

HHS Public Access

Author manuscript

Sleep Health. Author manuscript; available in PMC 2021 March 02.

Published in final edited form as:

Sleep Health. 2017 June; 3(3): 170–177. doi:10.1016/j.sleh.2017.03.003.

Associations between midlife insomnia symptoms and earlier retirement

Lauren Hale, PhD¹, Lee Singer, MPH², Jodi H. Barnet, MS³, Paul E. Peppard, PhD³, Erika W. Hagen, PhD³

² New York City Department of Health and Mental Hygiene

Abstract

Background: Insomnia symptoms are prevalent and associated with impaired health and wellbeing. However, scant research has investigated whether midlife insomnia symptoms are also associated with earlier retirement, thereby contributing to additional economic consequences.

Participants and Methods.—We analyzed data from a community-based sample of 1,635 Wisconsin State employees (51.6% female) that were collected from 1988 until 2014. Study participants were asked about insomnia symptoms (difficulty getting to sleep, difficulty getting back to sleep, repeated nocturnal awakenings, and early morning awakenings) in midlife, with prospective follow-up questions about the specific reasons for retirement between 2010 and 2014. Using Cox proportional hazards models, we investigated longitudinal associations between insomnia symptom measures (i.e. each individual insomnia symptom, any insomnia symptom, and number of insomnia symptoms) and rates of retirement. We also investigated reasons for retirement and the potentially mediating role of depression.

Results: For most of our insomnia measures, after adjusting for confounding variables, we did not find that insomnia symptoms at age 50 were predictive of earlier overall retirement. One exception is that early morning awakening at age 50 is associated with an increased rate of overall retirement (hazard ratio=1.22; 95% CI 1.04–1.43). With regard to reason for retirement, we found that all measures of insomnia were associated with increased rates of retirement due to poor health/disability. For example, the presence of at least one insomnia symptom was associated with a hazard ratio of 1.38 (95% CI 1.13–1.68). We also found evidence that depressive symptoms mediate the association between insomnia symptoms and retirement due to poor health/disability.

Discussion: Our study finds an association between insomnia symptoms in midlife and retirement due to poor health/disability whereas there is less compelling evidence between insomnia symptoms and retirement due to other reasons. Future research on insomnia should consider how earlier retirement affects the social and economic consequences of insomnia.

^{3.} University of Wisconsin-Madison

^{1.}Corresponding author: Lauren Hale, Associate Professor of Family, Population, and Preventive Medicine, Program in Public Health, HSC Level 3, Room 071, Stony Brook, NY 11794-8338, lauren.hale@stonybrook.edu,.

INTRODUCTION

Insomnia symptoms, including difficulty falling asleep, staying asleep, having trouble falling back asleep, or waking up too early, are common among adult middle-aged and elderly populations. Any of these insomnia symptoms, accompanied by a report of compromised daytime function, can result in a diagnosis of either acute or chronic insomnia, depending on the duration of the symptoms. The prevalence of insomnia diagnosis in the general population ranges between 6% and 18%, depending on the definition (1).

Insomnia is associated with a range of adverse physical and mental health outcomes, including hypertension, cancer, depression, anxiety and mood disorders, impaired cognitive functioning, diminished immune functioning, metabolic syndrome, and arthritis (2–13). While there is a substantial literature linking insomnia to health and well-being, less research has examined the economic and social consequences of insomnia. In this study, we investigate whether mid-life insomnia is associated with earlier exit from the workforce (hereafter, "earlier retirement"), an important economic and social outcome among Americans.

INSOMNIA AND RETIREMENT

Prior research has found associations between insomnia symptoms and retirement (14–22). Two general approaches exist: One approach seeks to understand how sleep characteristics change after retirement (Scenario A: Retirement affects sleep quality) (14–17), while the alternative pathway seeks to understand how sleep characteristics affect retirement itself (Scenario B: Sleep quality affects retirement) (14, 18–21).

Among the studies that investigate Scenario A, the general finding is that people have fewer sleep disturbances and longer sleep duration after retirement than they did before retiring (14–16). One study examined the association between retirement and sleep patterns by comparing the occurrence of sleep disturbances among nearly 15,000 French natural gas and electric employees seven years after retirement to seven years before retirement (14). Individuals had 26% lower odds of reporting sleep disturbances after retirement than before retirement (OR=0.74; 95% CI 0.71–0.77). The largest reductions in sleep disturbances after retirement (OR=0.55; 95% CI 0.52–0.60) compared to before retirement were found among those with depression or mental fatigue prior to retirement (14). Another study in France found that the symptom of premature awakening was reduced after retirement (15). Finally, a study investigating the Wisconsin Sleep Cohort observed a change in sleep behaviors after retirement that showed longer sleep duration, later wake times, and later bedtimes (16), but does not report on insomnia symptoms after retirement.

Among the studies that investigate Scenario B, the general finding is that insomnia symptoms during employment are not positively associated with overall earlier retirement (e.g., based on one study in France) (14) but insomnia is positively associated with disability pension in three northern European countries (e.g. Sweden, Finland, Norway) (17, 18, 19). One study observed Swedish workers approaching the age of retirement over a 12-year period to examine the impact of insomnia symptoms and sleep duration on subsequent

disability pension award (17). From a sample of over 4,000 employees in Sweden, 41% of the women studied showed symptoms of insomnia, which were associated with increased disability pension award (fully-adjusted HR=1.4 95% CI 1.1–1.7). In a similar cohort of nearly 6,000 employees in Finland, reports of frequent sleep problems were associated with all-cause disability retirement with an adjusted hazard ratio (HR) of 3.22 (95% CI 2.26–4.60) (18). Sleep problems were also associated with the development of mental disorders and musculoskeletal disorders with HRs of 9.06 (95% CI 3.27–25.1) and 3.27 (95% CI 1.91–5.61), respectively. A follow-up analysis of these data showed a joint association between insomnia symptoms and short sleep duration predicting subsequent retirement due to a disability (19). Finally, a four-year study of almost 6600 Norwegian employees found that insomnia strongly predicted permanent work disability (20).

