Hypertensive Disorders in Pregnancy

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Objectives

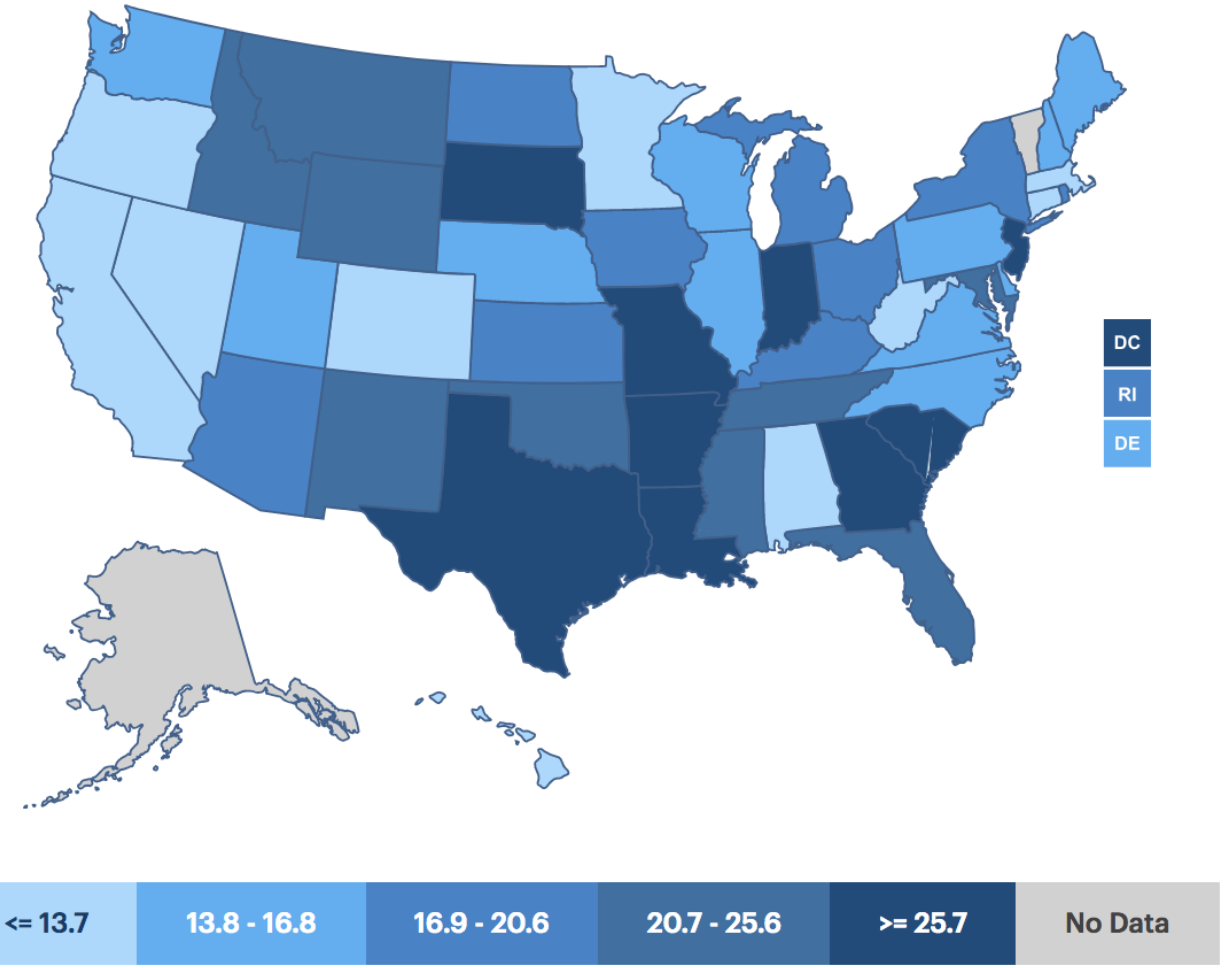
- Define the various hypertensive disorders in pregnancy (HDP)
- Review risk assessment and prevention of hypertensive morbidity
- Review antepartum surveillance and management of pregnancies complicated by hypertension
- Review management of severe hypertension during pregnancy and the postpartum period

Epidemiology

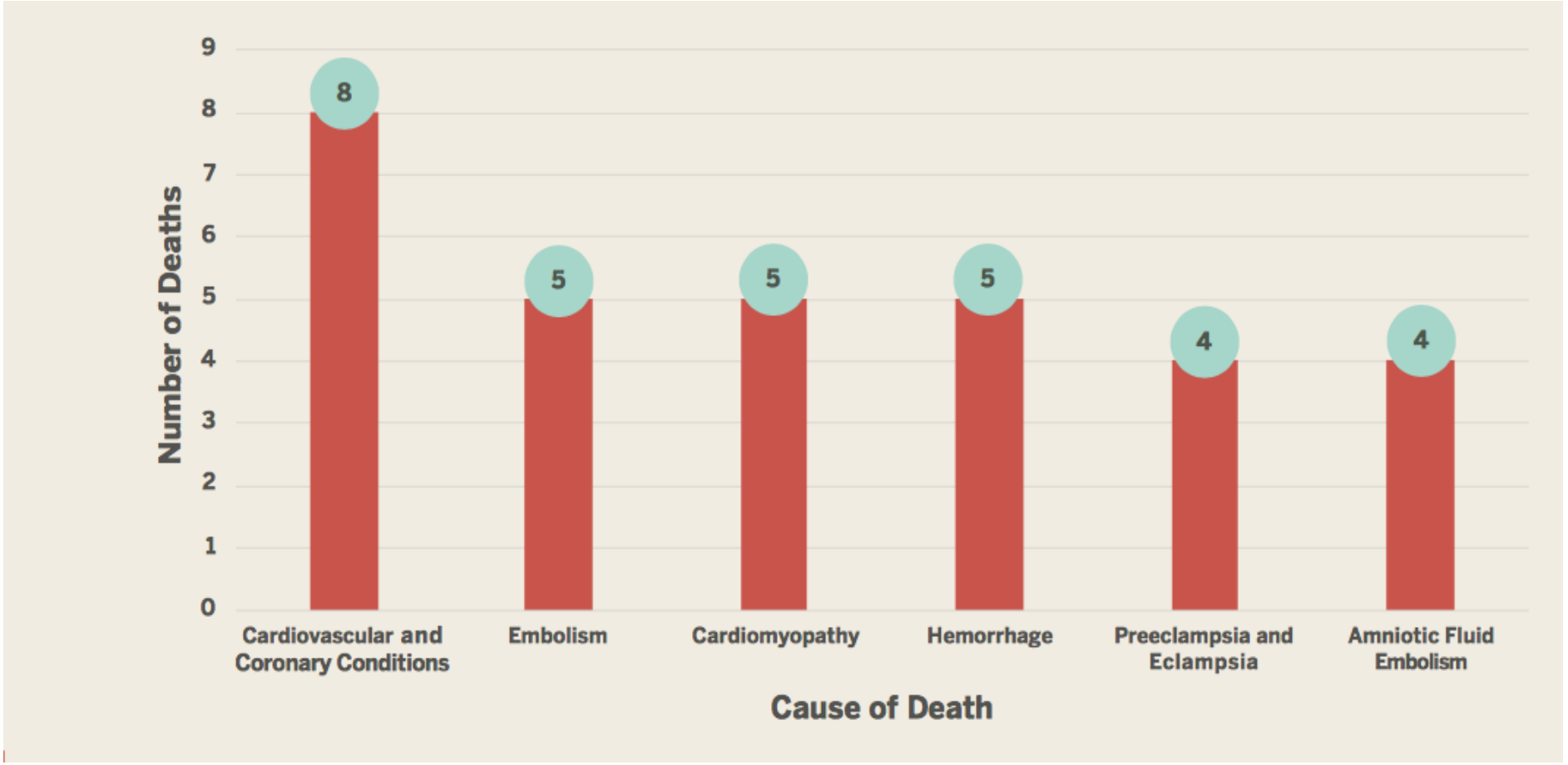
- Chronic Hypertension complicates up to 10% of pregnancies and increases risk of adverse outcomes 8 – 13 –fold
- Hypertensive Disorders of Pregnancy (gestational hypertension, preeclampsia) affect 5 – 7% of births and
- Incidence of preeclampsia increasing from 57.3 per 1000 delivery hospitalizations in 1994 to 86.5 per 1000 delivery hospitalizations in 2013.

Maternal mortality is rising in U.S.

