

SCIENTIFIC INVESTIGATIONS

## Maternal habitual snoring and blood pressure trajectories in pregnancy

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**Study Objectives:** Habitual snoring has been associated with hypertensive disorders of pregnancy. However, exactly when blood pressure (BP) trajectories diverge between pregnant women with and without habitual snoring is unknown. Moreover, the potentially differential impact of chronic vs pregnancy-onset habitual snoring on maternal BP trajectories during pregnancy has not been examined. This study compared patterns of BP across pregnancy in 3 groups of women: those with chronic habitual snoring, those with pregnancy-onset habitual snoring, and nonhabitual snoring “controls.”

**Methods:** In a cohort study of 1,305 pregnant women from a large medical center, participants were asked about habitual snoring ( $\geq 3$  nights/week) and whether their symptoms began prior to or during pregnancy. Demographic, health, and BP data throughout pregnancy were abstracted from medical charts. Linear mixed models were used to examine associations between habitual snoring-onset and pregnancy BP trajectories.

**Results:** A third of women reported snoring prior to pregnancy (chronic snoring) and an additional 23% reported pregnancy-onset snoring. Mean maternal age (SD) was 29.5 (5.6), 30 (6), and 30.5 (5.7) years in controls, chronic, and pregnancy-onset snoring, respectively. Overall, women with pregnancy-onset snoring had higher mean systolic BP and diastolic BP compared to those with chronic habitual snoring or nonhabitual snoring. In gestational week-specific comparisons with controls, systolic BP became significantly higher around 18 weeks' gestation among women with pregnancy-onset snoring and in the third trimester among women with chronic snoring. These differences became detectable at 1 mm Hg and increased thereafter, reaching 3 mm Hg-BP difference at 40 weeks' gestation in women with pregnancy-onset snoring relative to controls. Pairwise mean differences in diastolic BP were significant only among women with pregnancy-onset snoring relative to controls, after 15 weeks' gestation.

**Conclusions:** Pregnancy-onset and chronic maternal snoring are associated with higher BPs beginning in the second and third trimester, respectively. Pregnancy BP trajectories could identify critical windows for enhanced BP surveillance; the divergent BP trajectories suggest that the 2 groups of women with habitual snoring in pregnancy may need to be considered separately when gestational time intervals are evaluated for increased BP monitoring.

**Keywords:** pregnancy, sleep, blood pressure, hypertension

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### BRIEF SUMMARY

**Current Knowledge/Study Rationale:** Habitual snoring has been associated with hypertensive disorders of pregnancy. However, blood pressure trajectories along the gestational age in pregnant women with or without habitual snoring have not been examined. Whether chronic (prepregnancy) and pregnancy-onset habitual snoring are differentially associated with maternal blood pressure trajectories is also unknown.

**Study Impact:** Chronic and pregnancy-onset habitual snoring are associated with divergent and differential trajectories of maternal blood pressure in comparison with non-habitual snoring. Divergent blood pressure trajectories of women with habitual snoring in pregnancy should be considered when evaluating gestational “windows” for increased blood pressure monitoring and provide insight into pathophysiologic changes.

### INTRODUCTION

Sleep-disordered breathing (SDB) is a common nocturnal respiratory condition caused by complete or partial airway obstruction and ranges from snoring, at one end of the spectrum, to obstructive sleep apnea (OSA) at the other. Habitual snoring, a characteristic symptom of OSA, occurs at least 3 nights/week.<sup>1</sup> During pregnancy and in menopause, a woman's risk of developing SDB increases, likely due to hormonal changes and weight gain.<sup>2–4</sup> The rising levels of estrogen in pregnancy could contribute to lower extremity edema, vasodilation, and nasal congestion that in turn could affect the upper airway.

