



Management of Cardiovascular Risk Factors during Pregnancy

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Disclosures

- Research support from Amgen, Boehringer Ingelheim, Cleerly, Egglund's Best, Eli Lilly, Novartis, Novo Nordisk, Verily Life Sciences
- Consultation/Advisory Panels for Boehringer Ingelheim, CRISPR Therapeutics, Eli Lilly, AstraZeneca, Merck, Novartis, and Novo Nordisk.
- Executive Committee member for trials sponsored by Novo Nordisk and by Amgen.



Why does CV health during pregnancy matter?



- CVD is the leading cause of death in peri- and post-partum women (26.5% of US pregnancy-related deaths)¹
- CV risk factors during pregnancy have strong implications for future CVD in women²
- CV risk factors lead to worse pregnancy outcomes (e.g. preterm delivery, pregnancy loss)²
- Long-term increased risk for CV risk factors and CVD in offspring³

1. ACOG Practice Bulletin No. 212: Pregnancy and Heart Disease. *Obstet Gynecol.* 2019;133(5):e320-e56
2. Parikh et al. *Circulation* 2021; 143.
3. Turbeville et al. *AJP Renal Physiol.* 2020; 318.



Outline

- Obesity
- Hyperlipidemia
- Diabetes
- Hypertension



Obesity

- >50% of pregnant women have overweight or obesity
 - Greater burden among Black and Hispanic women
- Associated with increased complications:

During pregnancy	During labor and delivery	Postpartum/long-term complications
Spontaneous miscarriage	Difficult external fetal monitoring	Postpartum hemorrhage
Birth defects	Cesarean delivery	Wound infection
Limitations to ultrasound	Decreased success of vaginal birth after cesarean delivery	Obesity in offspring
Gestational diabetes	Difficult anesthesia	
Hypertensive disease		
Stillbirth		
Fetal growth abnormalities		

1. Kominiarek et al. Am J Perinatol. 2016, 33: 43.
2. ACOG Practice Bulletin 230. Obesity in Pregnancy



Weight Gain during Pregnancy

- 46% of women with obesity have excessive weight gain during pregnancy

Table 4. Recommendations for Total and Rate of Weight Gain during Pregnancy by Pregnancy Body Mass Index

Prepregnancy Weight Category	Body Mass Index*	Recommended Range of Total Weight Gain (lb)	Recommended Rates of Weight Gain [†] in the Second and Third Trimesters (lb) (Mean Range [lb/wk])
Underweight	Less than 18.5	28–40	1 (1–1.3)
Normal weight	18.5–24.9	25–35	1 (0.8–1)
Overweight	25–29.9	15–25	0.6 (0.5–0.7)
Obese (includes all classes)	30 and greater	11–20	0.5 (0.4–0.6)

1. ACOG Practice Bulletin 230. Obesity in Pregnancy



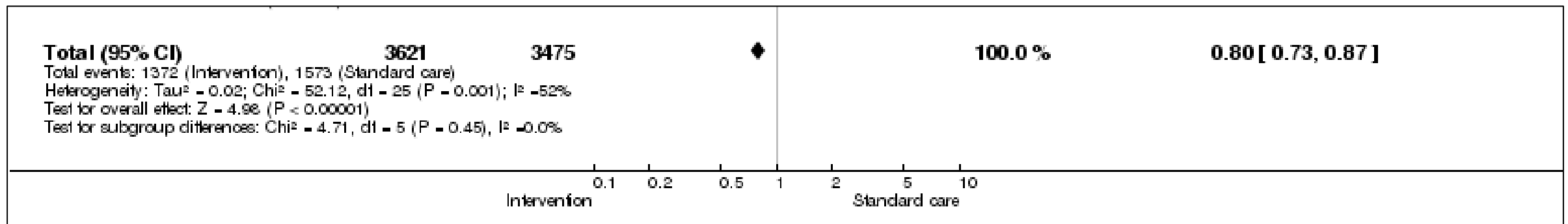
Management of Obesity in Pregnancy

- Weight management *prior* to pregnancy is key!
 - BMI $<30\text{kg/m}^2$, or at least 10% weight loss, is recommended prior to conception for risk reduction
- During pregnancy
 - Lifestyle modification is first line
 - Anti-obesity medications not recommended
 - Metformin does not improve pregnancy or birth outcomes in those without diabetes



Management of Obesity in Pregnancy

- Cochrane meta-analysis of 49 randomized trials in 11,444 women
- Interventions: diet only (low glycemic index or low calorie), exercise only (supervised or unsupervised), vs. both
- Outcome: Excessive weight gain during pregnancy





Management of Obesity *between* Pregnancies

Opinion

VIEWPOINT

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Obesity Management in Women of Reproductive Age

The prevalence of obesity has continued to increase among women of reproductive age in the US and has serious implications for pregnancy health.^{1,2} Nearly 25% of women in the US who become pregnant have obesity, with the highest prevalence among underrepresented racial and ethnic groups.² Women with obesity-related adverse pregnancy outcomes (APOs), such as gestational diabetes (GD) and hypertensive disorders of pregnancy (HDP), from prior pregnancies may benefit from aggressive weight management during the postpartum and interpregnancy period. However, current US obesity guidelines do not consider pregnancy history or intention or account for obesity-related APOs in the decision to escalate obesity therapies. This omission represents a potentially missed opportunity to initiate aggressive weight loss intervention and reduce postpartum weight retention, which is strongly associated with incident and persistent obesity, as well as prepregnancy obesity for future pregnancies.

