A population-based study of reduced sleep duration and hypertension: the strongest association may be in premenopausal women
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\textbf{Objectives} Recent evidence indicates that reduced sleep duration may be associated with an increased risk of hypertension with possibly stronger effects among women than men. We therefore examined cross-sectional sex-specific associations of sleep duration with hypertension in a large population-based sample from the Western New York Health Study (1996–2001).

\textbf{Methods} Participants were 3027 white men (43.5\%) and women (56.5\%) without prevalent cardiovascular disease (median age 56 years). Hypertension was defined as blood pressure at least 140 or at least 90 mmHg or regular use of antihypertensive medication. Multivariate logistic regression analyses were performed to estimate odds ratios (ORs) of hypertension comparing less than 6 h of sleep per night versus the reference category (≥6 h) while accounting for a number of potential confounders.

\textbf{Results} In multivariate analyses, less than 6 h of sleep was associated with a significant increased risk of hypertension compared to sleeping at least 6 h per night, only among women [OR = 1.66 (1.09 to 2.53)]. No significant association was found among men [OR = 0.93 (0.62 to 1.41)].

In subgroup analyses by menopausal status, the effect was stronger among premenopausal women [OR = 3.25 (1.37 to 7.76)] than among postmenopausal women [OR = 1.49 (0.92 to 2.41)].

\textbf{Conclusion} Reduced sleep duration, by increasing the risk of hypertension, may produce detrimental cardiovascular effects among women. The association is independent of socioeconomic status, traditional cardiovascular risk factors, and psychiatric comorbidities, and is stronger among premenopausal women. Prospective and mechanistic evidence is necessary to support causality.

\textbf{Introduction} Growing epidemiological evidence indicates that reduced sleep duration and/or sleep deprivation may be associated with a number of cardiovascular disease (CVD) and cardiovascular risk factors such as hypertension [1–11]. Specifically, in a prospective analysis of the first US National Health and Nutrition Examination Survey (NHANES-I), sleeping 5 h or less per night was associated with a 60\% increased risk of incident hypertension in middle-aged US adults of both sexes without overt sleep disorders during a mean follow-up of 8–10 years [7]. In agreement with this, in a cross-sectional analysis from the Sleep Heart Health Study on a large sample of US adults of both sexes, individuals sleeping less than 6 h per night reported a 66\% higher prevalence of hypertension as compared to those sleeping between 7 and 8 h per night [8]. These results were further supported by recent findings from the CARDIA study showing that reduced sleep duration, measured by wrist actigraphy, predicted higher blood pressure levels and adverse changes in blood pressure over time [9].

\textbf{Keywords:} blood pressure, epidemiology, hypertension, sex differences, sleep duration

\textbf{Abbreviations:} BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; CI, confidence interval; CVD, cardiovascular disease; HCFA, Healthcare Financing Administration; MONICA, Monitoring trends and determinants on cardiovascular diseases; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio; SDB, sleep-disordered breathing; SES, socioeconomic status; SF-36, Short Form-36; SPSS, Statistical Package for Social Sciences; WNYHS, Western New York Health Study

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pressure over 5 years among 578 African Americans and whites aged 33–45 years at baseline [9].

Furthermore, the Whitehall II Study in the UK showed potential sex differences in the association of reduced sleep duration with hypertension risk, with a significant effect only among women [10]. In particular, in cross-sectional analyses, the odds ratio (OR) of hypertension among women sleeping 5 h or less per night was 1.72 [95% confidence interval (CI) 1.07–2.75] compared with the group sleeping 7 h, whereas no association was detected in men (OR 0.88, 95% CI 0.63–1.23). In agreement with this, a cross-sectional analysis of the Heinz Nixdorf Recall Study in Germany [11] showed a significant association between reduced sleep duration (≤5 h per night) and hypertension only among women (OR 1.24, 95% CI 1.04–1.46).

