Original Research

Treating Mild Chronic Hypertension During Pregnancy

A Cost-Effectiveness Analysis

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OBJECTIVE: To assess the cost effectiveness of targeting a blood pressure of less than 140/90 mm Hg compared with 160/105 mm Hg.

METHODS: A decision-analytic model was constructed to compare the treatment of chronic hypertension in pregnancy at mild-range blood pressures (140/90 mm Hg) with the treatment of chronic hypertension before 20 weeks of gestation at severe-range blood pressures (160/105 mm Hg) in a theoretical cohort of 180,000 patients with mild chronic hypertension. Probabilities, costs, and utilities were derived from literature and varied in sensitivity analyses. Primary outcomes included incremental cost per quality-adjusted life-year (QALY), cases of preeclampsia, preeclampsia with severe features, severe maternal morbidity (SMM), preterm birth, maternal death, neonatal death, and neurodevelopmental delay. The cost-effectiveness threshold was $100,000 per QALY.

RESULTS: Treating chronic hypertension in a population of 180,000 pregnant persons at mild-range blood pressures, compared with severe-range blood pressures, resulted in 14,177 fewer cases of preeclampsia (43,953 vs 58,130), 11,835 of which were cases of preeclampsia with severe features (40,530 vs 52,365). This led to 817 fewer cases of SMM (4,375 vs 5,192), and 18 fewer cases of maternal death (102 vs 120). Treating at a lower threshold also resulted in 8,078 fewer cases of preterm birth (22,000 vs 30,078), which led to 26 fewer neonatal deaths (276 vs 302) and 157 fewer cases of neurodevelopmental delay (661 vs 818). Overall, treating chronic hypertension at a lower threshold was a dominant strategy that resulted in decreased costs of $600 million and increased effectiveness of 12,852 QALYs.

CONCLUSION: Treating chronic hypertension at a threshold of mild-range blood pressures is a dominant (lower costs, better outcomes) and cost-effective strategy that results in fewer neonatal and maternal deaths compared with the standard treatment of treating at severe range blood pressures.

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Chronic hypertension in pregnancy affects 3–5% of pregnancies in the United States.[1–3] The condition is characterized by elevated blood pressure present before pregnancy or is diagnosed before 20 weeks of gestation.[1–5] Chronic hypertension is associated with increased risk of several adverse maternal, fetal, and neonatal outcomes including preeclampsia, maternal death, fetal growth restriction, and preterm birth.[1–5] Although treatment for chronic hypertension in pregnancy is essential to reduce the risk of complications, the optimal approach to management has remained a topic of debate.[4,5]

There are many forms of treatment for chronic hypertension, including weight loss, diet modification, and exercise. For nonpregnant patients, treatment for chronic hypertension with antihypertensives traditionally has been indicated once blood pressures are consistently higher than 140/90 mm Hg and has recently shifted to a threshold of 130/80 mm Hg if a patient has high-risk factors for future cardiovascular disease. Several countries have adapted this recommendation in pregnancy, but practitioners in the

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United States have been hesitant to do so.[3,5] Several studies have examined the effects of antihypertensive treatment during pregnancy without clear evidence of improved perinatal outcomes.[5–7] Furthermore, one study found an increased risk of small-for-gestational-age birth weight with tighter blood pressure control, leading to mixed recommendations for management strategies. However, this risk is still theoretical because it has not been seen in follow-up studies.[8] In patients with *severe chronic hypertension*, defined as blood pressure higher than 160/110 mm Hg, treatment with antihypertensives has long been the standard of care; however, for those with mild chronic hypertension, it is only recently that clinicians in the United States have considered antihypertensive treatment.[6,7]

The move to embrace hypertension treatment at a lower blood pressure threshold is primarily due to the recent CHAP (Chronic Hypertension and Pregnancy) trial, a randomized trial of patients with mild chronic hypertension that compared treating chronic hypertension in pregnancy to a target of less than 140/90 mm Hg with treating to a target of less than 160/105 mm Hg. Targeting a blood pressure of less than 140/90 mm Hg was associated with better pregnancy outcomes, with no increase in risk of adverse outcomes, including incidence of small-for-gestational-age neonates. However, the effects on the patient population and economic implications of this strategy remains unknown.[1] There are potential increased costs associated with this treatment, including the cost of antihypertensive medication and increased obstetric intervention. Therefore, we sought to assess the cost effectiveness of targeting a blood pressure of less than 140/90 mm Hg as compared with a blood pressure of less than 160/105 mm Hg.

