Healthcare Resource Utilization Associated with Major Depressive Disorder with Insomnia Symptoms: A Retrospective Cohort Study in Hungary

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INTRODUCTION

- Insomnia is a core symptom of an acute mood episode in major depressive disorder (MDD) and the prevalence of insomnia is much higher in patients with MDD than in the general population (~10%).[1]
- Insomnia symptoms (IS) in MDD are associated with higher risk of suicidality and IS as residual symptoms (i.e., persistent insomnia in the absence of current mood symptoms) are linked to greater risk of relapse of depression.[2,3]
- Given its clinical implications, the presence of IS has been associated with incremental healthcare resource use and costs among patients with MDD.[4]

OBJECTIVES

- To compare the healthcare resource utilization and overall survival in Hungary among patients with MDD with IS (MDD-IS) vs patients with MDD without IS (MDD-nonIS).

METHODS

Data Source

- This study used data from the Hungarian National Health Insurance Fund (NHIF) database that were collected longitudinally.
  - The NHIF database contains detailed healthcare provision data for the whole population of approximately 10 million citizens in Hungary, as the mandatory public health insurance covers the entire Hungarian population.
  - These provision data include the basic demographic data (e.g., date of birth, region, gender, date of death, etc.) and all reimbursed health care services (inpatient and outpatient care) and medications.
- Data of patients between January 1, 2009 and December 31, 2020 were used in this study.

Study Patients

- MDD was identified as the presence of at least
  - 1 record of a diagnosis of MDD (ICD10 F32*/F33*) and 1 prescription of antidepressant(s) or
  - 2 records of the diagnosis of MDD

  within 90 days of each other between January 1, 2010 and December 31, 2020.
- Only patients aged between ≥18 and <65 years were included.
- **Patients were classified into 2 groups:**
  - **MDD-IS:** patients with MDD plus a diagnosis of insomnia (ICD10 G47*, F51*) and/or prescriptions for hypnotics.
    - The index date was the date of first diagnosis of insomnia or first prescription for hypnotics after the MDD diagnosis.
  - **MDD-nonIS:** patients with MDD with no prescriptions for hypnotics and no diagnosis of insomnia.
    - The index date was randomly selected from the days within the first year from the MDD diagnosis when the patient had any healthcare-related encounter.
- Patients in the MDD-IS and MDD-nonIS groups were matched using a 1:1 propensity score matching algorithm based on age, gender, location (region) of residence, and comorbidities.

Study Measures

- Number of all-cause outpatient events and inpatient stays, and number of days spent in hospital were evaluated for the total available follow-up and per patient per year metrics were calculated.
- In addition to all-cause resource use, MDD-related healthcare resource utilization (defined as the primary diagnosis, the code being F32*/F33*) was also calculated.
- Overall survival was measured from the index date to the death of patients due to any cause within 2 years; patients were censored if they were alive at the end of 2 years from the index date.

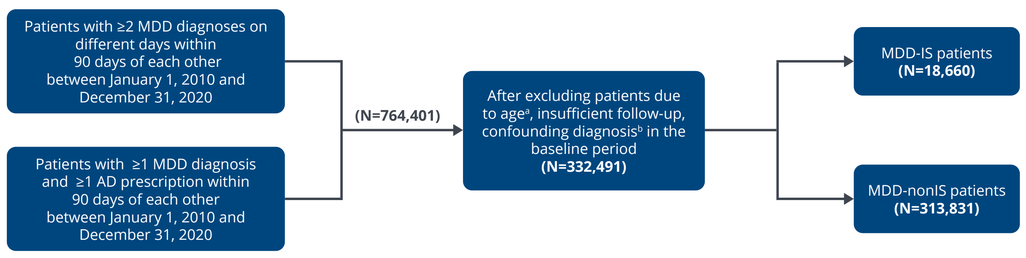
Statistical Analyses

- Means, standard deviations (SD), medians, and interquartile ranges were reported for continuous variables; frequencies and percentages were reported for categorical variables.
- Healthcare resource use was compared using chi-square tests for proportions of patients with a given type of healthcare encounter and using t-tests for number of visits and length of stay.
- Overall survival was estimated using Kaplan-Meier estimation and was compared between MDD-IS and MDD-nonIS using a log-rank test. Cox proportional hazards regression was used to estimate the hazard ratio (HR) of MDD-IS vs MDD-nonIS.
- Data analysis was conducted using R version 4.2.2. (R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.)