- GA ranks the highest at 46.2 deaths per 100,00 live births



Cardiovascular conditions are the leading cause of preventable pregnancy-related deaths in Georgia



Preventability of cardiac deaths

- Approximately 28.1 - 50% of maternal cardiac deaths deemed preventable
- Delays to timely intervention involve:
  - Health providers (failure to consider cardiac disease)
  - Patient (increasing obesity, nonadherence)
  - Healthcare system (insurance barriers, availability of providers)

Defining Hypertensive Disorders in Pregnancy

Chronic Hypertension	SBP ≥ 140 or DBP ≥ 90 Pre-pregnancy, prior to < 20 weeks GA, > 12 weeks postpartum
Gestational Hypertension	SBP ≥ 140 or DBP ≥ 90 (> 4 hours apart) 20 weeks GA No proteinuria or systemic signs/symptoms
Preeclampsia	SBP ≥ 140 or DBP ≥ 90 AND New onset proteinuria (P:C ≥ 0.3 mg/dL, or ≥ 300mg/dL 24 hrs) OR Systemic signs or symptoms
Chronic Hypertension and Superimposed Preeclampsia	Chronic hypertension as defined above ≥ 20 weeks GA Worsening hypertension New onset proteinuria

Defining Hypertensive Disorders in Pregnancy

Preeclampsia with severe features	○ Systolic BP of 160 mm Hg or higher or diastolic BP of 110 mm HG or higher on 2 occasions at least 4 hours apart (unless antihypertensive therapy is initiated before this time) ○ Thrombocytopenia (platelet count less than 100,000/microliter) ○ Impaired liver function as indicated by abnormally elevated blood concentrations of liver enzymes (to twice normal concentration), severe persistent right upper quadrant or epigastric pain unresponsive to medication and not accounted for by alternative diagnoses, or both ○ Progressive renal insufficiency (serum creatinine concentration greater than 1.1 mg/dL or a doubling of the serum creatinine concentration in the absence of other renal disease) ○ Pulmonary edema ○ New-onset cerebral or visual disturbances ○ Eclamptic seizure

Pregnancy physiology causes cardiac stress

Table 1. Cardiovascular Changes in a Normal Pregnancy*

	First Trimester	Second Trimester	Third Trimester	Stage 1 Labor	Stage 2 Labor	Early Postpartum	3–6 months Postpartum
Cardiac output	↑5–10%	↑↑35–45%		↑30%	↑↑50%	↑↑↑60–80% immediately, then rapidly decreases within the first hour	Return to prepregnancy values
Heart rate	↑3–5%	↑10–15%	↑15–20%	During uterine contractions: ↑40–50%		↓5–10% within 24 hours; continues to decrease throughout the first 6 weeks	Return to prepregnancy values
Blood pressure	↓10%	↓5%	↑5%	During uterine contractions: ↑SBP 15–25% ↑DBP 10–15%		↓SBP 5–10% within 48 hours; may increase again between days 3–6 due to fluid shifts	Return to prepregnancy values
Plasma volume	↑	↑↑40–50%		↑	↑↑	↑↑↑500 mL due to autotransfusion	Return to prepregnancy values

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure.

*Hemodynamic changes that occur during pregnancy, labor, and postpartum (compared with prepregnancy) should be understood to identify early interventions (such as blood pressure control and diuresis) that may be needed to prevent clinical deterioration in a woman with cardiovascular disease.

Maternal/fetal risks associated with chronic HTN

Outcome	Incidence	Relative Risk[a] (Compared With No Chronic Hypertension)
Preeclampsia	25%–30%	3–4
Acute renal failure	0.59%	12–17
Stroke	0.27%	4–6
Pulmonary edema	0.15%	6–12
In-hospital maternal mortality	0.04%	3–11
Abruption	1.5%	2–3
Preterm birth <35 weeks	18–22%	3–4
Intrauterine growth restriction	11%	2–3
Perinatal death	6–8%	3–5

Early pregnancy prediction and risk reduction of preeclampsia

- Universal routine BP monitoring
- Risk-factor based identification
- Evaluate baseline end organ damage
- Low dose Aspirin
- Interventions

Risk factors for Preeclampsia

Risk Factor (vs. Reference Group)	Unadjusted Relative Risk (95% CI)
Nulliparity (vs. multiparity)	2.91 (1.28–6.61)
Maternal age ≥40 (vs. <40), nulliparous women	1.68 (1.23–2.29)
Maternal age ≥40 (vs. <40), multiparous women	1.96 (1.34–2.87)
Previous preeclampsia (vs. none)	7.19 (5.85–8.83)
Twin (vs. singleton pregnancy)	2.93 (2.04–4.21)
Preexisting diabetes (vs. none)	3.56 (2.54–4.99)
Antiphospholipid antibodies	9.72 (4.34–21.75)

Preexisting renal disease and Systemic lupus erythematosus as well

Risk factors for CV mortality

- Race/Ethnicity: black women have 3.4 times higher risk off death due from CV-related pregnancy complications
- Age: >40 years increases the risk of CV-related maternal death 30x over the risk for women < 20 years
- Hypertension: HDP affect 10% of pregnancies, contribute to 8-13-fold increased risk of MI and heart failure
- Obesity: 60% of CV-related deaths occur in women with prepregnancy BMI >35

Initial evaluation

- Assess baseline target organ damage:
  - Baseline cardiac evaluation (i.e. ECG)
  - Baseline liver function tests and platelets for reference
  - Baseline renal function with baseline serum creatinine and urine protein has both referent and prognostic value
- Consider evaluation for secondary hypertension if:
  - Hypertension is resistant to treatment
  - Hypokalemia
  - Strong family history of renal disease
  - Serum creatinine is 1.1 mg/dL or greater.

Association of baseline renal function with early onset severe preeclampsia

- Creatinine >0.75 mg/dL → 35% incidence of preeclampsia, 15% PreE w/ SF < 34 weeks
- Urine P:C > 0.12 →49% incidence of preeclampsia, 16% PreE w/ SF < < 34 weeks.

Relative risks and adjusted odds ratios for baseline serum creatinine using the Liu method cutoff

Outcomes	Cr < 0.75 mg/dL n = 584	Cr ≥ 0.75 mg/dL n = 171	RR (95% CI)	aOR (95% CI)
Severe PE < 34 weeks GA *	27 (4.6)	27 (15.7)	3.4 (2.1–5.7)	**3.5 (1.9–6.3)**
Severe PE, any GA *	76 (13.0)	46 (26.9)	2.1 (1.5–2.9)	**2.3 (1.5–3.5)**
PE, any GA *	126 (21.6)	61 (35.7)	1.7 (1.3–2.1)	**1.9 (1.3–2.7)**
Preterm birth < 35 weeks GA †	115 (20.0) ‡	44 (25.7) ‡	1.3 (1.0–1.8)	1.1 (0.7–1.7)
Indicated PTB<35 weeks GA †	92 (22.1) §	38 (30.2) §	1.4 (1.0–1.9)	1.2 (0.8–2.0)
Small for gestational age //	93 (16.0)	39 (22.8)	1.4 (1.0–2.0)	1.5 (0.9–2.6)
Primary neonatal composite ¶	82 (14.0)	27 (15.8)	1.1 (0.75–1.68)	1.1 (0.7–1.8)

Kuper et al, 2016

Investigational Approaches

- Historical risk factors only predict ~ 30 percent of women who will develop preeclampsia
- Laboratory/imaging tests have failed to reliably predict women at high risk of developing preeclampsia
  - Angiogenic markers (VEGF, PIGF, sEng, sFLT-1) sensitivity ranges 5 – 18% with 5% false positive rate
  - Second trimester elevated uterine artery Doppler resistance index best predicts risk of severe preeclampsia with 80% sensitivity, 78% specificity but no established normative standards by gestational age and no standards for Doppler sampling technique, definition of abnormal flow velocity waveform, and criteria for diagnosis
  - Risk prediction models: https://fetalmedicine.org/research/assess/preeclampsia/first-trimester

Interventions

- Modifiable approaches:
  - Pre-pregnancy weight reduction
  - Optimize glycemic control in diabetics
  - Aspirin prophylaxis

Low Dose Aspirin

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Aspirin versus Placebo in Pregnancies at High Risk for Preterm Preeclampsia

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- ASA 150mg prophylaxis to women at increased risk of preeclampsia associated with 62% reduced risk of preeclampsia prior to 36 weeks

SMFM Recommendations for Aspirin in pregnancy

Risk Level	Risk Factors	Recommendation
High[†]	• History of preeclampsia, especially when accompanied by an adverse outcome • Multifetal gestation • Chronic hypertension • Type 1 or 2 diabetes • Renal disease • Autoimmune disease (systemic lupus erythematosus, antiphospholipid syndrome)	Recommend low-dose aspirin if the patient has one or more of these high-risk factors
Moderate[‡]	• Nulliparity • Obesity (body mass index greater than 30) • Family history of preeclampsia (mother or sister) • Sociodemographic characteristics (African American race, low socioeconomic status) • Age 35 years or older • Personal history factors (eg, low birthweight or small for gestational age, previous adverse pregnancy outcome, more than 10-year pregnancy interval)	Consider low-dose aspirin if the patient has more than one of these moderate-risk factors[§]
Low	• Previous uncomplicated full-term delivery	Do not recommend low-dose aspirin

