

NEW GUIDELINES: TREATMENT OF HYPERTENSION IN PREGNANCY

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THE INTERNATIONAL GUIDELINES:

1–The American College of Obstetricians and Gynecologists (ACOG).

2–American College of Cardiology/American Heart Association (ACC/AHA).

3–European Society of Cardiology/European Society of Hypertension(ESC/ESH).

4–National Institute for Health and Care Excellence(NICE).

CLASSIFICATION OF HYPERTENSION IN PREGNANCY

ACOG GUIDELINES	ESC GUIDELINES
1- Pre-eclampsia-eclampsia.	1-Pre-existing hypertension.
2-Chronic hypertension(of any cause).	2-Gestational hypertension.
3- Chronic hypertension with superimposed pre-eclampsia.	3-Pre-existing hypertension plus superimposed gestational hypertension with proteinuria.
4- Gestational hypertension.	4-Pre-eclampsia.
	5-Antenatally unclassifiable hypertension.

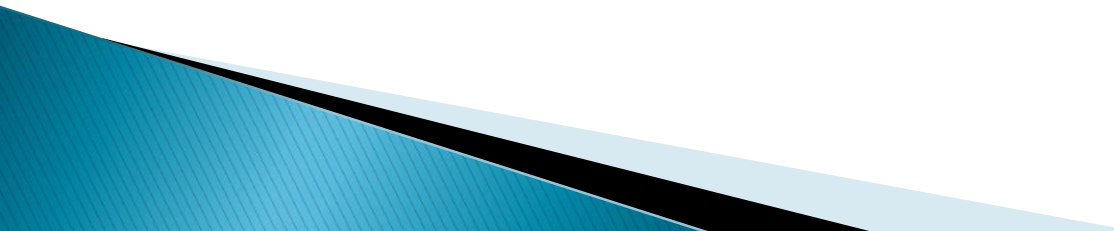
In 2019, the American College of Obstetricians and Gynecologists (ACOG) published updated guidelines on the diagnosis and management of chronic hypertension, gestational hypertension and preeclampsia.



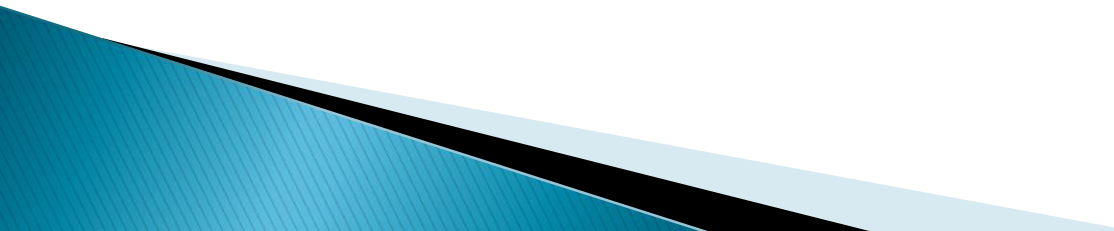
*Prevention of preeclampsia is the first goal, and ACOG outlined recommendations for the use of low-dose aspirin for preeclampsia prophylaxis in a separate committee opinion published in 2018.

*Aspirin 81 mg is recommended for high-risk women between 12 - 28 weeks gestation.

ACOG defines chronic hypertension as hypertension diagnosed before pregnancy or before 20 weeks gestation with blood pressure (BP) $\geq 140/90$ mmHg on at least 2 occasions 4 or more hours apart.



*New diagnostic criteria for stage 1 hypertension—systolic blood pressure (SBP) 130 – 139 mmHg or diastolic blood pressure (DBP) 80 – 89 mmHg—from the 2017 American College of Cardiology / American Heart Association guideline, but they state that the significance of these parameters in pregnancy is not certain.



