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Original Article

# Longitudinal changes in insomnia status and incidence of physical, emotional, or mixed impairment in postmenopausal women participating in the Women's Health Initiative (WHI) study

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ABSTRACT

*Objectives/Background:* We assessed prevalence and correlates of insomnia; associations between changes in insomnia with incidence of physical, emotional, and mixed impairments (PI, EI, and MI, respectively); and age as a moderator in these relationships.
*Participants/Methods:* The Women's Health Initiative (WHI) clinical trial (CT) and observational study (OS) cohorts with 1- and 3-year follow-ups, respectively, were studied. Participants included 39,864 CT and 53,668 OS postmenopausal women free of PI or EI at baseline. Insomnia Rating Scale (IRS), with a cutoff score of ≥9 indicated insomnia. Normal–Normal, Abnormal–Abnormal, Normal–Abnormal, and Abnormal–Normal categories indicated change in insomnia over time. PI, EI, and MI were constructed using Short Form-36 (SF-36) Physical and Emotional subscales (cutoff ≤60) and the modified Center for Epidemiological Studies Depression scale (cutoff ≤0.06).
*Results:* Among 93,532 women, 24.5% had insomnia at baseline. The highest odds ratios (ORs) for impairments were found in the Normal–Abnormal and Abnormal–Abnormal categories. In the CT cohort, Normal–Abnormal category, ORs were 1.86 (95% CI = 1.57–2.20) for PI, 4.11 (95% CI = 3.59–4.72) for EI, and 6.37 (95% CI = 4.65–8.74) for MI. Respective ORs for the OS cohort were 1.70 (95% CI = 1.51–1.89), 3.80 (95% CI = 3.39–4.25), and 4.41 (95% CI = 3.56–5.46). Interactions between changes in insomnia and age showed distinct albeit nonsignificant patterns.
*Conclusions:* The results suggest that exposure to insomnia increases vulnerability to impairment. Future studies are needed to understand the directionality of these relationships.


## 1. Introduction

Gender differences in sleep disturbances have repeatedly demonstrated a greater frequency of sleep complaints in women than in men [1–3], which has often been attributed to hormonal changes, particularly during the midlife years [4–7]. Increasing age has also been associated with increased frequency of sleep disturbance; however, this relationship is considerably modified when screening for comorbidity [2,8] and depends on the specific definition provided for the assessment of sleep disturbance [1,9]. In a recent cross-sectional investigation of sleep disturbances across the lifespan ($n$ = > 155,000 participants of the Behavioral Risk Factor Surveillance System – BRFSS), a nonlinear, bimodal distribution emerged, with the highest rates of self-reported sleep disturbance found for young (ages 18–24) and midlife (ages 50–59) men and women [2]. Rates of sleep disturbance were lowest in the oldest age group, were significantly higher in women, and were associated with poor general health and depression. In a systematic review of the literature, symptoms of insomnia were shown to increase with age, whereas self-reported sleep dissatisfaction was unrelated to age [1].

Numerous cross-sectional and longitudinal population studies have investigated disturbed sleep, in both quality and quantity, in

*Abbreviations:* BMI, body mass index; CESD, Center for Epidemiological Studies Depression; CT, clinical trial; EI, emotionally impaired; EW, Emotional Well-Being; IRS, Insomnia Rating Scale; KoGES, Korean Genome and Epidemiology study; MI, mixed impairment; OS, observational study; PF, Physical Functioning; PI, physically impaired; QOL, quality of life; UI, unimpaired; WHI, Women's Health Initiative.

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association with a wide array of medical [10–14] and mental disturbances [14–16], but few have investigated the associations between sleep disturbance and physical and mental quality of life (QOL) and functioning in community-dwelling men and women [17]. As health-related QOL has been found to be an important predictor of healthy aging and cardiovascular morbidity [18,19], understanding the long-term dynamics between poor sleep, health, and QOL may be of interest for epidemiological and clinical purposes. Findings from a cross-sectional study of >4000 adults (ages 18–65) demonstrate that comorbid sleep disturbance with physical illness increases the likelihood of poor health-related QOL, compared to the presence of physical illness alone, even after adjusting for sociodemographic factors and mental and medical comorbidities [17]. In a cross-sectional analysis of women aged 32–58 in Finland, more severe physical and mental QOL conditions incurred higher risks for self-reported sleep problems [20]. Similar findings were reported in a sample of postmenopausal women in Australia [21].

Taken together, a growing body of evidence suggests that sleep disturbance may have adverse long-term effects on health and functioning. Sleep disturbance is more prevalent in women, and findings indicate that such effects may also be more pronounced in women. Yet studies using longitudinal data and powered by large population-based samples aimed to address the dynamics of sleep disturbance and physical and mental aspects of QOL in older women are currently lacking. Thus, the present investigation aims to enhance the empirical evidence regarding the longitudinal impact of insomnia on physical and mental health and functioning among postmenopausal women (aged 50+) participating in the Women's Health Initiative (WHI) clinical trial (CT) and observational studies (OS). The presence of insomnia symptoms (hereafter insomnia) in the WHI study was based on the frequency of insomnia-related symptoms during the past 4 weeks using previously validated Insomnia Rating Scale (IRS) instrument [22].

The study aims were to describe baseline prevalence and correlates of insomnia in otherwise physically and emotionally unimpaired women; to evaluate the association of 1- and 3-year changes in insomnia status with physical, emotional, or mixed impairment (PI, EI, and MI, respectively) incidence; and to assess age categories as the moderator in the relationship between changes in insomnia status and rates of impairment.

