



ORIGINAL ARTICLE

Untreated insomnia increases all-cause health care utilization and costs among Medicare beneficiaries

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Abstract

Study Objectives: To examine the impact of untreated insomnia on health care utilization (HCU) among a nationally representative sample of Medicare beneficiaries.

Methods: Our data source was a random 5% sample of Medicare administrative data for years 2006–2013. Insomnia was operationalized as the presence of at least one claim containing an insomnia-related diagnosis in any given year based on International Classification of Disease, Version 9, Clinical Modification codes or at least one prescription fill for an insomnia-related medication in Part D prescription drug files in each year. We compared HCU in the year prior to insomnia diagnosis to HCU among to non-sleep disordered controls during the same period.

Results: A total of 151 668 beneficiaries were found to have insomnia. Compared to controls ($n = 333\,038$), beneficiaries with insomnia had higher rates of HCU across all point of service locations. Rates of HCU were highest for inpatient care (rate ratio [RR] 1.61; 95% confidence interval [CI] 1.59, 1.64) and lowest for prescription fills (RR 1.17; 95% CI 1.16, 1.17). Similarly, compared to controls, beneficiaries with insomnia demonstrated \$63,607 (95% CI \$60,532, \$66,685) higher all-cause costs, which were driven primarily by inpatient care (\$60,900; 95% CI \$56,609, \$65,191). Emergency department (\$1,492; 95% CI \$1,387, \$1,596) and prescription costs (\$486; 95% CI \$454, \$518) were also elevated among cases relative to controls.

Conclusions: In this randomly selected and nationally representative sample of older Medicare beneficiaries and compared to non-sleep disordered controls, individuals with untreated insomnia demonstrated increased HCU and costs across all points of service.

Statement of Significance

Although the health-related consequences of insomnia are well-documented, relatively less is known about the economic consequences of the disorder, particularly among older adults. This population-level study utilized a randomly selected, nationally representative 5% sample of Medicare administrative claims data for years 2006–2013. Compared to non-sleep disordered controls, beneficiaries with insomnia demonstrated increased HCU across all categories. This study adds to the growing body of literature documenting the substantial economic costs of insomnia among older adults. Future studies should evaluate the potential economic benefit from treating insomnia in this population.

Key words: sleep; insomnia; health care utilization; health economics; costs; Medicare; older adults

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Introduction

Sleep quality worsens with age, and half of older adults report sleep complaints [1–4]. Among this population, the prevalence of insomnia disorder, defined as difficulty initiating or maintaining sleep with associated daytime impairment, ranges from 25% to 40% [1]. By contrast, prevalence estimates for the general population range from 9% to 12% [5]. Further, in the United States, the prevalence of insomnia among older adults appears to be increasing [3, 6, 7]. Among Medicare beneficiaries in particular, the prevalence of diagnosed insomnia increased by over 150% between 2006–2013 [8]. Yet despite well-documented associations with adverse health consequences including depression [9–11], pain [9, 12], cognitive decline [13, 14], fall risk [15, 16], pulmonary and cardiovascular disease [17–20], and worsened health-related quality of life [12, 21], insomnia remains under-recognized and undertreated, especially among older adults [22]. One possible barrier to more widespread awareness and treatment is a lack of awareness of the economic costs of the disorder [22, 23]. In light of the aging US population, such insight could provide valuable guidance to payers, policy-makers, and health systems leaders seeking to allocate scarce resources and manage population health policy in the future [22–24].

Several studies have evaluated the economic impact of insomnia among older adults [2, 23, 25, 26]. In a seminal study, Ozminkowski and colleagues analyzed data from a large, self-insured employer database and found that among older adults, 6-month direct medical expenditures were \$1143 (in 2007 USD) higher among individuals with insomnia ($n = 75\,558$), relative to matched non-insomnia controls [25]. Kaufmann and colleagues found that among adults age >55 years in the Health and Retirement Study and after controlling for demographic variables, self-reported insomnia symptoms were associated with increased risk of hospitalizations, use of home health care services, nursing home placement, and a composite health care utilization (HCU) measure reflecting any of these three outcomes [2]. In a study of patients with comorbid insomnia and depression, Asche and colleagues found direct medical costs to be \$1007 (in 2009 USD) higher among older adults with comorbid insomnia and depression ($n = 2\,756$), relative to those with depression alone [23]. More recently, Gamaldo and colleagues analyzed data from over 35 million older adult participants in the Nationwide Inpatient Sample database and found that total health care costs associated with insomnia-related hospital admissions increased from \$22 500 in 2002 to \$31 527 in 2012 [27]. In aggregate, these results demonstrate that insomnia among older adults is associated with significant economic burden.