Stages of Hypertension

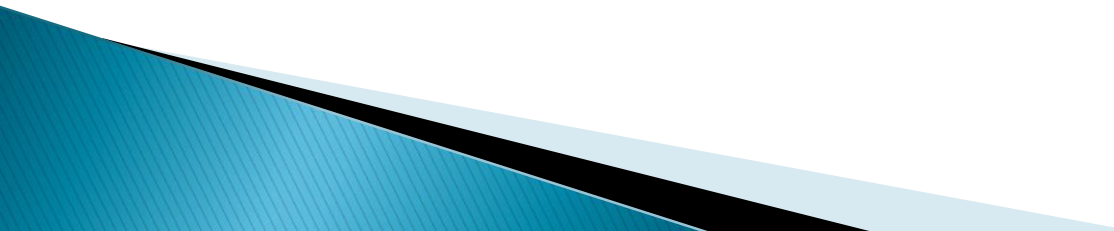
	<120/80 mm Hg	SBP 120-129 and DBP <80 mm Hg	SBP 130- 139 and/or DBP 80-89 mm Hg	SBP 140- 159 and/or DBP 90-110 mm Hg	≥ 160/110 mm Hg
ACOG →	Normal	Prehypertension		HTN	Severe HTN
2017 ACC/AHA →		Elevated BP	Stage 1 HTN	Stage 2 HTN	

ACOG recommends maintaining BP <160/110 mmHg with labetalol and nifedipine, the two first-line oral agents for long-term control.

*ACOG distinguishes gestational hypertension from preeclampsia.

*Gestational hypertension is defined as new onset hypertension with BP $\geq 140/90$ on 2 occasions at least 4 hours apart after 20 weeks gestation.

Preeclampsia is defined as hypertension with proteinuria or other end-organ effects, including thrombocytopenia $<100 \times 10^9 / L$, renal insufficiency with serum Cr >1.1 mg/dL or doubling from baseline, impaired liver function with transaminases greater than twice normal, pulmonary edema, and new onset headache unresponsive to medications or visual symptoms.



*In both chronic hypertension and gestational hypertension, ACOG recommends antihypertensive medications when BP $\geq 160/110$ mmHg with goal BP below this threshold.

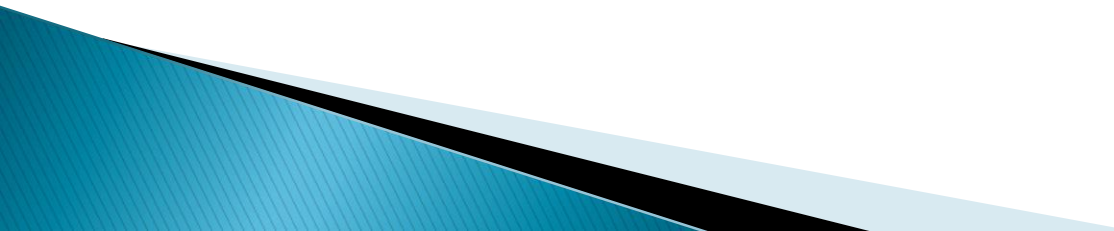
*Intravenous hydralazine and labetalol and oral nifedipine are recommended for acute hypertensive urgency, and oral labetalol and calcium channel blockers are recommended for long-term control.

Common antihypertensive medications used in pregnancy.

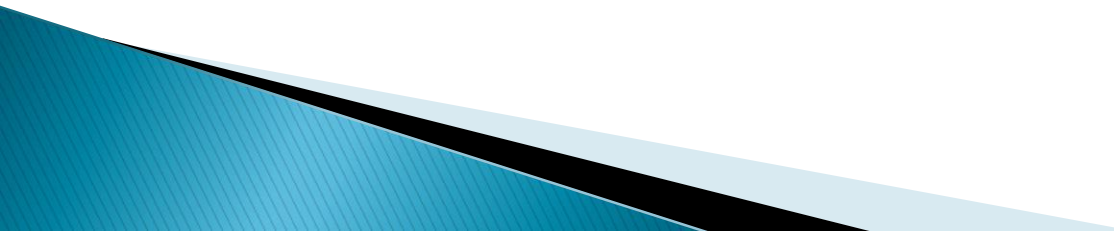
Urgent BP lowering			Outpatient BP control	
Labetalol	Intravenous	10-20 mg, then 20-80 mg every 10-30 min, maximum 300 mg OR 1-2 mg/min infusion	Oral	200-2400 mg/day, divided into two to three doses
Hydralazine	Intravenous	5 mg, then 5-10 mg every 20-40 min, maximum 20 mg OR 0.5-10 mg/h infusion	Not commonly used first-line	
Nifedipine	Oral <i>Immediate release</i>	10-20 mg every 2-6 h*, maximum 180 mg/day *May repeat initial dose after 20 min if needed	Oral <i>Extended Release</i>	30-120 mg/day
Methyldopa	Not commonly used first-line		Oral	500-3000 mg/day, divided into two to four doses

Adapted from the American College of Obstetricians and Gynecologists Practice Bulletin Number 2019,^{3,12}

ACOG specifies that outpatient management is an option for women diagnosed with gestational hypertension or preeclampsia without severe features dependent on adherence to frequent outpatient visits.