INSOMNIA, DEPRESSION, AND RETIREMENT

Prior literature has shown that insomnia symptoms and depression are commonly comorbid (21–23). Combined, they are positively associated with disability pension (24), though some researchers suggest that insomnia symptoms and depression may have independent roles in predicting retirement due to a disability (25). Other studies show the association between poor sleep and an increased risk of retirement disability due to the presence of depression (26). In a large sample of the Finnish Twin Cohort, the onset of poor sleep predicted increased odds of developing depression, as defined by the Beck Depression Inventory (OR = 4.5, 95% CI 2.7–7.4) and Negative Attitudes Towards Self measurement (OR = 2.0, 95% CI 1.4–2.7). Additionally, onset of poor sleep increased the risk of subsequent disability retirement due to the presence of depression (OR = 2.9, 95% CI 1.8–4.9). A similar risk for retirement due to a disability was seen among those who had persistent poor sleep (OR = 2.7, 95% 1.3–5.7). A secondary aim of our analysis is to investigate the potentially mediating role of depression in explaining the association between insomnia symptoms and retirement (26).

RESEARCH QUESTIONS AND HYPOTHESES

In the present manuscript, we investigate the longitudinal association of insomnia symptoms with earlier retirement in a US-based cohort of more than 1,600 workers with a broad range of blue-to-white collar job classifications. Insomnia symptoms evaluated at age 50 in employed participants are examined for associations with rate of retirement (i.e., earlier or later age-at-retirement) or a mean follow-up period of 11.0 years (SD=4.7 years).

Research Question 1: Do insomnia symptoms during midlife (age 50) predict earlier retirement? If so, what are the reasons for this earlier retirement? Is earlier retirement due to poor health/disability a major contributing factor to earlier retirement among those with insomnia symptoms?

Hypothesis: While the association between insomnia symptoms and earlier retirement was not observed in the GAZEL study of French natural gas and electric employees, there are reasons to predict that impaired functioning and mental health due to insomnia symptoms will affect performance in the workplace as well as interpersonal relationships and thus increase rate of retirement. Thus, we

hypothesize that insomnia symptoms will be predictive of earlier overall retirement. Based on the empirical research from Sweden, Finland and Norway showing that insomnia predicts disability pension, we further hypothesize that the association between insomnia symptoms and rate of retirement for disability or poor health will be a primary reason for why those with insomnia symptoms in midlife are retiring earlier than those without insomnia symptoms.

Research Question 2: Is there a mediating role of depression in explaining an association between insomnia symptoms and retirement?

Hypothesis: Based on the frequent comorbidity of insomnia symptoms, depression and poor health, we hypothesize that increased levels of depression, which are more prevalent among those with insomnia symptoms, will help explain earlier retirement due to poor health/disability, consistent with previous research (26)

PARTICIPANTS AND METHODS:

Sample and Data Collection

Participant information was collected as part of The Retirement and Sleep Trajectories (REST) Study, a longitudinal survey of the sampling frame (i.e., a superset) of the Wisconsin Sleep Cohort Study that collects information on sleep disorders and sleep habits of a community-based sample of Wisconsin State employees at baseline. Study participants were followed up regardless of whether they stayed employed within the state system or left the public sector for private sector work, self-employment, or retirement. Approval for the study protocols and informed consent forms were obtained by the University of Wisconsin-Madison Health Sciences Institutional Review Board.

The sample for the REST study was collected from the Wisconsin Sleep Cohort (WSC) study-sampling frame. Study participants of previous WSC study protocols were eligible for the current study based on being alive after September 2010 and either a) having completed one or more mailed surveys and an overnight sleep study or b) having completed 3 or more mailed surveys. A total of 2,427 participants were eligible, ranging from the ages of 25 and 60 years old in the year 1988, the year of inception of the Wisconsin Sleep Cohort study. Subjects were aged 25 to 60 years old at the start of the Wisconsin Sleep Cohort Study in 1988. At the time of the current analysis, subjects were aged 46 to 82 years old.

The study includes 4 surveys sent via mail at one-year intervals. The surveys included questions on socio-demographic information, occupational status, reasons for and date of retirement (if retired), health, and sleep.

Variables:

Primary Predictor Variable: Insomnia symptoms at approximately age 50 (+/- 4 yrs) is the independent predictor sleep problem for this analysis. Insomnia symptoms were measured at several time points. For each study subject, we used insomnia data collected at the survey time point closest to age 50. The analysis takes into account follow up on employment/retirement information from this insomnia measurement moving forward.

We asked the following four questions about insomnia:

- 1. Do you have difficulty getting to sleep?
- 2. Do you wake up during the night and have a hard time getting back to sleep (difficulty getting back to sleep)?
- **3.** Do you wake up repeatedly during the night (repeated nocturnal awakenings)?
- **4.** Do you wake up too early in morning and can't get back to sleep (early morning awakenings)?

For each of these questions, individuals were able to answer, Never, Rarely (once a month), Sometimes (2–4 times a month), Often (5–15), and Almost Always (>15 times a month). We then recoded each of these 4 questions into the following predictor variables. First, for each individual insomnia symptom, we created a dichotomous variable for presence of the symptom as determined by Never/Rarely/Sometimes=0 and Often/Almost Always=1. Second, we created a dichotomous variable to mark whether the individual reported any insomnia symptom. Individuals were coded as such if they answered Often or Almost Always on any of the four questions above. Third, we created a variable that counted the number of reported insomnia symptoms, listed from the 4 variables above, allowing for a range of 0 to 4. If responses to any of the specific symptom questions were missing, the insomnia summary variables were left missing.

Additional covariates: Based on prior studies predicting retirement (28–32), we included a range of covariates known to predict retirement age. These include variables for sex (male/female), education level (some college vs. no college), body mass index, marital status (e.g. married, divorced, single), and current smoking status. In addition, we included self-reported measures of comorbidities prior to insomnia assessment for the following conditions:

- Any CVD coronary artery disease, atherosclerosis, heart attack, congestive heart failure, coronary bypass surgery, angioplasty, stent, or pacemaker
- Diabetes mellitus type 1 or type 2
- Prior cancer diagnosis
- Emphysema or Obstructive Lung Disease

For our mediation models, we used a subset of participants who completed the Zung Depression Scale. The Zung Scale is a 20-question self-administered survey that rates symptoms associated with depression. Scores range from 20 (no depression) to 80 (severely depressed) (33). The Zung Depression Scale was only administered during overnight sleep studies (i.e., in REST participants that were also Wisconsin Sleep Cohort participants) and thus was available on a subset (N=814=50%) of the sample used for primary analyses here.

