

Section 1: Further information relating to methods

Covariates. Based on a review of the literature, variables that were potential confounders, that is, associated with both insomnia and dyslipidemia, were identified.¹⁻⁵ These variables included: sex, age, race, total household income, ever smoking (defined as having smoked at least 100 cigarettes in one's life), alcohol consumption over the past year, frequency of experiencing depressed mood and anhedonia over the previous 2 w, current self-reported use of any sleeping pill or pill to help with sleep (either prescription or nonprescription), ever doctor-diagnosed self-reported high cholesterol, current receipt of lipid-lowering medication, ever doctor-diagnosed diabetes, current receipt of diabetes pills or insulin, and, items contained in the Berlin Questionnaire (i.e., body mass index based on measured height and weight; frequency of reported snoring and/or apneas; frequency of reported daytime fatigue; frequency of daytime sleepiness; and, hypertension [based ever doctor-diagnosis or current receipt of antihypertensive medications]). The Berlin Questionnaire is a validated screening instrument for obstructive sleep apnea (for a respiratory distress index ≥ 5 events per hour, the sensitivity and specificity of the Berlin Questionnaire are 86% and 77%).⁶ Individuals for whom covariate information was missing (which represented a small proportion of all survey participants) were included in unadjusted analyses and excluded from multivariable analyses.

Sensitivity analyses. Several sensitivity analyses were performed. First, dyslipidemia was evaluated separately for men and women, since a previous study found increased dyslipidemia among women with insomnia symptoms, but not men.⁷ Second, dyslipidemia was evaluated separately by insomnia symptom subtype experienced (i.e., difficulty falling asleep versus prolonged nocturnal awakening versus early morning awakening). This analysis was

undertaken because a few previous studies have found difficulty falling asleep, but not difficulty maintaining sleep or early morning awakening, to be associated with increased cardiovascular mortality.⁸⁻¹¹ If a participant reported more than one type of insomnia symptom, he or she was included and analyzed in each of the reported insomnia symptom subgroups. Third, analyses were undertaken distinguishing by the frequency of insomnia symptoms experienced (i.e., 0 to 4 times in the past month versus 5 to 15 times in the past month versus 16 to 30 times in the past month). This analysis was undertaken because a few previous studies have found increased risk of negative cardiovascular outcomes among those experiencing insomnia symptoms frequently, but not among individuals experiencing insomnia symptoms occasionally or less.^{7,11-13} If a participant reported experiencing more than one type of insomnia symptom, participants' insomnia frequency status was based on the most frequent insomnia symptom experienced. Fourth, the association between insomnia symptoms and dyslipidemia was examined distinguishing by whether or not individuals were recently receiving sleeping pills or pills to help with sleep (defined as medication receipt within the past month, either prescription or non-prescription). This analysis was undertaken because receipt of sleeping pills may be a marker of having more severe insomnia and identifying a possible 'symptom severity-response' relationship is relevant. Receipt of sleeping pills may also potentially influence the presence of dyslipidemia (i.e., sleeping pills, which can improve insomnia symptoms, might lessen dyslipidemia if a true link between insomnia and dyslipidemia exists, but at the same time use of sleeping pills has also been linked with increased all-cause mortality).^{14,15} Fifth, analyses were separately conducted among individuals experiencing (or not) concomitant daytime fatigue. Individuals with combined insomnia and daytime fatigue likely reflect a subgroup experiencing more severe insomnia and/or of insomnia of more chronic duration and it is relevant to evaluate for possible

dyslipidemia among this more symptomatic subgroup. Sixth, dyslipidemia was examined by distinguishing the presence or not of short sleep time on most nights (defined as < 6 h of sleep). Individuals with insomnia symptoms coupled with short sleep time may reflect another more symptomatic subset of individuals worthy of evaluating. A cutoff of less than 6 h of sleep to denote short sleep time has been previously used in the literature.^{16,17} Seventh, the association between insomnia symptoms and dyslipidemia was examined separately among individuals with and without doctor-diagnosed dyslipidemia. Individuals with previously diagnosed dyslipidemia may have made lifestyle modifications or be on lipid-lowering pharmacotherapy, which could in turn influence the finding of dyslipidemia. Finally, the association between insomnia symptoms and dyslipidemia was examined by distinguishing whether or not individuals were receiving lipid-lowering medications at the time of survey administration.

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Section 2: Analysis examining the relationship between insomnia symptoms and self-reported current receipt of lipid-lowering agents

Insomnia symptoms in relation to self-reported receipt of any lipid-lowering medication at the time of survey administration was also examined. Forced entry multiple logistic regression was used. Unadjusted odds ratios (OR) and 95% confidence intervals (CI) were first calculated. A second regression model was run that included the following covariates: sex, age, race, education level, total household income, ever smoking, alcohol consumption over the past year, depressed mood and anhedonia over the previous 2 w, body mass index, doctor-diagnosed hypertension, current receipt of antihypertensive medication, doctor-diagnosed diabetes, current receipt of diabetes pills or insulin, current receipt of any sleeping pill, and frequency of reported snoring and/or apneas. A third regression model was run including all of the variables in the second model, plus frequency of reported daytime fatigue and frequency of daytime sleepiness. Several sensitivity analyses were performed, distinguishing results by sex, receipt of sleeping pills or not within the past month, concomitant presence or not of daytime fatigue symptoms, presence or not of short sleep time most nights (defined as < 6 h), insomnia symptom subtype (i.e., sleep initiation insomnia, sleep maintenance insomnia, early morning awakening insomnia), and insomnia symptom frequency category (i.e., 0 to 4 times in the past month versus 5 to 15 times in the past month versus 16 to 30 times in the past month).

