A population pharmacokinetic study	*Bjog*	No outcomes of interest
211	Salvatore	1967	5606799	['Postpartum curettage in severe toxemia with and without premature loosening of the placenta']	*Matern Infanc (Sao Paulo)*	Not an intervention of interest
212	Samal	2001	CN-00498615 (cochrane)	Management of eclampsia with magnesium sulphate and nifedipine	*Journal of obstetrics and gynaecology of india*	NRCS (no adjustment)
213	Sanghavi	2022	36269782	Telemedicine may increase visit completion rates in postpartum patients with preeclampsia	*PLoS One*	NRCS (no adjustment)
214	Sawhney	1998	9798355	Comparison of lytic cocktail and magnesium sulphate regimens in eclampsia: a retrospective analysis	*J Obstet Gynaecol Res*	NRCS (no adjustment)

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
215	Scholl	2019	L633843765 (embase)	Hydralazine Versus Labetalol for Acute Hypertension in the Peripartum Patient	*Obstetrics and Gynecology*	Abstract prior to 2020, unpublished
216	Seabe	1989	2781421	Nifedipine in acute hypertensive emergencies in pregnancy	*S Afr Med J*	Not population of interest
217	Shahul	2015	26636247	Racial Disparities in Comorbidities, Complications, and Maternal and Fetal Outcomes in Women With Preeclampsia/eclampsia	*Hypertens Pregnancy*	Not a comparison of interest
218	Shahzad	2017	L617626724 (embase)	Comparison of dexamethasone versus betamethasone for the management of females with HELLP syndrome	*Pakistan Journal of Medical and Health Sciences*	Not an intervention of interest
219	Shamsuddin	1997	CN-00234532 (cochrane)	Magnesium sulphate vs diazepam in the management of eclampsia	*Acta obstetricia ET gynecologica scandinavica. Supplement*	Abstract, subsequently published
220	Shao	2022	36277012	Effects of Nifedipine and Labetalol Combined with Magnesium Sulfate on Blood Pressure Control, Blood Coagulation Function, and Maternal and Infant Outcome in Patients with Pregnancy-Induced Hypertension	*Comput Math Methods Med*	No outcomes of interest
221	Sharma	2016	72164237 (embase)	Oral labetalol compared to oral extended release nifedipine for persistent postpartum hypertension: a randomized controlled trial	*American journal of obstetrics and gynecology*	Abstract, subsequently published
222	Sharma	2016	111975837 (cinahl)	40: Oral labetalol compared to oral extended release nifedipine for persistent postpartum hypertension: a randomized controlled trial	*American Journal of Obstetrics & Gynecology*	Abstract, subsequently published
223	Sheehan	2022	35365547	Understanding maternal postnatal blood pressure changes following hypertensive disorders in pregnancy: protocol for a prospective cohort study	*BMJ Open*	Protocol, no published study data
224	Shilva	2007	17368649	Safety and efficacy of low-dose MgSO4 in the treatment of eclampsia	*Int J Gynaecol Obstet*	No outcomes of interest
225	Shreya	2014	L600120053 (embase)	Evaluation of single dose magnesium sulphate and pritchard regimen in the treatment of eclampsia - A comparative study	*Biomedicine (India)*	Full text unavailable
226	Shumard	2016	111976183 (cinahl)	718: Peripartum anti-hypertensive choice affects time to blood pressure control in treating hypertensive disorders of pregnancy	*American Journal of Obstetrics & Gynecology*	Abstract prior to 2020, unpublished

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
227	Sibai	1984	6496595	A comparison of intravenous and intramuscular magnesium sulfate regimens in preeclampsia	*Am J Obstet Gynecol*	Less than 10 participants per group
228	Simon	2006	16411990	Cost-effectiveness of prophylactic magnesium sulphate for 9996 women with pre-eclampsia from 33 countries: economic evaluation of the Magpie Trial	*BJOG: An International Journal of Obstetrics & Gynaecology*	Not population of interest
229	Sioufi	1984	6487485	Oxprenolol placental transfer, plasma concentrations in newborns and passage into breast milk	*Br J Clin Pharmacol*	Not a comparative study
230	Smyth	2009	19366459	Magpie Trial in the UK: methods and additional data for women and children at 2 years following pregnancy complicated by pre-eclampsia	*BMC Pregnancy Childbirth*	No outcomes of interest
231	Socrates	2022	157436712 (cinahl)	FEASIBILITY, ACCEPTANCE AND SAFETY OF A HOME BASED TELEMONITORING STRATEGY IN WOMEN WITH POSTPARTUM HYPERTENSION. INTERIM ANALYSIS OF THE SWISS REGISTER FOR WOMEN WITH PPHT	*Journal of Hypertension*	Abstract, 2020 or later, not yet published
232	Song	2019	31993405	Magnesium Sulfate Combined with Nifedipine Is Effective in Pregnancy-Induced Hypertension and Reduces Levels of Serum β2-Microglobulin and Retinol Binding Protein 4	*Iran J Public Health*	NRCS (no adjustment)
233	Sullivan	2022	34187284	Duration of postpartum magnesium sulfate for seizure prophylaxis in women with preeclampsia: a systematic review and meta-analysis	*J Matern Fetal Neonatal Med*	Not a primary study
234	Sun	2016	L629421770 (embase)	Peripartum anti-hypertensive choice affects time to blood pressure control in treating hypertensive disorders of pregnancy	*Journal of Obstetrics and Gynaecology Research*	Abstract prior to 2020, unpublished
235	Suneja	2008	None	A prospective randomized controlled trial to individualize the duration of post partum magnesium sulfate therapy	*Hypertension in Pregnancy*	Abstract prior to 2020, unpublished
236	Suresh	2021	34619718	Postpartum Outcomes With Systematic Treatment and Management of Postpartum Hypertension	*Obstet Gynecol*	Not an intervention of interest
237	Suzuki		35974173	A multicenter prospective study of home blood pressure measurement (HBPM) during pregnancy in Japanese women	*Hypertens Res*	Not population of interest

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
238	Sylvester	2018	L621268597 (embase)	A study to compare the clinical efficacy of antihypertensive agents during the postpartum period	*Reproductive Sciences*	Abstract prior to 2020, unpublished
239	Taylor	2001	12044311	Evaluation of ambulatory and self-initiated blood pressure monitors by pregnant and postpartum women	*Hypertens Pregnancy*	Not a comparison of interest
240	Taylor	2020	CN-02075394 (cochrane)		*American journal of obstetrics and gynecology*	Not population of interest
241	PACTR		CN-02413027 (cochrane)	Furosemide for prevention 72 hours postpartum hypertension in women with preeclampsia with severe features: A randomized controlled trial	*https://trialsearch.who.int/Trial2.aspx?TrialID=TCTR20220419002*	PACTR record only
242	Thapa	2008	19079372	Magnesium sulphate: a life saving drug	*JNMA J Nepal Med Assoc*	Not a comparative study
243	The	2004	15113445	The Magpie Trial follow up study: outcome after discharge from hospital for women and children recruited to a trial comparing magnesium sulphate with placebo for pre-eclampsia [ISRCTN86938761]	*BMC Pregnancy Childbirth*	No outcomes of interest
244	Tikhova	2012	L71084555 (embase)	Effects of maternal magnesium sulfate therapy in preeclampsia/eclampsia on clinical outcomes in neonate	*European Journal of Anaesthesiology*	Not a primary study
245	Triebwasser	2020	CN-02075400 (cochrane)	221: successful implementation of remote blood pressure monitoring for postpartum hypertension	*Pregnancy Hypertens*	Abstract, subsequently published
246	Triebwasser	2022	L2016043348 (embase)	Nudge intervention to transition care after hypertensive disorders of pregnancy: a randomized clinical trial	*American Journal of Obstetrics and Gynecology*	Abstract, 2020 or later, not yet published
247	Tudela	2013	23344281	Effect of maternal body mass index on serum magnesium levels given for seizure prophylaxis	*Obstetrics & Gynecology*	Not a comparison of interest
248	Tukur	2010	20232764	Management of eclampsia at AKTH: before and after magnesium sulphate	*Niger J Med*	NRCS (no adjustment)
249	Ueda	2016	26513699	Magnesium sulphate can prolong pregnancy in patients with severe early-onset preeclampsia	*J Matern Fetal Neonatal Med*	NRCS (no adjustment)
250	Vadnais	2012	22247820	The Impact of Magnesium Sulfate Therapy on Angiogenic Factors in Preeclampsia	*Pregnancy Hypertens*	NRCS (no adjustment)

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
251	Vaishnav	2019	L2002766696 (embase)	Making magnesium sulfate therapy safer in eclampsia: A comparative study of zuspan regime vs low-dose intravenous MgSO4 regime	*Journal of SAFOG*	NRCS (no adjustment)
252	Vargas Ayala	1998	9745191	[Efficacy of isosorbide in aerosol form in the management of hypertensive crisis in severe preeclampsia].	*Ginecologia y obstetricia de Mexico*	Not population of interest
253	Varol	2001	11336737	HELLP syndrome and postpartum corticosteroids	*Int J Gynaecol Obstet*	Not an intervention of interest
254	Vermillion	1999	10521742	A randomized, double-blind trial of oral nifedipine and intravenous labetalol in hypertensive emergencies of pregnancy	*Am J Obstet Gynecol*	Not population of interest
255	Verschueren	2020	32979728	Why magnesium sulfate 'coverage' only is not enough to reduce eclampsia: Lessons learned in a middle-income country	*Pregnancy Hypertens*	Not a comparative study
256	Vigil-De Gracia	1997	9486510	Dexamethasone in the post-partum treatment of HELLP syndrome	*Int J Gynaecol Obstet*	Not an intervention of interest
257	Vigil-De Gracia	2006	106243203 (cinahl)	Dexamethasone treatment and HELLP syndrome...Fonseca JE, Méndez F, Cataño C, Arias F. Dexamethasone treatment does not improve the outcome of women with HELLP syndrome: a double-blind, placebo-controlled, randomized clinical trial. AM J Obstet Gynecol 2005;193:1591-8	*American Journal of Obstetrics & Gynecology*	Not an intervention of interest
258	Viteri	2018	127386297 (cinahl)	42: Torsemide for prevention of persistent postpartum hypertension in preeclampsia: a randomized, placebo-controlled trial	*American Journal of Obstetrics & Gynecology*	Abstract, subsequently published
259	Wacker	1994	8023622	[Anti-hypertensive therapy in pregnancy-induced hypertension with urapidil]	*Zentralbl Gynakol*	Not a comparative study
260	Wagner	2019	30887426	Socioeconomic, Racial, and Ethnic Disparities in Postpartum Readmissions in Patients with Preeclampsia: a Multi-state Analysis, 2007-2014	*J Racial Ethn Health Disparities*	Not a comparison of interest
261	Walss Rodriguez	1992	1478512	[Anticonvulsant treatment in severe preeclampsia. Comparison between diazepam and magnesium sulfate]	*Ginecol Obstet Mex*	Full text unavailable
262	Walss Rodríguez	1991	1769603	[Management of severe pre-eclampsia in the puerperium. Comparative study of sublingual nifedipine and hydralazine]	*Ginecol Obstet Mex*	Full text unavailable

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
263	Walss Rodríguez	1993	8454221	Severe pre-eclampsia management during puerperium. Comparative study between sublingual nifedipine and hydralazine] [Spanish	*Ginecologia y obstetricia de mexico*	Not population of interest
264	Wang	2008	18293201	Prostacyclin and thromboxane levels in women with severe preeclampsia undergoing magnesium sulfate therapy during antepartum and postpartum periods	*Hypertens Pregnancy*	No outcomes of interest
265	Wang	2020	33200001	Effect of magnesium sulfate combined with labetalol on serum sFlt-1/PlGF ratio in patients with early-onset severe pre-eclampsia	*Exp Ther Med*	NRCS (no adjustment)
266	Wang	2021	34790247	Clinical Effects of Integrated Traditional Chinese and Western Medicine in Treating Severe Preeclampsia and Its Influence on Maternal and Infant Outcomes after Cesarean Section under Combined Lumbar and Epidural Anesthesia	*Evidence-based Complementary and Alternative Medicine*	Not a comparison of interest
267	Wang	2022	36407738	Analysis on Clinical Outcomes of Low-Molecular Weight Heparin Combined with Magnesium Sulfate in Patients with Pre-Eclampsia	*Iran J Public Health*	No outcomes of interest
268	Warren	2004	CN-00526960 (cochrane)	First interim report on the labetalol versus magnesium sulfate for the prevention of eclampsia trial (LAMPET)	*Hypertension in pregnancy*	Full text unavailable
269	Wei	2021	148434503 (cinahl)	108 An automated home blood pressure monitoring program: a pilot study to improve postpartum hypertension care	*American Journal of Obstetrics & Gynecology*	Abstract, 2020 or later, not yet published
270	Weiner	1984	6377898	Control of preeclamptic hypertension by ketanserin, a new serotonin receptor antagonist	*Am J Obstet Gynecol*	Not an intervention of interest
271	Wen	2019	L626672099 (embase)	Effect of oral labetalol versus nifedipine on blood pressure control and length of stay	*Reproductive Sciences*	Abstract prior to 2020, unpublished
272	Wen	2019	30823948	Effect of Magnesium Sulfate Combined with Phentolamine and Nifedipine for Gestational Hypertension and Serum Levels of LIF and Apelin	*J Coll Physicians Surg Pak*	Not population of interest
273	West	2005	15933313	Do clinical trials improve quality of care? A comparison of clinical processes and outcomes in patients in a clinical trial and similar patients outside a trial where both groups are managed according to a strict protocol	*Qual Saf Health Care*	Not a comparison of interest

No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
274	Westermann	2022	L2016042494 (embase)	Comparison of magnesium sulfate loading dose on ability to achieve a therapeutic level	*American Journal of Obstetrics and Gynecology*	Abstract, 2020 or later, not yet published
275	Wu	2020	32432770	Regulation of magnesium sulfate combined with nifedipine and labetalol on disease-related molecules in serum and placenta in the treatment of preeclampsia	*Eur Rev Med Pharmacol Sci*	Not population of interest
276	Xiang	2020	34174970	Treatment of pregnancy-induced hypertension compared with labetalol, low dose aspirin and placebo	*Cell Mol Biol (Noisy-le-grand)*	Not population of interest
277	Xiang	2020	32063925	Magnesium Sulfate in combination with Nifedipine in the treatment of Pregnancy-Induced Hypertension	*Pak J Med Sci*	Not population of interest
278	Yalcin	1998	9639218	Effects of postpartum corticosteroids in patients with HELLP syndrome	*Int J Gynaecol Obstet*	Not an intervention of interest
279	Ybarra	2016	116760252 (cinahl)	Postpartum Preeclampsia	*JOGNN: Journal of Obstetric, Gynecologic & Neonatal Nursing*	Abstract prior to 2020, unpublished
280	Young	1977	865731	Effects of magnesium sulfate on toxemic patients in labor	*Obstet Gynecol*	Full text unavailable
281	Zhang	2019	31602207	Efficacy and safety of combination of magnesium sulfate, phentolamine and nifedipine in treatment of patients with hypertensive disorder complicating pregnancy	*Exp Ther Med*	NRCS (no adjustment)
282	Zhao	2020	32742411	Changes and clinical significance of serum inflammatory factors in the treatment of pregnancy hypertension syndrome with magnesium sulfate combined with nifedipine	*Exp Ther Med*	NRCS (no adjustment)
283	Zhao	2021	34733460	Effects of Compound Danshen Injection Combined with Magnesium Sulfate on Pregnancy-Induced Hypertension Syndrome under the Guidance of Empirical Mode Decomposition Algorithm-Based Ultrasound Image	*J Healthc Eng*	Not a comparison of interest
284	Zheng	2015	26485911	[Effect of Magnesium Sulfate, Nifedipine Tablet Combined Salvia Injection on ET-1/NO, TXA2/PGI2 and Hemorheology of Preeclampsia Patients]	*Chinese Journal of Integrated Traditional and Western Medicine*	No outcomes of interest

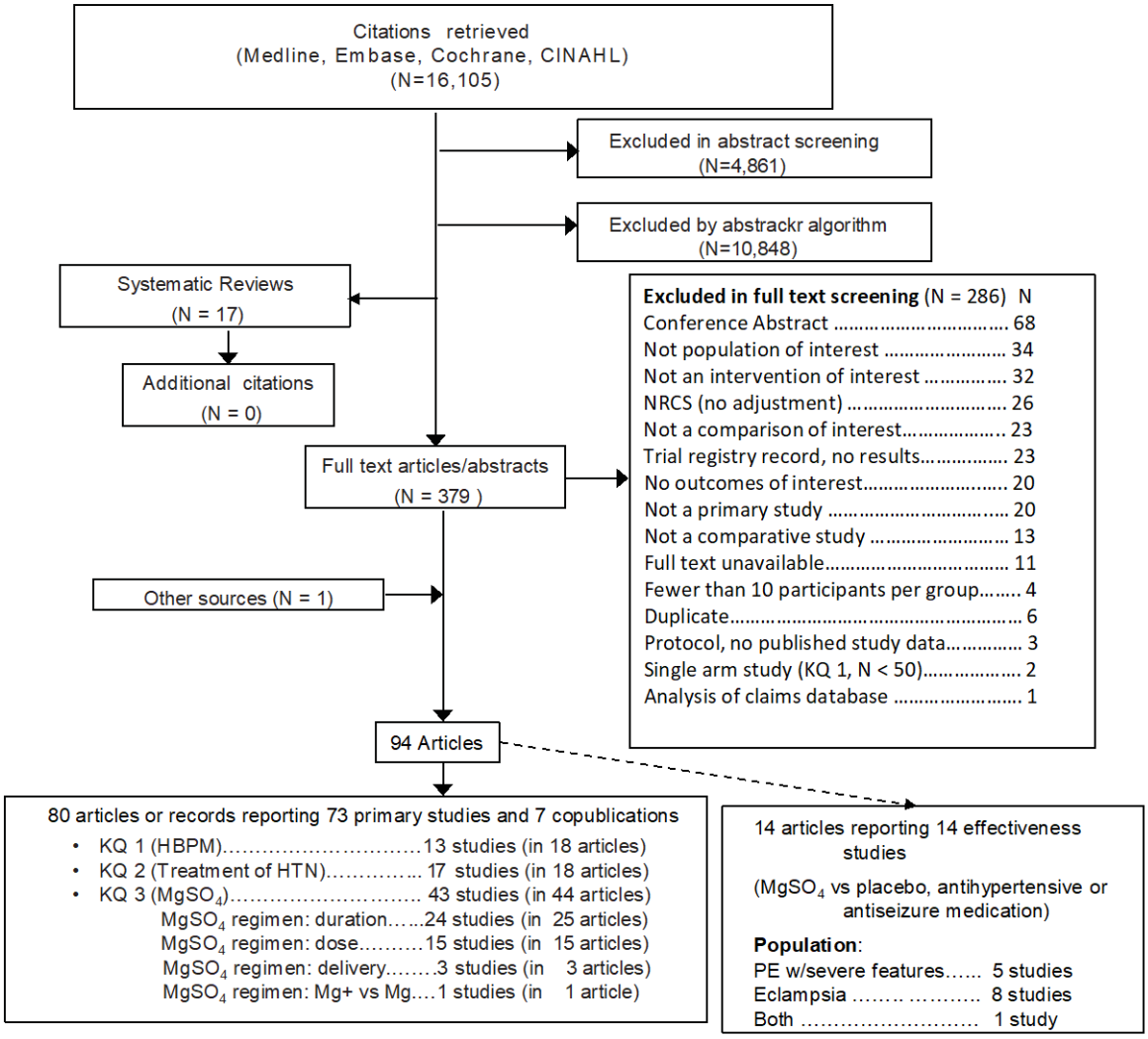
No.	Author	Year	PMID or (Other) ID	Title	Journal	Reason for Exclusion
285	Zhong	2018	30372830	Effect of intravenous magnesium sulfate on bupivacaine spinal anesthesia in preeclamptic patients	*Biomed Pharmacother*	No outcomes of interest
286	Zielinska	2022	35969213	Remote multimodality monitoring of maternal physiology from the first trimester to postpartum period: study results	*J Hypertens*	Single arm study (N < 50)

Appendix C. Results: Design, Arm, and Sample Details

C.1 Results of Literature Searches

As illustrated by Figure C–1, our citation search retrieved a combined 16,105 citations. Of these, 379 were deemed potentially relevant and retrieved in full text. After full-text screening, and the addition of 1 additional study from another source, our review includes 74 eligible studies, with results reported in 79 articles and 2 ClinicalTrials.gov records.

Figure C–1. Flow diagram for studies



Abbreviations: CINAHL = Cumulative Index of the Nursing and Allied Health Literature, NRCS = nonrandomized comparative study

C.2 Description of Included Studies

C.2.1 Overall Summary of Study and Patient Characteristics

Appendix Figure C–1 summarizes the results of the search and screening processes. We extracted data from 73 studies (reported in 80 articles or records) that met our inclusion criteria. [2-81] These 73 studies, published between 1982 and 2022, included 13,542 participants. Sixty-one were randomized controlled trials (RCTs), 4 were nonrandomized comparative studies (NRCSs), and 8 (all pertaining to KQ 1) were single arm studies.

