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Insomnia symptoms predict both future hypertension and depression

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ABSTRACT

The prevalence of hypertension and depression is high in older populations. Moreover, their comorbidity may significantly increase morbidity and mortality. However, the risk factors contributing to both health conditions are not well understood. Older individuals are prone to insomnia; thus we hypothesized that having more insomnia symptoms increases risk for incident hypertension and depression over time.

The sample consisted of a longitudinal population-based study of community-dwelling older individuals, from the 2008–2016 waves of the Health and Retirement Study, sampled across the United States.

A total of 18,123 subjects, aged 50+, were stratified into three age groups, ages 50–60, 61–74, and 75 and older years. Subjects were excluded for reporting baseline hypertension or depression at the first wave 2008. Center for Epidemiologic Studies-Depression (CES-D) score ≥ 4 was the cutoff for elevated depressive symptomatology. Subjective insomnia symptoms were evaluated.

Cox proportional hazards regression revealed that SBP (1.02[1.01, 1.02]) and more insomnia symptoms (1.11[1.01, 1.21]) were significant predictors of hypertension for all age groups. For depression, only insomnia symptoms were significant predictors (9.91[6.37, 15.41]). Kaplan-Meier curves revealed that 9.2% of the overall cohort had both hypertension and depression within 8 years and more insomnia symptoms predicted greater incidences of both conditions (p-values < 0.001).

In this older prospective cohort, insomnia symptoms are consistent predictors of future hypertension and depression in all age groups, who were not hypertensive and depressed at baseline. Insomnia may contribute to the etiology and comorbidity of hypertension and depression in older individuals.

1. Introduction

Worldwide prevalence of hypertension and depression is high. Hypertension is the leading cause of morbidity and mortality globally; while, depression is associated with impaired cognitive and physical functions as well as increased morbidity and mortality. Moreover, their comorbidity significantly increases risks for poor health prognosis, low quality of life and high mortality, particularly in older populations. Hypertensive subjects with depressive symptoms had 83.0% higher adjusted risk for major adverse cardiovascular events, including myocardial infarction, stroke, and death, than hypertensive subjects without depressive symptoms in a cohort of 35,537 subjects (Jani et al., 2016). A meta-analysis of 30,796 hypertensive subjects observed the prevalence of depression in hypertensive patients to be 26.8% (Li et al., 2015).

Despite the high prevalence of depression in hypertensive patients, it is still estimated to be undiagnosed in majority of these patients (Kretchy et al., 2014). Furthermore, few longitudinal studies have examined changes in blood pressure (BP) before onset of depression and reviews have highlighted the need for more of these studies to elucidate the complex relationship between blood pressure and depression with emphasis on modifiable factors (Gao et al., 2013). In a depression-free cohort of older primary care patients followed for 18 years, Gao et al. reported an increase in systolic blood pressure (SBP) which preceded the diagnosis of depression suggesting that BP may act as an independent risk factor for late-life depression (Gao et al., 2013). Cross-sectional studies however have reported inconsistent results with some reporting no association between BP and depression (Wiehe et al., 2006; Maatouk et al., 2016). Another important contributor and potential modifiable factor for both hypertension and depression is insomnia (Bathgate and Fernandez-Mendoza, 2018; Khurshid, 2018; Gebara et al., 2018). Insomnia is more common in the older population with studies suggesting that > 50% of the population, aged 65 or older, may have sleep problems (Neikrug and Ancoli-Israel, 2010). A study comparing somatic diseases found that only hypertension was significantly associated with insomnia (Jarrin et al., 2018). Insomnia may

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contribute to the development of hypertension via mechanisms including chronic inflammation and physiological hyperarousal from over-activation of the sympathetic nervous system and hypothalamic-pituitary-adrenal axis (Bathgate and Fernandez-Mendoza, 2018). Moreover, in the older population, sleep disturbances increase risks for common causes of mortality and morbidity, including cardiovascular diseases, cancer, and suicide (Foley et al., 2004; Hawton et al., 2013).

Despite the high prevalence of insomnia, little is known, particularly not in the older population, about the relationship between SBP, diastolic blood pressure (DBP), and insomnia and their risks for hypertension or depression (LaGrotte et al., 2016). Most studies have either investigated the association between sleep and BP or sleep and depression but not both (LaGrotte et al., 2016; Grandner et al., 2018). Thus, we hypothesized that having more insomnia symptoms increases risk for incident hypertension and depression over time.

