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Pregnancy-Onset Habitual Snoring, Gestational Hypertension, and Pre-eclampsia: Prospective Cohort Study

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Abstract

Objective—This study aimed to prospectively examine the impact of chronic vs. pregnancy-onset habitual snoring on gestational hypertension, pre-eclampsia, and gestational diabetes.

Study Design—Third trimester pregnant women were recruited from a large, tertiary medical center, between March 2007 and December 2010 and screened for the presence and duration of habitual snoring, as a known marker for sleep-disordered breathing. Clinical diagnoses of gestational hypertension, pre-eclampsia, and gestational diabetes were obtained.

Results—Of 1,719 pregnant women, 34% reported snoring, with 25% reporting pregnancy-onset snoring. After adjusting for confounders pregnancy-onset, but not chronic snoring, was independently associated with gestational hypertension (odds ratio 2.36, 95%CI 1.48–3.77, p<0.001) and pre-eclampsia (odds ratio 1.59, 95%CI 1.06–2.37 p=0.024) but not gestational diabetes.

Conclusion—New-onset snoring during pregnancy is a strong risk factor for gestational hypertension and pre-eclampsia. In view of the significant morbidity and healthcare costs associated with hypertensive diseases of pregnancy, simple screening of pregnant women may have clinical utility.

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Dr. O'Brien has received equipment support from Philips Respironics Inc. and has served on an advisory board for GlaxoSmithKline. Dr. Chervin receives educational grants from Philips Respironics Inc., Fisher Paykel Inc., is named in patents owned by the University of Michigan for signal analysis diagnostic algorithms and hardware relevant to the assessment and treatment of sleep disorders, and serves on the Board of Directors of the American Academy of Sleep Medicine. None of the other authors have conflicts to disclose.

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Keywords

pregnancy; snoring; gestational hypertension; pre-eclampsia; gestational diabetes

INTRODUCTION

Sleep-disordered breathing, a spectrum of respiratory abnormalities during sleep ranging from habitual snoring to obstructive sleep apnea, is common yet often undiagnosed, especially in women.[1] Increased weight promotes SDB and, strikingly, a weight gain of only 10% has been associated with a 6-fold increase in the development of significant SDB.[2] This observation is particularly relevant to pregnancy as weight gain >10% occurs in most women. Habitual snoring, the hallmark symptom of SDB, increases during pregnancy[3–5] and is particularly common in pre-eclampsia.[6]

The cardiovascular implications of untreated SDB are substantial and complex. Several large, population-based studies such as the Sleep Heart Health Study and the Wisconsin Sleep Cohort Study have provided clear evidence for an independent association between SDB and cardiovascular disease, particularly hypertension and metabolic dysfunction.[7–11] The Nurses Health Study found that snoring increased the risk of incident hypertension independent of age or body mass index (BMI).[12] The mechanisms linking SDB and cardiovascular disease are likely multifactorial, involving sympathetic over-activity, inflammation, and endothelial dysfunction.

Hypertensive disorders of pregnancy are a leading cause of maternal and infant morbidity[13] and cost billions of dollars annually to treat. An emerging literature of cross-sectional studies support an association between sleep-disordered breathing and hypertension during pregnancy.[5, 14–17] The association between SDB and hypertension is particularly relevant during pregnancy as such morbidities jeopardize the health of mother and fetus, with major public health impact. Furthermore, new onset SDB during pregnancy conceivably could have health ramifications that exceed those of chronic SDB, to which cardiovascular systems might have time to adapt. An improved understanding of some vulnerabilities unique to pregnancy may offer opportunities to improve the health of both mothers and infants.

The goals of this study were to determine the prevalence and incidence of snoring during pregnancy and to examine associations with maternal health. We hypothesized that snoring, and especially pregnancy-onset rather than chronic snoring, would be associated with gestational hypertension, pre-eclampsia, and gestational diabetes.

METHODS

In this prospective study pregnant women were recruited from prenatal clinics within the University of Michigan between March 2007 and December 2010. Women were eligible if they were ≥18 years old and ≥28 weeks pregnant with a single fetus. There were no other exclusion criteria. Written informed consent was obtained to access medical records. A comparison group of non-pregnant control women was recruited from women aged 18–45 years attending routine gynecology visits. This study was approved by the University of Michigan Institutional Review Board.

Pregnant women completed a questionnaire about the presence of habitual snoring and whether they had "stopped breathing or gasped for air" (Appendix 1). They were also asked whether a bed-partner had complained. Habitual snoring was defined as snoring at least 3–4

times per week.[18, 19] Similarly witnessed apneas were considered present if women "stopped breathing or gasped for air" at least 3–4 times per week. Enquiry was made about the timing of snoring to identify incident cases. Pregnancy-onset snoring was considered present when habitual snoring began during pregnancy. Chronic snoring was defined as habitual snoring both before *and* during pregnancy. A single question item about snoring was chosen instead of a multi-item SDB questionnaire for several reasons: a single question is strongly and reliably associated with the overnight polysomnogram (PSG)-derived apnea/hypopnea index (AHI, number of apneic events per hour of sleep);[8, 20] in women a report of "often" or "usually (always or almost always)" snoring is associated with PSG-confirmed SDB with respective odds ratios of 3.8 and 16.3;[20] its use provides an approach easily and immediately translated into clinical settings; no study has failed to associate snoring with objective measures of SDB from a PSG; validation of complex SDB screening tools in pregnancy has not been performed; most SDB scales emphasize weight, which in pregnancy will be necessarily high; and several scales rely on gender or hypertensive status, the major outcome in the current study. Non-pregnant women completed the same screening tools, with the exception of symptoms in relation to pregnancy. Pregnant women received a $10 gift card for participating.

Pre-pregnancy BMI was calculated from maternal self-report of height and weight just prior to conception and cross-checked with documented BMI from the initial obstetric visit in the first trimester. Serial weights throughout the pregnancy were obtained from clinical visits and, following delivery, the total amount of weight gain was calculated. Key variables abstracted from medical records included demographics, previous or family history of gestational hypertension or pre-eclampsia, smoking status, and the presence of a diagnosis of chronic hypertension, gestational hypertension, pre-eclampsia, or gestational diabetes. The latter diagnoses were obtained from medical coding using the International Classification of Diseases, 9th edition (ICD-9).[21] In reporting this study, guidelines from Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) group[22] were followed.

