

# Association of Major Depressive Disorder With Insomnia Symptoms With Healthcare Resource Use and Cardiovascular and Metabolic Conditions – Analysis of the National Health & Nutrition Examination Survey

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## Introduction

- Major depressive disorder (MDD) is a prevalent mental health condition with a prevalence of 8.2% (21.4 million adults) in the US<sup>1</sup>
- MDD is a heterogeneous condition with varying symptoms such as depressed mood, anhedonia, poor appetite, concentration difficulties and sleep disturbances<sup>1,2</sup>
- Insomnia is one of the key symptoms of MDD and worsening of depressed mood exacerbates insomnia symptoms and vice versa<sup>2,3</sup>
- Previous research has found that MDD with insomnia symptoms (MDDIS) is associated with increased risk of relapse, poor health-related quality of life and greater economic burden<sup>4-6</sup>
- Cardiovascular and metabolic conditions are common co-existing conditions in patients with MDD; however, little is known about the impact of MDDIS on the prevalence and worsening of these comorbidities in patients with MDD

## Objective

- To examine the association of MDDIS with cardiovascular and metabolic (CVM) conditions and healthcare resource utilization using nationally representative data from the National Health and Nutrition Examination Survey (NHANES)

## Methods

### Data source

- This study analyzed data from the NHANES database (2013-2014, 2015-2016, 2017-2018), which is a publicly available survey of the noninstitutionalized civilian US population
- The NHANES sample is selected using a complex, 4-stage sample design and the sample weights can be used to derive national estimates

### Study design

- This was a cross-sectional study of adults identified from the NHANES database
- The study considered survey questions that were administered during the 3 survey cycles mentioned above
- Patients with MDD were identified using a 9-item Patient Health Questionnaire (PHQ-9) total score  $\geq 10$  (score range 0–27)
- The PHQ-9 instrument asks participants about the frequency of depressive symptoms during the previous 2 weeks
- Response categories for PHQ-9 include the following
  - 0: “not at all”
  - 1: “several days”
  - 2: “more than half the days”
  - 3: “nearly every day”
- Insomnia symptoms were identified based on self-report of trouble sleeping, using the question: “Have you ever told a doctor or other health professional that you have trouble sleeping?”
- The study sample was selected based on the following inclusion criteria:
  - Patients aged  $\geq 18$  years
  - Patients having nonmissing data for both:
    - PHQ-9 score
    - Self-report of trouble sleeping
- Among patients with MDD,
  - MDDIS was defined as having MDD and answering “Yes” to the ‘trouble sleeping’ question
  - MDD w/o IS was defined as having MDD and answering “No” to the ‘trouble sleeping’ question

### Study outcomes

- Healthcare resource utilization included inpatient stays, outpatient office visits (all-cause) and mental health professional visits
- Inpatient use was defined as an overnight hospital stay in the past year
- Outpatient visits were defined as the number of times patients received healthcare in an outpatient/office-based setting
- Mental health professional visit was defined as presence of any mental health professional visit in the past year
- Work productivity limitation was defined as the patient being unable to work during the past week due to health reasons
- CVM conditions were defined as below
  - Diabetes was defined as either a self-reported diagnosis by a physician (ever told by a doctor that you have diabetes), plasma hemoglobin A1c (HbA1c)  $\geq 6.5\%$ , or fasting plasma glucose  $\geq 7.0$  mmol/L
  - Prediabetes was defined as the presence of any of the following criteria: 1) had been told by a doctor that you have prediabetes; 2) HbA1c between 5.7% and 6.4%; 3) fasting blood glucose between 5.6 to 6.9 mmol/L in subjects without the defined diabetes
  - Hypertension was defined as systolic blood pressure (SBP)  $\geq 130$  mm Hg, diastolic blood pressure (DBP)  $\geq 80$  mm Hg, self-reported diagnosis by a physician (had been told by a doctor that you have hypertension on 2 or more different visits), or self-reported prescriptions for hypertension
  - Presence of coronary heart disease and stroke was reported if the doctor or healthcare professional ever told the patient that they had those conditions

### Statistical analysis

- MDDIS and MDD w/o IS were balanced using propensity score–based inverse probability of treatment weighting (IPTW), controlling for baseline demographics
- Study outcomes were compared between MDDIS and MDD w/o IS using descriptive statistics and weighted (IPTW and sample weights) logistic regression models
- The findings reported here include sample counts and weighted percentages