Despite the consistency of these findings of increased costs associated with insomnia, we are unaware of any study that has evaluated the population-level impact of insomnia on overall HCU and costs among older adults. Such insight is desperately needed by payers, policy-makers, and health systems leaders who seek to make evidence-based decisions regarding sleep and population health care management. Further, previous studies have been limited in assessing only subpopulations [28] or costs of specific points of service [27, 29]. Thus, the purpose of the present study was to evaluate the economic consequences of untreated insomnia including all-cause inpatient and outpatient visits, ED visits, nursing home stays, prescription medication use, and costs among a randomly selected sample of older adult Medicare beneficiaries in the United States. Our primary

hypothesis was that compared to non-sleep disordered controls, beneficiaries with untreated insomnia demonstrate higher HCU.

Methods

Data source

The primary source of data for this study was a random 5% sample of Medicare administrative data obtained from the Centers for Medicare & Medicaid Services (CMS) Chronic Condition Data Warehouse (CCW) for years 2006–2013. This 5% sample is derived from the Medicare population through random processes [30].

Study design and population

We used a case-control design to assess all-cause HCU and costs over an 11-month period, comparing beneficiaries with untreated insomnia to non-sleep disordered controls. Consistent with prior work, we defined untreated insomnia as the 12 months prior to the month of first insomnia diagnosis or first prescription fill for an insomnia medication [23, 25]. This design, common in the insomnia literature [22, 25, 28, 31], is predicated on the understanding that insomnia is a chronic condition, and most insomnia patients have had the condition for years prior to diagnosis or treatment [32, 33]. All participants had continuous Medicare Parts A, B, and D, with no Part C (Medicare Advantage) coverage for a 36-month period comprising the 12 months pre-insomnia diagnosis and 24 months post-diagnosis. Based on our research question, the present analyses included only data from the 12-month pre-diagnosis period.

Insomnia cases

Insomnia was defined using diagnostic codes and medication fills. We searched inpatient and outpatient claims for the presence of at least one claim containing International Classification of Disease, Version 9, Clinical Modification (ICD-9-CM) codes 307.41, 307.42, 307.49, 327.00, 327.01, 327.09, 780.52, V69.4. We also searched the Part D prescription drug files for insomnia-related medications including barbiturates—amobarbital, butobarbital, pentobarbital, secobarbital, phenobarbital, mephobarbital; benzodiazepines—alprazolam, clonazepam, estazolam, flurazepam, lorazepam, oxazepam, quazepam, temazepam, triazolam; chloral hydrate; hydroxyzine; non-benzodiazepine sedative hypnotics (NBSH)—eszopiclone, zaleplon, zolpidem; ramelteon; and sedating antidepressants—amitriptyline, nortriptyline, doxepin, clomipramine, trazodone, nefazodone, and mirtazapine. The first date of a recoded insomnia diagnosis or insomnia-related medication fill served as the index date.

Non-sleep disordered controls

Non-sleep disordered controls were identified based on the absence of sleep-related diagnosis (insomnias, sleep-related breathing disorders, sleep-related movement disorders, parasomnias, central disorders of hypersomnolence, and other sleep disorders), treatment, or diagnostic procedure during the

entire study period (2006–2013). To ensure similar distributions of cases and controls across years, non-sleep disordered controls were frequency matched on index date to insomnia cases.

HCU and costs

HCU was operationalized as counts of claims over the 1-year period prior to the month of the index date. We excluded the month of the index date to avoid counting claims related to the insomnia diagnosis. We created an “any HCU” category and also categorized HCU by point of service (inpatient, emergency department [ED], outpatient, nursing home, prescriptions) using information available on the claims. We summed costs occurring during the year prior to insomnia diagnosis, excluding the month of insomnia diagnosis. Total all-cause costs represent all costs paid out by Medicare. Costs were also categorized by point of service. To account for inflation during the 8-year study period, all costs were converted to 2013 dollars using the consumer price index produced by the United States Bureau of Labor.

Data analysis

Distributions and frequencies of all variables were assessed. Next, we tested bivariate comparisons between cases and controls using Chi-square Goodness of fit and Student’s *t*-tests. Unadjusted mean HCU and costs were presented with their standard deviations overall and by point of service. We identified age, sex, and race a priori as potential confounders and included them in our adjusted regression models.

HCU counts are highly skewed with many zero values, leading to overdispersion. To accommodate this distribution, we modeled overall HCU as well as HCU by point of service using generalized linear models with a negative binomial distribution and a log link. These unadjusted models contained an indicator variable for insomnia case status and year of diagnosis (i.e. to adjust for matching on index date). Next, we added age, sex, and race. Due to the large number of potential variables, the fully adjusted model was generated using stepwise selection with a *p*-value for entry/exit set at 0.001. Final models were generated separately for each point of service.