Also increasing along the pregnancy, progesterone enhances respiratory drive but could contribute to airway collapsibility. Narrowing of the maternal airway has been attributed to progressive gestational weight gain.<sup>5,6</sup>

Hypertension is a common pregnancy complication, affecting up to 10% of pregnancies, with subsequent and long-term implications for maternal and infant health.<sup>7–9</sup> Both a diagnosis of OSA as well as its key symptom of habitual snoring have been linked to hypertensive disorders of pregnancy,<sup>10–12</sup> gestational diabetes,<sup>13</sup> and poor fetal outcomes.<sup>14,15</sup> The presence of habitual snoring onset—chronic or pregnancy-induced—has been associated with a shortened gestation.<sup>16</sup>

Women with habitual snoring have an approximately 2-fold greater risk of gestational hypertension relative to nonsnorers, though snoring onset—prepregnancy or pregnancy—appears to be of significance.<sup>11,17</sup> While earlier investigations of maternal habitual snoring focused on its link to diagnoses of hypertensive disorders of pregnancy, less is known about its relation to changes in blood pressure (BP) over the course of pregnancy. Distinct BP trajectories among women with essential hypertension, gestational hypertension/pre-eclampsia, and normal BP are apparent as early as the first trimester of pregnancy and continuing into the second and third trimesters.<sup>18</sup> Earlier timing of elevated BP onset carries significant maternal morbidity.<sup>19,20</sup> Further, trimester-specific maternal BP is positively correlated with offspring BP patterns in the first years of their life.<sup>21</sup> Thus, the use of BP trajectories along pregnancy, rather than diagnostic categories for hypertension, reveals the presence and timing of departure from gestational BP norms. These points of departure may provide clues to gestational age-specific etiologies of rising BP and their consequences as well as highlight critical windows for enhanced BP surveillance and perhaps interventions among subsets of women with distinct characteristics such as habitual snoring.

While differential patterns of gestational BP have been previously reported in racial/ethnic minorities and in relation to cardiometabolic markers,<sup>22,23</sup> their association with habitual snoring, a key symptom of obstructive sleep apnea, has not been examined. To elucidate associations between habitual snoring and maternal BP, this study compares BP patterns across pregnancy in 3 groups of women: those with chronic habitual snoring, those with pregnancy-onset habitual snoring, and nonhabitual snoring “controls.” Serial BP measures, obtained as part of routine obstetrical practice, are used to examine variations in BP trajectories among women with habitual snoring, as these BP variations may carry risks of adverse maternal and fetal health that are not revealed solely by the diagnostic categories of hypertensive disorders of pregnancy. We hypothesized that women with gestational-onset snoring would have the highest BP trajectory, in comparison to those who reported chronic snoring or nonhabitual snoring.

## METHODS

### Study population

Pregnant women in the third trimester of a singleton pregnancy were recruited from prenatal clinics within the University of Michigan medical system. Exclusion criteria were <18 years of age and <28 weeks' gestation. Sleep characteristics were collected via medical charts and questionnaires, then linked to demographic, health, and gestational BP data abstracted from medical charts. Of the 1,611 women included in this cohort, 11 had 2 pregnancies during the study period. For these women, the first pregnancy was considered in the analyses. All women provided written informed consent. The study was approved by the University of Michigan Institutional Review Board (HUM00009271).

### Exposure: onset of habitual snoring

Study participants provided information about their sleep via questionnaires. Sleep questions covered the frequency of snoring

and whether snoring onset began prior to or during pregnancy, and if so, in which trimester. Possible responses to snoring frequency were “almost daily,” “3–4 times per week,” “1–2 times per week,” “1–2 times per month,” or “never.” Prior epidemiologic studies in the general population have demonstrated that self-reported habitual snoring is strongly and reliably associated with OSA severity.<sup>24,25</sup> In the second trimester of pregnancy, snoring was highly prevalent in pregnant women with obstructive sleep apnea.<sup>26</sup>

Habitual snoring was defined as snoring frequency  $\geq 3$  days per week. Based on these data, we classified women into 3 groups: chronic habitual snoring (habitual snoring that began before pregnancy), pregnancy-onset habitual snoring, and nonhabitual snoring controls.

