Effects of Immediate Postpartum Diuretic Treatment on Postpartum Blood Pressure among Individuals with Hypertensive Disorders of Pregnancy: A Systematic Review and Meta-Analysis

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Word count: 5791

Short title: Postpartum diuretics and pregnancy hypertension

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ABSTRACT

Background: Hypertensive disorders of pregnancy (HDP) are associated with ongoing postpartum hypertension (HTN) and increased morbidity. Extravascular water and sodium mobilization is implicated in postpartum blood pressure (BP) elevation, however trials of postpartum diuretics in HDP have had mixed results. Our meta-analysis aimed to analyze the impact of postpartum diuretics on postpartum hypertension following HDP.

Methods: Systematic review identified randomized controlled trials (RCTs) studying the efficacy of diuretics in the treatment of postpartum BP. Meta-analysis outcomes included persistent HTN up to 10 days postpartum, mean postpartum systolic and diastolic BPs, and use of additional antihypertensive medications.

Results From 9 RCTs, 1273 subjects were included in the meta-analysis. Postpartum diuretic use was associated with lower systolic BP (SMD standard mean difference]: -0.36; 95% confidence interval [CI]: -0.72; -0.01) without a difference in diastolic BP (SMD: 0.01; 95% CI: -0.22; 0.23) compared with controls. There was no difference in rates of persistent HTN between the postpartum diuretics group versus controls (OR: 0.70; 95% CI: 0.4; 1.05) or in antihypertensive medication use (OR: 0.66; 95% CI: 0.42; 1.05).

Conclusion: Postpartum diuretic use was associated with lower systolic BP compared with controls and non-significant trends of lower rates of persistent HTN and postpartum antihypertensive medication use. Due to the low certainty of evidence, uniform postpartum diuretic use with HDP cannot be recommended. Future studies are needed to evaluate specific HDP subgroups who may benefit from diuretic use.

ABBREVIATIONS

HDP: hypertensive disorder of pregnancy

HTN: hypertension

BP: blood pressure

RCT: randomized controlled trials

INTRODUCTION

Hypertensive disorders of pregnancy (HDP) impact 10-20% of pregnant individuals in the United States and are associated with increased morbidity in the peripartum period including increased risk of hospital readmission, severe hypertension (HTN), heart failure, and stroke.[1-4] Preeclampsia and gestational HTN comprise the majority of these cases, while chronic HTN and superimposed preeclampsia account for the remainder.[5] Postpartum HTN most commonly occurs among individuals with antenatally diagnosed HDP but can also be due to the development of a de novo postpartum process.[4]

Normal pregnancy is characterized by a 40-50% expansion of the circulating blood volume which is associated with retention of sodium and water in the interstitial tissues and a gradual rise in systolic and diastolic blood pressure (BP) towards the end of pregnancy.[6, 7] BP rises after delivery, peaking at 3 to 10 days postpartum.[8, 9] This postpartum BP elevation has been attributed to extravascular water and sodium mobilization into the intravascular space and may be compounded by iatrogenic administration of intravenous fluid during labor or cesarean section.[10] Further, signs and symptoms of volume overload are prevalent among individuals with HDP, including dyspnea (20-30%), pulmonary edema (11%), and peripheral edema (11-18%).[4] Therefore, diuretics have been proposed to theoretically accelerate postpartum BP recovery among individuals with HDP through urinary sodium and water excretion, thereby decreasing intravascular volume.[11, 12] Interventions that improve postpartum BP may reduce associated maternal morbidity.

While several clinical guidelines have put forth recommendations for BP monitoring in the postpartum period, namely, checking an ambulatory BP within 10 days of delivery, there is a paucity of specific recommendations for postpartum BP management. According to the

American College of Obstetricians and Gynecologists, treatment of postpartum HTN is recommended for systolic BP ≥150 mm Hg or diastolic BP ≥100 mm Hg with the choice of medication primarily limited by compatibility with breastfeeding and use of contraception.[5] Current guidance on the management of HDP focuses on the use of calcium channel blockers and nonselective beta blockers but does not include specific recommendations for diuretic use. As a result, diuretic use is typically reserved for postpartum management of pulmonary edema or systemic volume overload. Given a proposed pathophysiology of HDP through intravascular volume expansion and increased sodium body sodium content, there is an opportunity to improve BP control with diuretics.

Randomized controlled trials evaluating the effectiveness of diuretic treatment for individuals with HDP in the postpartum period have been small. Further, studies have reported mixed results regarding BP effects. The latest meta-analysis found postpartum loop diuretics was associated with no difference in persistent hypertension or need for antihypertensive therapy at discharge.[7] With the recent publication of new, relevant studies as well as the lack of inclusion of all diuretic classes in prior meta-analyses, there is a need for a contemporary investigation on the role of diuretics in the postpartum setting after HDP. In this study, we performed an updated systematic review and meta-analysis to compare the effect of immediate postpartum diuretic treatment to placebo or alternative therapies on reducing persistent postpartum HTN, systolic and diastolic BP, need for additional antihypertensive medication, and postpartum complications among individuals with HDP.

METHODS

Data Sources and Searches

We registered the protocol for this review in the PROSPERO database (no. CRD42021253740). Searches were developed by a health sciences librarian and performed in the Ovid Medline, Embase.com, Web of Science Core Collection, and Cochrane CENTRAL databases (see Supplemental Appendix for full search strings). The search strings included natural language and database-specific controlled vocabulary covering the concepts HDP and diuretic medications. The searches were limited to the English language as well as the years 1980 to present. Additionally, clinicaltrials.gov was searched for relevant trials. On May 11, 2021, 3718 references were downloaded into the EndNote reference management software. The references were deduplicated twice: first using the Amsterdam Efficient Deduplication method and then the Bramer et al. method, resulting in a total of 2994 citations.[13, 14] These citations were uploaded to the DistillerSR software (Distiller, Evidence Partners, Ottawa, Canada) for screening. To supplement these electronic searches, reference lists of pertinent articles were reviewed to identify any additional potential eligible studies. Ongoing surveillance was conducted using PubMed article alerts to identify any potential additional studies published through December 1, 2024. The search was rerun on June 29, 2022, and after deduplication of the search, 246 new citations were uploaded to Distiller.[15]

Study Selection

In Distiller, two of four cardiology or obstetric physician investigators (SK, MC, AK, and AH) independently reviewed each title, abstract, and full text article when needed using prespecified inclusion and exclusion criteria (Supplemental Table 1). Disagreements were resolved by discussion. Randomized controlled trials (RCTs) and observational cohort studies (prospective or retrospective) were eligible for inclusion. Case control studies, cross-sectional

studies, case reports, conference presentations or posters, and narrative review articles were excluded. Eligible interventions included intravenous or oral diuretics or diuretics in conjunction with another antihypertensive pharmacotherapy, while eligible comparators included placebo or non-diuretic antihypertensive pharmacotherapy. Primary outcomes included "persistent HTN" defined as two BP readings taken four hours apart with systolic BP $\geq$ 140 mmHg or diastolic BP $\geq$ 90 mmHg before delivery hospitalization discharge (day 0) or up to 10 days postpartum. As guidelines recommend checking an ambulatory BP within 10 days of delivery in individuals with HDP, we performed our analysis by grouping persistent HTN from 0-10 days postpartum. Additional outcomes include systolic and diastolic BP, persistent HTN at 30 days or 6 weeks postpartum, need for additional antihypertensive medication, length of hospitalization, hospital readmission, emergency department visits, heart failure, b-type natriuretic peptide levels, and lactation outcomes.

Data Extraction and Quality Assessment

For each included study, one of four reviewers (SK, MC, AK, or KS) abstracted relevant study characteristics into a structured form. A second reviewer (SK, MC, AK, or KS) verified all data for accuracy. For each included study, two reviewers (SK, MC, AK, or KS) independently assessed methodological quality. As only RCT studies reached the full text screening stage, the Cochrane collaboration's risk-of-bias tool for randomized trials version 2-0 was used.[16] This tool allowed reviewers to assess bias in 5 categories including bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. Through a series of yes/no questions, a risk of bias score (low, some concerns, high) was assigned per domain for

each study. A low risk of bias meant that the study was judged to be a low risk of bias in all domains. A "some concern" risk of bias meant that the study was judged to have risk of concerns in some domains but no high risk of bias in any domains. Finally, a high risk of bias meant that the study was judged to have at least one high risk domain or multiple domains with some concern of bias overall lowering the confidence of the results. In turn, these domain-level judgements provided the basis for an overall risk-of-bias judgment for the specific trial result being assessed through an algorithm built in the tool. At the end of this thorough review, two reviewers (SK and KS) compared risk of bias scores per trial and any disagreements in data extraction or study quality assessments were resolved by consensus or with a third reviewer.

Statistical Analyses

Bias corrected standardized mean differences (Hedges' g) were used to present the difference between outcomes. A random effects model was used to estimate a pooled relative risk for persistent postpartum HTN. A Forest plot was used to illustrate the individual and pooled relative risk, estimate the confidence interval for the pooled relative risk, and report an overall p-value. Secondary continuous outcomes were assessed using a random effects model to compute a pooled mean difference. All statistical tests were performed in R 4.4.1 (R version 4.4.1 (2024-06-14 ucrt).[17] A pooled treatment effect model (theta) p-value <0.05 was considered significant.