Costs were similarly skewed with multiple zero values. We tested the distribution and link using the modified Park test and the Box-Cox test. Mean total and point of service charges were modeled using a generalized linear model with a gamma distribution and log link. The unadjusted model contained an indicator variable for insomnia case status and year of diagnosis (to adjust for matching on index date). Next, we added age, sex, and race. Final models were generated separately for each point of service by starting off with all covariates in the model and removing those with *p*-value ≥ 0.001 whose removal did not change the effect estimate of case by $>10\%$. We calculated adjusted mean charges, marginal effects and 95% confidence intervals (CIs) using the delta method.

Sensitivity analyses

We conducted sensitivity analyses to test assumptions regarding our insomnia definition. We reran all analyses using four additional insomnia definitions: receipt of two insomnia diagnoses within 12 months, receipt of two insomnia-related medication fills within 12 months, receipt of both an insomnia

diagnosis and an insomnia-related medication fill within 12 months, and receipt of either an insomnia diagnosis or a US Food and Drug Administration (FDA) approved insomnia medication (butabarbital, doxepin, estazolam, eszopiclone, flurazepam, quazepam, ramelteon, secobarbital, temazepam, triazolam, zaleplon, zolpidem) within 12 months.

Covariate imbalance between insomnia cases and non-sleep disordered controls could result in residual confounding of our effect estimates. Thus, we assessed whether residual confounding was biasing effect estimates. First, we constructed inverse probability of treatment weights (IPTW) [34, 35] by modeling the odds of being an insomnia case as a function of baseline covariates. Next, we reran all of our models using the weights. We also stratified the models by deciles of IPTW.

Analyses were performed with SAS version 9.3 (SAS Institute, Cary, NC) and Stata 14 (StatCorp LP, College Station, TX). This study was approved by the Institutional Review Board of the University of Maryland, Baltimore.

Results

Participants

We identified 151668 beneficiaries with insomnia who met inclusion criteria between the years 2007–2011. We also identified 333038 non-sleep disordered controls, resulting in a total sample size of 484707. Among beneficiaries with insomnia, 25784 (17%) received a diagnosis on the index date while 125884 (83%) received a fill for a sleep-related medication (Table 1).

Beneficiaries with insomnia were younger than controls (69.4 [standard deviation (SD) 15.0] years vs. 71.2 [SD 13.7] years, $p < 0.001$) and more likely to be female (67.6% vs. 60.6%, $p < 0.001$; Table 1). Most of the cohort was white (81.4%). Beneficiaries with insomnia had a higher burden of comorbid illness, with significantly elevated prevalence of every comorbidity measured. Notably, psychological and pain disorders such as depression (27.4% vs. 10.2%), anxiety (22.6% vs. 8.1%), migraine (4.8% vs. 1.8%), and fibromyalgia (21.6% vs. 11.3%) were almost doubled among those with insomnia, relative to non-sleep disordered controls.

HCU and costs

Unadjusted mean all-cause HCU and costs during the year prior to diagnosis were higher among insomnia cases (Table 2). In fully adjusted negative binomial models (Table 3, model 3) and relative to non-sleep disordered controls, beneficiaries with untreated insomnia had higher 11-month (month of diagnosis excluded) rates of HCU across all point of service locations. Rates of HCU were highest for inpatient care (rate ratio [RR] 1.61; 95% CI 1.59, 1.64) and lowest for prescription fills (RR 1.17; 95% CI 1.16, 1.17). All variables included in the final negative binomial models are displayed in Appendix 1.

Similar patterns were observed when comparing all-cause costs between beneficiaries with untreated insomnia and non-sleep disordered controls (Table 4). Specifically, total 11-month adjusted marginal costs for insomnia cases were significantly higher relative to controls (\$63,607; 95% CI \$60,532, \$66,685). The additive costs for insomnia were driven primarily by inpatient care (\$60,900; 95% CI \$56,609, \$65,191). Although much lower than inpatient care costs, marginal adjusted emergency department (\$1,492; 95% CI \$1,387, \$1,596) and prescription costs (\$486; 95% CI

Table 1. Baseline characteristics of insomnia cases diagnosed 2007–2011 and non-sleep disordered controls