## Results

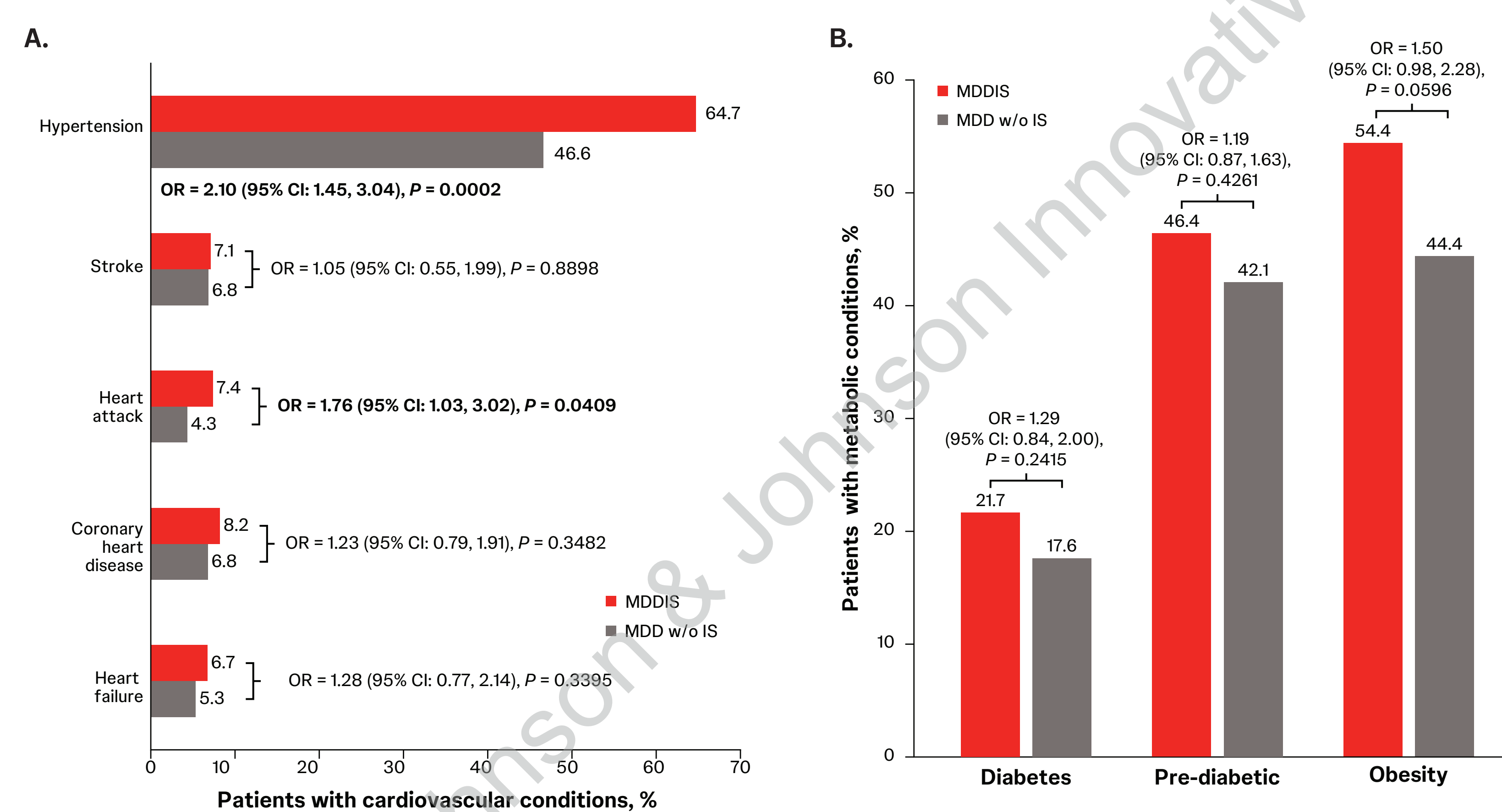
### Patient characteristics

- From a sample of 15,574 adults, 1383 (8.2%) had MDD (PHQ-9  $\geq 10$ ) and 853 (5.4%) had MDDIS
- Of 1383 patients with MDD, 853 (66%) were categorized as having MDDIS and 530 (34%) were categorized as having MDD w/o IS
- Compared with patients with MDD w/o IS, patients with MDDIS were older (mean, 49.0 vs 43.3 years), White (68.3% vs 53.5%), married (39.5% vs 29.8%) and college educated (17.1% vs 13.4%) (Table 1)
- The proportion of females was similar between those with MDDIS (64.6%) and MDD w/o IS (62.9%)