Hospitalization is recommended until delivery for those with severe disease (end-organ damage or severe hypertension) and for those who cannot undergo close outpatient monitoring.



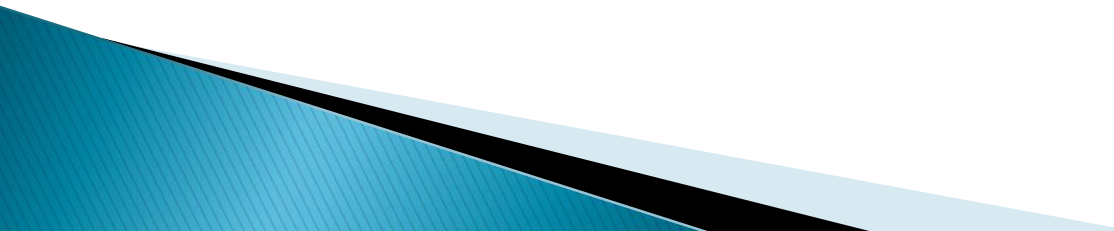
ACOG recommends fetal growth ultrasound measurements every 3–4 weeks, measurement of amniotic fluid at least weekly and antenatal testing once or twice weekly.



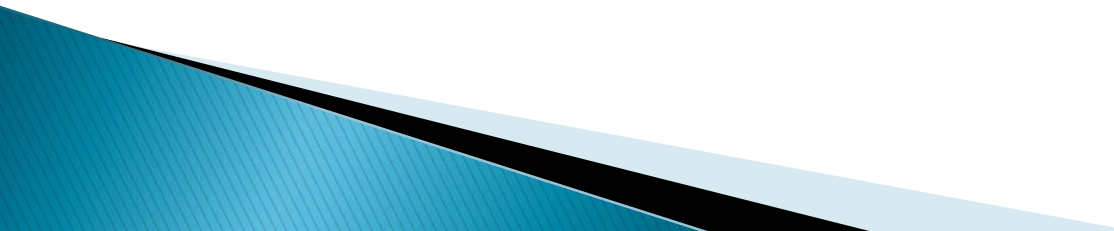
Delivery is recommended at 37 weeks gestation for women with gestational hypertension and preeclampsia without severe features and at 34 weeks for women with preeclampsia with severe features.



Indications for earlier delivery include: uncontrolled severe-range BP, refractory headaches or upper abdominal pain, visual disturbances, stroke, myocardial infarction, hemolysis elevated liver enzyme low platelet (HELLP) syndrome, worsening renal dysfunction, pulmonary edema, eclampsia or fetal distress.

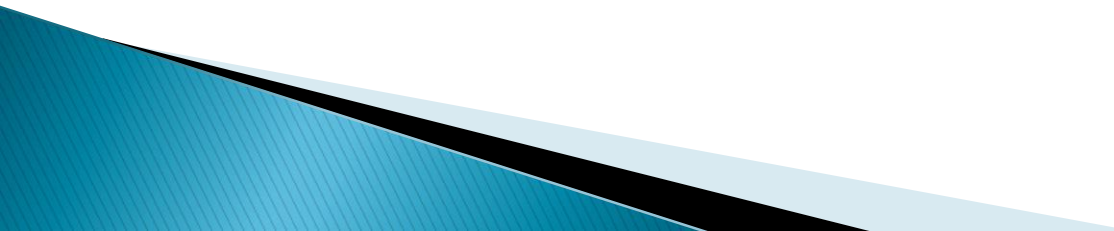


Magnesium sulfate is recommended for women with preeclampsia with severe features for eclampsia prophylaxis during labor and delivery and continued until 24 hours postpartum.