	Total (N = 484 707)	Insomnia cases (n = 151 668)	Healthy sleep controls (n = 333 039)	P-value ^a
Age, mean (SD)	70.6 (14.1)	69.4 (15.0)	71.2 (13.7)	<0.001
Index diagnosis, n (%)				
Diagnosis	n/a	25 784 (17.0)	n/a	
Medication	n/a	125 884 (83.0)	n/a	
Sex, n (%)				<0.001
Male	180 316 (37.2)	49 200 (32.4)	131 116 (39.4)	
Female	304 391 (62.8)	102 468 (67.6)	201 923 (60.6)	
Race, n (%)				<0.001
White	394 439 (81.4)	123 814 (81.6)	270 625 (81.3)	
Black	53 329 (11.0)	15 739 (10.4)	37 590 (11.3)	
Asian	11 913 (2.5)	3 985 (2.6)	7 928 (2.4)	
Hispanic	13 704 (2.8)	4 926 (3.2)	8 778 (2.6)	
Other	11 322 (2.3)	3 204 (2.1)	8 118 (2.4)	
Comorbid conditions, n (%)				
Migraine	13 354 (2.8)	7 264 (4.8)	6 090 (1.8)	<0.001
Fibromyalgia	70 285 (14.5)	32 800 (21.6)	37 485 (11.3)	<0.001
TBI	26 054 (5.4)	11 460 (7.6)	14 594 (4.4)	<0.001
Depression	75 731 (15.6)	41 595 (27.4)	34 136 (10.2)	<0.001
Anxiety	61 214 (12.6)	34 215 (22.6)	26 999 (8.1)	<0.001
Schizophrenia	15 363 (3.2)	7 480 (4.9)	7 883 (2.4)	<0.001
Bipolar disorder	15 830 (3.3)	9 697 (6.4)	6 133 (1.8)	<0.001
Alcohol dependence	11 510 (2.4)	5 606 (3.7)	5 904 (1.8)	<0.001
Substance dependence	50 179 (10.3)	23 433 (15.4)	26 746 (8.0)	<0.001
Myocardial infarction	19 103 (3.9)	6 827 (4.5)	12 276 (3.7)	<0.001
Alzheimer's and related dementias	53 616 (11.1)	22 479 (14.8)	31 137 (9.3)	<0.001
Anemia	207 876 (42.9)	77 630 (51.2)	130 246 (39.1)	<0.001
Asthma	47 542 (9.8)	21 969 (14.5)	25 573 (7.7)	<0.001
Atrial fibrillation	50 372 (10.4)	18 053 (11.9)	32 319 (9.7)	<0.001
Cataracts	280 800 (57.9)	89 865 (59.2)	190 935 (57.3)	<0.001
Heart failure	104 834 (21.6)	41 289 (27.2)	63 545 (19.2)	<0.001
Chronic kidney disease	69 306 (14.3)	26 918 (17.8)	42 388 (12.7)	<0.001
Endometrial cancer	3 787 (0.8)	1 331 (0.9)	2 456 (0.7)	<0.001
Breast cancer	23 543 (4.9)	8 191 (5.4)	15 352 (4.6)	<0.001
Colorectal cancer	12 036 (2.5)	3 950 (2.6)	8 086 (2.4)	<0.001
Lung cancer	3 995 (0.8)	1 647 (1.1)	2 348 (0.7)	<0.001
Prostate cancer	17 084 (3.5)	4 608 (3.0)	12 476 (3.8)	<0.001
COPD	101 669 (21.0)	43 121 (28.4)	58 548 (17.6)	<0.001
Diabetes	148 912 (30.7)	52 518 (34.6)	96 394 (28.9)	<0.001
Glaucoma	96 048 (19.8)	31 101 (20.5)	64 947 (19.5)	<0.001
Hip fracture	15 555 (3.2)	6 133 (4.0)	9 422 (2.8)	<0.001
Hyperlipidemia	317 514 (65.5)	105 386 (69.5)	212 128 (63.7)	<0.001
Benign prostate hyperplasia	52 376 (10.8)	15 940 (10.5)	36 436 (10.9)	<0.001
Hypertension	346 185 (71.4)	116 593 (76.9)	229 592 (68.9)	<0.001
Hypothyroidism	96 367 (19.9)	35 782 (23.6)	60 585 (18.2)	<0.001
Ischemic heart disease	200 015 (41.3)	72 954 (48.1)	127 061 (38.1)	<0.001
Osteoporosis	151 656 (31.3)	53 792 (35.5)	97 864 (29.4)	<0.001
Rheumatoid arthritis	215 337 (44.4)	82 822 (54.6)	132 515 (39.8)	<0.001
Stroke	59 825 (12.3)	23 267 (15.3)	36 558 (11.0)	<0.001

^ap-value from Student's t-test or Chi-square goodness of fit.

(\$454, \$518) were also elevated among insomnia cases. All variables included in the final cost models are displayed in Appendix 2.