RESULTS

- A total of 332,491 patients with MDD were identified, of which, 18,660 were MDD-IS and 313,831 were MDD-nonIS (**Figure 1**).

Figure 1. Sample selection



[a]Patients aged between ≥18 and <65 years were included; [b]Bipolar disorder, schizophrenia, dementia, or organic mood disorders.
AD, antidepressant; MDD, major depressive disorder; MDD-IS, major depressive disorder with insomnia symptoms; MDD-nonIS, major depressive disorder without insomnia symptoms.

- MDD-IS and MDD-nonIS groups were well balanced after the propensity score matching, with standardized differences of <0.1 for all variables included in the propensity score (**Table 1**).

Table 1. Baseline characteristics

	Before matching			After matching		
	MDD-IS	MDD-nonIS	p	MDD-IS	MDD-nonIS	Standardized difference
Total patients, n	18,660	313,831		18,660	18,660	
Age, years						
Mean	49.2	46.3	<0.001	49.2	49.2	0.005
SD	11.1	12.1				
Median	51.5	48.1				
Range (min, max)	(18.0, 64.9)	(18.0, 64.9)				
IQR (Q25, Q75)	(41.8, 58.2)	(37.4, 56.6)				
Women, %	62.3	64.7	<0.001	62.3	62.9	−0.011
Comorbidities, %						
Malignant neoplasms (C*)	5.0	4.2	<0.001	5.0	5.0	0.002
Acute myocardial infarction (I21)	0.7	0.6	0.259	0.7	0.6	0.009
Other acute ischaemic heart diseases (I24)	0.4	0.3	0.094	0.4	0.3	0.004
Cerebrovascular diseases (I60 – I64, G45)	6.8	5.7	<0.001	6.8	6.9	−0.003
Bronchitis, emphysema, asthma (J40, J41, J42, J43, J45)	6.7	6.2	0.014	6.7	6.7	−0.003
Diabetes mellitus (E10 – E14)	9.2	8.1	<0.001	9.2	9.0	0.007
Atherosclerosis (I70)	3.0	2.4	<0.001	3.0	3.0	−0.001
Liver disease (K70 – K77)	2.1	1.6	<0.001	2.1	2.1	−0.002
Epilepsy (G40, G41)	2.6	2.0	<0.001	2.6	2.6	0.000
Substance use disorders (F10 – F19)	4.8	3.2	<0.001	4.8	4.9	−0.002
Anxiety and stressor-related disorders (F40 – F43)	37.8	30.7	<0.001	37.8	37.7	0.001
Personality disorders (F60, F61, F62, F68, F69)	1.3	0.9	<0.001	1.3	1.4	−0.007

IQR, interquartile range; MDD-IS, major depressive disorder with insomnia symptoms; MDD-nonIS, major depressive disorder without insomnia symptoms; SD, standard deviation.

Healthcare Resource Utilization

- Patients with MDD-IS received significantly more all-cause and MDD-related inpatient care and all-cause outpatient specialist visits per year than patients with MDD-nonIS (**Table 2**).