We found 14 trials (in 14 publications) trials (all RCTs) compared the effects of $MgSO_4$ versus placebo, antiseizure medications or antihypertensive medications.[82-93, 94] We briefly extracted the seizure event rate from the $MgSO_4$ treatment arms of each study. These data were meta-analyzed and used to inform separate estimates of the risk of seizure in patients with preeclampsia with severe features, and the risk of subsequent seizures in patients with eclampsia.

For all 67 included studies, Appendix Tables C-1.1 to C–3.1 summarize the design, arm, and patient characteristics in separate tables for each KQ. Detailed search strategies, inclusion and exclusion criteria and a list of excluded studies (with reasons for their exclusion) are in Appendices A.1.1 and Appendix B.

Twenty-three studies enrolled patients in the United States (U.S.) and 2 studies enrolled patients in the United Kingdom (U.K.). For KQ 3, evidence derived from 4 studies conducted in the U.S. that enrolled 609 participants.[16, 28, 31, 57]

Table C–1.1. Key Question 1: Home blood pressure monitoring – summary of design details

Study	Comparators	Design (Timing)	Trial Registration	Inclusion Criteria	Exclusion Criteria	Total N
Burgess 2021, 34397475, USA	N/A	Single Arm (10/2018 – 05/2019)	None	Preeclampsia in PP period and received care from a Wellspan health obstetric care provider and enrolled/willing to enroll in myWellSpan. English-speaking	NR	54
Cairns 2018, 29967037, England	HBPM with self-titration of medications vs. usual care	RCT (04/2015 - 04/2016)	NCT02333240	Age ≥18 years Gestational HTN or preeclampsia. Requiring antihypertensive medication during pregnancy, which needs to continue in the postpartum period.	Prescription of >3 antihypertensive medications at discharge from hospital Self-report of HTN diagnosed outside of pregnancy Inability to speak English Became ineligible because of the cessation of antihypertensive treatment, hypertension prior to pregnancy	91
Deshpande 2022, 35340907, India	N/A	Single Arm (11/2020 – 04/2021)	None	Vaginal delivery after uncomplicated HDP	Complications, C/S, readmitted for neonatal complication	
Hacker 2022, 35283352 (ad hoc), US	N/A	Single Arm (07/2020 - 06/2021)	None	All postpartum discharges	No blood pressure cuff Pre-pregnancy diagnosis of HTN or prior HDP diagnosis	1,192
Hauspurg 2019, 31503166, USA	N/A	Single Arm (02/2018 - 01/2019)	None	Any HDP English-speaking Access to a text messaging-enabled smartphone device	NR	409
Hirshberg 2018, 29703800, USA	HBPM vs. usual care	RCT (08/2016 - 01/2018)	NCT03185455	Age ≥18 Able to read and speak English Delivered at home institution access to a cellphone with unlimited text message capabilities	Readmission for new onset postpartum HTN	206
Hoppe 2019, 30825917, USA	N/A	Single Arm (03/2017 - 07/2017)	None	HDP Age ≥18 years	Readmitted after their primary hospital admission for delivery	55
Hoppe 2020, 32439388, USA	HBPM vs. usual care	NRCS (04/2017 – 06/2018)	None	HDP	NR	428
Janssen 2021, 34329800, USA	N/A	Single Arm (NA - NA)	None	PP HDP English speaking	NR	199

Study	Comparators	Design (Timing)	Trial Registration	Inclusion Criteria	Exclusion Criteria	Total N
Khosla 2022, 35121193	Log vs. audio-only telehealth	NRCS (12/2019 – 06/2020)	None	HDP	NR	473
Rhoads 2017, 28475431, USA	N/A	Single Arm (NA - NA)	None	Age ≥ 18 Preeclampsia], language English speaking	Psychiatric disorder No telephone access	48
Spiegelman 2020, CN-02075381 (cochrane), USA	RPM vs. HBPM paper Log	RCT (11/2018 - 07/2019)	NCT03728790	Age ≥ 18 Speaks English or Spanish	Not planning postpartum care Unable to hold or use tablet No working phone, unwilling or unable to set up escalation pathway Lives out-of-state Postpartum diagnosis of HTN	213
Triebwasser 2020, 32980623, USA	N/A	Single Arm (09/2018 – 02/2019)	None	Age > 18 [over HDP at the time of their delivery admission English speaking Access to a cell phone with unlimited text message capabilities]	NR	333

Table C–1.2. Key Question 1: Home blood pressure monitoring – summary of arm details

Study	Design	Category	Trial Name	Arm Name	Remote Medication Management N (%)	Arm N
Hirshberg 2018, 29703800, USA	RCT	Effectiveness	HeartSafe Motherhood	HBPM	Yes, details N/R	103
	RCT	Effectiveness	HeartSafe Motherhood	Usual care	Yes, details N/R	103
Cairns 2018, 29967037, England	RCT	Effectiveness	SNAP-HT	Self-management of Postnatal HTN Management	Yes, 45 (100%)	45
	RCT	Effectiveness	SNAP-HT	Usual care	Yes, 45 (100%)	46
Hoppe 2020, 32439388, USA	NRCS	Effectiveness	none	Telehealth	No	214
	NRCS	Effectiveness	none	Standard outpatient care	No	214
Spiegelman 2020, CN-02075381, USA	RCT	Comparative effectiveness	none	HBPM	N/R	101
	RCT	Comparative effectiveness	none	Prescription for BP cuff with manual log	N/R	112
Khosla 2022, 35121193, USA	NRCS	Comparative effectiveness	none	Audio-only telehealth	No	258
	NRCS	Comparative effectiveness	none	Manual BP log	No	215
Burgess 2021, 34397475, USA	single arm	Feasibility	none	BP self-monitory via eHealth	N/R	54
Deshpande 2022, 35340907, India	single arm	Feasibility	none	N/R	N/R	N/R
Hoppe 2019, 30825917, USA	single arm	Feasibility	none	Telehealth with Remote BP Monitoring	Yes, 25 (45%)	55
Rhoads 2017, 28475431, USA	single arm	Feasibility	none	m-health Device User	N/R	50
Hauspurg 2019, 31503166, USA	single arm	Implementation	none	Remote Hypertension Monitoring	Yes, 172 (40%)	409
Janssen 2021, 34329800, USA	single arm	Implementation	HeartSafe Motherhood	Text-based PP BP monitoring	Yes, 32 (16.1%)	199
Triebwasser 2020, 32980623, USA	single arm	Implementation	HeartSafe Motherhood	Heart Safe Motherhood (implementation cohort)	Yes, 28 (65.1%)	333
Hacker 2022, 35283352, US	single arm	QI initiative	none	HBPM	No	1192

Table C–1.3.1. Key Question 1: Home blood pressure monitoring – summary of sample details

Study	Arm Name	Sample Size	Chronic HTN	HDP Classification, N (%)	Timing of HDP Diagnosis	Race, N (%)	Age, Mean (SD)
Burgess 2021, 34397475, US	BP self-monitory via eHealth	54	NR	NR	Postpartum, 54 (100%)	White, 40; Black, 6; Asian, 3; Declined/other, 5	28.2 (5.2)
Cairns 2018, 29967037, UK	Self-management of Postnatal HTN Management	45	NR	Gestational hypertension, 20 (44.4); Preeclampsia without severe features, 25 (55.6)	Median 35.9 (IQR 31.9–37.7)	White, 41 (91.1); Black, 1 (2.2); Asian, 3 (6.7)	31.7 (5.3)
	Usual care	46	NR	Gestational hypertension, 22 (47.8); Preeclampsia without severe features, 24 (52.2)	Median 34.7 (IQR 31.7–36.9)	White, 43 (93.5); Black, 1 (2.2); Asian, 2 (4.3)	31.7 (5.3)
Deshpande 2022, 35340907, India	Postpartum BP monitoring by teleconsultation	60	NR	HDP without complications	Postpartum (100%)	NR	25.7 (5.7)
Hacker 2022, 35283352, US	HBPM	1,043	NR	NR	NR	White, 741 (71); Black, 144 (13.8); Asian, 94 (9)	30.8 (7.4)
	New elevated BP	149	NR	NR	NR	White, 100 (67.1); Black, 36 (24.2); Asian, 5 (3.4)	30.4 (5.4)
Hauspurg 2019, 31503166, USA	Remote Hypertension Monitoring	409	NR	Gestational hypertension, 168 (41.1); Preeclampsia without severe features, 136 (33.3); PE superimposed on chronic HTN, 49 (12); Preeclampsia with severe features, 43 (10.5)	NR	White, 305 (74.6); Black, 87 (21.3); Asian, 8 (2); Other, 9 (2.2)	31 (Range 27.0-35.0)
Hirshberg 2018, 29703800, USA	HBPM	103	14 (13.6)	PE superimposed on chronic HTN, 14 (13.6); Preeclampsia with severe features, 25 (24.3); HELLP, 0 (0); Eclampsia, 1 (1)	Median 38 (IQR 36, 39); Antepartum, 45 (43.7%); Intrapartum, 44 (42.7%); Postpartum, before discharge, 14 (13.6%)	White, 28 (27.2); Black, 68 (66); Asian, 2 (1.9); Other, 5 (4.8)	28; Median 6
	Usual care	103	13 (12.6)	PE superimposed on chronic HTN, 10 (9.7); Preeclampsia with severe features, 22 (21.4); HELLP, 3 (2.9); Eclampsia, 0 (0)	Median 38 (IQR 36, 39); Antepartum, 56 (54.4%); Intrapartum, 31 (30.1%); Postpartum, before discharge, 16 (15.5%)	White, 25 (24.3); Black, 73 (70.9); Other, 1 (1)	28; Median 5

Study	Arm Name	Sample Size	Chronic HTN	HDP Classification, N (%)	Timing of HDP Diagnosis	Race, N (%)	Age, Mean (SD)
Hoppe 2019, 30825917,USA	Telehealth with Remote BP Monitoring	55	6 (10.9)	Gestational hypertension, 17 (30.9); Preeclampsia without severe features, 16 (29.1); PE superimposed on chronic HTN, 3 (5.5); Preeclampsia with severe features, 19 (34.5)	NR	White, 51 (92.7); Hispanic, 5 (9.1)	31.8 (4.9)
Hoppe 2020, 32439388, USA	Telehealth	214	NR	NR	NR	NR	NR
	Standard outpatient care	214	NR	NR	NR	NR	NR
Janssen 2021, 34329800, USA	Text-based PP BP monitoring	199	53 (26.6)	Gestational hypertension, 89 (44.7); ; PE superimposed on chronic HTN, 29 (14.6); Preeclampsia with severe features, 63 (31.7); HELLP, 4 (2); Eclampsia, 22 (11.1)	Prenatal, 199 (100%)	White, 84 (42.2); Black, 67 (33.7); Asian, 4 (2); Hispanic, 23 (11.6); Other or not listed, 21 (10.6);	31.2 (6.4)
Khosla 2022, 35121193, USA	Post-COVID (audio-only telemedicine)	258	Chronic HTN 29 (11.3),	Gestational HTN 113 (44.1), PE w/SF 75 (65.8), Superimposed PE 29 (11.3), HELLP 85 (33.2), Chronic HTN 59 (22.9)	All antepartum or intrapartum	Non-Hispanic White 30 (11.6) Non-Hispanic Black 190 (73.6) Hispanic or Latinx 17 (6.6) Asian 9 (3.5) Other/unknown 12 (4.7)	Median 30 Range 24 to 34
	Pre-COVID (manual BP log)	215	Chronic HTN 29 (13.5)	Gestational HTN 81 (37.7), PE w/SF 71 (67.6), Superimposed PE 38 (17.7), HELLP 67 (31.2), Chronic HTN 68 (31.6)	All antepartum or intrapartum	Non-Hispanic White 26 (12.1) Non-Hispanic Black 171 (79.5) Hispanic or Latinx 12 (5.6) Asian 2 (0.9) Other/unknown 4 (1.9)	Median 29 Range 24 to 33
Rhoads 2017, 28475431, USA	m-health Device User	25	NR	Preeclampsia without severe features, 25 (100)	Mean 33.1 (SD 3.3)	White, 12 (48)	26.8 (5.2)

Study	Arm Name	Sample Size	Chronic HTN	HDP Classification, N (%)	Timing of HDP Diagnosis	Race, N (%)	Age, Mean (SD)
Spiegelman 2020, CN-02075381, USA	HBPM	101	15 (14.9)	Gestational hypertension, 33 (32.7); Preeclampsia without severe features, 17 (16.8); PE superimposed on chronic HTN, 9 (8.9); Preeclampsia with severe features, 26 (25.7); Eclampsia, 0 (0); DC on BP medication, 41 (40.6)	NR	White, 55 (54.5); Black, 32 (31.7); Asian, 5 (5); American Indian or Pacific Islander, 1 (0.5); Hispanic, 53 (52.5); More than one, 0 (0); Unknown or NR, 9 (6.9)	Median 33 (IQR 28, 36)
	Usual Care	112	14 (12.5)	Gestational hypertension, 38 (33.9); Preeclampsia without severe features, 12 (10.7); PE superimposed on chronic HTN, 12 (10.7); Preeclampsia with severe features, 36 (32.1); DC on BP medication, 47 (42)	NR	Asian, 11 (9.8); American Indian or Pacific Islander, 0 (0); Hispanic, 67 (52.5); More than one, 1 (0.9); Unknown or NR, 19 (17)	Median 32 (IQR 19, 36)
Triebwasser 2020, 32980623, USA	Heart Safe Motherhood (implementation cohort)	333	26 (7.8)	PE superimposed on chronic HTN, 33 (9.9); Preeclampsia with severe features, 74 (22.2)	NR	Black, 136 (40.8); Hispanic, 192 (57.7)	31.1 (5.8)

Table C–1.3.2. Key Question 1: Home blood pressure monitoring – summary of additional sample details

Study	Arm Name	BMI, Mean (SD)	Co-occurring Disorders, N (%)	Parity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Gestational Age at Delivery, Mean (SD)	Preterm Birth, N (%)	Social Determinants Health, N (%)
Burgess 2021, 34397475, USA	BP self-monitory via eHealth	NR	NR	NR	NR	NR	NR	NR	NR	NR
Cairns 2018, 29967037, UK	Self-management of Postnatal HTN Management	29 (7.5)	NR	Nulliparous, 32 (71.1); Parity ≥1, 13 (28.9)	NR	NR	NR	Median 37.6 (IQR 36.2, 39.2)	NR	NR
	Usual care	28 (8.3)	NR	Nulliparous 31 (67.2); Parity ≥1, 15 (32.6)	NR	NR	NR	Median 37.2 (IQR 36.3, 39.1)	NR	NR
Deshpande 2022, 35340907, India	PP BP monitoring by teleconsultation	NR	NR	Primiparous 42 (66.6) Multiparous 21 (33.4)	NR	NR	NR	NR	NR	Class 3, 43 (68.3) Class 4, 20 (31.7)
Hacker 2022, 35283352, USA	HBPM	25.2 (IQR 22.4, 30.1)	Gestational diabetes, 85 (8.1)	Nulliparous, 594 (57)	Cesarean, 289 (28.8)	17 (1.7)	NR	39 (3)	NR	NR
	New elevated BP	29.2 (IQR 25, 34.5)	Gestational diabetes, 10 (6.7)	Nulliparous, 81 (54.4)	Cesarean, 41 (27.5)	1 (0.7)	NR	39.1 (1.8)	NR	NR
Hauspurg 2019, 31503166, USA	Remote Hypertension Monitoring	27.8 (Range 23.6, 34.6)	Pregestational diabetes, 9 (2.2); Gestational diabetes, 45 (11.2)	NR	Vaginal, 322 (80); Cesarean, 80 (20)	NR	NR	37.7 (Range 36.9, 39.1)	NR	Private insurance, 274 (67); Medicaid, 128 (31.3); Insurance status: Other, 7 (1.7)

Hirshberg 2018, 29703800, USA	HBPM	Median 31 (IQR 25.1, 38.3)	Pregestational diabetes, 5 (4.8); Gestational diabetes, 6 (5.8); Renal disease, 5 (4.8)	NR	Cesarean, 33 (32)	NR	3 (2.9)	Median 38 (IQR 37, 39)	NR	Private insurance, 44 (42.7); Medicaid, 59 (57.3)
	Usual care	Median 30.1 (IQR 24.3, 33.8)	Pregestational diabetes, 3 (2.9); Gestational diabetes, 8 (7.8); Renal disease, 5 (4.8)	NR	Cesarean, 34 (33)	NR	3 (2.9)	Median 38 (IQR 37, 39)	NR	Private insurance, 42 (40.8); Medicaid, 61 (59.2)
Hoppe 2019, 30825917, USA	Telehealth with Remote BP Monitoring	32.6; Median 8.3	NR	Nulliparous, 34 (61.8)	Vaginal, 23 (41.8); Cesarean, 32 (58.2)	NR	NR	37.3 (3.1)	NR	NR
Janssen 2021, 34329800, USA	Text-based PP BP Monitoring (Heart Safe Motherhood)	29.9; Median 8.1	Pregestational diabetes, 19 (9.5); Gestational diabetes, 21 (10.6)	NR	Vaginal, 119 (59.8); Cesarean, 80 (40.2)	NR	NR	37.2 (3.1)	Preterm delivery (< 37 weeks), 27 (13.6)	Private insurance, 108 (54.3); Medicaid, 71 (35.7); Insurance status: Other, 20 (10.1)
Rhoads 2017, 28475431, USA	m-health Device User	NR	NR	NR	Vaginal, 4 (16); Cesarean, 21 (84)	NR	NR	NR	NR	Education >High school, 14 (56); Income (>$30,000 per year), 7 (28); Work, 11 (44); Rural, 11 (44)
Khosla 2022, 35121193, USA	Audio-only telehealth (post-COVID)	NR	Pregestational diabetes 16 (6.3) Gestational diabetes, 25 (9.7) Cardiac disease, 7 (2.7)	Nulliperous, 114 (44.2)	Cesarean delivery, 86 (33.9)	NR	NR	Median 38.4 (IQR 37.0 to 39.4)	NR	NR
	Manual log (pre-COVID	NR	Pregestational diabetes 14 (6.5) Gestational diabetes, 17 (8) Cardiac disease, 4 (1.9)	Nulliperous, 92 (43)	Cesarean delivery, 87 (40.5)	NR	NR	Median 38.4 (IQR 37.0 to 39.3)	NR	NR

Spiegelman 2020, CN-02075381, USA	HBPM	NR	Pregestational diabetes, 1 (1); Gestational diabetes, 15 (14.9)	Multiparous, 83 (82.2)	Vaginal, 44 (43.6); Cesarean, 57 (56.4)	NR	NR	NR	NR	NR
	Usual Care	NR	Pregestational diabetes, 5 (4.5); Gestational diabetes, 13 (11.7)	Multiparous, 81 (72.3)	Vaginal, 56 (50); Cesarean, 56 (50)	NR	NR	NR	NR	NR
Triebwasser 2020, 32980623, USA	Heart Safe Motherhood	32.5 (Range 29.0, 37.3)	NR	Nulliparous, 203 (61)	Vaginal, 184 (55.3); Cesarean, 147 (44.1)	NR	NR	38.7 (Range 37.4, 39.9)	Preterm delivery (< 37 weeks), 54 (16.2)	Private insurance, 215 (64.6); Medicaid, 111 (33.3); Uninsured, 7 (2.1)

Table C–2.1. Key Question 2: Postpartum treatment of hypertension – summary of design details

Study	Group	Comparators	Design (Timing)	Trial Registration	Inclusion Criteria	Exclusion Criteria	Total N
Ainuddin 2019, 31489020, Pakistan	PP HTN	labetalol vs. nifedipine	RCT (01/2015 - 12/2015)	NCT02426177	Age [any age], gestational age, ≥20 weeks]	History of heart block or arrhythmia, heart failure, asthma, uncontrolled diabetes, hypothyroidism, chronic hypertension treated with antihypertensive medication prior to pregnancy, renal disease with serum creatinine level >1mg/dl, allergies to either nifedipine or labetalol and those not willing to participate in the study.	124
Arias-Hernández 2020, 32774912, Mexico	Severe acute	diltiazem vs. nifedipine	RCT (1/2009 - 5/2009)	NCT04222855	Age, 18 to 40yr	Patient falls outside of the inclusion criteria and parameters, subjects with unstable medical conditions.	42
Ascarelli 2005, 15625138, USA	Diuretic	furosamide+K vs. placebo	RCT (7/1997 - 3/1998)	NR	Gestational age [delivered at or greater than 20 weeks gestation], specific treatment needed [PP preeclampsia]	Less than 20 weeks of gestation, hypokalemia (k < 3.0 meq/l) on admission, already taking diuretics or potassium supplements for any reason, any hemodynamic instability surrounding the events of delivery, unable to understand and sign the informed consent	264
Barton 1990, 2316590, US	Severe acute	PO nifedipine vs. placebo	RCT (5/1988 - 5/1989)	NR	Severe preeclampsia	NR	31
Dabaghi 2019, L2002160304 (embase), Iran	Diuretic	furosamide+K vs. none	RCT (3/2013 - 3/2014)	Iranian Register Clinical Trials under the number 2014031717041N1	Gestational age [delivery at or greater than 20 wks of gestation], specific treatment needed [severe preeclampsia or HELLP]	Gestational age less than 20 weeks, hypokalemia(k<3 meq/l) on admission, taking diuretics or potassium supplements recently, any hemodynamic instability before or after delivery	