Sensitivity analyses

Because administrative claims lack standardized clinical assessment, we conducted sensitivity analyses to assess the

impact of our insomnia definition on estimates of all-cause HCU and costs. Four alternate definitions were considered in multiple sensitivity analyses. Requiring two diagnoses of insomnia in 12 months decreased the effect of untreated insomnia on increased HCU in all point of service locations, but all associations remained statistically significant. Smaller decreases in the effect estimates were observed for insomnia

Table 2. Annual all-cause health care utilization and costs in the year prior to insomnia diagnosis or matched index date among Medicare beneficiaries 2007–2011, N = 484 707

	Insomnia cases, n = 151 668	Non-sleep disordered controls, n = 333 039
Health care utilization ^a , mean (SD)		
Inpatient	0.49 (1.06)	0.19 (0.60)
Emergency department	0.94 (2.05)	0.38 (1.03)
Outpatient	5.48 (7.07)	3.50 (5.41)
Prescriptions	24.73 (17.66)	17.53 (15.32)
Costs in \$, for 2013, mean (SD)		
Hospital	99357 (368 983)	34428 (180055)
Emergency department	2947 (13 321)	1058 (4884)
Outpatient	36834 (175 507)	18676 (122 113)
Prescriptions	3450 (4924)	2185 (3635)
Total	142 586 (436 349)	56 346 (234 113)

^aOperationalized as number of claims.

Table 3. Adjusted rate ratios (95% confidence intervals) of all-cause health care utilization among insomnia cases compared to non-sleep disordered controls in the year prior^a to insomnia diagnosis or matched index date among Medicare beneficiaries 2007–2011, N = 484 707

	Model 1 ^b	Model 2 ^c	Model 3 ^d
Inpatient	2.56 (2.52, 2.60)	2.66 (2.62, 2.70)	1.61 (1.59, 1.64)
Emergency department	2.48 (2.45, 2.51)	2.41 (2.38, 2.44)	1.49 (1.47, 1.51)
Outpatient	1.56 (1.55, 1.57)	1.56 (1.54, 1.57)	1.20 (1.19, 1.21)
Prescriptions	1.41 (1.40, 1.41)	1.44 (1.43, 1.45)	1.17 (1.16, 1.17)

^aMonth of diagnosis excluded.

^bAdjusted for year of diagnosis.

^cAdjusted for year of diagnosis, age, sex, and race.

^dAdjusted for year of diagnosis, age, sex, race, and comorbidities listed in Appendix 1.

definitions requiring at least two fills for insomnia medication in the past 12 months or requiring an insomnia diagnosis and an insomnia medication fill. Restricting to FDA approved medications did not change effect estimates. Similar patterns were observed in sensitivity analyses for cost data. Similarly, including IPTW in our regression models for all-cause HCU and costs did not significantly change our effect estimates. In the interest of simplicity we presented the models without the IPTWs.

Discussion

In this large national analysis of Medicare beneficiaries, insomnia was associated with multiple medical and psychiatric comorbidities. Even after controlling for these comorbid conditions and after adjusting all costs to 2013 USD, when compared to non-sleep disordered controls, beneficiaries with untreated insomnia demonstrated significantly higher all-cause HCU and significantly greater costs across all points of service. The greatest disparities in costs between beneficiaries with insomnia and controls were found in inpatient-related HCU and costs, novel findings that have not previously been reported in the literature.

Our results are consistent with and build upon prior investigations that have found insomnia to be associated with increased all-cause HCU and costs among older adults. For example, like Kaufmann and colleagues, we found that insomnia increases risk for hospitalizations. However, whereas Kauffman defined HCU as hospitalizations, home health care services, and nursing home placement, we employed a robust

definition of HCU and found insomnia to increase HCU across a very broad range of points of service. In terms of costs, our results suggest that all-cause costs of insomnia are higher than previously reported. For example, whereas Ozminkowski and colleagues found 6-month health care costs to be \$1143 higher among older adults with insomnia than among non-insomnia controls [25], in the present study insomnia was associated with \$63 607 higher costs over 11 months. This dramatic increase in all-cause costs in the present study was driven primarily by inpatient costs, which were \$60 900 higher among beneficiaries with insomnia than among non-sleep disordered controls. Notably, Ozminkowski and colleagues did not assess inpatient costs and followed respondents for a much shorter period of time (i.e. 6 months), which might explain why we found greater costs at all points of service included in our study [25]. Of note, both insomnia as well as certain insomnia medications have been found to increase risk for fall-related injury, which likely increases inpatient costs [15, 16]. A final possible explanation for our findings is our operational definition of insomnia, which included insomnia-related ICD-9 diagnoses as well as prescription fills; it is possible that the medication fill component of our insomnia definition was overly sensitive and included high-cost beneficiaries without insomnia. That said, our methodology is commonly employed in the literature, and we conducted multiple sensitivity analyses to assess the robustness of results. Thus, our operational definitions alone are unlikely to explain the substantial costs of insomnia observed in this study.