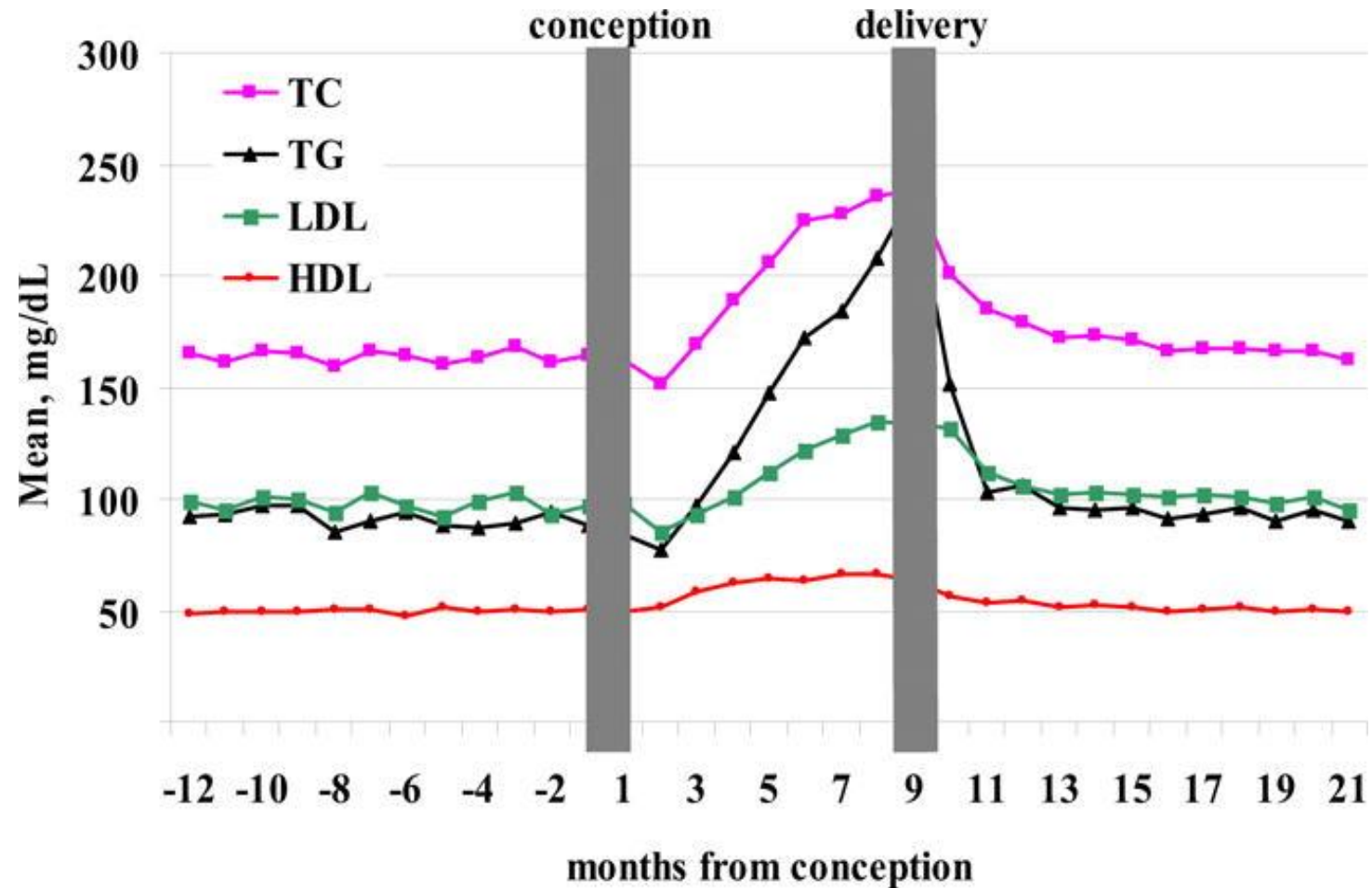
Obesity guidelines should specifically consider women of reproductive age and their pregnancy history because (1) this life stage is often the time of greatest weight gain, (2) aggressive weight loss interventions among women with obesity may reduce incident and recurrent APOs, and (3) in utero exposure to obe-

diovascular disease.⁴ In general, an obesity-related comorbidity assessment is based on whether obesity is a major modifiable risk factor for the condition and whether the condition is associated with increased morbidity or mortality. For an APO to qualify as an obesity-related comorbidity based on this rationale, obesity must be a modifiable risk factor for the APO (meaning weight loss should result in a reduction of the APO risk or recurrence) and the APO must be associated with morbidity or mortality.

Several pregnancy complications either have obesity as an associated modifiable risk factor (eg, cesarean delivery and large for gestational age infant)¹ or are associated with cardiovascular disease (eg, intrauterine growth restriction, preterm birth, and small for gestational age infant) (eTable in the [Supplement](#)).⁵ Conversely, GD and HDP meet both criteria and are subsequently classified as obesity-related comorbidities. The incidence of GD, which affects 6% to 7% of pregnancies in the US, increases with higher prepregnancy BMI. An analysis of National Vital Statistics System birth data⁶ showed that 3.6% of 1 699 751 women with a normal prepregnancy BMI (range, 18.5-24.9) developed GD vs 6.1% of 997 977 women with an overweight prepregnancy BMI (range, 25.0-29.9), 8.8% of