RESULTS

Characteristics of Included Studies

The searches yielded 3973 citations as summarized in the PRISMA flow diagram (Figure 1). After removing duplicates, 3240 unique studies were screened and 95 were sought for

retrieval. Out of these 95 studies, 86 were excluded due to various ineligibilities including study design, population, timing of intervention, comparison, outcomes, interventions, and additional duplicate records. In addition, one recently concluded clinical trial (DIUPRE) registered on clinicaltrials.gov met inclusion criteria. Unpublished study results were obtained from trial investigators and included in the meta-analysis.

The main characteristics of included studies are summarized in Table 1. A total of 1273 subjects were included from 9 RCTs. Three studies were conducted in the United States[18-20], 2 studies in Iran[21, 22], 1 study in Bangladesh,[23] 1 study in India,[24] 1 unpublished study in Brazil (DIUPRE), and 1 in the UK.[25] Patients in the intervention group received diuretics for a period of 5 to 7 days. All studies assigned their intervention group to furosemide 20-40 mg daily except for Viteri et al.[19] who assigned intervention group patients to torsemide 20 mg daily. Matthews et al.[25], Viteri et al.[19], Perdigao et al.[20], and the DIUPRE study assigned their control groups to placebo. Three studies assigned their control groups to alternative antihypertensive medications. The control groups in Veena et al.[18] and Bozorgan et al.[22] were assigned to nifedipine 10 mg every 8 hours and the control group in Siamansoori et al.[21] was assigned to methyldopa 250 mg three times daily. The control groups in Ascarelli et al.[18] and Dabaghi et al.[23] were assigned to no medication. The mean number of study participants was 115. The trials with the largest number of subjects had 384[20] and 264[18] subjects, respectively. The study with the least number of participants had 19 subjects.[25]

Primary outcomes varied between studies and included mean systolic and diastolic BPs, reduction in mean BPs, and persistent HTN at various time points up to 10 days post-hospital discharge. Observation periods varied among studies and lasted up to 6 weeks post-delivery and post-hospitalization.

Primary Outcome

The primary outcome, persistent HTN at 0-10 days post-delivery, was available in 7 studies.[18-25] Persistent HTN was significantly less frequent in the intervention group for the two most recent studies,[20, 22] including the largest study in our analysis.[20] However, in our random effects model there was no significant difference in persistent HTN among individuals who received postpartum diuretics compared with controls (odds ratio [OR]: 0.70; 95% confidence interval [CI]: 0.46-1.05), shown in Figure 2. Study heterogeneity was moderate for the primary outcome (I^2 of 40%, tau ^2 0.1208, p=0.12).

Secondary Outcomes

Systolic and diastolic blood pressure in the postpartum period

The systolic and diastolic BP measurements were available for 3 studies which encompassed 23% of patients included in the analysis (n=306).[21-23] BP measurements were monitored for 3 to 7 days postpartum. Postpartum diuretic use was associated with lower systolic BP (square mean difference [SMD]: -0.36; 95% CI: -0.72; -0.01) (Figure 3) without a difference in diastolic BP (SMD: 0.01; 95% CI: -0.22; 0.23) (Figure 4) compared with controls. The lower systolic BP effect was largest in the Bozorgan et al. study.

Antihypertensive use postpartum

Additional antihypertensive medication use during an observation period up to 10 days was reported in 8 studies (Figure 5). Although Veena et al. and Bozorgan et al. reported significantly lower use of additional antihypertensive drugs in the intervention group compared with the control group, there was no significant difference in the remaining studies.[22, 24] This

effect was largest in the Bozorgan et al. study (OR: 0.23; 95% CI: 0.08-0.67). Pooling data from all 8 studies, there was no significant difference in postpartum antihypertensive use in patients who received diuretics compared with controls (OR: 0.66; 95% CI: 0.42-1.05; p=0.08). Study heterogeneity was moderate with I^2 of 34%.

Length of hospital stay

Although 6 studies commented on length of hospital stay, there was significant heterogeneity in these reports which precluded the ability to calculate a pooled effect size for this secondary outcome. In brief, three studies reported postpartum hospital length of stay[19, 20, 24] while three others reported total hospital length of stay.[18, 23, 25] No studies reported a significant difference in these outcomes between treatment groups.

Postpartum maternal complications

There was limited reporting of our additional secondary outcome variables of interest including hospital readmission, emergency department visits, heart failure, b-type natriuretic peptide levels, and lactation outcomes. Therefore, analyses were not performed on these outcomes.

Three studies did report outcomes related to emergency department visits or hospital readmissions without any significant differences between treatment groups, however their variations in outcome definitions and the inclusion of a CI or standard error in only one of these studies precluded the calculation of pooled estimates.[19, 20, 25]

Risk of Bias Assessment Results

Detailed study quality assessments are provided in Table 2. Five studies received a low risk of bias.[19, 20, 24, 25] Two studies received some concerns of risk of bias around reporting of

missing outcome data and bias around measurement of the outcomes.[18, 21] Lastly, two studies received an overall high risk of bias for significant concerns with multiple domains including the randomization process, intervention assignment, missing outcome data, and outcome measurement.[22, 23]

DISCUSSION

In this meta-analysis, we assessed the role of postpartum diuretics after HDP on improving postpartum HTN and BP. We found that postpartum diuretic use was not associated with reduced postpartum hypertension but was associated with reduced systolic BP compared with controls without a statistically significant difference diastolic BP, or use of additional antihypertensive medications. However, the available data to assess the impact of postpartum diuretics in individuals with HDP remains limited. The number of available studies was relatively small, with some studies including only a small number of patients and some with concerns about risk of bias. Despite these limitations, there was a non-significant trend of reduced persistent postpartum HTN with an OR of 0.70 and of reduced use of antihypertensive medications with an OR of 0.66. While these findings did not reach statistical significance, they indicate potentially impactful trends. A well-conducted, sufficiently powered RCT could provide more definitive data on the potential benefit of postpartum diuretics in this population.

A recent systematic review and meta-analysis on the use of loop diuretics in the context of HDP similarly found no reduction in persistent HTN at 1 or 6 weeks postpartum and no reduction in the need for additional antihypertensive medications at discharge.[7] Our meta-analysis expands on these findings with the inclusion of three additional studies. We assessed 9 trials comparing loop diuretics to controls, including the unpublished results of one completed

registered clinical trial. Most of the included trials were individually limited by smaller sample size and short-term follow-up.

Our finding of reduced systolic BP is novel and although the effect size is small, improved BP control in the immediate short-term postpartum period may confer durable clinical benefit. Pharmaceutical intervention in the immediate postpartum period has been shown to result in improved BP control sustained up to 3-4 years postpartum[26, 27] and be associated with more favorable left atrial and left ventricular remodeling, suggesting that prompt postnatal BP control may reverse the adverse remodeling known to result from HDP.[28] Nonetheless, the lack of a diastolic BP benefit is relevant in this patient population. The association between HDP and later-life cardiovascular disease is partially mediated through the development of chronic HTN, with up to 37% of individuals with a HDP developing chronic HTN at 2-7 years after delivery.[29-31] In a study of BP trajectories in the first year postpartum following a HDP, the majority of those with persistent HTN had isolated diastolic HTN, which may suggest that targeting an improvement in postpartum diastolic BP is of particular importance following an HDP.[32]

Efficacy of postpartum diuretics may vary by severity of HDP. Perdigao et al. found that reduction in persistent HTN at 7 days postpartum was more significant when results were stratified to only individuals with non-severe HDP. Interestingly, there was no difference in persistent HTN in the severe HDP group (systolic BP ≥160 mm Hg or diastolic BP ≥110 mm Hg).[20] In contrast, Ascarelli et al. found that reduction in persistent HTN 2 days postpartum was more significant in patients with severe preeclampsia only.[18] There was heterogeneity among the studies in their inclusion of only severe versus both severe and non-severe HDP, and future studies should give particular attention to or perform subgroup analyses for these subgroups of HDP severity to define which group may particularly benefit from postpartum

diuretics. There was also variation in the spectrum of HDP subtypes which were included in the studies. Importantly, some studies included chronic HTN which may be less diuretic responsive with regards to BP recovery and thus attenuate the measured benefit by the total studied population of individuals with HDP.

Ongoing RCTs will hopefully contribute to narrowing knowledge gaps about the benefits of postpartum diuretics among individuals with HDP. The largest randomized placebo-controlled trial of postpartum diuretics in individuals with HDP will include an estimated 612 participants and will compare hydrochlorothiazide 50 mg daily to placebo for 14 days after delivery (NCT03298802). Primary outcomes include need for additional antihypertensive drug and rate of readmission or triage visits 1-6 weeks postpartum. As our meta-analysis included only 1273 subjects, the results of this trial would expand the number of subjects to more definitively assess the utility of postpartum diuretics in HDP, however the effect on blood pressure may be different with thiazide diuretics compared with loop diuretics.