Table 2. Healthcare resource utilization

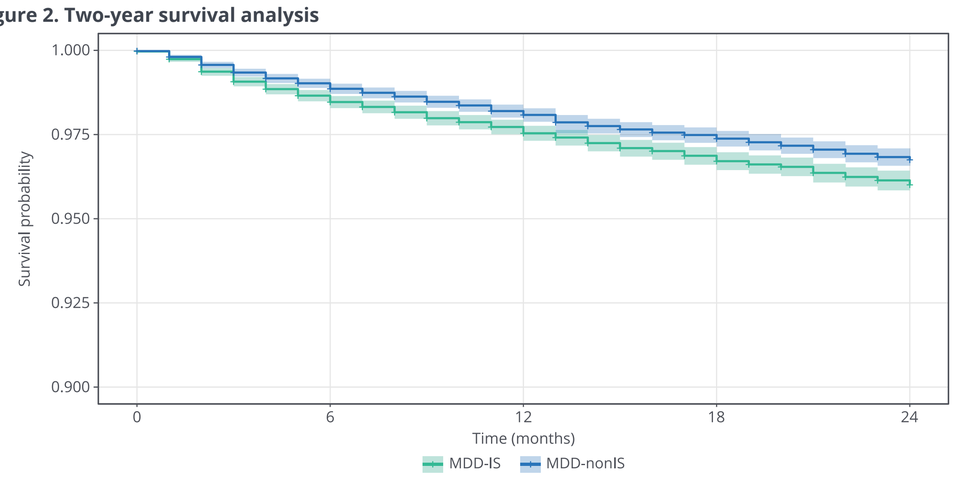
	MDD-IS	MDD-nonIS	p
Total patients, n	18,660	18,660	
All-cause			
Patients with ≥1 inpatient admission, n (%)	12,031 (64.5)	11,582 (62.1)	<0.001
Inpatient admissions (per year)			
Mean (SD)	3.4 (29.0)	0.9 (5.0)	<0.001
Median (Q25, Q75)	0.3 (0.0, 0.9)	0.2 (0.0, 0.6)	
Hospital days (per year)			
Mean (SD)	44.4 (412.1)	11.4 (74.8)	<0.001
Median (Q25, Q75)	1.3 (0.0, 9.0)	0.8 (0.0, 5.6)	
Patients with ≥1 outpatient visit, n (%)	18,095 (97.0)	18,286 (98.0)	<0.001
Outpatient visits (per year)			
Mean (SD)	12.9 (17.0)	12.0 (16.3)	<0.001
Median (Q25, Q75)	9.0 (4.3, 16.4)	8.3 (4.0, 15.2)	
MDD-related			
Patients with ≥1 inpatient admission, n (%)	2,857 (15.3)	1,223 (6.6)	<0.001
Inpatient admissions (per year)			
Mean (SD)	0.2 (1.7)	0.1 (1.4)	<0.001
Hospital days (per year)			
Mean (SD)	2.7 (19.8)	0.8 (10.2)	<0.001

MDD, major depressive disorder; MDD-IS, major depressive disorder with insomnia symptoms; MDD-nonIS, major depressive disorder without insomnia symptoms; Q, quartile; SD, standard deviation.

Survival Analysis

- Compared to patients with MDD-nonIS, patients with MDD-IS had worse survival in the first two years after diagnosis (HR=1.23 [95% CI: 1.11-1.38]) (**Figure 2**).

Figure 2. Two-year survival analysis



MDD-IS, major depressive disorder with insomnia symptoms; MDD-nonIS, major depressive disorder without insomnia symptoms.

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Presented at ISPOR Europe 2023; November 12-15, 2023; Copenhagen, Denmark

CONCLUSIONS

Patients with MDD-IS had significantly higher healthcare resource utilization than those with MDD-nonIS.

Findings demonstrate the real-world burden of IS among Hungarian patients with MDD, emphasizing the importance of systematic evaluation and treatment of IS in these patients.

STRENGTHS AND LIMITATIONS

- The Hungarian NHIF database utilized in this study has nationwide coverage, encompassing all major segments of healthcare and provides longitudinal follow-up data of 12 years for research.
- As information on death is essential to the termination of patient insurance, death data are considered reliable in the database; however, data on cause of death are not available for all deaths or are inconsistent even when they are available.
- The primary aim of the data collection is for financial and reimbursement purposes not for clinical evaluation of patients; thereby, no data are available on clinical values, such as disease severity indices.
- Propensity score matching adjusts for bias due to observed covariates, but it does not adjust for bias caused by unobserved covariates.

ACKNOWLEDGEMENTS:
Priya Ganpathy, MPH, CMPP (SIRO Clinpharm UK Ltd) and Harry Ma, PhD, CMPP (Janssen Global Services, LLC) provided editorial support. Amit Kavle (SIRO Clinpharm Pvt. Ltd., India) provided graphic design/poster layout support.

DISCLOSURES:
PK, **JGO**, **QC**, **JR**, **ND** and **ZZ** are employees of Janssen and may hold company stock or stock options. **LF** was an employee of Janssen at the time of study. **GS** received consulting fees from Janssen/Janssen-Cilag and KRKA; speaker's honoraria from Janssen/Janssen-Cilag, Lundbeck, KRKA, Gedeon Richter, Mylan and Egis/Servier. **PD** received consulting fees from Janssen/Janssen-Cilag. **KV** has nothing to disclose.

This study was supported by Janssen Global Services, LLC