Bringing Treatment-Resistant OM Depression to Light: AI-Driven Patient Discovery in Real-World Data

Innovative approaches to uncovering unseen TRD patients using AI & RWD



Client Challenges

- Difficulty identifying treatment-resistant depression (TRD) patients in real-world data sources
- Limited insights into the patient journey due to TRD disease complexity and the absence of a standardized disease definition
- Bridging the disconnect between clinical trial research and real-world practice

OM1 Solution

- Develop, test, and validate AI algorithms to identify TRD in OM1's real-world dataset of Major Depressive Disorder patients
- Characterize and identify TRD patients in a real-world cohort

Introduction

An estimated 5-55% of patients who are diagnosed with major depressive disorder (MDD) have treatmentresistant depression (TRD), a severe and persistent form of depression that does not respond adequately to treatment.¹ TRD is associated with a higher risk of disability, decreased quality of life, and increased healthcare utilization. Given the severity of TRD and high unmet need, the discovery, development, and commercialization of new and existing treatments is critical. In recent years, the advent of new therapeutic approaches, such as psilocybin and ketamine, has prompted a reevaluation of this population.

A leading biotechnology company focused on innovation in mental health sought to better understand treatment-resistant depression to inform their program development strategy.

OM1 developed a robust AI patient finding algorithm to successfully identify and characterize TRD patients in a real-world dataset.

Project Goals

- Develop, test, and validate Al-powered algorithms to identify TRD in OM1's MDD patient population
- Characterize and identify TRD patients in the realworld setting to inform program strategy

Scientific Opportunities

- Bridge existing evidence gaps in TRD research
- Understand TRD treatment patterns and outcomes, offering new pathways for research and future treatments
- Identify potential beneficiaries of innovative TRD treatments that are currently undiagnosed or unrecognized

Challenge #1

Hard to Define, Harder to Find

TRD presents significant challenges in both clinical and research settings due to its complex nature and the lack of a standardized definition. These challenges include:

- Definitions of TRD vary across clinical care, treatment guidelines, reimbursement, and regulatory contexts.² The lack of consensus definition greatly limits the comparison and generalizability of clinical trial results across populations.
- In real-world settings, the identification of TRD is often delayed, as clinicians typically identify TRD only after multiple treatment failures. Patient outcomes, such as remissions, are infrequently measured.
- TRD is not included in the Diagnostic and Statistical Manual of Mental Disorders (DSM), nor does it have a specific diagnosis code.

Given these challenges, patients with TRD are often undiagnosed and remain unseen in real-world data sets.



Challenge #2

Finding Fit-For-Purpose RWD

The mental health dataset landscape can be challenging to navigate, with subjective disease endpoints, limited use of evidence based care, and historically high placebo response rates contributing to difficulties showing clear treatment effects. **Given the complexity of mental health conditions, optimally identifying patients with TRD using accurate, specialized, and high-quality real-world data is critical.** When evaluating potential partners, the client prioritized finding a partner with disease-specific outcomes data, expertise in mental health, and innovative technology capabilities including novel applications of Al.

"The OM1 team was already involved in 'tip of the spear' research in TRD through their work with [PhenOM[®]], an NLP algorithm which aims to identify undiagnosed patients by correlating unstructured data with structured data...

The inclusion of PROs and the impressive longitudinality of the [OM1] dataset makes it a unique offering, especially in the world of behavioral health datasets."

-VP, Value and Outcomes Research, Client



The Solution

Leveraging Specialized Depression Data

OM1's clinically rich depression data, with its robust patient-reported outcomes (PROs), extensive longitudinal follow-up, and unstructured clinical notes from psychiatrists, served as the foundation for developing an advanced TRD patient-finding algorithm.