American College of Cardiology / American Heart Association (ACC/AHA)

The 2017 ACC/AHA Guideline makes two specific recommendations for the treatment of hypertension in pregnancy:

1. “Women with hypertension who become pregnant, or are planning to become pregnant, should be transitioned to methyldopa, nifedipine, and/or labetalol during pregnancy.”
 2. “Women with hypertension who become pregnant should not be treated with ACE inhibitors, ARBs, or direct renin inhibitors.”
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The guideline states that the reasons for antihypertensive treatment during pregnancy are twofold:

1 – To prevent severe hypertension.

2 – To potentially prolong pregnancy for fetal benefit.

It recommends that in women with hypertensive crises, for example severe preeclampsia or eclampsia, SBP should be reduced to <140 mmHg during the first hour of treatment.



European Society of Cardiology/ European Society of Hypertension

*The 2018 European Society of Cardiology/European Society of Hypertension Guidelines for HDP similar to ACOG.

*Variations include recommending a higher dose of aspirin of 100 - 150 mg for preeclampsia prevention.

*Initiation of antihypertensives for BPs persistently $\geq 150/95$.

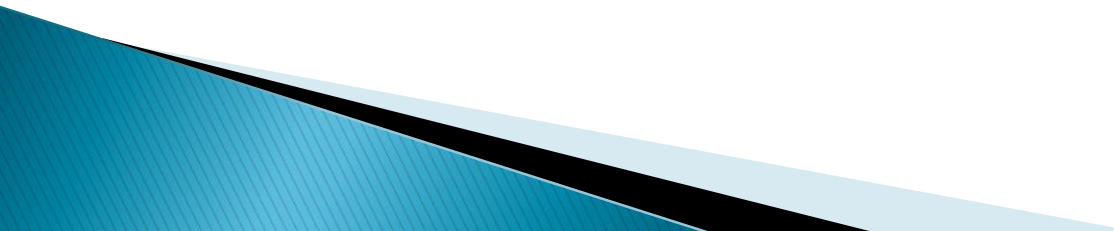
*They suggest a target BP of $<140/90$, noting that the optimal BP target in pregnancy is unknown.

*They recommend that Doppler ultrasound of the uterine arteries can be utilized after 20 weeks gestation to detect higher risk of intrauterine growth retardation.

*They recommend methyldopa, labetalol and calcium antagonists for the treatment of hypertension in pregnancy.

*I.v. labetalol, oral methyldopa, or nifedipine should be initiated in sever hypertension.

*I.v. hydralazine is no longer the drug of choice as its use is associated with more perinatal adverse effects than other drugs.



*Use of i.v. Urapidil can also be considered.

*Sodium nitroprusside should only be used as the drug of last choice since prolonged treatment is associated with an increased risk of foetal cyanide poisoning.

*The drug of choice when pre-eclampsia is associated with pulmonary oedema is nitroglycerin (glyceryl trinitrate), given as an i.v. infusion.

Recommendations for the management of hypertension

Recommendations	Class ^a	Level ^b
Low-dose aspirin (100–150 mg daily) is recommended in women at high or moderate risk of pre-eclampsia from week 12 to weeks 36–37. ^{343,344}	I	A
In women with gestational hypertension or pre-existing hypertension superimposed by gestational hypertension, or with hypertension and subclinical organ damage or symptoms, initiation of drug treatment is recommended at SBP >140 mmHg or DBP >90 mmHg. ³⁰⁵ In all other cases, initiation of drug treatment is recommended if SBP ≥150 mmHg or DBP ≥95 mmHg. ^{348,375}	I	C
SBP ≥170 mmHg or DBP ≥110 mmHg in a pregnant woman is an emergency, and hospitalization is recommended.	I	C
Methyldopa (B), labetalol (C), and calcium antagonists (C) are recommended for the treatment of hypertension in pregnancy. ^{51,379,389}	I	B (methyldopa)
		C (labetalol and calcium antagonists)
In women with gestational hypertension or mild pre-eclampsia, delivery is recommended at 37 weeks. ³⁸³	I	B
It is recommended to expedite delivery in pre-eclampsia and with adverse conditions such as visual disturbances or haemostatic disorders.	I	C
In pre-eclampsia associated with pulmonary oedema, nitroglycerin given as an intravenous infusion is recommended. ³⁶¹	I	C
In severe hypertension, drug treatment with intravenous labetalol, or oral methyldopa or nifedipine, is recommended. ⁵¹	I	C
Limitation of weight gain to <6.8 kg should be considered in obese women. ³⁷⁷	IIa	C
ACE inhibitors, ARBs, or direct renin inhibitors are not recommended. ^{51,385,361}	III	C

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BP = blood pressure; DBP = diastolic blood pressure; SBP = systolic blood pressure.