Statistics

Sample size was calculated based on literature available at the time of study design. We predicted the frequency of snoring as 4% in non-pregnant women and 25% in pregnant women.[5, 6, 23] With a sample size ≥1,400 pregnant women and 200 controls there would be a power of almost 100% to detect this difference with a 2-tailed significance level of 5%. If the frequency of snoring in non-pregnant women was 16% and that in pregnant women remained at 25%, the targeted sample sizes would provide 82% power to detect a difference. We anticipated that approximately 4% of women without snoring would develop hypertension compared to 10% of women with snoring.[5] Thus a test for equal frequency of hypertension based on this study (test for equality of binomial proportions) would have power of over 95%. We planned to recruit unequal group sizes because the non-pregnant controls would serve only as a comparison for frequency of snoring.

As BMI is strongly associated with SDB, and BMI changes across pregnancy, pre-pregnancy or early first trimester BMI was categorized according to Institute of Medicine (IOM) recommendations.[24] Subjects were classified as underweight (BMI<18.5kg/m^2); normal weight (BMI 18.5–24.9kg/m^2); overweight (BMI 25.0–29.9kg/m^2); or obese (BMI ≥30.0kg/m^2). Absolute weight gain was determined and subjects were classified according to whether they exceeded the IOM recommendations for gestational weight gain; 28–40lbs for underweight women, 25–35lbs for normal weight women, 15–25lbs for overweight women, and 11–20lbs for obese women.

All data obtained were double-entered into a database to ensure accuracy and analyzed with SPSS (version 18.0, Chicago, IL). Histograms, box-plots, and descriptive methods were used to examine data for errors and outliers. Between-group comparisons of continuous variables (maternal age, BMI, and gestational age) were conducted with t-tests (snoring vs. no snoring) and ANOVA (chronic snoring, pregnancy-onset snoring, and no snoring). Dichotomized variables were compared with Chi-Squared tests. Logistic regression was used to determine associations between snoring and maternal outcomes after adjusting for potential covariates (maternal age, race, pre-pregnancy BMI, weight gain in excess of IOM recommendations, gravidity, smoking, educational level, previous or family history of gestational hypertension/pre-eclampsia). Odds ratios (OR) and 95% Confidence Intervals (CI) were calculated. A p-value <0.05 was considered statistically significant. Population attributable risk percent (PAR%) was calculated; this represents the proportion of disease (hypertension/pre-eclampsia) among the total population that would not have occurred in the absence of exposure (snoring), assuming that the exposure contributes in a causal manner to the disease. The following formula was used:

$$\mathrm{PAR\%}=(\mathrm{Incidence}_{\mathrm{total\_population}}-\mathrm{Incidence}_{\mathrm{unexposed}})/\mathrm{Incidence}_{\mathrm{total\_population}}$$

RESULTS

In total, 2,038 pregnant women were invited to participate; 1,719 (84%) agreed to complete the surveys, 98% of whom consented to medical record access. There were no differences in maternal age, gestational age, parity, or BMI between women who did or did not participate or who did/did not consent to medical record access (data not shown). Five women were subsequently excluded because they were <28 weeks' gestation and two women were excluded because they were <18 years. In addition, 9 women moved out of the area before delivery. Thus, the total sample was 1,712 for prevalence data and 1,673 for pregnancy outcomes (Figure 1). In total, 202 non-pregnant women were enrolled. Overall, 94% of women had bed partners; only 2% of partners complained about snoring when women classified themselves as non-snorers. This did not alter the association with outcomes and thus the analyses were performed with maternal self-report only.

Table 1 shows population demographics. Pregnant women were more than twice as likely as controls to snore: 34.1% vs. 14·9%, p<0.0001.

Overall, 34.1% of third-trimester women reported snoring; 66% were non-snorers at both pre-pregnancy and in the 3rd trimester, 25% started snoring during pregnancy, and 9% reported chronic snoring (Table 2). Snorers in general, as well as those with pregnancy-onset snoring specifically, were more likely to have chronic hypertension, gestational hypertension, and pre-eclampsia, than non-snorers. In contrast, although snorers were more likely to have gestational diabetes compared to non-snorers, further analysis revealed that it was the chronic, not pregnancy-onset, snorers who appeared to drive this relationship.

In unadjusted analyses, pregnancy-onset, but not chronic, snoring was independently associated with gestational hypertension; OR 2.57, 95%CI 1.69–3.53, p<0.001, and pre-eclampsia; OR 1.71, 95%CI 1.20–2.44, p=0.003. There was no relationship with pregnancy-onset snoring and gestational diabetes; OR 1.29, 95%CI 0.96–1.74, p=0.09. However, chronic snoring was associated with gestational diabetes; OR 1.67, 95%CI 1.10–2.52, p=0.015.

A logistic regression model that controlled for potential covariates (maternal age, race, pre-pregnancy BMI, weight gain in excess of IOM recommendations, gravidity, smoking,

education level, previous or family history of gestational hypertension or pre-eclampsia) showed that pregnancy-onset, but not chronic, snoring was independently associated with gestational hypertension, OR 2.36, 95%CI 1.48–3.77, p<0.001. In this model exceeding the IOM weight gain guidelines, but not pre-pregnancy BMI, was also independently associated with gestational hypertension; OR 2.68, 95%CI 1.72–4.18, p<0.001. Table 3a.

Similarly, in a logistic regression model controlling for the same covariates and including chronic hypertension and gestational diabetes, pregnancy-onset – but not chronic - snoring was independently associated with pre-eclampsia; OR 1.59, 95%CI 1.06–2.37; p=0.024; Table 3b. No interactions were found between snoring and pre-pregnancy BMI for gestational hypertension or pre-eclampsia. Similarly, no interactions were found between snoring and weight gain in excess of IOM recommendations.

