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Patient Life Engagement Improvements Associated with Brexpiprazole

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Background

- Patients with major depressive disorder (MDD) have impaired functioning across multiple domains, including work, social, and family functioning[1,2]

- Improving patient life engagement and functioning are important goals in treating MDD

- Brexpiprazole, an atypical antipsychotic, was approved by the US Food and Drug Administration as adjunctive treatment to antidepressant therapy (ADT) for MDD[3]

- Efficacy and safety of brexpiprazole have been demonstrated in Phase 3 randomized controlled studies[4]
  - Post-hoc analysis of trial data showed improvement in overall life engagement and four domains of life engagement following initiation of treatment with brexpiprazole[5]

Objective

This study examined changes in life engagement following initiation of adjunctive brexpiprazole in patients with MDD using real world data

Methods

Data

The present study was a retrospective real-world study using NeuroDB[6], which contains:

- Longitudinal behavioral health patient records from ≥25 hospitals/ care systems, including more than 560,000 patients and over 14 million visits

- Demographic and clinical information including the Clinical Global Impression – Severity scale (CGI-S) and the Global Assessment of Functioning (GAF)

- Structured labels from the Mental Status Examination (MSE), which were processed using natural language processing (NLP) models to further enrich the database

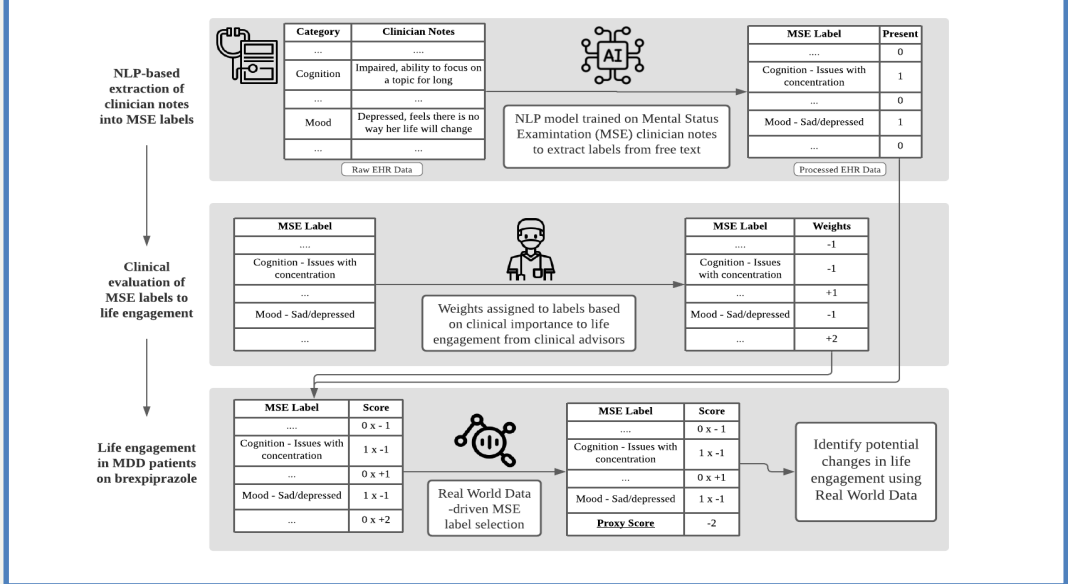## Methods, Continued

Inclusion/Exclusion Criteria

- We included patients diagnosed with MDD who were aged ≥18 years at the time of first brexpiprazole prescription (index event) and were prescribed brexpiprazole for at least 30 days between 2014 and 2020
  - Only patients with available MSE records around the index event (+/- 7 days) and at ≥1 point of time within 6 months from the index event were included in the analysis

- Patients with bipolar disorder, schizophrenia, and other psychotic disorders were excluded from the analysis

Data Analysis

Development of Life Engagement Score (Figure 1)

- Based on previous work leveraging MSE, 241 clinical labels were generated using NLP models, which were further mapped and simplified into 86 dichotomous labels with inputs from clinicians

- To identify clinical labels relevant to life engagement, the labels were selected and validated as follows.
  - Clinicians identified labels relevant to life engagement based on clinical estimation
  - Data processing and statistical models, including bivariate, variance inflation factor (VIF), and multivariable analyses, were applied to further assess the relevance of these clinical labels
  - A life engagement score was developed using the clinical labels, defined as the weighted sum for the presence of the labels relevant to life engagement
    - The weights were assigned with clinicians input based on its perceived positive or negative effect on life engagement

Figure 1: Life Engagement Score Development from MSE

- Patient life engagement in four domains (emotional, physical, social, and cognitive) were also derived from the MSE labels
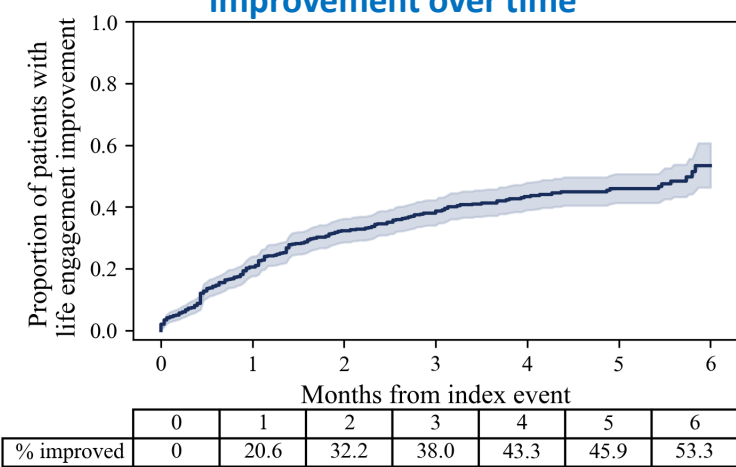
Methods, Continued