We expected to observe a relationship between changes in insomnia status and development of PI and EI. Specifically, we anticipated an increased risk of PI and/or EI among those who developed insomnia as compared to the healthy group. Moreover, we hypothesized that the risk of impairment in the persistent insomnia group would be similar to that in the incident insomnia group. Likewise, we expected that the risk of impairment in the healthy (i.e., non-insomnia) group would be comparable to that in the remissive insomnia group. Finally, we expected to observe an interaction between age categories and changes in insomnia status, so that an increased risk of impairment would be found in older incident and persistent insomnia participants compared to their younger counterparts.

## 2. Methods

### 2.1. Study population

The WHI is a study of postmenopausal women's health and risk factors for cancer, heart disease, and osteoporotic fractures. It was designed as a set of randomized controlled CTs and an OS. Details of the design, recruitment strategies, data collection methods, and baseline data are available elsewhere [23]. Briefly, women aged 50–79 were recruited for the WHI from 1993 to 1998 at 40 clinical centers in the USA, which yielded a diverse population of postmenopausal women, of whom 18% were from underrepresented racial and ethnic groups. Women were excluded for medical conditions with a predicted survival of three years or less, for conditions limiting adherence or retention (eg, alcohol or drug dependency and dementia), or for active participation in any other intervention study. The CTs ($N = 68,132$) included three overlapping components: the hormone therapy, the dietary modification, and the calcium and vitamin D trials. Women who were ineligible or unwilling to join the CTs were invited to join the OS, in addition to those who were specifically recruited for the OS ($N = 93,676$). The CT and OS women attended baseline and protocol-defined clinical visits. All WHI participants provided written informed consent, and institutional review board approval was obtained at each of the 40 WHI clinical centers and at the Clinical Coordinating Center at the Fred Hutchinson Cancer Research Center, Seattle, WA, USA. Analyses for this study were limited to the subset of CT and OS participants who were free of PI or EI at baseline and who had available IRS, RAND 36-Item (SF-36) [24] Health Survey Physical Functioning (PF) and Emotional Well-Being (EW) subscales, and the depression index based on six items for the Center for Epidemiological Studies Depression (CESD) scale and two items from the diagnostic interview schedule at the following measurement occasions: baseline (CT cohort; $N = 46,022$; OS cohort; $N = 62,579$), year 1 (CT cohort; $N = 39,864$), and year 3 (OS cohort; $N = 53,668$; see Fig. 1). Impairment was defined as scores ≤60 on each of the SF-36 subscales and, similarly, scores ≥0.06 on the modified CESD scale.

### 2.2. Measures

#### 2.2.1. Impairment

The outcomes of interest are four mutually exclusive groups representing normal impairment, PI, EI, or MI. The groups were constructed using SF-36 PF and EW subscales with a cut point of 60, indicating impairment. The cut point was selected as indicating low functioning in comparable-age cohorts [25]. In addition, the modified CESD scale scores were used to define EI with a cut point of 0.06 and higher, in accordance with Burnam's algorithm suggestive of depression [26]. Further details about these classifications are described below:

Unimpaired (UI) group: This group consisted of women who scored >60 on both the PF and EW subscales and <0.06 on the modified CESD scale.

Physically impaired (PI) group: This group comprised women who scored ≤60 on the PF, but >60 or <0.06 on the EW and the modified CESD, respectively.

Emotionally impaired (EI) group: This group included women who scored ≤60 or ≥0.06 on the EW and the modified CESD scales, respectively, and >60 on the PF scale.

Mixed impairment (MI) group: This group consisted of women who scored either ≤60 or ≥0.06 on the EW and the modified CESD scales, respectively, and also ≤60 on the PF scale.

The UI group was assigned as the reference category.

#### 2.2.2. Insomnia rating scale

The IRS scores were the primary exposure variables. The IRS consists of five items pertaining to quality of sleep, trouble falling asleep, waking up several times, waking up earlier than planned, and trouble getting back to sleep in the past four weeks [22]. The items are measured on a scale of 0–4, with higher scores representing more frequent or more severe symptoms. A final score, ranging from 0 to 20, is calculated by summing the scores for the five items. IRS measures were collected at baseline for all WHI participants and in year 1 for CT participants, and in year 3 in the OS cohort. Insomnia was defined using the IRS cut point of 9 [22]. This threshold has been widely used in previous studies investigating insomnia and health-related outcomes among WHI cohorts [27–29]. Categories