### Outcome: systolic and diastolic blood pressure readings

This study was designed to collect and track BP measures in clinical practice. During a routine prenatal care visit, pregnant women sat in a quiet room before their blood pressure was taken by trained medical assistants using standard clinical protocols. In all women, blood pressure was measured once in a seated position using an automatic sphygmomanometer, routinely maintained by biomedical engineering. However, if a blood pressure reading was abnormal, the medical assistant repeated the measurement to ensure that the reading was valid.

Exclusion criteria were implemented to remove BP readings less than 3 days prior to delivery or outside of clinic hours (before 7 AM or after 5 PM). Women with <60 days of follow up or <3 BP measures in their medical charts also were excluded and multiple daily BP readings per woman were averaged. After all exclusions, the final sample included 1,305 pregnant women. The majority of these women (80%) had >10 BP readings across pregnancy.

### Covariates

Selection of potential confounding variables was guided by a review of relevant prior literature and by the creation of a directed acyclic graph that maps hypothesized relations among exposure, outcomes, and covariates. Maternal demographic and health characteristics, ie, age, parity, and prepregnancy body mass index (BMI) were included in the regression models as confounders. To account for the circadian patterns of systolic blood pressure (SBP) and diastolic blood pressure (DBP), we also controlled for the timing of the BP measurement, AM or PM.

### Statistical analyses

We used descriptive statistics to examine the demographic and health characteristics of women across the 3 exposure groups—chronic, pregnancy-onset habitual snoring, and controls. A one-way analysis of variance model was used to compare the means for the continuous variables, and a chi-square test was used for the categorical variables. To examine the association between habitual snoring and trajectories of SBP and DBP along pregnancy, we fitted linear mixed-effect models. In these models, BP readings were the repeated outcome while habitual snoring (coded as non/chronic/pregnancy-onset) was the exposure. Adjusted regression models controlled for maternal age, race/

ethnicity, prepregnancy BMI (kg/m<sup>2</sup>), time of BP reading (AM or PM), and gestational week. To capture quadratic associations between BP and gestational week we included gestational week squared as a covariate to the regression model. Finally, we assessed gestational week as a potential effect modifier of the association between habitual snoring and BP by adding gestational week\*habitual snoring as an interaction term. Based on the adjusted models, we plotted predicted mean SBP and DBP along the gestational age continuum for each exposure group. In these plots, the reference was non-Hispanic White, 30-year-old women with prepregnancy BMI of 25 (due to additivity, the same pattern would be seen for any other subgroup of women, with an additive shift). Additional plots show gestational week-specific mean differences of SBP and DBP between the snoring groups, along with their pointwise 95% confidence bands, holding all other covariates constant.

**RESULTS**

Of the 1,305 women included in the analytic sample, chronic or pregnancy-onset habitual snoring was reported by nearly a third and a quarter, respectively (Table 1). The majority of women were non-Hispanic White and college educated. Mean maternal age (standard deviation [SD]) was 29.5 (5.6), 30 (6), and 30.5 (5.7) years in controls, chronic, and pregnancy-onset habitual snoring, respectively. Habitual snoring was more common in Black non-Hispanic women, high school graduates, smokers, and those with chronic or gestational hypertension. Mean

pregnancy BMI was higher in chronic and pregnancy-onset habitual snoring groups in comparison to controls: 29.7 (8.9), 26.8 (7.2), and 24.4 (5.7), respectively.

Predicted mean SBP and DBP trajectories along the gestational age showed a U-shape form, with the lowest BP readings found at approximately week 20 to week 25. These trajectories resembled BP patterns in normotensive pregnancies.<sup>18</sup> The pregnancy-onset snoring group had the highest BP over time, followed by the chronic group and the control group for both SBP and DBP. In these plots, the reference was non-Hispanic White, 30-year-old women with prepregnancy BMI of 25 (Figure 1).