METHODS

We created a decision-analytic model using TreeAge Pro 2022 to compare two strategies: 1) treating chronic hypertension in pregnancy to a target systolic blood pressure of lower than 140 mm Hg or diastolic blood pressure of lower than 90 mm Hg or 2) treating chronic hypertension in pregnancy to target systolic blood pressure of lower than 160 mm Hg or diastolic blood pressure of lower than 105 mm Hg. We used a cohort size of 180,000, the approximate number of pregnancies in the United States per year affected by chronic hypertension per Centers for Disease Control and Prevention (CDC) birth certificate data.[9] All model inputs were derived from the literature (Table 1). Because we did not involve human subjects in this theoretical model, the study was deemed exempt from approval by the institutional review board at Oregon Health & Science University.

In our model, we first assigned the cohort to each of the strategies being compared (Fig. 1). The data informing our model inputs regarding the main obstetric outcomes were obtained directly from the CHAP trial–rates of preeclampsia, and preterm birth in either cohort. Other clinical outcomes included preeclampsia with severe features, severe maternal morbidity, maternal death, neonatal death, and neurodevelopmental delay.

Costs were derived from the literature and adjusted to 2022 U.S. dollars using the medical care component of the consumer price index. Costs were considered from a societal perspective, incorporating all costs incurred rather than just patient or health care system costs. Cost of treatment was estimated in either arm using a weighted average of the costs of the medications and the proportions of patients treated from the original CHAP trial.[1,10] Cost of preeclampsia was derived from a large cohort study in Pennsylvania that examined the maternal and infant costs associated with preeclampsia.[11] The costs for delivery, both term and preterm, were derived from a large retrospective population-based California study that estimated birth hospitalization costs for mothers and neonates.[12] The cost of neurodevelopmental delay was derived from a Morbidity and Mortality Weekly Report by the CDC that analyzed and reported lifetime costs associated with people with cerebral palsy.[13]

Effectiveness was evaluated by using quality-adjusted life-years (QALYs) from a maternal perspective. The QALYs were calculated by applying utilities to the length of time associated with a particular health state or scenario. Utilities range from 0 to 1, with 0 representing death, and 1 a state of ideal health. The utility of preeclampsia with (0.89) and without (0.99) severe features was obtained from a previous cost-effectiveness analysis.[14] These utilities were applied for a duration of 15 days, which was the average hospitalization time for patients with preeclampsia with severe features.[15] The utility of neonatal death from a maternal perspective (0.92) was applied for the remainder of the mother's lifespan.[16] The QALYs were discounted at a standard rate of 3%. Baseline life expectancies were obtained from CDC data. Maternal life expectancy was calculated by using average reproductive age subtracted from average female life expectancy.[17]

We calculated the number of cases of preeclampsia and number of preterm births for each treatment strategy, as well as the total costs and number of QALYs associated with each strategy. Our willingness to pay threshold, or the point at which we would

