**Longitudinal associations between time-varying insomnia symptoms and all-cause healthcare services utilization among middle-aged and older adults in the US**

Online Supplementary Materials

***Supplementary* Figure 1**. A flowchart displaying the study’s inclusion/exclusion criteria.

***Supplementary* Figure 2.** A Schematic diagram depicting the study design, temporal sequence of events, and the associations between time-varying primary exposure (insomnia symptoms), time-dependent variables, and the outcomes (healthcare services utilization; overnight hospital stays, nursing home stays, and home healthcare services) at each study wave.

***Supplementary* Methods 1.** The marginal structural model (MSM) formula and estimation of the weights.

***Supplementary* Methods 2.** Sensitivity Analyses.

***Supplementary* Results 1.** Longitudinal associations between the time-varying number and type of insomnia symptoms and overnight hospital stays, nursing home stays, and home healthcare services, employing untruncated MSM weights.

***Supplementary* Results 2.** Longitudinal associations between the time-varying number and type of insomnia symptoms and overnight hospital stays, nursing home stays, and home healthcare services, employing truncated MSM weights at 5th and 95th percentiles.

***Supplementary* Results 3.** Longitudinal associations between the time-varying number and type of insomnia symptoms and overnight hospital stays, nursing home stays, and home healthcare services after excluding the effects of nonrestorative sleep symptom.

***Supplementary* Results 4.** Crude and adjusted associations between the time-varying number and type of insomnia symptoms and overnight hospital stays, nursing home stays, and home healthcare services using traditional models of analysis and without implementing the MSM weights.

***Supplementary* References.**

Excluded:

The Health and Retirement Study (HRS) respondents in 2002 (n= 18,165)

HRS respondents aged ≥50 years (n= 17,759)

Respondents aged <50 years (n= 406)

HRS self-respondents, aged ≥50 years at baseline (2002)

 (n= 13,666)

Respondents with nonpositive survey weights (n= 498)

Final analytical sample (n= 13,168). The HRS self-respondents, aged ≥50 years, who were present in the 2002 survey wave (baseline).

Proxy HRS respondents in 2002, 2004, 2006, 2008, 2010, 2012, 2014, and 2016 HRS waves (n= 4,093)

***Supplementary* Figure 1**. A flowchart displaying the study’s inclusion/exclusion criteria.

|  |  |
| --- | --- |
|  | **Follow–Up Year** |
|  | 2002 | 2004 | 2006 | 2008 | 2010 | 2012 | 2014 | 2016 | 2018 |
| **Healthcare Services Utilization**  | BaselineTime–invariant variables |   |   |   |   |   |   |  |  |
| **Insomnia Symptoms & Time–varying Covariates** |   |   |   |   |   |   |   |  |  |
|  |  |  |  |  |  |  |   |  |  |
|  |   | Wave A |  |  |  |  |  |  |  |
|  |   | Wave B |  |  |  |  |  |  |  |
|  |   | Wave C |  |  |  |  |  |  |  |
|  |   | Wave D |  |  |  |  |  |  |  |
|  |   | Wave E |  |  |  |  |  |  |  |
|  |   | Wave F |  |  |  |  |  |  |  |
|  |  | Wave G |  |  |  |  |  |  |  |
|  |  | Wave H |  |  |  |  |  |  |  |

***Supplementary* Figure 2.** A Schematic diagram depicting the study design, temporal sequence of events, and the associations between time-varying primary exposure (insomnia symptoms), time-dependent variables, and the outcomes (healthcare services utilization; overnight hospital stays, nursing home stays, and home healthcare services) at each study wave.