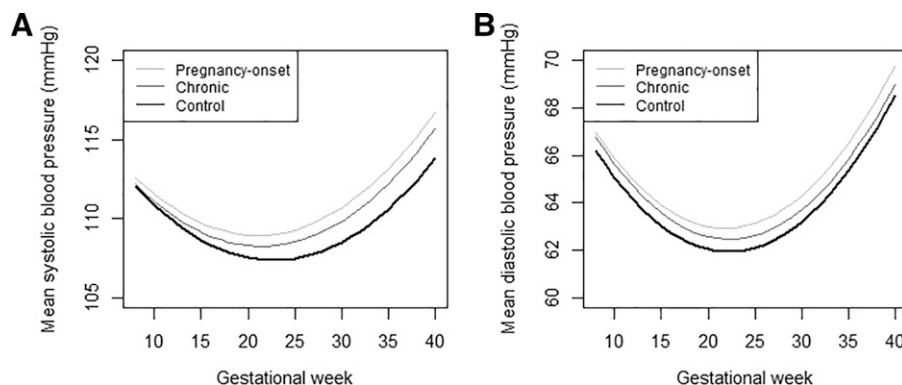
Gestational age-specific SBP was higher among women with pregnancy-onset habitual snoring in comparison to nonhabitual snoring controls, reaching a statistically significant difference at 18 weeks' gestation. These differences in SBP increased along the pregnancy and reached 3 mm Hg units by 40 weeks' gestation. A higher mean SBP among women with chronic habitual snoring vs controls became statistically significant in the third trimester. Overall, comparisons of mean SBP of women with chronic or pregnancy-onset habitual snoring were statistically insignificant (Figure 2).

A significantly higher mean DBP—by 1 mm Hg—was observed among women with pregnancy-onset habitual snoring in comparison to controls, after 15 weeks' gestation. However, other pairwise differences—chronic vs controls or chronic vs pregnancy-onset—were not statistically significant (Figure 3). Full model details are shown in Table S1 in the supplemental material, including all unadjusted and adjusted parameter estimates and 95% confidence intervals.

**Table 1**—Characteristics of pregnant women by timing of habitual snoring onset.

Maternal Characteristic	Habitual Snoring			P
	None	Chronic	Pregnancy-Onset	
Sample size, n (%)	615 (47)	396 (30)	294 (23)	
Maternal age, y, mean (SD)	29.5 (5.6)	30.0 (6.0)	30.5 (5.7)	.03
Race/ethnicity, n (%)				.01
White non-Hispanic	435 (71)	266 (67)	215 (73)	
Black non-Hispanic	78 (13)	80 (20)	35 (12)	
Asian	53 (9)	26 (7)	27 (9)	
Hispanic, American Indian, multiracial	49 (8)	24 (6)	17 (6)	
Education, n (%)				.0001
Less than high school	39 (6)	34 (9)	16 (6)	
High school	118 (19)	92 (24)	49 (17)	
Some college	114 (19)	107 (27)	64 (22)	
Bachelor's degree or higher	339 (56)	158 (40)	163 (56)	
Nulliparous, n (%)	273 (45)	170 (43)	128 (44)	.85
Smoking, n (%)	47 (8)	63 (16)	23 (8)	<.0001
Prepregnancy BMI, kg/m <sup>2</sup> , mean (SD)	24.4 (5.7)	29.7 (8.9)	26.8 (7.2)	<.0001
Chronic hypertension, n (%)	29 (5)	43 (11)	26 (9)	.0009
Hypertensive disorders of pregnancy, n (%)	74 (12)	85 (21)	67 (23)	<.0001

Hypertensive disorders of pregnancy include chronic, gestational hypertension, and preeclampsia. P value corresponds to the Pearson chi-square test of independence for each maternal characteristic. BMI = body mass index, SD = standard deviation.