There may also be a role for postpartum diuretics for prevention of HDP. The recently published Lasix for the Prevention of De Novo Postpartum Hypertension (LAPP) randomized placebo-controlled trial extends our understanding of the preventive role of postpartum diuretics by comparing primary prevention furosemide to placebo among 82 individuals at high risk for de novo postpartum HTN. The LAPP study found no difference in mean arterial pressure 24 hours prior to discharge or in the development of de novo postpartum HTN between the two groups.[33] As 42% of individuals with postpartum hypertension have preceding antepartum normotension, the identification of individuals at high risk to develop postpartum HTN and strategies to mitigate associated volume overload are needed.[34]

Limitations

The RCTs available for inclusion in our meta-analysis resulted in a modest sample size. Two of the studies, accounting for 16% of the patients included in the meta-analysis, were felt to have high risk of bias. There was heterogeneity in the control groups, with only four of the studies comparing diuretic to placebo and the remaining studies comparing diuretic to alternative antihypertensive or no medication, which could bias results towards the null hypothesis. Systolic and diastolic BP data were available from only three studies for inclusion in our analysis. Further, due to the lack of standardized guidance for postpartum BP monitoring, there was notable variation in the timing of study outcome assessments. Some studies reported this data at postpartum day 0-5, others at days 5-10, and others at 30 days. Consequently, study outcome heterogeneity was moderate per our random effect size analysis specifically regarding persistent postpartum HTN. Our analysis may have been affected by this heterogeneity in BP recording postpartum.

Conclusions

The data on the benefit of postpartum oral diuretics for the prevention of postpartum HTN among women with HDP remains inconclusive. Diuretic administration reduces systolic BP and may reduce the risk of HTN up to 10 days postpartum for some clinical subgroups. However, due to the low certainty of evidence, uniform postpartum use of diuretics among women with HDP cannot be recommended. Use of postpartum diuretics guided by thoughtful assessment of clinical volume status remains reasonable.

ACKNOWLEDGEMENTS

None.

SOURCES OF FUNDING

Dr. Countouris was supported by the National Institutes of Health (National Heart, Lung, and Blood Institute T32 Training Grant HL129964) and an American Heart Association CDA (941351). Dr. Koczo is supported by the American Heart Association (24CDA1266475). Dr. Hauspurg is funded by the NIH/ORWH Building Interdisciplinary Research Careers in Women's Health (BIRCWH) NIH K12HD043441 and NIH/ NHLBI K23HL168356.

DISCLOSURES

The authors report no conflicts.

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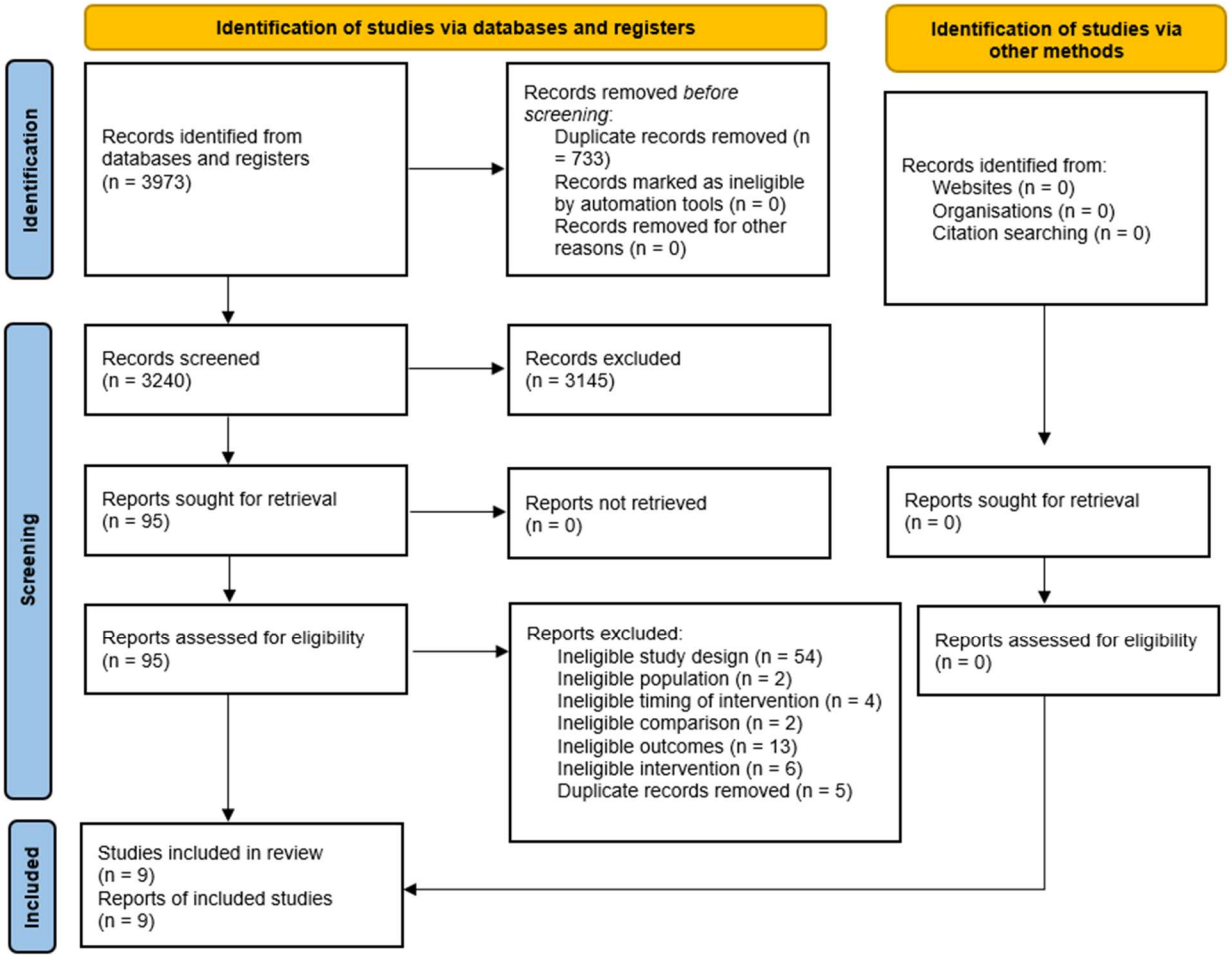

Figure 1. Literature search flow and study selection diagram

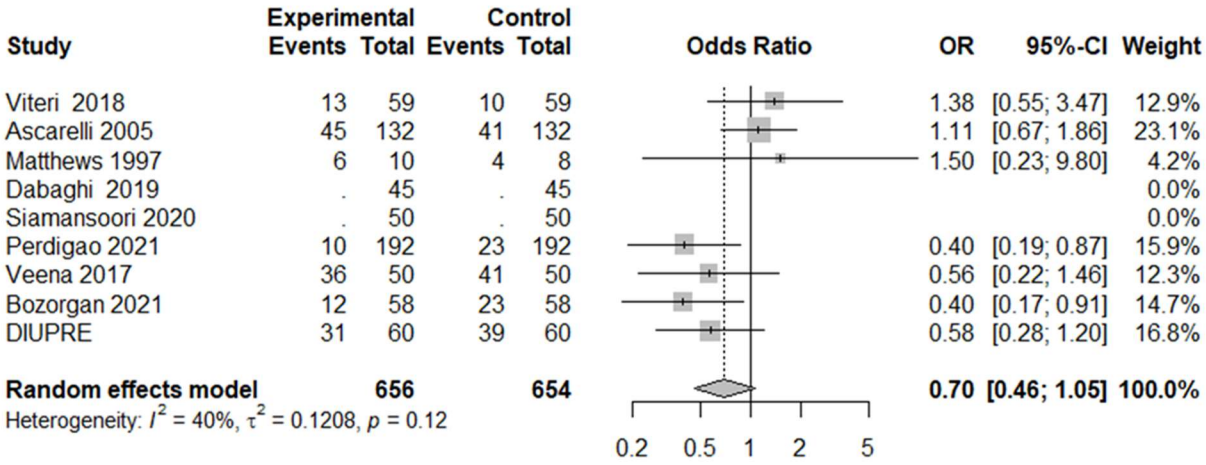

Figure 2. Persistent hypertension at 0-10 days postpartum among individuals with hypertensive disorders of pregnancy treated with diuretic versus control

OR: odds ratio; CI: confidence interval

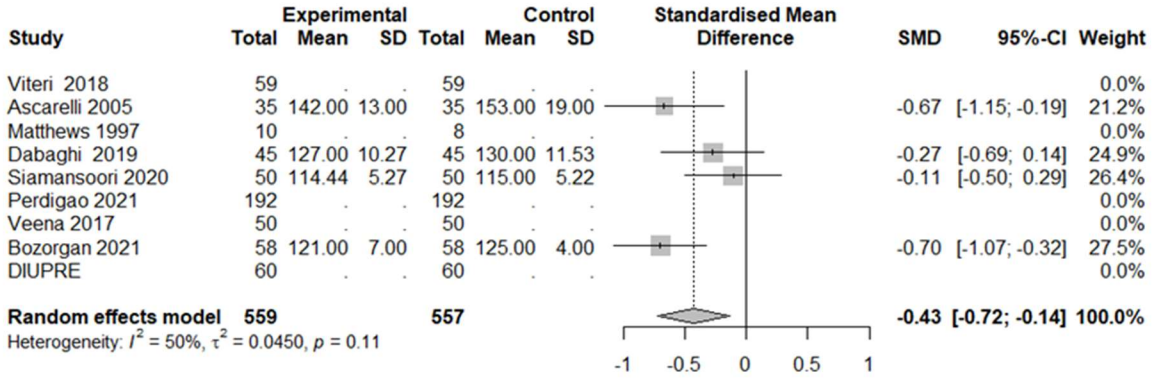

Figure 3. Mean difference in systolic blood pressure among individuals with hypertensive disorders of pregnancy with postpartum diuretic treatment compared with control

