Among European Individuals with Major Depressive Disorder, Higher Severity of Insomnia Symptoms is Independently Associated with Poorer Health-Related Outcomes

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Background

- Major depressive disorder (MDD) is the fifth leading cause of disability globally.[1]
- Insomnia is a common symptom of MDD[2] and a risk factor for new-onset or recurrent depression.[3–5]
- The presence of moderate-to-severe insomnia symptoms has been associated with poor health-related outcomes.[6]
- However, the impact of insomnia symptom severity on health-related outcomes among patients with MDD is not well understood.

Objective

To evaluate the relationship between insomnia symptom severity and health-related outcomes among individuals with MDD in Europe.

Methods

Data Source and Sample

Retrospective data were obtained from the 2020 National Health and Wellness Survey (NHWS), a nationally representative, self-reported, cross-sectional online survey of sample of adults (aged ≥18 years) in five European countries (EUR-5, France, Germany, UK, Italy, and Spain).

- A quota sampling procedure is used, with strata by sex and age, to ensure that the demographic composition of the NHWS sample is representative of the adult population.
- The NHWS was reviewed by Pearl Institutional Review Board (Indianapolis, IN) and granted exemption status.

Eligibility criteria:

- Self-reported physician diagnosis of depression and experience of depression in past 12 months
- Self-reported experience of insomnia in past 12 months
- Did not self-report diagnosis of bipolar disorder, schizophrenia, dementia or narcolepsy, or screen positive for bipolar disorder on the Mood Disorder Questionnaire

Measures

- Insomnia symptom severity was measured with Insomnia Severity Index (ISI);[7] higher scores correspond to more severe insomnia.
- Measured outcomes included: depression (Patient Health Questionnaire-9);[8] anxiety (Generalized Anxiety Disorder Assessment-7);[9] daytime sleepiness (Epworth Sleepiness Scale);[10] medication adherence (Medication Adherence Reasons Scale);[11] healthcare resource utilization; health-related quality of life (HRQoL; SF1v2 mental [MCS] and physical component [PCS] summary,[12] EQ-5D visual analog scale [EQ VAS][13] and health state utilities (SF-6D,[14] EQ-5D[13]); work productivity and activity impairment;[15] direct and indirect costs.

Statistical analysis

- Generalized linear models were used to assess the association of ISI score with outcomes, while controlling for age, sex, marital status, BMI, CCI, smoking, alcohol use, experience of daytime sleepiness, sleep apnea diagnosis, and restless legs syndrome diagnosis.

TARGETING NOVEL PATHWAYS IN DEPRESSION

Results

Sample Characteristics

- Analyses were conducted on 3,396 respondents with MDD and insomnia symptoms (mean age = 45.9 years; 66.8% female)
- Mean ISI score was 15.4 (range: 0-28)
- Higher ISI was associated with greater depression severity (r=0.53, p<0.001)

Table 1. Sample Characteristics (N = 3,396)

Characteristic			
Age (years), mean ± SD	45.9 ± 14.6	CCI, mean ± SD	0.37 ± 0.91
Female, %	67%	BMI, mean ± SD	25.9 ± 8.7
Married/living with Partner, %	52%	Smoking status, %	
University degree or higher, %	40%	Current smoker	38%
Employment status, %		Former smoker	28%
Employed*	53%	Never smoker	34%
Retired	16%	Alcohol use, %	
Short-term or long-term disability	10%	Daily	6%
Not employed, homemaker, student	20%	1 to 6 times/week	33%
Regularly experience daytime sleepiness, %	58%	Less often than 1x/week	33%
Diagnosed with sleep apnea, yes, %	8%	None	28%
Diagnosed with restless legs syndrome, %	8%	ISI score	15.4 ± 5.5

* Full-time, part-time, or self-employed

BMI, Body mass index; CCI, Charlson Comorbidity Index; ISI, Insomnia Severity Index; SD, standard deviation