Antihypertensive therapy to reduce maternal and fetal morbidity and mortality

- Treatment in nonpregnant adults to target < 140/90 is associated with reduction in stroke, MI, heart/renal failure, and death
- Lack of data showing maternal or perinatal benefits of treatment during pregnancy
- Ongoing concerns regarding safety of treatment for the fetus
- Current recommendation is for antihypertensive treatment for severe BP (>160/105 mmHg) or evidence of end organ damage

Target BP during pregnancy

- The Control of Hypertension in Pregnancy Study (CHIPS) 2015
  - Tight control (DBP < 85) vs Less Tight Control (DBP < 105)
  - Tight control had lower rates of severe maternal hypertension
  - Tight control had increased rates of small for gestational age neonates
  - No difference in primary outcome: pregnancy loss, need for >48 hour NICU admission
  - No difference in serious maternal complications (uncontrolled hypertension, stroke, pulmonary edema, renal failure, transfusion, development of preeclampsia, placental abruption)
- If on BP meds, target ~ 130 - 140/85 - 90

Common regimens used in pregnancy

- Labetalol: The initial dose is 100 mg twice daily, increasing to a maximum dose of 2.4 g/d in divided doses (usually 400 to 600 mg twice or three times daily)
- Nifedipine: Doses 30 to 120 mg of a sustained-release form is given once daily. If patients do not tolerate the single dose, the dose can be divided into twice daily
- Methyldopa: Doses of 500 to 1500 mg twice to three times daily to a maximum dose of 3 g/d

Obstetric management

- Surveillance for the development of superimposed preeclampsia
- Monitoring fetal wellbeing
- Timing of delivery

Surveillance for the development of superimposed preeclampsia

- Associated with worse maternal and fetal prognoses than either condition (cHTN or PET) alone
- Diagnosis is subtle and “tests the skills of the clinician”
- Suspected with worsening blood pressures or new onset/ worsening proteinuria after 20 weeks +/- objective organ involvement

Diagnostic Evaluation

- Symptoms: Headache, tinnitus, dizziness, scotomata, nausea, vomiting, epigastric pain
- SBP ≥ 140 or DBP ≥ 90
- Proteinuria (P:C ≥ 0.3 mg/dL, or ≥ 300mg/dL 24 hrs) OR
- Laboratory and physical exam
  - Thrombocytopenia
  - Impaired liver function
  - Progressive renal insufficiency
  - Pulmonary edema
  - New-onset cerebral or visual disturbances
  - Hyperreflexia
  - Eclamptic seizure

Accurate BP measurement

- Equipment
  - Mercury sphygmomanometer is the gold standard
  - Validated equivalent automated equipment
  - Correct size cuff: width of bladder is 40% of circumference and encircles 80% of arm
- Patient preparation
  - Sitting or semi-reclining position
  - Back supported and arm at heart level
  - Patient sits quietly for 5 minutes prior to measurement

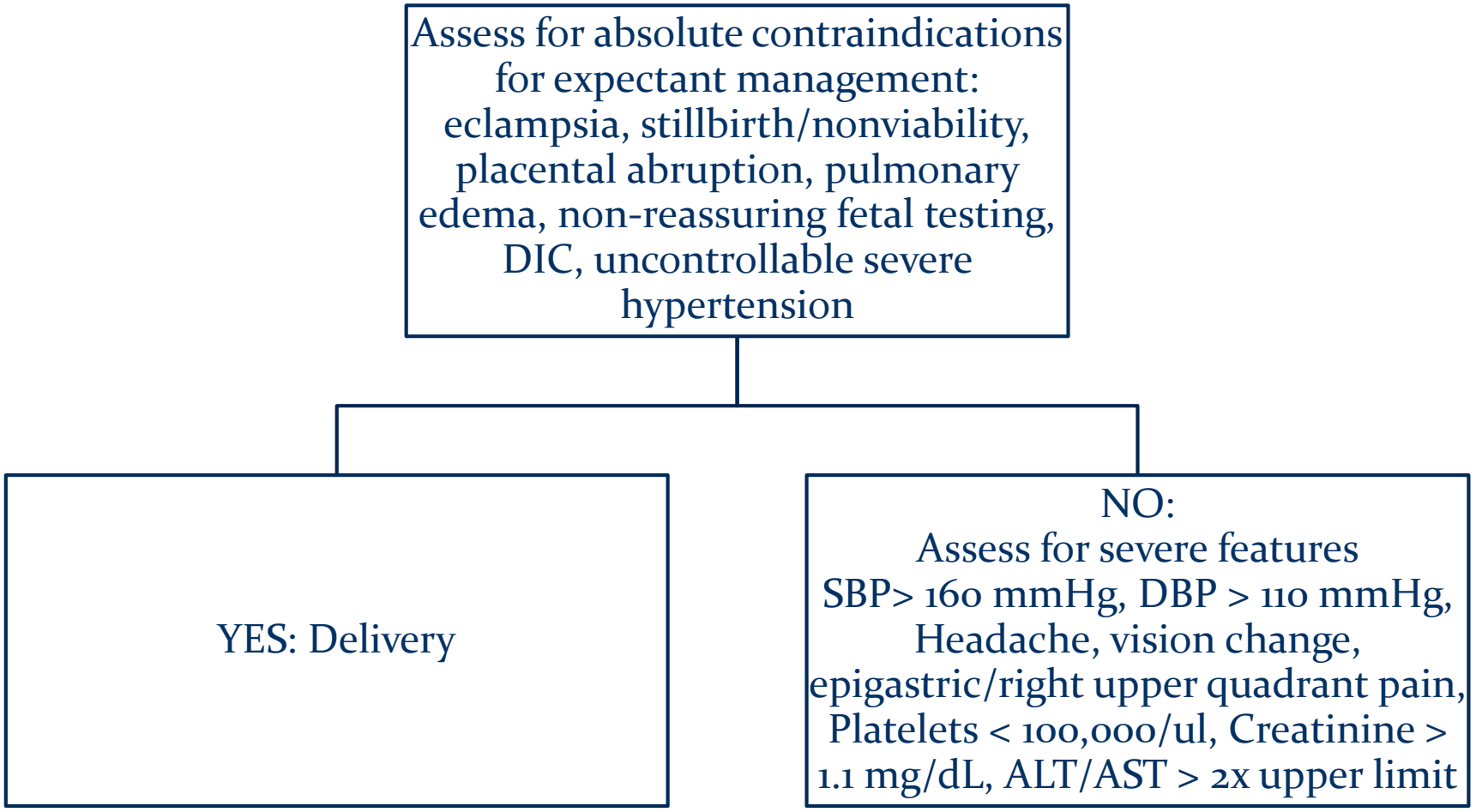
Monitoring fetal wellbeing

- Pregnancies complicated by chronic hypertension are at a 2-3x increased risk for stillbirth
- Serial growth ultrasounds to monitor onset FGR
- 1-2x weekly testing after 28 – 32 weeks

Timing of delivery in women with cHTN

- Delivery at 36 weeks → associated with a significant increase in the risk for perinatal morbidity and mortality
- Delivery after 39 weeks → associated with increased risk for preeclampsia
- Nadir of morbidity when delivery was planned between 38 and $38^{6/7}$ weeks
- Recommendation is for planned delivery of pregnancies complicated by chronic hypertension 38 to $39^{6/7}$ weeks