SD: standard deviation; SMD: standardized mean difference; CI: confidence interval

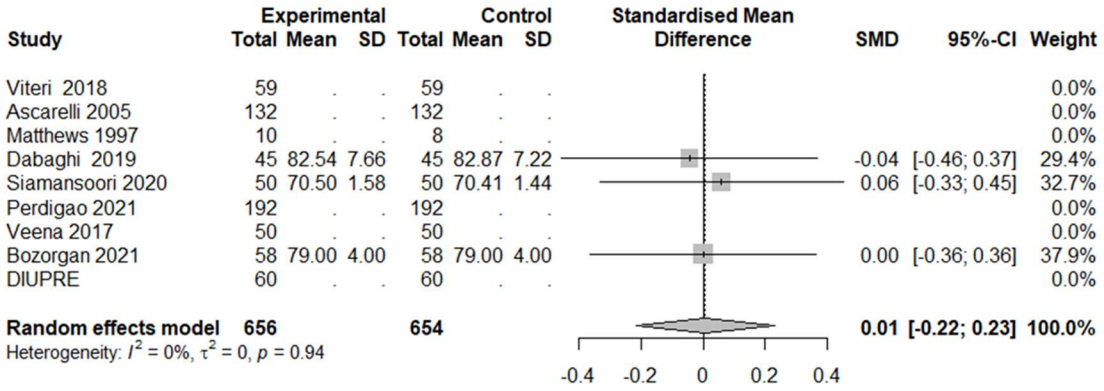

Figure 4. Mean difference in diastolic blood pressure among individuals with hypertensive disorders of pregnancy with postpartum diuretic treatment compared with control

SD: standard deviation; SMD: standardized mean difference; CI: confidence interval

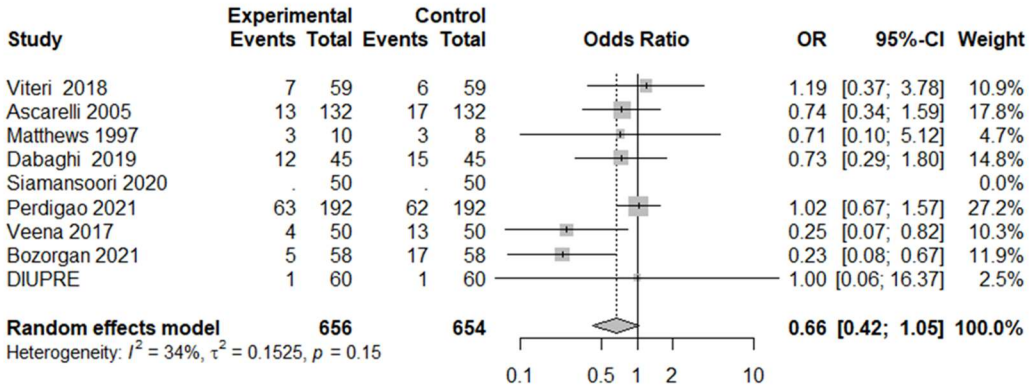

Figure 5. Use of additional antihypertensive medication among individuals with hypertensive disorders of pregnancy treated with diuretic compared with control

OR: odds ratio; CI: confidence interval

Table 1. Main characteristics of included studies

Year, author	Country	Included HDP	Important exclusion criteria	Total (n)	Intervention (n)	Comparison (n)	Primary outcome	Secondary outcomes
Matthews et al[25] (1997)	UK	Preeclampsia	Diabetes mellitus, renal or hepatic impairment, contraindication to diuretic	19	Furosemide 40 mg orally every 24 hours for 7 days (10)	Placebo orally every 24 hours for 7 days (8)	Mean and maximum BP	Postpartum antihypertensive usage Length of hospital stay
Ascarelli et al[18] (2005)	USA	Chronic HTN, gestational HTN, preeclampsia	Less than 20 weeks of gestation, hypokalemia (K < 3.0 mEq/L), already taking diuretics or potassium supplementation, hemodynamic instability	264	Furosemide 20 mg orally every 24 hours for 5 days (132)	No medication (132)	Systolic and diastolic BP	Length of hospital stay Postpartum antihypertensive usage
Veena et al[24] (2017)	India	Severe preeclampsia	Hemodynamic instability, hypokalemia (K< 3mEq/L), already on potassium supplementation and diuretics, expulsion of the fetus at <20 weeks	100	Furosemide 20 mg orally every 24 hours with nifedipine 10 mg orally every 8 hours until not needed (50)	Nifedipine 10 mg every 8 hours until not needed (50)	Reduction in mean, systolic, and diastolic BP	Length of hospital stay Postpartum antihypertensive usage Antihypertensive requirement at discharge
Viteri et al[19] (2018)	USA	Preeclampsia with or without severe features, superimposed preeclampsia with or without severe features	Oliguria, heart failure, hypokalemia (serum potassium below 3 mEq/L), diuretic use within the past 24 hours, hypersensitivity to torsemide or sulfonylureas, and pulmonary edema	118	Torsemide 20 mg orally every 24 hours for 5 days (59)	Placebo orally every 24 hours for 5 days (59)	BP >150/100 by day 5 or hospital discharge	Persistent HTN at discharge 7–10 days and 6 weeks after delivery Postpartum antihypertensive usage, Length of hospital stay Hospital readmission for HTN

								Adverse events to diuretics
Dabaghi et al[23] (2019)	Bangladesh	Severe preeclampsia HELLP syndrome	Gestational age under 20 weeks, hypokalemia (k < 3.0 mEq/L) on admission, history of diuretics or potassium supplements use, any hemodynamic instability surrounding the events of delivery	90	Furosemide 20 mg and potassium supplementation every 24 hours for 5 days (45)	No medication (45)	Mean systolic BP	Postpartum antihypertensive usage Length of hospital stay Eclampsia
Siamansoori et al[21] (2020)	Iran	Preeclampsia	Underlying cardiac disease, complicated pregnancies including gestational diabetes mellitus, renal disease, hypersensitivity to furosemide or methyldopa, major adverse drug complications	100	Furosemide 20 mg twice daily (50)	Methyldopa 250 mg three times daily (50)	Systolic and diastolic BP at 6 hours, 48 hours and one week	Diuresis at 24 and 48 hours post intervention
Perdigao et al[20] (2021)	USA	All forms of HDP: gestational HTN, preeclampsia with or without severe features, preeclampsia superimposed on chronic HTN with or without severe features	Underlying cardiac disease, rheumatologic disease, advanced diabetes, elevated creatinine (>1.2 mg/dL), significant hypokalemia (K<3 mEq/L), allergy to furosemide, or those who received diuretics before randomization	384	Furosemide 20 mg orally every 24 hours for 5 days (192)	Placebo orally every 24 hours for 5 days (192)	Persistent HTN 7 days postpartum (defined as at least 2 consecutive BP readings over 48 hours of systolic BP ≥140 mm Hg and diastolic BP ≥90 mm Hg) and the number of days required to achieve resolution of HTN (defined as at least 2 consecutive BP readings over 48 hours of systolic BP <140 mm Hg	Percentage of postpartum BP in the severe range (systolic BP ≥160 mm Hg or diastolic BP ≥110 mm Hg) Postpartum antihypertensive usage Hospital readmissions or ER visits for HTN Length of hospital stay HTN complications

							and diastolic BP <90 mm Hg)	
Bozorgan, et al[22] (2022)	Iran	Preeclampsia	Chronic HTN, BP less than 150/100 mmHg, administration of diuretics, renal disease, diabetes, hemodynamic instability, potassium level lower than 3 mEq/L, contraindication to furosemide, hematocrit more than 37%	116	Nifedipine 10 mg every 8 hours and furosemide 20 mg daily for 5 days (58)	Nifedipine 10 mg every 8 hours for 5 days (58)	Systolic and diastolic BP at day 2-5	Postpartum antihypertensive usage
DIUPRE (2024)	Brazil	Preeclampsia	Chronic HTN, blood pressure <140/90 mmHg, diuretic use, renal impairment, diabetes, sickle cell disease, rheumatologic disease, hemodynamic instability, potassium less than 3 mEq/L, contraindication for furosemide use	120	Furosemide 40 mg orally every 24 hours for 5 days (60)	Placebo orally every 24 hours for 5 days (60)	Mean blood pressure from 24 hours after delivery to first 15 days of delivery	Postpartum antihypertensive usage Time to blood pressure control Daily urine output Length of hospital stay Frequency of adverse events Frequency of maternal complications

BP: blood pressure; HDP: hypertensive disorders of pregnancy; HTN: hypertension; MAP: mean arterial pressure; ER: emergency room; HELLP: hemolysis, elevated liver enzyme, low platelet count

Table 2. Risk of bias assessments of included studies

	Risk of bias domains					
Studies	Randomization process	Assignment to intervention	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall risk of bias
Matthews et al[25] (1997)	Low	Low	Low	Low	Low	Low
Ascarelli et al[18] (2005)	Low	Low	Some concerns	Some concerns	Low	Some concerns
Veena et al[24] (2017)	Low	Low	Low	Low	Low	Low
Viteri et al[19] (2018)	Low	Low	Low	Low	Low	Low
Siamansoori et al[21] (2019)	Low	Low	Some concerns	Low	Low	Some concerns
Dabaghi et al[23] (2019)	Low	Some concerns	Some concerns	Some concerns	Low	High
Bozorgan et al[22] (2021)	Some concerns	Some concerns	Low	Low	Low	High
Perdigao et al[20] (2021)	Low	Low	Low	Low	Low	Low
DIUPRE (2024)	Low	Low	Low	Low	Low	Low