Clinical Outcomes

- After adjustments, higher severity of insomnia symptoms was associated with higher levels of depression severity (rate ratio [RR]=1.05), anxiety severity (RR=1.04), medication non-adherence (RR=1.06), and daytime sleepiness (R=1.01), all p<0.001 **(Figure 1).**
- Higher severity of insomnia symptoms was associated with more healthcare provider visits (RR=1.02, p<0.001), emergency room visits (RR=1.02, p=0.002), and hospitalizations (RR=1.04, p=0.003) **(Figure 2).**
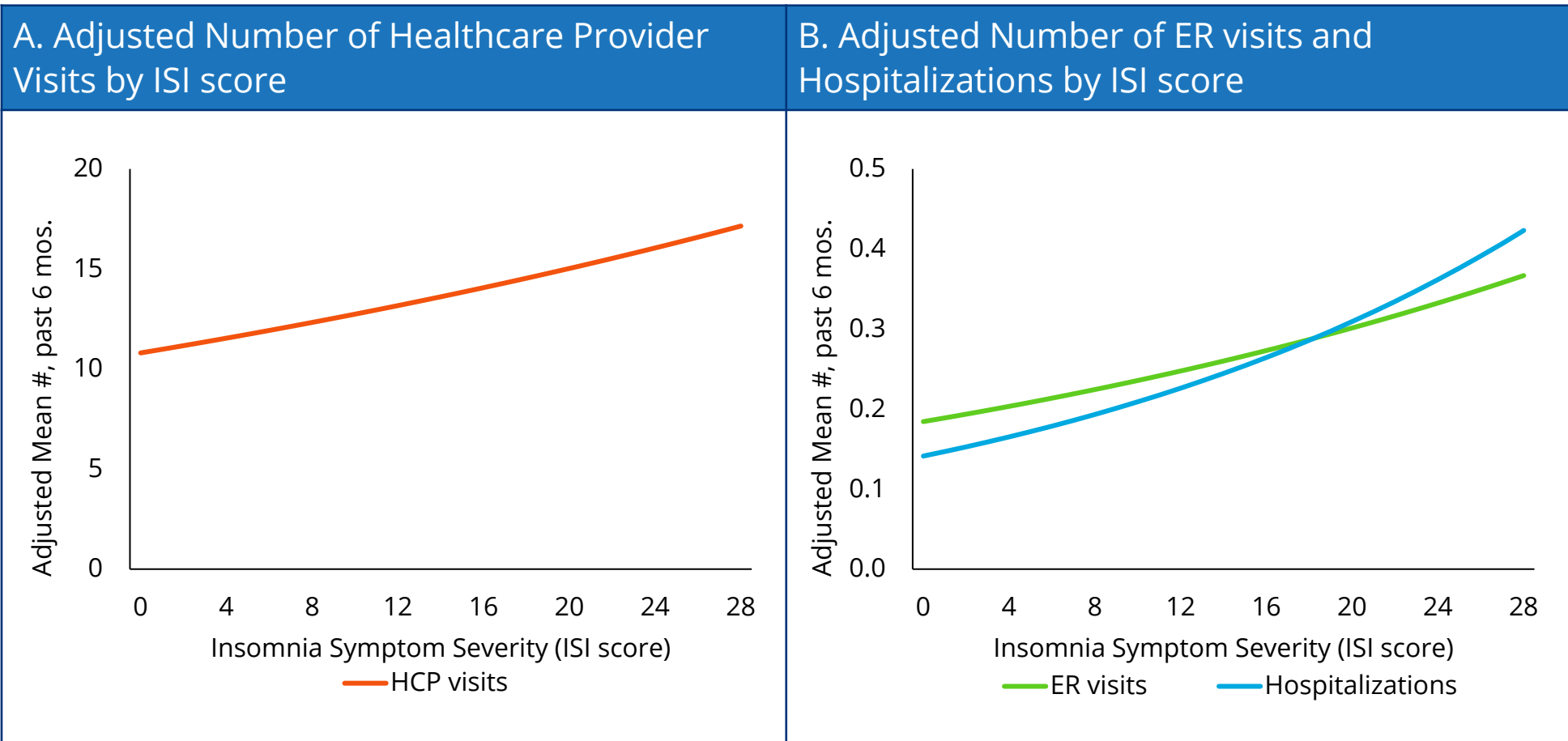
Figure 1. Adjusted Clinical Outcomes by Insomnia Symptom Severity: Depression, Anxiety, Adherence, and Daytime Sleepiness
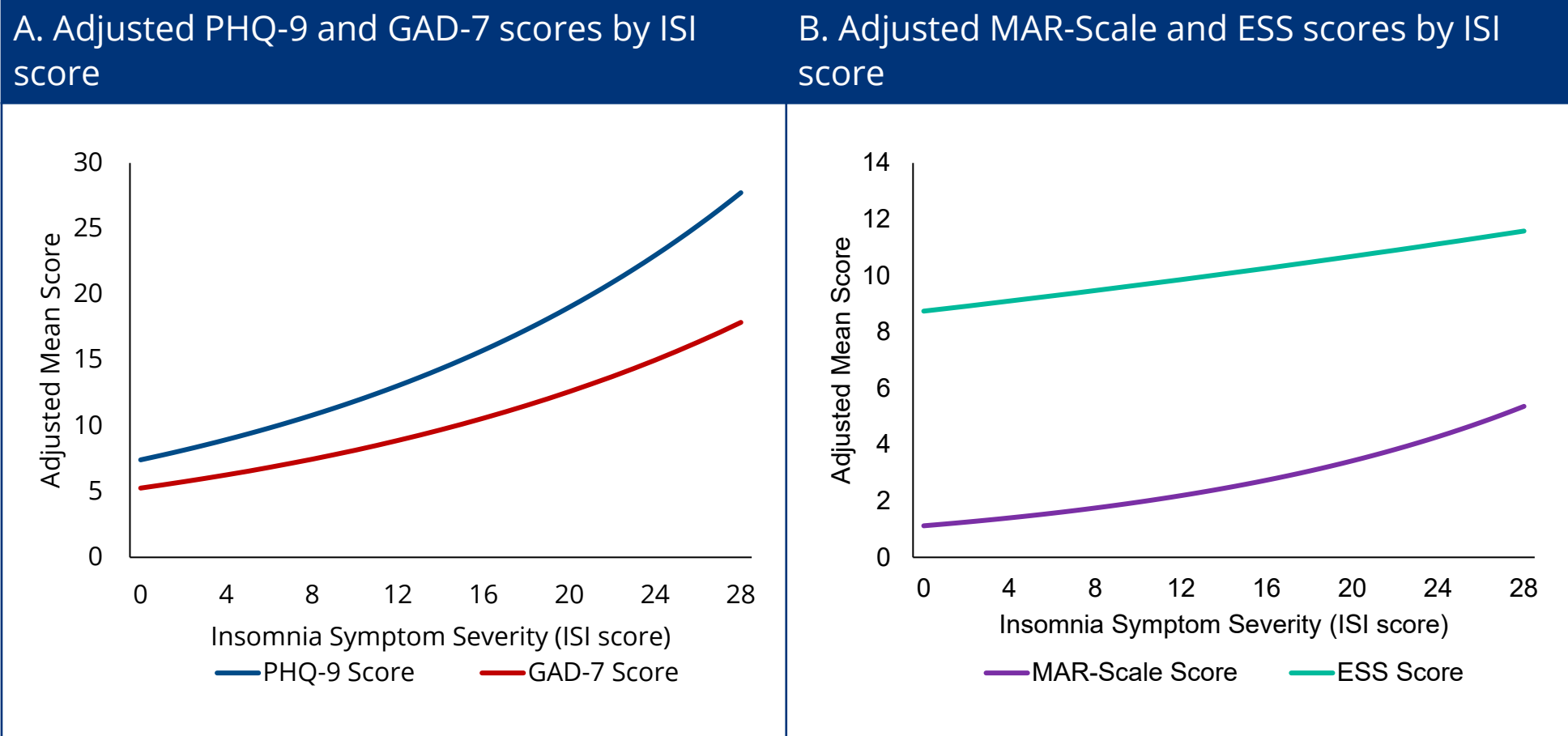
Note: Reference groups-- Age=47.00, Sex=Female, Marital Status=Married/living with a partner, BMI=25.70, CCI=0, Smoking Status=Current, Alcohol Use=Less often than once a week, Regularly experience daytime sleepiness=Yes, Restless legs syndrome diagnosis=Yes, Sleep apnea diagnosis=Yes