Altogether, these findings raise concern that reduced sleep duration might produce detrimental cardiovascular effects particularly in women, as supported by several independent studies evaluating sex-specific effects of sleep duration on CVD-related morbidity and mortality [12–16]. These findings may have considerable public health implications, given current declining trends in the average duration of sleep in the general population [17,18].

The mechanisms underlying the sex-specific association of reduced sleep duration with hypertension and other cardiovascular outcomes are unclear. Hormonal influences and psychosocial distress may contribute to the observed associations, particularly during periods marking shifts in the reproductive stages of women, such as menopause [19]. Moreover, methodological issues such as differential self-reporting of sleep habits between men and women may also play a role [20]. However, the possibility that reduced sleep duration may represent a risk marker rather than a casual risk factor for diseases cannot be ruled out at the present time [21].

In the present analysis we sought to examine cross-sectional sex-specific associations of sleep duration with hypertension in the Western New York Health Study (WNYHS), a large, well characterized population-based sample from the United States [21]. In chronic diseases, menopause represents an important effect modifier of the relation between exposure to endogenous factors and disease risk [22]. Therefore, unlike previous studies, we decided a priori to perform subgroup analyses by menopausal status among women to further investigate potential mechanisms for the observed sex-specific effect of reduced sleep duration on the risk of hypertension.

Methods

Study population

Participants in this study were originally enrolled as healthy control participants in the WNYHS, a series of case–control studies to examine risk factors for chronic disease, as described in detail elsewhere [21]. The following eligibility criteria were used to identify potential controls: residents of Erie and Niagara Counties; age 35–79 years; no cancer. Potential participants were identified through two sources: Department of Motor Vehicles of New York State for participants aged 35–64 years. This source was used because it is known that 95% of New York residents in this age group have a driver license; Healthcare Financing Administration (HCFA) lists for participants aged 65–79 years. This source was used because it includes virtually all individuals in the age range of interest. Between 1996 and 2001, a total of 6837 potential participants were identified, contacted and deemed eligible for the study. Of these, a total of 4065 agreed to participate and were examined, for a participation rate of 59.5%. All participants came to the Center for Preventive Medicine at the University at Buffalo for an interview and physical examination that lasted approximately 2.5 h. The study protocol was approved by the University at Buffalo Institutional Review Board.

The exclusion criteria applied to the present analysis were race other from white (N = 381); a self-reported history of prevalent coronary heart disease, that is previous myocardial infarction, coronary artery bypass graft surgery, angioplasty, or diagnosed angina pectoris (N = 502); missing sleep data (N = 155). The remaining 3027 participants (56.5% women), aged 35–79 years (median 56 years), were included in this study.

Sleep duration

Sleep duration in the past week was ascertained with the Seven-Day Physical Activity Recall questionnaire [23] by the question ‘On average, how many hours did you sleep each night during the last five weekday nights (Sunday–Thursday)?’ Response categories were collapsed in two main groups: less than 6 h and at least 6 h. In our sample, there were few individuals who reported sleeping more than 8 h per night (N = 92 among women, N = 81 among men). Therefore, these participants were grouped together with the mid-range category (6–8 h).

Covariates

The following covariates were examined: age, education (years), marital status, and annual household income, grouped as socio-demographics; body mass index (BMI), waist circumference, pulse rate, physical activity, drinking and smoking habits, and type 2 diabetes, grouped as CVD risk factors; Short Form-36 (SF-36) physical and mental health scores, and depressive symptoms, grouped as general health/psychiatric comorbidities.

Specifically, marital status was categorized as married/ unmarried. As a proxy measure of current or recent socioeconomic status (SES), annual household income was used and divided in three categories in order of decreasing income: above $70,000, $30,000–70,000, below $30,000. For women, menopausal status was determined using criteria taking into account age, surgical or natural cessation of menses, hormone use, and bilateral oophorectomy.
Hypertension was measured using a standard mercury sphygmomanometer by trained and certified technicians, according to a standardized protocol [26]. Briefly, participants were asked to remain seated, legs uncrossed, feet flat on the floor, for a period of 5 min and to refrain from talking during blood pressure measurement. The inflation pressure was 30 mmHg above the pulse obliteration pressure and the cuff was released at a rate of 2 mmHg/s. The onset of the first phase (systolic) and fifth phase (diastolic) Korotkoff sounds were recorded. The means of the second and third measures were used in the analyses. Hypertension was defined as blood pressure at least 140/90 mmHg or regular use of antihypertensive medication [27]. Pulse rate from the radial artery at the wrist was also recorded three times. The means of the second and third measures were used in the analyses.