### Cardiovascular and metabolic conditions

- Patients with MDDIS versus MDD w/o IS had significantly higher ( $P < 0.05$ ) odds for heart attack (7.4% vs 4.3%; odds ratio [OR]: 1.76) and hypertension (64.7% vs 46.6%; OR: 2.10) (Figure 1A)
- Findings for obesity (54.4% vs 44.4%; OR: 1.50) and diabetes (21.7% vs 17.6%; OR: 1.29) were not statistically significant but showed a similar trend (Figure 1B)

Figure 1: Associations between MDDIS and cardiovascular and metabolic conditions in patients with MDD



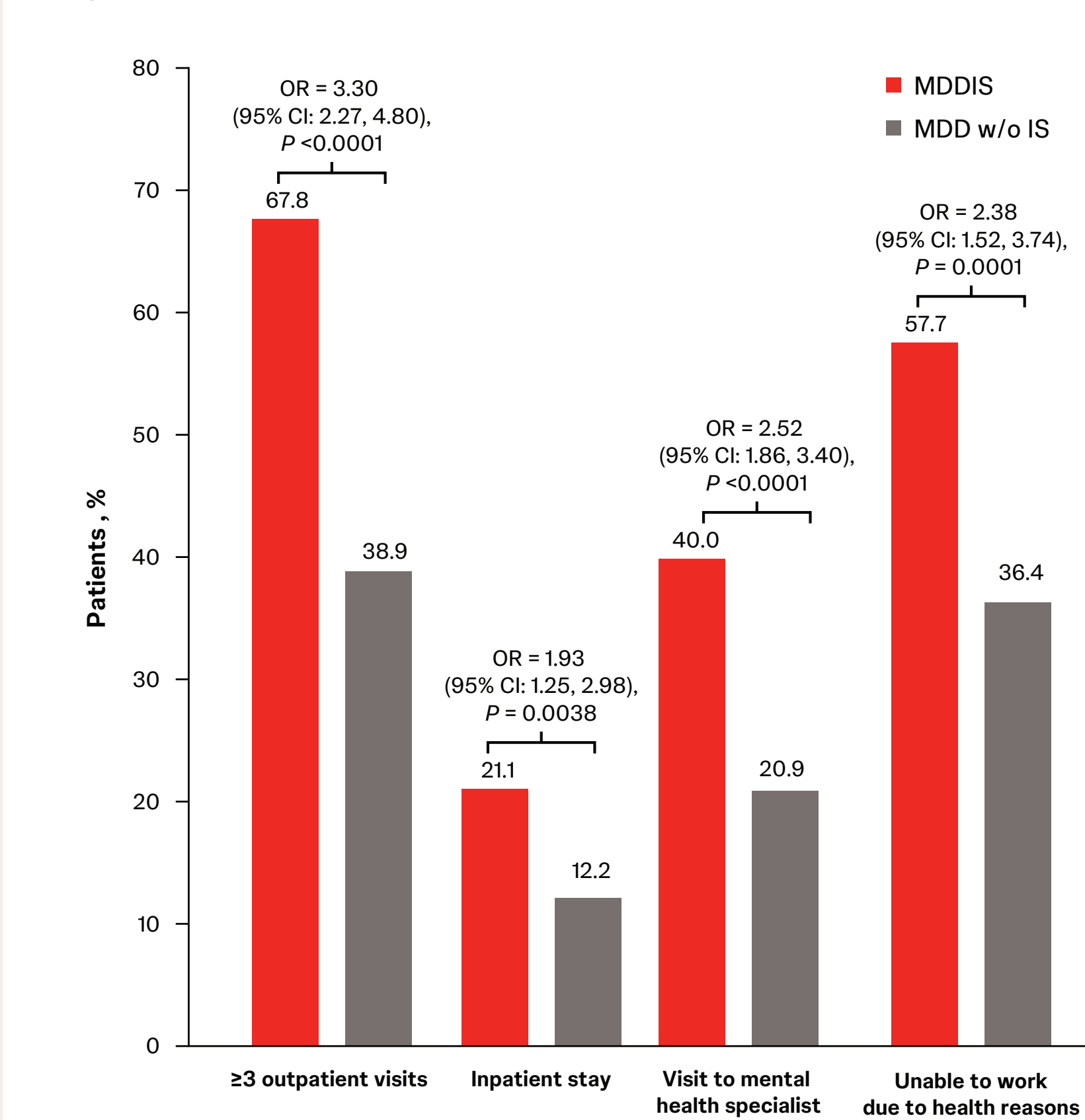
MDD, major depressive disorder; MDDIS, major depressive disorder with insomnia symptoms; MDD w/o IS, major depressive disorder without insomnia symptoms; OR, odds ratio.