2. Methods

2.1. Participants

This study sample consists of the 2008–2016 Health and Retirement Study (HRS) dataset. HRS is a longitudinal study surveying a prospective community-dwelling cohort of Americans, aged 50 years and older, every two years with follow-up interviews. This study is conducted by the University of Michigan. Details of the design and historical context of the HRS have been reported previously (Heeringa and Connor, 1995). Briefly, the HRS was designed to provide data regarding retirement, health insurance, physical health, and economic well-being and to help inform major policy-decisions. The study has been conducted via both telephone and in-person interviews (approximately 50% each method) (Crimmins et al., 2008). In our study, we utilized the first available data regarding SBP and DBP (2008 wave) and the most recent wave available (2016). To estimate the time-to-event of new cases of hypertension and depression, we selected only those who did not have hypertension nor depression in 2008 (n = 4275 excluded). A total of 18,123 participants were included in our study.

2.2. Outcome variables

2.2.1. Self-reported hypertension status

The HRS assessed for hypertension by asking a yes/no response-question, “Has a doctor ever told you that you have high blood pressure or hypertension?”

2.2.2. Elevated depressive symptomatology

Subjects were assessed for depressive symptomatology. A modified 8-item version of the *Centers for Epidemiologic Studies Depression Scale* (CES-D) was given. The CES-D scale is a measure of depressive symptoms with high internal consistency reliability (Hann et al., 1999). The eight items were as follows: felt depressed, everything was an effort, sleep was restless, happy, lonely, enjoyed life, felt sad, and feeling unmotivated. Participants recorded their answers as yes or no. The CES-D score was calculated based on the count of the 8 items, ranging from 0 to 8, with a cutoff ≥ 4 as elevated depressive symptomatology. The cut-score was determined by HRS investigators to be similar to the cut-score ≥ 16 on the full CES-D as clinically-relevant depressive symptoms and has been validated by prior research in older populations (Zivin et al., 2010).

2.3. Predictor variables

2.3.1. Blood pressure measurements

BPs were measured using automated sphygmomanometer by trained interviewers. Three BP readings, 45–60 s apart, were taken in a sitting position with both feet on the floor and the left arm supported with the palm facing up (Crimmins et al., 2008). The readings were then averaged. Responses for assessing taking antihypertensive medication were categorizing as “Yes” or “No.

2.3.2. Insomnia symptoms

The HRS assessed for insomnia symptoms by asking respondents four questions: how often they had trouble (Jani et al., 2016) falling asleep, (Li et al., 2015) waking up during the night, (Kretchy et al., 2014) waking up too early, and (Gao et al., 2013) how often they felt rested in the morning. The responses to these questions were categorized as “most of the time”, “sometimes”, and “rarely or never”. We defined subjects as experiencing an insomnia symptom if they answered “most of the time” or “sometimes” to the first three questions and “rarely or never” or “sometimes” to the fourth question. This method has been used in prior research for HRS studies (Kaufmann et al., 2013; Chen-Edinboro et al., 2014; Canham et al., 2015).

2.3.3. Other covariates

Age, sex, race, weight, BMI, smoking, alcohol, and physical activity were included as covariates. Sex was assessed and categorized as “male” or “female”. Race was self-reported and categorized as “white/Caucasian”, “black/African American”, “Other” (includes American Indian, Asian, something else). Smoking and drinking alcohol were self-reported as yes or no. Physical activity was self-reported as mild, moderate, or vigorous activity or no physical activity. Subsequently, we categorized subjects as participating or not participating in physical activity. Years of education were self-reported as an actual number.

2.4. Statistical analysis

Baseline characteristics of respondents were shown as mean ± standard deviation or frequency (%) as appropriate with subgroup analysis within ages 50–60, 61–74, and 75+ years old. Covariates included in this study were age, sex, race, weight, BMI, smoking, alcohol, physical activity, and years of education. BMI was the primary body weight marker. Analysis of variance assessed for differences in age, weight, BMI, years of education, SBP, and DBP among three age groups. For all categorical variables, Pearson Chi-squared test analyzed for significant associations among groups. Significance was determined when p-values were < 0.05.

Multivariable Cox proportional hazard models tested our hypothesis by calculating the risks for incident hypertension and depression with BP and the number of insomnia symptoms as predictors of interest with adjustments for covariates. Robust estimates of variances to obtain adjusted hazard ratios (HR) and 95% confidence intervals (95% CI) were reported.