Study	Group	Comparators	Design (Timing)	Trial Registration	Inclusion Criteria	Exclusion Criteria	Total N
Fidler 1982, 7171513, UK	PP HTN	timolol vs. methyldopa	RCT (NA - NA)	NR	Specific treatment needed [puerperal hypertension]	Had other complications of pregnancy, multiple pregnancy, diabetes, renal disease, already taking antihypertensive drugs, patient with heart failure or bronchial asthma	80
Griffis 1989, 2789542, US	Severe acute	IM hydralazine vs. IV methydopa	RCT (NA - NA)	NR	Gestational age > the 20 weeks preeclampsia	Previous antihypertensive use during pregnancy excluding that utilized for intrapartum management of pih, history of chronic hypertension or elevated blood pressure before 20 weeks of gestation, evidence of hepatic disease or dysfunction.	26
Lopes Perdigao 2021, 33550824, USA	Diuretic	furosamide vs. placebo	RCT (06/2018 - 10/2019)	NR	Age [≥ 18], gestational age [≥ 20], language spoken [English speaking]	Underlying cardiac or rheumatologic disease, advanced diabetes (white class c or higher), creatinine > 1.2 mg/dl, potassium < 3 meq/l, allergy to furosamide, diuretics given before randomization	384
Noronha-Neto 2017, 28125624, Brazil	Severe acute	captopril vs. clonidine	RCT (11/2012 - 6/2013)	NCT01761916	Age [18 years to 45 years], specific treatment needed [PP women with hypertensive disorders of pregnancy and very high bp episodes]	Heart disease, smoking, illicit drug use that could interfere with maternal hemodynamics, contraindications to captopril (acute or chronic renal disease, chronic liver disease and hypersensitivity to the drug), having used captopril/clonidine previously, prior to admission, contraindications to clonidine ((sinus node disease, chronic liver disease and hypersensitivity to the drug)	88
Ormesher 2020, 33012200, UK	Target organ protectio n	enalapril vs. placebo	RCT (9/2018 - 9/2020)	NCT03466333	Age ≥ 18 Gestational age < 37 weeks with preterm preeclampsia No known cardiac disease Creatinine <100 µmol/l]	Unable to consent, had known cardiac disease, had a contraindication to ace inhibitors, were currently taking ace inhibitor / angiotensin ii receptor blocker (arb), had known renal artery stenosis	60

Study	Group	Comparators	Design (Timing)	Trial Registration	Inclusion Criteria	Exclusion Criteria	Total N
Sayin 2005, L40874197 (embase), Turkey	PP HTN	nifedepine vs. alpha-methyldopa	RCT (01/1999 - 06/2004)	NR	Specific treatment needed [PP HTN in women who had various hypertensive disorders of pregnancy]	Pregnant women who received medical treatment were not included in the study	83
Sharma 2017, 27786578, US	PP HTN	labetalol vs. ER nifedipine	RCT (6/2014 –- 6/2015)	NCT02168309.	Age, ≥ 18 years], gestational age, ≥32 weeks' gestation], specific treatment needed [persistent PP hypertension]	Known heart block,, heart rate <60 or >120 beats per minute, absolute contraindication to nifedipine or labetalol such as allergy,, significant renal disease (creatinine >1.5 mg/dl),, heart failure, moderate persistent or severe asthma.	50
Vázquez-Rodríguez 2020, 34520145, Mexico	Target organ protection	losartin+hydralazine+methyldopa+metoprolol vs. hydralazine+methyldopa+metoprolol	RCT (01/2018 - 05/2018)	NR	NR	Prior comorbidity	49
Veena 2017, 27835048, India	Diuretic	furosamide+nifedipine vs. nifedipine	RCT (9/2011 - 8/2013)	NR	Severe preeclampsia with persistent high BP	Patients not willing to participate in the study, hemodynamically unstable patients,, hypokalemia (serum k+ < 3meq/l),, patients already on potassium supplementation and diuretics,, patients who expelled the fetus at < 20 weeks gestation	100

Study	Group	Comparators	Design (Timing)	Trial Registration	Inclusion Criteria	Exclusion Criteria	Total N
Vigil De Gracia 2007, 17469006, Panama	Severe acute	IV hydralazine vs. IV labetalol	RCT (NA - NA)	NR	Severe PP HTN, more than 24 hours after the last dose of intravenous Antihypertensive therapy received antenatal or intrapartum]. No concurrent oral antihypertensive medications No absolute contraindications to labetalol or hydralazine	NR	82
Viteri 2018, 30303905, US	Diuretic	torsemide vs. placebo	RCT (8/2016 - 9/2017)	NCT02813551	Age [aged 18 years and older], specific treatment needed [preeclampsia, antepartum/intrapartum or within 24 hours postpartum]	Oliguria (urine output less than 30 ml/h at the time of randomization), heart failure, hypokalemia (serum potassium below 3 meq/l), diuretic use within the past 24 hours, hypersensitivity to torsemide or sulfonylureas, and pulmonary edema., gestational hypertension, renal or cardiopulmonary failure	118
Yoselevsky, 2022, L2016043015, USA	PP HTN	Enalapril vs. Nifedipine	RCT (01/2020 – 01/2021)	NCT04236258	Age, ≥ 18 years, any Any HDP, chronic hypertension, provider wanting to initiate antihypertensive in the postpartum period. Not currently on >1 antihypertensive, and plans to receive PP care at the hospital or affiliated clinic	Pulse <60 or >120 BPM over four hours Allergy to any of the antihypertensives Creatinine ≥1.5 History of strict contraindication or failed treatment with enalpril or nifedipine	94

Table C–2.2. Key Question 2: Postpartum treatment of hypertension – summary of arm details

Study	Group	Medication	Route	Dosing Interval	Starting Dose	Maximum Dose	Treatment Duration	Protocol if BP Not Controlled
Ainuddin 2019, 31489020, Pakistan	PP HTN	Labetalol	PO	q24h	100mg	1200mg	NR	Add nifedipine 30 mg and give incremental increasing doses until desired BP achieved
	PP HTN	Nifedipine	PO	q24h	30 mg	90mg	NR	Add labetalol 100 mg and give incrementally increasing doses until desired BP achieved
Arias-Hernández 2020, 32774912, Mexico	Severe acute	Diltiazem	PO	q8h	60mg	60mg	N/R	In case of hypertensive crisis, 10 mg of hydralazine was administered IV three times (every 20 min);
	Severe acute	Nifedipine	PO	q8h	10mg	10mg	N/R	Same
Ascarelli 2005, 15625138, USA	Diuretic	Furosemide + oral K supplement	PO	q24h of Furosemide + q24h of K supplement	Furosemide 20mg + K supplement 20mEq	NR	Furosemide 5d + K supplement 5d	Antihypertensive therapy was administered to patients with intermittent or ≥2 elevations of SBP (≥150 mmHg) or DBP (≥100 mmHg) after assignment to receive either furosemide or no medication
	Diuretic	No Rx	N/A	N/A	N/A	NR	N/A	N/A
Barton 1990, 2316590, US	Severe acute	Nifedipine	PO	q4h	10mg	NR	48h	NR
	Severe acute	Placebo	PO	q4h	10mg	NR	48h	NR

Study	Group	Medication	Route	Dosing Interval	Starting Dose	Maximum Dose	Treatment Duration	Protocol if BP Not Controlled
Dabaghi 2019, L2002160304 (embase), Iran	Diuretic	Furosemide + K supply	PO	q24h	20mg	NR	5 days during hospitalization and after hospital discharge	Anti-hypertensive drugs were begun for patients in two groups if SBP was equal or greater than 160 mm-Hg and if DBP was equal or greater than 110 mm-Hg.
	Diuretic	No Rx	N/A	N/A	N/A	N/A	N/A	Same
Fidler 1982, 7171513, UK	PP HTN	Methyldopa	NR	q8h	250mg	1g/dose, 3g/d	Until attainment of the target blood pressure	Dose doubled and doubled again after a further 24 h if necessary. If the DBP >95 mmHg after successive doubling, oral hydralazine added
	PP HTN	Timolol	PO	q8h	5mg	20mg/dose, 60mg/d	Until attainment of the target blood pressure	Same

Study	Group	Medication	Route	Dosing Interval	Starting Dose	Maximum Dose	Treatment Duration	Protocol if BP Not Controlled
Griffis 1989, 2789542, US	Severe acute	Hydralazine	NR	q6h	20mg	40mg	NR	If on hydralazine, 20 mg IV every 6 hours, increase dosage to 40 mg IM every 6 hours
	Severe acute	Methyldopa	NR	q6h	250mg	500mg	NR	If on methyldopa, 250 mg IVPB every 6 hours, increase dosage to 500 mg IVPB every 6 hours.
Neto 2017, 28125624, Brazil	Severe acute	Clonidine	PO	q24h	0.1mg	0.6mg/day	Until it returned to levels before the episode (SBP) <180 mmHg and (DBP) <110 mmHg	NR
	Severe acute	Captopril	PO	q24h	25mg	150mg/day	Until it returned to levels before the episode (SBP) <180 mmHg and (DBP) <110 mmHg	NR
Ormesher 2020, 33012200, UK	Target organ protection	Enalapril	PO	q24h	5mg	20mg	6 months	NR
	Target organ protection	Placebo	PO	q24h	N/A	N/A	6 months	NR
Perdigao 2021, 33550824, USA	Diuretic	Furosamide	PO	q24h	20 mg	20 mg	5d	If BP ≥150/100 5 mg amlodipine or 30 mg nidefipine. IF BP ≥160/110 10 mg amlodipine
	Diuretic	Placebo	PO	q24	NA	20 mg	5d	Same

Study	Group	Medication	Route	Dosing Interval	Starting Dose	Maximum Dose	Treatment Duration	Protocol if BP Not Controlled
Sayin 2005, L40874197 (embase), Turkey	PP HTN	Alpha-methyldopa	NR	q8h	250mg	NR	Until control: treatment was discontinued if under treatment, SBP <150 and DBP <100 mmHg for 48 hours	Metoprolol (100 mg/day) was first added when >140/90 mmHg. If >140/90 mmHg despite the dual drug combination and the patient is refractory, a third antihypertensive drug was added: Amlodipine (5 mg/day) or Perindopril (4 mg/day)
	PP HTN	Nifedipine	NR	q6h	10ntil	NR	Until control: treatment was discontinued if under treatment, SBP <150 and DBP <100 mmHg for 48 hours	Same
Sharma 2017, 27786578, US	PP HTN	Labetalol	PO	q12h	200 mg	800 mg	NR	The use of concomitant intravenous (IV) antihypertensive medication for severe hypertension as well as the use of magnesium sulfate for seizure prophylaxis was decided by the treating medical team.
	PP HTN	Nifedipine	PO	q24h	30mg	90mg	NR	Same

Study	Group	Medication	Route	Dosing Interval	Starting Dose	Maximum Dose	Treatment Duration	Protocol if BP Not Controlled
Vázquez-Rodríguez 2020, 34520145, Mexico	Target organ protection	Losartan/Metoprolol/ Methyldopa/Hydralazine	PO	q12 h, q24h, q24h, q24h	100 mg/d, 200 mg/d, 1500 mg/d, 200 mg/d	NR	90 d	If hypotension (BP <110/70), suspend doses starting with methyldopa, then hydralazine, then metoprolol, then losartan, attempting to maintain at least 50 mg/d. If severe HTN (>160/110), nifedipine 10 mg sublingual q20 minutes until <140/90, then add oral nifedipine.
	Target organ protection	metoprolol, methyldopa hydralazine	PO	q24h all	200 mg/d, 1500 mg/d 200 mg/d	NR	90 d	Same
Veena 2017, 27835048, India	Diuretic	Furosemide + Nifedipine	PO	Furosemide q24h + Nifedipine q8h	20mg Furosemide + 10mg Nifedipine	20mg	NR	Any high blood pressure recording of ≥ 160/110 mm Hg was treated with an additional stat dose of nifedipine 10 mg.
	Diuretic	Nifedipine alone	PO	q8h	10mg	10mg	NR	Same

Study	Group	Medication	Route	Dosing Interval	Starting Dose	Maximum Dose	Treatment Duration	Protocol if BP Not Controlled
Vigil-De Gracia 2007, 17469006, Panama	Severe acute	Hydralazine	NR	Every 20 minutes, until the desired effect is achieved or to a maximum of five doses	5mg	5mg (But maximum total doses are 5doses= 25mg)	Until the desired effect is achieved or to a maximum of five doses	To receive the Labetalol and oral antihypertensive drug
	Severe acute	Labetalol	NR	Every 20 minutes, until the desired effect is achieved or to a maximum of five doses	20mg	80mg (But maximum total doses are 5doses= 300mg, first dose 20mg, second dose if needed is 40mg, then 80mg repeated 3 times)	Until the desired effect is achieved or to a maximum of five doses	To receive the Hydralazine and oral antihypertensive drug
Viteri 2018, 30303905, US	Diuretic	Torsemide	PO	q24h	20mg	20mg	NR	NR
	Diuretic	Placebo	PO	q24h	20mg	20mg	NR	NR

Study	Group	Medication	Route	Dosing Interval	Starting Dose	Maximum Dose	Treatment Duration	Protocol if BP Not Controlled
Yoselevsky 2022, L2016043015 (Embase), US	PP HTN	Enalapril	PO	q24h	10mg	40mg	NR	If > 40mg daily of enalapril without achieving BP goal or the patient's provider believes the assigned agent is ineffective, labetalol 200mg twice daily
	PP HTN	Nifedipine	PO	q24h	30mg	90mg	NR	If > 90mg nifedipine daily without achieving BP goal or the patient's provider believes the nifedipine (is ineffective, labetalol 200mg twice daily

Table C–2.3.1. Key Question 2: Postpartum treatment of hypertension – summary of sample details

Study	Arm Name	Sample Size	Chronic HTN, N (%)	HDP Classification N (%)	Timing of HDP Diagnosis, N (%)	BP Mean (SD)	Race and Ethnicity, N (%)
Ainuddin 2019 31489020 Pakistan	Labetalol	62	0 (0)	NR	NR	NR	NR
	Nifedipine	62	0 (0)	NR	NR	NR	NR
Arias-Hernández 2020 32774912 Mexico	Diltiazem	21	0 (0)	Patients without HTN antecedents during pregnancy 0 (0); Severe preeclampsia 21 (100); HELLP 0 (0);	Puerperium (the first 24 hours after delivery) 21 (100)	NR	NR
	Nifedipine	21	0 (0)	Patients without HTN antecedents during pregnancy 0 (0); Severe preeclampsia 21 (100); HELLP 0 (0);	Puerperium (the first 24 hours after delivery) 21 (100)	NR	NR
Ascarelli 2005 15625138 US	Furosemide + oral K supplement	132	NR	CPRE 16 (12.2); SPRE (severe preeclampsia including 3 patients with HELLP 35 (26.5); Mild Preeclampsia 81 (61.4)	NR	NR	NR
	No Therapy	132	NR	CPRE 9 (6.8); SPRE (severe preeclampsia including 3 patients with HELLP 35 (26.5); Mild Preeclampsia 88 (66.7)	NR	NR	NR

Study	Arm Name	Sample Size	Chronic HTN, N (%)	HDP Classification N (%)	Timing of HDP Diagnosis, N (%)	BP Mean (SD)	Race and Ethnicity, N (%)
Barton 1990 2316590 US	Nifedipine	16	NR	Severe preeclampsia 16 (100)	Antepartum 16 (100)	NR	NR
	Placebo	15	NR	Severe preeclampsia 15 (100)	Antepartum 15 (100)	NR	NR
Dabaghi 2019 Iran	Furosemide + K supply	NR	NR	NR	NR	NR	NR
	Control (no medication)	NR	NR	NR	NR	NR	NR
Fidler 1982 7171513 UK	Methyldopa	40	NR	Puerperal hypertension 40 (100)	Puerperal 40 (100)	147.6 (1.9)/101.3 (0.8)	NR
	Timolol	40	NR	Puerperal hypertension 40 (100)	Puerperal 40 (100)	143.8 (1.7)/99.8 (0.8)	NR
Griffis 1989 2789542 US	Hydralazine	12	NR	PP preeclampsia 12 (100)	After the 20th week of gestation 12 (100)	NR	NR
	Methyldopa	14	NR	PP preeclampsia 14 (100)	After the 20th week of gestation 14 (100)	NR	NR
Lopes Perdigao 2021 33550824 USA	Furosemide	192	19 (10)	PE superimposed on chronic HTN 19 (10); Gestational HTN/PE; Gestational HTN/PE 173 (90)	NR	NR	White 30 (16); Black 151 (79)
	Placebo	192	NR	PE superimposed on chronic HTN 11 (6); Gestational HTN/PE; Gestational HTN/PE 181 (94)	NR	NR	White 47 (24); Black 138 (72); Other 7 (4)

Study	Arm Name	Sample Size	Chronic HTN, N (%)	HDP Classification N (%)	Timing of HDP Diagnosis, N (%)	BP Mean (SD)	Race and Ethnicity, N (%)
Noronha 2017 28125624 Brazil	Clonidine	43	NR	Severe preeclampsia 27; Imminent eclampsia 4	Pregnancy 43	156.7 (16.7)/102.6 (12)	NR
	Captopril	45	NR	Severe preeclampsia 31; Imminent eclampsia 6	Pregnancy 45	161.2 (21.6)/102.6 (16.1)	NR
Ormesher 2020 33012200 PICk-UP UK	Enalapril	NR	NR	Preterm preeclampsia; Preterm preeclampsia 30 (100)	Preterm preeclampsia(before 37 weeks' gestation) 30 (100)	NR	White 21 (70); Black 4 (13.3); Asian 4 (13.3); Other 1 (3.3)
	Placebo	NR	NR	Preterm preeclampsia; Preterm preeclampsia 30 (100)	Preterm preeclampsia(before 37 weeks' gestation) 30 (100)	NR	White 17 (56.7); Black 4 (13.3); Asian 9 (30); Other 0 (0)
Sayin 2005 Turkey	Alpha-methyldopa	41	NR	Severe preeclampsia 15 (36.6); Preeclampsia 19 (46.3)	NR	NR	NR
	Nifedipine	42	NR	Severe preeclampsia 16 (38.1); Preeclampsia 20 (47.6)	NR	NR	NR

Study	Arm Name	Sample Size	Chronic HTN, N (%)	HDP Classification N (%)	Timing of HDP Diagnosis, N (%)	BP Mean (SD)	Race and Ethnicity, N (%)
Sharma 2017 27786578 US	Labetalol	25	3 (12)	NR	PP 25 (100)	NR	White 8 (32); Black 7 (28); Asian 3 (12); Latina 7 (28)
	Nifedipine	25	1 (4)	NR	PP 25 (100)	NR	White 9 (36); Black 11 (44); Asian 1 (4); Latina 4 (16)
Vázquez-Rodríguez 2020 34520145 Mexico	Losartan/Metoprolol/Methyldopa/Hydralazine	24	0 (0)	Preeclampsia with severe features (100)	NR	135.8 (14.39)/83.1 (9.58)	NR
	Metoprolol/Methyldopa/Hydralazine	25	0 (0)	Preeclampsia with severe features (100)	NR	135.5 (13.88)/85.7 (10.17)	NR
Veena 2017 27835048 India	Furosemide + Nifedipine	50	NR	Severe Preeclampsia 50 (100); PP Persistent high BP 50 (100)	Antenatal 50 (100)	NR	NR
	Nifedipine alone	50	NR	Severe Preeclampsia 50 (100); PP Persistent high BP 50 (100)	Antenatal 50 (100)	NR	NR

Study	Arm Name	Sample Size	Chronic HTN, N (%)	HDP Classification N (%)	Timing of HDP Diagnosis, N (%)	BP Mean (SD)	Race and Ethnicity, N (%)
Vigil-De Gracia 2007 17469006, Panama	Hydralazine	42	2 (4.8)	Gestational hypertension 8 (19); Superimposed preeclampsia 6 (14.3); Severe Preeclampsia 26 (61.9); SBP ≥ 160 mm Hg; SBP ≥ 160 mm Hg 33 (78.6); DBP ≥ 110 mm Hg 19 (45.2); BP ≥ 160/110 mm Hg 14 (33.3)	Severe hypertension antenatal 32 (76.1)	162 (9.4)/104 (9)	NR
	Labetalol	40	4 (10)	Gestational hypertension 3 (7.5); Superimposed preeclampsia 8 (20); Severe Preeclampsia 25 (62.5); SBP ≥ 160 mm Hg; SBP ≥ 160 mm Hg 37 (92.5); DBP ≥ 110 mm Hg 16 (40); BP ≥ 160/110 mm Hg 14 (35)	Severe hypertension antenatal 32 (80)	165 (8)/104 (9)	NR

Study	Arm Name	Sample Size	Chronic HTN, N (%)	HDP Classification N (%)	Timing of HDP Diagnosis, N (%)	BP Mean (SD)	Race and Ethnicity, N (%)
Viteri 2018 30303905 TROPHY US	Torsemide	59	NR	Preeclampsia without severe features 14 (23.7); Superimposed preeclampsia 15 (25.4); Preeclampsia with severe features 30 (50.8); Eclampsia 0 (0); Persistent severe hypertension 39 (66.1)	Postpartum (de novo, up to 24 h) 6 (10.2) Intrapartum 3 (5.1) Antepartum 50 (84.7)	NR	White 9 (15.3); Black 33 (55.9); Hispanic 16 (27.1); Other 1 (1.7)
	Placebo	59	NR	Preeclampsia without severe features 16 (27.1); Superimposed preeclampsia 15 (25.4); Preeclampsia with severe features 27 (45.8); Eclampsia 0 (0); Persistent severe hypertension 36 (61)	Postpartum (de novo, up to 24 h) 7 (11.9) Intrapartum 11 (18.6) Antepartum 41 (69.5)	NR	White 11 (18.6); Black 35 (59.3); Hispanic 13 (22); Other 0 (0)