Antepartum management



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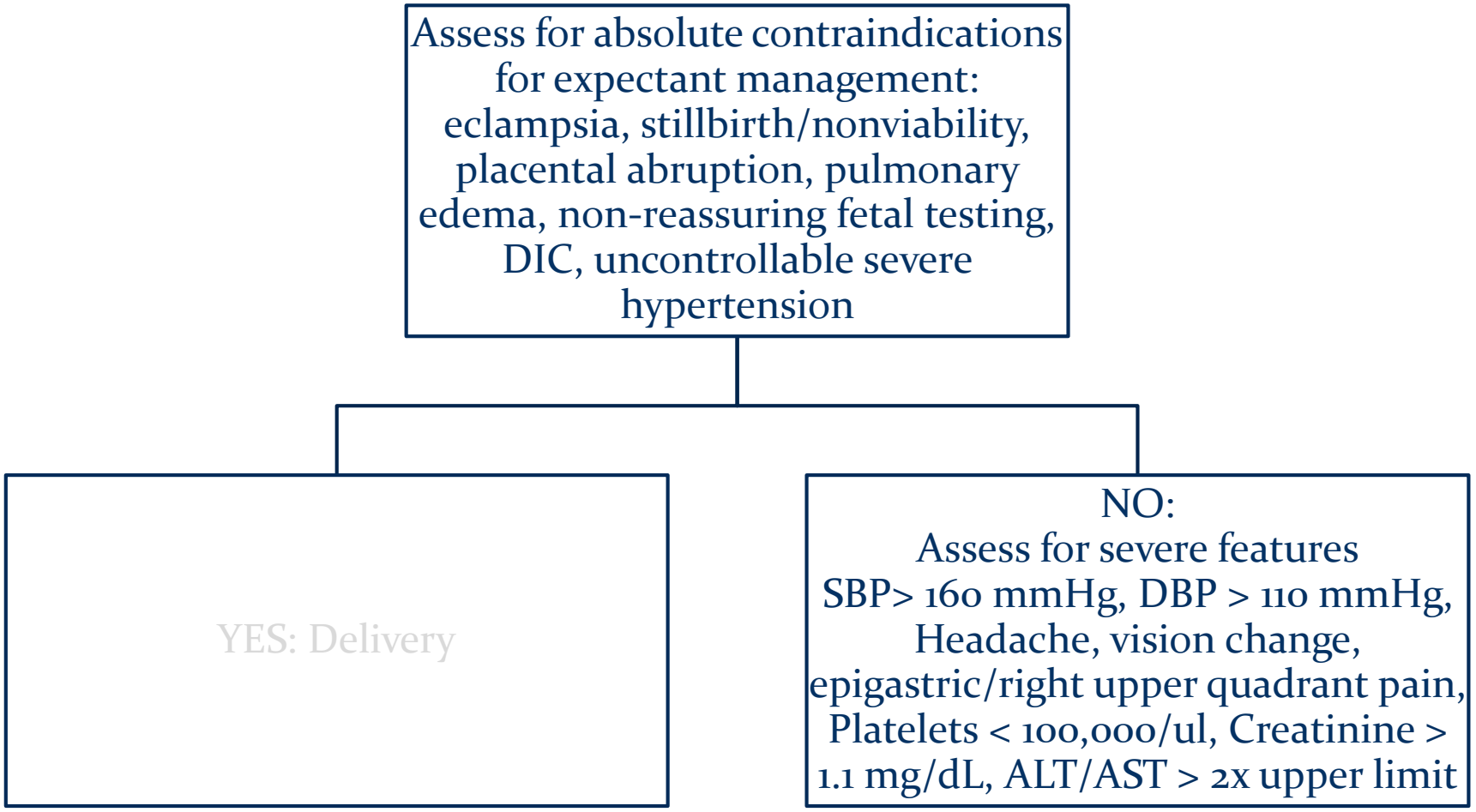

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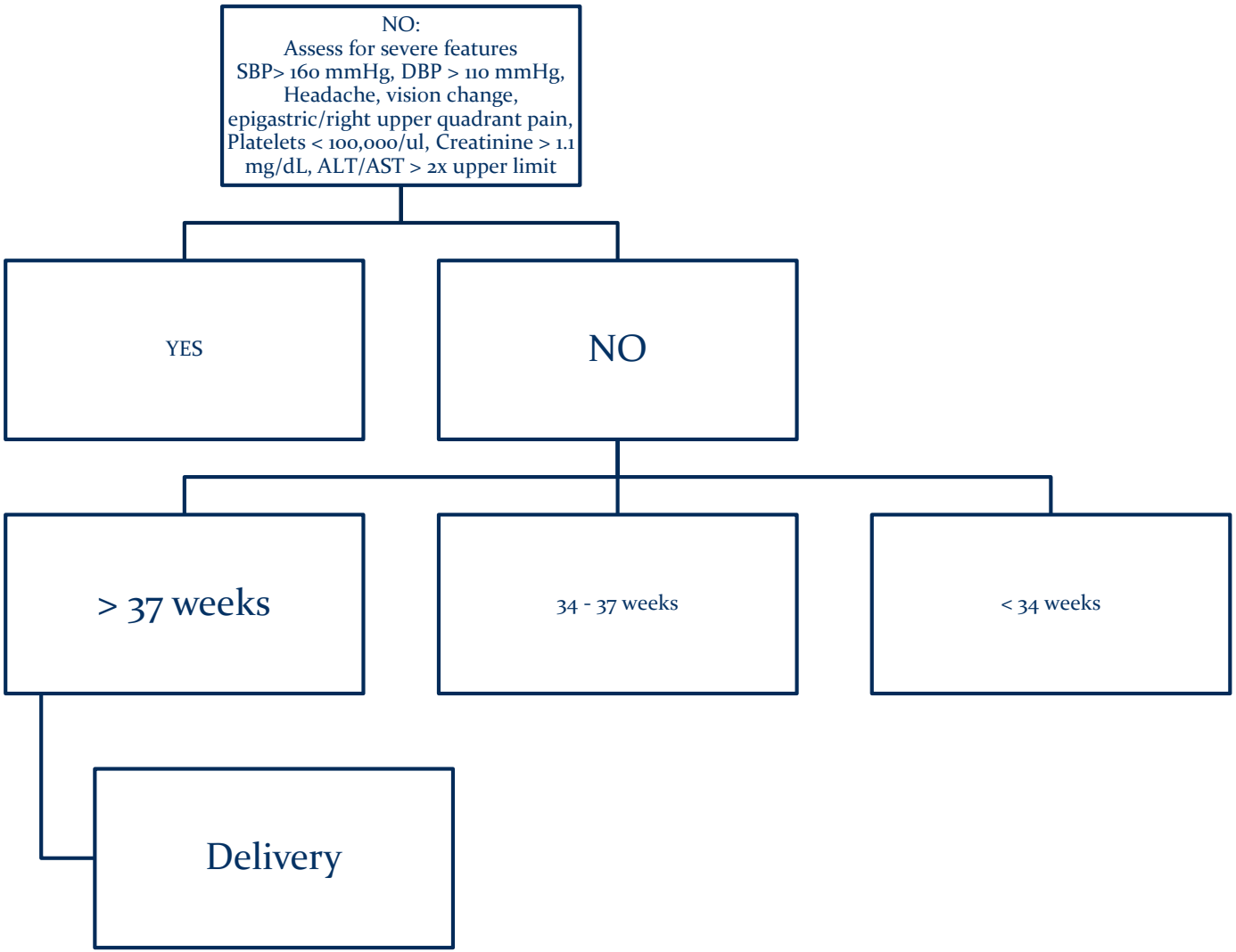

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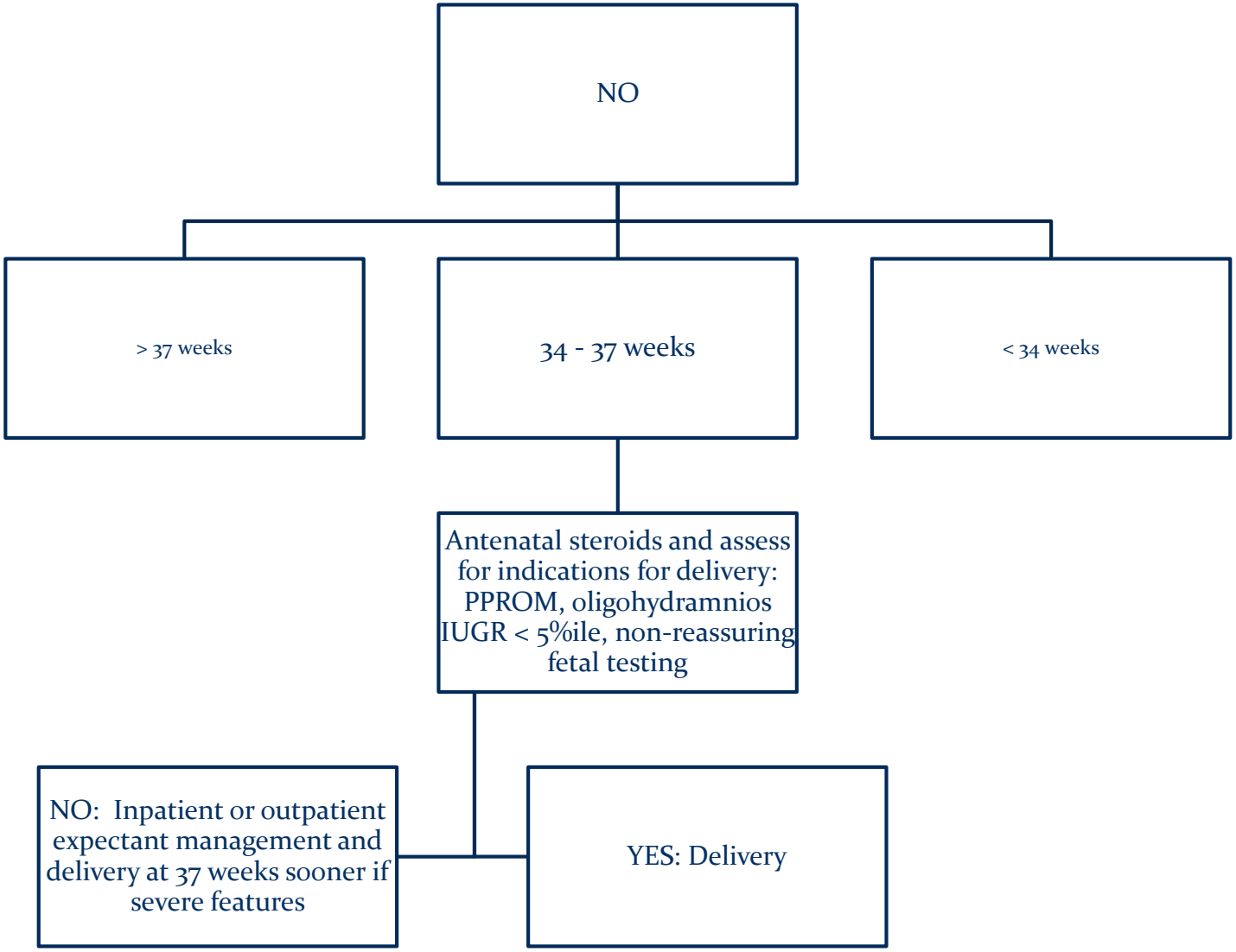