Kaplan-Meier unadjusted estimator computed survival distributions of being hypertension and depression-free in overall cohort with the number of insomnia symptoms as between-subjects factor. Log-ranked (Mantel-Cox) test assessed for significant differences in survival distributions.

All statistical analyses were performed via SPSS–IBM Software (version 24.0 SPSS Inc., Chicago, IL, USA) with the significance level set at $\alpha = 0.05$.

3. Results

3.1. General demographics

The characteristics of our participants at baseline (n = 18,123) were presented in Table 1 stratified by age groups 50–60, 61–74, and 75+ years old. The baseline average SBP and DBP were 132.3 mm Hg ± 20.5 and 79.0 mm Hg ± 11.7 respectively. Within 8 years, 60.0% of the cohort became hypertensive and of these individuals 89.1% were on antihypertensive medication, and 13.0% of our cohort had depression. Blacks had higher risks for hypertension and females had higher risks for depression.

Table 1
Baseline characteristics within age groups.

	Age groups		
	50–60	61–74	75+
Total number of participants	5874	7335	4914
General demographics			
Age	54.4 ± 4.6	67.6 ± 4.1	81.6 ± 5.4
BMI	34.4 ± 9.0	33.9 ± 8.4	31.4 ± 8.4
Sex (% females)	59.0%	57.7%	59.0%
Race (% blacks)	22.2%	17.2%	12.1%
Smoking (% yes)	22.5%	13.6%	5.1%
Drink alcohol (% yes)	58.5%	64.7%	68.8%
Physical activity (% yes)	97.0%	94.8%	83.6%
Years of education	13.0 ± 3.1	12.7 ± 3.2	12.2 ± 3.3
Blood pressure related measurements			
SBP (mm Hg)	125.7 ± 19.5	129.7 ± 19.3	133.6 ± 21.2
DBP (mm Hg)	81.3 ± 11.7	78.8 ± 11.0	75.6 ± 11.3
Insomnia symptoms:			
No symptom	18.7%	19.0%	16.8%
1 symptom	21.0%	21.4%	22.0%
2 symptoms	18.8%	20.5%	21.8%
3 symptoms	20.8%	21.1%	22.1%
4 symptoms	20.6%	18.0%	17.2%
Depression symptoms			
Felt depressed during past week? (%yes)	15.9%	12.0%	13.6%
Everything that you did was an effort during past week? (%yes)	30.5%	22.5%	24.3%
Restless sleep during past week? (%yes)	35.0%	29.3%	27.8%
Felt happy during past week? (%no)	16.9%	12.6%	11.8%
Felt lonely during past week? (%yes)	17.3%	14.6%	19.5%
Enjoyed life during past week? (%no)	10.8%	7.7%	7.9%
Felt sad during past week? (%yes)	21.8%	17.1%	18.3%
Felt unmotivated during past week? (%yes)	19.2%	19.0%	23.5%
CES-D score	1.5 ± 2.1	1.2 ± 1.9	1.3 ± 1.8

3.2. General trends among three age groups

Baseline values were reported in Table 1, comparing the three age groups. The youngest group smoked the most (22.5%) but drank the least alcohol (58.5%) (p-values < 0.001). The youngest group also exercised the most (97.0%) and attained most years of education (13.0 years) (p-values < 0.001). This group had the lowest SBP and highest DBP (125.7 and 81.3 mm Hg respectively) (p-values < 0.001).

The prevalence of one or more insomnia symptoms across the age groups from youngest to oldest were 81.3%, 81.0%, and 83.2% respectively. The prevalence of insomnia and depression symptoms showed U-shape relationships with the middle group reporting the lowest prevalence (p-values < 0.001).

3.3. Cox proportional hazard analysis

Table 2 showed results of Cox proportional hazard analysis in different age groups regarding SBP, DBP, number of insomnia symptoms, and their risks for hypertension with adjustments for sociodemographic and health behavior covariates. SBP, BMI, and insomnia symptoms were significant predictors of hypertension. Elevating 1 mm Hg in SBP increased incidence of hypertension by 1.0 to 2.0% depending on the age group. Having 4 insomnia symptoms increased incidence of hypertension by 11.0 to 27.0%. DBP was not a significant predictor.