Dependent Variables: On the surveys, respondents indicated their occupational status as follows: not working for pay/not retired/not currently looking for work, fully retired, partially retired, working part-time, or working full-time. For this investigation, we dichotomized the retirement status into those who were fully retired compared to those who were not, and we identified the age at the time of movement into this status for use in

survival analyses. Within this general category of full retirement, participants were also asked to identify their reasons for retirement, which included the following categories:

- Poor Health/Disability
- Wanted to do other things
- Did not like the work
- Wanted to spend more time with family and/or friends
- Wanted or needed to provide care for family or friend
- Financially secure and/or no need to work
- Hours reduced or laid off/ let go led to decision to retire (not available in the first mailings in year 1; it was added to the later mailings in year 1)

For reason of retirement, respondents were allowed to select which of the following response fit their reason for retirement: Very Important, Moderately Important, Somewhat Important, Not Important

• Responses were analyzed as 0=No (not important) vs 1=Somewhat, Moderate or Very Important

Methods

In order to answer the first research question of whether insomnia symptoms predict overall retirement, we conducted Cox Proportional Hazards models in which the outcome variable is full retirement (due to any reason), and among the predictor covariates we included the primary predictor variable (insomnia symptoms at approximately age 50 years old +/- 4 years) and the above-described socio-demographic factors. We subsequently estimated the same model in which the outcome variables were full retirement by reported reason of retirement as described above. For all models, follow-up time was computed as the time in years from the date of the insomnia questionnaire response to the date of retirement (or date of retirement by reported reason). For those who did not retire, follow-up was censored at the date of the last REST survey completed. For those who did retire but not for the specific reason of interest, follow-up was censored at the date of retirement.

To answer the second research question, we then conducted mediation analyses in which we investigated whether depressive symptoms might mediate the association between insomnia symptoms and retirement status by reason of retirement. We used the SAS Mediate macro written by Pazaris et al., which is designed for treatment effects estimated as relative risks in Cox Proportional Hazards models using PROC PHREG (34, 35). Because depression can be an underlying cause of both insomnia and early retirement (thus potentially acting as a confounder and mediator), by estimating possible mediating effects of depression on retirement, we are able to provide lower and upper estimates regarding the magnitude of the association between insomnia symptoms and retirement.

RESULTS:

Table 1 provides the descriptive statistics for the final analytic sample which includes 1,635 subjects with 51.6% female participants. Participants were predominantly Caucasian (96.9%) with some form of higher education (76.5%). Study participants tended to be non-smokers (87.2%) and married (70.4%) individuals. By the time of the final (fourth) wave of surveys, 68.4% of the sample had retired, with a mean age of retirement at 61 (with a standard deviation of 4.6) among those who had retired.

Table 2 provides similar descriptive statistics, stratified by retired/not retired and separately stratified by retired for health/disability reasons and not retired for this reason. Continuing to focus on those who retired due to poor health or disability, we also see differences with education, smoking status, history of cardiovascular disease, and history of diabetes. Specifically, retirement for health/disability reasons was more common among those with lower levels of education, current smoking status, history of cardiovascular disease, history of diabetes, and the presence of insomnia symptoms.

Table 3 shows the estimated model results for the insomnia symptom variables for each of the various types of retirement reason outcomes. The first column reflects the hazard ratio of "any retirement" as associated with various measures of insomnia symptoms (each measure of insomnia symptom is an independently estimated model). As shown, only one insomnia symptom was positively associated with retirement – early morning awakening. Specifically, those individuals who reported early morning awakening at age 50 had increased rate (HR=1.22; 95% CI 1.04–1.43) of retirement for any reason at the follow up waves. The subsequent columns reflect individual specific reasons for retirement as described above (e.g., due to poor health/disability, wanted to do other things, did not like work, etc.). Only the category of retiring due to poor health/disability was consistently associated with insomnia symptoms across the full range of measured insomnia symptoms. For example, reporting any symptoms of insomnia at age 50 was associated with a HR of 1.38 (95% CI 1.13-1.68) with similar magnitudes for all other observed symptoms. There was a doseresponse association between multiple symptoms of insomnia at age 50 and retirement for poor health/disability, such that compared to having 0 insomnia symptoms, having 1, 2, or 3–4 symptoms was associated with increased risks of 1.14, 1.54, and 1.90, respectively. Among the 4 reported insomnia symptoms, there was not one that stands out as the most predictive of earlier retirement. While symptoms of insomnia were associated with other individual reasons for retirement in some cases, these results were not observed for most of the measures of insomnia. One reported reason for retirement ("did not like work") was signficantly associated with 4 of the 8 insomnia measures variables. None of the other reported reasons for retirement were positively associated with more than 2 of the insomnia symptoms variables. Thus, in subsequent analyses, we focus on the association between insomnia symptoms and reasons for retirement due to poor health/disability.

Table 4 presents the full results for retirement due to health or disability. Among those who retired due to poor health or disability, there was an increased hazard ratio for those who had two or more symptoms of insomnia, difficulty falling asleep, difficulty falling back to sleep, and nocturnal awakenings as summarized in Table 3. The additional variables included in

Table 4 show that the other predictors of earlier retirement due to poor health/disability include: lower education, higher BMI, being single, being a current smoker, and having a history of cardiovascular disease. The magnitude of the coefficients here are substantively the same across all models, which only vary by the insomnia symptom included in the model. Gender was not associated with retirement due to poor health/disability.

In Table 5, displays the results of the mediation models in which we test whether the association between insomnia symptoms and retirement for poor health/disability is partially explained by the inclusion of measures of depression. Specifically, we find that depression is a significant mediator of the association between retirement for poor health/disability and any insomnia (p=0.035). The results were nuanced in the survival models. Specifically, two of the measures of insomnia symptoms (3–4 insomnia symptoms, and early morning awakenings) are associated with increased risk of retirement due to poor health/disability, even after adjustment for depression. However, the other insomnia symptoms measured had their effects fully attenuated when the depression measure was incorporated into the model.

We performed several supplemental and sensitivity analyses. We tested for interaction between insomnia and depression and did not find one. We tested for evidence of cardiovascular disease mediating the association between insomnia symptoms and retirement. While we found that cardiovascular disease was associated with increased risk of retirement, it did not change the coefficients on the insomnia symptoms, indicating no empirical evidence of mediation (or confounding). We tested whether adjusting for sleep apnea, anxiety symptoms, shiftwork, and depression and anxiety medications change the associations between insomnia symptoms; the results were essentially unchanged. We included an indicator of baseline (at age 50 years) menopausal status on a subset of women for whom these data were available and found that including the menopausal status indicator resulted in an greater association between insomnia symptoms and early retirement (larger coefficients), compared to models that do not include menopausal variables. In addition, we considered another test for robustness in which we excluded those individuals who were depressed at baseline. We found that even after excluding those who were depressed at the time of insomnia measurement, having 3-4 insomnia symptoms and early morning awakenings was a predictor of earlier retirement due to poor health/disability.