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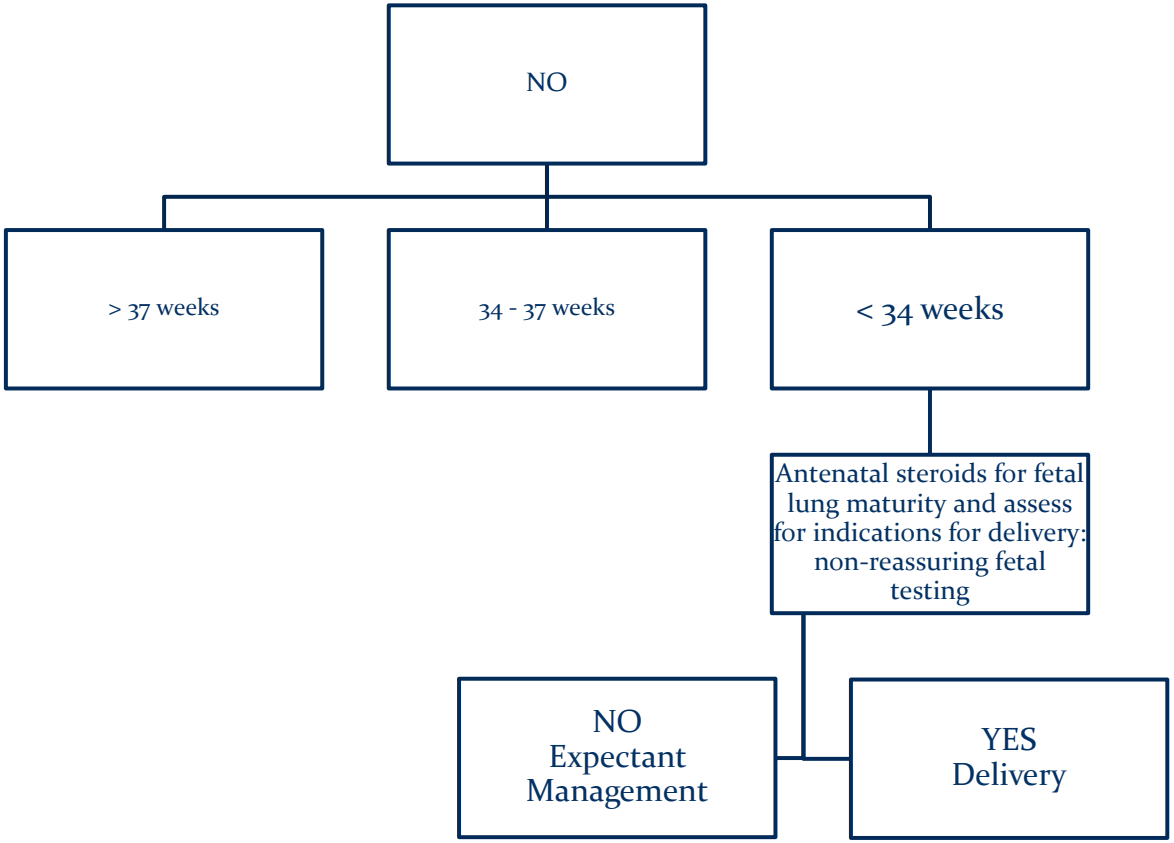
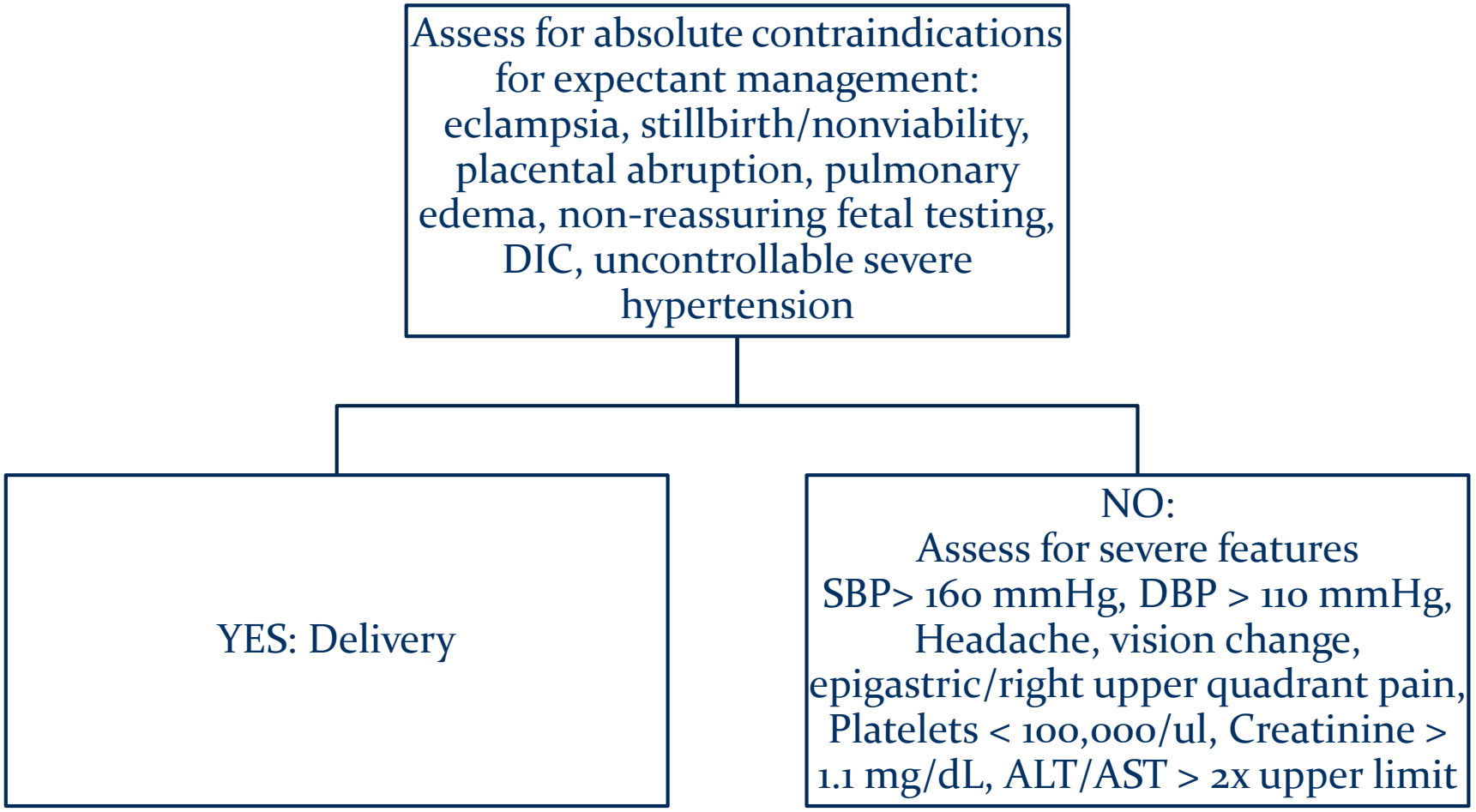


