Hypertensive Disorders of Pregnancy

Shaun Wesley, MD
Maternal-Fetal Medicine Fellow PGY-6
University of Rochester, NY

Disclosures

- None

Learning Objectives

- Define the current terms of hypertensive disorders of pregnancy
- Describe the pathophysiology of hypertensive disorders
- Assess for underlying etiologies and the associated therapies for each scenario
- Recognize the diagnosis of hypertensive emergency
- Apply appropriate interventions
- Prevent progression to adverse conditions if able

Epidemiology

Hypertension is the most common medical disorder occurring during pregnancy, complicating 5% to 10% of all pregnancies

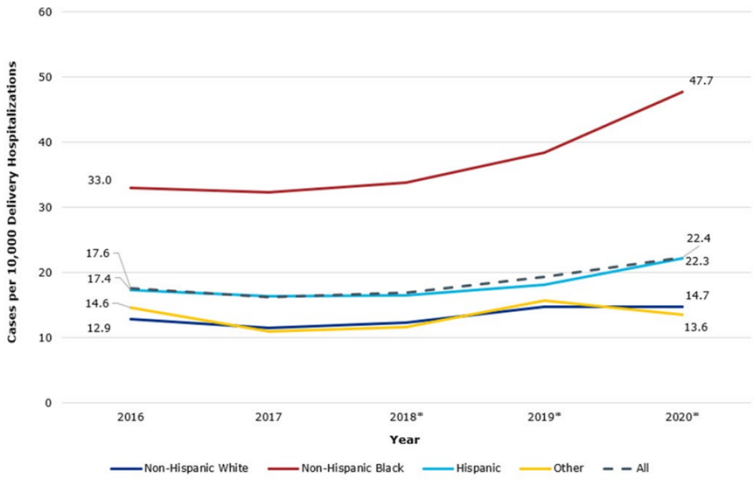
Further, hypertensive disorders of pregnancy account for approximately 7% of pregnancy related deaths

More specifically in Texas it is one of the leading causes of severe maternal morbidity and mortality

Ford ND, Cox S, Ko JY, et al. Hypertensive Disorders in Pregnancy and Mortality at Delivery Hospitalization — United States, 2017–2019. MMWR Morb Mortal Wkly Rep 2022;71:585–591. DOI: http://dx.doi.org/10.15585/mmwr.mm7117a1external icon

Texas Department of State Health Services Maternal Health and Safety Initiatives Biennial Report 2022. Dec 2022

Figure 4. Rate of Delivery Hospitalizations Involving SMM in Texas Associated with Preeclampsia, by Race and Ethnicity, per 10,000 Delivery Hospitalizations, 2016-2020



Texas Department of State Health Services Maternal Health and Safety Initiatives Biennial Report 2022. Dec 2022

Risk factors for adverse outcomes

- Chronic hypertension
- Hypertensive disorders of pregnancy
- Perioperative hypertension
- Renal disease
- Female gender
- Obesity
- Antihypertensive polypharmacy/non-adherence/acute cessation (particularly clonidine and beta-blockers)
- Stroke
- Head trauma
- Substance use, eg, cocaine, amphetamines, phencyclidine (PCP), etc.
- Pheochromocytoma
- Treatment with vascular endothelial growth factor (VEGF

Definition (general medicine)

Blood Pressure Categories

American Heart Association.

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER

Definition (general medicine)

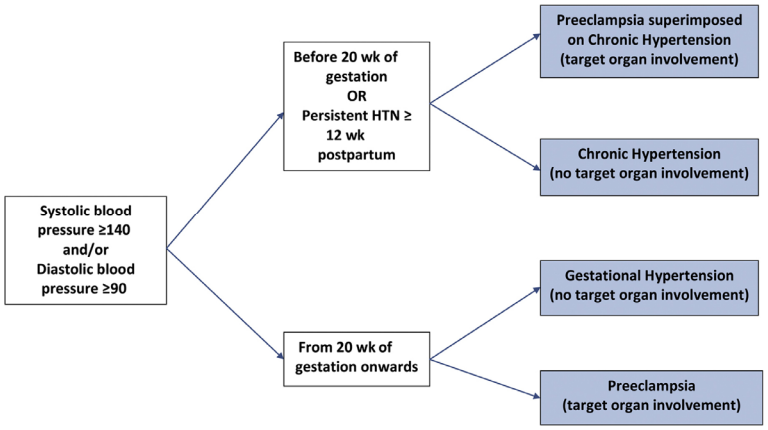
Hypertensive **urgency**:

- An elevated systolic **≥180 and/or**
- Diastolic blood pressure **≥120, WITHOUT** evidence of end-organ damage/dysfunction.

Hypertensive **emergency**:

- An elevated systolic **≥180 and/or**
- Diastolic blood pressure **≥120, WITH** evidence of end-organ damage/dysfunction.

Definition (pregnancy)



Khedagi AM, Bello NA. Hypertensive Disorders of Pregnancy. Cardiol Clin. 2021

Definition (pregnancy)

Hypertensive **urgency**:

- An elevated systolic **≥160 and/or**
- Diastolic blood pressure **≥110, WITHOUT** evidence of end-organ damage/dysfunction.

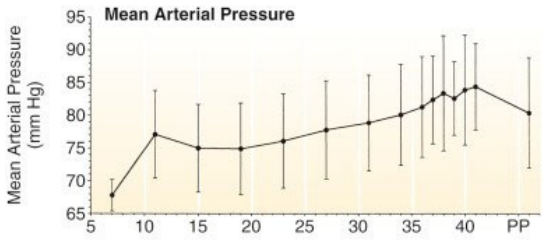
Hypertensive **emergency**:

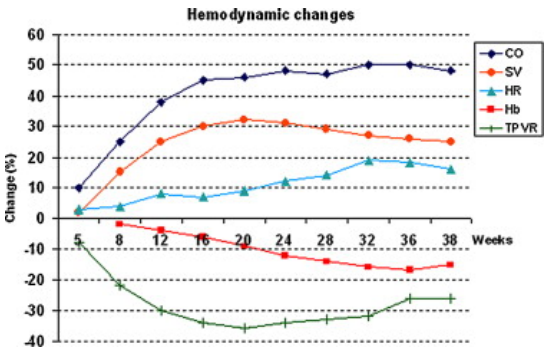
- An elevated systolic **≥160 and/or**
- Diastolic blood pressure **≥110, WITH** evidence of end-organ damage/dysfunction.

Examples of end-organ damage/dysfunction

- Neurological: headache, visual disturbances, seizures, altered mental status, altered sensorium, stroke/focal findings
- Cardiac: infarction, acute failure
- Vascular: dissection (aortic), peripheral ischemia
- Renal: acute renal insufficiency/failure
- Placental: insufficiency, abruption, preterm birth

Physiological changes in pregnancy



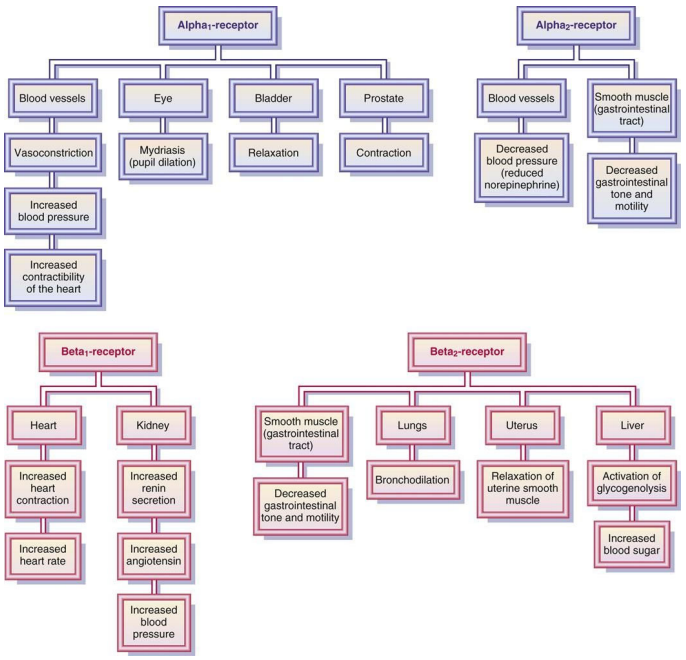


Ruys, Titia PE, Jérôme Cornette, and Jolien W. Roos-Hesselink. "Pregnancy and delivery in cardiac disease." *Journal of cardiology* 61.2 (2013): 107-112.