Table 3 showed results of Cox proportional hazard analysis in different age groups regarding SBP, DBP, antihypertensive medication, number of insomnia symptoms, and their risks for depression with adjustments for sociodemographic and health behavior covariates. Insomnia symptoms were most consistent predictors of depression with four symptoms increasing its incidence by 9.0 to 11.5-folds depending on age group. SBP, DBP, antihypertensive medication, and BMI were not significant predictors.

Table 2
Cox proportional hazard ratio for hypertension risk by age groups.

Predictor variables	Base model[a]	Model 1[b]
Age group 50 to 60 years old		
Age	N/A	0.97 (0.96, 0.98)
BMI	N/A	1.02 (1.01, 1.02)
Female	N/A	1.00 (0.91, 1.09)
Race: reference group (Black)		
White	N/A	0.75 (0.68, 0.83)
Other	N/A	0.80 (0.69, 0.92)
Smoking: Yes	N/A	1.03 (0.92, 1.15)
Drink alcohol: Yes	N/A	1.07 (0.97, 1.17)
Participates in physical activity: Yes	N/A	0.68 (0.54, 0.85)
Years of education	N/A	0.99 (0.97, 1.00)
SBP	1.02 (1.01, 1.02)	1.01 (1.01, 1.02)
DBP	1.01 (1.00, 1.01)	1.01 (1.00, 1.01)
Insomnia symptoms: reference group (No symptoms)		
1 symptom	1.08 (0.95, 1.23)	1.08 (0.93, 1.24)
2 symptoms	1.23 (1.08, 1.40)	1.26 (1.09, 1.46)
3 symptoms	1.21 (1.07, 1.37)	1.21 (1.05, 1.39)
4 symptoms	1.27 (1.12, 1.43)	1.26 (1.02, 1.45)
Age group 61 to 74 years old		
Age	N/A	1.03 (1.02, 1.04)
BMI	N/A	1.01 (1.01, 1.02)
Female	N/A	0.98 (0.92, 1.05)
Race: reference group (Black)		
White	N/A	0.87 (0.81, 0.95)
Other	N/A	0.77 (0.67, 0.88)
Smoking: Yes	N/A	1.07 (0.96, 1.18)
Drink alcohol: Yes	N/A	1.04 (0.97, 1.12)
Participates in physical activity: Yes	N/A	0.81 (0.69, 0.95)
Years of education	N/A	0.98 (0.97, 0.99)
SBP	1.01 (1.01, 1.02)	1.01 (1.01, 1.01)
DBP	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
Insomnia symptoms: reference group (No symptoms)		
1 symptom	1.09 (0.99, 1.20)	1.08 (0.98, 1.20)
2 symptoms	1.05 (0.95, 1.16)	1.06 (0.95, 1.18)
3 symptoms	1.12 (1.01, 1.23)	1.12 (1.00, 1.24)
4 symptoms	1.11 (1.01, 1.21)	1.11 (1.00, 1.24)
Age group 75+ years old		
Age	N/A	0.99 (0.99, 1.00)
BMI	N/A	1.01 (1.00, 1.01)
Female	N/A	1.07 (0.99, 1.16)
Race: reference group (Black)		
White	N/A	0.85 (0.77, 0.95)
Other	N/A	0.77 (0.61, 0.97)
Smoking: Yes	N/A	1.05 (0.88, 1.26)
Drink alcohol: Yes	N/A	0.99 (0.92, 1.07)
Participates in physical activity: Yes	N/A	1.00 (0.87, 1.14)
Years of education	N/A	0.99 (0.98, 1.00)
SBP	1.01 (1.00, 1.01)	1.01 (1.00, 1.01)
DBP	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)
Insomnia symptoms: reference group (No symptoms)		
1 symptom	1.02 (0.91, 1.14)	1.03 (0.90, 1.16)
2 symptoms	1.08 (0.97, 1.20)	1.11 (0.98, 1.25)
3 symptoms	1.13 (1.02, 1.26)	1.15 (1.02, 1.29)
4 symptoms	1.12 (1.00, 1.24)	1.13 (1.00, 1.26)

Hazard ratios given in 95% CI.
[a] Base Model: blood pressure measurements + insomnia symptoms.
[b] Model 1: Base Model + covariates.

3.4. Time-to-event of depression (not getting depression) within 8 years

The results from univariate Kaplan-Meier analysis showed

Table 3
Cox proportional hazard ratio for depression risk by age groups.