Statistical analysis

For continuous and categorical variables, respectively, Kruskal–Wallis and \( \chi^2 \) tests were used to determine the statistical significance of any difference in the distributions of selected variables by sex and sleep duration categories (<6 h; ≥6 h). Multivariate logistic regression analyses were performed to calculate ORs and 95% CIs of hypertension comparing less than 6 h sleep versus the reference category (≥6 h). We used three progressive levels of adjustment. Model 1 was adjusted for age, education, marital status, and household income (socio-demographics). Model 2 was further adjusted for BMI, waist circumference, pulse rate, physical activity, drinking status, smoking status, and type 2 diabetes (CVD risk factors). Model 3 was further adjusted for SF-36 physical and mental scores, and depressive symptoms (general health/psychiatric comorbidities). All analyses were stratified by sex (P < 0.001 for sex x sleep duration interaction). To further investigate potential mechanisms for the observed sex-specific effect of reduced sleep duration on hypertension risk, we decided a priori to perform subgroup analyses by menopausal status among women, despite lack of a statistically significant interaction. There was no statistically significant interaction between age (either as continuous or categorical variable) and sleep duration in either sex. Analyses were conducted using the Statistical Package for Social Sciences (SPSS-15.0; SPSS Inc., Chicago, Illinois, USA).

Results

Selected characteristics of participants by categories of sleep duration are reported in Table 1 for women and men separately. For both sexes, there were significant, consistent associations for several correlates of reduced sleep duration. For example, participants sleeping less than 6 h per night were less educated, heavier, more likely to be unmarried, noncurrent drinker and current...
smoker, reported lower SF-36 physical and mental scores and more frequent depressive symptoms than participants sleeping at least 6 h per night.

The prevalence of diabetes did not significantly differ between sleep duration categories. The prevalence of hypertension was significantly higher in participants sleeping less than 6 h per night only among women.

Table 2 displays ORs (95% CI) of prevalent hypertension by categories of sleep duration in women (N = 1710).

Table 3 displays ORs (95% CI) of prevalent hypertension by categories of sleep duration in men (N = 1317).

Discussion

Findings from the WNYHS corroborate the notion that reduced sleep duration may be associated with higher risk of hypertension only among women. Consistent with previous unrelated reports [10,11] from different countries (UK and Germany), we found a 66% higher prevalence of hypertension among women sleeping less than 6 h per night as compared to the group sleeping at least 6 h per night. This association was independent of socioeconomic status, traditional cardiovascular risk factors, and psychiatric comorbidities. As a novel finding,


Table 2 Odds ratiosa (95% CI) of hypertension by categories of sleep duration in women (N = 1710)