Supplement Table 1. Study selection criteria based on study design, population, interventions, comparators, outcomes, timing

	Eligible	Ineligible
Study design	Systematic reviews Randomized controlled trials Cohort studies	All other designs including single arm interventions, cross-sectional studies, case-control studies, narrative reviews, case reports, abstracts, editorials, letters
Population	Individuals with HDP including • Preeclampsia • Severe preeclampsia • Gestational hypertension • Chronic hypertension	
Intervention	Diuretic (including thiazide or loop diuretic) Diuretic in conjunction with another pharmacotherapy	Nondiuretic drug
Comparison	Placebo Nondiuretic antihypertensive	
Outcome	Primary outcomes: % with persistent hypertension before discharge % with persistent hypertension at 10 days after delivery Secondary outcomes: Systolic and diastolic blood pressure % With persistent hypertension at 30 days or 6 weeks post delivery Length of hospitalization Hospital readmission or emergency department visit Heart failure	N/A
Timing	Postpartum period	Antepartum period

Language	English	Non-English
Publication date	1980 or later	Before 1980

Search strategies

All searches performed on May 11, 2021 and reran on June 29, 2022

Ovid Medline

Ovid MEDLINE(R) ALL <1946 to May 10, 2021>		
#	**Search**	**Results**
1	HELLP Syndrome/ or hypertension, pregnancy-induced/ or pre-eclampsia/ or pregnancy complications/ or puerperal disorders/ or (gestational hyperten$ or HELLP or "hypertensive disorders of pregnancy" or pre-eclamp$ or preeclamp$ or (postpartum adj4 hyperten$) or (pregnan$ adj4 hyperten$) or pregnancy-induced hyperten$ or toxaemia$ or toxemia$).ti,ab,kw.	150596
2	(blood pressure/ and postpartum period/) or (blood pressure/ and pregnancy/) or (hypertension/ and postpartum period/) or (hypertension/ and pregnancy/) or ((((arterial or blood or diastolic or systolic) adj1 pressur$) and (post-partum or postpartum or puerper$)) or ((bp or dbp or sdp) and (perinatal or postnatal or postpartum or puerper$)) or (hyperten$ and (perinatal or postpartum or puerper$))).ti,ab,kw.	25132
3	1 or 2	161159
4	Bendroflumethiazide/ or Diazoxide/ or diuresis/ or diuretics/ or Eplerenone/ or furosemide/ or Hydrochlorothiazide/ or Metolazone/ or Mineralocorticoid Receptor Antagonists/ or Sodium Potassium Chloride Symporter Inhibitors/ or Spironolactone/ or thiazides/ or torsemide/ or (Aldosterone Antagonist$ or Diazoxide or diures#s or diuretic$ or Eplerenone or frusemide or furosemide or fursemide or hydrochlorothiazide$ or lasix or loop diuretic$ or metolazone or Mineralocorticoid Antagonist$ or Mineralocorticoid Receptor Antagonist$ or quinethazone or Spironolactone or thiazide$ or torsemide).ti,ab,kw.	101697
5	3 and 4	1394
6	limit 5 to english language	989
7	limit 6 to yr="1980-Current"	672

Embase.com

Embase.com		
#	**Search**	**Results**
1	'eclampsia and preeclampsia'/de OR 'hellp syndrome'/de OR 'maternal hypertension'/de OR 'preeclampsia'/de OR 'pregnancy complication'/de OR	174644

Embase.com		
#	Search	Results
	'pregnancy toxemia'/de OR 'puerperal disorder'/de OR 'gestational hyperten*':ab,ti,kw OR hellp:ab,ti,kw OR 'hypertensive disorders of pregnancy':ab,ti,kw OR 'pre eclamp*':ab,ti,kw OR preeclamp*:ab,ti,kw OR ((postpartum NEAR/4 hyperten*):ab,ti,kw) OR ((pregnan* NEAR/4 hyperten*):ab,ti,kw) OR 'pregnancy-induced hyperten*':ab,ti,kw OR toxaemia*:ab,ti,kw OR toxemia*:ab,ti,kw	
2	'blood pressure'/de AND 'puerperium'/de	475
3	'blood pressure'/de AND 'pregnancy'/de	7237
4	'hypertension'/de AND 'puerperium'/de	1396
5	'hypertension'/de AND 'pregnancy'/de	17135
6	(((arterial OR blood OR diastolic OR systolic) NEAR/1 pressur*):ab,ti,kw) AND ('post partum':ab,ti,kw OR postpartum:ab,ti,kw OR puerper*:ab,ti,kw)	2762
7	(bp:ab,ti,kw OR dbp:ab,ti,kw OR sdp:ab,ti,kw) AND (perinatal:ab,ti,kw OR postnatal:ab,ti,kw OR postpartum:ab,ti,kw OR puerper*:ab,ti,kw)	1847
8	hyperten*:ab,ti,kw AND (perinatal:ab,ti,kw OR postpartum:ab,ti,kw OR puerper*:ab,ti,kw)	11305
9	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	34243
10	#1 OR #9	189616
11	'aldosterone antagonist'/de OR 'bendroflumethiazide'/de OR 'diazoxide'/de OR 'diuresis'/de OR 'diuretic agent'/de OR 'eplerenone'/de OR 'furosemide'/de OR 'hydrochlorothiazide'/de OR 'metolazone'/de OR 'mineralocorticoid antagonist'/de OR 'loop diuretic agent'/de OR 'spironolactone'/de OR 'thiazide diuretic agent'/de OR 'torasemide'/de OR 'aldosterone antagonist*':ab,ti,kw OR diazoxide:ab,ti,kw OR diuresis:ab,ti,kw OR diuretic*:ab,ti,kw OR eplerenone:ab,ti,kw OR frusemide:ab,ti,kw OR furosemide:ab,ti,kw OR hydrochlorothiazide*:ab,ti,kw OR lasix:ab,ti,kw OR 'loop diuretic*':ab,ti,kw OR metolazone:ab,ti,kw OR 'mineralocorticoid antagonist*':ab,ti,kw OR 'mineralocorticoid receptor antagonist*':ab,ti,kw OR quinethazone:ab,ti,kw OR spironolactone:ab,ti,kw OR thiazide*:ab,ti,kw OR torsemide:ab,ti,kw	251632
12	#10 AND #11	3585
13	#10 AND #11 AND [english]/lim	2893
14	#10 AND #11 AND [english]/lim AND [1980-2021]/py	2542
15	33853402:ui OR 33848330:ui OR 33744967:ui OR 33550824:ui OR 33826400:ui OR 33753383:ui OR 33628547:ui OR 33832152:ui OR 33741059:ui OR 32755966:ui OR 33089031:ui OR 32724400:ui OR 32344245:ui OR 32747595:ui OR 32363336:ui OR 32963682:ui OR 32044579:ui OR 32532707:ui OR 32555118:ui OR 32199925:ui OR 32142824:ui OR 31715148:ui OR 32711486:ui OR 32558425:ui OR	639

Embase.com		
#	Search	Results
	31751313:ui OR 30762762:ui OR 30929513:ui OR 30854785:ui OR 31764732:ui OR 31724271:ui OR 31545168:ui OR 31431784:ui OR 31351941:ui OR 31023448:ui OR 31010554:ui OR 30944139:ui OR 30889588:ui OR 30497942:ui OR 30407107:ui OR 30352280:ui OR 29936563:ui OR 31915545:ui OR 31507531:ui OR 30797659:ui OR 30407356:ui OR 29974489:ui OR 29604124:ui OR 30371746:ui OR 30354705:ui OR 30303905:ui OR 30252182:ui OR 30248150:ui OR 29769494:ui OR 29694631:ui OR 29614490:ui OR 29587251:ui OR 29512817:ui OR 29292538:ui OR 29124624:ui OR 28514932:ui OR 30197974:ui OR 29850023:ui OR 29492141:ui OR 29187414:ui OR 29153692:ui OR 28402032:ui OR 28279449:ui OR 28271625:ui OR 28245343:ui OR 28181126:ui OR 28169090:ui OR 28099709:ui OR 28049556:ui OR 27835048:ui OR 26892095:ui OR 29284893:ui OR 30226702:ui OR 28863420:ui OR 28128088:ui OR 27766821:ui OR 27502863:ui OR 27479245:ui OR 27329098:ui OR 27276444:ui OR 27223308:ui OR 27156905:ui OR 27132428:ui OR 27106810:ui OR 27072935:ui OR 27072828:ui OR 27036652:ui OR 26976916:ui OR 26887881:ui OR 26818168:ui OR 26807737:ui OR 27695701:ui OR 26597737:ui OR 26574641:ui OR 26538126:ui OR 26242730:ui OR 26102343:ui OR 25855306:ui OR 25767291:ui OR 25735693:ui OR 25540137:ui OR 25482671:ui OR 25433575:ui OR 25367603:ui OR 25163723:ui OR 24435760:ui OR 25960654:ui OR 24402588:ui OR 25927843:ui OR 25436639:ui OR 25311173:ui OR 25260544:ui OR 25236748:ui OR 24956694:ui OR 24824702:ui OR 24791370:ui OR 24651072:ui OR 24554373:ui OR 24508521:ui OR 24384846:ui OR 24108204:ui OR 24102416:ui OR 26587434:ui OR 25210634:ui OR 24995192:ui OR 23884277:ui OR 24100222:ui OR 24068049:ui OR 24037634:ui OR 23978551:ui OR 23900968:ui OR 23871407:ui OR 23633317:ui OR 23563883:ui OR 23470109:ui OR 23466139:ui OR 23355577:ui OR 23216619:ui OR 23088788:ui OR 22941757:ui OR 22890415:ui OR 22418765:ui OR 24431648:ui OR 23741542:ui OR 26105246:ui OR 23316362:ui OR 23066416:ui OR 23011750:ui OR 22880472:ui OR 22779300:ui OR 22712170:ui OR 22594141:ui OR 22561779:ui OR 22544624:ui OR 22534703:ui OR 22533344:ui OR 22412221:ui OR 22270288:ui OR 22147655:ui OR 22146514:ui OR 21863227:ui OR 21730211:ui OR 26105605:ui OR 26105459:ui OR 26105333:ui OR 22988523:ui OR 22431946:ui OR 22164402:ui OR 22120097:ui OR 21896152:ui OR 21832180:ui OR 21619562:ui OR	