Predictor variables	Base model[a]	Model 1[b]
Age group 50 to 60 years old		
Age	N/A	0.95 (0.93, 0.98)
BMI	N/A	1.01 (0.99, 1.02)
Female	N/A	1.28 (1.01, 1.63)
Race: reference group (Black)		
White	N/A	0.97 (0.75, 1.25)
Other	N/A	1.35 (0.97, 1.93)
Smoking: Yes	N/A	1.50 (1.16, 1.87)
Drink alcohol: Yes	N/A	1.23 (0.99, 1.57)
Participates in physical activity: Yes	N/A	0.50 (0.34, 0.73)
Years of education	N/A	0.95 (0.92, 0.98)
Antihypertensive medication: Yes	0.93 (0.76, 1.15)	1.05 (0.79, 1.39)
SBP	1.00 (0.99, 1.01)	1.00 (0.99, 1.01)
DBP	1.01 (1.00, 1.02)	1.01 (1.00, 1.03)
Insomnia symptoms: reference group (No symptoms)		
1 symptom	3.37 (1.83, 6.19)	2.89 (1.38, 6.06)
2 symptoms	4.67 (2.59, 8.43)	4.84 (2.37, 9.87)
3 symptoms	7.63 (4.33, 13.45)	6.42 (3.22, 12.81)
4 symptoms	11.50 (6.59, 20.07)	9.96 (5.06, 19.62)
Age group 61 to 74 years old		
Age	N/A	0.99 (0.96, 1.01)
BMI	N/A	1.00 (0.99, 1.02)
Female	N/A	1.39 (1.11, 1.74)
Race: reference group (Black)		
White	N/A	0.92 (0.72, 1.16)
Other	N/A	0.95 (0.65, 1.38)
Smoking: Yes	N/A	1.51 (1.15, 1.97)
Drink alcohol: Yes	N/A	1.28 (1.04, 1.59)
Participates in physical activity: Yes	N/A	0.40 (0.29, 0.56)
Years of education	N/A	0.94 (0.91, 0.97)
Antihypertensive medication: Yes	0.82 (0.64, 1.04)	0.75 (0.54, 1.02)
SBP	1.00 (0.99, 1.00)	0.99 (0.98, 1.00)
DBP	1.01 (1.00, 1.02)	1.01 (0.99, 1.03)
Insomnia symptoms: reference group (No symptoms)		
1 symptom	2.02 (1.21, 3.37)	1.52 (0.79, 2.94)
2 symptoms	3.35 (2.19, 5.66)	3.21 (1.79, 5.78)
3 symptoms	6.02 (3.84, 9.46)	5.17 (2.96, 9.05)
4 symptoms	9.91 (6.37, 15.41)	7.96 (4.59, 13.80)
Age group 75+ years old		
Age	N/A	1.01 (0.99, 1.04)
BMI	N/A	1.01 (0.99, 1.02)
Female	N/A	1.25 (0.96, 1.63)
Race: reference group (Black)		
White	N/A	0.72 (0.54, 0.98)
Other	N/A	1.52 (0.89, 2.59)
Smoking: Yes	N/A	1.16 (0.68, 1.96)
Drink alcohol: Yes	N/A	1.01 (0.78, 1.31)
Participates in physical activity: Yes	N/A	0.51 (0.37, 0.71)
Years of education	N/A	0.92 (0.89, 0.96)
Antihypertensive medication: Yes	1.15 (0.77, 1.71)	1.37 (0.73, 2.59)
SBP	1.00 (0.99, 1.01)	1.00 (0.99, 1.01)
DBP	1.00 (0.99, 1.02)	1.00 (0.99, 1.02)
Insomnia symptoms: reference group (No symptoms)		
1 symptom	1.66 (0.91, 3.03)	1.07 (0.50, 2.30)
2 symptoms	3.68 (2.15, 6.32)	2.80 (1.48, 5.31)
3 symptoms	5.66 (3.37, 9.51)	4.44 (2.42, 8.15)
4 symptoms	9.01 (5.41, 15.03)	6.74 (3.70, 12.29)

Hazard ratios given in 95% CI.
[a] Base Model: blood pressure measurements + insomnia symptoms.
[b] Model 1: Base Model + covariates.

distributions for number of insomnia symptoms regarding incidences of both hypertension and depression within eight years in the overall cohort (Fig. 1). Having 2 to 4 insomnia symptoms showed higher incidences of both health conditions compared to having 0 to 1 symptom. Log-rank (Mantel-Cox) test showed significant differences between hypertension and depression-free among groups with different number of insomnia symptoms (p-value < 0.001). Overall, 9.2% of the cohort had both health conditions within 8 years. Stratification by the number of insomnia symptoms showed that 1.5% of the no symptom group, 3.6% of one symptom group, 6.7% of two symptoms group, 12% of three symptoms, and 21.5% of four symptoms group had both hypertension and depression.