Etiology

- Acute hypertension
- BP = flow x resistance
- Thus, elevated BP is a function/representation of either higher flow, higher resistance, or both simultaneously

Physiology



Evaluation

- Initial assessment
- Vital signs frequently (q2-5 mins if feasible)
- Exam to assess for end-organ dysfunction
  - Mental status (Glasgow coma scale; GCS)
  - Pulmonary edema
- Establish IV access quickly

Evaluation

Glasgow Coma Scale

BEHAVIOR	RESPONSE	SCORE
Eye opening response	Spontaneously	4
	To speech	3
	To pain	2
	No response	1
Best verbal response	Oriented to time, place, and person	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	No response	1
Best motor response	Obeys commands	6
	Moves to localized pain	5
	Flexion withdrawal from pain	4
	Abnormal flexion (decorticate)	3
	Abnormal extension (decerebrate)	2
	No response	1
Total score:	*Best response*	15
	Comatose client	8 or less
	Totally unresponsive	3

Evaluation

- Laboratory studies
- CBC, CMP, protein:creatinine ratio
- Consider coagulation studies if abruption concern:
  - PT/PTT, INR, fibrinogen
- Imaging as needed towards concerning etiologies; echocardiogram can be insightful
- Toxicology screening
- Fetal monitoring
- Continuous monitoring if viable while being stabilized

Evaluation

- When the patient is stabilized, thorough evaluation for the accurate underlying cause should be performed.
- Treatment may differ, and even be counterproductive, if the etiology is misdiagnosed
- No imaging is contraindicated solely due to pregnancy and should not be delayed to diagnose potential life-threatening conditions, e.g., stroke, vascular dissection, etc.
- Systematic and uniform approach is recommended to assess all patients thoroughly
- Discussion of clinical location for ongoing treatment, e.g. Labor & Delivery floor, ICU, intermediate level unit, etc.

Evaluation

- The “gestalt”/”vibes” of the BP

120 → Interaction of stroke volume (SV) and vascular resistance
80 → Degree of vasoconstriction

Pulse pressure = SBP – DBP = ~ ½ of the stroke volume

Evaluation

- Example

160 → Mildly hyperdynamic
110 → Significantly vasoconstricted

Pulse pressure of 50 = slight increase in SV, though issue is primarily driven by persistently elevated resistance

- Agents acting on α1 receptors, e.g. catecholamine, endocrine/hormonal, hypertensive disorders of pregnancy

Evaluation

- Example

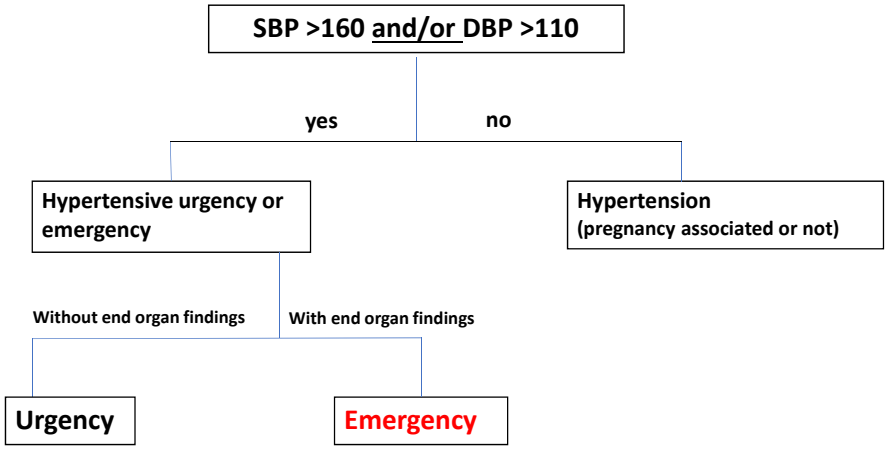
190 ⟹ Significantly hyperdynamic

100 ⟹ Moderately vasoconstricted

Pulse pressure of 90 = large increase in SV, therefore issue is primarily driven by substantially increased cardiac output

- Agents acting on β1 receptors, e.g. catecholamines, stimulants, endocrine/hormonal, pain, medical interventions

Algorithm



Management paradigm

Is the primary issue one of high flow or high resistance?

If flow, utilize something to slow the flow rate and/or reduce the volume

If resistance, utilize something to relax the vasculature

Therapy

- BP goal reduction:
- Blood pressure should be decreased by ~25% within the first few hours, then stabilized.
- Further decreases to “mild” or “normal” ranges should occur slowly over the course of 12-24 hours.
- This general principle may not apply in all cases, such as in post-stroke management depending on the type.
- Seek expert consultation and co-management from our colleagues in other specialties as indicated, eg, Anesthesiology, Critical Care/Intensivists, Cardiology, Surgery, Radiology/Interventional Radiology, Nephrology, etc.

First-Line Agents

- Labetalol
  - 20 mg IV, reassess and escalate dose (40-80 mg) every 10 minutes as needed
  - Beneficial for increased flow
- Hydralazine
  - 5 to 10 mg IV, reassess and escalate/repeat dose (5-10 mg) every 20 minutes as needed
  - Beneficial for increased resistance
- Nifedipine immediate release formulation
  - 10 mg PO, reassess and escalate/repeat dose (10-20 mg) every 20 minutes as needed
  - Beneficial for increased resistance
- May consider switching agents if inadequate response with second dose for any of these

Second-Line Agents

- Beta-blockers
  - Esmolol
    - 1000 mcg/kg IV bolus, then 150 mcg/kg/min infusion
  - Labetalol infusion
    - 10-20 mg IV bolus, then 2 mg/min infusion, may titrate to maximum of 6 mg/min
  - Beneficial for increased flow
- Calcium channel blockers
  - Nicardipine
    - 5 mg/hour, may increase every 15 minutes to maximum of 15 mg/hour
  - Clevidipine
    - 1-2 mg/hour, up to 6 mg/hour
  - Beneficial for increased resistance

These medications should be utilized by those with appropriate training in an appropriate clinical setting, most commonly an ICU

Second-Line Agents, continued

- Nitrates
  - Nitroglycerin
    - 5 mcg/min IV, may increase by 5 mcg/kg/min every 3-5 minutes to maximum of 20 mcg/kg/min
  - Sodium nitroprusside
    - 0.5 mcg/kg/min IV , may increase by 0.5 mcg/kg/min every 20-60 minutes to maximum of 2-10 mcg/kg/min
  - Beneficial for increased resistance
- Others
  - Fenoldapam
    - 0.1-0.3 mcg/kg/min IV, may increase by 0.05-0.1 mcg/kg/min every 15 minutes to maximum of 1.6 mcg/kg/min
  - Phentolamine
    - 5-20 mg, may increase by 5 mg every hour to a maximum of 40 mg/hour
  - Enalaprilat
    - 1.25 mg IV every 6 hours
  - Beneficial for increased resistance

  These medications should be utilized by those with appropriate training in an appropriate clinical setting, most commonly an ICU

Tertiary Agents

- Prior to initiating these therapies, ensure that the previous medications are actually infusing through a functioning IV and that they have had time to reach effect
- Sedatives that have antihypertensive effects:
  - propofol and dexmedetomidine; benzodiazepines in stimulant overdoses
- Neuromuscular blockade, ie, “paralytics” (rocuronium, vecuronium) may aid as well
- Patient should be intubated for airway protection when these medications are utilized
- These medications should be utilized by those with appropriate training in an appropriate clinical setting, most commonly an ICU

Adjuncts

- Diuretics
- Can benefit hypervolemic states, though are not immediate acting
- May bear risks related to renal and/or other end organ perfusion due to hypovolemia with high, frequent, or persistent dosing

Ongoing Assessments

- Follow up maternal monitoring:

Once BP is controlled (<160/110), measure

- Every 10 minutes for 1 hour
- Every 15 minutes for next hour
- Every 30 minutes for next hour
- Every hour for 4 hours

Resolution

- When blood pressure is stabilized below 160 systolic and 110 diastolic (thresholds for hypertensive crises) consistently, and there is no evidence of ongoing end-organ dysfunction, the emergency can be said to be resolved

- Transition to oral medications may occur when IV medications have not been needed for several vital signs assessments
    - Recommend titration of prior medications to maximum then additional agents as needed
    - If not on prior medications, recommend utilization of agent that was most efficacious during the emergency

Fetal Monitoring

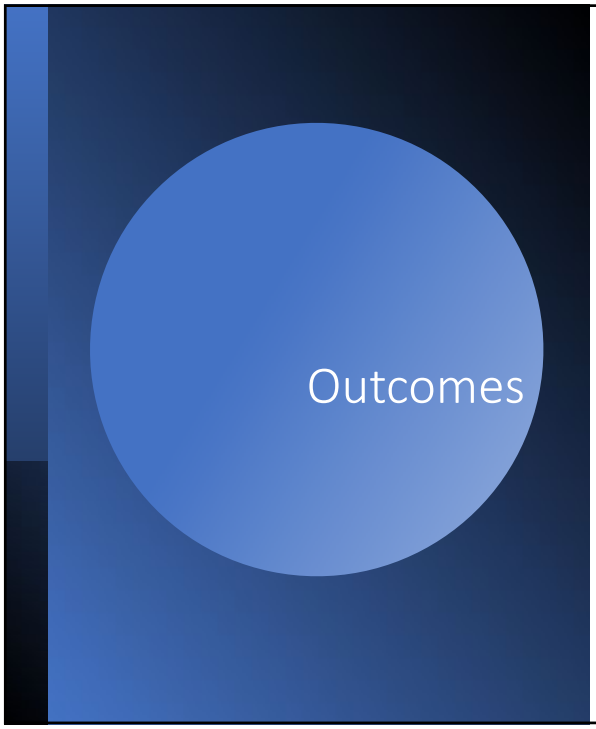
- Ideally continuous; should occur if feasible during acute treatment

- Goals:
    - To ensure fetal well-being and tolerance of treatment
    - To act as a surrogate marker of end-organ perfusion adequacy via the placenta

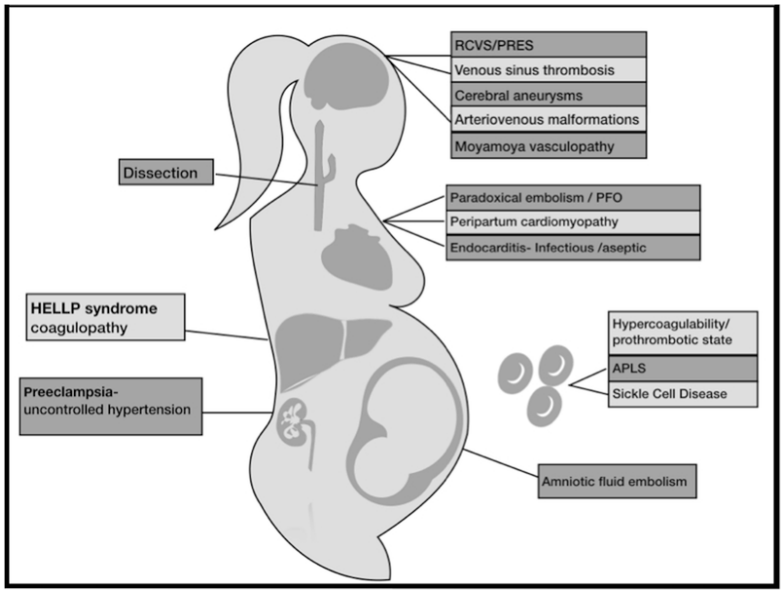
- If continuous monitoring is not available, intermittent Doppler heart tones and/or ultrasound every 5-10 minutes may be utilized

Evaluation for Associated Causes/Outcomes

- Should occur simultaneously with antihypertensive treatments
- Life-threatening events can occur with hypertensive emergencies, e.g. a head CT to evaluate for intracranial hemorrhage should not be delayed until the blood pressure is improved



- Prolonged hospitalization
- Separation of mother and neonate(s)
- Increased cost/resource utilization
- Long-term medical needs
- Increased needs in future gestations
- Foregoing future fertility
- Impact to mental health of the patient and family related to these



Zambrano MD, Miller EC. Maternal Stroke: an Update. Curr Atheroscler Rep. 2019

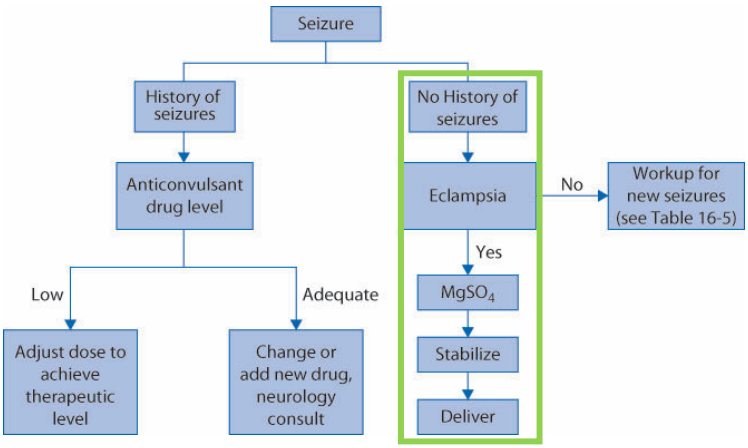
Eclampsia

Eclampsia is defined by **new-onset tonic-clonic, focal, or multifocal seizures in the absence of other causative conditions** such as epilepsy, cerebral arterial ischemia and infarction, intracranial hemorrhage, or drug use.

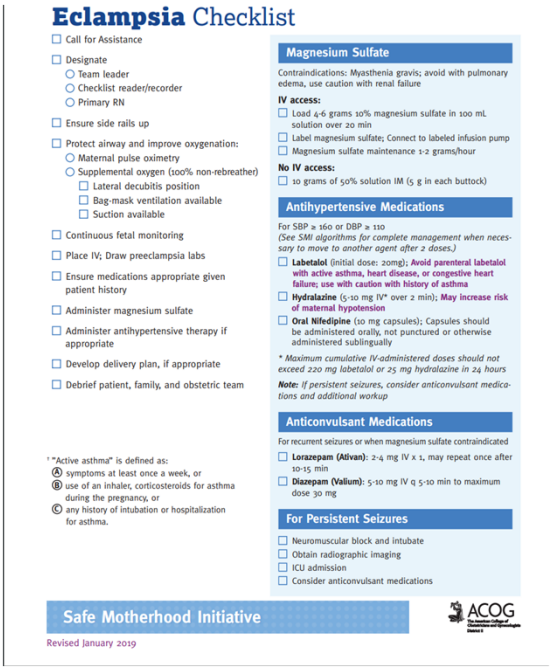
Eclampsia often (78–83% of cases) is preceded by premonitory signs of cerebral irritation such as severe and persistent occipital or frontal headaches, blurred vision, photophobia, and altered mental status.

However, eclampsia can occur in the absence of warning signs or symptoms

Seizure- workup



Foley Critical Care, 2018 Neurologic Emergencies



Eclampsia Checklist

- ☐ Call for Assistance
- ☐ Designate
  - ○ Team leader
  - ○ Checklist reader/recorder
  - ○ Primary RN
- ☐ Ensure side rails up
- ☐ Protect airway and improve oxygenation:
  - ○ Maternal pulse oximetry
  - ○ Supplemental oxygen (100% non-rebreather)
    - ☐ Lateral decubitis position
    - ☐ Bag-mask ventilation available
    - ☐ Suction available
- ☐ Continuous fetal monitoring
- ☐ Place IV; Draw preeclampsia labs
- ☐ Ensure medications appropriate given patient history
- ☐ Administer magnesium sulfate
- ☐ Administer antihypertensive therapy if appropriate
- ☐ Develop delivery plan, if appropriate
- ☐ Debrief patient, family, and obstetric team

† "Active asthma" is defined as:
Ⓐ symptoms at least once a week, or
Ⓑ use of an inhaler, corticosteroids for asthma during the pregnancy, or
Ⓒ any history of intubation or hospitalization for asthma.