Life Engagement Analysis

- Leveraging the derived life engagement score, two types of analyses were conducted to assess life engagement outcomes associated with brexpiprazole:
  - **Discrete timepoint analysis:** Directly compared scores at a population level between index event and follow-up (up to 6 months from the index event) using one directional paired t-tests
  - **Survival analysis:** Defined a binary endpoint that represented an improvement in life engagement relative to the index event; a threshold of 0.1 was chosen to demonstrate improvement based on data exploration
    - Kaplan-Meier analysis was used to estimate the proportion of patients whose life engagement had improved relative to the index event

- Both analyses were also conducted for the scores defined for each of the four life engagement domains

Results

- A total of 624 brexpiprazole users with MDD were identified (mean age 48 years; 67.9% female)

- A large proportion of patients had concomitant anxiety disorders (46.6%) and were taking anxiolytics at baseline (18.1%). Mean (standard deviation [SD]) GAF score was 50.1 (16.0) and mean (SD) CGI-S was 4.42 (1.00)

- Statistically significant changes in life engagement scores were observed from as early as one month after the index event (Mean = 0.37, SD = 1.73, $p < 0.001$)

- Within a month from the index date, 20.6% of patients demonstrated an improvement in life engagement score by more than 0.1 (Survival prob. = 0.79; 95% CI [0.76-0.82]) Subsequently, 37.9% (Survival prob. = 0.62; 95% CI [0.58-0.66]) and 53.3% (Survival prob. = 0.47; 95% CI [0.39-0.54]) demonstrated an improvement within the first three and six months, respectively (Figure 2)
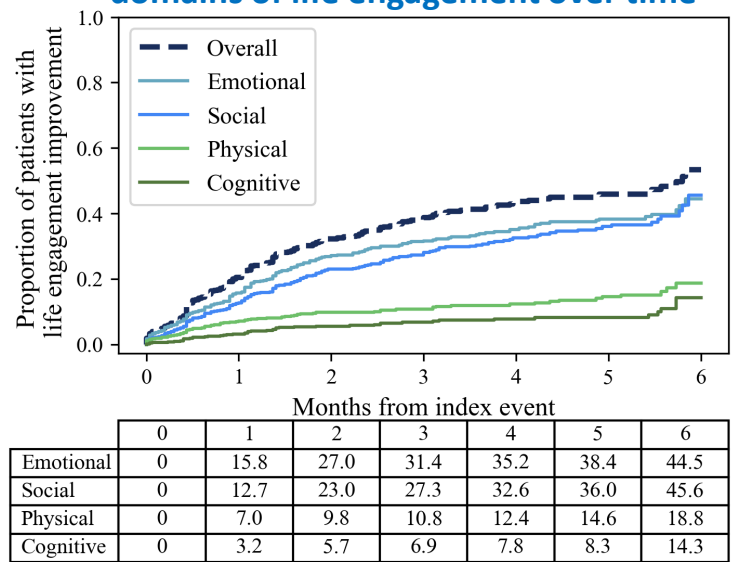

Figure 2: Proportion of brexpiprazole patients with life engagement improvement over time

	0	1	2	3	4	5	6
% improved	0	20.6	32.2	38.0	43.3	45.9	53.3

- Significant improvements were observed in the emotional and social domains, with 44.5% (Survival prob. = 0.56; 95% CI [0.48-0.62]) and 45.6% (Survival prob. = 0.54; 95% CI [0.45-0.63]) of patients demonstrating an improvement within the first six months, respectively

- Less profound improvements were observed in the physical (Survival prob. = 0.81; 95% CI [0.75-0.86]) and cognitive (Survival prob. = 0.86; 95% CI [0.79-0.91]) domains within the first 6 months

Results, Continued

Figure 3: Proportion of brexpiprazole patients with improvements on four domains of life engagement over time

	0	1	2	3	4	5	6
Emotional	0	15.8	27.0	31.4	35.2	38.4	44.5
Social	0	12.7	23.0	27.3	32.6	36.0	45.6
Physical	0	7.0	9.8	10.8	12.4	14.6	18.8
Cognitive	0	3.2	5.7	6.9	7.8	8.3	14.3

Limitations

- NeuroDB labels do not contain information about the severity of observations, which may limit the labels' ability to clearly represent impact on life engagement

- GAF scores are reported less frequently than MSE in NeuroDB, which may have introduced bias since the labels were correlated against GAF

- As different mental health disorders exhibit different symptoms, identifying labels significant to life engagement by utilizing data from all psychiatric patients may have skewed the final set of labels towards disorders with the highest prevalence in NeuroDB

- Use of survival analysis methodology required transformation of the continuous proxy measure into a binary variable, which defined the outcome as the first improvement in life engagement score, ignoring further changes as patients would have been considered to have undergone an "event"
  - It also did not assess the overall magnitude of change for a patient, which may have masked the extent to which brexpiprazole impacts life engagement outcomes

- While people who continue on treatment generally show improvement vs. those who do not, the analysis focused on patients with at least 30 days of brexpiprazole which reduced bias due to early discontinuation

Conclusions

- More than 50% of patients on brexpiprazole demonstrated an improvement in life engagement within 6 months, with significant improvement being observed from as early as 1 month from initiation

- Improvement was seen across the four domains of life engagement, with emotional and social domains showing the greatest level of improvement

- The present study demonstrated how real-world data enriched with NLP-derived information can be used to quantify outcomes such as life engagement that are not systematically measured elsewhere, allowing for a better understanding of treatment effectiveness

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