Blood glucose levels at the 24–26 week gestation 1-hour oral glucose tolerance test using a 50gram load were higher in snorers compared to non-snorers;124.0mg/dl vs. 117.2mg/dl, p<0.001, as was the proportion of women with abnormal glucose levels, defined as ≥140mg/dl; 30.2% vs. 22.1%, p=0.003. Glucose levels were not compared between women with and without pregnancy-onset snoring, as glucose was assessed in the second trimester. Neither pregnancy-onset nor chronic snoring was found to be associated with gestational diabetes in a multivariate model; however pre-pregnancy BMI and maternal age were associated (Table 3c).

Figure 2 graphically depicts the OR of pre-pregnancy obesity (BMI ≥ 30) and/or snoring in separate models for gestational hypertension, pre-eclampsia, and gestational diabetes after adjusting for covariates that were shown in Table 3 to be associated with the outcome of interest. For illustrative purposes data are shown as snorers (pregnancy-onset and chronic snoring) vs. non-snorers. Four groups are represented: lean, non-snorer (BMI<25kg/m^2, the reference group, n=689); lean snorer (n=195); obese, non-snorer, (n=189); and obese snorer (n=217). Compared to lean, non-snorers, both lean and obese snorers had significantly increased ORs for gestational hypertension: lean snorers OR 2.82, 95%CI 1.42–5.59, p=0.003, and obese snorers OR 2.39, 95%CI 1.22–4.71, p=0.012. Obese non-snorers were not at increased risk of gestational hypertension, OR 1.74, 95%CI 0.81–3.5, p=0.15. Figure 2A.

Compared to lean non-snorers, only obese snorers had increased risk for pre-eclampsia; OR 1.58, 95%CI 1.01–2.78 p=0.05; Figure 2B. Conversely, only obese women, regardless of snoring status, had increased risk for gestational diabetes; OR 2.31, 95%CI 1.01–5.36, p=0.05 for obese non-snorers and OR 4.12, 95%CI 1.78–9.52, p=0.001 for obese snorers; Figure 2C.

If snoring plays a causative role in hypertension, then the PAR% suggests that 15.0% of gestational hypertension and 14.4% of pre-eclampsia in this population could be ameliorated by elimination of snoring. Similarly, 18.7% of gestational hypertension and 11.6% of pre-eclampsia could be ameliorated by elimination of pregnancy-onset snoring.

A total of 1.2% of women reported witnessed apneas. Snorers (chronic or pregnancy-onset) were more likely than non-snorers to endorse this; 3.0% vs. 0.4% respectively; p<0.001. Women with gestational hypertension, pre-eclampsia, or gestational diabetes were no more likely to report apnea than women without these conditions. However, the total number of women who reported apnea was small, precluding use of regression models.

Comment

This is the first large, prospective study to demonstrate that pregnancy-onset snoring confers significant risk to maternal cardiovascular health. These novel findings strongly implicate a role not only for snoring in general but, more specifically, for pregnancy-onset snoring in both gestational hypertension and pre-eclampsia. Furthermore, the PAR% suggests that if snoring plays a causal role in maternal hypertension, approximately 12–19% of hypertensive disorders during pregnancy might be ameliorated through treatment of snoring and any associated SDB. In contrast, the data did not suggest any independent role for snoring in gestational diabetes.

Notably, weight gain in excess of IOM recommendations, but not pre-pregnancy BMI, was found to play an independent role in gestational hypertension. Both pre-pregnancy BMI and excessive weight gain were independent predictors of pre-eclampsia. Although excessive weight gain is a known risk factor for post-partum weight retention,[25] this is the first study to show its independent relationship to cardiovascular outcomes. This novel finding could have important implications for clinical care.

Our findings support and extend earlier observations that the frequency of snoring increases throughout pregnancy, peaks in the third trimester,[4] and is a risk for hypertension.[14, 15, 23, 26, 27] However, none of the previous studies investigated the impact of incident habitual snoring on maternal outcomes. Previous studies suggest that 14–23% of pregnant women habitually snore, compared to 4% of non-pregnant women,[5, 23] although more recent estimates suggest a considerably higher proportion[6,15] particularly in pre-eclampsia.[6] Potential explanations of the lower frequencies in earlier studies are that only women attending low risk clinics who had vaginal deliveries were included[5] and obesity was relatively infrequent in some populations.[5, 23]

Intriguing preliminary data suggest that new snoring during pregnancy is associated with increased erythropoesis and consequently increased levels of nucleated red blood cells in the umbilical cord.[28] Erythropoesis occurs during periods of hypoxia, and conditions such as uterine growth restriction and maternal hypertension are associated with elevated counts.[29] These findings in combination with our own implicate pregnancy-onset snoring as a particular concern.

Contrary to recent reports[15, 30, 31] we did not find that snoring is associated with gestational diabetes. This discrepancy may be explained in part by different methodologies including recruitment of postpartum women,[15] few women with the variable of interest,[30, 31] and the lack of information about pre-pregnancy BMI.[15] Nonetheless, the role of sleep in glucose control during pregnancy merits further investigation.

Although the pathogenesis of pre-eclampsia is not completely understood, the biological pathways include endothelial dysfunction, oxidative stress, and inflammation, with obesity being a major risk factor. The pathogenic process likely originates in the placenta during early pregnancy with abnormal implantation and vasculature development, leading to oxidative stress and inflammation with subsequent release of anti-angiogenic factors and widespread endothelial dysfunction.[32] Of note, the mechanisms of sleep disruption that affect cardiovascular morbidity in non-pregnant individuals are remarkably similar to the biological pathways for pre-eclampsia, with strong evidence for oxidative stress, inflammation, sympathetic nervous systemic activation, endothelial dysfunction, dyslipidemia, and obesity as major factors in the pathophysiology of cardiovascular morbidity in SDB.[33] These shared mechanistic pathways have been reviewed recently.[34]

Considering these overlapping risk factors, the finding that pregnancy-onset, but not chronic, snoring was associated with gestational hypertension and pre-eclampsia may be surprising. Sleep disruption and the consequent inflammatory cascade in early pregnancy may interfere with normal placental implantation,[35] although this may not completely explain our findings since the majority of women with pregnancy-onset snoring started in their second or third trimesters. The possibility remains, however, that pregnancy-onset snoring could exacerbate underlying inflammatory processes and enhance underlying cardiovascular dysfunction. Another possibility is that fluid shifts[36] or inflammation promotes the appearance of SDB. However, preliminary data show that treatment of SDB during pregnancy may improve blood pressure,[37, 38] suggesting that SDB is more likely to contribute to hypertensive disease, rather than result from it or from a third process that causes both hypertension and SDB.