Table 1. Probabilities, Utilities, and Costs Used in the Model

Variable	Value	Range in Sensitivity Analyses	Reference(s)
Probabilities			
Preeclampsia			
Treating at 140/90 mm Hg	0.252	0.15–0.35	1
Treating at 160/105 mm Hg	0.323	0.22–0.42	1
Preeclampsia with severe features			
Treating at 140/90 mm Hg	0.922	0.80–1	1
Treating at 160/105 mm Hg	0.901	0.80–1	1
SMM			
In the setting of preeclampsia with severe features	0.078	0.04–0.1	25
In the setting of no preeclampsia	0.0087	0.005–0.01	25
Maternal death			
In the setting of preeclampsia with severe features	0.0005	0.0001–0.0008	25
In the setting of no preeclampsia	0.000238	0.0001–0.0004	26
Preterm birth			
Treating at 140/90 mm Hg	0.122	0.05–0.25	1
Treating at 160/105 mm Hg	0.168	0.05–0.25	1
SGA			
Treating at 140/90 mm Hg	.112	0.05–0.25	1
Treating at 160/105 mm Hg	.104	0.05–0.25	1
Neonatal death			
Term, SGA	0.00265	0–0.05	27
Preterm, SGA	0.0190	0–0.05	27
Term, no SGA	0.000548	0–0.05	27
Preterm, no SGA	0.00316	0–0.05	27
Neurodevelopmental delay			
Preterm	0.0213	0–0.05	28
Term	0.00129	0–005	28
Costs (2022 U.S. dollars)			
Treatment			
Treating at 140/90 mm Hg	174.75	50–300	1, 10
Treating at 160/105 mm Hg	87.37	25–150	1, 10
Preeclampsia			
Without severe features	18,140	11,500–32,500	11
With severe features	24.280	13,000–46,000	11
SMM	7,153	5,000–20,000	29
Maternal death	4.220	2,000–10,000	12
Term delivery	3,625	500–15,000	12
Preterm delivery	44,550	10,000–100,000	12
Neonatal death	54.691	45,000–95,000	12
Neurodevelopmental delay	846,883.44	700,000–1,300,000	13
Utilities			
Preeclampsia			
Without severe features	0.99	0.9–1	14
With severe features	0.89	0.85–1	14
Neonatal death	0.92	0.85–1	16
Neurodevelopmental delay	0.76	0.5–1	30
Life expectancy			
Maternal	56.8	40–80	17

SMM, severe maternal morbidity; SGA, small for gestational age.

consider treating at a lower threshold to meet criteria for cost effectiveness, was set at a standard $100,000 per QALY.

We performed a tornado analysis that included all probabilities, costs, and utilities to determine which variables most affected the strength of our model. The range of values for each variable included three standard deviations above and below the mean, with values found in the literature (Fig. 2). We further investigated those found to be the most influential using univariable sensitivity analyses. We also examined the robustness of the model using a Monte Carlo multivariable simulation that used 1,000 samples (Fig. 3). Here, probabilities and utilities were varied

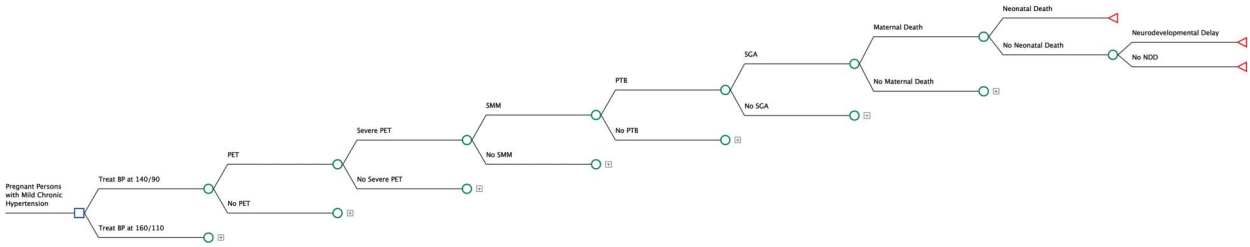

Fig. 1. Schematic tree created using TreeAge software. BP, blood pressure; PET, preeclampsia; SMM; severe maternal morbidity; PTB, preterm birth; SGA, small for gestational age; NDD, neurodevelopmental delay.

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according to a beta distribution to approximate a normal distribution with the set limits of 0–1. Costs were varied according to a gamma distribution to account for a start at $0 and a right skew in distribution. Life expectancies were varied according to a triangular distribution.

RESULTS

In this theoretical cohort of 180,000 pregnant individuals with chronic hypertension, treating at the lower blood pressure threshold of 140/90 mm Hg resulted in 43,953 cases of preeclampsia compared with the standard threshold of 160/105 mm Hg that resulted in 58,130 cases of preeclampsia. Of the preeclampsia cases in patients treated at a lower threshold, 40,529 were with severe features; of those treated at the standard threshold, 52,364 were with severe features. Treating at a lower threshold also resulted in 22,000 cases of preterm birth, compared with 30,078 cases of preterm birth in the standard