DISCUSSION:

We found that most of the insomnia symptoms measures at age 50 were not predictors of earlier overall retirement. The one insomnia symptom that was associated with an increased rate of earlier overall retirement was early morning awakening. When we analyzed the data by specific reported reasons for retirement, we found that when predicting retirement due to poor health or disability, all 8 of the measures of insomnia symptoms were positively associated with increased rate of earlier retirement. Most of the other reasons for retirement were only associated with one or two insomnia symptom measures. The reported reason of retirement being "not liking my job" was associated with 4 of the 8 insomnia measure variables.

Our findings are generally consistent with the research from Europe in which the association between insomnia symptoms and overall retirement is small or does not exist, and that insomnia symptoms are associated with disability retirement or retirement due to the presence of an existing disability (17–20). A similar hazard ratio was reported between insomnia symptoms and subsequent disability retirement in the study of Swedish employees (fully-adjusted HR=1.4; 95% CI 1.1–1.7) (17). A sample of Norwegian workers also found a similarly sized large association between insomnia symptoms and increased odds of permanent work disability when controlling for baseline exposure to disability, sick leave, and sleep duration (OR= 1.88; 95% CI 1.00–3.55) (20). In contrast, the HR of retirement reported in the Finnish study was substantially larger than those associations observed in this study. Specifically, the study of Finnish employees reported a more than 3-fold hazard ratio between frequent sleep problems and all-cause disability pension (adjusted HR= 3.22; 95% CI 2.26–4.60) (18).

For most of the insomnia symptoms (e.g., trouble falling asleep, trouble staying asleep), consistent with prior research (26), we observed a fully mediating role of depression in explaining the association between insomnia symptoms and retirement. Two measures of insomnia symptoms at age 50 still had predictive associations with retirement due to poor health/disability, even after adjustment for depression. Those two measures were: 3–4 symptoms and early morning awakenings. Reporting 3–4 symptoms of insomnia at the same time point reflects a higher level of severity of insomnia and may explain why it has an independent association with earlier retirement.

This research contributes to the current literature on insomnia symptoms and retirement through longitudinal study using a sample based in the US, with detailed follow-up questions at 4 waves on reasons for retirement. Future research should seek to understand the generalizability of these findings, as this study included primarily White, married non-smokers.

Compared to other studies on retirement, this study offers the most detailed questions about reasons for retirement. While the findings are longitudinal, and we are able to account for temporality, we cannot identify if there is a true causal association between insomnia symptoms in midlife and earlier retirement due to poor health or disability. Indeed, despite our statistical control for multiple health conditions, a range of underlying factors such as chronic life stressors and unmeasured physical and mental health factors (e.g., anxiety disorders) might cause increased risk of both insomnia symptoms and rate of retirement due to disability/poor health. These unmeasured factors may confound or mediate insomnia symptoms, or, alternatively, have their effects partially mediated by insomnia symptoms.

Other areas of future inquiry include investigating whether there are gender-differences in these associations or whether the duration of insomnia symptoms affects retirement risk. In addition, future research could look at different levels of retirement (i.e. from premature unemployment to partially retired to fully retired). Finally, it is worth investigating if the benefits of good sleep may have protective effects on employment such that those who regularly report high quality sufficient sleep are able to work longer and more productively into older ages.

Kessler et al (27) estimates a yearly burden of insomnia on US workers is \$63.5 billion, yet their study only accounts for the costs of absenteeism and presenteeism. Based on the findings in the current manuscript, future research on the economic costs of insomnia should consider the additional consequences of increased rate of retirement from the workforce—especially retirement due to poor health/disability—among those with mid-life insomnia symptoms.

Acknowledgements:

This work was supported by US National Institutes of Health (NIH) grants 1R01AG036838, R01HL62252, and 1UL1RR02501.

We thank the following people for their valuable assistance: Nicole Salzieder, Christine Harden, Rachel Steidl, Kayla Lacci, Haley Jelinski, Marni Sarazen, Kallie Waro, Dr. Mari Palta, Dr. F. Javier Nieto, and Robin Stubbs.

References

- 1. Morin CM, LeBlanc M, Daley M, Gregoire JP, & Merette C (2006). Epidemiology of insomnia: prevalence, self-help treatments, consultations, and determinants of help-seeking behaviors. Sleep Med, 7(2), 123–130. doi: 10.1016/j.sleep.2005.08.008 [PubMed: 16459140]
- 2. Ohayon MM (2002). Epidemiology of insomnia: what we know and what we still need to learn. Sleep Medical Review, 6(2), 97–111.
- 3. McCall WV (1995). Management of primary sleep disorders among elderly persons. Psychiatric Services, 46(1), 49–55. [PubMed: 7895121]
- Gislason T, Almqvist M. (1987) Somatic diseases and complaints: epidemiological study of 3201 Swedish men. Acta Medica Scandinavica; 221: 475–481. [PubMed: 3496735]
- 5. Ohayon M (1996). Epidemiological study on insomnia in the general population. Sleep, 19(3 Suppl), S7–15. [PubMed: 8723370]
- Ohayon MM, Caulet M, & Guilleminault C (1997). How a general population perceives its sleep and how this relates to the complaint of insomnia. Sleep, 20(9), 715–723. [PubMed: 9406323]
- 7. Ohayon MM, Caulet M, Priest RG, & Guilleminault C (1997). DSM-IV and ICSD-90 insomnia symptoms and sleep dissatisfaction. British Journal Psychiatry, 171, 382–388.
- 8. Andersson HI, Ejlertsson G, Leden I, & Schersten B (1999). Impact of chronic pain on health care seeking, self care, and medication. Results from a population-based Swedish study. Journal of Epidemiology & Community Health, 53(8), 503–509. [PubMed: 10562870]
- Foley DJ, Monjan A, Simonsick EM, Wallace RB, & Blazer DG (1999). Incidence and remission of insomnia among elderly adults: an epidemiologic study of 6,800 persons over three years. Sleep, 22 Suppl 2, S366–372. [PubMed: 10394609]
- Gislason T, Reynisdottir H, Kristbjarnarson H, & Benediktsdottir B (1993). Sleep habits and sleep disturbances among the elderly--an epidemiological survey. Journal of Internal Medicine, 234(1), 31–39. [PubMed: 8326287]
- 11. Altena E, Van Der Werf YD, Strijers RL, Van Someren EJ. (2008). Sleep loss affects vigilance: effects of chronic insomnia and sleep therapy. Journal of Sleep Research; 17:335–43. [PubMed: 18844819]
- 12. Savard J, Laroche L, Simard S, Ivers H, Morin CM. (2003). Chronic insomnia and immune functioning. Psychosomatic Medicine; 65:211–21. [PubMed: 12651988]
- 13. Jennings JR, Muldoon MF, Hall M, Buysse DJ, Manuck SB.(2007). Self-reported sleep quality is associated with the metabolic syndrome. Sleep. ;30:219–23. [PubMed: 17326548]
- Vahtera J, Westerlund H, Hall M, Sjösten N, Kivimäki M, Salo P, ... Zins M (2009). Effect of Retirement on Sleep Disturbances: the GAZEL Prospective Cohort Study. Sleep, 32(11), 1459– 1466. [PubMed: 19928385]