Normal Lipid Levels during Pregnancy



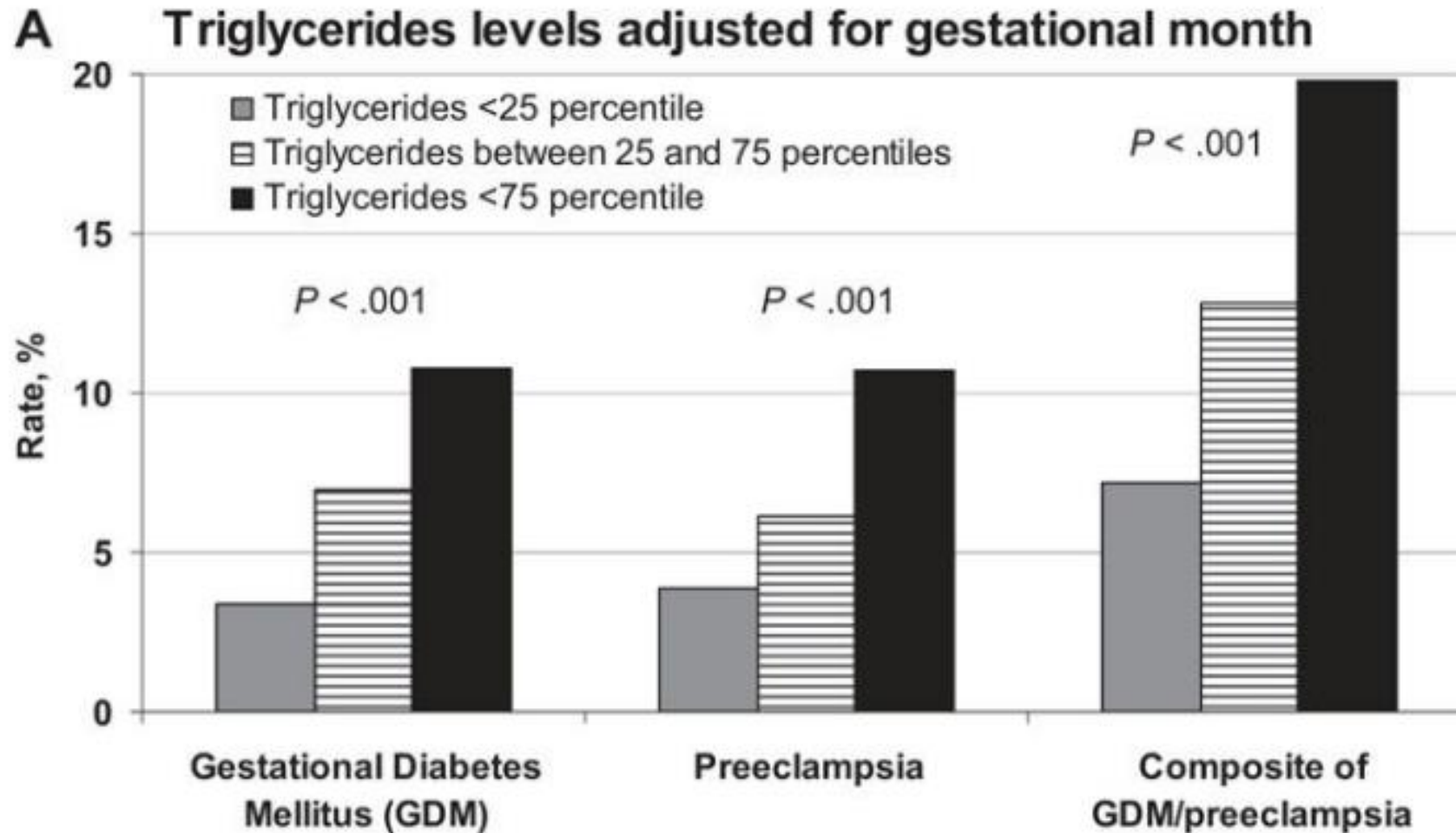


Management of Lipids during Pregnancy

- Only address in women with prior:
 - Hypertriglyceridemia
 - FH
 - ASCVD
- In all other women, no need to routinely check lipids levels during pregnancy



Hypertriglyceridemia in Pregnancy





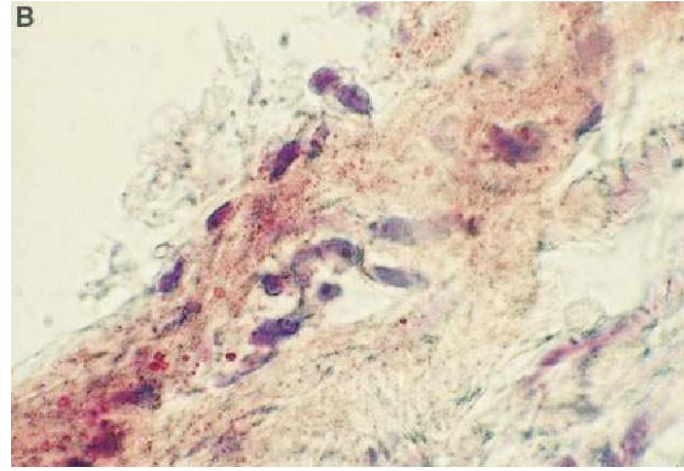
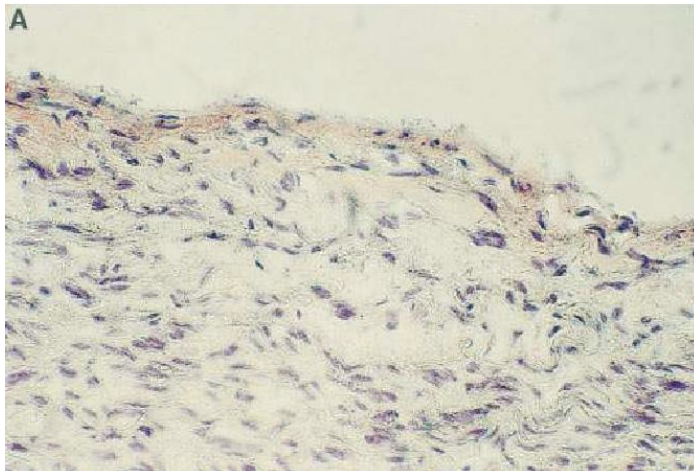
Hypertriglyceridemia in Pregnancy