Key strengths of the present study include the largest sample size to date, prospective design, high response rate, adjustment for other known risk factors for gestational hypertension/pre-eclampsia (particularly a previous and family history of these conditions), and a population pool representative of other major medical centers. The University of Michigan Health System is the largest of only two in Washtenaw County that provide maternity services. Therefore, selection bias of a tertiary referral center should be minimal.

Use of symptom-based screening not yet validated against PSG in pregnant women could be a limitation. However, the major goal was to validate the utility of snoring directly as a predictor of maternal outcomes. Self-report of snoring is strongly and reliably associated with the PSG-derived AHI[8, 20] and our own data confirm this in pregnancy.[39] The present large-sample focus on snoring is also a strength of the study design as queries about snoring can be readily adopted in clinical practice for little expense. However, elucidation of mechanisms that underlie any association between SDB and pregnancy outcomes require investigation in PSG-studies that allow assessment of whether respiratory effort, airflow limitation, sleep fragmentation, or gas exchange abnormalities best predict adverse outcomes and treatment response.

It is possible that some recall bias occurred with regards to snoring duration. Although information was obtained prospectively, women may have been less aware of their pre-pregnancy snoring. A further limitation is the temporal relationship between snoring onset and time of a diagnosis of gestational hypertension, pre-eclampsia, or gestational diabetes. This study cannot prove the direction of this relationship but clearly suggests an independent association.

In conclusion, pregnancy-onset rather than chronic snoring is independently associated with gestational hypertension and pre-eclampsia but not gestational diabetes. Rather than a multi-item composite SDB screen, two simple questions about snoring and the timing of its appearance could be an effective strategy in busy clinical settings to assist in identification of pregnant women at high risk for hypertensive disorders. These findings reinforce the need for a randomized controlled trial to investigate the impact of treatment interventions on maternal hypertension.

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References

1. Young T, Evans L, Finn L, Palta M. Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. Sleep. 1997; 20(9):705–6. [PubMed: 9406321]
2. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. Jama. 2000; 284(23):3015–21. [PubMed: 11122588]
3. Hedman C, Pohjasvaara T, Tolonen U, Suhonen-Malm AS, Myllyla VV. Effects of pregnancy on mothers' sleep. Sleep Med. 2002; 3(1):37–42. [PubMed: 14592252]
4. Pien GW, Fife D, Pack AI, Nkwuo JE, Schwab RJ. Changes in symptoms of sleep-disordered breathing during pregnancy. Sleep. 2005; 28(10):1299–305. [PubMed: 16295215]
5. Franklin KA, Holmgren PA, Jonsson F, Poromaa N, Stenlund H, Svanborg E. Snoring, pregnancy-induced hypertension, and growth retardation of the fetus. Chest. 2000; 117(1):137–41. [PubMed: 10631211]
6. Izci B, Martin SE, Dundas KC, Liston WA, Calder AA, Douglas NJ. Sleep complaints: snoring and daytime sleepiness in pregnant and pre-eclamptic women. Sleep medicine. 2005; 6(2):163–9. [PubMed: 15716220]
7. Young T, Peppard P, Palta M, Hla KM, Finn L, Morgan B, et al. Population-based study of sleep-disordered breathing as a risk factor for hypertension. Arch Intern Med. 1997; 157(15):1746–52. [PubMed: 9250236]
8. Nieto FJ, Young TB, Lind BK, Shahar E, Samet JM, Redline S, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. Jama. 2000; 283(14):1829–36. [PubMed: 10770144]
9. Nieto FJ, Peppard PE, Young TB. Sleep disordered breathing and metabolic syndrome. WMJ: official publication of the State Medical Society of Wisconsin. 2009; 108(5):263–5. [PubMed: 19743760]
10. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med. 2000; 342(19):1378–84. [PubMed: 10805822]
11. Shahar E, Whitney CW, Redline S, Lee ET, Newman AB, Javier Nieto F, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med. 2001; 163(1):19–25. [PubMed: 11208620]
12. Hu FB, Willett WC, Colditz GA, Ascherio A, Speizer FE, Rosner B, et al. Prospective study of snoring and risk of hypertension in women. Am J Epidemiol. 1999; 150(8):806–16. [PubMed: 10522651]
13. Khan KS, Wojdyla D, Say L, Gulmezoglu AM, Van Look PF. WHO analysis of causes of maternal death: a systematic review. Lancet. 2006; 367(9516):1066–74. [PubMed: 16581405]
14. Perez-Chada D, Videla AJ, O'Flaherty ME, Majul C, Catalini AM, Caballer CA, et al. Snoring, witnessed sleep apnoeas and pregnancy-induced hypertension. Acta Obstet Gynecol Scand. 2007; 86(7):788–92. [PubMed: 17611822]
15. Bourjeily G, Raker CA, Chalhoub M, Miller MA. Pregnancy and fetal outcomes of symptoms of sleep-disordered breathing. Eur Respir J. 2010; 36(4):849–55. [PubMed: 20525714]
16. Ursavas A, Karadag M, Nalci N, Ercan I, Gozu RO. Self-reported snoring, maternal obesity and neck circumference as risk factors for pregnancy-induced hypertension and preeclampsia. Respiration. 2008; 76(1):33–9. [PubMed: 17728529]
17. Louis JM, Auckley D, Sokol RJ, Mercer BM. Maternal and neonatal morbidities associated with obstructive sleep apnea complicating pregnancy. Am J Obstet Gynecol. 2010; 202(3):261, e1–5. [PubMed: 20005507]
18. Kump K, Whalen C, Tishler PV, Browner I, Ferrette V, Strohl KP, et al. Assessment of the validity and utility of a sleep-symptom questionnaire. Am J Respir Crit Care Med. 1994; 150(3):735–41. [PubMed: 8087345]