**Figure 1**—Mean blood pressure along the gestational week continuum by onset of maternal habitual snoring.**(A)** Systolic blood pressure. **(B)** Diastolic blood pressure.

## DISCUSSION

In this large cohort of pregnant women, we found that women with pregnancy-onset habitual snoring tended to have higher mean SBP and DBP in comparison to women with chronic snoring or controls. The BP trajectory of these women demonstrated a higher SBP from 18 weeks' gestation, compared to controls; the difference between these 2 groups peaked at 3 mm Hg prior to 40 weeks.

There is now a robust literature from both cross-sectional and prospective studies that demonstrate SDB as a consistent, strong, and positive predictor of gestational hypertension and preeclampsia,<sup>17</sup> similar to studies of SDB and hypertension in nonpregnant adults.<sup>27</sup> A systematic review reported a 2.4 (95% CI, 1.63–3.47) pooled odds ratio of pregnancy-related hypertension among women with habitual snoring or moderate to severe OSA.<sup>28</sup> However, previously published information on the impact of SDB on trajectories of gestational BP is limited.

In healthy pregnancies, a decrease in BP is apparent in the second trimester, between 20 and 26 weeks' gestation. This nadir is followed with an increasing trend throughout the third trimester.<sup>23</sup> Patterns of BP among women affected by gestational hypertension, preeclampsia, and chronic hypertension were compared along the pregnancy with normotensive patterns in the Avon longitudinal study of parents and children.<sup>18</sup> Higher first trimester BP was observed among women with chronic hypertension, gestational hypertension, or preeclampsia in comparison to normotensive women. Following a mild BP decrease, women with chronic or gestational hypertension and preeclampsia had a rapid increase in BP relative to normotensive women. This BP increase occurred earlier in women with gestational hypertension or preeclampsia vs those with chronic hypertension, starting at 18 and 30 weeks' gestation, respectively.<sup>18</sup>

Trajectories of BP in pregnancy in relation to BMI have been described among 57 White, healthy women whose BP was measured at 14–16, 22–24, 30–32, and 36 weeks' gestation, and 6 weeks postpartum. This study showed a drop in SBP and DBP midpregnancy, at 22–24 weeks' gestation, and positive relationships between prepregnancy BMI and SBP.<sup>29</sup> Trajectories of