- TG >1000 mg/dL → pancreatitis, hyperviscosity syndrome, severe preeclampsia
 - High Risk women: pre-pregnancy TG >500 mg/dL or familial hyperTG
- No guidelines!
- Check lipids at least every trimester + 6w postpartum
 - <500 mg/dL: excessive weight gain prevention
 - \geq 500 mg/dL: very low-fat diet, omega-3 FAs, fenofibrate (2nd trimester)



FH in Pregnancy

- Similar % rise in LDL-C as non-FH women, but higher absolute increase
- Norwegian registry with 2319 births in 1093 women with FH → no increased risk of preeclampsia, gestational hypertension, gestational diabetes

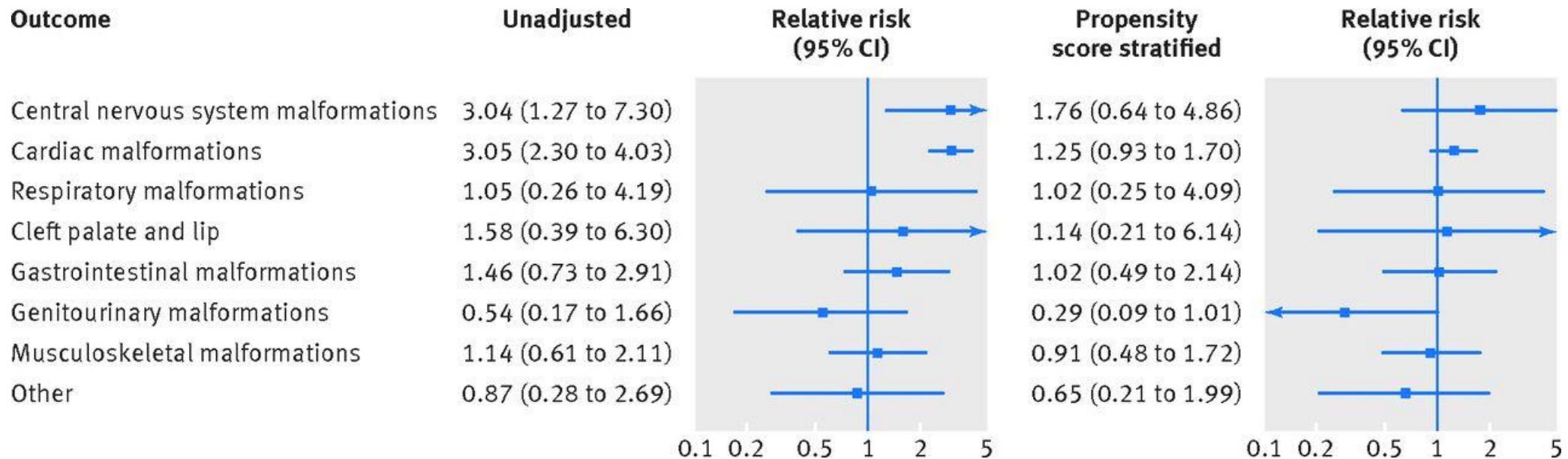




Statins during Pregnancy

Table 2 | Risk for major congenital malformations in infants of women who did or did not use statins during first trimester. Medicaid Analytic eXtract 2000–07

Statin use	Full cohort			Relative risk (95% CI)		
	Total No	No of congenital malformations	Risk (%)	Unadjusted	Stratified on diabetes	Propensity score stratified
No statins	885 844	31 416	3.55	Referent	Referent	Referent
Statins	1152	73	6.34	1.79 (1.43 to 2.23)	1.34 (1.07 to 1.68)	1.07 (0.85 to 1.37)