Expectant management: goal delivery at 37 weeks, sooner if development of non-reassuring fetal testing or severe features

Antepartum management



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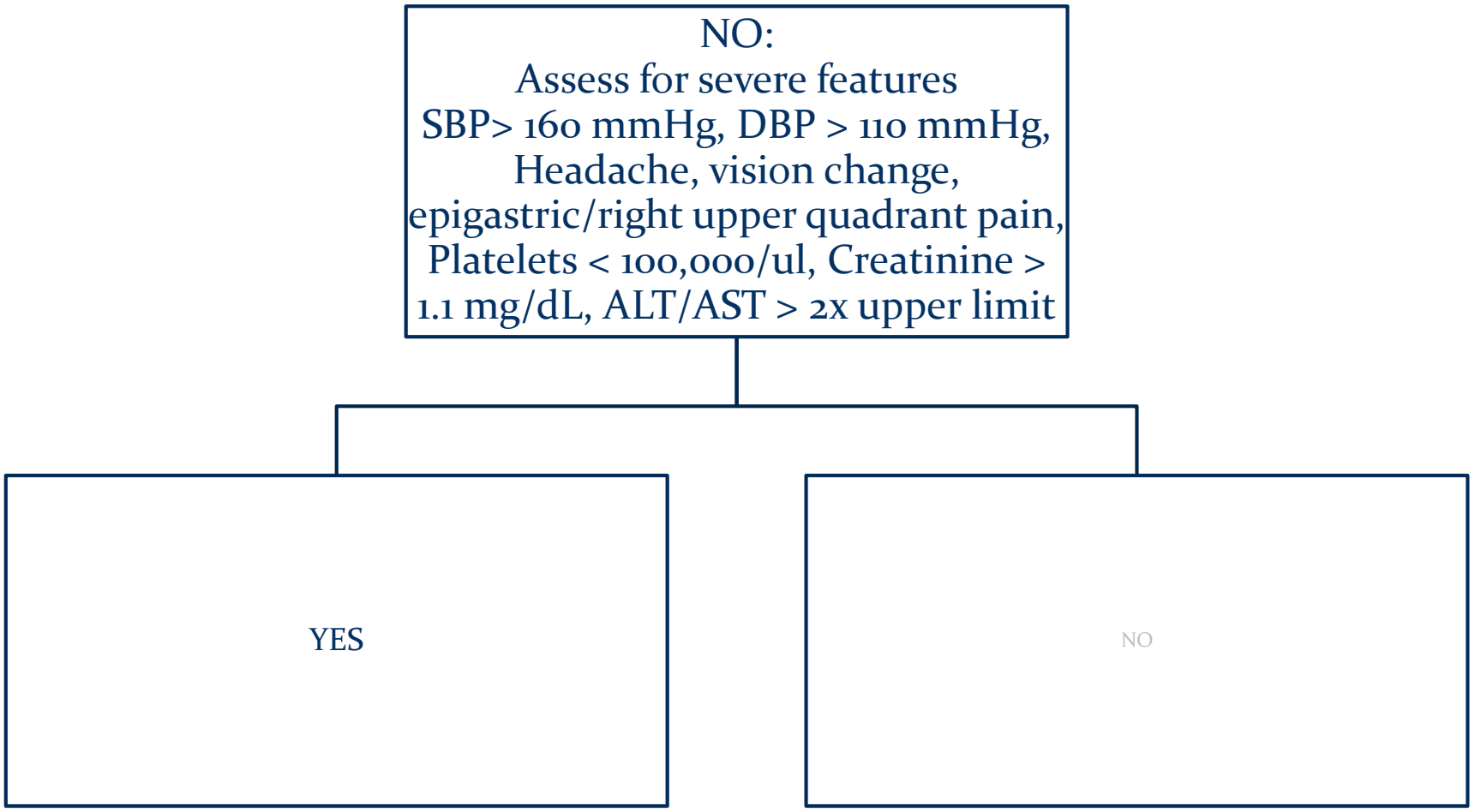

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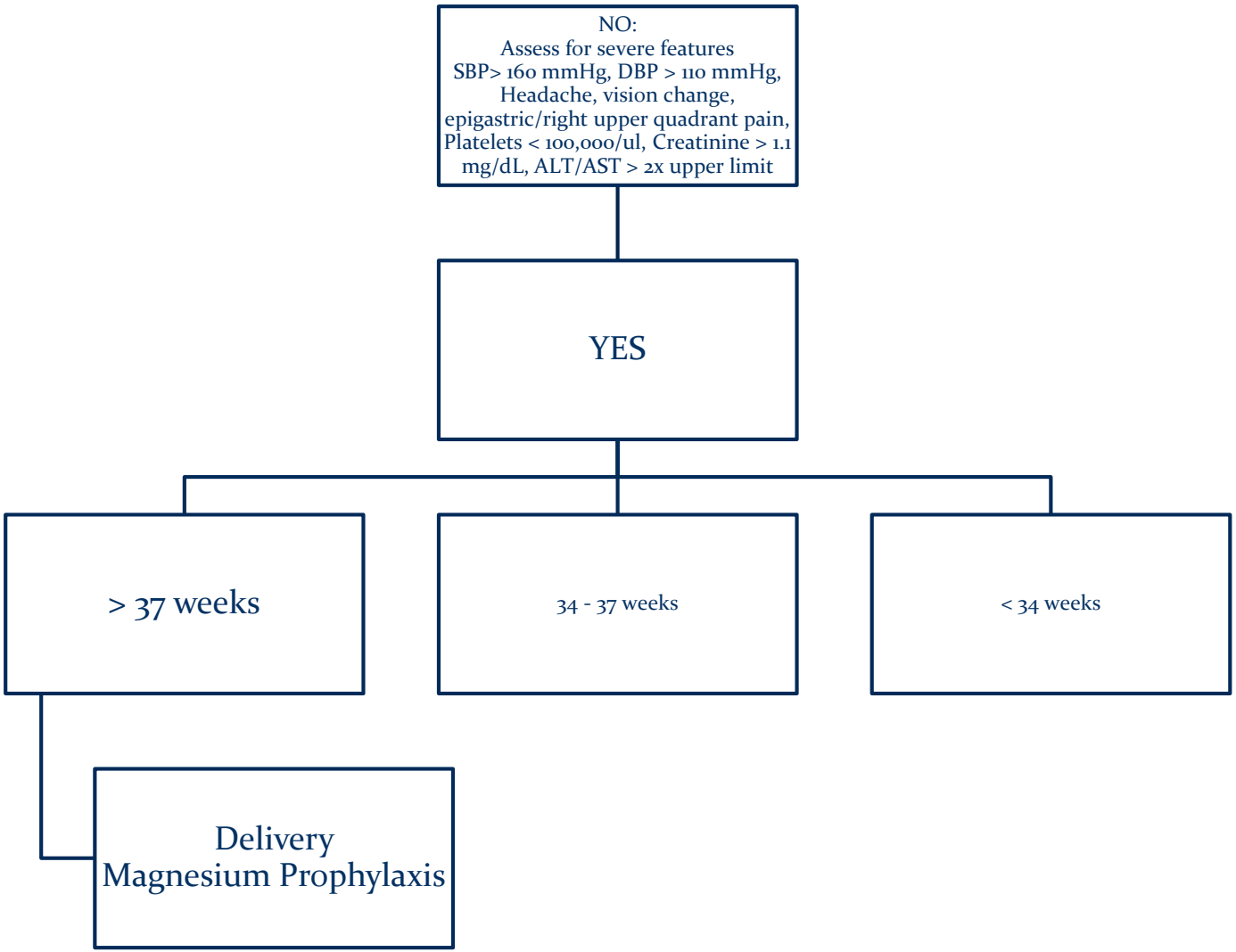

