Clinical Burden of Patients Diagnosed with Major Depressive Disorder with versus without Prominent Anhedonia Using a Real-World Dataset in the United States

Kale H[1], Severtson SG[2], Feldman BS[2], Drissen T[1], Dwibedi N[1], Cutler AJ[3], Marci CD[2, 4]

[1]Janssen Scientific Affairs, LLC, a Johnson & Johnson Company, Titusville, NJ, USA, [2]OM1, Inc., Boston, MA, USA, [3]SUNY Upstate Medical University, Lakewood Ranch, FL, USA, [4]Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

Background

- Major depressive disorder (MDD) is a highly prevalent disease in the United States general population, with a 20% lifetime prevalence among adults [1].
- Anhedonia is a common symptom and a diagnostic criterion in MDD. In the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition anhedonia is described as “markedly diminished interest or pleasure in all, or almost all activities most of the day, nearly every day.”
- Prevalence estimates of anhedonia among individuals with MDD are observed to be 40-70% [2,3].
- The goal of this study is to understand the symptom burden, characteristics and treatment patterns of patients diagnosed with MDD with prominent anhedonia (MDD-ANH) and patients with no/low levels of anhedonia (Other-MDD).

Methods

Data Source and Study Population

- Data are from a real-world dataset of over 500,000 patients with MDD in the US with linked claims and electronic medical record data (OM1, Inc. Boston MA).
- Newly diagnosed MDD patients with their first recorded PHQ-9 within one month of diagnosis (baseline score) were included.

Study Design

- This retrospective cohort study used the Patient Health Questionnaire 9-Items (PHQ-9) to assess depression symptoms at baseline and over time among MDD patients with prominent anhedonia (MDD-ANH) and with no or low anhedonia (Other-MDD) between January 2013 through August 2023.
- Prominent anhedonia was defined as a score of ≥2 on Item 1 ”Little interest or pleasure in doing things” of the PHQ-9 among moderately to severely depressed patients (PHQ-9 total score of ≥10) at baseline.

Outcome Definitions

- Remission (defined as PHQ-9 total score < 5) was assessed during four follow-up time windows (>0-3, >3-6, >6-9, and >9-12 months).
- If PHQ-9 scores were missing for patient encounters, a machine learning model was used to estimate PHQ-9 scores using routinely recorded information from relevant clinical notes [4].
- Symptom burden was assessed at baseline and >9-12-months after baseline, frequent symptoms were defined as a score of ≥2 on items 2 through 9 of the PHQ-9 (excluding Item 1).
- The following treatment patterns were assessed:
  - *Switching* to another line of antidepressant therapy was defined as starting a different antidepressant therapy after at least 30 days of continuous treatment on the previous line of therapy.
  - *Augmentation* was defined as the addition of another antidepressant or other augmentation medication to a given line of therapy after at least 30 days of continuous treatment with the original treatment.
  - *Combination* of antidepressants was the addition of another antidepressant treatment of adequate duration before 30 days of treatment is completed.
- Medications assessed included first and second-generation antipsychotics, selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), Tricyclic antidepressants, atypical antidepressants, and mood stabilizers.

Statistical analysis

- The likelihood of receiving antidepressant treatment, undergoing an antidepressant switch, an antidepressant augmentation, receiving combination of antidepressant treatments, or receiving other medications over the follow up period was assessed using bivariate and multivariable logistic regression.
- The number of unique antidepressants of adequate duration (≥30 days of treatment with no more than 14-day gap) were assessed and the average number of unique antidepressant treatments per patient during the 12-month follow up period was compared using bivariate and multivariable Poisson regression.
- Unadjusted and adjusted odds or rate ratios are presented for MDD-ANH relative to the Other-MDD cohort. Adjusted analysis controlled for age at baseline, insurance status (commercial, Medicare, Medicaid), attention-deficit/hyperactivity disorder (ADHD) diagnosis anytime prior to baseline, and Charlson comorbidity index score.

Results

Study Population

A total of 5,709 patients were included: 4,255 (74.5%) patients with MDD-ANH and 1,454 (25.5%) patients with Other-MDD. Patients in the MDD-ANH cohort were older, were more likely to have been insured by Medicaid or Medicare, tended to have slightly more medical comorbidities, and had a slightly lower, non-significant percentage of ADHD than patients with Other-MDD (Table 1).