Study	Arm Name	Sample Size	Chronic HTN, N (%)	HDP Classification N (%)	Timing of HDP Diagnosis, N (%)	BP Mean (SD)	Race and Ethnicity, N (%)
Yoselevsky 2022, L2016043015, US	Enalapril	47	3 (6.4)	Gestational HTN 9 (19.1) Preeclampsia without severe features 4 (8.5) Superimposed preeclampsia 1 (2.1) Preclampsia with severe features 30 (63.8)	NR	NR	White, 15 (31.9) Non-hispanic Black, 17 (36.2) Asian 0
	Nifedipine	47	3 (6.4)	Gestational HTN 16 (34.0) Preeclampsia without severe features 2 (4.3) Superimposed preeclampsia 5 (10.6) Preclampsia with severe features 21 (44.7)	NR	NR	White, 25 (53.2) Non-hispanic Black, 11 (23.2) Asian, 2 (4.3)

Table C–2.3.2. Key Question 2: Postpartum treatment of hypertension – additional summary of sample details

Study	Arm Name	Age Mean (SD)	BMI Mean (SD)	BMI (Timepoint) N(%) >30kg.m2	Co-occurring Disorders, N (%)	Parity/ Gravity	Delivery Char.	Other Birth Char. N (%)	GA at Delivery, Mean (SD)	Social Determinants of Health
Ainuddin 2019 31489020 Pakistan	Labetalol	26.7 (1.9)	25.7 (4.05)	Peripartum	Uncontrolled diabetes 0 (0); Renal disease, SCR >1mg/dl 0 (0)	NR	Vaginal delivery 38 (61.3) Cesarean delivery 24 (38.7)	Spontaneous or induced abortion 0 (0)	NR	NR
	Nifedipine	25.9 (1.8)	25.5 (3.9)	Peripartum	Uncontrolled diabetes 0 (0); Renal disease, SCR >1mg/dl 0 (0)	NR	Vaginal delivery 36 (58.1) Cesarean delivery 26 (41.9)	Spontaneous or induced abortion 0 (0)	NR	NR
Arias-Hernández 2020 32774912 Mexico	Diltiazem	21.6 (6.8)	NR	NR	Diabetes 0 (0); Gestational diabetes 0 (0); Renal disease 0 (0)	Primiparous 16 (76.2)	Vaginal delivery 1 (4.8) Cesarean delivery 20 (95.2)	NR	36.4 (3.5)	NR
	Nifedipine	23.2 (6.2)	NR	NR	Diabetes 0 (0); Gestational diabetes 0 (0); Renal disease 0 (0)	Primiparous 13 (61.9)	Vaginal delivery 0 (0) Cesarean delivery 21 (100)	NR	36.4 (2.1)	NR
Ascarelli 2005 15625138 US	Furosemide + oral K supplement	22.8 (6.1)	weight 199 lb (54)	Peripartum	NR	Parous (39.4)	Vaginal delivery (64.4) Cesarean delivery (35.6)	Spontaneous or induced abortion 0 (0)	NR	NR
	No Therapy	22.9 (6)	weight 206 lb (53)	Peripartum	NR	Parous (47)	Vaginal delivery (62.6) Cesarean delivery (37.4)	Spontaneous or induced abortion 0 (0)	NR	NR

Study	Arm Name	Age Mean (SD)	BMI Mean (SD)	BMI (Timepoint) N(%) >30kg.m2	Co-occurring Disorders, N (%)	Parity/ Gravity	Delivery Char.	Other Birth Char. N (%)	GA at Delivery, Mean (SD)	Social Determinants of Health
Barton 1990 2316590 US	Nifedipine	24	NR	NR	NR	NR	Vaginal delivery 9 (56.3) Cesarean delivery 7 (43.8)	NR	NR	NR
	Placebo	26.3	NR	NR	NR	NR	Vaginal delivery 8 (53.3) Cesarean delivery 7 (46.7)	NR	NR	NR
Dabaghi 2019 Iran	Furosemide + K supply	30 (6)	Weight 78kg (12.7)	Peripartum	NR	Parous (53.3)	Vaginal delivery (31) Cesarean delivery (69)	Spontaneous or induced abortion 0 (0)	NR	NR
	Control (no medication)	28.6 (6.9)	Weight 81kg (14.6)	Peripartum	NR	Parous (55.6)	Vaginal delivery (20) Cesarean delivery (80)	Spontaneous or induced abortion 0 (0)	NR	NR
Fidler 1982 7171513 UK	Methyldopa	27.8 (0.9)	NR	NR	Gestational diabetes 0 (0); Renal disease 0 (0); Asthma 0 (0); Heart failure 0 (0)	Primiparous 17 (42.5); Multiparous 23 (57.5)	NR	Multiple births 0 (0)	NR	NR
	Timolol	29.7 (1)	NR	NR	Gestational diabetes 0 (0); Renal disease 0 (0); Asthma 0 (0); Heart failure 0 (0)	Primiparous 18 (45); Multiparous 22 (55)	NR	Multiple births 0 (0)	NR	NR

Study	Arm Name	Age Mean (SD)	BMI Mean (SD)	BMI (Timepoint) N(%) >30kg.m2	Co-occurring Disorders, N (%)	Parity/ Gravity	Delivery Char.	Other Birth Char. N (%)	GA at Delivery, Mean (SD)	Social Determinants of Health
Griffis 1989 2789542 US	Hydralazine	NR	NR	NR	NR	Primigravidas 5 (41.7); Multigravidas 7 (58.3)	NR	Spontaneous or induced abortion 0 (0)	NR	NR
	Methyldopa	NR	NR	NR	NR	Primigravidas 6 (42.9); Multigravidas 8 (51.1)	NR	Spontaneous or induced abortion 0 (0)	NR	NR
Lopes 2021 33550824 US	Furosemide	Median 27 (IQR 22, 32)	36.5	NR	Diabetes 2 (1); Gestational diabetes 10 (6)	Nulliparous 93 (48)	Vaginal delivery 137 (71) Cesarean delivery 55 (29)	NR	38.6 (37.3, 39.7)	Private Insurance 47 (25); Medicaid 142 (75)
	Placebo	Median 27 (IQR 23, 33)	Median 34.6 (IQR 29.6, 42.1)	Postpartum (at delivery)	Diabetes 2 (1); Gestational diabetes 12 (7)	Nulliparous 101 (53)	Vaginal delivery 154 (80) Cesarean delivery 38 (20)	NR	38.4 (27.3, 39.7)	Private Insurance 65 (34); Medicaid 126 (66)
Noronha 2017 28125624 Brazil	Clonidine	NR	NR	NR	NR	Number of pregnancies: median 2; Parity: median 2	NR	NR	NR	NR
	Captopril	NR	NR	NR	NR	Number of pregnancies: median 2; Parity: median 2	NR	NR	NR	NR

Study	Arm Name	Age Mean (SD)	BMI Mean (SD)	BMI (Timepoint) N(%) >30kg.m2	Co-occurring Disorders, N (%)	Parity/ Gravity	Delivery Char.	Other Birth Char. N (%)	GA at Delivery, Mean (SD)	Social Determinants of Health
Ormesher 2020 33012200 PICk-UP UK	Enalapril	34.5 (6)	Median 28 (Range 19.4 - 37.3)	Peripartum > 30kg/m2 12 (40)	Diabetes 3 (10); Pre-existing renal disease 3 (10); Essential hypertension 6 (20); Renal hypertension 3 (10)	NR	NR	NR	NR	NR
	Placebo	30.9 (6.6)	Median 27.6 (Range 19.3 - 51.0)	Peripartum > 30kg/m2 11 (36.7)	Diabetes 2 (6.7); Pre-existing renal disease 0 (0); Essential hypertension 6 (20); Renal hypertension 0 (0)	NR	NR	NR	NR	NR
Sayin 2005 Turkey	Alpha-methyldopa	28.1 (5.9)	NR	NR	NR	Primigravid 21 (51.2)	NR	NR	NR	NR
	Nifedipine	27.1 (5.9)	NR	NR	NR	Primigravid 23 (54.8)	NR	NR	NR	NR
Sharma 2017 27786578 US	Labetalol	34 (7.4)	30.3 Median 4.1	Postpartum (Baseline)	Gestational diabetes 2 (8); Thyroid disorder 1 (4); Multiple sclerosis 0 (0)	Primiparous 9 (36); Grand multiparous 3 (12)	NR	Multiple births 3 (12)	NR	NR
	Nifedipine	33.3 (6.4)	33 Median 7.8	Postpartum (Baseline)	Gestational diabetes 3 (12); Thyroid disorder 2 (8); Multiple sclerosis 1 (4)	Primiparous 9 (36); Grand multiparous 4 (16)	NR	Multiple births 2 (8)	NR	NR

Study	Arm Name	Age Mean (SD)	BMI Mean (SD)	BMI (Timepoint) N(%) >30kg.m2	Co-occurring Disorders, N (%)	Parity/ Gravity	Delivery Char.	Other Birth Char. N (%)	GA at Delivery, Mean (SD)	Social Determinants of Health
Vázquez-Rodríguez 2020 34520145 Mexico	Losartan / Metoprolol / Methyldopa / Hydralazine	26.6 (5.36)	28.6 Median 4.6	NR	NR	Median parity (2)	NR	NR	33.8 (3.66)	NR
	Metoprolol / Methyldopa / Hydralazine	29.2 (5.87)	30.7 Median 7.01	NR	NR	Median parity (2)	NR	NR	31.8 (3.72)	NR
Veena 2017 27835048 India	Furosemide + Nifedipine	24.3 (4.3) < 20 (7.9); 21-25 (61.7)	NR	NR	Ascites 19 (38)	Nulliparous 32 (64); Multiparous 18 (36)	Vaginal delivery 28 (56) Cesarean delivery 22 (44)	Neonatal death 4 (8.3)	36 (3)	NR
	Nifedipine alone	24 (4.3) < 20 (20.5); 21-25 (45.6)	NR	NR	Ascites 5 (10)	Nulliparous 37 (74); Multiparous 13 (26)	Vaginal delivery 33 (66) Cesarean delivery 17 (34)	Neonatal death 5 (11)	36.1 (3)	NR
Vigil-De Gracia 2007 17469006 HYLA postpartum Panama	Hydralazine	29.9 (5.9)	NR	NR	NR	Parous 13 (40)	NR	NR	NR	NR
	Labetalol	31.3 (5.5)	NR	NR	NR	Parous 19 (47.5)	NR	NR	NR	NR

Study	Arm Name	Age Mean (SD)	BMI Mean (SD)	BMI (Timepoint) N(%) >30kg.m2	Co-occurring Disorders, N (%)	Parity/ Gravity	Delivery Char.	Other Birth Char. N (%)	GA at Delivery, Mean (SD)	Social Determinants of Health
Viteri 2018 30303905 TROPHY US	Torsemide	26.9 (6.1) Younger than 20 6 (10.2); 35 or older 7 (11.9)	NR	> 30kg/m2 44 (74.6)	Gestational diabetes 5 (8.5); Pregestational diabetes 7 (11.9); Asthma 4 (6.8)	Nulliparous 38 (64.4)	NR	NR	36.2 (3)	NR
	Placebo	28.2 (6.8) Younger than 20 4 (6.8); 35 or older 9 (15.3)	NR	> 30kg/m2 50 (84.7)	Gestational diabetes 5 (8.5); Pregestational diabetes 6 (10.2); Asthma 12 (20.3)	Nulliparous 31 (52.5)	NR	NR	36.7 (2.9)	NR
Yoselevsky 2022, L2016043015, US	Enalapril	32.4 (6.7)	35.2 (7)	NR	NR	1.9 (1.6)	NR	NR	37.4 (2.9)	NR
	Nifedipine	33.3 (6.3)	34.6 (8)	NR	NR	1.8 (1.7)	NR	NR	36.6 (2.3)	NR

Table C–3.1. Key Question 3: MgSO4 regimens – summary of design details

Study	Comparison	HDP Category	Design (Timing)	Trial Registration	Total N
Ali 2022, L2017937927, Pakistan	Duration	E	RCT (07/2016 – 12/2016)	NR	132
Anjum 2016, 26498603, India	Duration	sPE	RCT (11/2012 - 09/2014)	NR	119
Anjum 2016, 26604159, India	Duration	E	RCT 11/2012 – 09/2014)	NR	208
Anjum 2017, L616977819 (embase), India	Duration	sPE	RCT (01/2013 - 09/2014)	NR	91
Begum 2002, 12214831, Bangladesh	Duration	E	RCT (01/1999 – 11/1999)	NR	401
Beyuo 2022, 35304745 (ad hoc), Ghana	Duration	sPE	RCT (11/2018 - 11/2020)	PACTR201811515303983	1,176
Chama 2013, 24069775, Nigeria	Duration	E	RCT (01/2011 - 06/2011)	NR	98
Darngawn 2012, 22261127, India	Duration	sPE	RCT (09/2008 - 04/2010)	NR	150
Dasgupta 2021, CN-02320544 (cochrane), India	Duration	sPE	RCT (07/2015 – June 2016)	NR	90
Ehrenberg 2006, 17012443, USA	Duration	sPE	RCT (01/2001 - 08/2004)	NCT00344058	196
El-Khayat 2016, 25483417, Egypt	Duration	sPE	RCT (05/2013 - 04/2014)	NCT01846156	160
Fontenot 2005, 15970809, USA	Duration	sPE	RCT (N/R)	NR	98
Gracia 2017, 28738788, Panama	Duration	sPE	RCT (11/2013 - 10/2016)	NCT02317146	284
Kashanian 2016, 26364667, Iran	Duration	sPE	RCT (07/2012 – 01/2013)	Iran Registry of Clinical Trial (IRCT) (Trial registration number IRCT201207182624N10)	170
Keepanasseril 2018, 28974124, India	Duration	sPE	RCT (04/2011 - 04/2013)	NR	402
Khan 2021, L2011768439 (embase), Pakistan	Duration	E	RCT (06/2019 - 01/2021)	NR	100
Maia 2014, 24890747, Brazil	Duration	sPE	RCT (07/2011 - 10/2011)	NR	112

Study	Comparison	HDP Category	Design (Timing)	Trial Registration	Total N
Rao 2015, L606457038 (embase), Pakistan	Duration	E	RCT (06/2013 - 05/2014)	NR	120
Regmi 2010, 21744767, Nepal	Duration	E	RCT (07/2008 - 12/2009)	NR	80
Rimal 2017, 29453467, Nepal	Duration	sPE	RCT (08/2014 - 07/2015)	NR	60
Shoaib 2009, 19149977, Pakistan	Duration	sPE	NRCS	NR	100
Unwaha 2020, 31833059, Nigeria	Duration	sPE	RCT (05/2014 - 01/2020)	NR	80
Vigil-DeGracia 2018, 29878650, Dominican Republic, Ecuador, El Salvador, Panama, Peru	Duration	sPE	RCT (12/2014 - 12/2015)	NCT02307201	1,113
Abdul 2013, 22930148, Nigeria	Dose	E	RCT (01/2008 - 08/2002)	NR	72
Agarwal 2020, AH_001 (ad hoc), India	Dose	sPE, E	RCT (01/2017 - 01/2019)	NR	94
Bhattacharjee 2011, 21534749, India	Dose	E	RCT (09/2007 - 08/2009)	NR	137
Brookfield 2020, 33156201, USA	Dose	sPE	RCT (07/2016 - 06/2019)	NCT02835339	66
Charoenvidhya 2013, 23691692, Thailand	Dose	sPE	RCT (07/2011 - 08/2012)	NR	60
Easterling 2018, 29976161, Egypt	Dose	sPE	RCT (01/2015 - 02/2016)	NCT02091401	200
Gupta 2019, CN-01996873 (cochrane), India	Dose	E	RCT (NA - NA)	NR	60
Kitiyodom 2016, 29901967, Thailand	Dose	PE	RCT (NA - NA)	NR	38
Malapaka 2011, 21798536, India	Dose	sPE, E	RCT (06/2007 - 09/2009)	NR	126
Pascoal 2019, 31393402, Brazil	Dose	sPE	RCT (03/2015 - 03/2016)	NCT02396030	62
Saha 2017, 28714170, India	Dose	E	RCT (08/2008 - <2017)	CTRI/ 2009 000339, 05–08-2009	41
Singh 2011, L362772412 (embase), India	Dose	E	RCT (NA - <2010)	NR	109

Study	Comparison	HDP Category	Design (Timing)	Trial Registration	Total N
Sravani 2022, L2016942399, India	Dose	E	RCT (NA – NA)	NR	60
Sultana 2010, L365881919 (embase), Bangladesh	Dose	E	RCT (06/ 2007 - 05/2008)	NR	100
Tungmanowutthikul 2019, CN-01793189 (cochrane), Thailand	Dose	sPE	RCT (01/2018 - 09/2018)	NR	86
Manorot 1996, 8868017, Thailand	Delivery		RCT (07/1992 - 07/1993)	NR	50
Mundle 2012, 26104987, India	Delivery		RCT (04/2008 - 04/2009)	NR	300
Pippen 2020, 33179549, USA	Delivery		NRCS, retrospective	NR	249
Wang 2019, 31889791, NA	Mg Plus		RCT (03/2014 - 03/2017)	NR	220

Table C–3.2. Key Question 3: MgSO4 regimens – summary of arm details

Study	Comp	HDP Category	Reported as Subgroup	Arm Name	Regimen	Loading Dose	Maint. Dose	Duration	From	N arm
Ali 2022, L2017937927, (Pakistan)	duration	E	no	Loading dose	Pritchard Loading dose	4gIV then 10g IM	0	0	NA	66
	duration	E	no	24h	Pritchard 24 hr	4gIV then10g IM	5gm IV q4h	24	Last seizure	66
Anjum, 26604159 (India)	duration	E	no	12h MgSO4	Zuspan 12h	4g IV	1g/h	12	Total duration	132
	duration	E	no	24h MgSO4	Zuspan	4g IV	1g/h	24	Total duration	72
Anjum, 26498603 (India)	duration	sPE	no	Group A	Zuspan 6h	4g IV	1g/h	6	From delivery	76
	duration	sPE	no	Group B	Zuspan	4g IV	1g/h	24	From delivery	43
Anjum, L616977819 (India)	duration	sPE	no	MgSO4 until delivery	Zuspan	4g IV	1g/hr	0	From delivery	48
	duration	sPE	no	MgSO4 24h	Zuspan	4g IV	1g/hr	24	From delivery	43
Begum, 12214831 (Bangladesh)	duration	E	no	Loading dose only	NR	4g IV then 6g IM	0	0	Total duration	202
	duration	E	no	Standard regime	NR	4g IV then 6g IM	2.5g IM q4h	24	Total duration	199
Beyuo, 35304745 (Ghana)	duration	sPE	no	12-hour treatment group	Pritchard 12h	4g IV then 10g IM	5g IM q4h	12	Total duration	592
	duration	sPE	no	24-hour control group	Pritchard	4g IV then 10g IM	5g IM q4h	24	Total duration	584
Chama, 24069775 (Nigeria)	duration	E	no	Shortened Regimen	Pritchard 8h	4g IV then 10g IM	5g IM q4h	8	From delivery	48
	duration	E	no	Standard Pritchard Regimen	Pritchard	4g IV then 10g IM	5g IM q4h	24	From delivery	50
Darngawn, 22261127 (India)	duration	sPE	no	Intervention	mixed	NR	1g/h|4g IM q6h	12	From delivery	75
	duration	sPE	no	Control	mixed	NR	1g/h|4g IM q6h	24	From delivery	75
Dasgupta, CN-02320544 (India)	duration	sPE	no	Abbreviated Regimen	Pritchard	4g IV then 10g IM	5g IM q4h	8	From delivery	45
	duration	sPE	no	Traditional Regimen	Pritchard	4g IV then 10g IM	5g IM q4h	24	From delivery	45