***Supplementary* Methods 1.** The marginal structural model (MSM) formula and estimation of the weights.

The stabilized inverse probability of treatment weights (IPTWs) were calculated as follows 1–3:

$$SW^{E}\left(t\right)=\prod\_{k=0}^{t}\frac{Pr\{A(k)|\overbar{A}\left(k-1\right),V\}}{Pr\{A(k)|\overbar{A}\left(k-1\right),\overbar{L}(k)\}}$$

In this equation, *Pr(\*)* stands for the conditional probability function, $A(k)$ represents the time-varying treatment (exposure) at time *k,* $\overbar{A}\left(k-1\right)$ represents the treatment history prior to time *k,* $V$ represents a vector of baseline, time-invariant variables.$ \overbar{L}(k)$ represents an array of time-varying covariates through time *k* that can be potential mediators and confounders. $\overbar{L}(k)$ also incorporates ($V$) that represents time-invariant variables. The equation's denominator is the probability a subject is receiving his or her observed treatment (exposure) at time k, given prior treatment (exposure) history, time-varying covariates, and baseline time-invariant variables.The numerator is the probability a subject is receiving the observed treatment (exposure) at time k, given prior treatment history, and only baseline, time-invariant, covariates ($V$). Substituting the numerator with (1), the formula represents a standard IPTW. The numerator part is added to “stabilize” the standard IPTWs as they tend to be highly variable. Thus, adding the numerator reduces variability in the weights and increases precision.

As illustrated in the equation, to calculate the IPTWs in the current study, two pooled polynomial logistic regressions (the numerator and denominator models) were fit to output the predicted probability of the number of insomnia symptoms, “no symptoms, one, two, three, or four symptoms,” on a cumulative scale for each respondent and at each study wave. The numerator model was the predicted probability of the number of insomnia symptoms conditional on prior history of experienced insomnia symptoms and only the time-invariant, baseline characteristics for each respondent at each study wave. The denominator models the predicted probability of the number of insomnia symptoms, conditional on prior history of experienced insomnia symptoms, time-invariant, and time-varying variables, for each respondent and at each study wave. The numerator's predicted probabilities were then divided by the predicted probabilities of the denominator model to generate stabilized IPTWs to reduce variability in the weights and thus improve precision in the final outcomes.4

The stabilized IPCWs were calculated similar to IPTWs, except that pooled binary logistic regressions were fit to output the probability of respondents not being censored before the end of follow-up:

$$SW^{C}(t)=\prod\_{k=0}^{t}\frac{Pr\{C(k)|\overbar{C}\left(k-1\right),V\}}{Pr\{C(k)|\overbar{C}\left(k-1\right),\overbar{L}(k)\}}$$

Final total stabilized MSM weights were derived from multiplying stabilized IPTWs by stabilized IPCWs. The final weights represent a “pseudo-population” with all confounding removed as it appropriately incorporated both adjustments for time-dependent confounding and censoring,4 and made the design to obtain results which resemble that of a randomized controlled trial. The final MSM weights were truncated on both ends of the weight distribution at the 1st and 99th percentiles to have a mean weight (±standard deviation [SD]) of 1.00 ± 0.29 with a range of 0.64 to 2.54). MSM weights that deviate substantially from 1.0 indicate non-positivity or misspecification of the model.4 All regression models of the MSM weight estimation were fit using the SAS SURVEYLOGISTIC procedure to account for the complex sampling design features of the HRS, and to incorporate the original survey weights and the sample’s strata and clustering information.

Total stabilized MSM weights:

$$SW^{Total}\left(t\right)=SW^{E}\left(t\right)\*SW^{C}\left(t\right)$$

***Supplementary* Methods 2.** Sensitivity Analyses.

The validity of final MSM weights and the robustness of the findings were assessed by performing several sensitivity analyses. First, different combinations of the time-invariant “baseline-only,” and time-varying covariates were considered and examined during estimations of the MSM weights. These variables were alternatively and sequentially added to or dropped from the models to evaluate their effects on the variability of the final MSM weights. These steps also incorporated replacing time-varying age variable with a categorical term, and BMI, comorbid medical conditions, CES-D score, cognition score, ADL, and ADL limitations variables with their linear, quadratic, or three-knot spline terms, as well as adding meaningful interaction terms between the time-varying variables.