Magnesium Sulfate

Contraindications: Myasthenia gravis; avoid with pulmonary edema, use caution with renal failure

IV access:
- ☐ Load 4-6 grams 10% magnesium sulfate in 100 mL solution over 20 min
- ☐ Label magnesium sulfate; Connect to labeled infusion pump
- ☐ Magnesium sulfate maintenance 1-2 grams/hour

No IV access:
- ☐ 10 grams of 50% solution IM (5 g in each buttock)

Antihypertensive Medications

For SBP ≥ 160 or DBP ≥ 110
(See SMI algorithms for complete management when necessary to move to another agent after 2 doses.)
- ☐ **Labetalol** (initial dose: 20mg); **Avoid parenteral labetalol with active asthma, heart disease, or congestive heart failure; use with caution with history of asthma**
- ☐ **Hydralazine** (5-10 mg IV* over 2 min); **May increase risk of maternal hypotension**
- ☐ **Oral Nifedipine** (10 mg capsules); Capsules should be administered orally, not punctured or otherwise administered sublingually

** Maximum cumulative IV-administered doses should not exceed 220 mg labetalol or 25 mg hydralazine in 24 hours*

***Note:** if persistent seizures, consider anticonvulsant medications and additional workup*

Anticonvulsant Medications

For recurrent seizures or when magnesium sulfate contraindicated
- ☐ **Lorazepam (Ativan)**: 2-4 mg IV x 1, may repeat once after 10-15 min
- ☐ **Diazepam (Valium)**: 5-10 mg IV q 5-10 min to maximum dose 30 mg

For Persistent Seizures
- ☐ Neuromuscular block and intubate
- ☐ Obtain radiographic imaging
- ☐ ICU admission
- ☐ Consider anticonvulsant medications

Safe Motherhood Initiative

ACOG

Revised January 2019

Magnesium vs. other antiepileptics for preeclampsia

- Magnesium sulfate is mainstay of therapy
  - more effective than phenytoin, diazepam, or nimodipine in reducing eclampsia
  - drug of choice in the prevention of eclampsia-- intra/postpartum
  - RE-treatment after 24 hrs of therapy for new symptoms rarely indicated
- Benzodiazepines and phenytoin:
  - ONLY in context of antiepileptic treatment

    ---- OR -----
  - When magnesium contraindicated or unavailable
    - myasthenia gravis
    - Severe hypocalcemia
    - Moderate-to-severe renal failure
    - cardiac ischemia, heart block, or myocarditis

Outcomes - Eclampsia

Summary of maternal and neonatal outcomes in pregnancies complicated by eclampsia

Outcome	Frequency (percent)
Abruption	7 to 10
Disseminated intravascular coagulation	7 to 11
Pulmonary edema	3 to 5
Acute renal failure	5 to 9
Aspiration pneumonia	2 to 3
Cardiopulmonary arrest	2 to 5
Liver hematoma	1
HELLP syndrome	10 to 15
Perinatal death	5.6 to 11.8
Preterm birth	50

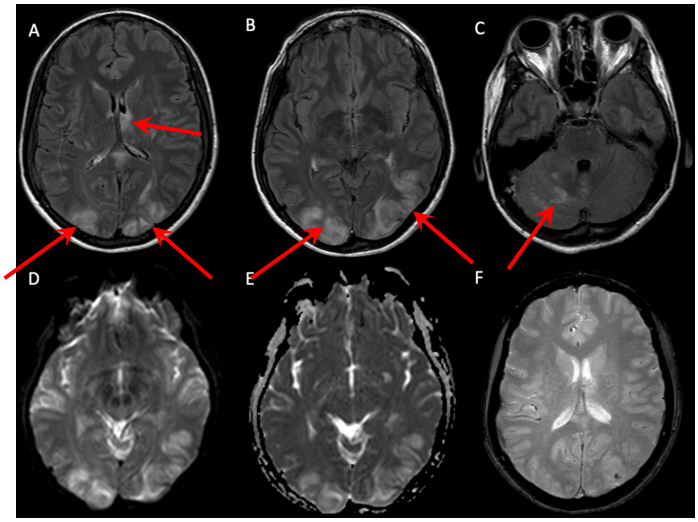
Adapted from: Sibai BM. Obstet Gynecol 2005; 105:402.

Graphic 70241 Version 3.0

PRES (Posterior reversible leukoencephalopathy syndrome)

- Constellation of a range of clinical neurologic signs and symptoms such as vision loss or deficit, seizure, headache, and altered sensorium or confusion
- Unclear precise incidence, though may be more common in women overall, especially related to pregnancy
- Thought to be due to cerebral vasculature autoregulatory dysfunction, particularly if acute
- Women are particularly at risk of PRES in the settings of eclampsia and preeclampsia with headache, altered consciousness, or visual abnormalities

Imaging findings in typical PRES. MR scan of the brain of a 39-year-old woman with PRES who presented with visual disturbance, seizure and fever.



James D Triplett et al. Pract Neurol 2022;22:183-189

PRES (Posterior reversible leukoencephalopathy syndrome)

Management focuses on blood pressure regulation and avoidance of subsequent sequelae

Consideration of seizure prophylaxis

Stroke

Rare diagnosis in pregnancy- 67/100,000 live births

- Second leading cause of death in women, 12% of maternal deaths
- Mortality as high as 25% (recent data lower)
  - Hemorrhagic > ischemic

Hypertensive disorders of pregnancy (increase 7x)

Peripartum highest risk

- 50% in the first 10 days PP
- 50% in late second and third trimester

Swartz 2017; Yoshida 2017, Caso 2017, Ban 2018

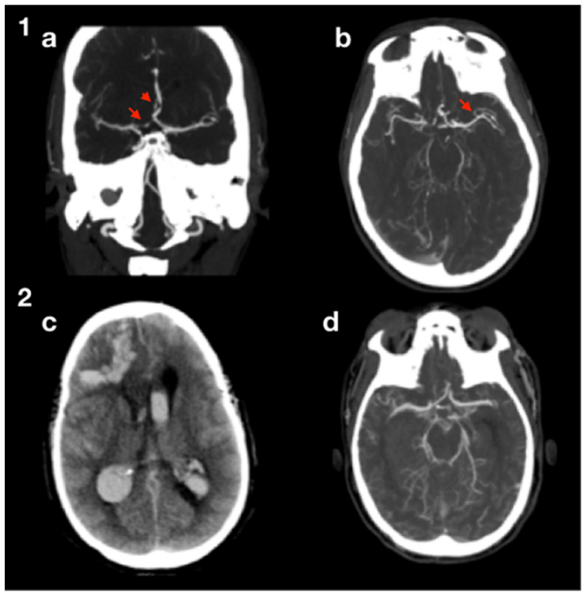
Stroke

- Up to 9-fold increased RR within 2 days of delivery
- Persistent 2-fold increased risk for the postpartum period (6 weeks from delivery)
- As high as ~18 fold higher OR of cerebral venous thrombosis in the postpartum period
- Most postpartum strokes occur within the first two weeks after delivery, with 50% of readmissions for postpartum stroke occurring within 8 days after delivery

Zambrano MD, Miller EC. Maternal Stroke: an Update. Curr Atheroscler Rep. 2019

Stroke Evaluation

- CT main imaging study for acute events
- Initial care:
  - ABC's
  - Stabilization of blood sugar
  - Maintain adequate BP to ensure cerebral perfusion
  - Treatment of increased ICP (if develops)
    - Dexamethasone, Mannitol
- Minimal risk to fetus (if no vascular instability)