Study	Comp	HDP Category	Reported as Subgroup	Arm Name	Regimen	Loading Dose	Maint. Dose	Duration	From	N arm
Ehrenberg, 17012443 (USA)	duration	sPE	no	12 Hours PP Magnesium Sulfate Therapy	Zuspan	4g IV	2g/h	12	Total duration	101
	duration	sPE	no	24 Hours Magnesium Sulfate Therapy	Zuspan	4g IV	2g/h	24	Total duration	95
El-Khayat, 25483417 (Egypt)	duration	sPE	no	Loading dose only	NR	6g IV	0	0	Total duration	80
	duration	sPE	no	12h protocol	NR	6g IV	1g/h	12	Total duration	80
	duration	sPE	no	24h protocol	NR	6g IV	1g/h	24	Total duration	80
Fontenot, 15970809 (USA)	duration	sPE	no	Study group	Zuspan	4g IV	2g/h	until UO > 100 ml/h	From delivery	48
	duration	sPE	no	Control group	Zuspan	4g IV	2g/h	24	From delivery	50
Kashanian, 26364667 (Iran)	duration	sPE	no	MgSO4 for 12 hours	Pritchard	4g IV then 10g IM	5g IM q4h	12	From delivery	79
	duration	sPE	no	MgSO4 for 24 hours	Pritchard	4g IV then 10g IM	5g IM q4h	24	From delivery	91
Keepanasseril, 28974124 (India)	duration	sPE	no	Loading dose only (group B)	Dhaka	4g IV then 6g IM	0	0	Total duration	201
	duration	sPE	no	Low-dose Dhaka (group A)	Dhaka	4g IV then 6g IM	2.5g IM q4h	24	Total duration	201
Khan, L2011768439 (Pakistan)	duration	E	no	12-hour protocol	Zuspan	4g IV	1g/h	12	From delivery	50
	duration	E	no	24-hour protocol	Zuspan	4g IV	1g/h	24	From delivery	50
Maia, 24890747 (Brazil)	duration	sPE	no	12 hours	NR	6g IV	1g/h	12	From delivery	56
	duration	sPE	no	24 hours	NR	6g IV	1g/h	24	From delivery	56
Rao, L606457038 (Pakistan)	duration	E	no	12h regimen (A)	Zuspan	4g IV	1g/h	12	Total duration	60
	duration	E	no	24h regimen (B)	Zuspan	4g IV	1g/h	24	Total duration	60
Regmi, 21744767 (Nepal)	duration	E	yes	Loading dose	Pritchard	4g IV then 10g IM	0	0	Total duration	43
	duration	E	yes	Loading and maintenance dose of Mg Sulfate	Pritchard	4g IV then 10g IM	5g IM q4h	24	Total duration	37

Study	Comp	HDP Category	Reported as Subgroup	Arm Name	Regimen	Loading Dose	Maint. Dose	Duration	From	N arm
Rimal, 29453467 (Nepal)	duration	sPE	yes	Loading dose only	Pritchard	4g IV then 10g IM	0	0	NA	30
	duration	sPE	yes	Standard Pritchard Regimen	Pritchard	4g IV then 10g IM	5g IM q4h	24	Total duration	30
Shoaib, 19149977 (Pakistan)	duration	sPE	no	Loading dose only	Pritchard	4g IV then 10g IM	0	0	Total duration	50
	duration	sPE	no	Standard Pritchard regime	Pritchard	4g IV then 10g IM	5g IM q4h	24	Total duration	50
Unwaha, 31833059 (Nigeria)	duration	sPE	no	12 hour maintenance dose	Zuspan 12h	4g IV	1g/h	12	Total duration	40
	duration	sPE	no	24 hour maintenance dose	Zuspan	4g IV	1g/h	24	Total duration	40
Vigil-DeGracia, 29878650 (Latin America)	duration	sPE	no	Magnesium sulphate postdelivery group	Zuspa	4g IV	1g/h	8	Total duration	555
	duration	sPE	no	No magnesium sulphate postdelivery group	Zuspan	4g IV	1g/h	24	From delivery	558
Vigil-DeGracia, 28738788 (Panama)	duration	sPE	no	6h post-delivery	Zuspan	4g IV	1g/h	6	From delivery	141
	duration	sPE	no	24h post-delivery	Zuspan	4g IV	1g/h	24	From delivery	143
Abdul, 22930148 (Nigeria)	dose	E	no	MgSO4 Low Dose	NR	4g IV then 5g IM	2.5g IM q4h	24	From delivery	39
	dose	E	no	MgSO4 Standard Dose	Pritchard	4g IV then 10g IM	5g IM q4h	24	From delivery	33
Agarwal, AH 001 (India)	dose	sPE	yes	Pritchard	Pritchard	4g IV then 10g IM	5g IM q4h	24	From delivery	28
	dose	sPE	yes	Dhaka	Dhaka	4g IV then 5g IM	2.5g IM q4h	24	From delivery	25
	dose	E	yes	Pritchard	Pritchard	4g IV then 10g IM	5g IM q4h	24	From delivery	22
	dose	E	yes	Dhaka	Dhaka	4g IV then 5g IM	2.5g IM q4h	24	From delivery	21
Bhattacharjee, 21534749 (India)	dose	E	no	Group A: MgSO4 IV Low Dose	NR	4g IV	6g IM q8h	24	Total duration	67
	dose	E	no	Group B: MgSO4 IM Standard Regimen	NR	4g IV then 10g IM	5g IM q4h	24	Total duration	70
Brookfield, 33156201 (USA)	dose	sPE	BMI ≥ 35	Alternate	Zuspan	6g IV	2 g/h	NR	NR	19
	dose	sPE	BMI ≥ 35	Zuspan	Zuspan	4g IV	1 g/h	NR	NR	18

Study	Comp	HDP Category	Reported as Subgroup	Arm Name	Regimen	Loading Dose	Maint. Dose	Duration	From	N arm
Charoenvidhya, 23691692 (Thailand)	dose	sPE	no	Study group (2g/h)	NR	5g IV	2g/h	NR	NR	30
	dose	sPE	no	Control group (1g/h)	NR	5g IV	1g/h	NR	NR	30
Gupta, CN-01996873 (India)	dose	E	no	Low IV Dose of MgSO4	NR	4g IV	0.8 g/h	24	From delivery	30
	dose	E	no	MgSO4 per Conventional Pritchard's regimen	NR	4g IV then 10g IM	5g IM q4h	24	From delivery	30
Kitiyodom, 29901967 (Thailand)	dose	PE	no	Mg 2g/h	Zuspan	4g IV	2g/h	24	From delivery	19
	dose	PE	no	Mg 1g/h	Zuspan	4g IV	1g/h	24	From delivery	19
Malapaka, 21798536 (India)	dose	sPE	yes	Low-dose regimen	NR	4g IV	2g q3h IM	24	Total duration	37
	dose	sPE	yes	Pritchard regimen	NR	4g IV then 5g IM	5g IM q4h	24	Total duration	16
	dose	E	yes	Low-dose regimen	NR	4g IV	2g q3h IM	24	Total duration	35
	dose	E	yes	Pritchard regimen	NR	4g IV then 5g IM	5g IM q4h	24	Total duration	38
Pascoal, 31393402 (Brazil)	dose	sPE	no	2 g/h	NR	6g IV	2g/h	24		31
	dose	sPE	no	1 g/h	NR	6g IV	1g/h	24		31
Saha, 28714170 (India) Singh, L362772412 (India)	dose	E	no	Zuspan Regimen	Zuspan	4g IV	1g/h	24	From delivery	20
	dose	E	no	Dhaka Regimen	Dhaka	4g IV then 6g IM	2.5g IM q4h	24	From delivery	21
	dose	E	no	Pritchard regimen	NR	4g IV then 10g IM	5g IM q4h	24	Total duration	60
	dose	E	no	Zuspan regimen	NR	4g IV	1 g/h	24	Total duration	49
	dose	E	no	Sibai regimen	NR	6g IV	2 g/h	24	Total duration	49
Sravani 2022, L2016942399 (India)	dose	E	No	Low dose regimen	NR	4g IV	2g IV q3h	24	Total duration	30
	NR	NR	NR	Standard dose	Pritchard	4g IV then 10g IM	4g IM q4h	24	Total duration	30
Sultana, L365881919 (Bangladesh)	dose	E	no	Group –A: Lower Dose of MgSO4 (8g) (Case Group)	NR	8g IV	0	0	NR	48
	dose	E	no	Group - B: MgSO4 dose (10g) (Control Group)	NR	4g IV then 6g IM	0	0	From delivery	52

Study	Comp	HDP Category	Reported as Subgroup	Arm Name	Regimen	Loading Dose	Maint. Dose	Duration	From	N arm
Tangmanowutthikul, CN-01793189 (Thailand)	dose	sPE	no	MgSO4 by Weight-adjusted protocol	NR	4g IV	1.2 to 1.5 g/h*	24	From delivery	43
	dose	sPE	no	MgSO4 2g/h	NR	4g IV	2g/h	24	From delivery	43
Agarwal, AH 001 (india)	delivery	sPE	yes	Zuspan	Zuspan	4g IV	1g/h	24	From delivery	25
	delivery	E	yes	Zuspan	Zuspan	4g IV	1g/h	24	From delivery	19
Easterling, 29976161 (Egypt)	delivery	sPE	no	Serial bolus	Easterling 12h	6g IV	2g IV q2h	12	NA	100
	delivery	sPE	no	Continuous Infusion	Zuspan 12h	4g IV	1g/h	12	NA	100

Abbreviations: sPE = preeclampsia with severe features, E = eclampsia, subgroup = within-study subgroups reported, Maint. = maintenance, Regimen = Name, i.e., Zuspan, Pritchard loading dose

Table C–3.3.1. Key Question 3: MgSO4 regimens – summary of sample details

Study	Arm Name	Sample Size	Chronic HTN , N (%)	HDP Classification, N (%)	Gestational Age at HDP Diagnosis, Mean (SD)	Timing of HDP Diagnosis, N (%)	Race/Ethnicity, N (%)	Age, Mean (SD) [Range]
Abdul 2013, 22930148, Nigeria	MgSO4 Low Dose	39	NR	Eclampsia, 39 (100)	NR	NR	NR	NR
	MgSO4 Standard Dose	33	NR	Eclampsia, 33 (100)	NR	NR	NR	NR
Agarwal 2020, AH_001 (ad hoc), India	Pritchard	50	NR	Severe preeclampsia, 28 (56); Eclampsia, 22 (44)	NR	<37 wks, 25 (50); 37-40 wks, 24 (48); >40 wks, 10 (20)	NR	NR
	Zuspan	44	NR	Severe preeclampsia, 25 (57); Eclampsia, 19 (43)	NR	<37 wks, 22 (50); 37-40 wks, 16 (36); >40 wks, 6 (14)	NR	NR
	Dhaka	46	NR	Severe preeclampsia, 25 (54); Eclampsia, 21 (46)	NR	<37 wks, 19 (41); 37-40 wks, 20 (43); >40 wks, 7 (15)	NR	NR
	MgSO4 infusion for 6 hours	76	NR	Severe preeclampsia, 76 (100)	NR	Antepartum, 76 (100)	NR	25.2 (4.4)
Anjum 2016, 26498603, India	MgSO4 infusion for 24 hours	43	NR	Severe preeclampsia, 43 (100)	NR	Antepartum, 43 (100)	NR	25.8 (4.7)
	12h MgSO4	132	NR	Eclampsia, 132 (100)	NR	NR	NR	23.8 (3.4)
Anjum 2016, 26604159, India	24h MgSO4	76	NR	Eclampsia, 76 (100)	NR	NR	NR	24.5 (3.6)
Anjum 2017, L616977819 (embase), India	MgSO4 until delivery	48	NR	Severe preeclampsia, 48 (100)	NR	NR	NR	24.9 (4.2)
	MgSO4 24h	43	NR	Severe preeclampsia, 43 (100)	NR	NR	NR	25.8 (4.7)
Begum 2002, 12214831, Bangladesh	Loading dose only	202	NR	Eclampsia, 202 (100)	NR	NR	NR	22.4 (4.21)
	Standard regime	199	NR	Eclampsia, 199 (100)	NR	NR	NR	22.49 (4.67)

Study	Arm Name	Sample Size	Chronic HTN , N (%)	HDP Classification, N (%)	Gestational Age at HDP Diagnosis, Mean (SD)	Timing of HDP Diagnosis, N (%)	Race/Ethnicity, N (%)	Age, Mean (SD) [Range]
Beyuo 2022, 35304745 Ghana	12-hour treatment group	592	133 (22.5)	Severe preeclampsia, 539 (91.1); Eclampsia, 53 (8.9)	Median 37.1 (IQR 33.4, 39.0)	Antepartum, 491 (84.4); Intrapartum, 65 (11.2); Postpartum, 26 (4.5)	NR	Median 31 (IQR 27.0, 35.0)
	24-hour control group	584	146 (25)	Severe preeclampsia, 521 (89.2); Eclampsia, 63 (10.8)	Median 35.4 (IQR 32.1, 38.0)	Antepartum, 487 (84.7); Intrapartum, 52 (9); Postpartum, 36 (6.3)	NR	Median 32 (IQR 27.0, 35.0)
Bhattacharjee 2011, 21534749, India	Group A: MgSO4 IV Low Dose	67	NR	Eclampsia, 67 (100)	NR	Postpartum, 14 (20.9); Intrapartum, 16 (23.9); Antepartum, 37 (55.2)	NR	NR
	Group B: MgSO4 IM Standard Regimen	70	NR	Eclampsia, 70 (100)	NR	Postpartum, 16 (22.9); Intrapartum, 16 (22.9); Antepartum, 38 (54.3)	NR	NR
Brookfield 2020, 33156201, US	Zuspan Regimen	31	NR	NR	NR	NR	White, (83); Black (0); Other, (17)	30.9 (6.6)
	Alternative Dosing	35	NR	NR	NR	NR	White, (79); Black (1); Other, (16)	31.6 (7.1)
Chama 2013, 24069775, Nigeria	Standard Pritchard Regimen	50	NR	Eclampsia, 50 (100)	NR	NR	NR	NR
	Shortened Regimen	48	NR	Eclampsia, 48 (100)	NR	NR	NR	NR
Charoenvidhya 2013, 23691692, Thailand	Study group (2g/h)	30	NR	NR	NR	NR	NR	31.63
	Control group (1g/h)	30	NR	NR	NR	NR	NR	31.57

Study	Arm Name	Sample Size	Chronic HTN , N (%)	HDP Classification, N (%)	Gestational Age at HDP Diagnosis, Mean (SD)	Timing of HDP Diagnosis, N (%)	Race/Ethnicity, N (%)	Age, Mean (SD) [Range]
Darngawn 2012, 22261127, India	MgSO4 infusion for 6 hours	75	NR	Gestational HTN, 2 (2.7); Chronic hypertension with superimposed pre-eclampsia, 4 (5.3); Severe preeclampsia, 69 (92)	NR	Intrapartum, 75 (100)	NR	25.1 (4.2)
	MgSO4 infusion for 24 hours	75	NR	Gestational HTN, 3 (4); Chronic hypertension with superimposed pre-eclampsia, 2 (2.7); Severe preeclampsia, 70 (93.3)	NR	Intrapartum, 75 (100)	NR	24.8 (4.6)
Dasgupta 2021, CN-02320544 (cochrane), India	Abbreviated Regimen	45	1 (2.2)	Gestational HTN, 2 (4.4); Severe preeclampsia, 42 (93.3)	NR	NR	NR	19.84 (2.66)
	Traditional Regimen	45	1 (2.2)	Gestational HTN, 1 (2.2); Severe preeclampsia, 43 (95.6)	NR	NR	NR	19.93 (2.38)
Easterling 2018, 29976161, Egypt	Serial bolus	100	NR	NR	NR	NR	NR	29 (6)
	Continuous Infusion	100	NR	NR	NR	NR	NR	29 (6)
Ehrenberg 2006, 17012443, US	12 Hours PP Magnesium Sulfate Therapy	101	18 (17.8)	Mild preeclampsia, 101 (100)	NR	NR	Black, 48 (47.5)	24.4 (6.5)
	24 Hours Magnesium Sulfate Therapy	95	13 (13.7)	Mild preeclampsia, 96 (100)	NR	NR	Black, 48 (50.5)	25.2 (6.5)
El-Khayat 2016, 25483417, Egypt	Loading dose only	80	0 (0)	NR	35.75 (2.85)	NR	NR	26.75 (5.26)
	12h protocol	80	0 (0)	NR	35.91 (2.93)	NR	NR	26.56 (4.98)
	24h protocol	80	0 (0)	NR	35.59 (2.68)	NR	NR	26.64 (5.15)

Study	Arm Name	Sample Size	Chronic HTN , N (%)	HDP Classification, N (%)	Gestational Age at HDP Diagnosis, Mean (SD)	Timing of HDP Diagnosis, N (%)	Race/Ethnicity, N (%)	Age, Mean (SD) [Range]
Fontenot 2005, 15970809, US	MgSO4 until diuresis	48	NR	Severe preeclampsia, 48 (100)	32.1 (4)	NR	White, 26 (54)	23.6 (6.1)
	24h MgSO4 post-delivery	50	NR	Severe preeclampsia, 50 (100)	33.4 (4.2)	NR	White, 28 (56)	25 (6.3)
Gracia 2017, 28738788, Panama	6h post-delivery	143	NR	Superimposed preeclampsia, 25 (17.7)	NR	NR	NR	28.7 (6.8)
	24h post-delivery	141	NR	Superimposed preeclampsia, 28 (19.5)	NR	NR	NR	28.3 (7.5)
Gupta 2019, CN-01996873 (cochrane), India	Low IV Dose of MgSO4	30	NR	Eclampsia, 30 (100)	NR	Postpartum, 5 (16.7); Intrapartum, 0 (0); Antepartum, 25 (83.3)	NR	24.4
	MgSO4 per Conventional Pritchard's regimen	30	NR	Eclampsia, 30 (100)	NR	Postpartum, 4 (13.3); Intrapartum, 0 (0); Antepartum, 26 (86.7)	NR	25.4
Kashanian 2016, 26364667, Iran	MgSO4 for 12 hours	79	8 (10.1)	NR	NR	NR	Afghani, 20 (25.3)	28.9 (6.1)
	MgSO4 for 24 hours	91	7 (7.7)	NR	NR	NR	Afghani, 20 (22)	29.9 (6.1)
Keepanasseril 2018, 28974124, India	Loading dose only	201	NR	NR	NR	NR	NR	24.7 (0.3)
	low-dose Dhaka regimen	201	NR	NR	NR	NR	NR	24.5 (0.3)
Khan 2021, L2011768439 (embase), Pakistan	12-hour protocol	50	NR	Eclampsia, 50 (100)	NR	NR	NR	NR
	24-hour protocol	50	NR	Eclampsia, 50 (100)	NR	NR	NR	NR

Study	Arm Name	Sample Size	Chronic HTN , N (%)	HDP Classification, N (%)	Gestational Age at HDP Diagnosis, Mean (SD)	Timing of HDP Diagnosis, N (%)	Race/Ethnicity, N (%)	Age, Mean (SD) [Range]
Kitiyodom 2016, 29901967, Thailand	MgSO4 1g/h maintenance dose	19	NR	Preeclampsia without severe features, 19 (100)	NR	NR	NR	28 (6.6)
	MgSO4 2g/h maintenance dose	19	NR	Preeclampsia without severe features, 19 (100)	NR	NR	NR	26 (7.6)
Maia 2014, 24890747, Brazil	Magnesium sulfate 12 hours	56	NR	Severe preeclampsia, 56 (100)	NR	Peripartum, 56 (100)	NR	24.7 (6.3)
	Magnesium sulfate 24 hours	56	NR	Severe preeclampsia, 56 (100)	NR	Peripartum, 56 (100)	NR	26.3 (7.6)
Malapaka 2011, 21798536, India	Low-dose regimen	72	NR	Imminent eclampsia, 37 (51.4); Eclampsia, 35 (48.6)	34 (5.17)	NR	NR	25 (4.57)
	Pritchard regimen	54	NR	Imminent eclampsia, 16 (29.6); Eclampsia, 38 (70.4)	32.9 (5.22)	NR	NR	24.54 (3.92)
Manorot 1996, 8868017, Thailand	MgSO4 IV Maintenance Regimen	25	NR	Severe preeclampsia, 25 (100)	35.6 (4.26) [range 25, 40]	NR	NR	26 (5) [20-43]
	MgSO4 IM Maintenance Regimen	25	NR	Severe preeclampsia, 25 (100)	37 (2.43) [range 33, 41]	NR	NR	28 (5.8) [20-42]
Mundle 2012, 26104987, India	MgSO4 via Springfusor Pump	147	NR	Preeclampsia without severe features, 147 (100)	33.8 (3.6)	NR	NR	25 (4) [19–38]
	MgSO4 via Standard of Care	153	NR	Preeclampsia without severe features, 153 (100)	34.1 (4.2)	NR	NR	24 (4) [18–35]
Pascoal 2019, 31393402, Brazil	MgSO4 1g/h	31	NR	Severe preeclampsia, 31 (100)	NR	NR	NR	29.6 (7.1)
	MgSO4 2g/h	31		Severe preeclampsia, 31 (100)	NR	NR	NR	27.3 (7.6)