Second, we further truncated the final selected weights at the 5st and 95th percentiles and compared the final products using untruncated weights (mean=1.05; SD=0.36; minimum=0.224; maximum=13.98), weights truncated at 1st and 99th percentiles (our selected MSM weights, mean=1.00; SD=0.29; minimum=0.64; maximum=2.54), and weights truncated at 5th and 95th percentiles (mean=0.99; SD=0.20; minimum=0.77; maximum=1.56) to evaluate the bias-variance tradeoff in the final results.4 The direct effect of weight truncation is a reduction in the instability of the weights and an increase in precision in model outcomes; however, with further truncation the probability of introducing bias to the estimated weights increases.4 Third, since information on three out of the four insomnia symptoms were not collected during the 2008 and 2012 survey waves, we completely dropped the observations representing those two waves from the pooled data and restricted the analyses to the remaining waves of data. Finally, since the fourth insomnia symptom in our study, nonrestorative sleep, is believed to have different functional and epidemiological correlates than other three insomnia symptoms and because it is considered as a broad complaint of poor sleep,5–7 we dropped it from the MSM weight estimation and from the analyses of final results. Then, the abovementioned steps were repeated for the three other symptoms and their associations with the three measures of healthcare services utilization (i.e., overnight hospital stay, nursing home stay, and home healthcare services) were examined at follow-up.

***Supplementary* Results 1.** Longitudinal associations between the time-varying number and type of insomnia symptoms and overnight hospital stays, nursing home stays, and home healthcare services, employing untruncated MSM weights.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Overnight hospital stays | Nursing home stays | Home healthcare services |
|   | Adjusted OR (95% CI)† | *P* | Adjusted OR (95% CI)† | *P* | Adjusted OR (95% CI)† | *P* |
| Number of insomnia symptoms (ref: no symptoms) |  |  |  |  |  |  |
| One | 1.24 (1.19–1.30) | <.001 | 1.19 (1.07–1.32) | <.001 | 1.29 (1.20–1.38) | <.001 |
| Two | 1.38 (1.30–1.48) | <.001 | 1.27 (1.10–1.46) | <.001 | 1.50 (1.36–1.65) | <.001 |
| Three | 1.62 (1.48–1.77)  | <.001 | 1.39 (1.16–1.67) | <.001 | 1.72 (1.51–1.95) | <.001 |
| Four | 1.77 (1.51–2.08)  | <.001 | 1.49 (1.11–2.00) | .008 | 1.66 (1.35–2.04) | <.001 |
| Individual insomnia symptoms |  |  |  |  |  |  |
| Difficulty initiating sleep (ref: no) | 1.24 (1.16–1.32) | <.001 | 1.20 (1.05–1.37) | .01 | 1.24 (1.13–1.37) | <.001 |
| Difficulty maintaining sleep (ref: no) | 1.17 (1.12–1.23) | <.001 | 1.14 (1.03–1.27) | .01 | 1.17 (1.09–1.26) | <.001 |
| Early-morning awakenings (ref: no) | 1.07 (1.00–1.14) | .05 | 0.90 (0.78–1.03) | .12 | 1.06 (0.96–1.16) | .25 |
| Nonrestorative sleep (ref: no) | 1.25 (1.17–1.33) | <.001 | 1.30 (1.16–1.47) | <.001 | 1.33 (1.22–1.45) | <.001 |
| *Abbreviations*: CI, Confidence Interval; OR, Odds Ratio; MSM, Marginal Structural Model; ref, reference. |  |
| †Stabilized MSM weights were applied. The models incorporated a general specification for the main effect of time and were adjusted for all time-invariant “baseline-only” respondent characteristics (sex, race and ethnicity, level of education, marital status, family poverty threshold, and census region). |