This study possesses several strengths. First, we employed a large national sample spanning 8 years. Indeed, the present

Table 4. Adjusted marginal effects (95% confidence intervals) of Medicare all-cause costs in 2013 dollars among insomnia cases compared to non-sleep disordered controls in the year^a prior to insomnia diagnosis or matched index date among Medicare beneficiaries 2007–2011, *N* = 484707

	Model 1 ^b	Model 2 ^c	Model 3 ^d
Inpatient	64917 (62429, 67406)	68238 (65508, 70697)	60900 (56609, 65191)
Emergency department	1888 (1819, 1957)	2016 (1935, 2096)	1492 (1387, 1596)
Outpatient	18433 (17265, 19601)	18187 (17119, 19255)	10336 (9312, 11361)
Prescriptions	1252 (1222, 1282)	1170 (1142, 1199)	486 (454, 518)
Total	86248 (83391, 89104)	89627 (866994, 92559)	63607 (60532, 66685)

^aMonth of diagnosis excluded.

^bAdjusted for year of diagnosis.

^cAdjusted for year of diagnosis, age, sex, and race.

^dAdjusted for year of diagnosis, age, sex, race, and comorbidities listed in Appendix 2.

results reflect the largest analysis of the economic impact of insomnia among older adults to date. Second, in addition to being large, our CCW population is also highly generalizable, representing a random sample that generalizes to approximately 75% of older adults in the United States. Third, we successfully captured a broad range of expenditures from the payer perspective, including HCU and costs related to outpatient, inpatient, ED, nursing home, and medication prescriptions.

At the same time, several limitations to the present investigation must be noted. First, our operational definition of insomnia was based on physician-assigned diagnoses and medication fills. To date, there is no validated algorithm to identify insomnia cases within administrative claims data. Second, we were unable to determine insomnia symptoms, subjective or objective measures of sleep, or other clinical variables of interest. From a diagnostic perspective the ICD-9 diagnostic codes included in our data do not differentiate between acute and chronic insomnia, so we were unable to assess duration of sleep complaints. Similarly, we were unable to identify clinical indications for the prescribed medications. Many medications used to treat insomnia (e.g. sedating antidepressants, benzodiazepines) are also used to treat other conditions, so while our insomnia definition was highly sensitive, it was less specific. However, our administrative methodology is well-established in the insomnia literature [22, 25, 28, 31], and results remained consistent throughout multiple sensitivity analyses. Third, given the very high inpatient costs, another limitation is that we were unable to ascertain reasons why beneficiaries were hospitalized. Fourth, although our administrative design provides valuable insight into HCU and direct medical costs from the payer perspective (i.e. all-cause costs borne by Medicare), we were unable to measure important direct and indirect costs from other perspectives. For example, from the patient perspective, insomnia treatments are associated with travel-related costs and co-pays and diminished health-related quality of life, which were unable to be included in the present study. Similarly, among adults the majority of insomnia-related costs are associated with lost workplace productivity, including days missed from work (i.e. absenteeism) as well as subpar performance on the job (i.e. presenteeism) [36, 37]. Although changes in sleep have also been associated with early retirement among older adults [38], we were unable to assess the impact of insomnia on workplace or employment productivity factors in our study. Insomnia is associated with increased costs to society, such as increased risk for motor vehicle crashes [22, 39], which were not included in the present study. Unfortunately, our claims data are unable to answer these and other important questions

from the patient, employer, and societal perspectives. This is an inherent limitation to an administrative review design such as ours. Fifth, our administrative design precludes determination of causality. For example, it could not be determined whether insomnia leads to comorbid conditions, which increases costs, or whether comorbidities lead to insomnia, which increases costs. Nonetheless, treating comorbid insomnia has been shown to provide positive economic benefit [22]. Similarly, insomnia cases differed significantly from controls, including significantly higher rates of all comorbid conditions. To minimize the effects of this potential confounding, we controlled for comorbid illnesses and employed IPTW to enhance exchangeability between insomnia cases and non-sleep disordered controls. Nonetheless, despite our multiple efforts, residual confounding might have been present. Finally, although our 5% sample was large and randomly selected from the Medicare population, it remains unknown how well this randomly generated 5% sample generalizes to all older adults, or adults in Medicare advantage plans.