Study	Arm Name	Sample Size	Chronic HTN , N (%)	HDP Classification, N (%)	Gestational Age at HDP Diagnosis, Mean (SD)	Timing of HDP Diagnosis, N (%)	Race/Ethnicity, N (%)	Age, Mean (SD) [Range]
Pippen 2020, 33179549, US	Paused	171	40 (23)	NR	NR	NR	White, 124 (73); Black, 22 (13); Asian, 5 (3); Hispanic, 7 (4); Other, 13 (8)	Median 28 (IQR 24, 32)
	Continued	78	1 (1)	NR	NR	NR	White, 53 (67); Black, 17 (22); Asian, 0 (0); Hispanic, 7 (9); Other, 1 (1)	Median 28 (IQR 24, 33)
Rao 2015, L606457038 (embase), Pakistan	12h regimen (A)	60	NR	Eclampsia, 60 (100)	NR	NR	NR	NR
	24h regimen (B)	60	NR	Eclampsia, 60 (100)	NR	NR	NR	NR
Regmi 2010, 21744767, Nepal	Loading dose	43	NR	Eclampsia, 43 (100)	37 (2.4)	Postpartum, 7 (16.3); Antepartum, 36 (83.7)	NR	NR
	Loading and maintenance dose of Mg Sulfate	37	NR	Eclampsia, 37 (100)	35.4 (3.8)	Postpartum, 4 (10.8); Antepartum, 33 (89.2)	NR	NR
Rimal 2017, 29453467, Nepal	Loading dose only	30	NR	Severe preeclampsia, 30 (100)	37.1 (3.55)	NR	NR	24.57 (4.96)
	Standard Pritchard Regimen	30	NR	Severe preeclampsia, 30 (100)	37.2 (4.11)	NR	NR	25.03 (5.7)
Saha 2017, 28714170, India	Zuspan Regimen	20	NR	Eclampsia, 20 (100)	NR	NR	NR	24 (2.2)
	Dhaka Regimen	21	NR	Eclampsia, 21 (100)	NR	NR	NR	24 (3.8)
Shoaib 2009, 19149977, Pakistan	Loading dose only	50	NR	Severe preeclampsia, 50 (100)	33.28 (4.24)	NR	NR	26.06 (5.01) [19-40]
	Standard Pritchard regime	50	NR	Severe preeclampsia, 50 (100)	34.43 (2.5)	NR	NR	28.06 (5.5) [19-38]

Study	Arm Name	Sample Size	Chronic HTN , N (%)	HDP Classification, N (%)	Gestational Age at HDP Diagnosis, Mean (SD)	Timing of HDP Diagnosis, N (%)	Race/Ethnicity, N (%)	Age, Mean (SD) [Range]
Singh 2011, L362772412 (embase), India	Pritchard regimen	60	NR	Eclampsia, 60 (100)	NR	NR	NR	NR
	Zuspan regimen	49	NR	Eclampsia, 49 (100)	NR	NR	NR	NR
	Sibai regimen	49	NR	Eclampsia, 49 (100)	NR	NR	NR	NR
Sravani 2022, L2016942399 (embase), India	Low dose	30	NR	Eclampsia, 30 (100)	NR	NR	NR	18-20y: 2 (6.7) 21-25y: 60 (18) 25-30y, 10 (33.3)
	Pritchard	30	NR	Eclampsia, 30 (100)	NR	NR	NR	18-20y, 4 (13.7) 21-25y, 17 (56.5) 25-30y, 9 (30.0)
Sultana 2010, L365881919 (embase), Bangladesh	Group –A: Lower Dose of MgSO4 (8g) (Case Group)	48	NR	Eclampsia, 48 (100)	NR	Intrapartum, 14 (29.2); Antepartum, 34 (70.8)	NR	22.9 (3.83) [18-36]
	Group - B: MgSO4 dose (10g) (Control Group)	52	NR	Eclampsia, 52 (100)	NR	Intrapartum, 9 (17.3); Antepartum, 43 (82.7)	NR	22.4 (4.11) [18-35]
Tungmanowutthikul 2019, CN-01793189 (cochrane), Thailand	MgSO4 by Weight-adjusted protocol	43	7 (16.3)	Severe preeclampsia, 43 (100)	NR	NR	NR	29.2 (7.3) [16-44]
	MgSO4 2g/h	43	5 (11.6)	Severe preeclampsia, 43 (100)	NR	NR	NR	27.8 (7.3) [15-42]
Unwaha 2020, 31833059, Nigeria	12 hour maintenance dose	40	NR	Severe preeclampsia, 40 (100)	NR	NR	NR	34.1 (4.47)
	24 hour maintenance dose	40	NR	Severe preeclampsia, 40 (100)	NR	NR	NR	32.3 (6.35)

Study	Arm Name	Sample Size	Chronic HTN , N (%)	HDP Classification, N (%)	Gestational Age at HDP Diagnosis, Mean (SD)	Timing of HDP Diagnosis, N (%)	Race/Ethnicity, N (%)	Age, Mean (SD) [Range]
Vigil-DeGracia 2018, 29878650, Dominican Republic, Ecuador, El Salvador, Panama, Peru	Magnesium sulphate postdelivery group	555	NR	Superimposed preeclampsia, 55 (10); Severe preeclampsia, 500 (90)	NR	NR	Latin American (100)	26.8 (7.1)
	No magnesium sulphate postdelivery group	558	NR	Superimposed preeclampsia, 51 (9.1); Severe preeclampsia, 507 (90)	NR	NR	Latin American (100)	26.4 (7)
Wang 2019, 31889791, China	Nifedipine & MgSO4	110	NR	Gestational HTN, 110 (100)	34.6 (4.2)	NR	NR	27.2 (2.8)
	MgSO4	110	NR	Gestational HTN, 110 (100)	33.9 (5)	NR	NR	28 (2.1)

Table C–3.3.2. Key Question 3: MgSO4 regimens – summary of additional sample details

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Abdul 2013, 22930148, Nigeria	NR	NR	NR	Cesarean, 13 (33.3)	NR	NR	NR	NR	NR	NR
	NR	NR	NR	Cesarean, 9 (27.2)	NR	NR	NR	NR	NR	NR
Agarwal 2020, AH_001 (ad hoc), India	NR	NR	NR	Vaginal, 35 (70); Cesarean, 15 (30)	NR	NR	NR	NR	NR	NR
	NR	NR	NR	Vaginal, 34 (77); Cesarean, 10 (23)	NR	NR	NR	NR	NR	NR
Agarwal 2020,	NR	NR	NR	Vaginal, 34 (74); Cesarean, 12 (26)	NR	NR	NR	NR	NR	NR
Anjum 2016, 26498603, India	NR	Diabetes, 0 (0); Gestational diabetes, 0 (0); Renal disease, 0 (0)	NR	NR	NR	NR	NR	NR	NR	NR
	NR	Diabetes, 0 (0); Gestational diabetes, 0 (0); Renal disease, 0 (0)	NR	NR	NR	NR	NR	NR	NR	NR

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Anjum 2016, 26604159, India	NR	NR	Gravidity: 1, 94 (71.2); Gravidity: 2-4, 30 (22.7); Gravidity: >=5, 8 (6.1)	NR	NR	NR	NR	NR	NR	NR
	NR	NR	Gravidity: 1, 60 (78.9); Gravidity: 2-4, 14 (18.4); Gravidity: >=5, 2 (2.6)	NR	NR	NR	NR	NR	NR	NR
Anjum 2017, L616977819 (embase), India	NR	NR	NR	NR	NR	NR	NR	37.04 (3.1)	NR	NR
	NR	NR	NR	NR	NR	NR	NR	37.2 (3.5)	NR	NR
Begum 2002, 12214831, Bangladesh	NR	NR	Nulliparous, 147 (72.77); Parity 1-5, 55 (27.23)	Vaginal, 51 (29.82); Cesarean, 117 (68.42)	NR	25 (14.62)	NR	NR	Low birth weight, 56 (32.75)	NR
	NR	NR	Nulliparous, 140 (70.35); Parity 1-5, 59 (29.65)	Vaginal, 53 (31.18); Cesarean, 114 (67.05)	NR	22 (12.94)	NR	NR	Low birth weight, 63 (37.06)	NR

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Beyuo 2022, 35304745, Ghana	Underweight (<18.5), 6 (1.1%); Normal weight (18.5–24.9), 119 (21%); Overweight (25–29.9), 141 (24.8%); Obese (≥30), 302 (53.2)	Diabetes, 27 (4.6); Sickle cell disease, 18 (3)	Nulliparous, 197 (33.3); Primiparous, 134 (22.7); Multiparous (2–4), 234 (39.6); Grand Multiparity (≥5), 26 (4.4)	Vaginal, 214 (36.7); Cesarean, 369 (63.3)	34 (5.8)	75 (12.2)	NR	36.6 (13.8)	NR	NR
	Underweight (<18.5), 9 (1.6%); Normal weight (18.5–24.9), 134 (24.1%); Overweight (25–29.9), 146 (26.2%); Obese (≥30), 268 (48.1)	Diabetes, 38 (6.5); Sickle cell disease, 15 (2.6)	Nulliparous, 179 (30.7); Primiparous, 149 (25.6); Multiparous (2–4), 230 (39.5); Grand Multiparity (≥5), 25 (4.3)	Vaginal, 172 (30.2); Cesarean, 398 (69.9)	32 (5.6)	73 (12.2)	NR	35.5 (4.1)	NR	NR
Bhattacharjee 2011, 21534749, India	NR	Proteinuria: +2, 34 (50.7)	Nulliparous, 51 (76.1); Parity: > or = 1, 16 (23.9)	Vaginal, 4 (7.5); Cesarean, 39 (73.6)	NR	5 (9.4)	NR	NR	<36 week, 18 (26.9); 36–40 week, 49 (73.1)	NR
	NR	Proteinuria: +2, 34 (48.6)	Nulliparous, 55 (78.6); Parity: > or = 1, 15 (21.4)	Vaginal, 5 (9.3); Cesarean, 41 (75.9)	NR	6 (11.1)	NR	NR	<36 week, 19 (27.1); 36–40 week, 51 (72.9)	NR
Brookfield 2020, 33156201, USA	Median 41 (IQR 37, 46)	NR	Multiparous, 11 (61)	NR	NR	NR	NR	NR	NR	NR
	Median 42 (IQR 37, 45)	NR	Multiparous, 11 (58)	NR	NR	NR	NR	NR	NR	NR

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Chama 2013, 24069775, Nigeria	NR	NR	Nulliparous, 32 (64); 1-4, 16 (32); 5+, 2 (4)	Vaginal, 41 (82); Cesarean, 9 (18)	NR	5 (10)	NR	NR	NR	Education: no formal education, 42 (84); primary, 3 (6); secondary, 5 (10); tertiary, 0 (0)
	NR	NR	Nulliparous, 28 (58); 1-4, 18 (38); 5+, 2 (4)	Vaginal, 35 (73); Cesarean, 13 (27)	NR	4 (8.34)	NR	NR	NR	Education: no formal education, 40 (83.33); primary, 5 (10.45); secondary, 2 (4.17); tertiary, 1 (2.08)
Charoenvidhya 2013, 23691692, Thailand	NR	NR	Nulliparous, 20 (66.7); Multiparous, 10 (33.3)	NR	NR	NR	NR	36.17NR	NR	NR
	NR	NR	Nulliparous, 18 (60); Multiparous, 12 (40)	NR	NR	NR	NR	36.27NR	NR	NR
Darngawn 2012, 22261127, India	NR	NR	Primiparous (1), 47 (62.7); Multiparous, 2 (37.3)	Vaginal, 28 (37.3); Cesarean, 31 (41.3)	NR	NR	0 (0)	35.4 (3.6)	NR	NR
	NR	NR	Primiparous (1), 50 (66.7); Multiparous, 25 (33.3)	Vaginal, 27 (36); Cesarean, 32 (42.7)	NR	NR	0 (0)	35.6 (3.8)	NR	NR

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Dasgupta 2021, CN-02320544 (cochrane), India	NR	Diabetes, 0 (0); Renal disease, 0 (0)	Primiparous, 33 (73.3); Multipara, 12 (26.7)	Vaginal, 7 (15.6); Cesarean, 36 (80)	NR	NR	NR	35.85 (0.89)	NR	NR
	NR	Diabetes, 0 (0); Renal disease, 0 (0)	Primiparous, 39 (86.7); Multipara, 6 (13.3)	Vaginal, 9 (20); Cesarean, 33 (73.3)	NR	NR	NR	35.79 (0.94)	NR	NR
Easterling 2018, 29976161, Egypt	NR	NR	NR	Vaginal, 22 (22.2); Cesarean, 76 (76.8)	6NR	0 (0)	NR	35.7 (2.8)	NR	NR
	NR	NR	NR	Vaginal, 15 (16.5); Cesarean, 73 (80.2)	2NR	1 (1.1)	NR	35.2 (3.3)	NR	NR
Ehrenberg 2006, 17012443, USA	30.3	Diabetes, 11 (10.9)	Primiparous, 48 (47.5)	Cesarean, 22 (21.8)	NR	0 (0)	0 (0)	38.7 (1.7)	NR	NR
	28.3	Diabetes, 9 (9.5)	Primiparous, 45 (47.4)	Cesarean, 25 (26.3)	NR	0 (0)	0 (0)	38.7 (1.7)	NR	NR
El-Khayat 2016, 25483417, Egypt	NR	Diabetes, 0 (0); Renal disease, 0 (0)	NR	Vaginal, 45 (56.3); Cesarean, 35 (43.8)	NR	NR	NR	NR	Prematurity, 35 (46.1)	NR
	NR	Diabetes, 0 (0); Renal disease, 0 (0)	NR	Vaginal, 37 (46.3); Cesarean, 43 (53.8)	NR	NR	NR	NR	Prematurity, 31 (39)	NR
	NR	Diabetes, 0 (0); Renal disease, 0 (0)	NR	Vaginal, 35 (43.8); Cesarean, 45 (56.3)	NR	NR	NR	NR	Prematurity, 31 (43.7)	NR
Fontenot 2005, 15970809, USA	NR	NR	Nulliparous, 29 (58)	Vaginal, 31 (62)	NR	NR	NR	34.4 (3.9)	NR	NR
	NR	NR	Nulliparous, 23 (48)	Vaginal, 27 (56)	NR	NR	NR	33.4 (3.7)	NR	NR

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Vigil-De Gracia 2017, 28738788, Panama	NR	NR	Mean 2.2 (SD 1.6)	Cesarean, 92 (64.3)	NR	NR	NR	36.2 (2.8)	NR	NR
	NR	NR	Mean 2.5 (SD 1.7)	Cesarean, 96 (68)	NR	NR	NR	36.1 (3.1)	NR	NR
Gupta 2019, CN-01996873 (cochrane), India	NR	NR	Primiparous (60)	Vaginal, 20 (80); Cesarean, 5 (20)	NR	10 (40)	NR	NR	NR	Middle class (40)
	NR	NR	Primiparous (66.7)	Vaginal, 19 (73.1); Cesarean, 6 (23.1)	NR	9 (34.6)	NR	NR	NR	Middle class (33.3)
Kashanian 2016, 26364667, Iran	29.9	Diabetes, 4 (5.1); Gestational diabetes, 5 (6.3); Renal disease, 0 (0)	Primiparous (1), 65 (82.3); Parity 2, 12 (15.2); Parity 3, 2 (2.5)	NR	NR	NR	NR	NR	NR	NR
	30.5	Diabetes, 4 (4.4); Gestational diabetes, 6 (6.6); Renal disease, 0 (0)	Primiparous (1), 79 (86.8); Parity 2, 8 (8.8); Parity 3, 4 (4.4)	NR	NR	NR	NR	NR	NR	NR
Keepanasseril 2018, 28974124, India	NR	NR	Nulliparous, 65 (32.4)	Cesarean, 48 (23.9)	0 (0)	NR	NR	35.1 (0.3)	NR	NR
	NR	NR	Nulliparous, 53 (26.4)	Cesarean, 45 (22.4)	0 (0)	NR	NR	35.4 (0.25)	NR	NR

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Khan 2021, L2011768439 (embase), Pakistan	NR	Diabetes, 0 (0); Gestational diabetes, 0 (0); Renal disease, 0 (0)	NR	Vaginal, 15 (30); Cesarean, 35 (70)	NR	NR	NR	36.7 (1.25)	NR	NR
	NR	Diabetes, 0 (0); Gestational diabetes, 0 (0); Renal disease, 0 (0)	NR	Vaginal, 19 (38); Cesarean, 31 (62)	NR	NR	NR	36.6 (1.65)	NR	NR
Kitiyodom 2016, 29901967, Thailand	33.5	Gestational diabetes, 1 (5.3)	Primigravida, 7 (36.8); Multigravida, 9 (47.4)	Vaginal, 1 (5.3); Cesarean, 18 (94.7)	NR	NR	NR	NR	gestational age <37 weeks, 8 (42.1)	NR
	38.	Gestational diabetes, 4 (21.1)	Primigravida, 12 (63.2); Multigravida, 10 (52.6)	Vaginal, 3 (15.8); Cesarean, 16 (84.2)	NR	NR	NR	NR	gestational age <37 weeks, 6 (31.6)	NR
Maia 2014, 24890747, Brazil	NR	Diabetes, 0 (0); Gestational diabetes, 0 (0); Renal disease, 0 (0)	NR	Cesarean, 36 (64.3)	NR	1 (1.8)	NR	36.8 (3)	NR	NR
	NR	Diabetes, 0 (0); Gestational diabetes, 0 (0); Renal disease, 0 (0)	NR	Cesarean, 33 (58.9)	NR	1 (1.8)	NR	37.2 (4.9)	NR	NR

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Malapaka 2011, 21798536, India	22.9 (3.35)	NR	NR	NR	NR	4 (5.6)	1 (1.4)	NR	preterm, 27 (37.5)	NR
	23.5 (3.77)	NR	NR	NR	NR	4 (7.4)	1 (1.9)	NR	preterm, 29 (53.7)	NR
Manorot 1996, 8868017, Thailand	NR	Diabetes, 0 (0); Gestational diabetes, 0 (0); Renal disease, 0 (0)	NR	NR	0 (0)	NR	NR	NR	NR	NR
	NR	Diabetes, 0 (0); Gestational diabetes, 0 (0); Renal disease, 0 (0)	NR	NR	0 (0)	NR	NR	NR	NR	NR
Mundle 2012, 26104987, India	NR	NR	NR	Vaginal, 66 (44.9); Cesarean, 72 (49)	4 (2.7)	NR	NR	NR	NR	NR
	NR	NR	NR	Vaginal, 79 (51.6); Cesarean, 65 (42.5)	5 (3.3)	NR	NR	NR	NR	NR
Pascoal 2019, 31393402, Brazil	NR	NR	Median 2 (IQR 1-3)	Vaginal, 12 (38.7); Cesarean, 19 (61.3)	NR	NR	NR	36.7 (1.9)	NR	NR
	NR	NR	Median 2 (IQR 1-3)	Vaginal, 10 (32.3); Cesarean, 21 (67.7)	NR	NR	NR	34.8 (4.5)	NR	NR

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Pippen 2020, 33179549, USA	33.4 (8.39)	Diabetes, 24 (14)	Median 0 (IQR 0-1)	Vaginal, 0 (0); Cesarean, 171 (100)	0 (0)	NR	NR	Median 33 (IQR 31, 36)	NR	NR
	35.4 (9.59)	Diabetes, 10 (13)	Median 1 (IQR 0-1)	Vaginal, 0 (0); Cesarean, 78 (100)	0 (0)	NR	NR	Median 34 (IQR 31, 36)	NR	NR
Rao 2015, L606457038 (embase), Pakistan	NR	NR	Nulliparous, 46 (76.7); Primiparous, 5 (8.3); P2+, 9 (15)	NR	NR	NR	NR	NR	NR	NR
	NR	NR	Nulliparous, 44 (73.3); Primiparous, 4 (6.6)	NR	NR	NR	NR	NR	NR	NR
Regmi 2010, 21744767, Nepal	NR	NR	NR	Vaginal, 24 (64.9); Cesarean, 13 (35.1)	NR	NR	NR	NR	NR	NR
	NR	NR	NR	Vaginal, 23 (53.5); Cesarean, 20 (46.5)	NR	NR	NR	NR	NR	NR
Rimal 2017, 29453467, Nepal	NR	NR	Primiparous, 19 (63); Multiparous, 11 (37)	Vaginal, 16 (53.3); Cesarean, 14 (46.7)	NR	1 (3.3)	NR	NR	NR	NR
	NR	NR	Primiparous, 21 (70); Multiparous, 9 (30)	Vaginal, 18 (60); Cesarean, 12 (40)	NR	3 (10)	NR	NR	NR	NR

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Saha 2017, 28714170, India	23.3 (5)	NR	NR	Vaginal, 13 (65); Cesarean, 5 (25)	NR	4 (20)	NR	36.5 (3.3)	NR	NR
	23.2 (6)	NR	NR	Vaginal, 14 (66.6); Cesarean, 7 (33.4)	NR	1 (5)	NR	35.4 (3.8)	NR	NR
Shoaib 2009, 19149977, Pakistan	NR	NR	Mean 1.95 (SD 3.25) [range 0-13]	Cesarean, 6 (12)	NR	9 (18)	NR	33.8 (3.73)	NR	NR
	NR	NR	Mean 2.46 (SD 1.54) [range 0-7]	Cesarean, 15 (30)	NR	14 (28)	NR	35.56 (2.76)	NR	NR
Singh 2011, L362772412 (embase), India	NR	NR	NR	Vaginal, 46 (76.7); Cesarean, 14 (23.3)	2 (3.3)	16 (26.7)	NR	NR	NR	NR
	NR	NR	NR	Vaginal, 41 (83.7); Cesarean, 8 (16.3)	3 (5)	17 (28.3)	NR	NR	NR	NR
	NR	NR	NR	Vaginal, 35 (72.9); Cesarean, 13 (27.1)	4 (6.7)	17 (28.3)	NR	NR	NR	NR
Sravani 2022, L201694239 (embase), India	NR	NR	Primigravida 30 (100)	NR	NR	NR	NR	NR	NR	NR
	NR	NR	Primigradida, 30 (100)	NR	NR	NR	NR	NR	NR	NR