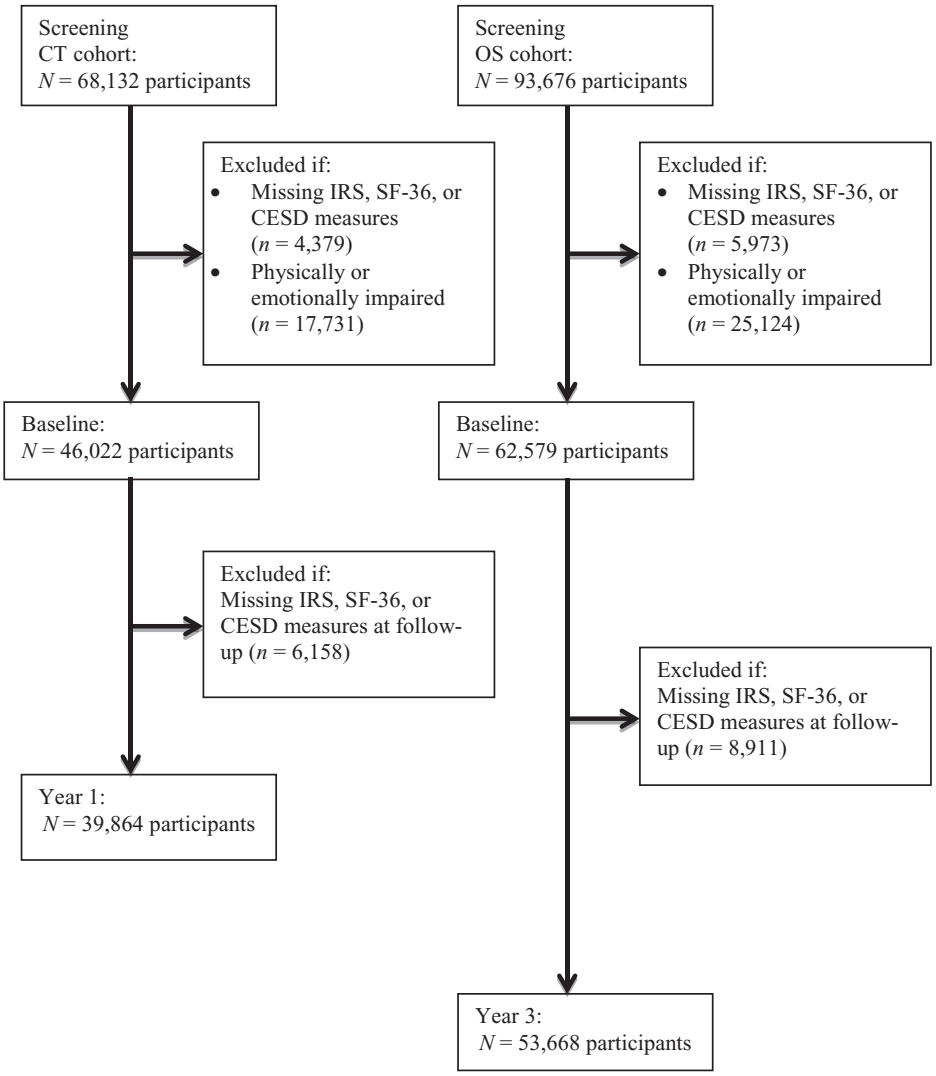


**Fig. 1.** Participants' flow chart. CT = clinical trial; OS = observational study; IRS = Insomnia Rating Scale; SF = Short Form; CESD = Center for Epidemiological Studies Depression scale.

of change were constructed based on insomnia statuses at baseline and follow-up (ie, year 1 for the CT, and year 3 for the OS cohorts, respectively). Based on the IRS scores at both time points, four mutually exclusive categories were created and labeled according to baseline and follow-up insomnia status (above/below a threshold of 9). Thus, the Normal–Normal and Abnormal–Abnormal groups, respectively, represent participants with below-threshold (no insomnia) and above-threshold (persistent insomnia) scores at both time points. The Normal–Abnormal (incident insomnia) category represents participants with below-threshold baseline scores and above-threshold follow-up scores; and the Abnormal–Normal (remissive insomnia) group represents participants with above-threshold scores at baseline and below-threshold scores at follow-up.

### 2.2.3. Covariates

Existing literature suggests that race/ethnicity, income, education level, living arrangement, chronic conditions, body mass index (BMI), sleep duration, hormone replacement therapy, and behavioral characteristics such as smoking or alcohol intake are all possible confounders of the relationship between sleep disturbances and functional outcomes. Comprehensive data on demographic, behavioral, health status, and other factors were collected using well-established self-reported measures at WHI baseline [30]. Smoking was a three-category variable: never smoker/past smoker/current smoker. Alcohol intake was a four-category variable: nondrinker (nondrinker and past drinker), mild drinker (<one drink per week), moderate drinker (<seven drinks per week), and heavy drinker (seven+ drinks per week). Coffee consumption was a six-category variable representing a respective number of regular cups of coffee per day. Chronic conditions included self-reported history of cardiovascular disease, stroke, or treated diabetes mellitus. BMI was objectively measured at baseline and calculated as weight in kilograms divided by height in meters squared and rounded up to the nearest tenth. Self-reports on sleep duration included the following categories indicating hours of sleep per night: ≤ 5, 6, 7, 8, and 9, and ≥10. Living arrangement was a binary variable indicating whether a participant lives alone. Hormone therapy was classified as either current or past/never user based on self-reported use of estrogen with or without progestin in the OS cohort, or as a treatment assignment into one of the hormone replacement therapy groups in the CT participants.

## 2.3. Statistical analysis

The analyses included three steps: 1) We described baseline characteristics by insomnia status (ie, insomnia vs. no insomnia).