4. Discussion

We investigated the relationships among blood pressure, insomnia symptoms, and future hypertension and depression in a prospective older cohort, who were not hypertensive nor depressed at baseline, in an eight-year follow-up. This is the first study to investigate all three health factors in the HRS cohort. We observed a U-shaped relationship among three age groups, 50–60, 61–74, and 75 and older; for the prevalence of baseline insomnia and CES-D score with lowest values in the middle group. In all three age groups, SBP was a significant predictor for hypertension but not depression. DBP was not a predictor for either health conditions. Furthermore, subjective poor sleep symptoms were consistently significant predictors of incident hypertension and depression as well as their co-occurrences.

In our population, the average SBP and DBP were respectively 132 and 79 mm Hg with 60% of the cohort becoming hypertensive, which were consistent with other studies in older populations (Lin et al., 2016). SBP increased with age while DBP decreased, which had been found in other geriatric studies (Pinto, 2007). A possible explanation is the accelerated stiffening of large arteries, which may contribute to both higher SBP and lower DBP (Pinto, 2007). We observed that SBP was a significant predictor for hypertension but not for depression and DBP was not a significant predictor for either. This may be explained by the physiological arterial stiffening and higher prevalence of isolated systolic hypertension associated with increasing age (Franklin, 2012). It is important to note that because majority of hypertensive subjects used antihypertensive medication, we could not account for risks of uncontrolled high BP as a confounder. However, studies with a wide range of ages have reported inconsistent associations of BP and depression with some finding similar results to ours (Gao et al., 2013; Maatouk et al., 2016; Yan et al., 2003; Gross et al., 2018). Additionally, BP of patients with lifetime major depressive episodes were found not to be significantly different from those of patients without episodes (Wiehe et al., 2006). Blacks had higher risk for hypertension in our cohort, which has been well-documented in other studies (Krakoff et al., 2014). Taken together, hypertensive subjects may have risk factors, other than blood pressure, which contribute more to the development of late-onset depression.

Approximately 13% of our cohort had depressive symptomatology. This prevalence was similar to that of other studies (Smith et al., 2018). Our average CES-D score was also comparable to other cross-sectional studies from this prospective cohort (Mezuk et al., 2011; Barry et al., 2012). The risks of depression may have devastating consequences, including suicide, which is twice as frequent in the older population compared to the general population (Alexopoulos, 2005). In our study, prevalence of depressive symptoms was highest in the age group 75 or older. Possible explanations for late-old age depression include chronic and acute health conditions, cognitive impairment, and loneliness (Fiske et al., 2009). The prevalence was lowest in the age group, 61–74. This may be explained by their abilities to continue to work and exercise, and maintain social support (Fiske et al., 2009). Being female was also a significant predictor for incident depression compared to being male. Other studies have found similar results (Hall and Reynolds, 2014). Depression is multifactorial and its risk factors may change over time; thus more studies are needed to investigate the risk factors contributing to the onset of depression.

More than 81% of our cohort has one or more insomnia symptoms.

