Impact of Major Depressive Disorder with Prominent Anhedonia on Polypharmacy, Resource Utilization, and Humanistic Outcomes in the United States

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Background

- Major depressive disorder (MDD) is a serious mental health condition that imposes vast economic, medical, and personal burdens.[1–5]
- About 21 million adults in the US had at least one depressive episode in 2020; the 12-month prevalence was approximately 9.2%.[6,7]
- Anhedonia, a key symptom and diagnostic criterion of MDD, is characterized by deficits in pleasure and/or interest[8] and has been linked to worse prognosis, lower rate of remission, and higher functional impairments and suicidality in individuals with MDD.[9–12]
- Although 40%–70% of individuals with MDD exhibit symptoms of anhedonia,[13,14] little is known about the clinical and humanistic burden associated with prominent anhedonia in individuals with MDD.

Objectives

Assess the clinical and humanistic burden associated with prominent anhedonia in patients with MDD.

Methods

Study Design and Data Source

- Pooled cross-sectional study using data from the Medical Expenditure Panel Survey (MEPS) (2016 through 2019).

Study Cohorts and Measures

- Respondents with MDD were identified as those with at least one record in the MEPS medical conditions file containing an International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) code of F32* (depressive episode) or F33* (major depressive disorder, recurrent).
- The presence and degree of anhedonia were assessed using the first item of the Patient Health Questionnaire-2 (PHQ-2), administered during the second and fourth interview rounds of each MEPS panel ("During the past two weeks, bothered by having little interest or pleasure in doing things").
- We classified respondents with MDD into two groups, based on their MDD and anhedonia status:
  - Respondents with MDD who reported more than half the days (2) or nearly every day (3) were classified as having MDD with prominent anhedonia (MDD-ANH).
  - Respondents with MDD who reported not at all (0) or several days (1) were classified as having MDD with no/low anhedonia (other-MDD).

Table 1. Pooled Prevalence of Anhedonia in Patients with MDD

Study Cohort	PHQ-2 item 1 score	Unweighted N (%)	Weighted %
Other-MDD	0 (none) 1 (several days)	4,037 (79.0)	81.0
MDD-ANH	2 (more than half the days) 3 (almost every day)	1,075 (21.0)	19.0

Abbreviation: PHQ-2 = Patient Health Questionnaire-2

Sample Selection

Included

- Respondents who were at least 18 years of age during the first interview round of each year.

Excluded

- Respondents with bipolar disorder, dementia, Alzheimer's disease, and other neurological conditions during the calendar year.

Use of Healthcare Services

- Use of pharmacologic treatments (medications) was measured by the proportion of respondents who used specific medications or medication classes and by the number of unique medications respondents used.
  - Medications were classified as psychotropic or non-psychotropic; psychotropic medications were further classified into MDD or non-MDD (other) treatment.
- Polypharmacy was defined as the concomitant use of two or more psychotropic medications during the same calendar year.
- The numbers of visits and hospitalizations (per 100 persons) were assessed for office-based/outpatient visits, emergency department (ED) visits, inpatient hospitalizations, and home health services.
  - These measures were also defined for mental health- and non-mental health-related services.

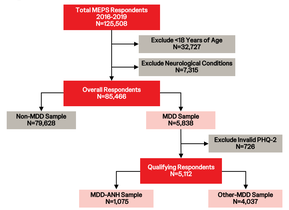
Health-related Quality of Life (HRQoL)

- HRQoL was assessed using the 12-item Short Form Health Survey Version 2 (SF-12v2) instrument.
  - The Physical Component Summary (PCS) score.
  - The Mental Component Summary (MCS) score.
  - The PCS and MCS scores range from 0 to 100, with 0 representing the worst and 100 representing the best health status; 50 represents the national average.

Statistical Analyses

- The MDD-ANH and other-MDD groups were compared using propensity score-based inverse probability weighting to minimize the effect of confounding and selection bias on outcomes.
- All outcomes were summarized by their weighted means (continuous variables) or weighted proportions (categorical variables) and their corresponding 95% confidence intervals (CIs).
- Weighting accounted for the non-MDD group as well; findings presented in this poster focus on respondents with MDD-ANH and other-MDD, only

Figure 1. Sample Selection Flowchart



Results

Respondent Characteristics (Tables 1–2; Figure 1)

- We identified 5,838 (7.2%) respondents with MDD, of whom 5,112 respondents had a valid response for presence and degree of anhedonia in the first item of PHQ-2.
  - 1,075 individuals with MDD had MDD-ANH.
  - 4,037 individuals with MDD had other-MDD.
- Selected respondents were, on average (mean), 50 years of age, 70% were female, >87% were White, and about 66% were covered by private health insurance plans.
- Respondents with MDD-ANH were mostly Black (9.0% vs. 5.9%), previously married (36.6% vs. 28.5%), had low to negative income (44.8% vs. 27.9%), and had more comorbid conditions as measured by the Charlson comorbidity Index (0.8 vs. 0.6) than those in the other-MDD group.