^aClass of recommendation.

^bLevel of evidence.

National Institute for Health and Care Excellence(NICE)

*Guideline was published in 2019 in the United Kingdom. Overall, the NICE guideline is similar to ACOG.

*Differences include antihypertensive therapy for women with chronic hypertension with BPs persistently $\geq 140/90$.

*Women with gestational hypertension and preeclampsia not already treated should be offered medication following birth if BP $\geq 150/110$.

*Target BP is 135/85 in all HDP patients.

Aspirin: Preeclampsia Risk-reducing Recommendations by Hypertension Guideline

Guideline	Year	Daily Dose	GA (weeks)		Who Qualifies
			Begin	End	
ACOG	2019	81 mg	12 – 28	Delivery	≥ 1 high risk factor (1), or > 1 moderate risk factor (2)
USPSTF	2017	81 mg	12		≥ 1 high risk factor (1)
WHO	2011	75 mg	< 20		≥ 1 high risk factor (1, 3)
NICE	2019	75 – 150 mg	12	Birth	≥ 1 high risk factor (4), or > 1 moderate risk factor (5)
ESC/ESH	2018	100–150mg	12	36	High (4) or moderate (5) risk
Ireland	2019	75 – 100 mg	12 – 16	Birth	≥ 1 high risk factor (4), or > 1 moderate risk factor (5)
FIGO	2019	150 mg	11 – 14	36, or delivery, or preeclampsia	High risk (locally defined), or Risk ≥ 1 in 100
Queensland	2016	100 mg	< 16	37, or Birth	Moderate to high risk (6)
SOMANZ	2014	Low dose		37	Moderate to high risk (7)
ISSHP	2018	75 – 162 mg	16 – 20		Strong risk factors (8)
Brazil	2016	75 – 150 mg	12		Intermediate or increased risk (9)
DGGG	2015	100 mg		Up to 34	
ACC/AHA	2017	No specific recommendation, refer to ACOG recommendations			
Canada	2018	No recommendations			

(1) High risk factors (per ACOG, USPSTF, WHO): history of preeclampsia, multi-fetal gestation, chronic hypertension, type 1 or 2 diabetes, renal disease, autoimmune disease.

(2) Moderate risk factors (per ACOG): nulliparity, obesity (BMI >30), preeclampsia in the patient's mother or sister, African American race, low socioeconomic status, age > 35 years, history of a small for gestational age neonate, previous adverse pregnancy outcome, or >10 year pregnancy interval.

(4) High risk factors (per NICE, ESC/ESH, Royal College of Physicians of Ireland):

hypertensive disease during previous pregnancy, chronic kidney disease, autoimmune disease, type 1 or 2 diabetes, chronic hypertension.

(5) Moderate risk factors (per NICE, ESC/ESH, Royal College of Physicians of Ireland): first pregnancy, age ≥ 40 , pregnancy interval > 10 years, BMI ≥ 35 at first visit, family history of preeclampsia, multi-fetal pregnancy.

Antepartum Antihypertensive Medication Initiation and Blood Pressure Goals by Hypertensive Disorder of Pregnancy Guideline and / or Country

Guideline and / or Country	Recommended Medication Initiation (mmHg)	Target BP (mmHg)
ACOG [11, 12]	≥ 160 ≥ 110	<160 <110
ISSHP [27]	≥ 140 ≥ 90	110 – 140 85
Queensland [32]	≥ 140 ≥ 90	<140 <90
Canada [29]	≥ 140 ≥ 90	NR 85
SOMANZ [30]	≥ 160 ≥ 110	<160 <110
Brazil [33]	>150 >100	130 – 150 80 – 100
Germany [34] Ireland [32, 33]	≥ 150 ≥ 100	<150 80 – 100
NICE [36]	≥ 140 ≥ 90	135 85
ESC/ESH [37]	≥ 150 ≥ 95	<140 <90

Treatment for Mild Chronic Hypertension during Pregnancy

Tita AT et al. DOI: 10.1056/NEJMoa2201295

CLINICAL PROBLEM

Chronic hypertension during pregnancy increases risk of poor pregnancy and birth outcomes. Although pharmacologic antihypertensive therapy is standard treatment for severe hypertension during pregnancy, its benefits and safety are unclear for mild chronic hypertension in pregnant women.