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Sultana 2010, L365881919 (embase), Bangladesh	NR	NR	Gravidity: Primi, 36 (75); Gravidity: Multi, 10 (20.8); Gravidity: Grandmulti, 2 (4.2)	NR	NR	NR	NR	NR	<32 weeks, 14 (29.2); 33-36 weeks, 22 (45.8); >37 weeks, 12 (25)	Lower class, 34 (70.8); Middle class, 14 (29.2)
	NR	NR	Gravidity: Primi, 37 (7); Gravidity: Multi, 12 (23.1); Gravidity: Grandmulti, 3 (5.8)	NR	NR	NR	NR	NR	<32 weeks, 14 (26.9); 33-36 weeks, 17 (32.7); >37 weeks, 21 (40.4)	Lower class, 45 (86.5); Middle class, 7 (13.5)
Tungmanowutthikul 2019, CN-01793189 (cochrane), Thailand	31.9 (5.5) <18.5, 0 (0%); 18.5 to <25, 3 (7%); 25 to <30, 15 (34.9%); 30 to <40, 23 (53.5)	Gestational diabetes, 6 (14); Autoimmune disease, 0 (0)	Nulliparous, 18 (41.9); Primigravida, 13 (30.2)	Vaginal, 10 (23.3); Cesarean, 31 (72.1)	NR	NR	NR	36.4 (3.2) [27-41]	NR	NR
	30.2 (5.8) <18.5, 0 (0%); 18.5 to <25, 9 (20.9%); 25 to <30, 13 (30.2%); 30 to <40, 19 (44.2)	Gestational diabetes, 6 (14); Autoimmune disease, 1 (2.3)	Nulliparous, 29 (67.4); Primigravida, 22 (51.2)	Vaginal, 17 (39.5); Cesarean, 26 (60.5)	NR	NR	NR	36.1 (3.5) [26-41]	NR	NR

Study	BMI, Mean (SD) [Range]	Co-Occurring Disorders, N (%)	Parity / Gravidity, N (%)	Delivery Characteristics, N (%)	Multiple Births, N (%)	Stillbirth, N (%)	Spontaneous or Induced Abortion, N (%)	Gestational Age at Delivery, Mean (SD) [Range]	Prematurity, N (%)	Social Determinants of Health, N (%)
Unwaha 2020, 31833059, Nigeria										
	NR	NR	Primiparous (1), 11 ()	Vaginal, 15 (37.5); Cesarean, 25 (62.5)	NR	NR	NR	34.4 (3.99)	NR	Education: secondary or lower, 10 (25); tertiary, 30 (75)
	NR	NR	Primiparous (1), 11 ()	Vaginal, 10 (25); Cesarean, 30 (75)	NR	NR	NR	34.1 (4.53)	NR	Education: secondary or lower, 12 (30); tertiary, 28 (70)
Vigil-DeGracia 2018, 29878650, Dominican Republic, Ecuador, El Salvador, Panama, Peru	NR	NR	Nulliparous, 325 (58.6)	Vaginal, 218 (39); Cesarean, 337 (61)	9 (1.6)	NR	NR	36.3 (3.6)	NR	NR
	NR	NR	Nulliparous, 327 (58.6)	Vaginal, 215 (39); Cesarean, 343 (61.4)	11 (1.9)	NR	NR	36.3 (4.9)	NR	NR
Wang 2019, 31889791, China	NR	Diabetes, 0 (0); Gestational diabetes, 0 (0); Renal disease, 0 (0)	Primiparous, 81 (73.6); Multiparous, 29 (26.4)	NR	0 (0)	NR	0 (0)	NR	NR	NR
	NR	Diabetes, 0 (0); Gestational diabetes, 0 (0); Renal disease, 0 (0)	Primiparous, 83 (75.5); Multiparous, 27 (24.5)	NR	0 (0)	NR	0 (0)	NR	NR	NR

Appendix D. Results Risk of Bias and Assessment of Methodological Quality

Risk of Bias Assessments

Appendix Tables D-1.1 to D-1.3 summarize the risk of bias assessment or methodological quality (KQ 1: single-arm studies) of all 73 studies.

Among the 61 RCTs we rated 16 at low risk of bias, 24 at moderate risk, and 21 at high risk. Moderate and high-risk ratings were generally related to the lack of blinding of participants, care providers, and outcome assessors, incomplete outcome data or generally unclear reporting.

Among the 4 NRCSs, we rated 1 at high risk and 3 at moderate risk, due serious risk of confounding and lack of blinding of participants, care providers, and outcome assessors.
We did not assess RoB in the 8 noncomparative single-arm studies. In the 4 feasibility studies, participation rates were low (≤ 55%) or unclear.

Table D–1.1. All Key Questions: Risk of bias assessment – randomized controlled trials

KQ	Study, Year, Citation ID (Database)	Overall RoB	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessor	Incomplete Outcome Data	Selective Reporting	Intention-to-Treat Analysis	Other Bias
1	Cairns 2018, 29967037	Moderate	Low	Low	High	High	Low	Low	Low	Low
1	Hirshberg 2018, 29703800	Moderate	Low	Low	High	High	Low	Low	Low	Low
1	Spiegelman 2020, CN-02075381 (cochrane)	High	Low	High	High	High	High	Low	Low	High
2	Ainuddin 2019, 31489020	High	Unclear	Low	Unclear	Unclear	Low	Unclear	Low	Low
2	Arias-Hernández 2020, 32774912	Low	Low	Low	Low	High	Low	Low	Unclear	Low
2	Ascarelli 2005, 15625138	Moderate	Unclear	Low	High	High	Low	Low	Unclear	Low
2	Barton 1990, 2316590	High	Unclear	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Low
2	Dabaghi 2019, L2002160304 (embase)	High	Unclear	Low	High	High	Unclear	Unclear	Unclear	Low
2	Fidler 1982, 7171513	High	Unclear	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Low
2	Griffis 1989, 2789542	Moderate	Unclear	Low	High	High	Unclear	Low	Unclear	Low
2	Noronha Neto 2017, 28125624	Low	Low	Low	Low	Low	Low	Low	Low	Low
2	Ormesher 2020, 33012200	Low	Low	Low	Low	Low	Low	Low	Low	Low
2	Lopes Perdigao 2021, 33550824	Low	Low	Low	Low	Low	Low	Low	Low	Low
2	Sayin 2005, L40874197 (embase)	High	Unclear	Unclear	Unclear	Unclear	Low	Low	Unclear	Low
2	Sharma 2017, 27786578	Moderate	Low	Low	High	High	Low	Low	Low	Low
2	Veena 2017, 27835048	Low	Low	Low	Unclear	Unclear	Low	Low	Unclear	Low
2	Vigil-De Gracia 2007, 17469006	Low	Low	Low	High	High	Low	Low	Unclear	Low
2	Viteri 2018, 30303905	Moderate	Low	Low	Low	Low	Low	Low	Low	Low
2	Vázquez-Rodríguez 2020, 34520145	Moderate	Unclear	Unclear	High	Unclear	Low	Low	Low	Low

KQ	Study, Year, Citation ID (Database)	Overall RoB	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessor	Incomplete Outcome Data	Selective Reporting	Intention-to-Treat Analysis	Other Bias
2	Yoselevsky 2022, L2016043015 (embase)	High	Unclear	Unclear	High	High	Low	Low	Unclear	Low
3	Abdul 2013, 22930148	Moderate	Low	Low	High	High	Low	Unclear	Unclear	Low
3	Agarwal 2020, AH_001 (ad hoc)	Moderate	Low	Unclear	Low	Low	Low	Low	Low	Low
3	Ali 2022, L2017937927 (embase)	Moderate	Low	Unclear	Low	Low	Low	Low	Unclear	Low
3	Anjum 2016, 26604159	Moderate	Low	Low	Unclear	Unclear	Low	Low	Low	Low
3	Anjum 2016, 26498603	High	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low
3	Anjum 2017, L616977819 (embase)	High	Unclear	Unclear	Low	Low	Low	Unclear	Low	Low
3	Begum 2002, 12214831	High	Low	Unclear	Low	Low	Low	Low	Low	Low
3	Beyuo 2022, 35304745	Low	Low	Low	Low	Low	Low	Low	Low	Low
3	Bhattacharjee 2011, 21534749	Moderate	Low	Low	High	High	Low	Unclear	Low	Low
3	Brookfield 2020, 33156201	Low	Low	Low	Low	Low	Low	Low	Low	Low
3	Chama 2013, 24069775	Low	Low	Low	Low	Low	Low	Low	Low	Low
3	Charoenvidhya 2013, 23691692	High	Unclear	Unclear	Low	Low	Unclear	Unclear	Low	Low
3	Darngawn 2012, 22261127	Moderate	Low	Unclear	High	High	Low	Low	Unclear	Low
3	Dasgupta 2021, CN-02320544 (cochrane)	Low	Low	Low	Low	Low	Low	Low	Low	Low
3	Easterling 2018, 29976161	Low	Low	Low	Low	Low	Low	Low	Low	Low
3	Ehrenberg 2006, 17012443	Moderate	Low	Low	High	High	Low	Low	Low	Low
3	El-Khayat 2016, 25483417	Low	Low	Low	Low	Low	Low	Unclear	Low	Low
3	Fontenot 2005, 15970809	Low	Low	Low	Low	Low	Low	Low	Low	Low

KQ	Study, Year, Citation ID (Database)	Overall RoB	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessor	Incomplete Outcome Data	Selective Reporting	Intention-to-Treat Analysis	Other Bias
3	Gupta 2019, CN-01996873 (cochrane)	High	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low
3	Kashanian 2016, 26364667	High	Unclear	Unclear	High	Low	Low	Low	Unclear	Low
3	Keepanasseril 2018, 28974124	Low	Low	Low	Low	Low	Low	Low	Low	Low
3	Khan 2021, L2011768439 (embase)	High	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low
3	Kitiyodom 2016, 29901967	High	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Unclear	Low
3	Maia 2014, 24890747	Moderate	Low	Low	High	High	Low	Low	Low	Low
3	Malapaka 2011, 21798536	High	Unclear	Unclear	Low	Low	Low	Low	Low	Low
3	Manorot 1996, 8868017	Moderate	Low	Unclear	Low	Low	Low	Low	Low	Low
3	Mundle 2012, 26104987	Moderate	Low	Low	High	High	Low	Low	Low	Low
3	Pascoal 2019, 31393402	Low	Low	Unclear	Low	Low	Low	Low	Low	Low
3	Rahat 2022, L2017656012 (embase)	Moderate	Low	Unclear	Low	Low	Low	Unclear	Low	Low
3	Rao 2015, L606457038 (embase)	High	Unclear	Unclear	Low	Low	Unclear	Low	Low	Low
3	Regmi 2010, 21744767	Moderate	Low	Unclear	Unclear	Unclear	Low	Low	Unclear	Low
3	Rimal 2017, 29453467	High	Unclear	Unclear	Low	Low	Low	Low	Low	Low
3	Saha 2017, 28714170	Moderate	Low	Unclear	Low	Low	Low	Unclear	Low	Low
3	Singh 2011, L362772412 (embase)	Moderate	Low	Unclear	Low	Low	Low	Low	Low	Low
3	Sravani 2022, L2016942399 (embase)	High	Unclear	Unclear	Low	Low	High	Low	Unclear	Low
3	Sultana 2010, L365881919 (embase)	High	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Low

KQ	Study, Year, Citation ID (Database)	Overall RoB	Random Sequence Generation	Allocation Concealment	Blinding of Participants and Personnel	Blinding of Outcome Assessor	Incomplete Outcome Data	Selective Reporting	Intention-to-Treat Analysis	Other Bias
3	Tungmanowutthikul 2019, CN-01793189 (cochrane)	Moderate	Low	Low	Unclear	Unclear	Low	Low	Unclear	Low
3	Unwaha 2020, 31833059	Moderate	Low	Low	Low	Low	Low	Low	Low	Low
3	Vigil-De Gracia 2017, 28738788	Moderate	Low	Low	Low	Low	Low	Low	Low	Low
3	Vigil-De Gracia 2018, 29878650	Moderate	Low	Low	Low	Low	Low	Low	Low	Low
3	Wang 2019, 31889791	High	Unclear	Unclear	Unclear	Unclear	Low	Low	Low	Low

Abbreviations: Citation ID = PubMed identifier when available. Otherwise, identifier is specific to database in parentheses. Ratings are color coded for emphasis only. The colors do not impart unique information.

From the Cochrane Risk of Bias Tool (each item rated as Low, High, Unclear, or N/A [Not applicable]

- Random sequence generation (selection bias): Selection bias (biased allocation to interventions) due to inadequate generation of a randomized sequence.
- Allocation concealment (selection bias): Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.
- Blinding of participants (performance bias): Performance bias due to knowledge of the allocated interventions by participants during the study.
- Blinding of personnel/care providers (performance bias): Performance bias due to knowledge of the allocated interventions by personnel/care providers during the study.
- Blinding of outcome assessor (detection bias): Detection bias due to knowledge of the allocated interventions by outcome assessors during the study.
- Incomplete outcome data (attrition bias): Attrition bias due to amount, nature, or handling of incomplete outcome data.
- Selective outcome reporting (outcome reporting bias): Bias arising from outcomes being selectively reported based on the direction and/or strength of the results.
- Other Bias: Bias due to problems not covered elsewhere in the table.

Each study is rated as High, Moderate, or Low.

Table D–1.2. Risk of bias assessment for all Key Questions: nonrandomized comparative studies

KQ	Study, Year, Citation ID (Database)	Overall Risk of Bias	1.2 Potential for Time-Varying Confounding	1.3 Intervention Switches Related to Prognostic Factors?	1.4 Appropriate Analysis Method for Confounding?	1.5. Appropriate Adjustment Variables Used	1.6. Inappropriate Adjustment for Post-Intervention Variables	1.7. Judgment – Risk of Bias Related to Residual Confounding	1.8. If Y/PY to 1.7: Were Adjustment Variables Measured Reliably	2.1 Participant Selection Based on Post-Intervention Variables?	2.2 Start and Follow-Up (Duration) Coincide	2.3 Post-Intervention Variables Associated With Intervention?	2.4 Post-Intervention Variables	2.5. Appropriate Adjustment for Selection Bias
1	Hoppe 2020, 32439388	High	N	N/A	PY	N/A	PY	Y	N/A	N	Y	N/A	Y	N
1	Khosla 2022, 35121193	Moderate	N	N/A	Y	Y	PY	PY	Y	N	N/A	N/A	N/A	N
3	Pippen 2020, 33179549	Moderate	N	N	Y	Y	N	Y	Y	N	N/A	N/A	Y	N/A
3	Shoaib 2009, 19149977	Moderate	N	N/A	Y	Y	N	N	N/A	N	Y	N/A	N/A	N/A

Abbreviations: KQ = Key Question, N/A = Not applicable, NI = no information, Citation ID = PubMed identifier when available. Otherwise, identifier is specific to database in parentheses, PN = probably no, PY = probably yes, Y = yes.

Table D–1.3. KQ 1: Methodologic quality assessment for single arm studies

KQ	Study, Year, Citation ID (Database)	Was There Evidence of INCOMPLETE OUTCOME DATA?	Was there Evidence of SELECTIVE OUTCOME REPORTING?	Was there Evidence Suggesting OTHER BIAS?	Were the Participant ELIGIBILITY CRITERIA Prespecified and Clearly Described?	Was the INTERVENTIONS(s) Clearly Described and Delivered Consistently to All Participants?	Were the OUTCOMES Prespecified, Clearly Defined, Valid, Reliable, and Assessed Consistently?
1	Rhoads 2017, 28475431	High	Low	Yes, 52.1% participation rate	Yes	To some extent “yes”	Yes
1	Hoppe 2019, 30825917	Low	Low	Yes, 55% participation rate	Yes	To some extent "yes"	Yes
1	Burgess 2021, 34397475	Low	Low	Yes, unclear participation rate	Yes	Yes	Yes
1	Deshpande 2022 35340907	High	Low	Yes, 52.1% participation rate	Yes	To some extent “yes”	Yes
1	Hauspurg 2019, 31503166	Low	Low	Yes, Unclear participation rate	Yes	Yes	Yes
1	Triebwasser, 2020, 32980623	Low	Low	Yes, 47% participation rate	Yes	Yes	Yes
1	Janssen 2021, 34329800	High	Low	Yes, unclear participation rate	Yes	Yes	Yes
1	Hacker 2022, 35283352	High	Unclear	Yes, high nonresponse and refusal rates	Yes	Yes	Yes

Abbreviations: KQ = Key Question, N/A = Not applicable, NI = no information, Citation ID = PubMed identifier when available. Otherwise, identifier is specific to database in parentheses, PN = probably no, PY = probably yes, Y = yes.

Appendix E. Results: Evidence Tables

Evidence Tables: KQ 1

Table E–1.1. Evidence Table – Key Question 1: Categorical outcomes

Outcome Measure	Study, Design	Arm	Sub-group	Time Point	n/N (%) or [95% CI]	Effect Measure	Effect Size (95% CI)	Reported P–Value
BP reporting: At least one BP during first 10 PP days	Hirshberg, 2018, RCT	HBPM	All	10d	95/103 (92.2%)	OR aOR	15.31 (6.74, 34.75) 58.20 (6.2, 208.1)	NR
	Hirshberg, 2018, RCT	Office-based follow up	All	10d	45/103 (43.7%),	OR aOR	Ref	NR
	Hirshberg, 2018, RCT	HBPM	Black	10d	63/68 (93%)	NR	NR	NR
	Hirshberg, 2018, RCT	Office-based follow up	Black	10d	NR	NR	NR	NR
	Hirshberg, 2018, RCT	HBPM	Non-black	10d	32/35 (91%)	NR	NR	NR
	Hirshberg, 2018, RCT	Office-based follow up	Non-black	10d	21/30 (70%)	NR	NR	NR
	Hoppe 2020, NRCS	HBPM	All	10d	202/214 (94.4%)	aRR	1.59 (1.36, 1.77)	**P=0.02**
	Hoppe 2020, NRCS	Standard care	All	10d	129/214 (60.3%)	NR	Ref	NR
	Khosla 2022, NRCS	HBPM (audio-only telehealth)	All (reported by race/ ethnicity)	by 6 wks	76.3% non-Hispanic Black 76.7% non-Hispanic White	racial gap 0.4%	NR	**P<0.0001**, adjusted overall improvement in adherence for non-Hispanic-Black patients
	Khosla 2022, NRCS	HBPM (paper log)	All (reported by race/ ethnicity)	by 6 wks	48% non-Hispanic Black 73.1% non-Hispanic White	racial gap 24.6%	NR	NR
Adherence to BP surveillance	NCT03728790	HBPM (transmitted)	All	14d	61.1% of BPs reported (range 0.0, 92.3)	NR	NR	NR
	NCT03728790	HBPM (paper log)	All	14d	0% of BPs reported (range 0.0, 0.0)	NR	NR	NR

Outcome Measure	Study, Design	Arm	Sub-group	Time Point	n/N (%) or [95% CI]	Effect Measure	Effect Size (95% CI)	Reported P–Value
BP treatment (initiation)	Hirshberg, 2018, RCT	HBPM	All	NR	17/103 (16.5%)	aOR	1.0 (0.3, 3.1)	NR
	Hirshberg, 2018, RCT	Office-based follow up	All	NR	10/45 (22.2%)	aOR	Ref	NR
BP treatment (initiation)	NCT03728790	HBPM (transmitted)	All	NR	24/60 (40%)	RR	2.60 (1.36, 4.98)	NR
	NCT03728790	HBPM (paper log)	All	NR	10/65 (15%)	RR	Ref	NR
Unplanned healthcare utilization: ***re-admissions***	Hirshberg, 2018, RCT	HBPM	All	NR	0/103 (0%)	RR	0.11 (0.01 to 2.04)	NR
	Hirshberg, 2018, RCT	Office-based follow up	All	NR	4/103 (3.9%)	RR	Ref	NR
	NCT03728790	HBPM (transmitted)	All	NR	13/101 (12.9%)	RR	2.50 (0.79 to 7.85)	NR
	NCT03728790	HBPM (paper log)	All	NR	7/112 (6.3%)	RR	Ref	NR
	Khosla 2022, NRCS	HBPM (audio-only telehealth)	All	NR	17.44%	RR	NR	NR
	Khosla 2022, NRCS	HBPM (paper log)	All	NR	17.84%	RR	NR	NR
Unplanned healthcare utilization: ***ED visits***	NCT03728790	HBPM (transmitted)	All	14 d	25/101 (24.8%)	RR	1.63 (0.94, 2.84)	NR
	NCT03728790	HMPM (paper log)	All	14 d	17/112 (15.2%)	RR	Ref	NR
Satisfaction with PP care	Hirshberg, 2018, RCT	HBPM	All	NR	N/R	RR	N/R	NR
	Hirshberg, 2018, RCT	Office-based follow up	All	NR	N/R	RR	NR	NR
Maternal M&M: PE related complications	NCT03728790	HBPM (transmitted)	All	14d	9/101 (8.9%)	RR	2.5 (0.79, 7.85)	NR
	NCT03728790	HMPM (paper log)	All	14d	4/112 (3.6%)	RR	Ref	NR

Abbreviations: OR = odds ratio, aOR = adjusted OR, Citation = PubMed, Cochrane ID, EMBASE ID, RoB = risk of bias