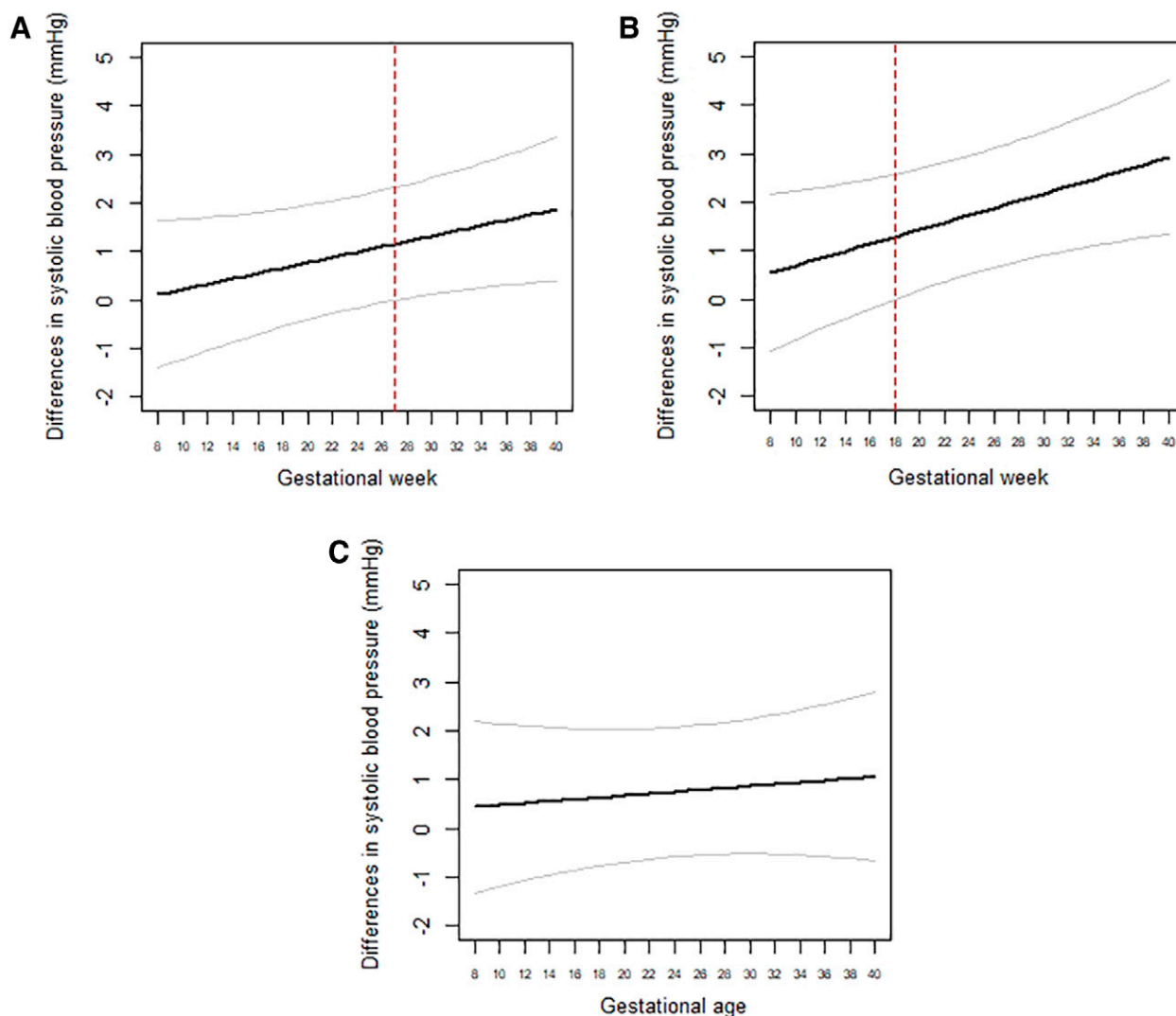
BP also have been associated with cardiometabolic markers. In a cohort of 199 healthy Brazilian women, trimester-specific SBP measures were positively associated with prepregnancy BMI, homeostatic model assessment for insulin resistance (HOMA-IR), total cholesterol, and leptin.<sup>22</sup> In another report, 418 young pregnant women age 14–25 years, race, prepregnancy BMI, and weight gain were examined in relation to BP trajectories.<sup>23</sup> Findings showed higher pregnancy BP measures across pregnancy in African American women compared with other racial/ethnic groups. Further, while both BMI and excessive weight gain were associated with pregnancy BP trajectories, each was a unique predictor of pregnancy BP patterns.<sup>23</sup>

Differential BP patterns may identify groups that should be monitored more closely in early gestation for subsequent onset of hypertensive disorders of pregnancy. Also, repeated BP readings across gestational weeks could provide additional information, beyond the categorical hypertension diagnosis, in studies of adverse perinatal outcomes and later-life cardiometabolic risks for mother and offspring. To this end, gestational weight gain, BMI, and dietary patterns have been studied in association to BP trajectories.<sup>23,30</sup> However, despite strong relationships between sleep health and hypertension in children<sup>31</sup> and adults,<sup>28,32</sup> as well as pregnant<sup>33</sup> women, examinations of BP trajectories in relation to sleep disturbances are scant. The present study suggests that women with pregnancy-onset habitual snoring have a unique BP trajectory in pregnancy that is not fully explained by prepregnancy BMI or pregnancy weight gain.