Statistical significance was evaluated using analysis of variance for continuous variables and the Pearson's chi-squared test for categorical variables; 2) We examined baseline insomnia status and categories of change in insomnia status by incident impairment; 3) As the outcome comprised four nominal categories, the association of baseline insomnia status and categories of change with the patterns of impairment was examined using multinomial logistic regression. Multinomial logistic regression uses maximum likelihood to estimate the log odds of being in a given impairment category (Normal–Abnormal, Abnormal–Normal, and Abnormal–Abnormal) compared with the reference category (Normal–Normal), allowing for separate slope estimates [31]. The model adjusted for age was the first model to fit. In the partially adjusted model, we added indicators of race, income, education, hormone replacement therapy, alcohol use, smoking, coffee consumption, BMI, sleep duration, and whether a participant lives alone (see Supplementary Table S1). Finally, in the fully adjusted model, we also added indicators of chronic conditions. The interactions between categories of change in insomnia status and the age categories were explored by testing the significance of cross-product terms. The adjusted prediction of change categories and age by the impairment groups was computed and plotted using coefficients estimated from the fully adjusted multinomial model. In the second and third steps, we performed separate analyses for CT and OS cohorts. All *p*-values reported are for two-tailed tests. Complete-case analysis was implemented; only participants who provided complete data on sleep-related and functional measures were included for analysis. The statistical software STATA, version 11.2 (StataCorp, College Station, TX, USA), was used for the statistical analysis.

## 3. Results

Of the 93,530 women who met the inclusion criteria for this study, 22,866 (24.5%) had insomnia and 70,664 (75.5%) were free of insomnia, based on the IRS cutoff, at study baseline.

Correlates of the insomnia and non-insomnia status at the WHI study baseline in physically or emotionally unimpaired participants are shown in Table 1. There were significant differences at $p < 0.05$ across insomnia status groups for most variables, except for living alone, BMI categories, and diabetes. In general, those who had insomnia at baseline were older, more likely to be white, had lower income and education levels, tended to be past smokers, drank none or one cup of coffee per day, were more likely to consume seven+ alcoholic drinks per week, and had experienced cardiovascular disease or stroke. In addition, they had lower PF and EW scores compared to the non-insomniac group (87.2 vs. 89.6, $p < 0.001$) and (81.5 vs. 85.0, $p < 0.001$) for the PF and EW scores, respectively.

Cross-tabulation of the insomnia status categories by impairment group is presented in Table 2. The results demonstrate that the percentage of individuals reporting incident (ie, Normal–Abnormal) or persistent (ie, Abnormal–Abnormal) insomnia is relatively high in the MI group. The findings are consistent among CT and OS participants: 28.3% and 26.1% for incident and 26.71% and 32.9% for persistent insomnia in each cohort, respectively. Among UI participants, there was the highest percentage of women reporting consistently normal (68.7% and 66.4%) sleep status after one and three years of follow-up.

Table 3 shows adjusted odds ratios (ORs) for the insomnia categories. Consistently high ORs for the PI, EI, or MI categories versus the UI were found in those assigned to the Normal–Abnormal category as compared with the Normal–Normal category. For example, women in the 1-year follow-up cohort who were in the Normal–Abnormal category had about a twofold risk of being in the PI, a 4.1-fold risk of being in the EI, and a 6.4-fold risk of being in the MI categories, compared with their counterparts in the Normal–Normal and UI reference categories. Longer follow-up attenuated the associations; 3-year estimates were OR = 1.70 (95% CI = 1.51–1.89), OR = 3.80 (95% CI = 3.29–4.25), and OR = 4.41 (95% CI = 3.56–4.46) for the PI, EI, and MI groups, respectively.

Similarly, persistent 1- and 3-year insomnia status increased the likelihood of being in PI groups by factors of 1.90 (95% CI = 1.64–2.20) and 1.68 (95% CI = 1.50–1.87); in EI groups by factors of 3.66 (95% CI = 3.22–4.18) and 3.59 (95% CI = 3.21–4.03); and in MI groups