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#	Search	Results
	10873690:ui OR 10832736:ui OR 10804495:ui OR 10796261:ui OR 10796237:ui OR 10785880:ui OR 10752764:ui OR 10659912:ui OR 10726809:ui OR 10604545:ui OR 10587770:ui OR 10584919:ui OR 10546718:ui OR 10517776:ui OR 10438406:ui OR 10411809:ui OR 10338062:ui OR 10232722:ui OR 10214821:ui OR 10192478:ui OR 10102171:ui OR 10070145:ui OR 10027136:ui OR 9829161:ui OR 9822515:ui OR 9790377:ui OR 9775990:ui OR 9746952:ui OR 9715225:ui OR 9699772:ui OR 9653867:ui OR 9646008:ui OR 9523918:ui OR 9506418:ui OR 9453359:ui OR 9406146:ui OR 9375317:ui OR 9337637:ui OR 9247750:ui OR 9222458:ui OR 9185112:ui OR 9101586:ui OR 15511760:ui OR 8937816:ui OR 8928917:ui OR 8887185:ui OR 8863696:ui OR 8858082:ui OR 8834992:ui OR 8829069:ui OR 8763317:ui OR 8754607:ui OR 8732994:ui OR 8731004:ui OR 8708776:ui OR 8677094:ui OR 8623791:ui OR 8572029:ui OR 8600604:ui OR 8522630:ui OR 8522430:ui OR 7900841:ui OR 7889632:ui OR 7789292:ui OR 7789210:ui OR 7771516:ui OR 7755100:ui OR 7735900:ui OR 7658037:ui OR 7589906:ui OR 9419773:ui OR 8194181:ui OR 8140955:ui OR 8066479:ui OR 8033511:ui OR 8008721:ui OR 7941985:ui OR 7911388:ui OR 7865984:ui OR 7852058:ui OR 7810772:ui OR 7802082:ui OR 7802067:ui OR 7786695:ui OR 7704688:ui OR 7697403:ui OR 20301710:ui OR 8512045:ui OR 8498970:ui OR 8482941:ui OR 8469485:ui OR 8423956:ui OR 8420337:ui OR 8319988:ui OR 8285327:ui OR 8259081:ui OR 8161250:ui OR 8108188:ui OR 7692954:ui OR 1627208:ui OR 1597875:ui OR 1590427:ui OR 1558222:ui OR 1527352:ui OR 1525094:ui OR 1504688:ui OR 1503669:ui OR 1495716:ui OR 1443232:ui OR 1438342:ui OR 1357989:ui OR 1317759:ui OR 1315815:ui OR 1299557:ui OR 2021561:ui OR 2003559:ui OR 1985355:ui OR 1927295:ui OR 1912987:ui OR 1882820:ui OR 1872345:ui OR 1870805:ui OR 1836984:ui OR 1836470:ui OR 1787718:ui OR 1772563:ui OR 1747801:ui OR 1685783:ui OR 2386594:ui OR 2381609:ui OR 2372338:ui OR 2358562:ui OR 2352253:ui OR 2316590:ui OR 2303281:ui OR 2300341:ui OR 2260686:ui OR 2258788:ui OR 2222622:ui OR 2216215:ui OR 2205429:ui OR 2194868:ui OR 2138415:ui OR 2120648:ui OR 2083513:ui OR 1983424:ui OR 1978541:ui OR 1967892:ui OR 2789543:ui OR 2789542:ui OR 2698145:ui OR 2693848:ui OR 2693046:ui OR 2691556:ui OR 2650515:ui OR 2648928:ui OR 2640226:ui OR 2634992:ui OR 2604661:ui OR 2604652:ui OR 2603913:ui OR 2595797:ui OR 2565758:ui OR 3402018:ui OR 3394805:ui OR 3374914:ui OR 3348280:ui OR 3280299:ui OR 3275209:ui OR 3264036:ui OR 3243334:ui OR 3179582:ui OR 3140400:ui OR 3060295:ui OR 2974682:ui OR 2973251:ui OR 2971147:ui OR 2901276:ui OR 2853660:ui OR 8816071:ui OR 3828257:ui OR 3799742:ui OR 3653042:ui OR 3578420:ui	

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#	Search	Results
	OR 3549116:ui OR 3453763:ui OR 3428473:ui OR 3326631:ui OR 3310099:ui OR 3038429:ui OR 2884053:ui OR 3945429:ui OR 3787894:ui OR 3783079:ui OR 3777057:ui OR 3777045:ui OR 3763091:ui OR 3746936:ui OR 3737046:ui OR 3728580:ui OR 3524548:ui OR 3510974:ui OR 3145669:ui OR 3081538:ui OR 3015491:ui OR 3011343:ui OR 2940080:ui OR 2938487:ui OR 2873916:ui OR 2861558:ui OR 12340716:ui OR 4032197:ui OR 4010599:ui OR 3993711:ui OR 3970085:ui OR 3926008:ui OR 3921117:ui OR 3920596:ui OR 3918757:ui OR 3917318:ui OR 3911376:ui OR 3905268:ui OR 3905080:ui OR 3902341:ui OR 3891306:ui OR 2982541:ui OR 2867049:ui OR 2866859:ui OR 2865023:ui OR 2864852:ui OR 2858815:ui OR 6745529:ui OR 6729610:ui OR 6726706:ui OR 6722062:ui OR 6713869:ui OR 6711634:ui OR 6702928:ui OR 6695297:ui OR 6693547:ui OR 6607630:ui OR 6593821:ui OR 6539432:ui OR 6512661:ui OR 6507509:ui OR 6505964:ui OR 6496581:ui OR 6470917:ui OR 6399864:ui OR 6398986:ui OR 6388556:ui OR 6387886:ui OR 6379886:ui OR 6377825:ui OR 6371619:ui OR 6371091:ui OR 6369038:ui OR 6369037:ui OR 6151891:ui OR 6147240:ui OR 6145669:ui OR 6145284:ui OR 6143542:ui OR 6877689:ui OR 6840923:ui OR 6839690:ui OR 6682726:ui OR 6679230:ui OR 6639460:ui OR 6613573:ui OR 6575306:ui OR 6571369:ui OR 6571365:ui OR 6400108:ui OR 6369342:ui OR 6353297:ui OR 6341219:ui OR 6340942:ui OR 6338150:ui OR 6338137:ui OR 6310529:ui OR 6138151:ui OR 6136361:ui OR 12266217:ui OR 7173295:ui OR 7165975:ui OR 7106893:ui OR 7092455:ui OR 7076342:ui OR 7055161:ui OR 7049589:ui OR 7041548:ui OR 7032445:ui OR 6963155:ui OR 6960780:ui OR 6950309:ui OR 6927128:ui OR 6803918:ui OR 6764393:ui OR 6176563:ui OR 6135521:ui OR 6133267:ui OR 7335755:ui OR 7333693:ui OR 7315905:ui OR 7282808:ui OR 7270102:ui OR 7259339:ui OR 7258240:ui OR 7257377:ui OR 7246657:ui OR 7226825:ui OR 7209737:ui OR 7049522:ui OR 6949162:ui OR 6942826:ui OR 6942817:ui OR 6907263:ui OR 6265487:ui OR 6119955:ui OR 6116219:ui OR 6115739:ui OR 6111403:ui OR 7438580:ui OR 7428567:ui OR 7392200:ui OR 7373797:ui OR 7350798:ui OR 7239963:ui OR 7211625:ui OR 7190936:ui OR 7189324:ui OR 7003203:ui OR 7003202:ui OR 7003197:ui OR 7000473:ui OR 6996161:ui OR 6992177:ui OR 6988746:ui OR 6988156:ui OR 6985679:ui OR 6937086:ui OR 6111311:ui OR 6105720:ui	
16	#14 NOT #15	2166