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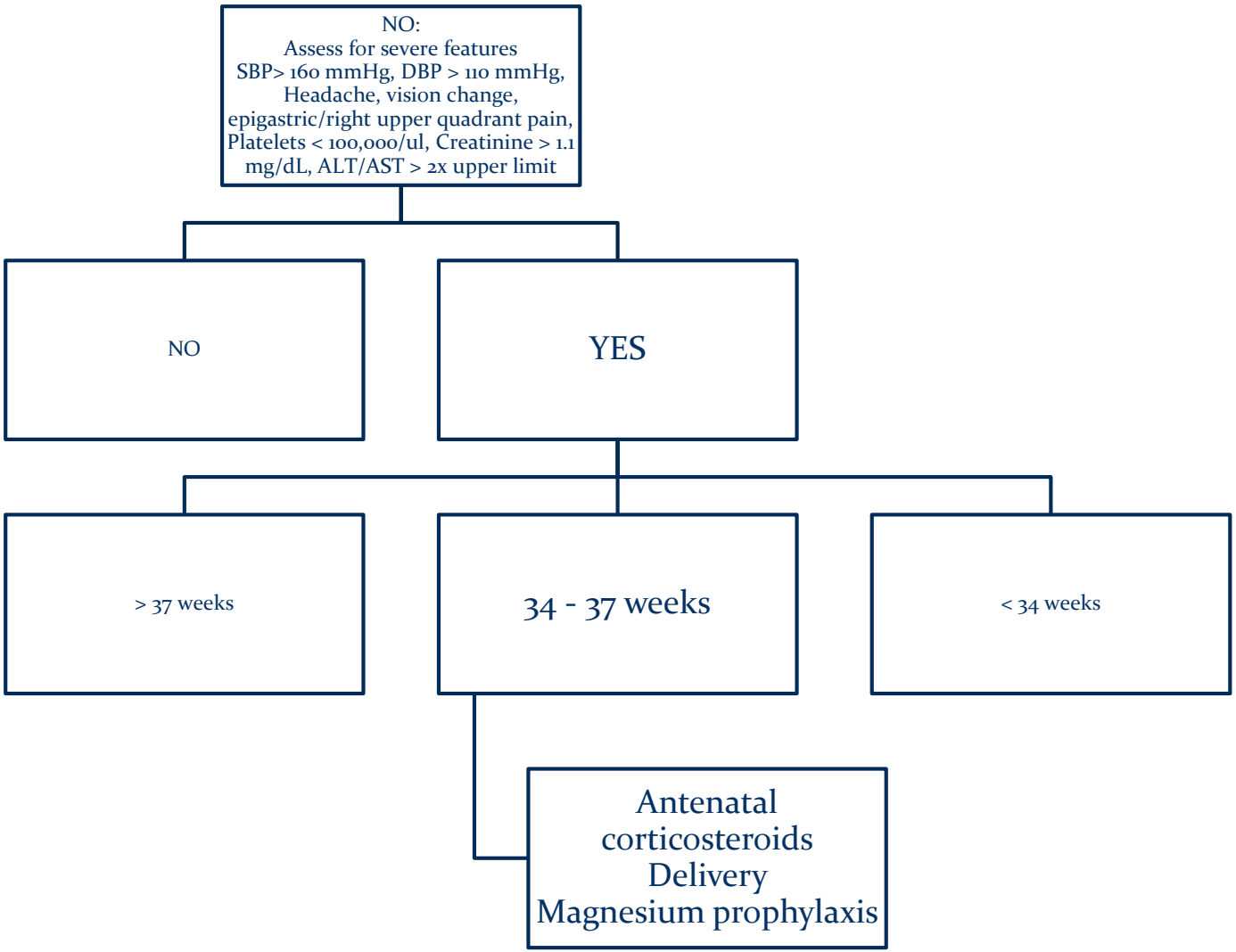

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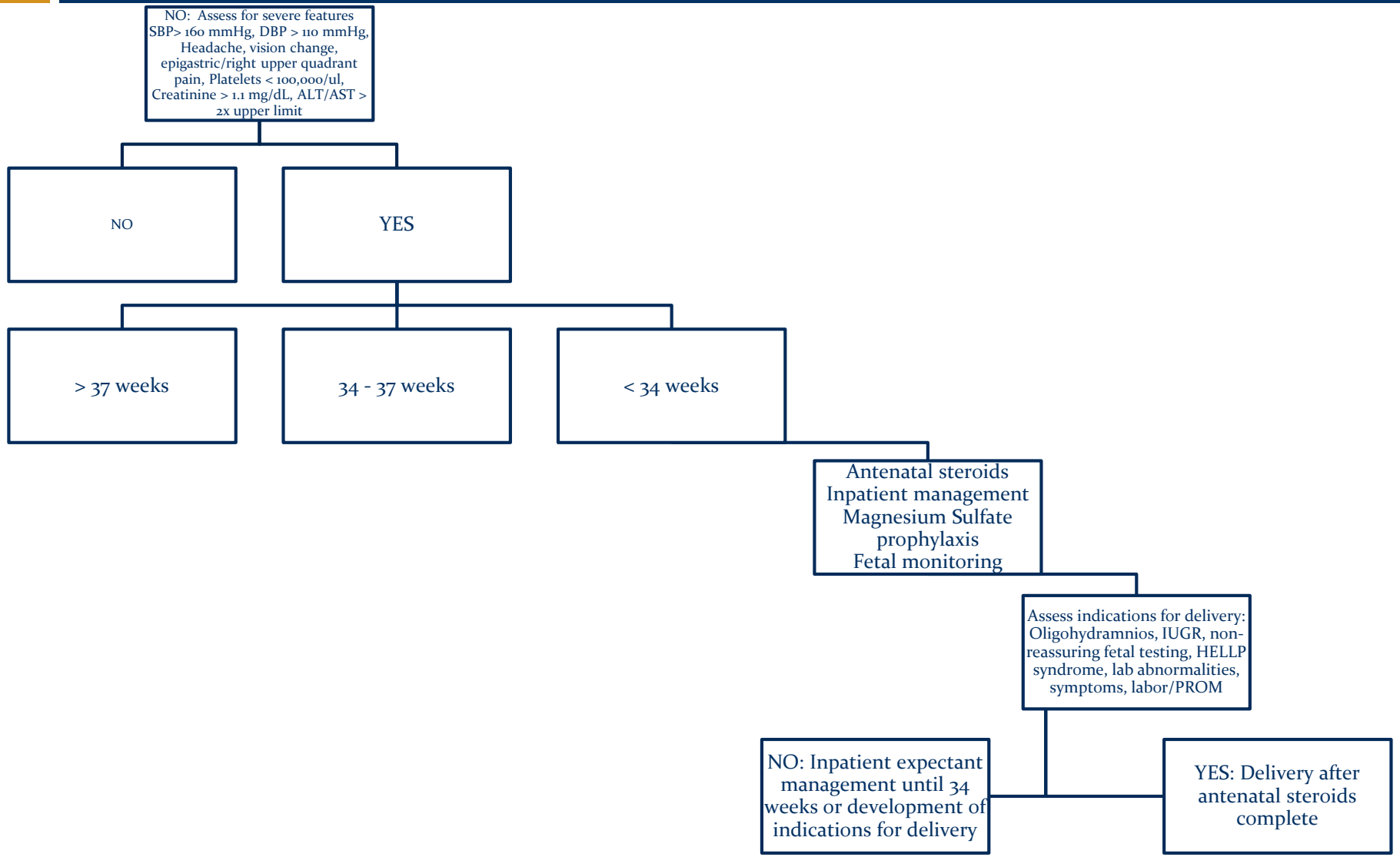
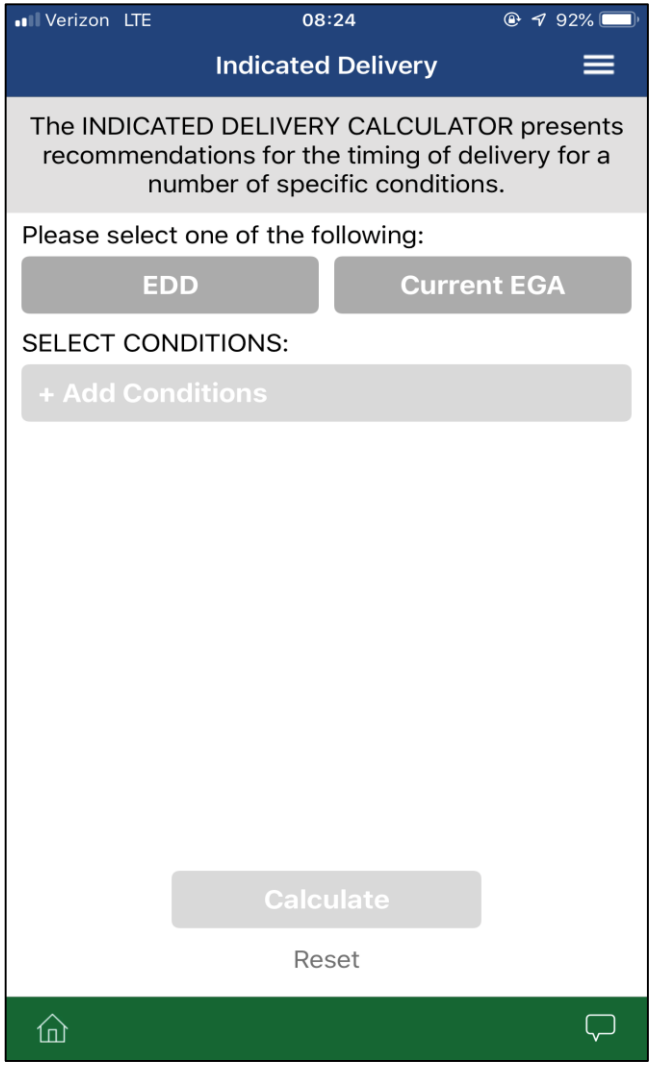