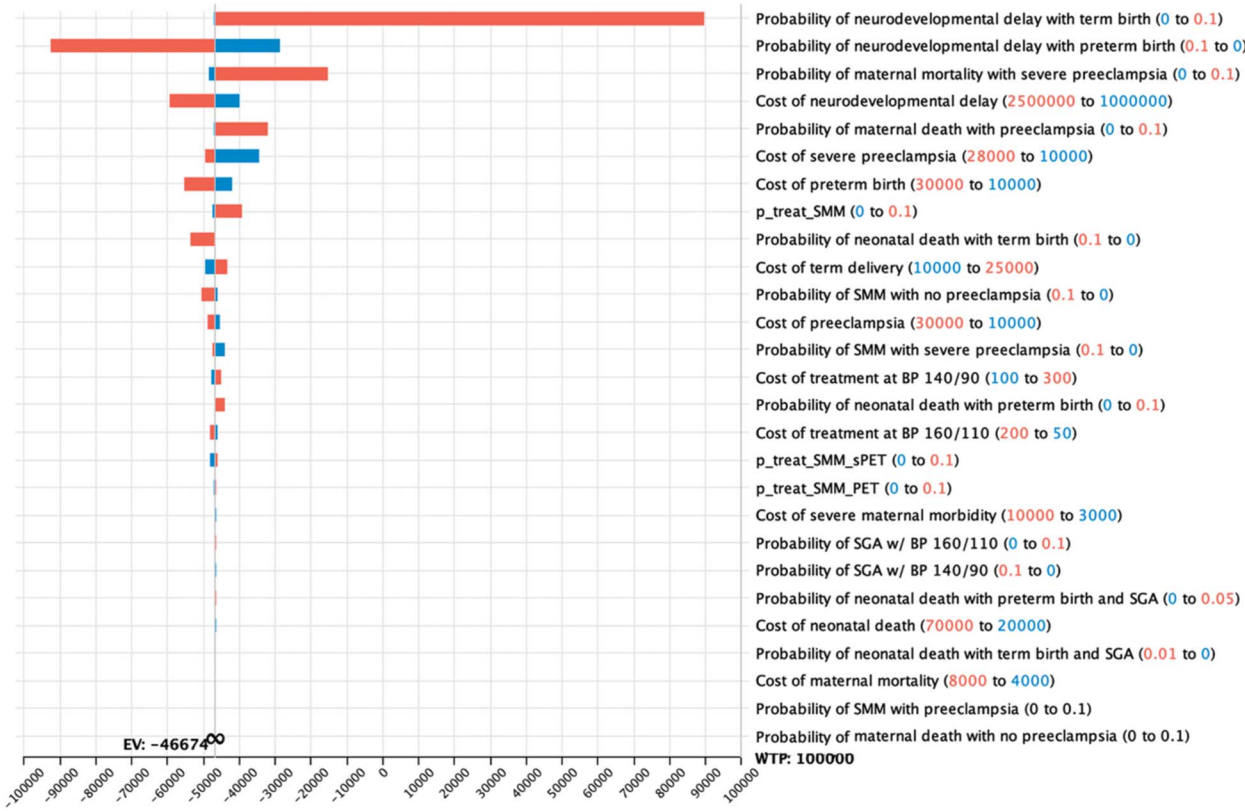

Fig. 2. Tornado diagram created using TreeAge software. Incremental cost-effectiveness ratio (ICER) to treat blood pressure (BP) at 140/90 mm Hg vs 160/105 mm Hg (willingness to pay [WTP]: 100,000). SMM, severe maternal morbidity; PET, preeclampsia; sPET, severe preeclampsia; SGA, small for gestational age; EV, expected value of ICER.

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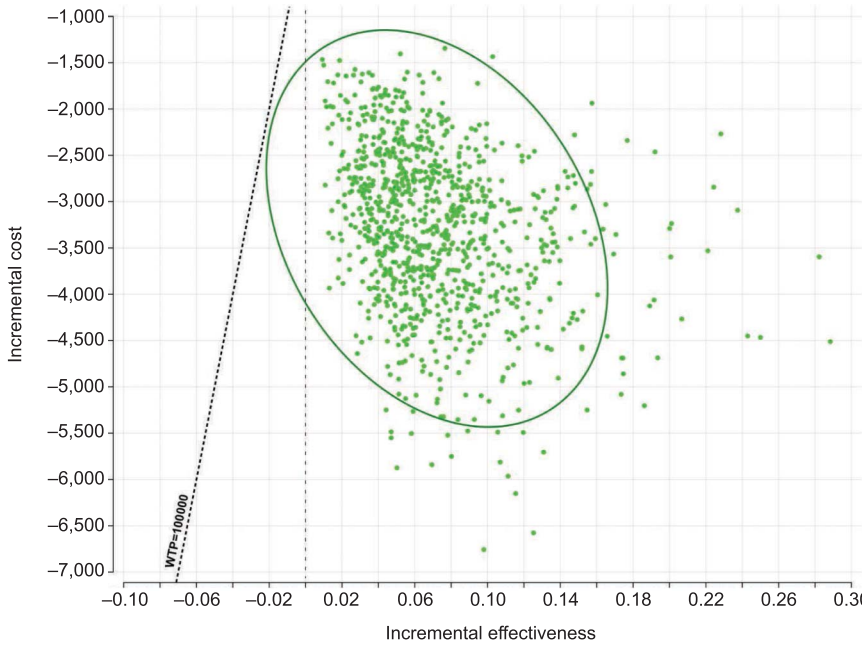