 Marquiae JC, Folkard S, Ansiau D, & Tucker P (2012). Effects of age, gender, and retirement on perceived sleep problems: results from the VISAT combined longitudinal and cross-sectional study. Sleep, 35(8), 1115–1121. doi: 10.5665/sleep.2000 [PubMed: 22851807]

- Hagen EW, Barnet JH, Hale L, & Peppard PE (2016). Changes in Sleep Duration and Sleep Timing Associated with Retirement Transitions. Sleep, 39(3), 665–673. doi: 10.5665/sleep.5548 [PubMed: 26564125]
- Canivet C, Staland-Nyman C, Lindeberg SI, Karasek R, Moghaddassi M, & Ostergren PO(2014).
 Insomnia symptoms, sleep duration, and disability pensions: a prospective study of Swedish workers. Int J Behav Med, 21(2), 319–328. doi: 10.1007/s12529013-9315-0 [PubMed: 23595781]
- Lallukka T, Haaramo P, Lahelma E, & Rahkonen O (2011). Sleep problems and disability retirement: a register-based follow-up study. American Journal of Epidemiology, 173(8), 871–881. doi: 10.1093/aje/kwq462 [PubMed: 21415034]
- Haaramo P, Rahkonen O, Lahelma E, & Lallukka T (2012). The joint association of sleep duration and insomnia symptoms with disability retirement—a longitudinal, register-linked study. Scandinavian Journal of Work, Environment & Health, 38(5), 427–435. doi:10.5271/sjweh.3269
- Sivertsen B, Overland S, Pallesen S, Bjorvatn B, Nordhus IH, Maeland JG, & Mykletun A (2009). Insomnia and long sleep duration are risk factors for later work disability. The Hordaland Health Study. Journal of Sleep Research, 18(1), 122 128. doi:10.1111/j.1365-2869.2008.00697.x [PubMed: 19021852]
- 21. Cole MG, & Dendukuri N (2003). Risk Factors for Depression Among Elderly Community Subjects: A Systematic Review and Meta-Analysis. American Journal of Psychiatry, 160(6), 1147–1156. doi: doi:10.1176/appi.ajp.160.6.1147
- Perlis ML, Smith LJ, Lyness JM, Matteson SR, Pigeon WR, Jungquist CR, & Tu X (2006).
 Insomnia as a risk factor for onset of depression in the elderly. Behavioral Sleep Medicine, 4(2), 104–113. doi: 10.1207/s15402010bsm0402_3 [PubMed: 16579719]
- 23. Stepanski EJ, Rybarczyk B. (2006). Emerging research on the treatment and etiology of secondary or comorbid insomnia. Sleep Medicine Review. 10:7–18
- 24. Overland S, Glozier N, Sivertsen B, Stewart R, Neckelmann D, Krokstad S, & Mykletun A (2008). A comparison of insomnia and depression as predictors of disability pension: the HUNT Study. Sleep, 31(6), 875–880. [PubMed: 18548833]
- 25. Sivertsen B, Overland S, Neckelmann D, Glozier N, Krokstad S, Pallesen S, ... Mykletun A (2006). The long-term effect of insomnia on work disability: the HUNT-2 historical cohort study. Am J Epidemiol, 163(11), 1018–1024. doi: 10.1093/aje/kwj145 [PubMed: 16611665]
- Paunio T, Korhonen T, Hublin C, Partinen M, Koskenvuo K, Koskenvuo M, & Kaprio J (2014).
 Poor sleep predicts symptoms of depression and disability retirement due to depression. Journal of Affect Disorders, 172C, 381–389. doi: 10.1016/j.jad.2014.10.002
- 27. Kessler RC, Berglund PA, Coulouvrat C, Hajak G, Roth T, Shahly V, ... Walsh JK (2011). Insomnia and the Performance of US Workers: Results from the America Insomnia Survey. Sleep, 34(9), 1161–1171. doi: 10.5665/SLEEP.1230 [PubMed: 21886353]
- 28. Dahl SÅ, Nilsen ØA, & Vaage K (2003). Gender Differences in Early Retirement Behaviour. European Sociological Review, 19(2), 179–198. doi: 10.1093/esr/19.2.179
- 29. Crystal S, Shea D, & Krishnaswami S (1992). Educational attainment, occupational history, and stratification: Determinants of later-life economic outcomes. Journal of Gerontology: Social Sciences, 47, S213–S221.
- 30. Houston DK, Cai J, & Stevens J (2009). Overweight and obesity in young and middle age and early retirement: the ARIC study. Obesity (Silver Spring), 17(1), 143–149. doi: 10.1038/oby.2008.464 [PubMed: 19107127]
- Szinovacz ME, Deviney S. (2000) Marital characteristics and retirement decisions. Res Aging; 22: 470–98
- 32. Husemoen LL, Osler M, Godtfredsen NS, & Prescott E (2004). Smoking and subsequent risk of early retirement due to permanent disability. Eur J Public Health, 14(1), 86–92. [PubMed: 15080398]
- 33. Zung WW (1965). "A self-rating depression scale". Archives of General Psychiatry 12: 63–70. [PubMed: 14221692]

34. Pazaris M, Hertzmark E, Fauntleroy J, Skinner S, Jacobson D, & Spiegelman D (2012). Channing Laboratory. Harvard University.