Zambrano MD, Miller EC. Maternal Stroke: an Update. Curr Atheroscler Rep. 2019

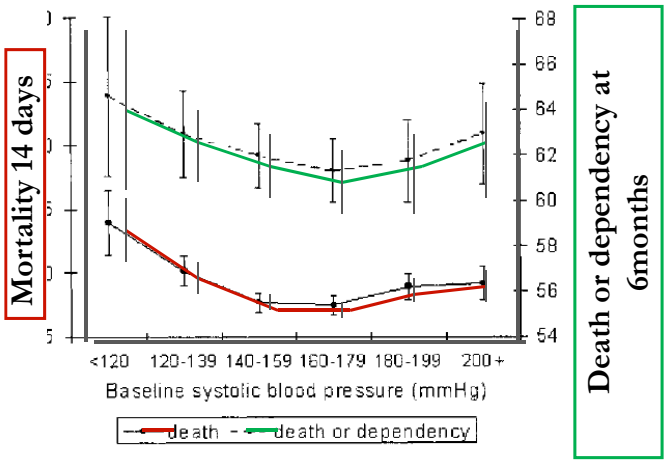
Stroke in the setting of hypertension

Hypertensive Emergency Treatment
Disease-specific Recommendations

Conditions	Preferred Agent	Goal	Risks
Acute ischemic stroke	Nicardipine, labetalol	Treat when > 220/ 120 except w/thrombolytics > 185/ 110	Excessive BP decrease may worsen ischemia
Intracranial Hemorrahge	Nicardipine, labetalol, esmolol	Treat to target MAP 130	Precipitous BP fall may increase mortality
SAH	Nicardipine, labetalol, esmolol	SBP < 160	Keep SBP > 120 to maintain CPP
Hypertensive Encephalopathy	Nicardipine, labetalol, esmolol	Decrease MAP 15 - 20%	Aggressive BP fall may produce ischemia

Ischemic Stroke (not a tPA candidate)	Ischemic Stroke (tPA candidate)
Treat SBP > 220 mmHg and/or DBP >120 mmHg only	Treat SBP > 185 mmHg and/or DBP >110 mmHg
Acute Aortic Dissection (can have stroke-like symptoms)	**Subarachnoid or Intracranial Hemorrhage**
Rapid reduction (5 – 10 minutes) to a SBP between 100 – 120 mmHg (if tolerated)	Balance risk of re-bleeding with risk of reducing cerebral perfusion pressure

Chobanian A, et al. Hypertension 2003;42:1206-1252



Leonardi-Bee *Stroke* 2002:33;1351-1357

Ischemic/Thrombotic Stroke- Thrombolytics

No RTC data on therapy	rt-PA	Risks/benefits depends on gestational age, size of stroke, prognosis for mother without therapy

• rt-PA and urokinase are both used; neither cross placenta
  • Risks: intrauterine hematoma, miscarriage and maternal intracranial hemorrhage/death
• Thrombectomy is also described
	• VTE data:
	  • 8% complication rate, 27% bleeding risk
	  • 6-23% pregnancy loss risk
	• Stroke data:
	  • Outcomes/risks = to those not pregnant	

VanAlebeek 2018, Reining-Festa 2017, Landais 2018

Stroke- anticoagulation

- Does not appear helpful in acute phase
- ASA and LMWH/heparin are sometimes utilized
- For Embolic Stoke:
  - Anticoagulation can prevent recurrence
  - Likely should be delayed 7-10 days to prevent acute hemorrhage into infarct

Definitive Management

Depends on the etiology

- Delivery for refractory hypertensive disorders of pregnancy
- Optimization of medical management for poorly controlled chronic hypertension without associated preeclampsia, pain, etc.
- Potential surgical intervention for intracranial bleeding, pheochromocytoma, renal hypoperfusion due to vascular causes, etc.
- Removal/counteraction of offending illicit substances, i.e., cocaine, phenylcyclidine, amphetamines, etc.

Definitive Management

Depends on the etiology

- Continue to optimize blood pressure control, in a controlled manner, while determining the underlying cause and further indicated interventions
- Care for such patients should be multidisciplinary, with consultation to Critical Care, Anesthesiology, Surgery as indicated, etc.
- Such patients should be cared for in the clinical setting most appropriate to treat the gravest immediate threat to patient and pregnancy, eg, Labor & Delivery, ICU, operating room, transfer to another facility, etc., and this decision should be made collaboratively as a multidisciplinary team

Prevention

- Should there be a goal BP in pregnancy to reduce the risk of severe hypertension?
- Can we detect patients before they approach this level?
- Can we intervene in early preeclampsia to prevent more severe blood pressures later?

Prevention – CHAP trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 12, 2022 VOL. 386 NO. 19

Treatment for Mild Chronic Hypertension during Pregnancy

A.T. Tita, J.M. Szychowski, K. Boggess, L. Dugoff, B. Sibai, K. Lawrence, B.L. Hughes, J. Bell, K. Aagaard, R.K. Edwards, K. Gibson, D.M. Haas, L. Plante, T. Metz, B. Casey, S. Esplin, S. Longo, M. Hoffman, G.R. Saade, K.K. Hoppe, J. Foroutan, M. Tuuli, M.Y. Owens, H.N. Simhan, H. Frey, T. Rosen, A. Palatnik, S. Baker, P. August, U.M. Reddy, W. Kinzler, E. Su, I. Krishna, N. Nguyen, M.E. Norton, D. Skupski, Y.Y. El-Sayed, D. Ogunyemi, Z.S. Galis, L. Harper, N. Ambalavanan, N.L. Geller, S. Oparil, G.R. Cutter, and W.W. Andrews, for the Chronic Hypertension and Pregnancy (CHAP) Trial Consortium*

ABSTRACT

BACKGROUND

The benefits and safety of the treatment of mild chronic hypertension (blood pressure, <160/100 mm Hg) during pregnancy are uncertain. Data are needed on whether a strategy of targeting a blood pressure of less than 140/90 mm Hg reduces the incidence of adverse pregnancy outcomes without compromising fetal growth.

METHODS

In this open-label, multicenter, randomized trial, we assigned pregnant women with mild chronic hypertension and singleton fetuses at a gestational age of less than 23 weeks to receive antihypertensive medications recommended for use in pregnancy (active-treatment group) or to receive no such treatment unless severe hypertension (systolic pressure, ≥160 mm Hg; or diastolic pressure, ≥105 mm Hg) developed (control group). The primary outcome was a composite of preeclampsia with severe features, medically indicated preterm birth at less than 35 weeks' gestation, placental abruption, or fetal or neonatal death. The safety outcome was small-for-

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Tita can be contacted at atita@uab.edu or at the Department of Obstetrics and Gynecology, Center for Women's Reproductive Health, Marnix E. Heersink School of Medicine, University of Alabama at Birmingham, 619 19th St. S., Birmingham, AL 35249.

*A complete list of the investigators in the CHAP Trial Consortium is provided in the Supplementary Appendix, available at NEJM.org.

This article was published on April 2, 2022, at NEJM.org.

Prevention – CHAP trial

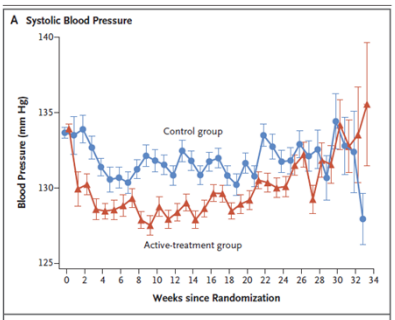


Figure 1. Mean Blood Pressure after Randomization.
Between randomization and delivery, the overall mean blood-pressure level was lower in the active-treatment group than in the control group, both for systolic pressure (129.5 mm Hg vs. 132.6 mm Hg) and for diastolic pressure (79.1 mm Hg vs. 81.5 mm Hg). I bars indicate standard errors.

Prevention – CHAP trial

Table 2. Primary and Safety Outcomes.