Table E–1.2. Evidence Table – Key Question 1: Continuous outcomes

Outcome Measure (Unit)	Study	Arm	N	Time Point	Mean (SD)	Effect Measure	Effect Size (95% CI)	Reported P–Value
Adherence to BP surveillance	NCT03728790	HBPM (transmitted)	All	14d	Median 61.1% (Range 0, 92.3%)	N/R	N/R	NR
	NCT03728790	HBPM (paper log)	NR	NR	Median 0% Range 0, 100%	NR	N/R	NR
BP IAD: mean treatment duration (d)	Cairns 2018	HBPM with self-titration	NR	Variable	29d IQR:12, 49	aMD	–12d (–39, 6)	NR
	Cairns 2018	Usual care	NR	NR	41 IQR: 23, 58	NR	Ref	NR
BP control: mean DBP (mmHg)	Cairns 2018	HBPM with self-titration	NR	4 wk 6 wk 12 wk 3–4 yr	NR	NR	NR	NR
	Cairns 2018	Usual care	NR		NR	NR	Ref	NR

Abbreviations: CI = confidence interval, d = days, PMID = PubMed ID, RoB = risk of bias, SD = standard deviation

Evidence Tables: KQ 2

Table E–2.1. Evidence Table – Key Question 2: Categorical outcomes

Outcome Measure	Study (Overall RoB)	Arm	Subgroup	Time Point	n/N (%) or [95% CI]	Effect Measure	Effect Size (95% CI)	Reported P–Value
BP control: persistent HTN	Lopes Peredigao 2021 (Low)	PO furosemide	All	PP Day-7	23/192 (12%)	aRR	**0.40 (0.20 to 0.81)**	NR
	Lopes Peredigao 2021 (Low)	Placebo	All	PP Day-7	12/192 (5.2%)	aRR	Ref	NR
BP control: persistent HTN	Viteri 2018	PO torsemide	PE (48% severe)	PP Day 7–10	12/34 (38%)	RR	1.1 (0.6, 2.1)	NR
	Viteri 2018	Placebo	PE (48% severe)	PP Day 7–10	10/28 (36%)	RR	NR	NR
BP control: need for rescue medication	Veena 2017	PO furosemide + nifedipine	PE (20% severe)	DC	4/50 (8%)	RR	0.31 (0.11, 0.88)	NR
	Veena 2017	nifedipine alone	PE (20% severe)	DC	13/50, (26%)	RR	NR	NR
Length of PP hospital stay	NCT04236258	enalapril	All	Beyond “length of normal stay”	17/47 (36.2%)	RR	1.39 (0.76, 2.54)	NR
	NCT04236258	XR nifedipine	All	.	13/47 (27.7)	RR	NR	NR
Unplanned health care utilization: re-admissions	Lopes Perdigao 2021	PO furosemide	PE (32% severe)	N/R	9/192 (5%)	RR	0.55 (0.25, 1.21)	NR
	Lopes Perdigao 2021	Placebo	PE (32% severe)	.	16/192 (8%)	RR	NR	NR
	NCT04236258 (moderate)	enalapril	All	N/R	4/47 (8.5%)	RR	1.33 (0.32, 5.64)	NR
	NCT04236258	XR nifedipine	All	N/R	3/47 (6.4%)	RR	NR	NR

Outcome Measure	Study (Overall RoB)	Arm	Subgroup	Time Point	n/N (%) or [95% CI]	Effect Measure	Effect Size (95% CI)	Reported P–Value
Unplanned heathcare utilization: obstretrical triage area or clinic visits	NCT04236258 (moderate)	enalapril	All	N/R	32/47 (68%)	RR	1.06 (0.82, 1.38)	NR
	NCT04236258	ER nifedipine	All	N/R	34/42 (72%)	RR	NR	NR

Abbreviations: OR = odds ratio, aOR = adjusted OR, Citation = PubMed, Cochrane ID, EMBASE ID, RoB = risk of bias

Table E–2.2. Evidence Table – Key Question 2: Continuous outcomes

Outcome Measure (Unit)	Study Year Citation, Design, (Overall RoB)	Comparison	Subgroup	N	Time Point	Mean (SD)	Effect Measure	Effect Size (95% CI)	Reported P–Value
BP control: Days to resolution of HTN	Lopes Peredigao 2021 (low)	PO furosemide vs. placebo	All	.	Variable	N/R	aHR	1.20 (0.95, 1.51)	NR
	NCT04236258 (moderate)	Enalapril vs. ER nifedipine	All	47 vs. 47	No need for changes in antihypertensive regimen for 24 hours	.	MD	1.2 (–0.3, 2.7)	NR
BP control: mean SBP	Ascarelli 2005 (moderate)	PO furosemide vs. no treatment	All severe PE	.	PP Day-2	142 vs. 153mmHg	N/R	N/R	**P < 0.004**

Abbreviations: CI = confidence interval, d = days, PMID = PubMed ID, RoB = risk of bias, SD = standard deviation

Evidence Table: KQ 3

Table E–3.1. Evidence Table – Key Question 3: Seizure outcomes

Study	Category	HDP Category	Subgroup	Arm	Regimen	Duration of MgSO4	Counts (x/N)	Estimate (95% CI)
Altman, 2002, 12057549	Effect	sPE	no	placebo	placebo	N/A	37/1345	0.028 (95% CI: 0.019, 0.038)
	Effect	sPE	no	Mg	Zuspan / Pritchard	24	15/1297	0.012 (95% CI: 0.006, 0.019)
Belfort, 2003, 12540643	Effect	E	no	nimodipine	nimodipine	N/A	21/819	0.026 (95% CI: 0.016, 0.039)
	Effect	E	no	Mg	Zuspan*	24	7/831	0.008 (95% CI: 0.003, 0.017)
Bhalla, 1994, 7980301	Effect	E	no	Menon	Lytic Cocktail	N/A	11/45	0.244 (95% CI: 0.129, 0.395)
	Effect	E	no	Mg	Bhalla	24	1/45	0.022 (95% CI: 0.001, 0.118)
Chen, 1995, L362772412	Effect	sPE	no	usual care	usual care	N/A	0/30	0 (95% CI: 0, 0.116)
	Effect	sPE	no	Mg	Zuspan	24	0/34	0 (95% CI: 0, 0.103)
Coetzee, 1998, 9532990	Effect	sPE	no	placebo	placebo	N/A	11/340	0.032 (95% CI: 0.016, 0.057)
	Effect	sPE	no	Mg	Zuspan	24	1/345	0.003 (95% CI: 0, 0.016)
Crowther, 1990, 2180472	Effect	E	no	diazepam	diazepam	N/A	5/27	0.185 (95% CI: 0.063, 0.381)
	Effect	E	no	Mg	Pritchard	24	7/24	0.292 (95% CI: 0.126, 0.511)
Dommisse, 1990, 2317464	Effect	E	no	phenytoin	phenytoin	N/A	4/11	0.364 (95% CI: 0.109, 0.692)
	Effect	E	no	Mg	Zuspan	24	0/11	0 (95% CI: 0, 0.285)
Hangarga, 2001, CN-00498563	Effect	E	no	phenytoin	phenytoin	N/A	2/32	0.062 (95% CI: 0.008, 0.208)
	Effect	E	no	Menon	Lytic Cocktail	N/A	18/34	0.529 (95% CI: 0.351, 0.702)
	Effect	E	no	Mg	Hangarga	24	3/24	0.125 (95% CI: 0.027, 0.324)

Study	Category	HDP Category	Subgroup	Arm	Regimen	Duration of MgSO4	Counts (x/N)	Estimate (95% CI)
Khooshideh, 2017, 29114367	Effect	sPE	yes	phenytoin	phenytoin	N/A	7/65	0.108 (95% CI: 0.044, 0.209)
	Effect	sPE	yes	Mg	Zuspan 4-2	24	0/65	0 (95% CI: 0, 0.055)
	Effect	E	yes	phenytoin	phenytoin	N/A	3/25	0.12 (95% CI: 0.025, 0.312)
	Effect	E	yes	Mg	Zuspan 4-2	24	0/25	0 (95% CI: 0, 0.137)
Moodley, 1994, L25017558	Effect	sPE	no	usual care	usual care	N/A	0/112	0 (95% CI: 0, 0.032)
	Effect	sPE	no	Mg	Pritchard	24	1/116	0.009 (95% CI: 0, 0.047)
Ola, 2005, CN-00713435	Effect	E	no	diazepam	diazepam	N/A	13/30	0.433 (95% CI: 0.255, 0.626)
	Effect	E	no	Mg	Zuspan	24	0/30	0 (95% CI: 0, 0.116)
Sawhney, 1999, 10533328	Effect	E	no	phenytoin	phenytoin	N/A	18/25	0.72 (95% CI: 0.506, 0.879)
	Effect	E	no	Mg	Bhalla	24	7/25	0.28 (95% CI: 0.121, 0.494)
Shamsuddin, 1998, 9926482	Effect	E	no	diazepam	diazepam	N/A	26/100	0.26 (95% CI: 0.177, 0.357)
	Effect	E	no	Mg	Dhaka	24	5/100	0.05 (95% CI: 0.016, 0.113)
Ali 2022, L201793792	duration	E	no	Loading dose only	.	0	8/66	0.12 (95% CI: 0.054, 0.225)
	duration	.		Standard24	Prichard	24	4/66	0.06 (95% CI: 0.017, 0.148)
Anjum, 2016, 26604159	duration	E	no	12h MgSO4	Zuspan 12h	12	0/132	0 (95% CI: 0, 0.028)
	duration	E	no	24h MgSO4	Zuspan	24	0/72	0 (95% CI: 0, 0.05)
	duration	sPE	no	Group A	Zuspan 6h	6	0/76	0 (95% CI: 0, 0.047)
	duration	sPE	no	Group B	Zuspan	24	0/43	0 (95% CI: 0, 0.082)
Anjum, 2017, L616977819	duration	sPE	no	MgSO4 until delivery	Zuspan	0	0/48	0 (95% CI: 0, 0.074)
	duration	sPE	no	MgSO4 24h	Zuspan	24	0/43	0 (95% CI: 0, 0.082)

Study	Category	HDP Category	Subgroup	Arm	Regimen	Duration of MgSO4	Counts (x/N)	Estimate (95% CI)
Begum, 2002, 12214831	duration	E	no	Loading dose only	NR	0	8/202	0.04 (95% CI: 0.017, 0.077)
	duration	E	no	Standard regime	NR	24	7/199	0.035 (95% CI: 0.014, 0.071)
Beyuo, 2022, 35304745	duration	sPE	no	12-hour treatment group	Pritchard 12h	12	2/592	0.003 (95% CI: 0, 0.012)
	duration	sPE	no	24-hour control group	Pritchard	24	5/584	0.009 (95% CI: 0.003, 0.02)
Chama, 2013, 24069775	duration	E	no	Shortened Regimen	Pritchard 8h	8	3/48	0.062 (95% CI: 0.013, 0.172)
	duration	E	no	Standard Pritchard Regimen	Pritchard	24	2/50	0.04 (95% CI: 0.005, 0.137)
Darngawn, 2012, 22261127	duration	sPE	no	Intervention	mixed	12	0/75	0 (95% CI: 0, 0.048)
	duration	sPE	no	Control	mixed	24	0/75	0 (95% CI: 0, 0.048)
Dasgupta, 2021, CN-02320544	duration	sPE	no	Abbreviated Regimen	Pritchard	8	0/45	0 (95% CI: 0, 0.079)
	duration	sPE	no	Traditional Regimen	Pritchard	24	0/45	0 (95% CI: 0, 0.079)
Ehrenberg, 2006, 17012443	duration	sPE	no	12 Hours PP Magnesium Sulfate Therapy	Zuspan 4-2 12hr	12	0/101	0 (95% CI: 0, 0.036)
	duration	sPE	no	24 Hours Magnesium Sulfate Therapy	Zuspan 4-2	24	0/95	0 (95% CI: 0, 0.038)
El-Khayat, 2016, 25483417	duration	sPE	no	Loading dose only	Zuspan 6 1	0	0/80	0 (95% CI: 0, 0.045)
	duration	sPE	no	12h protocol	Zuspan 6 1	12	1/80	0.013 (95% CI: 0, 0.068)
	duration	sPE	no	24h protocol	Zuspan 6 1	24	0/80	0 (95% CI: 0, 0.045)
Fontenot, 2005, 15970809	duration	sPE	no	Study group	Zuspan 4-2	until UO > 100 ml/h	0/48	0 (95% CI: 0, 0.074)
	duration	sPE	no	Control group	Zuspan 4-2	24	0/50	0 (95% CI: 0, 0.071)
Kashanian, 2016, 26364667	duration	sPE	no	MgSO4 for 12 hours	Pritchard	12	1/79	0.013 (95% CI: 0, 0.069)
	duration	sPE	no	MgSO4 for 24 hours	Pritchard	24	0/91	0 (95% CI: 0, 0.04)
Keepanasseril, 2018, 28974124	duration	sPE	no	Loading dose only (group B)	Dhaka	0	6/201	0.03 (95% CI: 0.011, 0.064)
	duration	sPE	no	Low-dose Dhaka (group A)	Dhaka	24	3/201	0.015 (95% CI: 0.003, 0.043)

Study	Category	HDP Category	Subgroup	Arm	Regimen	Duration of MgSO4	Counts (x/N)	Estimate (95% CI)
Khan, 2021, L2011768439	duration	E	no	12-hour protocol	Zuspan 12h	12	0/50	0 (95% CI: 0, 0.071)
	duration	E	no	24-hour protocol	Zuspan	24	0/50	0 (95% CI: 0, 0.071)
Maia, 2014, 24890747	duration	sPE	no	12 hours	Zuspan 6-1	12	0/56	0 (95% CI: 0, 0.064)
	duration	sPE	no	24 hours	Zuspan 6-1	24	0/56	0 (95% CI: 0, 0.064)
Rao, 2015, L606457038	duration	E	no	12h regimen (A)	Zuspan 12h	12	0/60	0 (95% CI: 0, 0.06)
	duration	E	no	24h regimen (B)	Zuspan	24	0/60	0 (95% CI: 0, 0.06)
Regmi, 2010, 21744767	duration	E	yes	Loading dose	Pritchard LD	0	2/43	0.047 (95% CI: 0.006, 0.158)
	duration	E	yes	Loading and maintenance dose of Mg Sulfate	Pritchard	24	0/37	0 (95% CI: 0, 0.095)
Rimal, 2017, 29453467	duration	sPE	yes	Loading dose only	Pritchard LD	0	2/30	0.067 (95% CI: 0.008, 0.221)
	duration	sPE	yes	Standard Pritchard Regimen	Pritchard	24	1/30	0.033 (95% CI: 0.001, 0.172)
Shoaib, 2009, 19149977	duration	sPE	no	Loading dose only	Pritchard LD	0	0/50	0 (95% CI: 0, 0.071)
	duration	sPE	no	Standard Pritchard regime	Pritchard	24	1/50	0.02 (95% CI: 0.001, 0.106)
Unwaha, 2020, 31833059	duration	sPE	no	12 hour maintenance dose	Zuspan 12h	12	0/40	0 (95% CI: 0, 0.088)
	duration	sPE	no	24 hour maintenance dose	Zuspan	24	0/40	0 (95% CI: 0, 0.088)
Vigil-DeGracia, 2018, 29878650	duration	sPE	no	Magnesium sulphate postdelivery group	Zuspan 8h	8	1/555	0.002 (95% CI: 0, 0.01)
	duration	sPE	no	No magnesium sulphate postdelivery group	Zuspan	24	2/558	0.004 (95% CI: 0, 0.013)
Vigil-DeGracia, 2017, 28738788	duration	sPE	no	6h post-delivery	Zuspan	6	0/141	0 (95% CI: 0, 0.026)
	duration	sPE	no	24h post-delivery	Zuspan	24	0/143	0 (95% CI: 0, 0.025)
Abdul, 2013, 22930148	dose	E	no	MgSO4 Low Dose	NR	24	2/39	0.051 (95% CI: 0.006, 0.173)
	dose	E	no	MgSO4 Standard Dose	Pritchard	24	1/33	0.03 (95% CI: 0.001, 0.158)

Study	Category	HDP Category	Subgroup	Arm	Regimen	Duration of MgSO4	Counts (x/N)	Estimate (95% CI)
Agarwal, 2020, AH 001	dose	sPE	yes	Pritchard	Pritchard	24	0/28	0 (95% CI: 0, 0.123)
	dose	sPE	yes	Dhaka	Dhaka	24	0/25	0 (95% CI: 0, 0.137)
Agarwal, 2020, AH 001	dose	E	yes	Pritchard	Pritchard	24	1/22	0.045 (95% CI: 0.001, 0.228)
	dose	E	yes	Dhaka	Dhaka	24	1/21	0.048 (95% CI: 0.001, 0.238)
Bhattacharjee, 2011, 21534749	dose	E	no	Group A: MgSO4 IV Low Dose	NR	24	5/67	0.075 (95% CI: 0.025, 0.166)
	dose	E	no	Group B: MgSO4 IM Standard Regimen	NR	24	6/70	0.086 (95% CI: 0.032, 0.177)
Brookfield, 2020, 33156201	dose	sPE	BMI ≥ 35	Alternate	Zuspan 6-2	NR	0/19	0 (95% CI: 0, 0.176)
	dose	sPE	BMI ≥ 35	Zuspan	Zuspan	NR	0/18	0 (95% CI: 0, 0.185)
Charoenvidhya, 2013, 23691692	dose	sPE	no	Study group (2g/h)	NR	NR	0/30	0 (95% CI: 0, 0.116)
	dose	sPE	no	Control group (1g/h)	NR	NR	0/30	0 (95% CI: 0, 0.116)
Gupta, 2019, CN-01996873	dose	E	no	Low IV Dose of MgSO4	NR	24	4/30	0.133 (95% CI: 0.038, 0.307)
	dose	E	no	MgSO4 per Conventional Pritchard's regimen	NR	24	0/30	0 (95% CI: 0, 0.116)
Kitiyodom, 2016, 29901967	dose	PE	no	Mg 2g/h	Zuspan 4-2	24	0/19	0 (95% CI: 0, 0.176)
	dose	PE	no	Mg 1g/h	Zuspan	24	0/19	0 (95% CI: 0, 0.176)
Malapaka, 2011, 21798536	dose	sPE	yes	Low-dose regimen	NR	24	0/37	0 (95% CI: 0, 0.095)
	dose	sPE	yes	Pritchard regimen	NR	24	0/16	0 (95% CI: 0, 0.206)
	dose	E	yes	Low-dose regimen	NR	24	6/35	0.171 (95% CI: 0.066, 0.336)
	dose	E	yes	Pritchard regimen	NR	24	0/38	0 (95% CI: 0, 0.093)
Pascoal, 2019, 31393402	dose	sPE	no	2 g/h	Zuspan 6-2	24	0/31	0 (95% CI: 0, 0.112)
	dose	sPE	no	1 g/h	Zuspan 6-1	24	0/31	0 (95% CI: 0, 0.112)

Study	Category	HDP Category	Subgroup	Arm	Regimen	Duration of MgSO4	Counts (x/N)	Estimate (95% CI)
Saha, 2017, 28714170	dose	E	no	Zuspan Regimen	Zuspan	24	2/20	0.1 (95% CI: 0.012, 0.317)
	dose	E	no	Dhaka Regimen	Dhaka	24	1/21	0.048 (95% CI: 0.001, 0.238)
Singh, 2011, L362772412	dose	E	no	Pritchard regimen	NR	24	0/60	0 (95% CI: 0, 0.06)
	dose	E	no	Zuspan regimen	NR	24	1/49	0.02 (95% CI: 0.001, 0.109)
	dose	E	no	Sibai regimen	NR	24	0/49	0 (95% CI: 0, 0.073)
Sravani, 2022, L2016942399	dose	E	no	Low dose	NR	24	NR/60	N/A
	dose	E	no	Standard	Pritchard	24	NR/60	N/A
Sultana, 2013, L365881919	dose	E	no	Group –A: Lower Dose of MgSO4 (8g) (Case Group)	NR	0	6/48	0.125 (95% CI: 0.047, 0.252)
	dose	E	no	Group - B: MgSO4 dose (10g) (Control Group)	NR	0	9/52	0.173 (95% CI: 0.082, 0.303)
Tangmanowutthikul, 2019, CN-01793189	dose	sPE	no	MgSO4 by Weight-adjusted protocol	NR	24	0/43	0 (95% CI: 0, 0.082)
	dose	sPE	no	MgSO4 2g/h	NR	24	0/43	0 (95% CI: 0, 0.082)
Agarwal, 2020, AH 001	delivery	sPE	yes	Zuspan	Zuspan	24	0/25	0 (95% CI: 0, 0.137)
	delivery	E	yes	Zuspan	Zuspan	24	0/19	0 (95% CI: 0, 0.176)
Easterling, 2018, 29976161	delivery	sPE	no	Serial bolus	Easterling 12h	12	0/100	0 (95% CI: 0, 0.036)
	delivery	sPE	no	Continuous Infusion	Zuspan 12h	12	0/100	0 (95% CI: 0, 0.036)

Abbreviations: Study = First author, year published, Citation ID, Estimate = proportion with exact confidence interval for proportion of seizures (or recurrent seizures in HDP category = "E"), CI = confidence interval, Category = Effect (effectiveness studies, MgSO4 vs. placebo, antiseizure medication, antihypertensive medication), E = eclampsia, sPE = severe preeclampsia

Appendix F. Appendix References

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