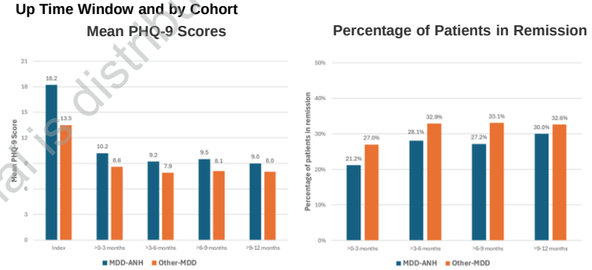
Table 1: Baseline Characteristics

Variable	Characteristic	MDD-ANH (N=4,255)	Other-MDD (N=1,454)	p-value
Age (years)	N	4,255	1,454	<.001
	Mean (SD)	41.0 (15.8)	37.8 (15.0)	
Sex	Female	3,065 (72.0%)	1,077 (74.1%)	0.133
	Male	1,190 (28.0%)	377 (25.9%)	
Race	Asian	29 (1.4%)	8 (1.1%)	0.468
	Black/AA	159 (7.5%)	47 (6.2%)	
	Caucasian	1,834 (87.0%)	664 (87.9%)	
	Other (including multiple)	85 (4.0%)	36 (4.8%)	
	Unknown/Not Reported	2,148	699	
Ethnicity	Hispanic/Latino	203 (10.0%)	82 (11.3%)	0.319
	Non-Hispanic/Latino	1,822 (90.0%)	641 (88.7%)	
	Unknown/Not Reported	2,230	731	
Insurance: Commercial	N (%)	2,014 (47.3%)	718 (49.4%)	0.177
Insurance: Medicare	N (%)	384 (9.0%)	80 (5.5%)	<.001
Insurance: Medicaid	N (%)	313 (7.4%)	83 (5.7%)	0.033
Comorbid Anxiety	N (%)	1,915 (45.0%)	656 (45.1%)	0.941
Comorbid ADHD	N (%)	413 (9.7%)	164 (11.3%)	0.086
Comorbid Post-Traumatic Stress Disorder	N (%)	286 (6.7%)	89 (6.1%)	0.425
Charlson Comorbidity Index	N	4,255	1,454	0.020
	Mean (SD)	0.6 (1.3)	0.5 (1.1)	

PHQ-9 Scores

At baseline, patients with MDD-ANH had a mean PHQ-9 score of 18.2 (SD=4.2) compared to 13.5 (SD=2.9) for Other-MDD (Figure 1). Descriptive analysis shows that the percentage of patients in remission at the four follow-up windows was lower among patients with MDD-ANH (21.2%, 28.1%, 27.2%, and 30.0%) compared to patients with Other-MDD (27.0%, 32.9%, 33.1%, and 32.6%), respectively (Figure 1).

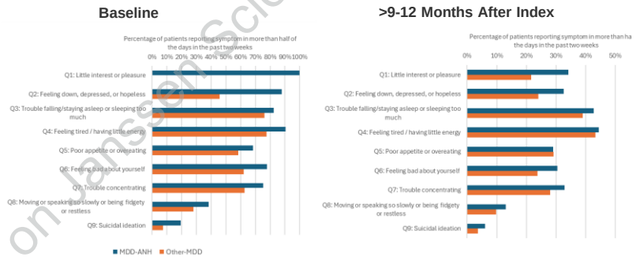
Figure 1: Mean PHQ-9 Scores and Percentage of Patients in Remission by Follow Up Time Window and by Cohort



Symptom Burden

At baseline, a greater percentage of patients with MDD-ANH reported experiencing other depressive symptoms frequently compared to patients with Other-MDD (Figure 2). At >9-12 months, the percentage reporting frequent depressive symptoms declined for both groups for all symptoms, however, the MDD-ANH group continued to report more frequent symptoms.

Figure 2: Percentage of Patients Reporting Frequent Symptoms of Depression Based on PHQ-9 Items (Score of ≥2) at Baseline and at >9-12 Month Follow Up by Cohort



Treatment Patterns

In the adjusted analyses, patients with MDD-ANH were treated with more antidepressants on average (rate ratio [RR]=1.10, p<0.001), were more likely to switch medications (odds ratio [OR]=1.24, p=0.004), were more likely to receive treatment augmentation (OR=1.16, p=0.021), and were more likely to receive combinations of antidepressant treatments (OR=1.23, p=0.004) compared to patients with Other-MDD (Table 2). Patients with MDD-ANH were more likely to be treated with SNRIs (OR=1.29 , p<0.001), tricyclic antidepressants (OR=1.31, p=0.003), atypical antidepressants (OR=1.24, p<0.001), mood stabilizers (OR=1.32, p<0.001), and second-generation antipsychotics (OR=1.51, p<0.001) during follow-up than Other-MDD patients.