ESS, Epworth Sleepiness Scale; GAD7, 7-item Generalized Anxiety Disorder Assessment; ISI, Insomnia Severity Index; MAR-Scale, Medications Adherence Reasons Scale; PHQ, 9-item Patient Health Questionnaire

Figure 2. Adjusted Clinical Outcomes by Insomnia Symptom Severity: Healthcare Resource Utilization in the Past 6 Months

Note: Reference groups-- Age=47.00, Sex=Female, Marital Status=Married/living with a partner, BMI=25.70, CCI=0, Smoking Status=Current, Alcohol Use=Less often than once a week, Regularly experience daytime sleepiness=Yes, Restless legs syndrome diagnosis=Yes, Sleep apnea diagnosis=Yes

ER, emergency room; HCP, healthcare provider; ISI, Insomnia Severity Index, mos., months

Humanistic Outcomes

- After adjustments, higher severity of insomnia symptoms was associated with poorer HRQoL (MCS: β=-0.462; PCS: β=-0.354; EQ VAS: β=-1.089) and health state utilities (SF-6D: β=-0.005; EQ-5D: β=-0.016), all p<0.001 **(Figure 3)**.
- Higher severity of insomnia symptoms was associated with greater absenteeism (RR=1.07), presenteeism (RR=1.03), overall work productivity impairment (RR=1.03), and non-work-related activity impairment (RR=1.03), all p<0.001 **(Figure 4)**.

Figure 3. Adjusted Humanistic Outcomes by Insomnia Symptom Severity: HRQoL and Health State Utilities

Note: Reference groups-- Age=47.00, Sex=Female, Marital Status=Married/living with a partner, BMI=25.70, CCI=0, Smoking Status=Current, Alcohol Use=Less often than once a week, Regularly experience daytime sleepiness=Yes, Restless legs syndrome diagnosis=Yes, Sleep apnea diagnosis=Yes

ISI, Insomnia Severity Index; MCS, mental component summary; PCS, physical component summary; VAS, visual analog scale

Figure 4. Adjusted Humanistic Outcomes by Insomnia Symptom Severity: Work Productivity and Activity Impairment

Note: Reference groups-- Age=47.00, Sex=Female, Marital Status=Married/living with a partner, BMI=25.70, CCI=0, Smoking Status=Current, Alcohol Use=Less often than once a week, Regularly experience daytime sleepiness=Yes, Restless legs syndrome diagnosis=Yes, Sleep apnea diagnosis=Yes

ISI, Insomnia Severity Index; MCS, mental component summary; PCS, physical component summary; VAS, visual analog scale

Economic Outcomes

- After adjustments, higher severity of insomnia symptoms was associated with higher direct (RR=1.04) and indirect (RR=1.04) costs, both p<0.001 **(Figure 5)**.

Figure 5. Adjusted Economic Outcomes by Insomnia Symptom Severity

Note: Reference groups-- Age=47.00, Sex=Female, Marital Status=Married/living with a partner, BMI=25.70, CCI=0, Smoking Status=Current, Alcohol Use=Less often than once a week, Regularly experience daytime sleepiness=Yes, Restless legs syndrome diagnosis=Yes, Sleep apnea diagnosis=Yes

ISI, Insomnia Severity Index

CONCLUSIONS

- **This large scale, representative survey study provides novel insight into the burden associated with insomnia symptoms among adults with MDD in Europe.**
- **In patients with MDD, higher levels of insomnia symptoms are associated with worse health-related outcomes.**
- **These results suggest that MDD treatments that better target insomnia symptoms in individuals with depression may improve health-related outcomes.**

LIMITATIONS

- Data from the NHWS are self-reported and may be subject to methodological limitations, such as recall bias.
- As this was a cross-sectional study, no causal relation between insomnia symptoms in MDD and outcomes can be made.

ACKNOWLEDGMENTS

DISCLOSURES

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