Statins during Pregnancy

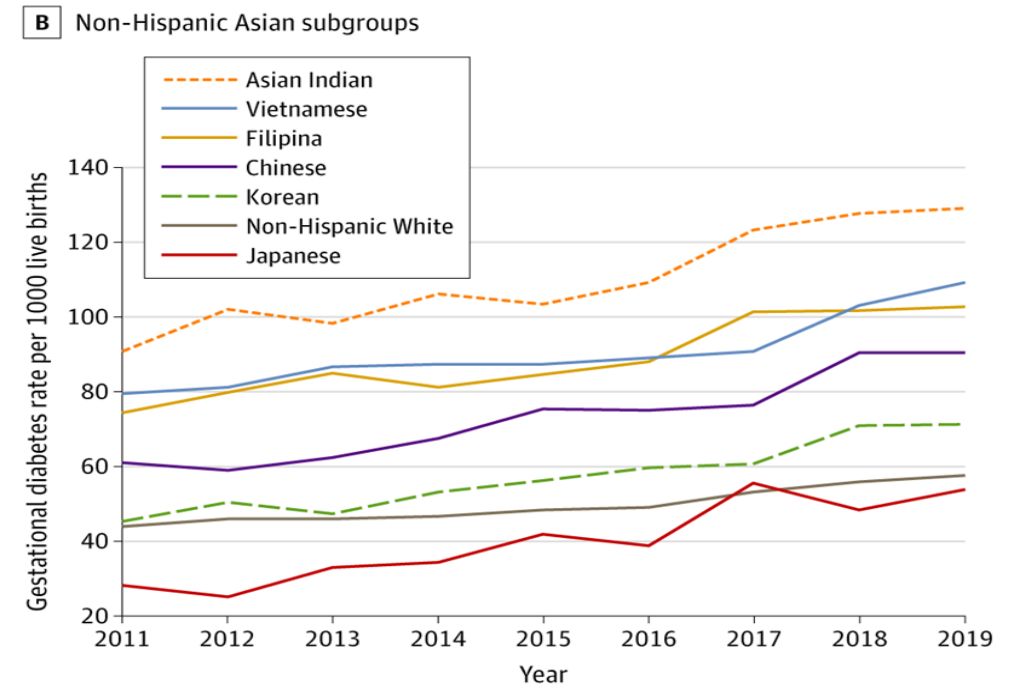
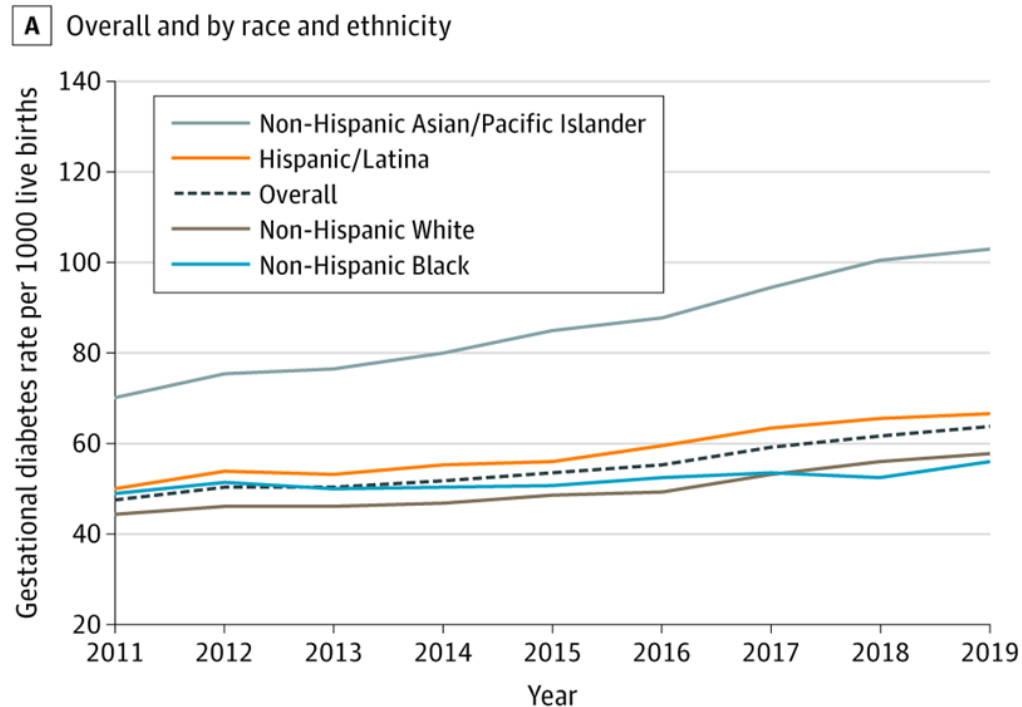
FDA requests removal of strongest warning against using cholesterol-lowering statins during pregnancy; still advises most pregnant patients should stop taking statins

Breastfeeding not recommended in patients who require statins



Gestational Diabetes

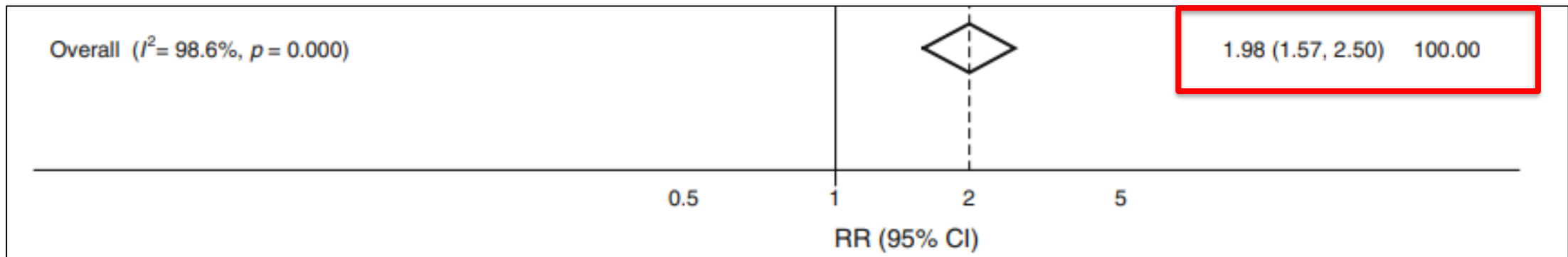
- Pregestational diabetes (1-2%)
- Gestational diabetes: (6-9%)





Gestational Diabetes

- ↑ risk of preeclampsia and gestational hypertension
- ↑ risk of large-for-gestational age, macrosomia, polyhydramnios, and stillbirth; ↑ future obesity and insulin insensitivity in children
- >7-fold increased risk of future T2DM
- 2-fold increased risk of CVD within first decade postpartum





Management of Gestational Diabetes

- Routine screening 24-28 weeks
 - 2-step diagnosis:
 - 50-g oral GTT: $>135\text{mg/dL}$ at 1-hour, followed by:
 - 100-g oral GTT, if ≥ 2 of the following values:
 - Fasting: $>95\text{mg/dL}$
 - 1-hour: $>180\text{mg/dL}$
 - 2-hours: $>155\text{mg/dL}$
 - 3-hours: $>140\text{mg/dL}$