35. Lin DY, Fleming TR, & De Gruttola V (1997). Estimating the proportion of treatment effect explained by a surrogate marker. Stat Med, 16(13), 1515–1527. [PubMed: 9249922]

Table 1

Baseline Characteristics of the Final Sample

Subject Characteristics	n (%) or Mean [Standard Deviation]
Final Sample	1635
Gender	
Female	843 (51.6%)
Male	792 (48.4%)
Race	
Caucasian	1417 (96.9%)
Non-Caucasian	46 (3.1%)
Education	
Through High School	384 (23.5%)
Some College	1251 (76.5%)
Current Smoker	
No	1425 (87.2%)
Yes	210 (12.8%)
Marital Status	
Divorced, Separated, Widowed	307 (18.8%)
Married	1151 (70.4%)
Single	177 (10.8%)
BMI (kg/m^2)	29[6.6]
Retired	
No	517 (31.6%)
Yes	1118 (68.4%)
Age at Retirement (years)	61 [4.6]
Age of Insomnia (years)	50 [1.8]
Years Between Insomnia and Retirement	11 [4.7]

Hale et al. Page 14

 $\label{eq:Table 2} \textbf{Baseline Characteristics by Reason for Retirement (bolded indicates that there are differences across groups at p<.05)}$

		Retired (N=1118)	Not Retired (N=517)	P value	Retired for Health/ Disability Reasons (N=415)	Not Retired For This Reason (N=703)	P value
Age at Retirement/ Follow-up (years)	Mean (SD)	60.5(4.2)	62.2(5.2)	0.000	59.9(4.4)	60.8(4.0)	0.001
Age at Insomnia Measurement (years)	Mean (SD)	50.1(1.8)	49.7(1.8)	0.000	50.0(1.8)	50.2(1.8)	0.293
BMI (kg/m^2)	Mean (SD)	28.6(6.3)	29.7(7.1)	0.007	30.1(7.4)	27.8(5.4)	0.000
Years Between Insomnia and Retirement	Mean (SD)	10.4(4.3)	12.5(5.1)	0.000	9.9(4.3)	10.7(4.2)	0.002
# of Days Without Insomnia Symptoms	Mean (SD)	15.5(16.1)	14.2(14.8)	0.309	18.5(17.9)	13.7(14.7)	0.000
Age at REST Survey 1 (years)	Mean (SD)	67.4(4.7)	62.2(5.2)	0.000	67.0(4.8)	67.6(4.6)	0.044
Sex							
Female	N (%)	588(52.6)	255(49.3)	0.218	225(54.2)	363(51.6)	0.404
Male	N (%)	530(47.4)	262(50.7)		190(45.8)	340(48.4)	
Education							
Through High School	N (%)	275(24.6)	109(21.1)	0.119	117(28.2)	158(22.5)	0.032
Some College	N (%)	843(75.4)	408(78.9)		298(71.8)	545(77.5)	
Caucasian							
Caucasian	N (%)	972(97.4)	445(95.7)	0.083	365(97.3)	607(97.4)	0.925
Non-Caucasian	N (%)	26(2.6)	20(4.3)		10(2.7)	16(2.6)	
Current Smoking Status							
No	N (%)	963(86.1)	462(89.4)	0.070	343(82.7)	620(88.2)	0.010
Yes	N (%)	155(13.9)	55(10.6)		72(17.3)	83(11.8)	
Marital Status							
Divorced	N (%)	210(18.8)	97(18.8)	0.984	78(18.8)	132(18.8)	0.541
Married	N (%)	788(70.5)	363(70.2)		287(69.2)	501(71.3)	
Single	N (%)	120(10.7)	57(11.0)		50(12.0)	70(10.0)	
Any CVD Prior to Insomnia							
No	N (%)	1076(96.2)	508(98.3)	0.029	391(94.2)	685(97.4)	0.006
Yes	N (%)	42(3.8)	9(1.7)		24(5.8)	18(2.6)	
Diabetes Prior to Insomnia							
No	N (%)	1062(95.0)	488(94.4)	0.611	383(92.3)	679(96.6)	0.001
Yes	N (%)	56(5.0)	29(5.6)		32(7.7)	24(3.4)	
Any Cancer Prior to Insomnia							
No	N (%)	1075(96.2)	487(94.2)	0.075	396(95.4)	679(96.6)	0.328
Yes	N (%)	43(3.8)	30(5.8)		19(4.6)	24(3.4)	
Emphysema or Lung Disease Prior to Insomnia							
No	N (%)	1111(99.7)	516(99.8)	0.244	410(98.8)	701(99.7)	0.059
Yes	N (%)	7(0.6)	1(0.2)		5(1.2)	2(0.3)	

		Retired (N=1118)	Not Retired (N=517)	P value	Retired for Health/ Disability Reasons (N=415)	Not Retired For This Reason (N=703)	P value
Insomnia Information Survey							
Health Interview	N (%)	168(15.0)	155(30.0)	0.000	71(17.1)	97(13.8)	0.459
Outcomes Survey	N (%)	9(0.8)	71(13.7)		3(0.7)	6(0.9)	
Survey 1	N (%)	242(21.6)	25(4.8)		81(19.5)	161(22.9)	
Survey 2	N (%)	356(31.8)	82(15.9)		129(31.1)	227(32,3)	
Survey 3	N (%)	343(30.7)	184(35.6)		131(31.6)	212(30.2)	
Any Insomnia Symptoms							
No	N (%)	655(58.6)	312(60.3)	0.500	212(51.1)	443(63.0)	0.000
Yes	N (%)	463(41.4)	205(39.7)		203(48.9)	260(37.0)	
Number of Insomnia Symptoms							
0	N (%)	655(58.9)	312(60.6)	0.125	212(51.3)	443(63.4)	0.000
1	N (%)	226(20.3)	117(22.7)		89(21.5)	137(19.6)	
2	N (%)	115(10.3)	50(9.7)		51(12.3)	64(9.2)	
3	N (%)	73(6.6)	27(5.2)		36(8.7)	37(5.3)	
4	N (%)	43(3.9)	9(1.7)		25(6.1)	18(2.6)	
3 or 4 Insomnia Symptoms							
No	N (%)	996(89.6)	479(93.0)	0.027	352(85.2)	644(92.1)	0.000
Yes	N (%)	116(10.4)	36(7.0)		61(14.8)	55(7.9)	
Difficulty Falling Asleep							
Never/Rarely/Sometimes	N (%)	976(87.3)	464(89.7)	0.155	342(82.4)	634(90.2)	0.000
Often/Always	N (%)	142(12.7)	52(10.3)		73(17.6)	69(9.8)	
Difficulty Getting Back to Sleep							
Never/Rarely/Sometimes	N (%)	904(81.0)	439(84.9)	0.055	314(75.8)	590(84.0)	0.001
Often/Always	N (%)	212(19.0)	78(15.1)		100(24.2)	112(16.0)	
Repeated Nocturnal Awakenings							
Never/Rarely/Sometimes	N (%)	806(72.4)	372(72.2)	0.960	274(66.2)	532(76.0)	0.000
Often/Always	N (%)	308(27.6)	143(27.8)		140(33.8)	168(24.0)	
Early Morning Awakenings							
Never/Rarely/Sometimes	N (%)	925(82.8)	454(87.8)	0.010	327(78.8)	598(85.2)	0.006
Often/Always	N (%)	192(17.2)	63(12.2)		88(21.2)	104(14.8)	