The physiological mechanisms linking SDB to hypertension include oxidative stress, systemic inflammation, sympathetic nervous system overactivity, and endothelial dysfunction, with obesity being a major risk factor.<sup>34</sup> Of note, the mechanisms by which sleep disruption may play a role in cardiovascular morbidity in the nonpregnant population are remarkably similar to the biological pathways for preeclampsia.<sup>35–39</sup>

It is plausible that pregnancy-onset snoring and any associated OSA could exacerbate underlying inflammatory processes during pregnancy and contribute to cardiovascular dysfunction. We speculate that without time for cardiovascular adaptation, women with pregnancy-onset snoring are at higher risk of

**Figure 2**—Pairwise differences among snoring groups in systolic blood pressure, with 95% pointwise confidence bands, along the gestational week continuum.



Red dotted line marks the gestational age where differences in blood pressure trajectories are statistically significant. **(A)** Chronic habitual snoring vs controls. **(B)** Pregnancy-onset habitual snoring vs controls. **(C)** Pregnancy-onset vs chronic habitual snoring.

elevated BP sooner in pregnancy, unlike those with chronic snoring who have had time to adapt. This speculation parallels maternal physiological adaptation to chronic hypoxia, attributed to residency in high-altitude areas, that confers fetal resilience to compromised development.<sup>40</sup>

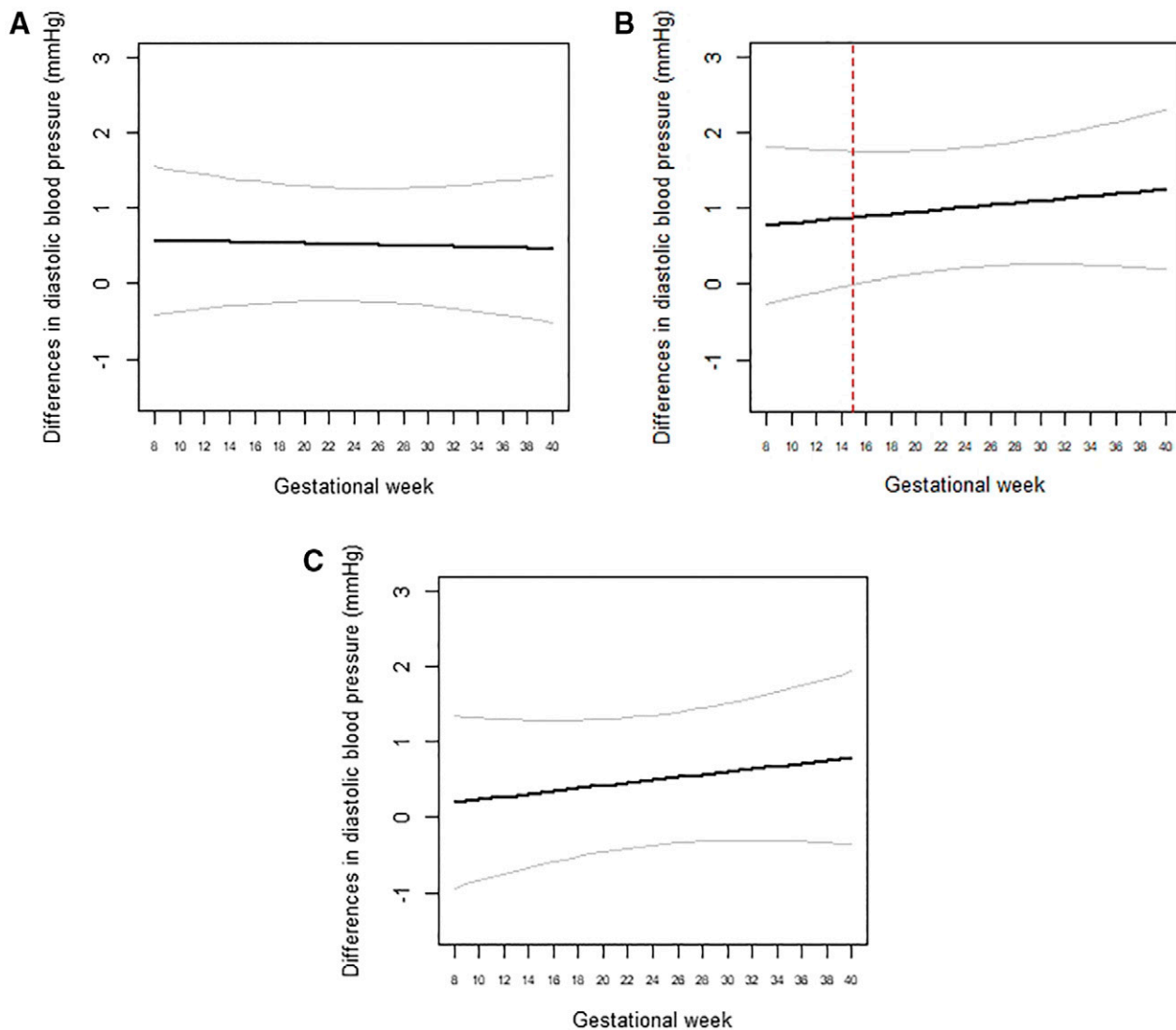
The mean BP differences between snoring groups in our study were modest, ie, 1, 2, or 3 mm Hg. While differences of this magnitude are less consequential at the level of the individual, they can have a substantive impact on population health.<sup>41,42</sup> Moreover, even mild increases in maternal BP recently have been linked to higher BP levels in their offspring.<sup>21</sup>