Management of Gestational Diabetes

- HbA1c <6% → ↓large-for-gestational age infants, preterm delivery, and preeclampsia
- Lifestyle modification (70-85%)
- Next line: Insulin (debated)
 - Metformin: crosses the placenta; may lead to increased obesity in offspring



Hypertensive Disorders of Pregnancy

Chronic Hypertension	Hypertension prior to pregnancy or diagnosed <20 weeks gestational age
Gestational Hypertension	Hypertension diagnosed >20 weeks gestational age but <i>without</i> proteinuria or signs of end-organ dysfunction
Pre-eclampsia	Hypertension diagnosed >20 weeks gestational age <i>with</i> the following: <ul style="list-style-type: none">• Proteinuria <u>and/or</u>• End-organ dysfunction, including:<ul style="list-style-type: none">• Acute kidney injury• Liver dysfunction• Neurologic abnormalities (e.g. confusion, seizures)• Hemolysis or thrombocytopenia• Fetal growth restriction



HDP Prevalence and Disparities

2019:

- Overall prevalence: 14.6% (rising ~1%/year)
- Black women: 20.9%
- Native American women: 16.4%
- Rural: 15.5%
- Lowest median household income: 16.4%
- South: 15.0%



HDP Pregnancy/Fetal Consequences

Women:

- 1.5x risk of gestational diabetes
- 2x risk of postpartum hemorrhage
- 5x risk of peripartum stroke
- ↑risk of renal failure, acute heart failure, pulmonary edema, and seizures

Fetus:

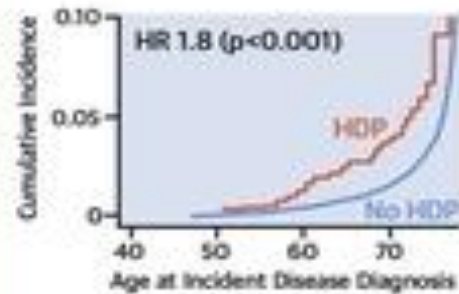
- ↑ risk of preterm delivery, small-for-gestational-age, stillbirth, and neonatal death.



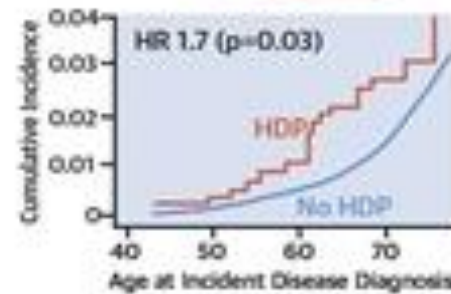
HDP Long-Term CV Consequences

CENTRAL ILLUSTRATION: Hypertensive Disorders of Pregnancy Are Associated With Long-Term Risk of Diverse Cardiovascular Diseases

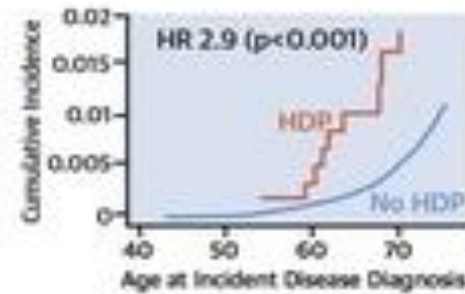
Coronary Artery Disease



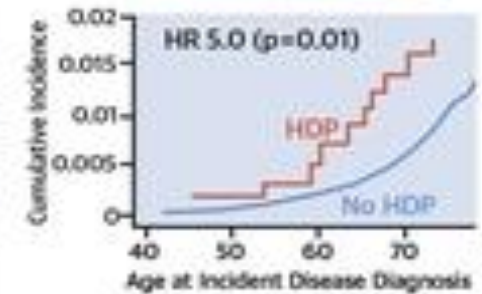
Heart Failure



Aortic Stenosis



Mitral Regurgitation

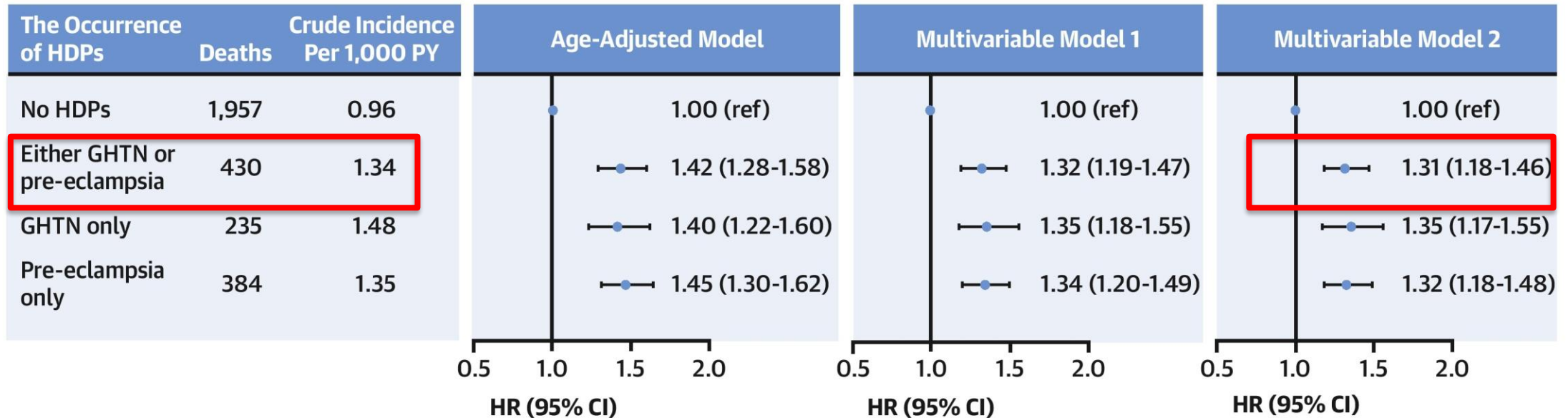


Honigberg, M.C. et al. J Am Coll Cardiol. 2019;74(22):2743-54.