Outcome	Imputation Analysis (N=2408)*		Complete-Case Analysis (N=2325)†			
	Adjusted Risk Ratio (95% CI)	P Value	Active Treatment	Control	Risk Ratio (95% CI)	P Value
			no./total no. (%)			
Primary composite outcome	0.82 (0.74–0.92)	<0.001	353/1170 (30.2)	427/1155 (37.0)	0.82 (0.73–0.92)	<0.001
Preeclampsia with severe features	0.80 (0.70–0.92)		272/1170 (23.3)	336/1155 (29.1)	0.80 (0.70–0.92)	
Medically indicated preterm birth at <35 wk	0.73 (0.60–0.89)		143/1170 (12.2)	193/1155 (16.7)	0.73 (0.60–0.89)	
Placental abruption	0.88 (0.49–1.59)		20/1170 (1.7)	22/1155 (1.9)	0.90 (0.49–1.64)	
Fetal or neonatal death at <28 days	0.81 (0.54–1.22)		41/1170 (3.5)	50/1155 (4.3)	0.81 (0.54–1.21)	
Safety outcome						
Small for gestational age						
<10th percentile	1.04 (0.82–1.31)	0.76	128/1146 (11.2)	117/1124 (10.4)	1.07 (0.85–1.36)	0.56
<5th percentile	0.89 (0.62–1.26)	0.51	58/1146 (5.1)	62/1124 (5.5)	0.92 (0.65–1.30)	0.63

* Shown are the results of multiple imputation analysis performed with the use of multivariable log-binomial regression models to calculate adjusted risk ratios. The missing values were modeled within treatment group with the use of baseline characteristics that included diabetes status (yes or no), treatment status at enrollment (receiving or not receiving blood-pressure medication), age, body-mass index, and elevated blood pressure (≥150 mm Hg systolic or ≥100 mm Hg diastolic) at the first visit.
† Complete-case analysis of the primary outcome included 2325 patients with sufficient data (1170 in the active-treatment group and 1155 in the control group). Complete-case analysis of the safety outcome included 2270 patients with sufficient data (1146 in the active-treatment group and 1124 in the control group); included in this analysis were assessments of data obtained during delivery.

Prevention – Cochrane review

Cochrane Library

Cochrane Database of Systematic Reviews

Antihypertensive drug therapy for mild to moderate hypertension during pregnancy (Review)

Abalos E, Duley L, Steyn DW, Gialdini C

Abalos E, Duley L, Steyn DW, Gialdini C.
Antihypertensive drug therapy for mild to moderate hypertension during pregnancy.
Cochrane Database of Systematic Reviews 2018, Issue 10. Art. No.: CD002252.
DOI: 10.1002/14651858.CD002252.pub4.

Prevention – Cochrane review

Cochrane Library

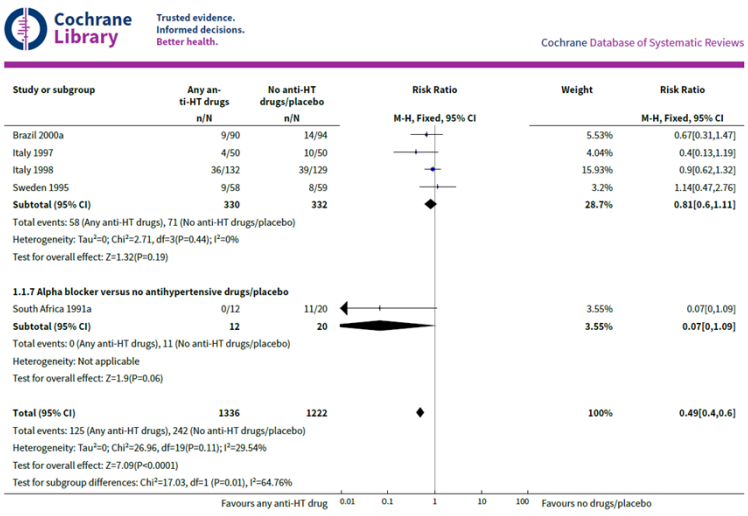
Trusted evidence.
Informed decisions.
Better health.

Cochrane Database of Systematic Reviews

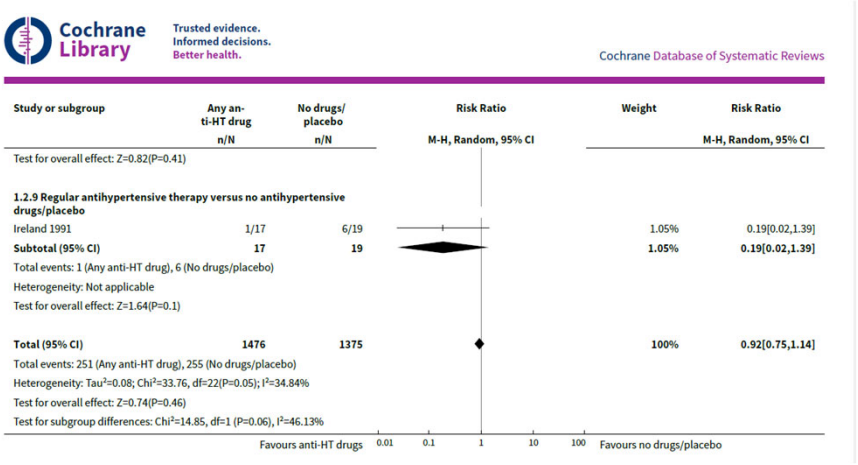
Analysis 1.1. Comparison 1 Any antihypertensive drug versus no antihypertension drugs/placebo (subgrouped by class of drug), Outcome 1 Severe hypertension.

Study or subgroup	Any anti-HT drugs n/N	No anti-HT drugs/placebo n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Beta blocker versus no antihypertensive drugs/placebo					
Hong Kong 1990	6/20	10/21		3.94%	0.63[0.28,1.41]
Israel 1992a	6/30	15/30		6.06%	0.4[0.18,0.89]
Sweden 1984	1/26	0/26		0.2%	3[0.13,70.42]
UK 1982	3/64	13/62		5.33%	0.22[0.07,0.75]
UK 1983a	2/60	7/60		2.83%	0.29[0.06,1.32]
UK 1989	5/70	15/74		5.89%	0.35[0.14,0.92]
UK 1990	0/16	2/17		0.98%	0.21[0.01,4.1]
USA 1987a	5/92	14/94		5.59%	0.36[0.14,0.97]
Subtotal (95% CI)	**378**	**384**		**30.81%**	**0.38[0.26,0.57]**
Total events: 28 (Any anti-HT drugs), 76 (No anti-HT drugs/placebo)					
Heterogeneity: $Tau^2=0$; $Chi^2=4.2$, $df=7(P=0.76)$; $I^2=0\%$					
Test for overall effect: Z=4.81(P<0.0001)					
1.1.2 Beta blocker + other drug versus no antihypertensive drugs/ placebo					
Caribbean Is.1990	5/78	11/76		4.5%	0.44[0.16,1.21]
Sweden 1985	0/86	6/82		2.69%	0.07[0,1.28]
Subtotal (95% CI)	**164**	**158**		**7.18%**	**0.3[0.12,0.77]**
Total events: 5 (Any anti-HT drugs), 17 (No anti-HT drugs/placebo)					
Heterogeneity: $Tau^2=0$; $Chi^2=1.48$, $df=1(P=0.22)$; $I^2=32.39\%$					
Test for overall effect: Z=2.52(P=0.01)					
1.1.3 Methyldopa versus no antihypertensive drugs/placebo					
Sudan 2002	3/34	18/36		7.06%	0.18[0.06,0.55]
UK 1976	9/117	22/123		8.66%	0.43[0.21,0.9]
Subtotal (95% CI)	**151**	**159**		**15.72%**	**0.32[0.17,0.58]**
Total events: 12 (Any anti-HT drugs), 40 (No anti-HT drugs/placebo)					
Heterogeneity: $Tau^2=0$; $Chi^2=1.7$, $df=1(P=0.19)$; $I^2=41.24\%$					
Test for overall effect: Z=3.73(P=0)					
1.1.4 Methyldopa + other drug versus no antihypertensive drugs/ placebo					
USA 1979	2/29	3/29		1.21%	0.67[0.12,3.7]
Subtotal (95% CI)	**29**	**29**		**1.21%**	**0.67[0.12,3.7]**
Total events: 2 (Any anti-HT drugs), 3 (No anti-HT drugs/placebo)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.46(P=0.64)					
1.1.5 Beta blocker or methyldopa versus no antihypertensive drugs/ placebo					
India 2012	10/99	14/50		7.51%	0.36[0.17,0.75]
USA 1990a	10/173	10/90		5.31%	0.52[0.22,1.2]
Subtotal (95% CI)	**272**	**140**		**12.82%**	**0.43[0.25,0.74]**