19. Young T, Shahar E, Nieto FJ, Redline S, Newman AB, Gottlieb DJ, et al. Predictors of sleep-disordered breathing in community-dwelling adults: the Sleep Heart Health Study. Arch Intern Med. 2002; 162(8):893–900. [PubMed: 11966340]
20. Bliwise DL, Nekich JC, Dement WC. Relative validity of self-reported snoring as a symptom of sleep apnea in a sleep clinic population. Chest. 1991; 99(3):600–8. [PubMed: 1995215]
21. World Health Organization. Family of International Classifications.
22. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007; 370(9596):1453–7. [PubMed: 18064739]
23. Loube DI, Poceta JS, Morales MC, Peacock MD, Mitler MM. Self-reported snoring in pregnancy. Association with fetal outcome. Chest. 1996; 109(4):885–9. [PubMed: 8635365]
24. Rasmussen, KM.; Yaktine, AL., editors. Institute of Medicine (US) and National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines. Weight Gain During Pregnancy: Reexamining the Guidelines. Washington D.C: The National Academies Press; 2009.
25. Nehring I, Schmoll S, Beyerlein A, Hauner H, von Kries R. Gestational weight gain and long-term postpartum weight retention: a meta-analysis. The American journal of clinical nutrition. 2011; 94:1225–31. [PubMed: 21918221]
26. Champagne KA, Kimoff RJ, Barriga PC, Schwartzman K. Sleep disordered breathing in women of childbearing age & during pregnancy. Indian J Med Res. 2010; 131:285–301. [PubMed: 20308754]
27. Guilleminault C, Querra-Salva M, Chowdhuri S, Poyares D. Normal pregnancy, daytime sleeping, snoring and blood pressure. Sleep medicine. 2000; 1(4):289–97. [PubMed: 11040461]
28. Tauman R, Many A, Deutsch V, Arvas S, Ascher-Landsberg J, Greenfeld M, et al. Maternal snoring during pregnancy is associated with enhanced fetal erythropoiesis--a preliminary study. Sleep medicine. 2011; 12(5):518–22. [PubMed: 21440495]
29. Hermansen MC. Nucleated red blood cells in the fetus and newborn. Arch Dis Child Fetal Neonatal Ed. 2001; 84(3):F211–5. [PubMed: 11320052]
30. Facco FL, Grobman WA, Kramer J, Ho KH, Zee PC. Self-reported short sleep duration and frequent snoring in pregnancy: impact on glucose metabolism. Am J Obstet Gynecol. 2010; 203(2):142, e1–5. [PubMed: 20510182]
31. Qiu C, Enquobahrie D, Frederick IO, Abetew D, Williams MA. Glucose intolerance and gestational diabetes risk in relation to sleep duration and snoring during pregnancy: a pilot study. BMC Womens Health. 2010; 10:17. [PubMed: 20470416]
32. Powe CE, Levine RJ, Karumanchi SA. Preeclampsia, a disease of the maternal endothelium: the role of antiangiogenic factors and implications for later cardiovascular disease. Circulation. 2011; 123(24):2856–69. [PubMed: 21690502]
33. Lavie L. Oxidative stress–a unifying paradigm in obstructive sleep apnea and comorbidities. Prog Cardiovasc Dis. 2009; 51(4):303–12. [PubMed: 19110132]
34. Izci-Balserak B, Pien GW. Sleep-disordered breathing and pregnancy: potential mechanisms and evidence for maternal and fetal morbidity. Curr Opin Pulm Med. 2010; 16(6):574–82. [PubMed: 20859210]
35. Okun ML, Roberts JM, Marsland AL, Hall M. How disturbed sleep may be a risk factor for adverse pregnancy outcomes. Obstet Gynecol Surv. 2009; 64(4):273–80. [PubMed: 19296861]
36. Su MC, Chiu KL, Ruttanaumpawan P, Shiota S, Yumino D, Redolfi S, et al. Difference in upper airway collapsibility during wakefulness between men and women in response to lower-body positive pressure. Clin Sci (Lond). 2009; 116(9):713–20. [PubMed: 19007335]
37. Edwards N, Blyton DM, Kirjavainen T, Kesby GJ, Sullivan CE. Nasal continuous positive airway pressure reduces sleep-induced blood pressure increments in preeclampsia. Am J Respir Crit Care Med. 2000; 162(1):252–7. [PubMed: 10903250]
38. Poyares D, Guilleminault C, Hachul H, Fujita L, Takaoka S, Tufik S, et al. Pre-eclampsia and nasal CPAP: part 2. Hypertension during pregnancy, chronic snoring, and early nasal CPAP intervention. Sleep medicine. 2007; 9(1):15–21. [PubMed: 17644475]

39. O'Brien LMBA, Hewlett MM, Martel K, Arastu F, Kempf LA, Shelgikar A, Chames MC, Chervin RD. Associations Between Habitual Snoring and PSG-Defined SDB in Pregnant Women. Sleep. 2011; 34:A320.