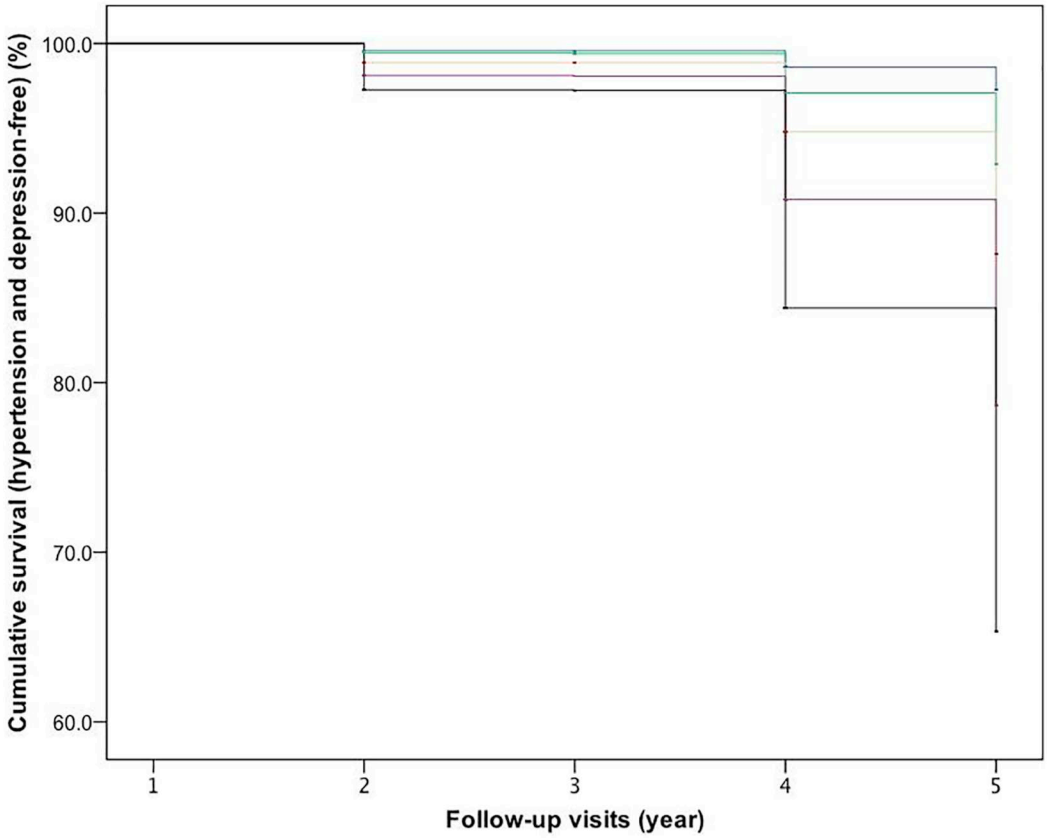

Fig. 1. Kaplan-Meier eight-year cumulative survival for both hypertension and depression-free in overall cohort.
Follow-up visits (year):
1 = 2008
2 = 2010
3 = 2012
4 = 2014
5 = 2016
Insomnia symptoms:
No symptom
1 symptom
2 symptom
3 symptom
4 symptom

Number at risk for both hypertension and depression	2008	2010	2012	2014	2016
No insomnia symptoms	3,242	2,775	2,290	1,684	537
One insomnia symptom	3,749	3,204	2,628	1,930	616
Two insomnia symptoms	3,623	3,156	2,644	1,961	630
Three insomnia symptoms	3,958	3,503	2,969	2,261	758
Four insomnia symptoms	3,551	3,224	2,795	2,241	811

Log-rank (Mantel-Cox) test for all age groups, $p < 0.001$

Insomnia predicted the incidence of both hypertension and depression. Other studies have shown similar prevalence of insomnia and its association with hypertension (Jarrin et al., 2018). A multicenter epidemiologic study conducted by the National Institute on Aging among 9000 non-institutionalized older individuals reported similar insomnia symptoms to our study and found that 43% of the population had difficulty initiating or maintaining sleep, 19% had trouble falling asleep, 19% woke up too early, and 13% woke up feeling not rested (McCall, 2004).

Moreover, meta-analyses have shown that the coupling of insomnia and objective short sleep duration is a severe phenotype of insomnia and significantly increases the risk for incident hypertension (Javaheri and Redline, 2017). Although obstructive sleep apnea (OSA) could not be assessed, insomnia and OSA have been found to co-exist, and both are risk factors for hypertension and depression (Heinzer et al., 2015; Lang et al., 2017). A study identified that the age group 60–80 had significantly higher risks for OSA (OR = 34.5) compared to younger age group 20–29 (Tufik et al., 2010). Another study found that the prevalence of OSA was 23.4% and 49.7% in females and males respectively and OSA was associated with hypertension and depression (Heinzer et al., 2015). These findings suggest that OSA, although not assessed in our population, may have high prevalence given the relatively older age of our subjects and its co-occurrence with insomnia. Insomnia is a major unresolved health condition particularly in older populations, and is associated with increased risks for poor health prognosis, including mental health conditions and mortality (Fiske et al., 2009; Reid et al.,

2006). Yet despite the significance of sleep disturbance as predictors of physical and mental health, currently common clinical practices do not evaluate sleep hygiene (Reid et al., 2006).