**Table 1**
Demographic data at baseline by insomnia status.

| Characteristic | Insomnia | Non-insomnia | *p* value |
|---|---|---|---|
| ***N* (%)** | 22,866 (24.5) | 70,664 (75.5) | |
| **CT, *n* (%)** | 9663 (24.2) | 30,201 (75.8) | |
| **OS, *n* (%)** | 13,203 (24.6) | 40,463 (75.4) | |
| **Age, years (SD)** | 63.5 (7.1) | 62.7 (7.0) | <0.001 |
| **White race, *n* (%)** | | | <0.001 |
| Yes | 20,361 (89.2) | 60,737 (86.1) | |
| No | 2463 (10.8) | 9779 (13.9) | |
| **Education, *n* (%)** | | | <0.001 |
| Some school | 7282 (32.1) | 18,920 (26.9) | |
| Some college | 8928 (39.3) | 27,980 (39.8) | |
| Some graduate | 6505 (28.6) | 23,330 (33.2) | |
| **Family income, *n* (%)** | | | <0.001 |
| < $20,000 | 2770 (12.6) | 7291 (10.7) | |
| $20,000 to <$50,000 | 9751 (44.4) | 29,183 (42.9) | |
| $50,000 or more | 9461 (43.0) | 31,623 (46.4) | |
| **Hormone replacement therapy, *n* (%)** | | | <0.001 |
| Yes | 9849 (44.2) | 31,750 (46.4) | |
| No | 12,426 (55.8) | 36,740 (53.6) | |
| **Live alone, *n* (%)** | | | 0.188 |
| Yes | 5272 (23.2) | 16,136 (22.9) | |
| No | 17,493 (76.8) | 54,231 (77.1) | |
| **Smoking behavior, *n* (%)** | | | <0.001 |
| Never smoked | 11,577 (51.1) | 36,711 (52.5) | |
| Past smoker | 9946 (43.9) | 29,095 (41.6) | |
| Current smoker | 1148 (5.1) | 4185 (6.0) | |
| **Alcohol intake, *n* (%)** | | | <0.001 |
| Nondrinker | 2093 (9.2) | 6861 (9.8) | |
| Past drinker | 3462 (15.2) | 10,781 (15.3) | |
| Less than 1 drink/week | 2707 (11.9) | 8585 (12.2) | |
| 1 or more drink/week | 4654 (20.5) | 14,820 (21.1) | |
| 1 to <7 drinks per week | 6458 (28.4) | 20,106 (28.6) | |
| 7 + drinks per week | 3365 (14.8) | 9135 (13.0) | |
| **Cups of coffee per day, *n* (%)** | | | <0.001 |
| 0 | 3429 (20.8) | 9353 (18.3) | |
| 1 | 3512 (21.3) | 10,717 (20.9) | |
| 2 | 4431 (26.9) | 13,904 (27.1) | |
| 3 | 2.697 (16.4) | 8859 (17.3) | |
| 4 | 1363 (8.3) | 4603 (9.0) | |
| 5 | 567 (3.4) | 1921 (3.8) | |
| 6 or more | 490 (3.0) | 1865 (3.4) | |
| **BMI category, *n* (%)** | | | 0.203 |
| Underweight | 197 (0.9) | 622 (0.9) | |
| Normal weight | 8766 (38.7) | 27,412 (39.1) | |
| Overweight | 8323 (36.7) | 25,143 (35.9) | |
| Obese | 5381 (23.7) | 16,917 (24.1) | |
| **Cardiovascular disease, *n* (%)** | | | <0.001 |
| Yes | 3669 (16.9) | 9404 (14.0) | |
| No | 18,037 (83.1) | 67,597 (86.0) | |
| **Stroke, *n* (%)** | | | < 0.001 |
| Yes | 206 (1.0) | 482 (0.7) | |
| No | 22,653 (99.0) | 70,163 (99.3) | |
| **Diabetes, *n* (%)** | | | 0.084 |
| Yes | 652 (2.9) | 1897 (2.7) | |
| No | 22,188 (97.2) | 68,726 (97.3) | |
| **Sleep duration, *n* (%)** | | | <0.001 |
| 5 or less hours | 3093 (13.5) | 2088 (2.9) | |
| 6 | 8649 (37.9) | 15,351 (21.7) | |
| 7 | 7750 (33.9) | 30,057 (42.6) | |
| 8 | 2938 (12.9) | 19,837 (28.1) | |
| 9 | 380 (1.7) | 3081 (4.4) | |
| 10 and more hours | 43 (0.2) | 217 (0.3) | |
| **SF-36 PF Subscale, mean (SD)** | 87.2 (10.4) | 89.6 (9.7) | <0.001 |
| **SF-36 EW Subscale, mean (SD)** | 81.5 (8.8) | 85.0 (8.4) | <0.001 |

*Note.* SF-36 = Short Form; PF = Physical Functioning; EW = Emotional Well-Being.

**Table 2**
Cross-tabulation of insomnia status categories by unimpaired (UI), physical impairment (PI), emotional impairment (EI), or mixed impairment (MI) groups among CT ($N = 43,212$) and OS ($N = 57,827$) WHI participants.

| Insomnia status categories, *n* (%) | UI group | PI group | EI group | MI group |
|---|---|---|---|---|
| **CT Cohort (1 year of follow-up)** | | | | |
| Normal–Normal | 23,645 (68.7) | 1302 (56.1) | 1117 (41.9) | 158 (35.8) |
| Normal–Abnormal | 2947 (8.6) | 324 (14.0) | 583 (21.9) | 125 (28.3) |
| Abnormal–Normal | 3434 (10.0) | 213 (9.2) | 236 (8.9) | 41 (9.3) |
| Abnormal–Abnormal | 4408 (12.8) | 484 (20.8) | 729 (27.4) | 118 (26.7) |
| **OS Cohort (3 years of follow-up)** | | | | |
| Normal–Normal | 29,458 (66.4) | 2642 (55.0) | 1387 (39.3) | 348 (37.3) |
| Normal–Abnormal | 4770 (10.7) | 758 (15.8) | 856 (24.3) | 244 (26.1) |
| Abnormal–Normal | 4213 (9.5) | 476 (9.9) | 302 (8.6) | 72 (7.7) |
| Abnormal–Abnormal | 5958 (13.4) | 930 (19.4) | 982 (27.8) | 270 (32.9) |

*Note.* Categories denote: consistently normal insomnia scores (Normal–Normal), incident insomnia (Normal–Abnormal), remissive insomnia (Abnormal–Normal), and persistent insomnia (Abnormal–Abnormal).

by staggering factors of 4.34 (95% CI = 3.12–6.02) and 3.69 (95% CI = 2.96–4.60) when comparing the estimates in the CT and OS cohorts, respectively. Finally, although remissive insomnia status (ie, Abnormal–Normal) overall had statistically significant effects on impairment rate, their magnitude was relatively modest and ranged from OR = 1.06 (95% CI = 0.87–1.29) when the PI outcome was modeled to OR = 2.05 (95% CI = 1.34–3.14) for the EI outcome among CT participants.

