



## Sleep maintenance difficulties in insomnia are associated with increased incidence of hypertension

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### ARTICLE INFO

#### Article history:

Received 2 November 2014

Received in revised form 18 November 2014

Accepted 21 November 2014

### ABSTRACT

**Study objectives:** We examined the relative contributions of sleep onset and sleep maintenance difficulties in insomnia as predictors of incidence and development of hypertension.

**Design:** This study is cross-sectional and longitudinal.

**Participants:** There were 967 adults with *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*-based current insomnia.

**Measurements and results:** At baseline, participants were divided into 2 groups based on current diagnosis of hypertension. Prevalence of hypertension in this sample was 34.7%, which is higher than the prevalence in the general population previously documented at approximately 28%. Participants completed a follow-up assessment 1 year later that revealed a 5.4% incidence of hypertension. Analyses revealed that increases in sleep maintenance difficulties, not sleep initiation difficulties, between baseline and follow-up significantly predicted increased risk for incidence of hypertension. Analyses at baseline also revealed that sleep maintenance rather than sleep initiation difficulties marginally predicted increased severity of hypertension. Results suggest that risk for hypertension may be conferred through disruptions to blood pressure with nightly repeated or prolonged awakenings.

**Conclusions:** This study provides novel information regarding the risk of hypertension in insomnia via sleep maintenance difficulties. Findings from this study provide preliminary evidence for examining nighttime fluctuations of blood pressure and concomitant physiological changes (ie, catecholamines, heart rate, and sympathetic activation) due to wake during sleep as a mechanism for subsequent hypertension.

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### Introduction

Insomnia is a commonly occurring sleep disorder that is characterized by chronic difficulties in initiating or maintaining sleep, resulting in impairments to daytime functioning. Such impairments include increased rates of absenteeism, decreased productivity, diminished quality of life, and impaired cognitive and emotional functioning.<sup>1</sup> However, insomnia also confers additional health risks beyond its acute consequences. Most notably, individuals with insomnia are at higher risk for developing medical morbidities,<sup>2</sup> especially cardiovascular illnesses such as hypertension.<sup>3–5</sup> Because of the high prevalence and mortality rates associated with cardiovascular illnesses, research has increasingly focused on insomnia as a risk factor for hypertension and similar comorbidities.

Research examining insomnia as a risk factor for hypertension has produced mixed results. Notably, although many studies find that

insomnia predicts increased incidence of hypertension,<sup>4</sup> some do not<sup>6–8</sup> One potential explanation may be the fact that the underlying mechanism of risk between insomnia and hypertension remains poorly understood, and studies may therefore find varying results based on differing variables used. Vgontzas et al<sup>9</sup> have argued that risk for hypertension may be conferred through decreased sleep duration, as well as in conjunction with insomnia, with an adjusted odds ratio estimated at 5.12, which is significantly higher than that for insomnia alone (range estimated between 1.05 and 2.24).<sup>4</sup> However, reduced sleep duration in insomnia may arise from difficulties falling asleep and/or difficulties maintaining sleep, and it is still unclear how risk may differ based on this distinction. There is evidence that specific patterns of sleep difficulties predict risk for hypertension. For example, one prospective study using a large sample of Japanese male workers found that both difficulty initiating and maintaining sleep independently predicted development of hypertension.<sup>10</sup> Another recent meta-analysis of prospective studies found that difficulties maintaining sleep and early morning awakening predicted incidence of hypertension, but no significant effect was detected for difficulty falling asleep.<sup>4</sup> However, these studies did not directly compare distinct patterns of sleep difficulties, thereby precluding discernment of their relative contribution in predicting hypertension.

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Such discernment is important because it may increase specificity and effectiveness of clinical interventions.

Among different endophenotypes of insomnia, the biological processes specific to sleep maintenance difficulties may be of particular relevance to hypertension. Although blood pressure decreases with sleep onset,<sup>11,12</sup> nighttime awakenings result in surges in the sympathetic nervous system. These surges trigger the release of catecholamines such as norepinephrine, which is associated with rises in blood pressure. Disruptions to blood pressure with nightly repeated or prolonged awakenings may increase risk for hypertension. To further explore this hypothesis, this study examined the relative contributions of sleep onset vs maintenance difficulties in insomnia as predictors of prevalence and incidence of hypertension. This was a prospective study of a large sample of individuals with insomnia that measured incidence of hypertension across 2 years. Two sets of analyses were used to examine risk of hypertension in insomnia. The first used a cross-sectional design in comparing sleep onset and maintenance difficulties between those with and without hypertension at baseline. We hypothesized that prevalence of hypertension will be higher compared with that of the general population and that individuals with increased sleep maintenance difficulties will have additionally increased risk for hypertension. The second set of analyses used a longitudinal design in examining incident hypertension at follow-up. If risk for hypertension is indeed augmented by sleep maintenance difficulties, exacerbation of sleep maintenance difficulties from baseline would increase risk for hypertension at follow-up.