CLINICAL TRIAL

Design: A U.S. multicenter, open-label, randomized, controlled trial assessed whether treatment of mild chronic hypertension in pregnant women, as compared with no treatment, would reduce adverse pregnancy outcomes without harming fetal growth.

Intervention: 2408 women with a known or new diagnosis of mild chronic hypertension and a singleton fetus at <23 weeks' gestation were randomly assigned to receive either active treatment with antihypertensive medications approved for pregnancy or standard treatment — i.e., no treatment, unless systolic blood pressure was ≥ 160 mm Hg or diastolic blood pressure was ≥ 105 mm Hg. The primary outcome was a composite of preeclampsia with severe features, medically indicated preterm birth at <35 weeks, placental abruption, fetal death, or neonatal death.

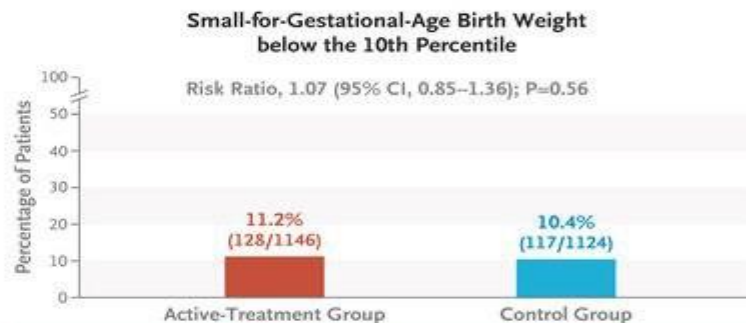
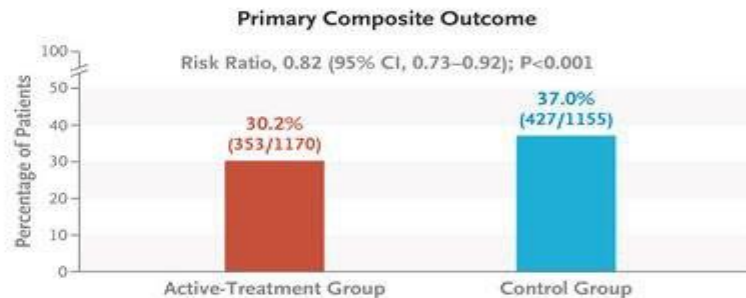
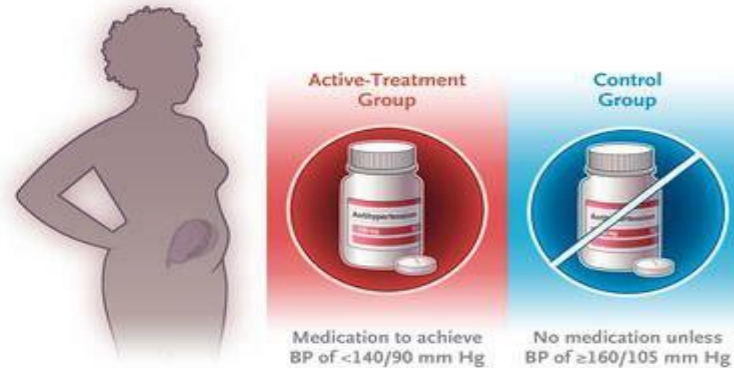
RESULTS

Efficacy: Active treatment of mild chronic hypertension reduced the frequency of primary outcome events.

Safety: The percentage of infants who were small for gestational age (<10th percentile) was similar in the active-treatment and control groups.

LIMITATIONS AND REMAINING QUESTIONS

- Patients were aware of their treatment group.
- There was a high ratio of women screened to women enrolled (12:1).
- The study was not powered to assess treatment effects across subgroups.



CONCLUSIONS

Treating mild chronic hypertension in pregnancy reduced adverse pregnancy outcomes without impairing fetal growth.

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THANK YOU