Prevention – Cochrane review



Prevention – Cochrane review



Prevention – BUMP trials

Research

JAMA | Original Investigation

Effect of Self-monitoring of Blood Pressure on Diagnosis of Hypertension During Higher-Risk Pregnancy

The BUMP 1 Randomized Clinical Trial

Katherine L. Tucker, PhD; Sam Mort, PGCert; Ly-Mee Yu, DPhil; Helen Campbell, DPhil; Oliver Rivero-Arias, DPhil; Hannah M. Wilson, MSc; Julie Allen, BSc; Rebecca Band, PhD; Alison Chisholm, PhD; Carole Crawford, MSc; Greig Dougall, PhD; Lazarina Engonidou, MSc; Marloes Franssen, PhD; Marcus Green, BA; Sheila Greenfield, PhD; Lisa Hinton, DPhil; James Hodgkinson, PhD; Layla Lavallee, MSc; Paul Leeson, MB BChir, PhD; Christine McCourt, PhD; Lucy Mackillop, BM, BCh; Jane Sandall, PhD; Mauro Santos, DPhil; Lionel Tarassenko, DPhil; Carmelo Velardo, PhD; Lucy Yardley, PhD; Lucy C. Chappell, MB BChir, PhD; Richard J. McManus, MBBS, PhD; for the BUMP Investigators

IMPORTANCE Inadequate management of elevated blood pressure (BP) is a significant contributing factor to maternal deaths. Self-monitoring of BP in the general population has been shown to improve the diagnosis and management of hypertension; however, little is known about its use in pregnancy.

OBJECTIVE To determine whether self-monitoring of BP in higher-risk pregnancies leads to earlier detection of pregnancy hypertension.

DESIGN, SETTING, AND PARTICIPANTS Unblinded, randomized clinical trial that included 2441 pregnant individuals at higher risk of preeclampsia and recruited at a mean of 20 weeks' gestation from 15 hospital maternity units in England between November 2018 and October 2019. Final follow-up was completed in April 2020.

INTERVENTIONS Participating individuals were randomized to either BP self-monitoring with telemonitoring (n = 1223) plus usual care or usual antenatal care alone (n = 1218) without access to telemonitored BP.

MAIN OUTCOMES AND MEASURES The primary outcome was time to first recorded hypertension measured by a health care professional.

RESULTS Among 2441 participants who were randomized (mean [SD] age, 33 [5.6] years; mean gestation, 20 [1.6] weeks), 2346 (96%) completed the trial. The time from randomization to clinic recording of hypertension was not significantly different between individuals in the self-monitoring group (mean [SD], 104.3 [32.6] days) vs in the usual care group (mean [SD], 106.2 [32.0] days) (mean difference, −1.6 days [95% CI, −8.1 to 4.9]; $P = .64$). Eighteen serious adverse events were reported during the trial with none judged as related to the intervention (12 [1%] in the self-monitoring group vs 6 [0.5%] in the usual care group).

Visual Abstract
Editorial page 1651
Multimedia
Related articles joi220035 and 1700
Supplemental content

Prevention – BUMP trials

Table 2. Primary Outcome: Time From Randomization to Diagnosis of Elevated Sustained Blood Pressure

	Self-monitoring group	Usual care group	Difference (95% CI)	*P* value[a]
Participants with primary outcome data	1171	1175		
Clinic hypertension, No. (%)[b]	179 (15.3)	184 (15.7)	0.0 (−3 to 2)[c]	.75
Time to clinic hypertension, d				
Mean (SD)	104.3 (32.6)	106.2 (32.0)	−1.6 (−8.1 to 4.9)	.64
Median (IQR)	109 (90 to 127)	115 (90 to 129)		

[a] Self-monitoring vs usual care: threshold level of significance $P = .05$.
[b] Sustained elevated blood pressure defined as 2 readings ≥140/90 mm Hg within 168 hours or a recorded diagnosis of pregnancy hypertension or prescription of an antihypertensive medication, whichever came first.
[c] Difference in percentage of having elevated blood pressure modeled against randomized group, parity, and site.

Table 3. Selected Secondary Maternal and Perinatal Outcomes by Randomized Group[a]

	No./total (%)		Adjusted absolute difference, % (95% CI)[b]	Adjusted risk ratio (95% CI)[b]	*P* value for treatment effect
	Self-monitoring group	Usual care group			
Maternal					
Severe hypertension	69/1171 (6.0)	57/1175 (4.9)	1.09 (−0.94 to 3.12)	1.22 (0.87 to 1.70)	.25
Preeclampsia	51/1209 (4.2)	51/1209 (4.2)	0.01 (−1.84 to 1.85)	1.00 (0.66 to 1.51)	>.99
≥1 Serious maternal complications[c]	15/1209 (1.2)	19/1209 (1.6)			
Perinatal					
Gestation at delivery, median (IQR), wk	39.3 (38.1 to 40.4) [1190]	39.3 (38.0 to 40.4) [1185]	0.14 (−0.01 to 0.30)[d]		
Stillbirth	5/1260 (0.4)	3/1248 (0.2)			
Neonatal death within 7 d	2/1248 (0.2)	0/1240			
Small for gestational age (<10th percentile)	104/1249 (8.3)	87/1235 (7.0)	1.10 (−1.09 to 3.29)	1.15 (0.87 to 1.53)	.32
Infant admitted to neonatal intensive care unit	161/1248 (12.9)	163/1240 (13.1)	−0.64 (−3.34 to 2.05)	0.95 (0.77 to 1.17)	.63

[a] See eTables 3 and 4 in Supplement 3 for additional maternal and perinatal outcomes.
[b] Statistical comparisons completed when >2% event rate for self-monitoring vs usual care. Log-Poisson generalized linear mixed-effects model with robust standard errors adjusted for randomized group and parity as fixed effects; and site as a random effect. Level of significance $P < .05$.
[c] One or more of the following: eclampsia, transient ischemic attack or stroke, HELLP syndrome (hemolysis, elevated liver enzymes, low platelets), liver involvement (ALT or AST >70 U/L), pulmonary edema, kidney involvement (creatinine >90 μmol/L), and hematological involvement (platelets < x100^9/L).
[d] Estimated median difference (95% CI) derived from quantile regression adjusted for randomized arm, parity, and site.

Key Points

Question Does self-monitoring of blood pressure (BP) by pregnant individuals at higher risk for preeclampsia lead to earlier detection of pregnancy hypertension compared with usual antenatal care?

Findings In this randomized clinical trial that included 2441 pregnant individuals at increased risk for preeclampsia, self-monitoring of BP with telemonitoring compared with usual care resulted in a mean time to clinic-based detection of hypertension of 104 vs 106 days, a difference that was not statistically significant.

Meaning Among pregnant individuals at higher risk of preeclampsia, self-monitoring of BP with telemonitoring did not lead to earlier clinic-based detection of hypertension.

Prevention – BUMP trials

Research

JAMA | Original Investigation

Effect of Self-monitoring of Blood Pressure on Blood Pressure Control in Pregnant Individuals With Chronic or Gestational Hypertension

The BUMP 2 Randomized Clinical Trial

Lucy C. Chappell, MB BChir, PhD; Katherine L. Tucker, PhD; Ushma Galal, MSc; Ly-Mee Yu, DPhil; Helen Campbell, DPhil; Oliver Rivero-Arias, DPhil; Julie Allen, BSc; Rebecca Band, PhD; Alison Chisholm, PhD; Carole Crawford, MSc; Greig Dougall, PhD; Lazarina Engonidou, MSc; Marloes Franssen, DPhil; Marcus Green, BA(Hons); Sheila Greenfield, PhD; Lisa Hinton, DPhil; James Hodgkinson, PhD; Layla Lavallee, MSc; Paul Leeson, MB BChir, PhD; Christine McCourt, PhD; Lucy Mackillop, BM BCh; Jane Sandall, PhD; Mauro Santos, DPhil; Lionel Tarassenko, DPhil; Carmelo Velardo, PhD; Hannah Wilson, MSc; Lucy Yardley, PhD; Richard J. McManus, MBBS, PhD; for the BUMP 2 Investigators

IMPORTANCE Inadequate management of elevated blood pressure is a significant contributing factor to maternal deaths. The role of blood pressure self-monitoring in pregnancy in improving clinical outcomes for the pregnant individual and infant is unclear.