**Methods**

*Participants*

Participants in this study were recruited as part of the Evolution of Pathways to Insomnia Cohort study, which was a longitudinal investigation examining insomnia in a large sample of adults living in southeastern Michigan (specific information regarding the larger investigation is detailed elsewhere).<sup>13</sup> Prospective participants were derived from a major health maintenance organization database, where a randomly selected sample of individuals (n = 36,002) were recruited by mail. Twenty-one percent (n = 7608) of these individuals responded by completing a Web-based survey that assessed eligibility for this study. Approximately 34% of these individuals (n = 2590) reported current/lifetime insomnia and were invited for study participation. Of all eligible individuals, 54% (n = 1388) elected to enroll and completed baseline questionnaires. See Table 1 for demographic and descriptive information for study participants and the Figure for the breakdown of sample by time points.

*Procedure and measures*

All study protocols were approved by the Henry Ford Hospital Institutional Review Board.

*Insomnia*

Diagnosis of insomnia was established based on *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* criteria, using the following questions: “Have you experienced difficulty falling asleep?,” and “Have you experienced difficulty staying asleep?,” Participants met *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* diagnostic criteria if 1 or more of the above symptoms were reported for at least 3 nights a week for a duration of 3 months or longer. In addition, insomnia criteria included daytime consequences or distress from sleep difficulties as determined by a response of 2 (“somewhat”) or higher on a 5-point Likert scale to the question: “To what extent do you consider your sleep problems to

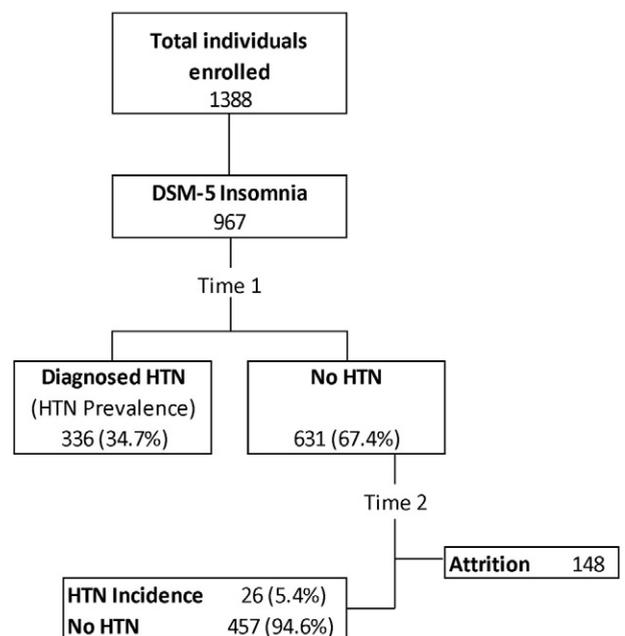
**Table 1**  
Demographic and descriptive information for study participants.

|  | No HTN<br>(n = 631) | HTN<br>(n = 336) | P     |
|--|---------------------|------------------|-------|
| Sex  | 452 ♀               | 216 ♀            | <.05  |
| Age  | 43.1 (12.7)         | 53.3 (8.9)       | <.001 |
| Race:  |                     |                  | <.001 |
| White  | 68.3%               | 59.2%            |       |
| African American   | 22.8%               | 39.0%            |       |
| Other  | 8.9%                | 2.0%             |       |
| High risk for OSA (%)  | 41.2%               | 61.0%            | <.001 |
| Use of antihypertensive medication   | –                   | 88.4%            | –     |
| Days of impairment due to physical/mental health difficulties in the last year | 4.7%                | 13.8%            | <.01  |
| SOL (min)  | 69.8 (65.5)         | 73.9 (77.3)      | NS    |
| No. of night awakenings  | 4.7 (8.0)           | 5.4 (9.0)        | NS    |
| WASO (min)   | 95.5<br>(100.8)     | 111.7<br>(108.5) | <.05  |
| Average sleep duration (min)   | 336.3<br>(78.1)     | 324.2 (83.0)     | <.05  |
| Sleep quality  | 1.84 (.5)           | 1.79 (.6)        | <.05  |
| Chronicity of insomnia (mo)  | 66.6 (83.2)         | 86.9 (104.5)     | <.01  |

Abbreviations: NS, not significant; HTN, hypertension.

interfere with your daily functioning?” Responses ranged from “0” (“not at all”) to “4” (“very much”).

Sleep onset and maintenance difficulties were quantified via questions that probed for average minutes to sleep onset and duration of wake after sleep onset (WASO) during the last month. Prior research has demonstrated high correlations between results attained from retrospective sleep questionnaires and sleep diaries,<sup>14</sup> suggesting accuracy in the use of retrospective sleep questions. Previous research using large samples of adults has also indicated that measurement of sleep-related impairments has higher sensitivity and specificity to quantitative thresholds.<sup>15,16</sup> The reported sleep variables were subsequently categorized based on quantitative measures of sleep difficulties to maximize sensitivity and specificity in detecting sleep-related impairment to blood pressure. Specifically, individuals who reported sleep onset latencies (SOLs) of longer than 30 minutes



**Figure.** Breakdown of sample by time point. HTN, hypertension.

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