Our results suggest several directions for future research. First, there is need for a validated algorithm to identify insomnia cases within administrative claims data. This will require a linkage between clinical and claims data. Second, our data suggest that insomnia is associated with greater inpatient HCU and costs than previously described. Future research should seek to illuminate the nature of these costs. For example, although insomnia is frequently comorbid with other costly medical conditions requiring inpatient care (e.g. cardiopulmonary diseases, mood disorders, neurodegenerative diseases, etc) [9–20], it is unclear whether insomnia exacerbates these conditions or by what mechanisms insomnia leads to more or longer inpatient stays. It is also possible that hospitalizations increase the risk for subsequent insomnia, and hospital, discharge, and recovery/follow-up factors warrant further investigation. Third, in addition to reasons for hospitalization and inpatient-specific costs, greater understanding of the economic impact of insomnia among older adults is needed more generally. A recent review of economic consequences of insomnia and the cost-effectiveness of insomnia treatments found that the cost of treating insomnia, including comorbid insomnia, is much less than the cost of not treating this disorder [22]. To advance understanding, we propose that measures of direct and indirect insomnia-related costs should be incorporated into all insomnia-related trials and outcomes studies among older adults. Even in the absence of administrative claims, direct and indirect costs from the payer perspective can be assessed via

self-reported HCU and measures of disability. Fourth, greater insight is needed into insomnia-related costs from the employer perspective. An increasing number of Medicare beneficiaries remain in the workforce, and understanding the impact of insomnia on workplace productivity and/or early retirement among older adults is an important research priority. Indeed, many insomnia treatments can be tailored for delivery in an occupational setting [40, 41], and insomnia in the workplace is of increasing interest to self-insured employers. Academic-industry partnerships are likely to be mutually beneficial in this regard. Fifth, there is a dramatic need for understanding the cost-benefit of insomnia treatment as well as the relative cost-effectiveness of various insomnia treatments among older adults [22]. Fifth, given the very high prevalence of comorbid insomnia, the economic impact of untreated insomnia and the cost-benefit of insomnia treatments in comorbid disease states warrant further attention [22]. Sixth, greater insight is needed into the potential impact of different methods of identifying insomnia cases, including various diagnostic codes, prescription types, provider types, and point of service. From a clinical perspective, future studies should consider clinical and causative variations among various insomnia subtypes. Finally, future studies should assess the economic impact of various pharmacologic and non-pharmacological treatments for insomnia, such as cognitive-behavioral therapy.

In conclusion, the present study reports the largest analysis to date of insomnia-related economic outcomes among older adults with comprehensive measurement of HCU. In our national sample, the prevalence of insomnia was high, and insomnia was significantly associated with multiple medical and psychiatric comorbidities. Even after controlling for these conditions and compared with non-sleep disordered controls, beneficiaries with insomnia demonstrated greater all-cause HCU and increased costs across all categories. These findings are consistent with and expand previous literature that suggests insomnia is a costly condition among older adults.

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References

1. Ancoli-Israel S. Sleep and its disorders in aging populations. *Sleep Med.* 2009;10(Suppl 1):S7–11.
2. Kaufmann CN, et al. Trends in prescribing of sedative-hypnotic medications in the USA: 1993–2010. *Pharmacoepidemiol Drug Saf.* 2016;25(6):637–645.
3. Maust DT, et al. National trends in antidepressant, benzodiazepine, and other sedative-hypnotic treatment of older adults in psychiatric and primary care. *J Clin Psychiatry.* 2017;78(4):e363–e371.
4. Olfson M, et al. Benzodiazepine use in the United States. *JAMA Psychiatry.* 2015;72(2):136–142.
5. Ford DE, et al. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? *JAMA.* 1989;262(11):1479–1484.
6. Ford ES, et al. Trends in outpatient visits for insomnia, sleep apnea, and prescriptions for sleep medications among US adults: findings from the National Ambulatory Medical Care survey 1999–2010. *Sleep.* 2014;37(8):1283–1293.
7. Moloney ME, et al. The medicalization of sleeplessness: a public health concern. *Am J Public Health.* 2011;101(8):1429–1433.
8. Albrecht JS, et al. Trends in insomnia diagnosis and treatment among medicare beneficiaries, 2006–2013. *Am J Geriatr Psychiatry.* 2018.
9. Dragioti E, et al. Insomnia severity and its relationship with demographics, pain features, anxiety, and depression in older adults with and without pain: cross-sectional population-based results from the PainS65+ cohort. *Ann Gen Psychiatry.* 2017;16:15.
10. Soehner AM, et al. Prevalence and clinical correlates of co-occurring insomnia and hypersomnia symptoms in depression. *J Affect Disord.* 2014;167:93–97.
11. Sunderajan P, et al. Insomnia in patients with depression: a STAR*D report. *CNS Spectr.* 2010;15(6):394–404.
12. Dragioti E, et al. Association of insomnia severity with well-being, quality of life and health care costs: A cross-sectional study in older adults with chronic pain (PainS65+). *Eur J Pain.* 2018;22(2):414–425.
13. Altena E, et al. Do sleep complaints contribute to age-related cognitive decline? *Prog Brain Res.* 2010;185:181–205.
14. Dzierzewski JM, et al. Sleep and cognition in older adults. *Sleep Med Clin.* 2018;13(1):93–106.
15. Helbig AK, et al. Association between sleep disturbances and falls among the elderly: results from the German Cooperative Health Research in the Region of Augsburg-Age study. *Sleep Med.* 2013;14(12):1356–1363.
16. Zhang Y, et al. Age- and gender-specific associations between insomnia and falls in Boston Puerto Rican adults. *Qual Life Res.* 2017;26(1):25–34.
17. Helbig AK, et al. Relationship between sleep disturbances and multimorbidity among community-dwelling men and women aged 65–93 years: results from the KORA Age Study. *Sleep Med.* 2017;33:151–159.
18. Khan MS, et al. The effects of insomnia and sleep loss on cardiovascular disease. *Sleep Med Clin.* 2017;12(2):167–177.
19. Routledge FS, et al. Insomnia symptoms are associated with abnormal endothelial function. *J Cardiovasc Nurs.* 2017;32(1):78–85.
20. Sofi F, et al. Insomnia and risk of cardiovascular disease: a meta-analysis. *Eur J Prev Cardiol.* 2014;21(1):57–64.
21. Kyle SD, et al. Insomnia and health-related quality of life. *Sleep Med Rev.* 2010;14(1):69–82.
22. Wickwire EM, et al. Health economics of insomnia treatments: the return on investment for a good night's sleep. *Sleep Med Rev.* 2016;30:72–82.
23. Asche CV, et al. The direct costs of untreated comorbid insomnia in a managed care population with major depressive disorder. *Curr Med Res Opin.* 2010;26(8):1843–1853.
24. Gaudette É, et al. Health and Health Care of Medicare Beneficiaries in 2030. *Forum Health Econ Policy.* 2015;18(2):75–96.