Web of Science Core Collection

Web of Science Core Collection Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI		
#	**Search**	**Results**
1	TS=("gestational hyperten*" OR HELLP OR "hypertensive disorders of pregnancy " OR (postpartum NEAR/4 hyperten*) OR pre-eclamp* OR preeclamp* OR (pregnan* NEAR/4 hyperten*) OR "pregnancy complication*" OR "pregnancy-induced hyperten*" OR "puerperal disorder*" OR toxaemia* OR toxemia*)	59563
2	TS=((((arterial OR blood OR diastolic OR systolic) NEAR/1 pressur*) AND (post-partum OR postpartum OR puerper*)) OR ("blood pressure" AND postpartum) OR ("blood pressure" and pregnan*) OR ((bp OR dbp OR sdp) AND (perinatal OR postnatal OR postpartum OR puerper*)) OR (hypertens* AND (perinatal OR postpartum OR puerper*)) OR (hypertens* AND postpartum) OR (hypertens* AND pregnan*))	37411
3	#2 OR #1	73042
4	TS=("Aldosterone Antagonist*" OR Bendroflumethiazide OR Diazoxide OR diures?s OR diuretic* OR Eplerenone OR frusemide OR furosemide OR hydrochlorothiazide* OR lasix OR "loop diuretic*" OR metolazone OR "Mineralocorticoid Antagonist*" OR "Mineralocorticoid receptor antagonist*" OR Spironolactone OR thiazide* OR torsemide)	70041
5	#4 AND #3	459
6	(#4 AND #3) AND LANGUAGE: (English)	418
7	(#4 AND #3) AND LANGUAGE: (English) Timespan=1980-2021	380
8	PMID=(33853402 OR 33848330 OR 33744967 OR 33550824 OR 33826400 OR 33753383 OR 33628547 OR 33832152 OR 33741059 OR 32755966 OR 33089031 OR 32724400 OR 32344245 OR 32747595 OR 32363336 OR 32963682 OR 32044579 OR 32532707 OR 32555118 OR 32199925 OR 32142824 OR 31715148 OR 32711486 OR 32558425 OR 31751313 OR 30762762 OR 30929513 OR 30854785 OR 31764732 OR 31724271 OR 31545168 OR 31431784 OR 31351941 OR 31023448 OR 31010554 OR 30944139 OR 30889588 OR 30497942 OR 30407107 OR 30352280 OR 29936563 OR 31915545 OR 31507531 OR 30797659 OR 30407356 OR 29974489 OR 29604124 OR 30371746 OR 30354705 OR 30303905 OR 30252182 OR 30248150 OR 29769494 OR 29694631 OR 29614490 OR 29587251 OR 29512817 OR 29292538 OR 29124624 OR 28514932 OR 30197974 OR 29850023 OR 29492141 OR 29187414 OR 29153692 OR 28402032 OR 28279449 OR 28271625 OR 28245343 OR 28181126 OR 28169090 OR 28099709 OR 28049556 OR 27835048 OR 26892095 OR 29284893 OR 30226702 OR 28863420 OR 28128088 OR 27766821 OR 27502863 OR 27479245 OR 27329098 OR 2727	553

Web of Science Core Collection Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI		
#	**Search**	**Results**
	6444 OR 27223308 OR 27156905 OR 27132428 OR 27106810 OR 27072935 OR 27072828 OR 27036652 OR 26976916 OR 26887881 OR 26818168 OR 26807737 OR 27695701 OR 26597737 OR 26574641 OR 26538126 OR 26242730 OR 26102343 OR 25855306 OR 25767291 OR 25735693 OR 25540137 OR 25482671 OR 25433575 OR 25367603 OR 25163723 OR 24435760 OR 25960654 OR 24402588 OR 25927843 OR 25436639 OR 25311173 OR 25260544 OR 25236748 OR 24956694 OR 24824702 OR 24791370 OR 24651072 OR 24554373 OR 24508521 OR 24384846 OR 24108204 OR 24102416 OR 26587434 OR 25210634 OR 24995192 OR 23884277 OR 24100222 OR 24068049 OR 24037634 OR 23978551 OR 23900968 OR 23871407 OR 23633317 OR 23563883 OR 23470109 OR 23466139 OR 23355577 OR 23216619 OR 23088788 OR 22941757 OR 22890415 OR 22418765 OR 24431648 OR 23741542 OR 26105246 OR 23316362 OR 23066416 OR 23011750 OR 22880472 OR 22779300 OR 22712170 OR 22594141 OR 22561779 OR 22544624 OR 22534703 OR 22533344 OR 22412221 OR 22270288 OR 22147655 OR 22146514 OR 21863227 OR 21730211 OR 26105605 OR 26105459 OR 26105333 OR 22988523 OR 22431946 OR 22164402 OR 22120097 OR 21896152 OR 21832180 OR 21619562 OR 21608428 OR 21596882 OR 21519980 OR 21454131 OR 21347876 OR 21342329 OR 21205934 OR 21113627 OR 21068161 OR 21045727 OR 22802371 OR 21294403 OR 20965396 OR 20804607 OR 20687095 OR 20629814 OR 20613487 OR 20587867 OR 20538570 OR 20500966 OR 20219345 OR 20132879 OR 20021530 OR 19915297 OR 19855426 OR 19781045 OR 19770791 OR 19615811 OR 19490287 OR 19403862 OR 19341836 OR 19293543 OR 19272222 OR 19241082 OR 19215236 OR 19155365 OR 19026715 OR 18840163 OR 18781561 OR 18768352 OR 18753755 OR 18645715 OR 18590935 OR 18588604 OR 18516803 OR 18501807 OR 18472157 OR 18466419 OR 18426576 OR 18400873 OR 18307755 OR 18194800 OR 18184763 OR 18034353 OR 17763862 OR 19668497 OR 17710582 OR 17627681 OR 17588579 OR 17550218 OR 17485266 OR 17469007 OR 17399682 OR 17398315 OR 17395120 OR 17362507 OR 17253507 OR 17177070 OR 16463355 OR 17087071 OR 17008838 OR 16885997 OR 16885996 OR 16855969 OR 16843085 OR 16760705 OR 16717105 OR 16612254 OR 16508324 OR 16500518 OR 16614664 OR 16359980 OR 16272671 OR 16199704 OR 16147831 OR 15970809 OR 15937436 OR 15841926 OR 15802428 OR 15696009 OR 15674943 OR 15653214 OR 15625138 OR 15590878 OR 15516453 OR 15478474 OR 15372830 OR 15354968 OR 15324607 OR 15277406 OR 15262369 OR 15223177 OR 15140513 OR 15135857 OR 15114685 OR 15050428 OR 14577830 OR 14667981 OR 14664423 OR	

Web of Science Core Collection Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI		
#	**Search**	**Results**
	14596636 OR 14520647 OR 12876067 OR 12827023 OR 12755529 OR 1271200 0 OR 12611826 OR 12594581 OR 12537992 OR 12517647 OR 12519557 OR 12 517329 OR 12459405 OR 12399443 OR 12358893 OR 12183847 OR 12163901 OR 12109847 OR 12082488 OR 12066100 OR 12060603 OR 12034156 OR 1201 2278 OR 11862056 OR 15321631 OR 12750764 OR 11704193 OR 11668076 OR 11530124 OR 11478816 OR 11423756 OR 11408849 OR 11399888 OR 1139639 0 OR 11388607 OR 11288383 OR 11267716 OR 11095476 OR 11093406 OR 11 003995 OR 10960640 OR 10919856 OR 10893382 OR 10873690 OR 10832736 OR 10804495 OR 10796261 OR 10796237 OR 10785880 OR 10752764 OR 1065 9912 OR 10726809 OR 10604545 OR 10587770 OR 10584919 OR 10546718 OR 10517776 OR 10438406 OR 10411809 OR 10338062 OR 10232722 OR 1021482 1 OR 10192478 OR 10102171 OR 10070145 OR 10027136 OR 9829161 OR 982 2515 OR 9790377 OR 9775990 OR 9746952 OR 9715225 OR 9699772 OR 9653 867 OR 9646008 OR 9523918 OR 9506418 OR 9453359 OR 9406146 OR 93753 17 OR 9337637 OR 9247750 OR 9222458 OR 9185112 OR 9101586 OR 155117 60 OR 8937816 OR 8928917 OR 8887185 OR 8863696 OR 8858082 OR 883499 2 OR 8829069 OR 8763317 OR 8754607 OR 8732994 OR 8731004 OR 8708776 OR 8677094 OR 8623791 OR 8572029 OR 8600604 OR 8522630 OR 8522430 O R 7900841 OR 7889632 OR 7789292 OR 7789210 OR 7771516 OR 7755100 OR 7735900 OR 7658037 OR 7589906 OR 9419773 OR 8194181 OR 8140955 OR 8 066479 OR 8033511 OR 8008721 OR 7941985 OR 7911388 OR 7865984 OR 78 52058 OR 7810772 OR 7802082 OR 7802067 OR 7786695 OR 7704688 OR 769 7403 OR 20301710 OR 8512045 OR 8498970 OR 8482941 OR 8469485 OR 842 3956 OR 8420337 OR 8319988 OR 8285327 OR 8259081 OR 8161250 OR 8108 188 OR 7692954 OR 1627208 OR 1597875 OR 1590427 OR 1558222 OR 15273 52 OR 1525094 OR 1504688 OR 1503669 OR 1495716 OR 1443232 OR 143834 2 OR 1357989 OR 1317759 OR 1315815 OR 1299557 OR 2021561 OR 2003559 OR 1985355 OR 1927295 OR 1912987 OR 1882820 OR 1872345 OR 1870805 O R 1836984 OR 1836470 OR 1787718 OR 1772563 OR 1747801 OR 1685783 OR 2386594 OR 2381609 OR 2372338 OR 2358562 OR 2352253 OR 2316590 OR 2 303281 OR 2300341 OR 2260686 OR 2258788 OR 2222622 OR 2216215 OR 22 05429 OR 2194868 OR 2138415 OR 2120648 OR 2083513 OR 1983424 OR 197 8541 OR 1967892 OR 2789543 OR 2789542 OR 2698145 OR 2693848 OR 2693 046 OR 2691556 OR 2650515 OR 2648928 OR 2640226 OR 2634992 OR 26046 61 OR 2604652 OR 2603913 OR 2595797 OR 2565758 OR 3402018 OR 339480 5 OR 3374914 OR 3348280 OR 3280299 OR 3275209 OR 3264036 OR 3243334	