***Supplementary* Results 2.** Longitudinal associations between the time-varying number and type of insomnia symptoms and overnight hospital stays, nursing home stays, and home healthcare services, employing truncated MSM weights at 5th and 95th percentiles.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Overnight hospital stays | Nursing home stays | Home healthcare services |
|   | Adjusted OR (95% CI)† | *P* | Adjusted OR (95% CI)† | *P* | Adjusted OR (95% CI)† | *P* |
| Number of insomnia symptoms (ref: no symptoms) |  |  |  |  |  |  |
| One | 1.26 (1.21–1.32) | <.001 | 1.23 (1.12–1.35) | <.001 | 1.34 (1.25–1.43) | <.001 |
| Two | 1.42 (1.33–1.51) | <.001 | 1.35 (1.18–1.54) | <.001 | 1.57 (1.43–1.72) | <.001 |
| Three | 1.65 (1.52–1.80) | <.001 | 1.44 (1.21–1.72) | <.001 | 1.75 (1.55–1.98) | <.001 |
| Four | 1.90 (1.63–2.19) | <.001 | 1.57 (1.20–2.05) | <.001 | 1.76 (1.44–2.14) | <.001 |
| Individual insomnia symptoms |  |  |  |  |  |  |
| Difficulty initiating sleep (ref: no) | 1.24 (1.17–1.32) | <.001 | 1.23 (1.08–1.40) | .002 | 1.24 (1.13–1.36) | <.001 |
| Difficulty maintaining sleep (ref: no) | 1.19 (1.13–1.24) | <.001 | 1.16 (1.05–1.28) | .003 | 1.20 (1.12–1.29) | <.001 |
| Early-morning awakenings (ref: no) | 1.08 (1.01–1.15) | .03 | 0.91 (0.80–1.04) | .17 | 1.06 (0.97–1.17) | .19 |
| Nonrestorative sleep (ref: no) | 1.27 (1.19–1.34) | <.001 | 1.33 (1.18–1.49) | <.001 | 1.36 (1.25–1.48) | <.001 |
| *Abbreviations*: CI, Confidence Interval; OR, Odds Ratio; MSM, Marginal Structural Model; ref, reference. |  |
| †Stabilized MSM weight were applied. The models incorporated a general specification for the main effect of time and were adjusted for all time-invariant “baseline-only” respondent characteristics (sex, race and ethnicity, level of education, marital status, family poverty threshold, and census region). |

***Supplementary* Results 3.** Longitudinal associations between the time-varying number and type of insomnia symptoms and overnight hospital stays, nursing home stays, and home healthcare services after excluding the effects of nonrestorative sleep symptom.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Overnight hospital stays | Nursing home stays | Home healthcare services |
|   | Adjusted OR (95% CI)† | *P* | Adjusted OR (95% CI)† | *P* | Adjusted OR (95% CI)† | *P* |
| Number of insomnia symptoms (ref: No symptoms) |  |  |  |  |  |  |
| One | 1.26 (1.20–1.32) | <.001 | 1.17 (1.05–1.30) | .004 | 1.29 (1.20–1.39) | <.001 |
| Two | 1.40 (1.30–1.50) | <.001 | 1.29 (1.11–1.50) | .001 | 1.46 (1.31–1.62) | <.001 |
| Three | 1.67 (1.51–1.85) | <.001 | 1.35 (1.10–1.64) | .004 | 1.62 (1.40–1.87) | <.001 |
| Individual insomnia symptoms |  |  |  |  |  |  |
| Difficulty initiating sleep (ref: no) | 1.30 (1.22–1.39) | <.001 | 1.30 (1.13–1.49) | <.001 | 1.32 (1.20–1.45) | <.001 |
| Difficulty maintaining sleep (ref: no) | 1.19 (1.13–1.25) | <.001 | 1.17 (1.05–1.30) | .004 | 1.20 (1.11–1.29) | <.001 |
| Early-morning awakenings (ref: no) | 1.10 (1.03–1.18) | .003 | 0.93 (0.81–1.07) | .30 | 1.09 (0.99–1.21) | .072 |
| *Abbreviations*: CI, Confidence Interval; OR, Odds Ratio; MSM, Marginal Structural Model; ref, reference. |  |
| †Stabilized MSM weight were applied. The models incorporated a general specification for the main effect of time and were adjusted for all time-invariant “baseline-only” respondent characteristics (sex, race and ethnicity, level of education, marital status, family poverty threshold, and census region). |

***Supplementary* Results 4.** Crude and adjusted associations between the time-varying number and type of insomnia symptoms and overnight hospital stays, nursing home stays, and home healthcare services using traditional models of analysis and without implementing the MSM weights.