Although cross-product terms representing the interactions between categories of change in insomnia status and the age categories failed to reach statistical significance, distinct patterns were observed. Figs. 2 and 3 illustrate the estimated probabilities of a WHI study participant being in the UI, PI, EI, and MI groups as a function of age and insomnia categories when holding all other variables in the model at their means. The lines are maximum-likelihood-based predicted probabilities. For insomnia trajectories in both the 1- and 3-year follow-up cohorts, the probability of being in the PI groups increases in older age with a trend toward divergence between insomnia categories, whereas the EI models demonstrate a downward pattern with a trend toward convergence among the insomnia categories. Furthermore, differences were observed with regard to MI groups between CT and OS participants: the 3-year follow-up was associated with increased probabilities of MI in older ages versus relative stability in probabilities over a shorter (1-year) follow-up term.

## 4. Discussion

This study is the first to investigate short- and long-term trajectories of insomnia on PI, EI, and MI in a large cohort of initially non-impaired postmenopausal women. A prevalence of one out of four women had insomnia at baseline, similar to that found in a mixed cohort of Korean-community adults aged 65 and above [32]. Consistent with other studies, correlates of insomnia status included socioeconomic factors, health behaviors, and comorbidities [27]. Findings demonstrate that incident and persistent insomnia similarly entail considerably increased risks for all types of impairment, whereas resolved insomnia also incurs elevated risks, albeit to a lesser extent, when compared with no insomnia. These findings suggest that any exposure to insomnia increases vulnerability to impairment.

Risks for EI following all trajectories of change in insomnia status were higher than those for PI, whereas risks for MI were highest. These findings are supported in numerous population-based studies that have demonstrated robust associations between sleep disturbances and impaired emotional and physical status [2,20,22,24–33]. In a cross-sectional study, Grandner et al. (2012 [2]) reported that poor general health incurred a fivefold increase in risk for sleep disturbance, whereas moderate to severe depressed mood was associated with ORs of 13.0 and 16.0 in risk for sleep disturbance in women and men, respectively, in adjusted models. In a longitudinal investigation based on the Korean Genome and Epidemiology study (KoGES) of nondepressed adults at baseline, the course of depression over four time points was significantly more elevated in those with persistent insomnia than in those with a single insomnia episode or no insomnia [34]. In a subsequent study using the same database and following insomnia trajectories over three time points, persistent insomnia was best predicted by poor sleep quality, sleep-interfering behaviors, and mental impairment [35]. Another 2-year longitudinal investigation reported that baseline depression and four or more physical disorders were similarly associated with increased prevalence, incidence, and persistence rates of

**Table 3**
Odd ratios (ORs) and 95% confidence intervals (CIs) from a multinomial logistic regression estimating the effect of insomnia status categories on the likelihood of being in the physical impairment (PI), emotional impairment (EI), or mixed impairment (MI) groups versus the unimpaired (UI) group among CT ($N = 39,864$) and OS ($N = 53,666$) WHI participants.

| Insomnia status categories | PI group | | EI group | | MI group | |
|---|---|---|---|---|---|---|
| | Model[a] OR (95% CI) | Model[b] OR (95% CI) | Model[a] OR (95% CI) | Model[b] OR (95% CI) | Model[a] OR (95% CI) | Model[b] OR (95% CI) |
| **CT cohort (1 year of follow-up)** | | | | | | |
| Normal–Normal | [Reference] | [Reference] | [Reference] | [Reference] | [Reference] | [Reference] |
| Normal–Abnormal | 1.97 (1.74–2.25) *** | 1.86 (1.57–2.20) *** | 4.20 (3.77–4.68) *** | 4.11 (3.59–4.72) *** | 6.35 (5.00–8.05) *** | 6.37 (4.65–8.74) *** |
| Abnormal–Normal | 1.11 (0.96–1.29) | 1.06 (0.87–1.29) | 1.46 (1.26–1.63) *** | 1.39 (1.16–1.68) *** | 1.79 (1.26–2.52) *** | 2.05 (1.34–3.14) *** |
| Abnormal–Abnormal | 1.88 (1.68–2.10) *** | 1.90 (1.64–2.20) *** | 3.62 (3.28–3.99) *** | 3.66 (3.22–4.18) *** | 4.00 (3.15–5.10) *** | 4.34 (3.12–6.02) *** |
| **OS cohort (3 years of follow-up)** | | | | | | |
| Normal–Normal | [Reference] | [Reference] | [Reference] | [Reference] | [Reference] | [Reference] |
| Normal–Abnormal | 1.76 (1.61–1.92) *** | 1.70 (1.51–1.89) *** | 3.82 (3.49–4.18) *** | 3.80 (3.39–4.25) *** | 4.32 (3.66–5.10) *** | 4.41 (3.56–4.46) *** |
| Abnormal–Normal | 1.21 (1.09–1.35) *** | 1.24 (1.09–1.42) *** | 1.54 (1.35–1.75) *** | 1.49 (1.27–1.75) *** | 1.42 (1.10–1.84) ** | 1.44 (1.04–1.99) * |
| Abnormal–Abnormal | 1.64 (1.51–1.77) *** | 1.68 (1.50–1.87) *** | 3.58 (3.29–3.91) *** | 3.59 (3.21–4.03) *** | 3.72 (3.16–4.37) *** | 3.69 (2.96–4.60) *** |

*Note.* Results are from multinomial logistic regression. Categories denote: consistently normal insomnia scores (Normal–Normal); incident insomnia (Normal–Abnormal), remissive insomnia (Abnormal–Normal), and persistent insomnia (Abnormal–Abnormal).

[a] adjusted for age.

[b] adjusted for age, race, income, education, hormone replacement therapy, selected chronic conditions, alcohol use, smoking, coffee consumption, BMI, sleep duration, and whether a participant lives alone.

ORs >1 denote risk of impairment.

*** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

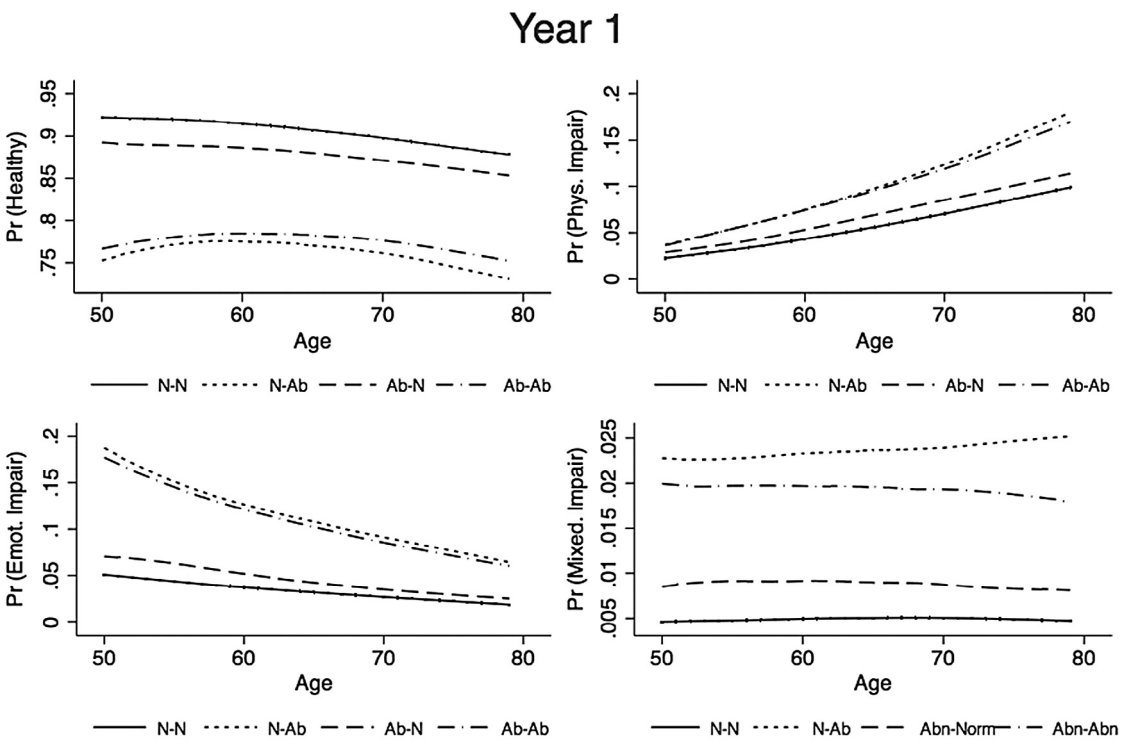


**Fig. 2.** Estimated adjusted probabilities for unimpaired (UI), physical impairment (PI), emotional impairment (EI), or mixed impairment (MI) groups in 1 year of follow-up by insomnia status categories and age among clinical trial (CT) Women's Health Initiative (WHI) participants ($N = 39{,}864$). Categories denote: consistently normal insomnia scores (Normal–Normal; N–N), incident insomnia (Normal–Abnormal; N–Ab), remissive insomnia (Abnormal–Normal; Ab–N), and persistent insomnia (Abnormal–Abnormal; Ab–Ab). Results are from multinomial logistic regression adjusted for race, income, education, hormone replacement therapy, selected chronic conditions, alcohol use, smoking, coffee consumption, body mass index (BMI), sleep duration, and whether a participant lives alone. Lines indicate likelihood-ratio-based estimates.

insomnia, and, conversely, baseline insomnia was associated with increased rates of depression and physical disorders [32].

For both of the WHI cohorts included, no significant interactions were found for age, lending strong support to previous investigations in which it was concluded that sleep disturbances are not a function of age per se [2,8,36,37]. However, distinct patterns were observed when modeling insomnia trajectories as a function of age for each of the impairment categories separately. Specifically, we show here for the first time that PI and EI outcomes demonstrated opposite longitudinal dynamics, so that with age, exposure to insomnia may not only subtly increase the risk of PI but also decrease the risk of EI. These patterns were highly consistent in both cohorts. Our findings demonstrate that increasing age may be considered a weak correlate of insomnia that should be interpreted in the context of PI and mental impairment separately. In an earlier study on risk factors in the incidence of insomnia, although depressed mood emerged as a major risk factor, poor physical health was the more prevalent risk factor in a sample of older adults [37]. Pending further investigation, one cautious interpretation is that insomnia is more closely related to mental health in younger adults and to physical health in older adults. These postulated associations may be moderated by gender.

Furthermore, insomnia trajectory groups clustered into pairs, with persistent and incident insomnia grouped into one pair, and no insomnia and resolved insomnia grouped into another. This clustering was most prominent in the EI and MI outcomes as well as in the healthy-outcome categories. Finally, the probability of being healthy at both follow-ups was lower with advanced age for all insomnia trajectories, yet this probability was consistently lower in the incident and persistent insomnia categories. To the best of our knowledge, these dynamics have not been described previously.

Short- and long-term follow-ups were highly similar, providing added validity to our findings. Increased risks of impairments were slightly attenuated at the longer (3-year) follow-up, particularly for the incident insomnia group. Pending further research, this may signify that, over time, adjustment to insomnia may somewhat reduce the risks for impairment.