Finally, our longitudinal analysis showed that insomnia symptoms increased risks for both hypertension and depression in the older population who were neither hypertensive nor depressed at baseline. Insomnia has been proposed to be a risk factor for both hypertension and depression (Batal et al., 2011). In fact, insomnia is a diagnostic criterion of major depressive disorder with 60 to 70% positive predictive value in diagnosis (Khurshid, 2018). Reviews have found insomnia to be a risk factor for hypertension (Bathgate and Fernandez-Mendoza, 2018; Jarrin et al., 2018). Individuals with depression are also likely to suffer from sleep disturbances, which complicates the differentiating of their casual relationships (Franzen and Buysse, 2008). Thus, we estimated the time-to-event of new hypertension and depression cases and excluded those with hypertension or depression in the first wave. Recent study has suggested that subjective sleep disturbance is associated with both hypertension and depression, and in particular may be a better predictor of depression than objective sleep measurements (Kenneth et al., 2018; Gould et al., 2018). More than 21% of individuals having four insomnia symptoms became both hypertensive and depressed compared to 1.5% of individuals having no symptom. Our study provided additional evidence that more number of insomnia symptoms may contribute to both the etiology and comorbidity of hypertension and late-onset depression in older populations within eight years.

5. Limitations

A major limitation of our study was that although clinical implications may be drawn from our findings, this study was based on a non-clinical sample with some self-reported measures of chronic health conditions. Another limitation was that despite asking questions related to insomnia, they are not diagnostic clinical markers and sleep duration and time frame were not collected. Nonetheless, a recent study using HRS data found that insomnia severity remained stable over an 8-year period, which may suggest that the reported insomnia symptoms persist in these individuals over time (Kaufmann et al., 2016). Objective sleep phenotype (i.e. OSA) was not collected in the HRS study. However, a recent study suggested that subjective sleep quality may be better associated with depression than objective sleep (Gould et al., 2018).

Because OSA and insomnia can co-occur, the reported associations with insomnia may partially have been mediated by OSA. The different types of antihypertensive medications were not reported; thus the types of blood pressure medication and their risks for depression could not be analyzed. Although the association between insomnia and autonomic dysregulation has been reported, currently existing literature lack empirical evidence for causation; therefore, the relationship between insomnia and hypertension requires more evidence (Dodds et al., 2017). At the time of writing this paper, the 2016 wave data has been released but their weights have not. As such we did not use weights in our final analysis; however, we compared analyses of previous waves using weights and without weights and found the results to be similar. Additional limitations include possible bias arising from lost to follow-up and the excluded data of subjects who did not have BP measured.

Despite these limitations, there were several notable strengths in our study. First, HRS was designed to be generalizable to the overall aging American population with a rich source of longitudinal data, which renders our results more likely applicable to the overall aging population. Second, we performed time-to-event analysis which provided evidence for possible causal and longitudinal relationships regarding insomnia, and risks for hypertension and depression. We believe this longitudinal study adds valuable information to the current literature by elucidating relationships among BP, insomnia, hypertension, and depression in older populations with.

6. Conclusions

The present study examined the roles of insomnia or BP in the development of hypertension and depression overtime in a prospective older cohort with eight-year follow-up. Our study shows (1) more insomnia symptoms are consistent predictors of both incident hypertension and depression, and (2) insomnia may contribute to the comorbidity of hypertension and depression, (3) neither blood pressure nor antihypertensive medications are associated with depression. Insomnia may be a major risk factor for hypertension and depression as well as their comorbidity. Our study promotes the importance of assessing insomnia symptoms as a risk factor in older individuals for their general well-being. Furthermore, these results suggest that sleep disturbance may play roles in the etiology between hypertension and late-onset depression and warrants clinical investigations to assess the cardiometabolic and psychosocial health prognosis of older individuals through reducing sleep disturbance and improve sleep quality as a potential intervention.

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Conflict of interest

The authors declare no conflicts of interest in the cover letter as well as in the manuscript.

Author contributions

YTD helped conceptualize, analyze data, and write the manuscript. FMY also helped conceptualize, analyze data, and write manuscript.

Sponsor's role

The sponsor was not involved in the design, analysis and interpretation of the present study.

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