|  |  |
| --- | --- |
|  | Overnight hospital stays |
|   | Crude OR (95% CI) | *P* | Adjusted OR (95% CI)† | *P* |
| Number of insomnia symptoms (ref: no symptoms) |  |  |  |  |
| One | 1.31 (1.25–1.38) | <.001 | 1.08 (1.03–1.14) | .002 |
| Two | 1.52 (1.41–1.64) | <.001 | 1.10 (1.02–1.19) | .01 |
| Three | 1.87 (1.69–2.06) | <.001 | 1.21 (1.09–1.34) | <.001 |
| Four | 2.16 (1.84–2.55) | <.001 | 1.24 (1.05–1.47) | .012 |
| Individual insomnia symptoms |  |  |  |  |
| Difficulty initiating sleep (ref: no) | 1.52 (1.42–1.62) | <.001 | 1.04 (0.97–1.12) | .25 |
| Difficulty maintaining sleep (ref: no) | 1.39 (1.32–1.46) | <.001 | 1.08 (1.02–1.14) | .006 |
| Early-morning awakenings (ref: no) | 1.44 (1.35–1.54) | <.001 | 1.05 (0.97–1.13) | .22 |
| Nonrestorative sleep (ref: no) | 1.47 (1.37–1.57) | <.001 | 1.05 (0.98–1.13) | .14 |
|  | Nursing home stays |
| Number of insomnia symptoms (ref: no symptoms) |  |  |  |  |
| One | 1.30 (1.17–1.44) | <.001 | 0.93 (0.83–1.04) | .2 |
| Two | 1.59 (1.37–1.84) | <.001 | 0.93 (0.79–1.09) | .37 |
| Three | 1.75 (1.44–2.12) | <.001 | 0.85 (0.68–1.05) | .14 |
| Four | 2.02 (1.51–2.68) | <.001 | 0.84 (0.62–1.14) | .26 |
| Individual insomnia symptoms |  |  |  |  |
| Difficulty initiating sleep (ref: no) | 1.52 (1.34–1.72) | <.001 | 0.93 (0.80–1.07) | .31 |
| Difficulty maintaining sleep (ref: no) | 1.40 (1.27–1.55) | <.001 | 1.04 (0.93–1.16) | .48 |
| Early-morning awakenings (ref: no) | 1.29 (1.13–1.47) | <.001 | 0.83 (0.72–0.97) | .02 |
| Nonrestorative sleep (ref: no) | 1.51 (1.33–1.72) | <.001 | 1.03 (0.89–1.18) | .72 |
|  | Home healthcare services |
| Number of insomnia symptoms (ref: no symptoms) |  |  |  |  |
| One | 1.37 (1.27–1.48) | <.001 | 1.06 (0.98–1.14) | .17 |
| Two | 1.75 (1.57–1.95) | <.001 | 1.11 (0.99–1.25) | .067 |
| Three | 1.97 (1.72–2.25) | <.001 | 1.07 (0.92–1.23) | .39 |
| Four | 2.05 (1.61–2.60) | <.001 | 0.95 (0.74–1.23) | .71 |
| Individual insomnia symptoms |  |  |  |  |
| Difficulty initiating sleep (ref: no) | 1.62 (1.48–1.78) | <.001 | 1.00 (0.90–1.11) | .98 |
| Difficulty maintaining sleep (ref: no) | 1.40 (1.30–1.50)  | <.001 | 1.05 (0.97–1.13) | .25 |
| Early-morning awakenings (ref: no) | 1.48 (1.34–1.64)  | <.001 | 0.97 (0.87–1.09) | .60 |
| Nonrestorative sleep (ref: no) | 1.60 (1.46–1.76) | <.001 | 1.07 (0.97–1.18) | .19 |
| *Abbreviations*: CI, Confidence Interval; OR, Odds Ratio; ref, reference group. |
| †Adjusted for all time-invariant and time-varying respondent characteristics. |  |

***Supplementary* References**

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