OBJECTIVE To evaluate the effect of blood pressure self-monitoring, compared with usual care alone, on blood pressure control and other related maternal and infant outcomes, in individuals with pregnancy hypertension.

DESIGN, SETTING, AND PARTICIPANTS Unblinded, randomized clinical trial that recruited between November 2018 and September 2019 in 15 hospital maternity units in England. Individuals with chronic hypertension (enrolled up to 37 weeks' gestation) or with gestational hypertension (enrolled between 20 and 37 weeks' gestation). Final follow-up was in May 2020.

INTERVENTIONS Participants were randomized to either blood pressure self-monitoring using a validated monitor and a secure telemonitoring system in addition to usual care (n = 430) or to usual care alone (n = 420). Usual care comprised blood pressure measured by health care professionals at regular antenatal clinics.

MAIN OUTCOMES AND MEASURES The primary maternal outcome was the difference in mean systolic blood pressure recorded by health care professionals between randomization and birth.

RESULTS Among 454 participants with chronic hypertension (mean age, 36 years; mean gestation at entry, 20 weeks) and 396 with gestational hypertension (mean age, 34 years; mean gestation at entry, 33 weeks) who were randomized, primary outcome data were available from 444 (97.8%) and 377 (95.2%), respectively. In the chronic hypertension cohort, there was no statistically significant difference in mean systolic blood pressure for the self-monitoring groups vs the usual care group (133.8 mm Hg vs 133.6 mm Hg, respectively; adjusted mean difference, 0.03 mm Hg [95% CI, −1.73 to 1.79]). In the gestational hypertension cohort, there was also no significant difference in mean systolic blood pressure (137.6 mm Hg compared with 137.2 mm Hg; adjusted mean difference, −0.03 mm Hg [95% CI, −2.29 to 2.24]). There were 8 serious adverse events in the self-monitoring group (4 in each cohort) and 3 in the usual care group (2 in the chronic hypertension cohort and 1 in the gestational hypertension cohort).

Visual Abstract
Editorial page 1651
Multimedia
Related articles pages 1656 and 1700
Supplemental content

Table 2. Primary Outcome: Mean Blood Pressure for Participants With Chronic Hypertension and Gestational Hypertension

	Self-monitoring	Usual care	Adjusted mean difference (95% CI)	*P* value
Chronic hypertension				
Primary outcome available, No. (%)[a]	229 (98.3)	215 (97.3)		
Blood pressure, mean (SD), mm Hg				
Systolic[b]	133.8 (10.3)	133.6 (11.1)	0.03 (−1.73 to 1.79)[c]	.97
Diastolic	84.0 (7.4)	84.3 (7.9)	−0.03 (−1.28 to 1.22)	.96
Gestational hypertension				
Primary outcome available, No. (%)[a]	187 (94.9)	190 (95.5)		
Blood pressure, mean (SD), mm Hg				
Systolic	137.6 (12.1)	137.2 (10.8)	−0.03 (−2.29 to 2.24)[d]	.98
Diastolic	86.1 (7.8)	86.3 (7.7)	−0.35 (−1.77 to 1.06)	.63

[a] Individuals with missing primary outcomes (10 in the chronic hypertension self-monitoring group, 6 in the chronic hypertension usual care group, 10 in the gestational hypertension self-monitoring group, and 9 in the gestational hypertension usual care group) were not included in this analysis; no imputation was undertaken.

[b] Mean blood pressure was defined as the mean of the means of all systolic blood pressure readings recorded by health care professionals, from after entry into the study until up to 1 day before the date of delivery. No self-recorded blood pressure was used.

[c] Chronic hypertension, self-monitoring vs usual care; estimated from linear mixed-effects model adjusting for mean baseline systolic blood pressure, parity, and recruitment site. Eleven participants not included in the model due to missing baseline systolic blood pressure reading (n = 7 from self-monitoring, n = 4 from usual care).

[d] Gestational hypertension, self-monitoring vs usual care; estimated from linear mixed-effects model adjusting for mean baseline systolic blood pressure, parity, transfer from BUMP 1, and recruitment site. Six participants not included in the model due to missing baseline systolic blood pressure reading (n = 4 from self-monitoring, n = 2 from usual care).

Key Points

Question Does self-monitoring of blood pressure by individuals with hypertension in pregnancy lead to better clinic blood pressure control compared with usual antenatal care?

Findings In this randomized clinical trial that included 850 pregnant individuals with chronic hypertension or gestational hypertension, use of self-monitoring of blood pressure with telemonitoring resulted in an adjusted mean difference in clinic-based systolic blood pressure, compared with usual care alone, of 0.03 mm Hg for chronic hypertension and −0.03 mm Hg for gestational hypertension. Neither difference was statistically significant.

Meaning Among pregnant individuals with chronic or gestational hypertension, blood pressure self-monitoring with telemonitoring did not lead to improved clinic-based blood pressure control.

Prevention – BUMP trials

Potential Pitfalls to Avoid

- Too frequent dosing/not allowing time for medication effect/overtreatment
- Incomplete evaluation
- Management directed at inaccurate etiology
- Not creating and utilizing the expertise of a multidisciplinary care team, and/or a delay in involving such teams
- Managing the patient in a lower resourced unit for their primary concern/not transferring patient when indicated
- ? Antihypertensive therapy for hypertensive disorders of pregnancy

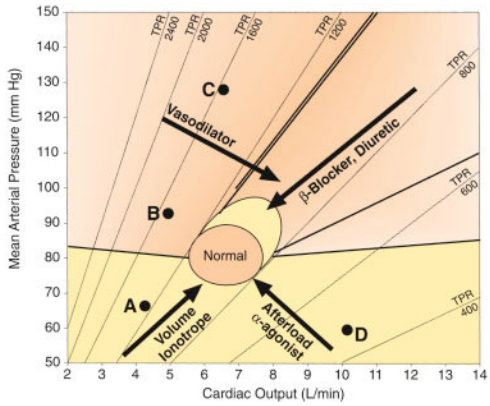
Overall assessment

- "Big picture view"
- Know the patient's initial "normal" reference point
  - i.e. how they are at home and how they came into the hospital
  - Goal is to stay here! (or at least not deteriorate below this level)
    - Harms are caused by rapid changes from what the body is accustomed to

Management plan

- Be prepared for catastrophes
  - Ensure all potentially necessary equipment is available and functional (have a system in place where such things are checked routinely).
    - Includes monitoring systems, AED, bedside US, bedside suction, etc., etc.
  - Obtain adequate access “before” it is needed.
  - Have all planned/potential medications available or on standby.
    - Diuretics, inotropes, pressors, anti-hypertensives, vasodilators, analgesia, fluids, etc.

Management in one picture



THINK ABOUT WHAT THE PROBLEM IS AND HOW TO GET BACK TO “NORMAL”.

Coordination of care

- Multidisciplinary teams
  - Pregnancy champions from Anesthesia, Cardiology, Intensivists working in conjunction with the Obstetrician and Maternal-Fetal Medicine specialists
  - Creates reliable points of contact to help guide care
  - Consistent team gains familiarity with and expertise in providing such care
  - Can offer direct patient care, or assist in remote consultation/transport coordination

Coordination of care

- Wealth of literature showing:
  - Improved outcomes
  - Less need for interventions
  - Greater patient and family satisfaction
  - Improved care team functioning with the use of protocols to promote greater and more clear, consistent communication in Critical Care

Coordination of care

The American College of Obstetricians and Gynecologists, along with the Society for Maternal-Fetal Medicine have put forth recommendations for levels of maternal care.

The fourth and highest level calls for well implemented collaboration between the Obstetrics and Critical Care teams, as well as the presence of a high-risk pregnancy specialist with expertise in Critical Care.

Thank you, keep up the good work!

Shaun Wesley, MD
Shaun.Wesley@ttuhsc.edu