P<0.05, *Kruskal Wallis Test, Pearson Chi-Square Test

Author Manuscript

Author Manuscript

Table 3.

Survival Analysis by Reasons of Retirement, fully adjusted model results

Insomnia Retirement	Any Reason	Due to Poor Health / Disability	Wanted to Do Other Things	Did Not Like Work	Wanted to Spend More Time with Family / Friends	Wanted / Needed to Provide Care to Family / Friends	Financially Secure and/or No Need to Work	Hours Reduced/ Laid Off/ Let Go
	HR (95% CI) [p-value]	HR (95% CI) [p-value]	HR (95% CI) [p-value]	HR (95% CI) [p-value]	HR (95% CI) [p-value]	HR (95% CI) [p-value]	HR (95% CI) [p-value]	HR (95% CI) [p-value]
Any Symptoms	1.07 (0.95, 1.32) [0.29]	1.38 (1.13 1.68) [0.001]	1.06 (0.94, 1.21) [0.35]	1.19 (1.01, 1.40) [0.035]	1.03 (0.90, 1.17) [0.67]	0.92 (0.77, 1.11) [0.39]	1.08 (0.95, 1.23) [0.25]	1.28 (0.88, 1.87) [0.20]
1 Symptom	0.98 (0.84, 1.15) [0.83]	1.14 (0.89, 1.47) [0.29]	1.00 (0.86, 1.37) [0.97]	1.12 (0.91, 1.37) [0.29]	0.95 (0.80, 1.11) [0.50]	0.80 (0.63, 1.02) [0.07]	1.02 (0.87, 1.19) [0.84]	1.08 (0.67, 1.74) [0.76]
2 Symptoms	1.16 (0.95, 1.41) [0.16]	1.54 (1.13, 2.10) [0.007]	1.11 (0.90, 1.37) [0.35]	1.17 (0.88, 1.54) [0.28]	1.12 (0.91, 1.39) [0.28]	1.10 (0.82, 1.48) [0.51]	1.09 (0.88, 1.36) [0.43]	1.69 (0.95, 3.00) [0.07]
3-4 Symptoms	1.22 (1.00, 1.49) [0.054]	$1.90\ (1.42,2.56)\\ [<\!0.001]$	1.22 (0.99, 1.39) [0.07]	1.46 (1.13, 1.90) [0.004]	1.18 (0.95, 1.46) [0.13]	1.03 (0.76, 1.40) [0.84]	$1.24 (1.00, 1.54) \\ [0.048]$	1.30 (0.68, 2.48) [0.43]
Difficulty Falling Asleep	1.01 (0.85, 1.21) [0.90]	1.37 (1.06, 1.78) [0.017]	1.03 (0.85, 1.24) [0.75]	1.22 (0.97, 1.32) [0.09]	0.99 (0.82, 1.20) [0.96]	1.07 (0.83, 1.39) [0.59]	1.03 (0.85, 1.25) [0.76]	1.71 (1.06, 2.77) [0.027]
Difficulty Falling Back to Sleep	1.15 (0.99, 1.34) [0.08]	1.57 (1.25, 1.99) [<0.001]	1.11 (0.94, 1.30) [0.21]	1.20 (0.98, 1.48) [0.08]	1.08 (0.92, 1.27) [0.37]	0.97 (0.77, 1.22) [0.79]	1.12 (0.95, 1.32) [0.16]	1.35 (0.85, 2.15) [0.20]
Repeated Nocturnal Awakenings	1.10 (0.96, 1.25) [0.18]	$1.38\ (1.12,1.70)\\ [0.003]$	1.10 (0.95, 1.26) [0.20]	1.24 (1.04, 1.48) [0.016]	1.08 (0.93, 1.24) [0.31]	0.95 (0.77, 1.16) [0.60]	1.09 (0.95, 1.26) [0.22]	1.20 (0.79, 1.83) [0.39]
Early Morning Awakening	1.22 (104, 1.43) [0.012]	$1.59\ (1.25, 2.02)\\[<\!0.001]$	1.20 (1.02, 1.42) [0.028]	1.24 (1.01, 1.54) [0.042]	$1.19\ (1.01,1.40)\\ [0.041]$	1.19 (0.94, 1.50) [0.14]	$1.24(1.05,1.46)\\ [0.012]$	1.07 (0.64, 1.78) [0.81]

Table 4.