Fig. 3. Monte Carlo simulation created using TreeAge software. WTP, willingness to pay.

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treatment group. Treating to a lower blood pressure threshold also resulted in 4,375 cases of severe maternal morbidity as compared with 5,195 in the standard treatment group, 102 cases of maternal death as compared with 120 in the standard treatment group, 276 cases of neonatal death as compared with 302 in the standard treatment group, and 661 cases of neurodevelopment delay as compared with 818 in the standard treatment group. Treating to a lower blood pressure threshold was associated with a decreased cost of $600 million and increased QALYs of 12,852 making it a dominant strategy (Table 2).

In a tornado diagram that assessed univariable sensitivity analyses of all inputs, we found that the rates of neurodevelopmental delay in neonates at term and preterm had the most effect on the model, but variation of these inputs through a realistic range still did not change the cost effectiveness of the strategy. The only variable that potentially could have affected the cost effectiveness of the strategy was the cost of treatment, which crossed the threshold of $100,00 per QALY only at a cost of $10,743–far higher than the cost estimated. Although there are several treatment side effects that could incur additional costs, these are rare and unlikely to cause the cost of treatment to increase by a factor of more than $10,000. Monte Carlo multivariable probabilistic simulation showed that treating to a lower blood pressure threshold was cost saving in

Table 2. Outcomes Associated With Treating Chronic Hypertension at 140/90 mm Hg Compared With 160/105 mm Hg in a Theoretical Cohort of 180,000 Pregnant Persons With Chronic Hypertension

Outcome	Early Treatment*	Standard Treatment†	Difference
Cases of preeclampsia	43,953	58,130	−14,177
Cases of preeclampsia with severe features	40,530	52,365	−11,835
SMM	4,375	5,192	−817
Preterm birth	22,000	30,078	−8,078
SGA	20,160	18,720	+1,440
Maternal death	102	120	−18
Neonatal death	238	265	−27
Neurodevelopmental delay	661	818	−157
Cost	$5,014,138,872	$5,613,990,649	−$599,851,777
Effectiveness (QALYs)	4,760,725	4,747,873	+12,852

SMM, severe maternal morbidity; SGA, small for gestational age; QALY, quality-adjusted life-year.
* Systolic blood pressure higher than 140 mm Hg, diastolic blood pressure higher than 90 mm Hg.
† Systolic blood pressure higher than 160 mm Hg, diastolic blood pressure higher than 105 mm Hg.

100% of trials. This suggests that the cost effectiveness of this strategy was not sensitive to the uncertainty in the probabilities, costs, and utilities in the model.

DISCUSSION

We found that treating chronic hypertension in pregnancy to a lower blood pressure threshold led to better outcomes and lower costs and, thus, was a dominant strategy. Treating to a lower threshold not only resulted in improved outcomes, but also decreased health care costs. The cost of antihypertensive medication is considerably less expensive than the accrued costs of the adverse outcomes of hypertensive diseases in pregnancy that were prevented. The model continued to be cost saving in multivariable analyses demonstrating the significant effect on costs for adverse perinatal outcomes from chronic hypertension when a lower BP target of 140/90 mm Hg is used.

Prior studies have examined the cost effectiveness of antihypertensive treatment in nonpregnant people. A systematic review conducted by the CDC examined more than 70 studies and determined that in all studies, treatment with antihypertensives was cost effective.[18] Different iterations of providing antihypertensive treatment to a variety of higher risk populations, such as veterans, or older Black men has also been shown to be cost effective.[19–21] The evidence of cost-effective antihypertensive treatment in the general population combined with the robust results of the CHAP trial, provide further strength to our results.