Web of Science Core Collection Indexes=SCI-EXPANDED, SSCI, A&HCI, ESCI		
#	**Search**	**Results**
	OR 3179582 OR 3140400 OR 3060295 OR 2974682 OR 2973251 OR 2971147 OR 2901276 OR 2853660 OR 8816071 OR 3828257 OR 3799742 OR 3653042 OR 3578420 OR 3549116 OR 3453763 OR 3428473 OR 3326631 OR 3310099 OR 3038429 OR 2884053 OR 3945429 OR 3787894 OR 3783079 OR 3777057 OR 3777045 OR 3763091 OR 3746936 OR 3737046 OR 3728580 OR 3524548 OR 3510974 OR 3145669 OR 3081538 OR 3015491 OR 3011343 OR 2940080 OR 2938487 OR 2873916 OR 2861558 OR 12340716 OR 4032197 OR 4010599 OR 3993711 OR 3970085 OR 3926008 OR 3921117 OR 3920596 OR 3918757 OR 3917318 OR 3911376 OR 3905268 OR 3905080 OR 3902341 OR 3891306 OR 2982541 OR 2867049 OR 2866859 OR 2865023 OR 2864852 OR 2858815 OR 6745529 OR 6729610 OR 6726706 OR 6722062 OR 6713869 OR 6711634 OR 6702928 OR 6695297 OR 6693547 OR 6607630 OR 6593821 OR 6539432 OR 6512661 OR 6507509 OR 6505964 OR 6496581 OR 6470917 OR 6399864 OR 6398986 OR 6388556 OR 6387886 OR 6379886 OR 6377825 OR 6371619 OR 6371091 OR 6369038 OR 6369037 OR 6151891 OR 6147240 OR 6145669 OR 6145284 OR 6143542 OR 6877689 OR 6840923 OR 6839690 OR 6682726 OR 6679230 OR 6639460 OR 6613573 OR 6575306 OR 6571369 OR 6571365 OR 6400108 OR 6369342 OR 6353297 OR 6341219 OR 6340942 OR 6338150 OR 6338137 OR 6310529 OR 6138151 OR 6136361 OR 12266217 OR 7173295 OR 7165975 OR 7106893 OR 7092455 OR 7076342 OR 7055161 OR 7049589 OR 7041548 OR 7032445 OR 6963155 OR 6960780 OR 6950309 OR 6927128 OR 6803918 OR 6764393 OR 6176563 OR 6135521 OR 6133267 OR 7335755 OR 7333693 OR 7315905 OR 7282808 OR 7270102 OR 7259339 OR 7258240 OR 7257377 OR 7246657 OR 7226825 OR 7209737 OR 7049522 OR 6949162 OR 6942826 OR 6942817 OR 6907263 OR 6265487 OR 6119955 OR 6116219 OR 6115739 OR 6111403 OR 7438580 OR 7428567 OR 7392200 OR 7373797 OR 7350798 OR 7239963 OR 7211625 OR 7190936 OR 7189324 OR 7003203 OR 7003202 OR 7003197 OR 7000473 OR 6996161 OR 6992177 OR 6988746 OR 6988156 OR 6985679 OR 6937086 OR 6111311 OR 6105720)	
9	#7 NOT #8	164

Cochrane Central Register of Controlled Trials (CENTRAL)

Cochrane CENTRAL		
#	**Search**	**Results**
#1	MeSH descriptor: [HELLP Syndrome] this term only	52
#2	MeSH descriptor: [Hypertension, Pregnancy-Induced] this term only	205

Cochrane CENTRAL		
#	**Search**	**Results**
#3	MeSH descriptor: [Pre-Eclampsia] this term only	995
#4	MeSH descriptor: [Pregnancy Complications] this term only	1736
#5	MeSH descriptor: [Puerperal Disorders] this term only	309
#6	gestational hyperten*:ti,ab,kw	1643
#7	hellp:ti,ab,kw	217
#8	hypertensive disorders of pregnancy:ti,ab,kw	257
#9	pre-eclamp*:ti,ab,kw	1928
#10	preeclamp*:ti,ab,kw	3537
#11	(postpartum NEAR/4 hyperten*):ti,ab,kw	111
#12	(pregnan* NEAR/4 hyperten*):ti,ab,kw	1849
#13	pregnancy-induced hyperten*:ti,ab,kw	732
#14	toxaemia*:ti,ab,kw	38
#15	toxemia*:ti,ab,kw	376
#16	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15	7362
#17	MeSH descriptor: [Blood Pressure] this term only	26829
#18	MeSH descriptor: [Postpartum Period] this term only	1212
#19	#17 AND #18	24
#20	MeSH descriptor: [Pregnancy] this term only	22025
#21	#17 AND #20	656
#22	MeSH descriptor: [Hypertension] this term only	17835
#23	#22 AND #18	10
#24	#22 AND #20	353
#25	(((arterial OR blood OR diastolic OR systolic) NEAR/1 pressur*) AND (post-partum OR postpartum OR puerper*)):ti,ab,kw	11361
#26	((bp OR dbp OR sdp) AND (perinatal OR postnatal OR post-partum OR postpartum OR puerper*)):ti,ab,kw	238
#27	(hyperten* AND (perinatal OR post-partum OR postpartum OR puerper*)):ti,ab,kw	1057
#28	#19 OR #21 OR #23 OR #24 OR #25 OR #26 OR #27	12620
#29	#16 OR #28	17859
#30	MeSH descriptor: [Bendroflumethiazide] this term only	207
#31	MeSH descriptor: [Diazoxide] this term only	79
#32	MeSH descriptor: [Diuresis] this term only	565
#33	MeSH descriptor: [Diuretics] this term only	2373
#34	MeSH descriptor: [Eplerenone] this term only	218
#35	MeSH descriptor: [Furosemide] this term only	1185

Cochrane CENTRAL		
#	**Search**	**Results**
#36	MeSH descriptor: [Hydrochlorothiazide] this term only	2055
#37	MeSH descriptor: [Metolazone] this term only	39
#38	MeSH descriptor: [Mineralocorticoid Receptor Antagonists] this term only	601
#39	MeSH descriptor: [Sodium Potassium Chloride Symporter Inhibitors] this term only	113
#40	MeSH descriptor: [Spironolactone] this term only	972
#41	MeSH descriptor: [Thiazides] this term only	19
#42	MeSH descriptor: [Torsemide] this term only	104
#43	Aldosterone Antagonist*:ti,ab,kw	418
#44	Diazoxide:ti,ab,kw	126
#45	diuresis:ti,ab,kw	2156
#46	diuretic*:ti,ab,kw	9331
#47	Eplerenone:ti,ab,kw	490
#48	frusemide:ti,ab,kw	355
#49	furosemide:ti,ab,kw	2651
#50	hydrochlorothiazide*:ti,ab,kw	3938
#51	lasix:ti,ab,kw	77
#52	loop diuretic*:ti,ab,kw	561
#53	metolazone:ti,ab,kw	78
#54	Spironolactone:ti,ab,kw	2079
#55	thiazide*:ti,ab,kw	1391
#56	torsemide:ti,ab,kw	141
#57	#30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56	16625
#58	#29 AND #57	135
#59	#29 AND #57 with Publication Year from 1980 to 2021, in Trials	106

Clinicaltrials.gov

Due to website constraints, each search was run separately using the “other terms” field. Results from each set were downloaded into Excel and deduplicated manually. The final 18 results were then added to EndNote to dedupe against all database results.

Clinicaltrials.gov		
#	**Search**	**Results**
1	(Diuretics OR frusemide OR furosemide OR fursemide OR Hydrochlorothiazide OR lasix OR "loop diuretic" OR "Sodium Potassium Chloride Symporter Inhibitor" OR torsemide) AND Preeclampsia	10

2	(Diuretics OR frusemide OR furosemide OR fursemide OR Hydrochlorothiazide OR lasix OR "loop diuretic" OR "Sodium Potassium Chloride Symporter Inhibitor" OR torsemide) AND "hypertensive disorders of pregnancy"	7
3	(Diuretics OR frusemide OR furosemide OR fursemide OR Hydrochlorothiazide OR lasix OR "loop diuretic" OR "Sodium Potassium Chloride Symporter Inhibitor" OR torsemide) AND "hypertension, pregnancy-induced"	12
4	(Diuretics OR frusemide OR furosemide OR fursemide OR Hydrochlorothiazide OR lasix OR "loop diuretic" OR "Sodium Potassium Chloride Symporter Inhibitor" OR torsemide) AND "Gestational Hypertension"	6