The present study has several strengths. First, this large, prospective cohort examined associations of maternal habitual snoring, chronic or pregnancy-onset, in relation to SBP and DBP measured repeatedly along the gestational age continuum, rather than focusing only on a diagnosis of hypertension. The repeated-

measure study design allows examination of between- and within-group BP variations. While BP measures were not collected according to a standard clinical protocol, these readings represent measures typically obtained in clinical practice and used by clinicians for decision-making on a daily basis; thus our approach increases the generalizability of our findings and their potential application in real-world settings.

A potential limitation in our study includes the reliance on self-reported habitual snoring; this may have produced some misclassification of women who snore as nonhabitual controls which could have resulted in an attenuation of effect estimates. This study utilized a symptom-based sleep-disordered breathing assessment, which is more prevalent in pregnant populations than conventionally assessed OSA.<sup>10</sup> Information on snoring onset could be influenced by recall bias. However, as women reported broadly whether their snoring began

**Figure 3**—Pairwise differences among snoring groups in diastolic blood pressure, with 95% pointwise confidence bands, along the gestational week continuum.



Red dotted line marks the gestational age where differences in blood pressure trajectories are statistically significant. **(A)** Chronic habitual snoring vs controls. **(B)** Pregnancy-onset habitual snoring vs controls. **(C)** Pregnancy-onset vs chronic habitual snoring.

prepregnancy or during pregnancy (trimester-specific), recall bias may be less significant. Finally, while the onset of pregnancy snoring typically was reported in the second or third trimester, we cannot determine whether it preceded the divergence in BP trajectories.

**CONCLUSIONS**

This study found that pregnancy-onset and chronic maternal snoring are associated with higher mean maternal BP in pregnancy, starting around 18 weeks’ and 27 weeks’ gestation, respectively. The findings of divergent BP trajectories suggest the 2 groups of women with habitual snoring in pregnancy should be

considered separately when evaluating gestational “windows” for increased BP monitoring and provide insight into pathophysiologic changes.

**ABBREVIATIONS**

- BMI, body mass index
- BP, blood pressure
- DBP, diastolic blood pressure
- OSA, obstructive sleep apnea
- SBP, systolic blood pressure
- SD, standard deviation
- SDB, sleep-disordered breathing

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