OM1 PremiOM MDD Dataset

600,000+

Patients with deep clinical data from specialists

Dataset highlights

- Linked EMR & claims data
- Unstructured clinical notes from psychiatrists
- Longitudinal data (~7 years average follow-up per patient)
- Demographically & geographically diverse population
- Diverse payer mix (1/3 Commercial, 1/3 Medicare, 1/3 Medicaid)
- Disease activity measures including PHQ-9, CGI-I, MDQ, GAD-7
- Documented psychiatric and medical comorbidities
- Extracted and estimated symptoms of depression and suicidal ideation
- Social determinants of health (SDOH) including race, ethnicity, household income, education level and credit score.



The Solution (continued)

Identifying Psychiatrist-Attested TRD

The OM1 team conducted a detailed analysis of the PremiOM MDD dataset, utilizing machine learning alongside text extraction and natural language processing (NLP) to identify patients with psychiatristattested TRD within unstructured clinical notes. This process involved detecting explicit affirmations such as "patient has treatment resistant depression" and negations such as "patient does not have TRD." These identified patients served as the "gold standard" TRDpositive cohort for Al model calibration and training.

Continue Xanax 0.5mg PO PRN Qhs for anxiety/insomnia [CR][LF] (uses sparingly) [CR][LF][CR][LF]4. Continue abilify to 7.5mg PO QHS for treatment resistent depression symptoms and irritibility/agitation

Sample of clinical note with psychiatrist-attested annotation.

Developing a Robust Digital Phenotyping Model with OM1 PhenOM[®]

PhenOM is an AI-powered digital phenotyping platform trained using OM1's Real-World Data Cloud repository of linked EMR, claims and other data covering more than 350 million patients. PhenOM builds digital phenotypes from complex signals and interactions shared by patients with similar conditions, characteristics, or outcomes, which help distinguish these patients from others and isolate patients of interest. The richness of the mental health specialty network within the OM1 data – including extracted and estimated disease measures like PHQ-9 scores – allows the model to create digital phenotypes that capture many complex facets of TRD patients and their journeys.

The OM1 team calibrated the PhenOM model using the gold-standard psychiatrist-attested TRD cohort. PhenOM identified features such as the specific sequences of failed treatments, nuanced clinical interactions, and other distinguishing characteristics, to highlight and ultimately identify similar TRD patients.

Evaluating the AI Model with Comparator Cohorts

To assess the PhenOM model's effectiveness in identifying TRD patients compared to other methods of identifying TRD in real-world datasets, the OM1 team constructed three comparator cohorts. One cohort used the common definition of TRD, one a simplified feature set, and the third cohort consisted of patients identified by the OM1 PhenOM model.

Cohort	Common Regulatory Definition	FDA criteria for TRD; commonly used definition cited in literature At least two failed sequences of antidepressant therapy of adequate dose and duration within the same depression episode, where failure includes switching or adding an augmentation therapy
Cohort 2	Data-driven Simple Definition	Simple definition with no requirement explicitly linking treatment to depression At least three different antidepressants OR at least one antidepressant AND at least one antipsychotic within one year, regardless of dose and duration
Cohort 3	OM1 PhenOM AI Model Definition	OM1 phenotypic model cohort Flagged by an AI-based TRD identification algorithm, calibrated on a set of patients with psychiatrist-attested TRD in their clinical narrative

Results

Uncovering Unseen TRD Patients

Out of 45,053 patients identified in the OM1 MDD dataset across the three cohorts, less than 1% (only 0.4%) of patients were identified by all three definitions, and 9.4% met two definitions. The low overlap across definitions underscores the significant variability in how TRD is defined across different criteria. Each definition captures different aspects of the TRD patient population, which can lead to inconsistencies in identifying and understanding these patients.

PhenOM identified 4,300 TRD patients that were not included in the regulatory or data-driven definition cohorts – patients that would have been missed using traditional RWD methods.

Overlap across the three cohorts of TRD patients identified in realworld data.