Results for this analysis are shown in Supplementary Table 1. Among individuals ages 20 y and older for whom insomnia data were available, data on current receipt of lipid-lowering drugs was available for 10,448 individuals, of whom 15.0% were taking lipid-lowering drugs at the time of survey administration. In unadjusted analyses, having any insomnia symptom at least five times in the past month was associated with increased odds of lipid-lowering medication

receipt (OR 1.16, 95% CI 1.01-1.34). However, these odds decreased and the statistical significance was lost after adjusting for covariates (OR 1.02, 95% CI 0.83-1.25). There was no association between insomnia symptoms and lipid-lowering drug receipt among men, but there were increased unadjusted odds of lipid-lowering drug use among women with any insomnia symptom at least five times in the past month (OR 1.21, 95% CI 1.01-1.44). This finding, however, became nonsignificant after adjusting for covariates (OR 1.08, 95% CI 0.80-1.46). Individuals with insomnia symptoms coupled with daytime fatigue had elevated unadjusted odds of lipid-lowering drug use (OR 1.64, 95% CI 1.28-2.11), but this result was rendered nonsignificant after covariate adjustment (OR 1.28, 95% CI 0.93-1.77). Individuals with sleep maintenance insomnia and early morning awakening insomnia subtypes had increased unadjusted odds of receipt of lipid-lowering medications, but these results too became nonsignificant after covariate adjustment. Individuals experiencing insomnia symptoms the most frequently (i.e., 16 to 30 times in the past month) had unadjusted increased odds of lipid-lowering medication receipt (OR 1.21, 95% CI 1.01-1.49), but significance was lost after controlling for covariates (OR 1.09, 95% CI 0.84-1.40). None of the remaining sensitivity analyses yielded significant results.

In summary, although increased odds of lipid-lowering medication receipt among individuals with insomnia symptoms were found for the entire group and for certain subgroups in unadjusted analyses, these results were related to covariate confounding. The absence of any significant association between insomnia symptoms and receipt of lipid-lowering medication after adjusting for covariates makes the main findings of this study even more robust, that there is no true link between insomnia symptoms and dyslipidemia.

Table S1. Frequency and odds of current lipid-lowering drug receipt among individuals with insomnia symptoms

	Number (%) with drug receipt	Unadjusted OR (95% CI) for drug receipt	Adjusted [†] OR (95% CI) for drug receipt	Adjusted [‡] OR (95% CI) for drug receipt
Any insomnia symptom, at least 5 times/month*				
All individuals	526 (5.0)	1.16 (1.01-1.34)	1.02 (0.83-1.25)	0.98 (0.81-1.19)
Men	209 (4.2)	1.13 (0.91-1.41)	0.92 (0.67-1.26)	0.87 (0.63-1.19)
Women	316 (5.8)	1.21 (1.01-1.44)	1.12 (0.82-1.52)	1.08 (0.80-1.46)
Individuals receiving sleeping pills	220 (10.9)	0.99 (0.74-1.32)	0.99 (0.68-1.44)	0.96 (0.65-1.41)
Individuals not receiving sleeping pills	305 (3.6)	1.08 (0.90-1.29)	1.04 (0.82-1.33)	0.98 (0.77-1.26)
Individuals with daytime fatigue	284 (10.2)	1.64 (1.28-2.11)	1.28 (0.93-1.77)	not applicable
Individuals without daytime fatigue	242 (3.2)	1.05 (0.88-1.25)	0.87 (0.69-1.11)	not applicable
Individuals with usually < 6 hours of total sleep time	144 (9.8)	1.31 (0.93-1.83)	0.89 (0.49-1.61)	0.76 (0.42-1.39)
Individuals with usually ≥ 6 hours of total sleep time	378 (4.2)	1.14 (0.97-1.35)	1.03 (0.82-1.30)	1.01 (0.81-1.25)
Insomnia symptom subtypes, at least 5 times/month*				
Initiation insomnia	291 (2.8)	1.10 (0.91-1.33)	1.17 (0.92-1.49)	1.14 (0.90-1.44)
Maintenance insomnia	373 (4.0)	1.23 (1.05-1.46)	1.09 (0.86-1.38)	1.04 (0.83-1.30)
Early morning awakening insomnia	310 (3.0)	1.24 (1.03-1.48)	1.09 (0.84-1.41)	1.05 (0.79-1.38)
Any insomnia symptom, by increasing frequency				
0-4 times/month	1046 (10.0)	1.00	1.00	1.00
5-14 times/month	298 (2.2)	1.12 (0.94-1.34)	0.98 (0.76-1.26)	0.95 (0.75-1.20)
16-30 times/month	227 (11.6)	1.22 (1.01-1.49)	1.09 (0.84-1.40)	1.03 (0.80-1.33)

*Reference group includes individuals without any insomnia symptoms or insomnia symptoms less than 5 times/month. †Adjusted for sex, age, race, education level, total household income, ever-smoking, ever alcohol consumption in the past year, depression symptoms in the past 2 weeks, measured body mass index, ever doctor-diagnosed hypertension, current receipt of antihypertensive medications, ever doctor-diagnosed diabetes, current receipt of diabetes pills or insulin, and self-reported history of apneas or snoring. ‡Adjusted for all the variables in the previous model, plus self-reported daytime fatigue and sleepiness.