In regards to treatment in pregnant persons, previous studies have indicated that treating hypertension at a lower threshold could lead to higher rates of fetal growth restriction.[8,22] The CHIPS (Control of Hypertension in Pregnancy Study) trial examined treating diastolic blood pressure at 100 mm Hg compared with 85 mm Hg and its effect on pregnancy loss and neonatal intensive care unit admission and found increased rates of newborns with birth weights less than the 10th percentile for gestational age.[22] However, these results had not been seen in a prior meta-analysis and were not mirrored in the CHAP trial.[1,22] Our model focused on the management approach to chronic hypertension from the CHAP trial rather than that used in the CHIPS trial and examined a large theoretical cohort to see whether this strategy of a lower blood pressure target would result in fewer adverse pregnancy outcomes and be cost effective. Similar cost-effectiveness studies have been shown to be cost saving in developed and developing countries demonstrating the cost effectiveness of an intervention for hypertension in pregnancy before it has the potential to progress to a severe hypertensive disorder.[23]

In our model, pregnant persons who were and were not diagnosed with preeclampsia were assumed to have the same preterm birth rates as in the original CHAP trial–preterm birth rates were not separated by preeclampsia status, simply by treatment group. However, in patients with preeclampsia with severe features, we expected that the preterm delivery rates would be increased compared with all patients. If this were the case, the model would in fact underestimate the extent to which treating at a lower threshold was cost saving. Our tornado diagram also showed that, if rates of preterm birth differed, this would only accentuate the robustness of the model (Fig. 2). Similarly, it is important to note that several of our inputs in the model were based on the population in the CHAP trial. Trial populations often are not entirely representative of the general population, because they may be in better overall health to avoid confounding data. In a sample measuring the general population, there is a high likelihood that there are higher rates of adverse outcomes, especially in individuals with higher blood pressures. Thus, our model would underestimate the cost-saving nature of treating blood pressure at a lower threshold.

Despite these compelling findings, our study is not without limitations. There is always uncertainty in the inputs for selected probabilities, costs, and utilities. For our model inputs to be as accurate as possible, many estimates were derived from large multicenter studies across the United States. Furthermore, the model cannot include all possible outcomes, and we did not account for all possible adverse outcomes, such as maternal sepsis or intensive care unit admission, because they do not tend to be associated with hypertension but could have costs that could influence the model. However, the inclusion of such outcomes would only have increased the extent to which the model was cost-saving, making our findings more robust. Further, we did not include any potential adverse effects of the specific antihypertensive medication because those were complications that were not analyzed in the original study and have yet to be analyzed in a large cohort study. Although the complication of historical concern–fetal growth restriction–was not different between the two arms of the trial, it was included in the model. However, because preeclampsia cases rise in the setting of treating at a higher threshold, it is likely that cases of fetal growth restriction would also increase, because there has been a proven association between preeclampsia

and neonates born small for gestational age. Additionally, it is important to note that the definition of chronic hypertension outside of pregnancy was recently changed to a target of 130/80 mm Hg.[24] Because this was during recruitment for the CHAP trial, this was not the threshold used in the trial, and the effect and cost effectiveness of this threshold would need to be examined in future studies.

It is important to note that chronic hypertension in pregnancy disproportionately affects Black pregnant individuals.[2–6] The population of the CHAP trial was representative of the racial demographic of pregnant individuals with chronic hypertension in pregnancy. Inequities such as those rooted in exposure to systemic and interpersonal racism, including medical racism, socioeconomic differences, and access to health care may contribute to chronic hypertension and to the complications seen with chronic hypertension in pregnancy.[19] Thus, in revising hypertension guidelines, equitable treatment must be prioritized. A large component of being able to treat to a lower blood pressure target will include monitoring blood pressure regularly, which may be difficult for individuals without the resources to access proper standardized blood pressure devices. Examining these potential care gaps are vital when thinking about changing overall treatment recommendations.

In conclusion, treating to a lower blood pressure target of 140/90 mm Hg for chronic hypertension in pregnancy was cost saving and led to better maternal and neonatal outcomes in our model. Our findings support adopting a treatment regimen to maintain blood pressures of less than 140/90 mm Hg for pregnant persons with chronic hypertension.

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