Table 2. Selected Respondent Characteristics (Unweighted)

Characteristic	MDD-ANH (N=1,075)	Other-MDD (N=4,037)
Age in years, mean	50.6	49.5
Sex, %		
Female	68.1	70.5
Male	31.9	29.5
Race, %		
White only	84.7	87.8
Black only	9.0	5.9
Other race	6.2	6.2
Marital status, %		
Never married	25.4	25.7
Married	38.0	45.9
Divorced, separated, widowed	36.6	28.5
Income level, %		
Low to negative (<200% FPL)	44.8	27.9
Middle (200% to <400% FPL)	27.4	29.8
High (≥400% FPL)	27.8	42.3
Insurance coverage during the year, %		
Any private coverage	53.1	69.5
Only public coverage	43.5	26.5
Uninsured	3.5	4.0
Charlson comorbidity index, mean	0.8	0.6

Abbreviations: FPL = federal poverty level; MDD = major depressive disorder; MDD-ANH = MDD with prominent anhedonia; other-MDD = MDD with no/low anhedonia

Use of Healthcare Services (Table 3; Figures 2-3)

- Respondents with MDD-ANH had more healthcare visits than those with other-MDD:
  - Office/outpatient visits: 1,305.2 per 100 persons vs. 896.9 per 100 persons
  - ED visits: 33.1 per 100 persons vs. 22.6 per 100 persons
  - Inpatient hospitalizations 14.3 per 100 persons vs. 9.9 per 100 persons
  - Home health visits: 38.1 per 100 persons vs. 18.9 per 100 persons

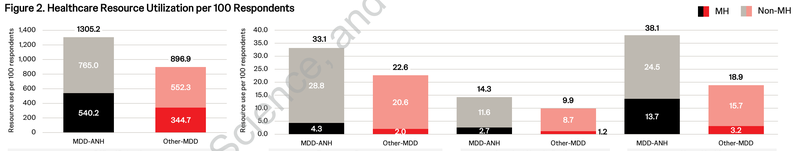
Use of Antidepressants and Psychotropic Medications (Table 4; Figure 4)

- Proportionately more respondents with MDD-ANH used serotonin modulators, tricyclic antidepressants, bupropion + serotonin modulators, and bupropion + selective serotonin reuptake inhibitors (SSRIs) than respondents with other-MDD.
- Respondents with MDD-ANH were also more likely to have used the following medications than those with other-MDD:
  - Any psychotropic medications: 75.7% vs. 71.7%
  - >1 psychotropic medications: 43.2% vs. 27.8%
  - Non-MDD psychotropic medications: 42.8% vs. 25.3%
  - Any non-psychotropic medications: 75.0% vs. 72.2%
- Polypharmacy was slightly more prevalent among respondents with MDD-ANH than other-MDD (43.2% vs. 27.8%); respondents with MDD-ANH were about twice as likely as those with other-MDD to have used medications from other classes in addition to antidepressants:
  - Mood stabilizers: 13.0% vs 7.1%
  - Antipsychotics: 6.2% vs 2.9%
  - Anxiolytics: 6.5% vs 3.2%
  - Attention-deficit hyperactivity disorder (ADHD) medications: 7.1% vs 4.3%

HRQoL (Figure 5)

- Mental HRQoL, as measured by the SF-12 MCS, was substantially lower for respondents with MDD-ANH (30.9) than for those with other-MDD (47.1).
- Physical HRQoL, as measured by the SF-12 PCS, was also lower for respondents with MDD-ANH (46.2) than for those with other-MDD (50.3).

Figure 2. Healthcare Resource Utilization per 100 Respondents



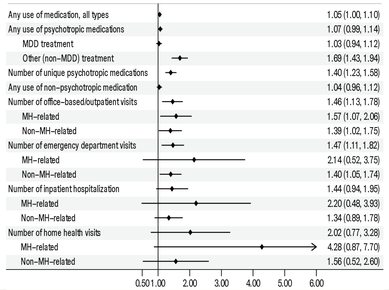
Abbreviations: MDD-ANH = MDD with prominent anhedonia; MH = mental health; other-MDD = MDD with no/low anhedonia