ACOG When To Deliver Smartphone App



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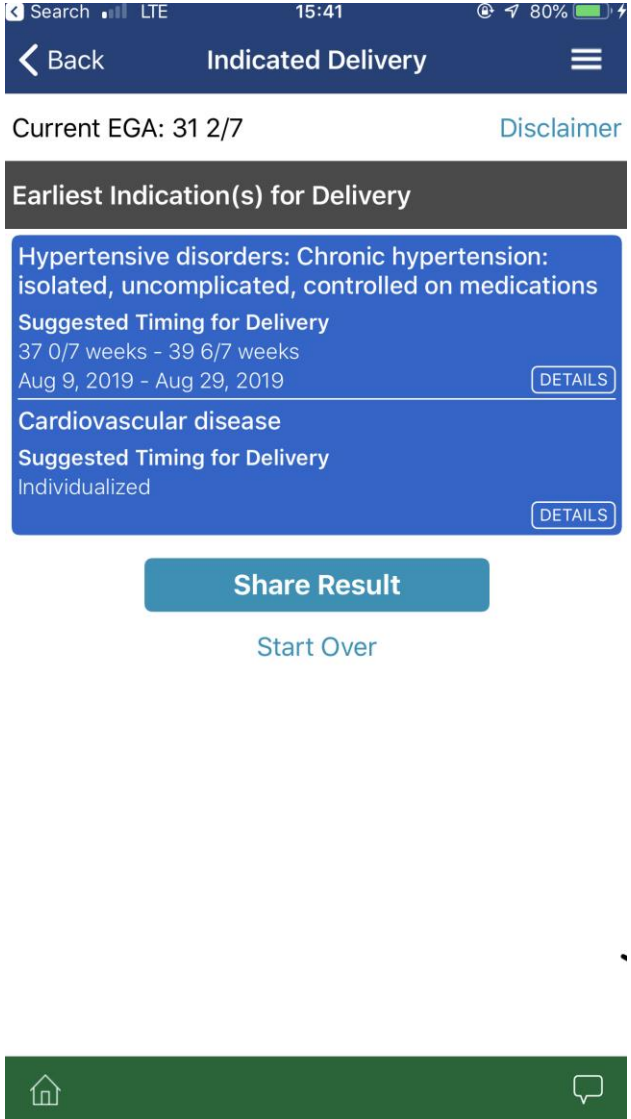


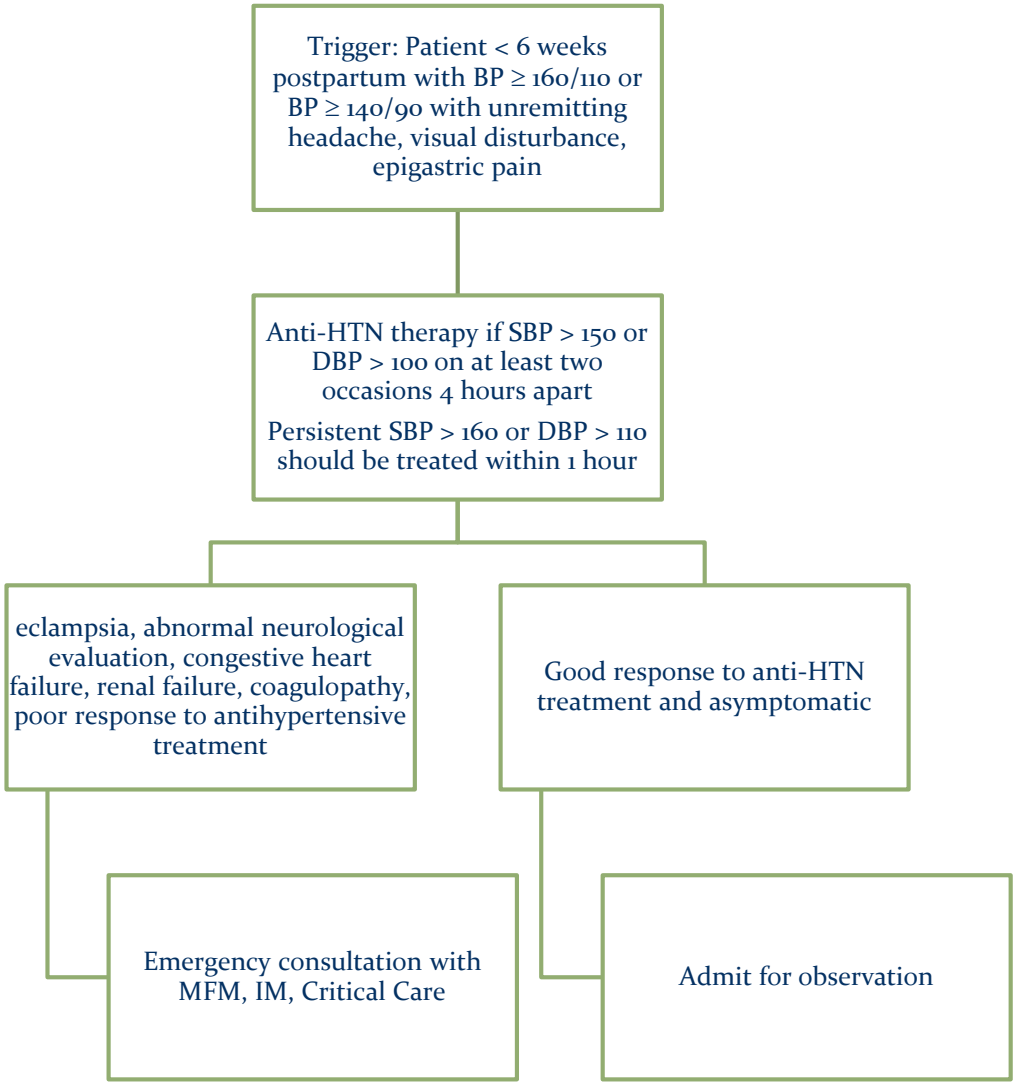
Intrapartum Management

- Routine administration of parenteral magnesium sulfate for seizure prophylaxis is recommended in women with preeclampsia with severe features
- IV antihypertensive therapies for severe hypertension
- Vaginal delivery, with cesarean reserved for the usual obstetric indications.
  - The decision to expedite delivery in the setting of severe preeclampsia does not mandate immediate cesarean birth
  - Success rate for all inductions less than 34 weeks is over 60%
  - For those at 24 to 28 weeks being induced for preeclampsia, the success rate is 39%

Postpartum presentation of severe hypertension / preeclampsia

- Approximately 75% of deaths secondary to hypertensive disorders of pregnancy occur after birth, with 41% occurring > 48 hours postpartum
- Up to half of woman diagnosed with postpartum preeclampsia are not diagnosed in the antepartum or immediate peripartum period
- Most women with postpartum preeclampsia present first to emergency department or primary care
- Timely recognition and timely treatment is necessary for preventing maternal morbidity and mortality

Management of postpartum preeclampsia



Discharge Planning

- ALL PATIENTS
  - Receive information on preeclampsia warning signs and symptoms in culturally competent language
  - Emphasize the importance of contacting a provider
- PATIENTS WITH PREECLAMPSIA
  - BP monitoring 72 hours after delivery
  - Outpatient surveillance (i.e. visiting nurse) within 3 – 5 days after discharge and again 7 – 10 days after discharge

*Maternal blood pressure has been shown to decrease for the first 48 hours and then increase with a peak 3–6 days after birth, thus peak blood pressures are likely to occur after most women have been discharged home

Hypertension and Pregnancy: Implications for future cardiovascular health

- The American Heart Association identifies a history of hypertension during pregnancy as an established risk factor for long term cardiovascular health
  - 50% will develop chronic hypertension 2 – 5 years after the affected pregnancy
  - Elevated risk for cardiovascular disease and renal disease
- CV Risk calculators (i.e. Framingham, ASCVD, Reynolds) do not yet incorporate adverse pregnancy outcomes into risks, however increasing recommendations for enhanced screening
  - Annual screening of blood pressure, lipids, and fasting glucose
- Ongoing area of investigation

Summary

- The prevalence of pregnancies complicated by hypertension are increasing
- Complications arising from hypertensive disorders of pregnancy are among the leading causes of preventable severe maternal morbidity and mortality.
- Timely and appropriate surveillance, diagnosis, and management has the potential to significantly reduce hypertension-related complications.
- Patients whose pregnancies are complicated by HDP should be aware of increased lifetime risk and undergo annual screening

Thank you!

For questions, please contact me at ntjose2@emory.edu