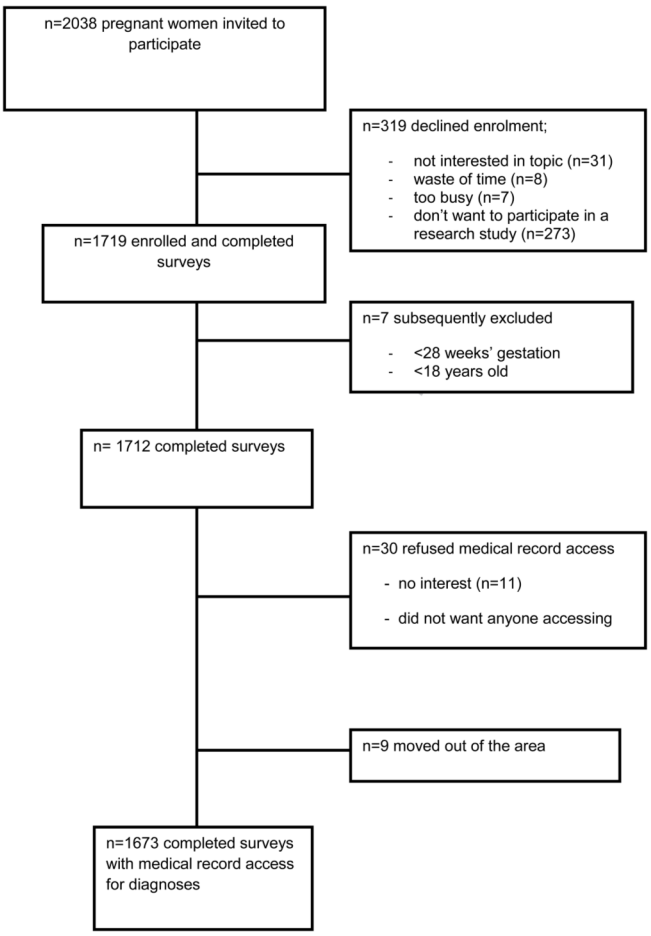
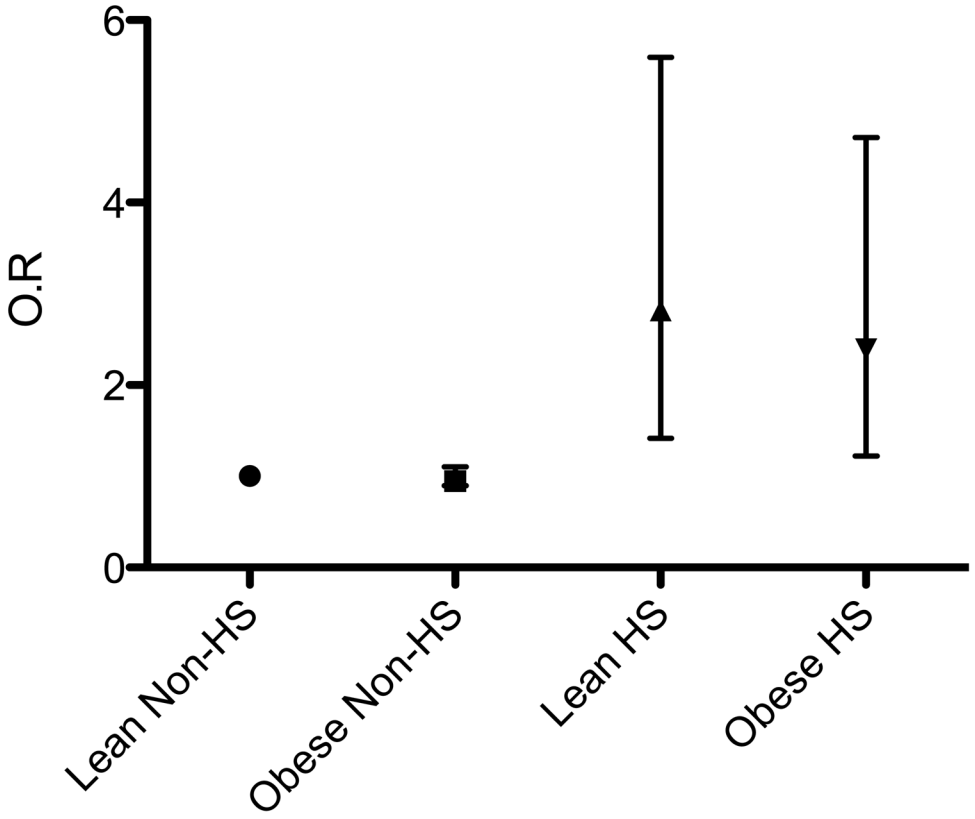
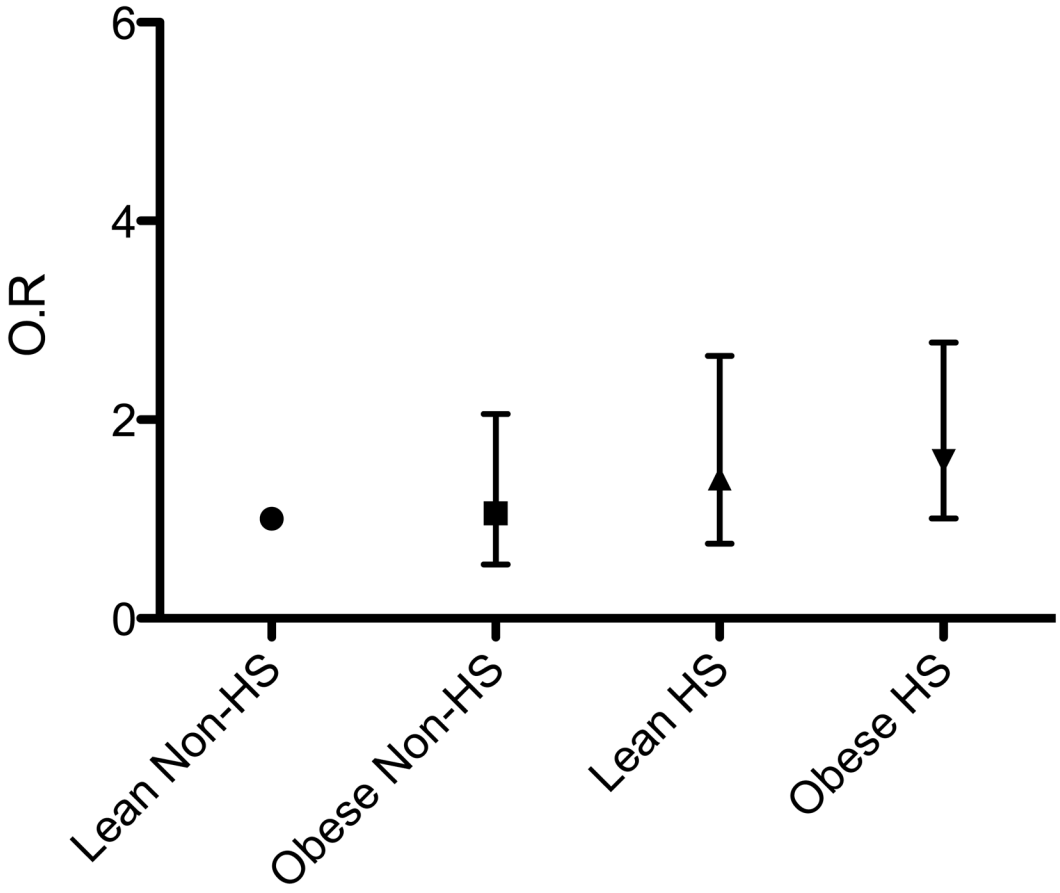