HDP Long-Term CV Consequences

CENTRAL ILLUSTRATION: Hazard Ratios for the Risk of All-Cause Premature Mortality According to the Occurrence of Hypertensive Disorders of Pregnancy



Wang, Y.-X. et al. J Am Coll Cardiol. 2021;77(10):1302-12.



Management of HDP

CHIPS Study:

Less-tight (dBP < 100 mmHg) vs tight (dBP < 85 mmHg) BP control among gestational hypertension

Outcome: pregnancy loss or NICU

No difference (but less severe hypertension)

Table 2. Primary and Other Perinatal Outcomes.*

Variable	Less-Tight Control (N=493)	Tight Control (N=488)	Adjusted Odds Ratio (95% CI)†
Primary outcome — no. (%)	155 (31.4)	150 (30.7)	1.02 (0.77–1.35)
Pregnancy loss — no. (%)	15 (3.0)	13 (2.7)	1.14 (0.53–2.45)
Miscarriage	0	1 (0.2)	
Ectopic pregnancy	0	0	
Elective termination‡	1 (0.2)	1 (0.2)	
Perinatal death	14 (2.8)	11 (2.3)	1.25 (0.56–2.81)
Stillbirth	12 (2.4)	7 (1.4)	
Neonatal death	2 (0.4)	4 (0.8)	
High-level neonatal care for >48 hr — no./total no. (%)§	141/480 (29.4)	139/479 (29.0)	1.00 (0.75–1.33)
Gestational age at delivery — wk	36.8±3.4	37.2±3.1	
Small-for-gestational-age newborns — no./total no. (%)¶			
Birth weight <10th percentile	79/491 (16.1)	96/488 (19.7)	0.78 (0.56–1.08)
Birth weight <3rd percentile	23/491 (4.7)	26/488 (5.3)	0.92 (0.51–1.63)
Other perinatal outcomes of liveborn infants			
Respiratory complications — no./total no. (%)			
Clinical respiratory problem	82/480 (17.1)	67/479 (14.0)	1.19 (0.83–1.71)
Administration of oxygen beyond the first 10 min of life	34/479 (7.1)	25/477 (5.2)	1.24 (0.72–2.14)
Ventilatory support (with or without intubation) beyond the first 10 min of life	35/478 (7.3)	38/479 (7.9)	0.86 (0.53–1.40)
Use of surfactant	28/480 (5.8)	26/479 (5.4)	0.97 (0.55–1.69)
At least one serious neonatal complication — no./total no. (%)	40/480 (8.3)	40/479 (8.4)	0.96 (0.60–1.52)



Management of HDP

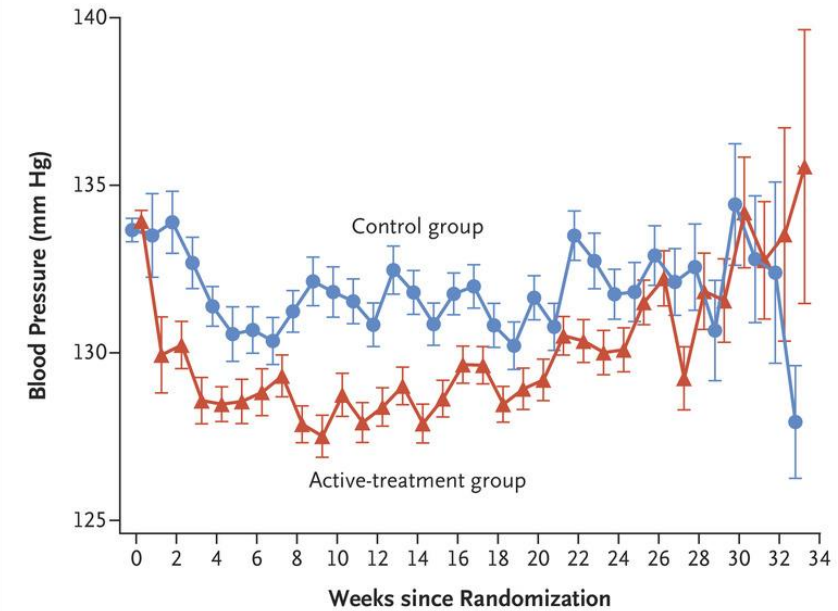
CHAP Study

Target BP <140/90 vs treat only if >160/105 among chronic or mild gestational hypertension (labetalol or nifedipine)