<table>
<thead>
<tr>
<th>Variable</th>
<th>&lt;6h</th>
<th>≥6h</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women (n = 1710)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>223</td>
<td>1487</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>56.7</td>
<td>55.6</td>
<td>0.178</td>
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<tr>
<td>Premenopausal (%)</td>
<td>29.3</td>
<td>34.4</td>
<td>0.068</td>
</tr>
<tr>
<td>Education (%)</td>
<td>12.9</td>
<td>13.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unmarried (%)</td>
<td>38.6</td>
<td>28.2</td>
<td>0.002</td>
</tr>
<tr>
<td>Lowest income (%)</td>
<td>45.6</td>
<td>32.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29.6</td>
<td>27.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>90.6</td>
<td>85.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pulse rate (beats/min)</td>
<td>71.5</td>
<td>70.9</td>
<td>0.380</td>
</tr>
<tr>
<td>Physical activity (h/week)</td>
<td>6.2</td>
<td>5.0</td>
<td>&lt;0.048</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>50.5</td>
<td>64.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>18.4</td>
<td>14.7</td>
<td>0.149</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>6.6</td>
<td>6.8</td>
<td>0.932</td>
</tr>
<tr>
<td>SF-36 Physical Score</td>
<td>44.9</td>
<td>49.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SF-36 Mental Score</td>
<td>50.4</td>
<td>52.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Depressive symptoms (%)</td>
<td>21.8</td>
<td>10.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>39.5</td>
<td>26.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 3 Odds ratiosa (95% CI) of hypertension by categories of sleep duration in men (N = 1317)

<table>
<thead>
<tr>
<th>Variable</th>
<th>&lt;6h</th>
<th>≥6h</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men (n = 1317)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>191</td>
<td>1126</td>
<td></td>
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<tr>
<td>Age (years)</td>
<td>54.9</td>
<td>57.6</td>
<td>0.003</td>
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<td>Education (%)</td>
<td>13.4</td>
<td>14.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Unmarried (%)</td>
<td>22.5</td>
<td>15.0</td>
<td>0.009</td>
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<tr>
<td>Lowest income (%)</td>
<td>28.9</td>
<td>23.7</td>
<td>0.139</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>28.7</td>
<td>28.1</td>
<td>0.192</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>99.3</td>
<td>98.1</td>
<td>0.314</td>
</tr>
<tr>
<td>Pulse rate (beats/minute)</td>
<td>68.5</td>
<td>68.5</td>
<td>0.984</td>
</tr>
<tr>
<td>Physical activity (h/week)</td>
<td>5.4</td>
<td>5.3</td>
<td>0.726</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>72.2</td>
<td>76.6</td>
<td>0.194</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>23.6</td>
<td>14.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>8.7</td>
<td>9.8</td>
<td>0.642</td>
</tr>
<tr>
<td>SF-36 Physical Score</td>
<td>45.3</td>
<td>50.5</td>
<td>0.071</td>
</tr>
<tr>
<td>SF-36 Mental Score</td>
<td>51.7</td>
<td>54.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Depressive symptoms (%)</td>
<td>12.8</td>
<td>4.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>30.9</td>
<td>36.7</td>
<td>0.134</td>
</tr>
</tbody>
</table>

Table 1 Selected characteristicsa of participants by categories of sleep duration (N = 3027)

Western New York Health Study, Buffalo, USA (1996–2001). a Data are expressed as the mean or as percentages. b P values for comparison between sleep duration categories using the X² test for categorical variables and the Kruskal–Wallis test for continuous variables.
in subgroup analyses by menopausal status, the effect of reduced sleep duration on hypertension was exacerbated and more than doubled (OR 3.25 versus 1.49) among premenopausal women as compared to postmenopausal counterparts. No significant associations were found among men.

Observational epidemiological studies suggest that both ‘short’ and ‘long’ sleep duration may be associated with an increased risk for health outcomes, such as total mortality, cardiovascular disease, type 2 diabetes mellitus, obesity, and poor general health status [1-16,21]. These studies have often shown a U-shaped relationship between sleep duration and health [28,29]. However, whereas findings on the associations of long sleep duration with health outcomes are not fully consistent and their underlying mechanisms are little understood [21,30], there is increasing recognition that reduced sleep duration (or chronic sleep restriction) may represent an emerging risk factor or risk marker for increased morbidity and mortality [31]. Specifically, consistent epidemiological evidence indicates that reduced sleep duration may be associated with a number of cardiovascular outcomes [2-11], and may increase mortality risk primarily through effects on CV death [1]. Furthermore, there is concern that reduced sleep duration may produce detrimental cardiovascular effects particularly among women, as supported by several unrelated studies examining sex-specific effects of sleep duration on cardiovascular endpoints [10-16]. For example, findings from the Monitoring trends and determinants on cardiovascular diseases (MONICA) Augsburg Study on a large sample of German adults showed a prospective association of reduced sleep duration (≤5 h per night) with incident myocardial infarction only among women (hazard ratio 2.98, 95% CI 1.48-6.03), as compared with the group sleeping 8 h [16]; the corresponding hazard ratio among men was 1.13 (95% CI 0.66-1.92). Moreover, two recently published studies, from the UK and Germany, consistently showed significant cross-sectional associations between reduced sleep duration (≤5 h per night) and hypertension only among women [10,11], though the effect size was somewhat different between the two samples (OR 1.72 versus 1.24, respectively). The present study additionally suggests that hypertensive effects of reduced sleep duration may be stronger in premenopausal women.