Figure 1.
Recruitment flow chart

A. Odds ratio for gestational hypertension by obesity and snoring status



B. Odds ratio for pre-eclampsia by obesity and snoring status



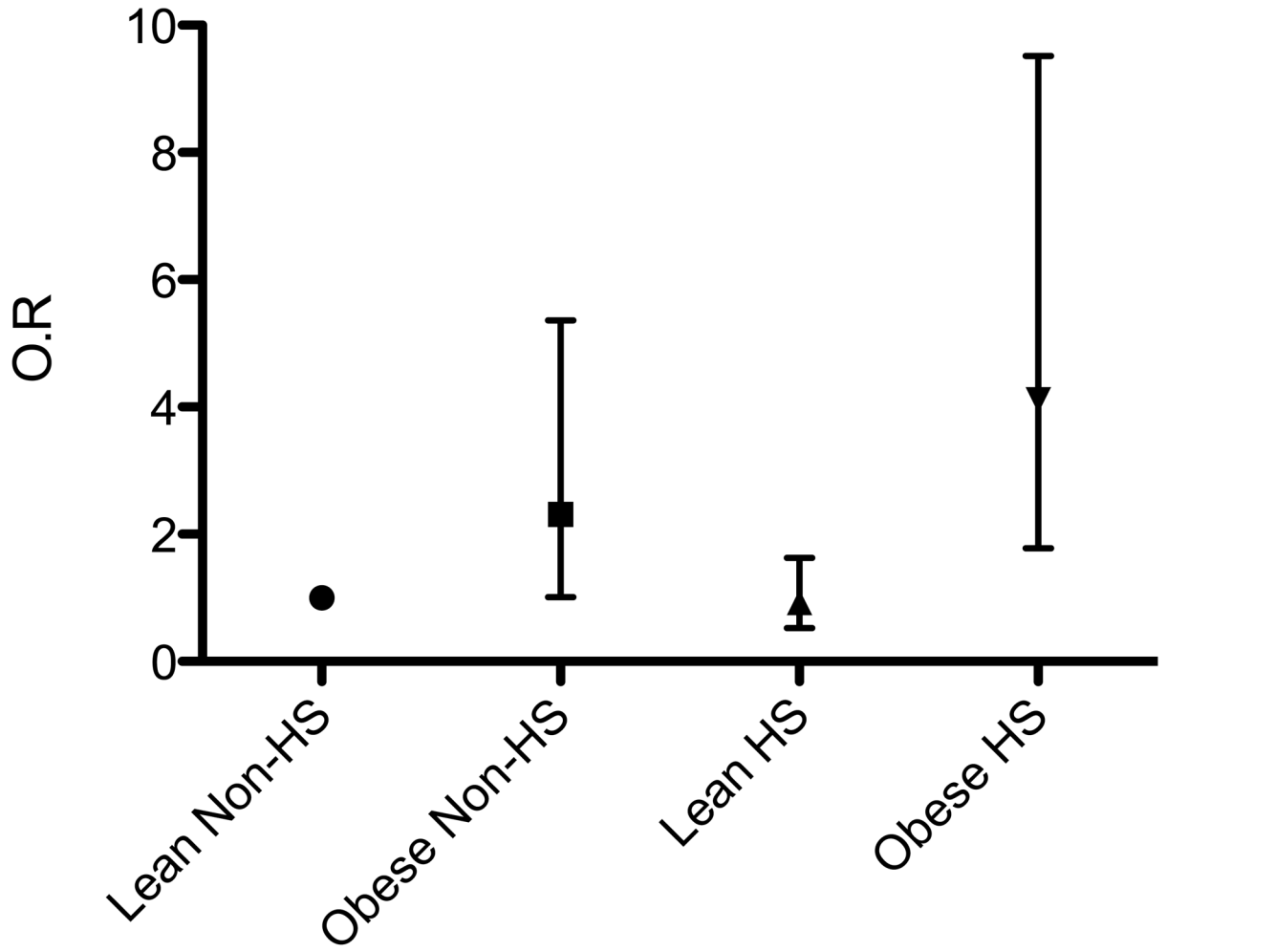


Figure 2.

Adjusted odds ratio, and 95%CI of maternal morbidity by obesity and snoring status
95%CI = 95% Confidence Intervals
A. Odds ratio for gestational hypertension by obesity and snoring status
HS = Habitual Snoring
Odds ratios are adjusted for weight gain in excess of IOM recommendations, gravidity, and history of gestational hypertension/pre-eclampsia.
B. Odds ratio for pre-eclampsia by obesity and snoring status
HS = Habitual Snoring
Odds ratios are adjusted for weight gain in excess of IOM recommendations, gravidity, race, history of gestational hypertension/pre-eclampsia, smoking, chronic hypertension, and gestational diabetes.
C. Odds ratio for gestational diabetes by obesity and snoring status
HS = Habitual Snoring
Odds ratios are adjusted for pre-pregnancy BMI and education level.

Table 1

Demographics of Participants

	Pregnant Women (n=1,712)	Controls (n=202)
Age (years)	29.7±5.9	31.2±7.8 *
Baseline BMI (kg/m^2)	26.5±7.4	25.3±6.3 *
3rd trimester BMI (kg/m^2)	31.2±7.1	N/A
Racial Background:		
Caucasian (%)	70.5%	75.1%
African American (%)	14.8%	14.7%
Asian (%)	7.4%	4.1%
Multi-racial/Other (%)	7.3%	6.1%
Gestational Age (weeks)	34.1±3.7	N/A
Smoker (%)	12.8%	15.0%
Snoring (%)	34.1%	14.9% ***

Data shown as mean ± standard deviation, or proportion as appropriate

* p<0.05;