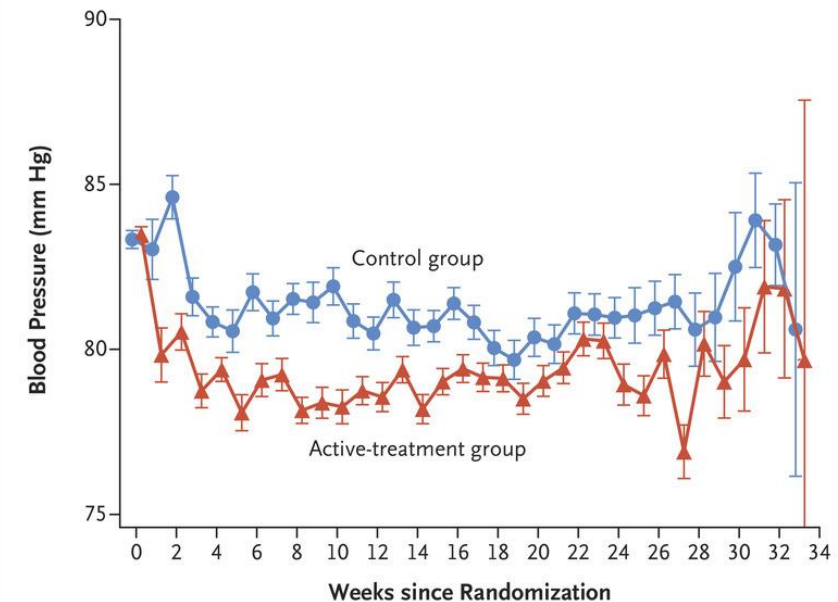
Outcome: composite of preeclampsia with severe features, medically indicated preterm birth <35w, placental abruption, or fetal or neonatal death

HR 0.82 (0.74-0.92)

A Systolic Blood Pressure



B Diastolic Blood Pressure





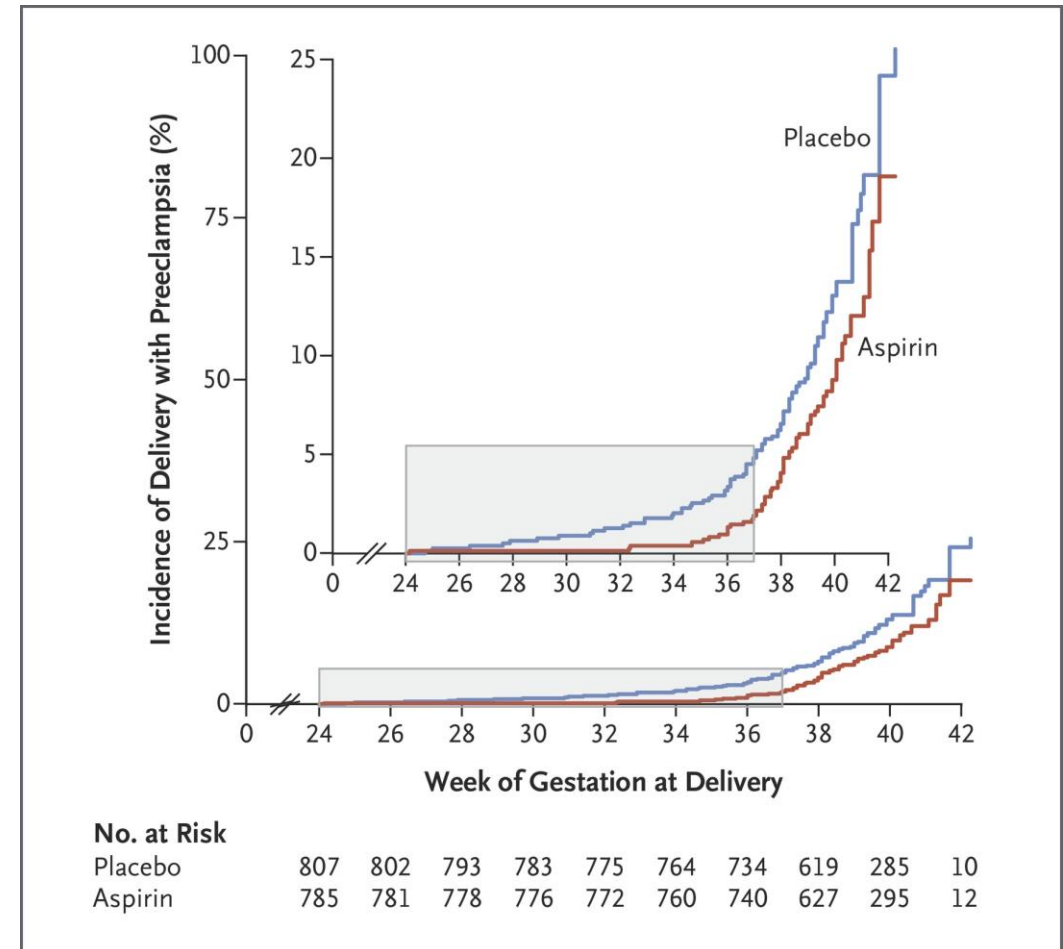
Prevention of Preeclampsia

ASPREE Trial:

ASA 150 mg/d in women 11-14w pregnant at high risk for preterm preeclampsia

Outcome: delivery with preeclampsia before 37w

HR 0.38 (0.20-0.74)





Prevention of Preeclampsia

Table 1. Clinical Risk Factors and Aspirin Use*

Level of Risk	Risk Factors	Recommendation
High [†]	<ul style="list-style-type: none">• History of preeclampsia, especially when accompanied by an adverse outcome• Multifetal gestation• Chronic hypertension• Type 1 or 2 diabetes• Renal disease• Autoimmune disease (ie, systemic lupus erythematosus, the antiphospholipid syndrome)	Recommend low-dose aspirin if the patient has one or more of these high-risk factors
Moderate [‡]	<ul style="list-style-type: none">• 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 birth weight 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	<ul style="list-style-type: none">• Previous uncomplicated full-term delivery	Do not recommend low-dose aspirin



Conclusion

- CV risk factors are common during pregnancy (and rising!)
 - Disproportionate impact on underserved populations
- They portend poor short-term maternal and fetal outcomes, as well as poor long-term CV outcomes
- Need further research to better guide treatment strategies
- Need effective strategies to improve post-partum and long-term follow up to reduce CV risk



Thank you!