Table 3. Use of Healthcare Services

Use Measure	MDD-ANH	Other-MDD
All medication types, any use, % (95% CI)	90.2 (86.4, 93.9)*	85.7 (83.7, 87.8)*
Psychotropic, any use, % (95% CI)	75.7 (70.7, 80.6)*	71.0 (68.4, 73.6)*
MDD treatment, %	67.8 (62.6, 73.1)	66.0 (63.2, 68.7)
NDRI	16.2 (11.6, 20.8)	12.7 (11.0, 14.4)
Serotonin modulator	7.0 (3.8, 10.2)*	2.7 (2.0, 3.3)*
SNRI	14.0 (10.2, 17.9)	11.2 (9.7, 12.6)
SSRI	47.8 (42.3, 53.3)	46.5 (43.6, 49.3)
Tetracyclic antidepressant	2.1 (0.7, 3.6)	1.3 (0.8, 1.8)
Tricyclic antidepressant	3.6 (1.5, 5.7)*	1.6 (1.2, 2.0)*
Bupropion + serotonin modulator	2.5 (0.03, 4.9)*	0.5 (0.2, 0.8)*
Bupropion + SNRI	1.9 (0.6, 3.2)	1.2 (0.7, 1.7)
Bupropion + SSRI	9.1 (5.5, 12.8)*	4.4 (3.2, 5.5)*
Other (non-MDD) treatment, %	42.8 (37.3, 48.3)*	25.3 (23.3, 27.4)*
No. of unique psychotropic medications, mean (95% CI)	6.8 (6.5, 7.1)*	6.3 (6.2, 6.5)*
Non-psychotropic medication, any use, % (95% CI)	75.0 (69.6, 80.5)*	72.2 (69.7, 74.7)*

* Statistically significant differences between MDD-ANH vs other-MDD, *ps* ≤ 0.01
Abbreviations: MDD = major depressive disorder; MDD-ANH = MDD with prominent anhedonia; NDRI = norepinephrine–dopamine reuptake inhibitor; other-MDD = MDD with no/low anhedonia; SNRI = serotonin–norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor

Figure 3. Rate Ratios Comparing Healthcare Resource Utilization between Study Cohorts



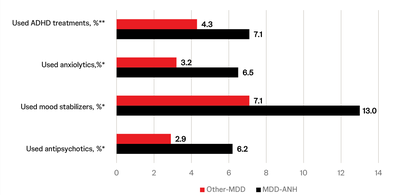
Abbreviations: ED = emergency department; MDD = major depressive disorder; MDD-ANH = MDD with prominent anhedonia; MH = mental health; other-MDD = MDD with no/low anhedonia

Table 4. Prevalence of Psychotropic Polypharmacy Use between Study Cohorts

Polypharmacy Use	MDD-ANH	Other-MDD
Polypharmacy, any use, % (95% CI)	43.2 (37.9, 48.5)	27.8 (25.6, 30.0)
Within same class, % (95% CI)		
Used 2 unique medications	17.2 (13.1, 21.3)*	11.3 (9.8, 12.8)*
Used 3 unique medications	4.3 (2.1, 6.5)*	0.9 (0.6, 1.2)*
Used ≥4 unique medications	0.9 (0.0, 1.8)*	0.03 (0.0, 0.08)*
Across different classes, % (95% CI)		
Used 2 unique classes	26.3 (21.4, 31.1)*	17.1 (15.4, 18.8)*
Used 3 unique classes	7.7 (4.9, 10.4)*	3.2 (2.6, 3.9)*
Used ≥4 unique classes	2.4 (1.1, 3.7)*	0.9 (0.4, 1.3)*

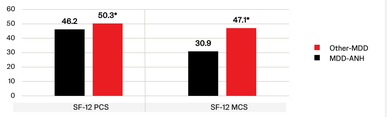
Note: Costs expressed in 2022 US dollars
* Statistically significant differences between MDD-ANH vs other-MDD, p<0.05
Abbreviations: MDD-ANH = MDD with prominent anhedonia; other-MDD = MDD with no/low anhedonia

Figure 4. Psychotropic Polypharmacy Use in Combination with MDD Treatment



* Statistically significant differences between MDD-ANH and other-MDD, *ps*≤*0.01*
** Statistically significant differences between MDD-ANH and other-MDD, *p<0.05*
Abbreviations: ADHD = attention-deficit hyperactivity disorder; MDD-ANH = MDD with prominent anhedonia; other-MDD = MDD with no/low anhedonia

Figure 5. Health-related Quality of Life



* Statistically significant differences between MDD-ANH vs other-MDD, *p*=0.05
Abbreviations: MCS = mental component summary; MDD-ANH = MDD with prominent anhedonia; other-MDD = MDD with no/low anhedonia; PCS = physical component summary; SF-12 = 12-item Short Form Health Survey

Conclusions

- Prominent anhedonia in MDD was associated with high psychotropic medication use, polypharmacy use, and healthcare resource use, as well as poor HRQoL.
- Higher psychotropic medication and polypharmacy use, along with poorer HRQoL, suggest that it is difficult to treat MDD — specifically patients with prominent anhedonia.
- Higher polypharmacy use in combination with MDD-related treatments indicates higher clinical burden and unmet needs among individuals with MDD with prominent anhedonia, compared to individuals without prominent anhedonia.
- The impact of MDD with prominent anhedonia extends beyond mental health, as reflected by higher use of non-MDD and non-mental health-related medications and healthcare services.
- These findings suggest that anhedonia severity should be considered in routine assessment of MDD; identifying targeted treatments may reduce clinical and humanistic burden associated with MDD

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Key Contributors

Study conception and design (HK, MLG, RG, TD, AC); data analysis (CSM); data interpretation (HK, MLG, RG); draft poster preparation (RG); final approval (HK, TD, AC)

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