25. Ozminkowski RJ, et al. The direct and indirect costs of untreated insomnia in adults in the United States. *Sleep*. 2007;**30**(3):263–273.
26. Pollack M, et al. Insomnia-related comorbidities and economic costs among a commercially insured population in the United States. *Curr Med Res Opin*. 2009;**25**(8):1901–1911.
27. Gamaldo AA, et al. Sleep disturbances among older adults in the United States, 2002–2012: nationwide inpatient rates, predictors, and outcomes. *Front Aging Neurosci*. 2016;**8**:266.
28. Asche CV, et al. The direct costs of untreated comorbid insomnia in a managed care population with major depressive disorder. *Curr Med Res Opin*. 2010;**26**(8):1843–1853.
29. Kaufmann CN, et al. Insomnia and health services utilization in middle-aged and older adults: results from the Health and Retirement Study. *J Gerontol A Biol Sci Med Sci*. 2013;**68**(12):1512–1517.
30. Buchaneer. *Chronic Conditions Data Warehouse Medicare Administrative Data User Guide. Version 3.5*. www.ccwdata.org/documents/10280/19002246/ccw-medicare-data-user-guide.pdf. Accessed September 5, 2018.
31. Pollack M, et al. Insomnia-related comorbidities and economic costs among a commercially insured population in the United States. *Curr Med Res Opin*. 2009;**25**(8):1901–1911.
32. Katz DA, et al. Clinical correlates of insomnia in patients with chronic illness. *Arch Intern Med*. 1998;**158**(10):1099–1107.
33. Mallon L, et al. Relationship between insomnia, depression, and mortality: a 12-year follow-up of older adults in the community. *Int Psychogeriatr*. 2000;**12**(3):295–306.
34. Cole SR, et al. Constructing inverse probability weights for marginal structural models. *Am J Epidemiol*. 2008;**168**(6):656–664.
35. Austin PC, et al. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Stat Med*. 2015;**34**(28):3661–3679.
36. Kessler RC, et al. Insomnia and the performance of US workers: results from the America insomnia survey. *Sleep*. 2011;**34**(9):1161–1171.
37. Sivertsen B, et al. The economic burden of insomnia at the workplace. An opportunity and time for intervention? *Sleep*. 2011;**34**(9):1151–1152.
38. Hagen EW, et al. Changes in sleep duration and sleep timing associated with retirement transitions. *Sleep*. 2016;**39**(3):665–673.
39. Barger LK, et al.; Harvard Work Hours Health and Safety Group. Common sleep disorders increase risk of motor vehicle crashes and adverse health outcomes in firefighters. *J Clin Sleep Med*. 2015;**11**(3):233–240.
40. Thiart H, et al. Internet-based cognitive behavioral therapy for insomnia: a health economic evaluation. *Sleep*. 2016;**39**(10):1769–1778.
41. Wickwire EM. Value-based sleep in the workplace. *Sleep*. 2016;**39**(10):1767–1768.