Retirement due to Poor Health/Disability
due to
Retirement of
redicting
for p
Results for
e R
with All covariate
٦A
with
'ull Models
Лo
11
Fu

Covariates	Retirement Due to Poor Health /Disability	Retirement Due to Poor Health /Disability	Retirement Due to Poor Health /Disability	Retirement Due to Poor Health /Disability	Retirement Due to Poor Health /Disability	Retirement Due to Poor Health /Disability
HR (95% CI) [p-value]	HR (95% CI) [p-value]	HR (95% CI) [p-value]	HR (95% CI) [p-value]	HR (95% CI) [p-value]	HR (95% CI) [p-value]	HR (95% CI) [p-value]
Sex (Female)	1.17 (0.95–1.44) [p=0.139]	1.15 (0.93–1.42) [p=0.198]	1.19 (0.96–1.46) [p=0.106]	1.14 (0.92–1.40) [p=0.228]	1.19 (0.97–1.47) [p=0.100]	1.20 (0.97–1.47) [p=0.086]
Baseline Age	$1.11 \ (1.05-1.17) \\ [p=0.000]$	1.11 $(1.05-1.18)$ [p=0.000]	$\begin{array}{c} 1.11(1.061.18) \\ [p=0.000] \end{array}$	1.11 $(1.05-1.18)$ [p=0.000]	1.11 (1.05-1.18) [p=0.000]	$1.12\ (1.06-1.18)\\ [p=0.000]$
Any College (vs no college)	0.75 (0.60-0.93) [p=0.010]	0.77 (0.61-0.95) [p=0.017]	$\begin{array}{c} 0.76 \; (0.610.94) \\ [p=0.014] \end{array}$	$\begin{array}{c} 0.77 \; (0.61 - 0.95) \\ [p=0.017] \end{array}$	0.75 (0.60-0.93) [p=0.008]	0.74 (0.59–0.92) [p=0.007]
BMI	$1.04\ (1.02{-}1.05)\\ [p=0.000]$	$1.04\ (1.02{-}1.05)\\ [p=0.000]$	$1.04\ (1.02{-}1.05)\\ [p=0.000]$	$1.04\ (1.02{-}1.06)\\ [p=0.000]$	$\begin{array}{c} 1.04 \; (1.02{-}1.05) \\ [p{=}0.000] \end{array}$	1.04 (1.02–1.06) [p=0.000]
Divorced (vs. single)	0.60 (0.42-0.86) [p=0.006]	0.58 (0.40-0.84) [p=0.004]	$\begin{array}{c} 0.61 \ (0.42 - 0.87) \\ [p=0.007] \end{array}$	0.59 (0.41-0.84) [p=0.004]	0.59 (0.41-0.86) [p=0.005]	$\begin{array}{c} 0.61 \; (0.42 - 0.88) \\ [p = 0.008] \end{array}$
Married (vs. Single)	0.71 (0.52-0.97) [p=0.033]	0.71 (0.52-0.97) [p=0.031]	0.72 (0.52-0.98) [p=0.037]	0.69 (0.51-0.95) [p=0.022]	$\begin{array}{c} 0.71\ (0.520.97) \\ [p=0.031] \end{array}$	0.70 (0.51–0.96) [p=0.027]
Current Smoker	$1.67 \ (1.28-2.17)$ [p=0.000]	1.73 (1.33–2.26) [p=0.000]	$1.66\ (1.28-2.16)\\[1mm] [p=0.000]$	1.71 $(1.31-2.22)$ [p=0.000]	1.73 (1.33–2.25) [p=0.000]	1.69 (1.30-2.19) [p=0.000]
Any CVD	1.56 (1.02–2.38) [p=0.042]	1.66 (1.07–2.58) [p=0.025]	1.59 (1.04-2.43) [p=0.033]	1.60 (1.04–2.46) [p=0.032]	$1.64\ (1.06{-}2.54)\\ [p{=}0.028]$	1.57 (1.02–2.41) [p=0.039]
Diabetes	1.36 (0.93–2.01) [p=0.117]	1.34 (0.90–1.98) [p=0.147]	1.36 (0.93–2.00) [p=0.117]	1.36 (0.92–2.00) [p=0.124]	1.34 (0.91–1.98) [p=0.141]	1.42 (0.96–2.09) [p=0.075]
Cancer	0.97 (0.61–1.55) [p=0.915]	1.01 (0.63–1.62) [p=0.958]	0.98 (0.61–1.56) [p=0.926]	1.05 (0.66–1.67) [p=0.844]	0.98 (0.62–1.57) [p=0.944]	0.99 (0.62–1.58) [p=0.976]
* Emphysema	1.83 (0.74–4.53) [p=0.194]	1.55 (0.61–3.92) [p=0.357]	2.17 (0.88–5.36) [p=0.091]	1.88 (0.75–4.71) [p=0.178]	1.76 (0.70–4.39) [p=0.226]	1.69 (0.67–4.23) [p=0.265]
Any Symptoms	1.38 (1.13-1.68) [p<0.001]					
1 symptom		1.14 (0.89–1.47) [p=0.291]			ı	
2 symptom		1.54 (1.13–2.10) [p=0.007]			I	
3-4 symptom		1.90 (1.42 – 2.56) [p=0.000]			I	
Difficulty falling asleep		ı	1.37 (1.06–1.78) [p=0.017]		I	

Covariates	Retirement Due to Poor Health /Disability	Retirement Due to Poor Health /Disability	Retirement Due to Poor Retirement Due to Poor Retirement Due to Poor Retirement Due to Poor Health / Disability	etirement Due to Poor Retirement Due to Poor Health /Disability Health /Disability	Retirement Due to Poor Health /Disability	Retirement Due to Poor Health /Disability
Difficulty falling back to sleep		1	1	1.57 (1.25-1.99) [p=0.000]	1	
Nocturnal awakenings		I	i	;	1.38 (1.12-1.70) [p=0.003]	
Early Morning Awakening						1.59 (1.25–2.02) P<.001

Hale et al.

Page 18

Table 5:

Mediation Modeling Results for the Association between Insomnia and Retirement for Poor Health Mediated by Depression (n=814)

Insomnia Variable	Exposure Effect Unadjusted for Mediator	Exposure Effect Adjusted for Mediator	Proportion of Insomnia Effect Mediated by Depression	Chi-Square P-value
Any Insomnia Symptom	1.39 (1.05–1.84)	1.18 (0.89–1.56)	49.5 % (3.4%-95.5%)	0.035
Number of Insomnia Symptoms	1.23 (1.10–1.37)	1.13 (1.01–1.27)	39.8% (11.1%-68-5%)	0.0065
Difficulty falling asleep	1.53 (1.07–2.18)	1.15 (0.79–1.68)	66.1% (2.3%–130.0%)	0.042
Difficulty falling back to sleep	1.60 (1.14–2.23)	1.35 (0.95–1.92)	35.6% (1.0%-70.2%)	0.044
Nocturnal awakenings	1.33 (0.99–1.79)	1.15 (0.86–1.54)	51.5% (-4.7% -107.7%)	0.072
Early Morning Awakening	1.75 (1.28–2.41)	1.51 (1.08–2.11)	26.6% (2.4%–50.7%)	0.031