Sleep-disordered breathing (SDB) has been linked to elevated blood pressure and risk of hypertension in several epidemiological studies [32-36]. The observational data have been corroborated by findings of mechanistic studies emphasizing the critical role of sympathetic overactivity in the cause of SDB-related hypertension [37,38], although other mechanisms are likely to be involved [39].

Potential mechanisms that may explain sex-specific effects of reduced sleep duration on cardiovascular health and hypertension risk are unknown at the present time; therefore any such discussion is highly speculative. However, it is possible that hormonal influences may play a role, especially during times such as the menopause when women are more vulnerable due to major hormonal fluctuations [19,22]. Moreover, there are sex differences in stress and reaction to stress [47]. Recent findings from the Whitehall II Study also point to potential sex differences in the association of sleep duration with inflammatory markers [48]. Furthermore, as shown in our descriptive analyses, the distribution of correlates of reduced sleep duration that have the potential to affect hypertension risk (e.g. BMI, waist, lowest SES, SF-36 physical and mental health, depressive symptoms) was somewhat different between sexes and may have partially contributed to the observed associations. Finally, the possibility of differential self-reporting of sleep habits between men and women cannot be ruled out, as suggested in a previous analysis of the Sleep Heart Health Study on the relationship of sex to subjective measures of sleepiness [20].

Altogether, most of the studies on the effect of reduced sleep duration on blood pressure levels and hypertension risk have found significant associations only in younger/middle-aged individuals [7,9,49,50]. Three studies were unable to find associations between sleep duration and hypertension in the elderly [7,51,52]. The present study suggests that menopausal status could represent a plausible explanation for the age-related effect of reduced sleep duration on hypertension risk at least in women.

The cross-sectional nature of the present study does not allow establishing causality and temporality of the observed associations. Given the self-reporting of sleep habits, we cannot disregard the likelihood that health outcomes such as hypertension may influence reports of habitual sleep habits [53] and impair sleep quality [54], and not vice versa. Nevertheless, self-report assessments
of sleep have been shown to be valid measures compared to quantitative sleep assessments with actigraphy or polysomnography [55,56]. As a further limitation, we were unable to control for the potential effect of SDB, which is clearly linked to elevated blood pressure and risk of hypertension [32–36]. Moreover, the suboptimal participation rate (59.5%) may leave the possibility for selection bias and restrict the generalizability of these findings to the general population. However, the consistency in the magnitude of the observed association between reduced sleep duration and hypertension risk with previous unrelated studies [10,11] strengthens the external validity and generalizability of these findings.

The strengths of this study include the extensive assessment of several covariates known to be related to either sleep habits or hypertension risk, and the large community-wide sample.

Perspectives
The present study corroborates sex-specific associations between sleep duration and hypertension risk. Specifically, reduced sleep duration (<6 h per night) was associated with a higher risk of hypertension only among women. As a novel observation, findings of the present study showed that this association may be stronger in premenopausal women. These findings raise additional concern that behavioral curtailment of sleep might produce detrimental effects on cardiovascular health particularly among women. This may have important public health implications given current declining trends in the average duration of sleep in the general population [17,18]. Prospective and mechanistic evidence is necessary to support causality.

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