### 4.1. Strengths and limitations

This study has a number of limitations. First, the concurrent association between changes in insomnia status and incident impairment precludes causality, as it is possible that women who experienced incident EI and/or PI also had a worsening in their insomnia symptoms. However, regardless of the directionality of the effects, the strengths of the observed associations have epidemiological and clinical merits and suggest areas for targeted intervention. Second, older women with low levels of physical and emotional functioning were less likely than women with higher levels of functioning to participate in follow-up visits. Loss to follow-up may result in underestimation of the proportion of women at risk of being in impairment groups. However, rather than determining the prevalence of impairments, the aim of this analysis was to describe the interplay between sleep disturbances and functioning over time, based on the conceptualized model. Third, diagnosis of insomnia in this study was based on the frequency of sleep problems during the past four weeks. Although these criteria are different from the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) criteria and did not explicitly address the duration and interference with daily functioning of insomnia symptoms, the WHI IRS scale was previously validated and used in other epidemiological studies [22,27–29]. Finally, although other factors such as cognitive status, medication regimen, or personality traits may have had

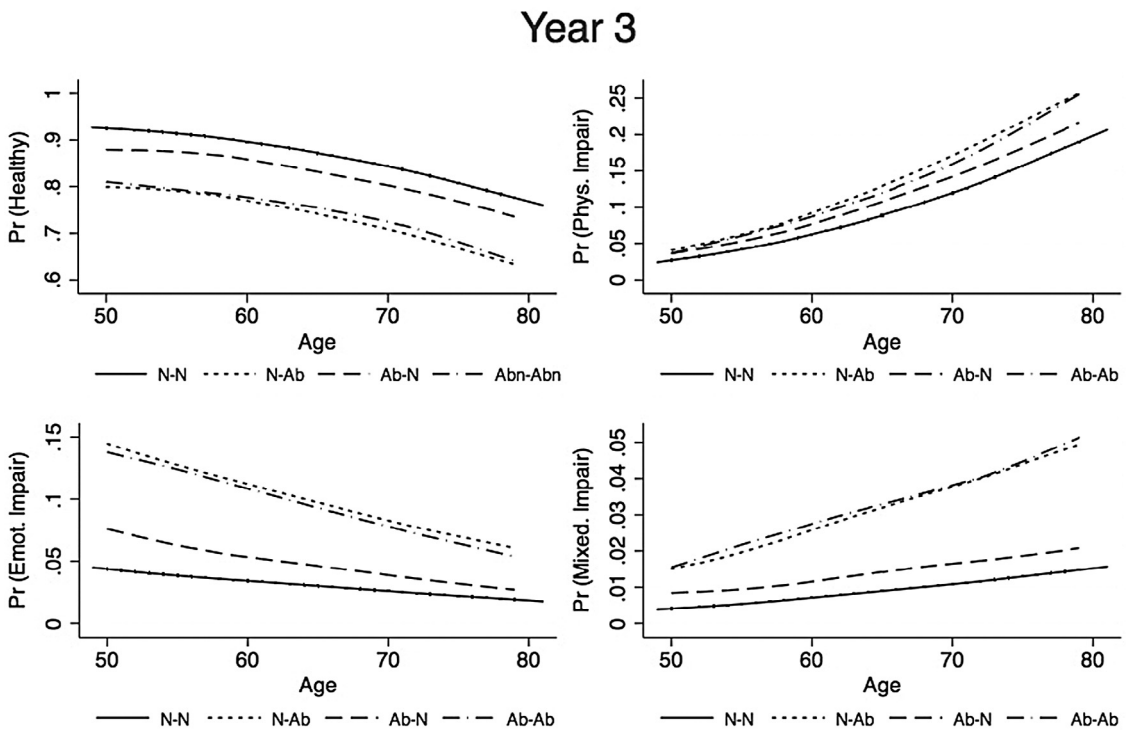


**Fig. 3.** Estimated adjusted probabilities for unimpaired (UI), physical impairment (PI), emotional impairment (EI), or mixed impairment (MI) groups in 3 years of follow-up by insomnia status categories and age among observational study (OS) Women's Health Initiative (WHI) participants ($N = 53,666$). Categories denote: consistently normal insomnia scores (Normal–Normal; N–N), incident insomnia (Normal–Abnormal; N–Ab), remissive insomnia (Abnormal–Normal; Ab–N), and persistent insomnia (Abnormal–Abnormal; Ab–Ab). Results are from multinomial logistic regression adjusted for race, income, education, hormone replacement therapy, selected chronic conditions, alcohol use, smoking, coffee consumption, body mass index (BMI), sleep duration, and whether a participant lives alone. Lines indicate likelihood-ratio-based estimates.

an effect on the relationships examined, the extensive list of sociodemographic, medical, and lifestyle adjustment variables included, the large sample size of more than 93,000 community-dwelling women, and the two separate cohorts with different lengths of follow-up reinforce the validity of the findings.

## 5. Conclusions

In summary, these results add to a growing literature on the negative effects of insomnia in postmenopausal and older women, and they suggest that any exposure to insomnia increases vulnerability to impairment. While EI may be more strongly associated with insomnia than PI, with advanced age, associations with PI may become more pronounced. Future prospective studies are needed to better understand the short- and long-term dynamics of trajectories of change in insomnia status and patterns of functional impairment in older age.

## Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.11.008.

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## Appendix: Supplementary material

Supplementary data to this article can be found online at doi:10.1016/j.sleep.2014.11.008.

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