Table 1: Demographics of study participants with MDD

|                       | MDDIS      |      | MDD w/o IS |      | P value |
|-----------------------|------------|------|------------|------|---------|
|                       | N          | %    | N          | %    |         |
| <b>Sex</b>            | 853        |      | 530        |      |         |
| Men                   | 308        | 35.4 | 207        | 37.1 | 0.6040  |
| Women                 | 545        | 64.6 | 323        | 62.9 |         |
| <b>Age</b>            |            |      |            |      |         |
| Mean (SD)             | 49.0 (0.8) |      | 43.3 (1.2) |      | <0.0001 |
| 18-24                 | 67         | 7.9  | 94         | 22.0 | 0.0002  |
| 25-44                 | 228        | 32.1 | 158        | 35.5 |         |
| 45-64                 | 375        | 42.4 | 162        | 25.3 |         |
| 65+                   | 183        | 17.7 | 116        | 17.1 |         |
| <b>Race</b>           |            |      |            |      |         |
| Mexican American      | 110        | 6.4  | 97         | 11.6 | <0.0001 |
| Other Hispanic        | 102        | 6.3  | 74         | 9.3  |         |
| Non-Hispanic White    | 384        | 68.3 | 178        | 53.5 |         |
| Non-Hispanic Black    | 168        | 10.1 | 120        | 15.3 |         |
| Non-Hispanic Asian    | 29         | 1.6  | 33         | 3.4  |         |
| Other                 | 60         | 7.2  | 28         | 7.0  |         |
| <b>Marital status</b> |            |      |            |      |         |
| Married               | 308        | 39.5 | 159        | 29.8 | 0.0040  |
| Not married           | 517        | 60.5 | 337        | 70.2 |         |
| <b>Education</b>      |            |      |            |      |         |
| Less than high school | 243        | 19.2 | 174        | 26.0 | 0.0228  |
| High school           | 485        | 63.8 | 262        | 60.6 |         |
| Above college         | 98         | 17.1 | 58         | 13.4 |         |

MDDIS, major depressive disorder with insomnia symptoms; MDD w/o IS, major depressive disorder without insomnia symptoms. Data are expressed as the unweighted number of participants and survey-weighted percentages to be nationally representative. Data represents frequency and percentages before inverse probability of treatment weighting (IPTW).

Figure 2: Associations between MDDIS and healthcare resource utilization and work productivity in patients with MDD



MDD, major depressive disorder; MDDIS, major depressive disorder with insomnia symptoms; MDD w/o IS, major depressive disorder without insomnia symptoms; OR, odds ratio.

### Healthcare resource utilization and work productivity

- Results from weighted logistic regression analyses (Figure 2) found that MDDIS patients had significantly ( $P < 0.05$ ) higher odds than those with MDD w/o IS for
  - $\geq 3$  office visits (67.8% vs 38.9%; OR: 3.30)
  - Hospitalization (21.1% vs 12.2%; OR: 1.93)
  - Mental health professional visit (40.0% vs 20.9%; OR: 2.52)
  - Inability to work due to health reasons (57.7% vs 36.4%; OR: 2.38)

## Key Takeaway



There remains a critical need for therapies that effectively address both depressive and insomnia symptoms in patients with MDD

## Limitations



NHANES is a cross-sectional database; therefore, only associations can be derived between presence of insomnia symptoms in MDD and outcomes; causality cannot be implied



Current findings do not distinguish between prevalent versus incident cardiovascular and metabolic conditions



The study did not assess depression treatment use due to lack of prescription medication data in NHANES



Study findings are subject to respondent recall and response bias due to the self-reported nature of the survey questionnaire data



Findings from this study may not be generalizable to institutionalized or nursing home populations

## Conclusions



MDDIS was associated with higher healthcare resource utilization, reduced work productivity, and poorer CVM health



Study findings indicate that the burden of MDDIS extends beyond mental health, contributing to broader clinical and societal impacts



There remains a critical need for therapies that effectively address both depressive and insomnia symptoms in patients with MDD

## Acknowledgments

The authors thank Alicia K Campbell, PharmD, for her assistance in writing the abstract and the study protocol. Editorial assistance was provided by ApotheCom, Yardley, PA, which was funded by Johnson & Johnson.

## Disclosures

HK, ZL, KJ, GL, CB, and ZZ are employees of Johnson & Johnson and hold stock in the company.

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This study was funded by Johnson & Johnson.

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