** p<0.01;

** p<0.001

BMI=Body Mass Index

Table 2

Comparison between pregnant women with and without snoring

	Snoring (n=584)	Chronic Snoring (n=150)	Pregnancy-Onset Snoring (n=434)	Non-Snoring (n=1,128)
Age (years)	30.3±5.9 **	29.7±6.2	30.6±5.8 **	29.4±5.8
Women ≥35 years (%)	24.6%	22.4%	25.4%	20.2%
Baseline BMI (kg/m^2)	29.3±8.6 **	31.9±9.2 ***	28.5±8.3 ***	25.0±6.1
Obese (%)	37.8% **	52.7% ***	32.8% ***¶¶	19.9%
3rd trimester BMI (kg/m^2)	34.0±6.0 **	35.5±8.5 ***	33.5±7.8 ***¶	29.9±6.2
Exceeded IOM weight gain (%)	45.1% ***	34.5%	48.9% ***	35.2%
Racial Background (%)				
Caucasian	71.2%	67.3%	72.8%	70.2%
African American	15.7%	21.6% *	13.5% ¶	13.9%
Asian	6.7%	5.2%	7.2%	7.9%
Multi-racial/Other	6.4%	5.9%	6.5%	8.0%
Educational Level (%):				
<12th grade	9.1%	14.9% *	7.4% ¶	8.3%
≥12th grade	20.9%	25.0% ***	19.7% ¶¶	21.5%
Some college	25.3% *	28.4% *	24.1%	19.6%
4-year college	35.7%	27.0% **	8.1% ¶¶	38.9%
Postgraduate	8.9%	4.7% *	10.8%	11.5%
Gestational Age (weeks) at enrollment	34.4±3.7 *	33.6±3.5	34.6±3.8 *¶	34.0±3.7
Gravidity	2.7±1.7	2.9±1.9 *	2.6±1.7	2.5±1.7
Parity	0.9±1.1	1.0±1.1	0.9±1.1	0.9±1.1
First pregnancy (%)	28.8%	23.6% *	30.5%	32.3%
Smoker (%)	16.7% ***	24.3% ***	13.9%	10.6%
Chronic Hypertension (%)§	16.4% ***	19.0% ***	15.4% ***	6.8%
Gestational Hypertension (%) §	9.8% ***	7.2%	10.6% ***	4.5%
Pre-eclampsia (%)§	12.9% **	11.8%	13.3% **	8.2%
Gestational Diabetes (%)§	19.7% *	22.9% *	18.7%	15.0%

Data shown as mean ± standard deviation, or proportion as appropriate

§ Diagnoses obtained from medical records for 1,673 women

* p<0.05;

** p<0.01;

*** p<0.001; for comparisons with non-snoring controls

¶ p<0.01;

¶¶ p<0.001 for comparisons with chronic snoring

Table 3a

Regression of gestational hypertension against snoring and other covariates

	Explanatory Variables			Adjusted Odds Ratio (95%CI)	
	Beta	**SE**	**p-value**		
Pregnancy-onset snoring	0.859	0.238	<0.001	2.36	1.48–3.77
Chronic snoring	0.542	0.393	0.168	1.72	0.80–3.71
Pre-pregnancy BMI	0.003	0.016	0.869	1.00	0.97–1.04
Excessive weight gain	0.985	0.227	<0.001	2.68	1.72–4.18
Maternal Age	0.000	0.000	0.898	1.00	1.00–1.00
Gravida	−0.255	0.083	0.002	0.78	0.66–0.91
African American	0.413	0.291	0.155	1.51	0.86–267
Smoker	0.211	0.311	0.498	1.24	0.67–2.27
Education level high school or less	0.258	0.243	0.289	1.29	0.80–2.08
History of GHTN/Pre-E	1.135	0.369	0.002	3.11	1.51–6.41
Family History of GHTN/Pre-E	0.91	1.151	0.607	1.81	0.19–17.23

BMI=Body Mass Index; GHTN=Gestational Hypertension; Pre-E=Pre-eclampsia; 95%CI=95% Confidence Intervals

Table 3b

Regression of pre-eclampsia against snoring and other covariates

	Explanatory Variables			Adjusted Odds Ratio (95%CI)	
	Beta	**SE**	**p-value**		
Pregnancy-onset snoring	0.462	0.205	0.024	1.59	1.06–2.37
Chronic snoring	0.109	0.333	0.745	1.12	0.58–2.14
Pre-pregnancy BMI	0.011	0.013	0.391	1.01	0.99–1.04
Excessive weight gain	0.398	0.185	0.032	1.49	1.04–2.14
Maternal Age	0.000	0.000	0.888	1.00	1.00–1.00
Gravida	−0.375	0.074	<0.001	0.69	0.59–0.80
African American	0.578	0.242	0.017	1.78	1.11–2.86
Smoker	0.541	0.251	0.031	1.72	1.05–2.81
Education level high school or less	−0.030	0.213	0.890	0.97	0.64–1.48
History of GHTN/Pre-E	1.524	0.304	<0.001	4.59	2.53–8.34
Family History of GHTN/Pre-E	−0.178	1.127	0.874	0.84	0.09–7.62
Chronic hypertension	1.686	0.303	<0.001	5.40	2.98–9.78
Gestational Diabetes	0.549	0.219	0.012	1.73	1.13–2.67

BMI=Body Mass Index; GHTN=Gestational Hypertension; Pre-E=Pre-eclampsia; 95%CI=95% Confidence Intervals

Table 3c

Regression of gestational diabetes against snoring and other covariates

	Explanatory Variables			Adjusted Odds Ratio (95%CI)	
	Beta	**SE**	**p-value**		
Pregnancy-onset snoring	0.004	0.167	0.982	1.00	0.72–1.39
Chronic snoring	−0.100	0.253	0.693	0.91	0.55–1.49
Pre-pregnancy BMI	0.076	0.010	<0.001	1.08	1.06–1.10
Excessive weight gain	−0.241	0.149	0.107	0.79	0.59–1.05
Maternal Age	0.000	0.000	0.847	1.00	1.00–1.00
Gravida	0.019	0.041	0.651	1.02	0.94–1.11
African American	−0.142	0.209	0.497	0.87	0.58–1.31
Smoker	−0.067	0.230	0.769	0.94	0.60–1.47
Education level high school or less	−0.397	0.175	0.023	0.67	0.48–0.95

BMI=Body Mass Index; 95%CI=95% Confidence Intervals