	Regulatory N = 6,230	Data-driven cohort N = 37,153	PhenOM cohort N = 6,222
One cohort	3,407 (54.7%)	32,945 (88.7%)	4,300 (69.1%)
Two cohorts			
Regulatory + data- driven	2,479 (39.8%)	2,479 (6.7%)	N/A
Regulatory + model	193 (3.1%)	N/A	193 (3.1%)
Data-driven + model	N/A	1,578 (4.2%)	1,578 (25.4%)
Three cohorts	151 (2.4%)	151 (0.4%)	151 (2.4%)

PhenOM displayed very strong analytic performance in isolating TRD patients, with an Area Under the Curve **(AUC) of 0.87**. This measure reflects how well the AI model balances sensitivity and specificity: 0.5 is no better than a coin flip, and 1.0 represents a perfect model.

When evaluated against sex, age, and race sub-cohorts, PhenOM's model performance remained consistent. The strong performance provides evidence that the PhenOM model successfully identified TRD patients similar to those psychiatrists attested are truly treatment-resistant. "PhenOM enables us to translate provider intuition into other things that are present in the data. We can run the algorithm on a million people, and have it show us in an instant 100 patients that psychiatrists had called out as TRD positive."

– Joseph Zabinski, PhD, MEM, VP, Head of Commercial Strategy & AI at OM1, CNS Summit Presentation Panel

Key Publications

Identification of Treatment-Resistant Major Depressive Disorder Using a Machine Learning Algorithm

Presented at the International Conference on Pharmacoepidemiology & Therapeutic Risk Management, 2023

Insights From a Large Real-World Cohort of TRD Patients

The PhenOM model was applied to the OM1 Real-World Data Cloud and identified over 52,000 patients likely to have TRD. Combined with OM1's robust outcomes data, including <u>estimated and extracted PHQ-9 scores</u>, this large real-world cohort enables further research and visibility into complex patterns in TRD disease progression, burden for patient sub-populations, treatment response, and comorbid disease evolution. With this study, the client significantly advanced their internal understanding of TRD and successfully refined their strategic positioning, enabling more informed decision-making.

Conclusion

Advancing TRD Identification through Real-World Data and AI

Clinically rich real-world data (RWD) are vital for the discovery, development, and commercialization of effective treatments in mental health. When combined with advanced Al solutions like PhenOM[®], these data provide deeper insights into patient journeys, enabling the identification of individuals who might be overlooked by traditional analytic methods.

This study is the first to evaluate the characteristics of patients meeting three different definitions of treatmentresistant depression (TRD) within a mental health specialty data network. The patients identified through PhenOM's digital phenotyping closely align with providerdefined TRD, demonstrating a reliable process for mapping physician-attested conditions to real-world data in a hard to define and harder to find patient population.

Improving Patient Outcomes and Addressing Unmet Needs

Patients with TRD experience higher healthcare resource utilization (HRU) and incur greater medical costs compared to non-TRD major depressive disorder (MDD) patients. A 2020 study showed that TRD patients had annual healthcare costs of \$22,541 compared to \$17,450 for non-TRD MDD patients³—a difference driven by more frequent hospitalizations, outpatient visits, and complex treatment regimens. By utilizing AI tools like PhenOM to identify these patients more accurately, there is a critical opportunity to intervene earlier and tailor treatments that better address the unique challenges of TRD.

For biopharma companies, this approach not only highlights the importance of developing therapies that meet the specific needs of TRD patients but also underscores the potential to close existing gaps in mental health treatment. Expanding the patient base for targeted therapies ensures that more individuals receive the care they need, which can lead to significant return on investment for developers of interventions and improvements in overall patient outcomes.

About OM1

OM1 is pioneering cutting-edge healthcare innovation through its insights-driven technology and data. It specializes in personalized medicine, evidence generation, and real-world evidence (RWE) research powered by next-generation AI platforms, regulatory-grade deep longitudinal data, and globally recognized thought leadership.



Sources:

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