Table 2: Analysis of Treatment Patterns and Medication Use in the 12 Month Follow Up Period by Cohort

Variable	MDD-ANH (N=4,255)	Other-MDD (N=1,454)	Unadjusted odds or rate ratio (95% CI) p value	Adjusted odds or rate ratio (95% CI) p value
Treatment Patterns				
On any antidepressant N (%)	3,677 (86.4%)	1,231 (84.7%)	1.15 (0.97, 1.36) p=0.097	1.14 (0.96, 1.35) p=0.123
Number of antidepressants Mean (SD)	1.583 (1.106)	1.433 (1.033)	1.11 (1.05, 1.16) p<0.001	1.10 (1.04, 1.15) p<0.001
Any antidepressant switch N (%)	975 (22.9%)	278 (19.1%)	1.26 (1.08, 1.46) p=0.003	1.24 (1.07, 1.44) p=0.004
Any augmentations N (%)	1,765 (41.5%)	546 (37.6%)	1.18 (1.04, 1.33) p=0.008	1.16 (1.02, 1.31) p=0.021
Any antidepressant combination N (%)	1,073 (25.2%)	306 (21.0%)	1.27 (1.10, 1.46) p=0.001	1.23 (1.07, 1.43) p=0.004
Medication Use				
SSRIs N (%)	2,491 (58.5%)	891 (61.3%)	0.89 (0.79, 1.01) p=0.067	0.93 (0.83, 1.06) p=0.283
SNRIs N (%)	1,514 (35.6%)	425 (29.2%)	1.34 (1.18, 1.52) p<0.001	1.29 (1.13, 1.47) p<0.001
Tricyclic antidepressants N (%)	736 (17.3%)	186 (12.8%)	1.43 (1.20, 1.70) p<0.001	1.31 (1.10, 1.56) P=0.003
Atypical antidepressants N (%)	1,754 (41.2%)	524 (36.0%)	1.24 (1.10, 1.41) p<0.001	1.24 (1.09, 1.40) p<0.001
Mood stabilizers N (%)	1,271 (29.9%)	352 (24.2%)	1.33 (1.16, 1.53) p<0.001	1.32 (1.15, 1.51) p<0.001
Second-generation antipsychotic N (%)	1,308 (30.7%)	325 (22.4%)	1.54 (1.34, 1.77) p<0.001	1.51 (1.31, 1.74) p<0.001

Adjustment is for age, ADHD, Charlson comorbidity index, and insurance status (commercial, Medicare, Medicaid).

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[Poster # 32]

Key takeaway

Significant clinical unmet need exists in patients with MDD with prominent anhedonia as reflected in higher symptom burden, higher use of antidepressants and lower rate of remission.

Conclusions

MDD patients with prominent anhedonia had more frequent depressive symptoms as measured by individual PHQ-9 items than MDD patients without prominent anhedonia at diagnosis and follow up.

MDD patients with prominent anhedonia had a lower rate of remission in the year following initial assessment than patients with MDD without prominent anhedonia.

MDD patients with prominent anhedonia on average received significantly more antidepressants and other psychotropic medications, switched antidepressant medications more often, and were more likely to have antidepressant treatments augmented than MDD patients without prominent anhedonia.

Strengths

- This is one of the first studies to examine the association between prominent anhedonia and clinical burden in MDD using a real-word dataset.
- Inclusion of medical and pharmacy claims and EMR data from multiple sources provides a rich real-world data source to assess patient outcomes.
- Data captured in a real-world setting from multiple sources and a geographically diverse population provides valuable assessment of treatment patterns.

Limitations

- Though the multi-source nature of the data increases the observation time for each patient; at a given time, patient data may not be complete, and the extent of missing data may vary over time.
- There is a potential bias in the cohort selection toward more severe cases as patients who receive a PHQ-9 score at baseline have higher severity of depression than patients without PHQ-9 data.
- These findings are generalizable to the MDD population seeking psychiatric care and may not reflect those accessing primary care.

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Disclosures

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Data Safety Monitoring Board (DSMB): COMPASS Pathways, Freedom Biosciences. HK and TD are employee and stock holders of Janssen (Johnson & Johnson Innovative Medicine).

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