Treatment Patterns and Patient Characteristics in Misdiagnosis of Bipolar I Disorder

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Abstract

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Background: Bipolar I disorder (BP-I) presents significant diagnostic challenges, often misdiagnosed as major depressive disorder (MDD) during initial evaluation. Misdiagnosis can lead to inappropriate treatment regimens, including the prescription of antidepressant monotherapy, which poses the risk of inducing manic episodes in BP-I patients. Understanding post-misdiagnosis treatment patterns among BP-I patients is necessary to improve diagnostic accuracy and treatment selection.

Objective: This retrospective cohort study aimed to characterize treatment patterns among the BP-1 patients who misdiagnosed with MDD during their misdiagnosis period and assess their associations with the time until correct BP-I diagnosis.

Methods: Utilizing the MarketScan database, we identified two cohorts: BP-I patients with the history of misdiagnosis with MDD, and BP-I patients without the history of MDD misdiagnosis. In the misdiagnosed group, we described the first and last treatment regimens during the misdiagnosis period. We performed multinomial logistic regression to investigate the associations between patients and provider characteristics and the first treatment regimen after misdiagnosis. We employed Cox Proportional Hazard Model to assess the associations between treatment patterns and time until BP-I diagnosis. We compared the first treatment regimen after BP-I diagnosis between the two groups.

Results: Among 21,771 misdiagnosed BP-I patients, 28.5% received antidepressant monotherapy initially, with 18.8% continuing this regimen before BP-I diagnosis. Conversely, 13.3% persisted with antidepressant monotherapy post-BP-I diagnosis. In the non-misdiagnosed BP-I cohort, 11.2% initiated antidepressant monotherapy. Notably, mood stabilizer/anticonvulsant monotherapy post-misdiagnosis had the highest hazard of BP-I diagnosis compared to antidepressant monotherapy (HR: 1.26, 95% CI: 1.19-1.34, $p<0.001$).

Conclusion: Our findings highlight disparities in initial diagnoses between acute care providers, internal medicine, and family practice versus mental health facilities, psychiatrists, and nurse practitioners. This may reflect differences in diagnostic expertise and referral patterns. Notably, prevalent use of antidepressants and anxiolytics contravenes current guidelines, underscoring the need for improved clinical practice. The lack of screening tools for BP-I compared to MDD emphasizes the necessity for more comprehensive assessment tools to improve diagnostic accuracy.

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1. Introduction

Bipolar I Disorder (BP-I) is a psychiatric disorder that is characterized by chronic mood episodes of mania that often alternate with major depressive episodes.[1] The estimated total annual national economic burden of BP-I is $219 billion (in 2018 USD), with a lifetime prevalence of ~1.0% of the adult population.[2] The majority (80%) of total healthcare costs were attributed to indirect costs such as losses in work productivity and caregiving. BP-I mood episodes are characterized as manic, depressive, or mixed features.[1] To classify a manic episode, individuals must present with an elevated, expansive, or irritable mood and exhibit at least three of the following symptoms: decreased need for sleep, faster speech, uncontrollable racing thoughts, distractibility, increased goal-directed activity, or increased risky behavior. During a major depressive episode, individuals must exhibit at least five of the following symptoms for a period of at least two weeks: Intense sadness or despair, loss of interest in activities they usually enjoy, feelings of worthlessness or guilt, fatigue, increased or decreased sleep, increased or decreased appetite, restlessness, difficulty concentrating, frequent thoughts of death or suicide.[3] These criteria are subjective and may be hard to gauge, which makes diagnosis challenging. BP-I is frequently misdiagnosed as major depressive disorder (MDD) because patients are more likely to seek office visits during their depressive episodes compared to their manic episodes.[4] One study showed that in a primary care clinic, 21% of patients being treated for depression screened positive for bipolar disorder.[5] These misdiagnosed patients may struggle for years before receiving a correct diagnosis and treatment, which highlights the need for a better clinical standard to differentiate MDD and BP-I.

Misdiagnosis negatively impacts health outcomes due to delayed, ineffective or inappropriate treatments. For example, misdiagnosed patients may be at risk of receiving an antidepressant monotherapy, which can induce a hypomanic or manic episode in patients with BP-I.[6] The standard of care for BP-I patients is an atypical antipsychotic or mood stabilizer, though an antidepressant may be used in combination with these to address unresolved depressive symptoms.[7] One study examined the medical costs of misdiagnosed patients to be $6,541 greater per patient-year compared to those correctly diagnosed with BP-I, on account of higher hospitalizations, ER visits, and outpatient visits.[8]

While previous studies focused on the burden of misdiagnosing BP-I, current literature lacks understanding of the treatment patterns during the misdiagnosis stage, which has both economic and

clinical implications. For example, the use of antidepressant monotherapy may induce a manic event in patients. This study will fill in that gap by analyzing treatment patterns during misdiagnosis of BP-I from MDD.

2. Methods

2.1 Study Design and Data Source

We conducted a retrospective cohort study, using health insurance claims data, to assess treatment patterns and patient characteristics during misdiagnosis of BP-I.

The MarketScan Commercial Claims and Encounters database was used to identify two cohorts: (1) BP-I patients with the history of being misdiagnosed with MDD; (2) BP-I patients without the history of being misdiagnosed with MDD. This database contains de-identified, patient-specific health data of reimbursed healthcare claims for employees, retirees, and their dependents of over 250 medium and large employers and health plans. approximately 30 million individuals are covered under private insurance plans. No Medicaid or Medicare data are included.

The study period was from January 1st, 2018 through January 1st, 2023 (Figure 7.1). The index period, defined to be the date of MDD or BP-I diagnosis of the study cohorts, was from January 1st, 2019, through October 1st, 2022, to allow for twelve months of continuous enrollment before the index date and three months of follow-up.

At the time of the analysis, MarketScan data met Health Insurance Portability and Accountability Act of 1996 (HIPAA) requirements for fully de-identified data sets.[9] Institutional Review Board (IRB) approval at the University of Washington was not required, as the study met criteria for non-human subjects research as specified by the Human Subjects Division at the University of Washington.

2.2 Sample Selection

Misdiagnosed Cohort

We included patients who were at least 18 years old, and who were diagnosed with MDD (ICD-10-CM), defined as ≥1 inpatient OR ≥2 outpatient medical followed by ≥1 inpatient OR ≥2 outpatient medical claims with a diagnosis of BP-I (ICD-10-CM). MDD and BP-I diagnosis defined the first and second index date in this cohort, respectively. We excluded all patients with prior diagnosis of BP-I and/or schizophrenia before our index date. We included patients with continuous enrollments in medical and prescription benefits 12 months prior to MDD diagnosis (first index date), throughout misdiagnosis, and 3 months after BP-I diagnosis (second index date). We provided the list of ICD-10-CM codes for MDD and BP-1 in **Table 9.1**.

Non-Misdiagnosed Cohort (Control)

For non-misdiagnosed patients, we included patients who were at least 18 years old, and who were diagnosed with BP-I (ICD-10-CM), defined as ≥1 inpatient OR ≥2 outpatient medical claims. We excluded patients with prior diagnosis of MDD and/or schizophrenia before our index date. We defined the index date to be the date of BP-I diagnosis in this group. We required continuous enrollment in medical and prescription benefits 12 months prior and 3 months after BP-I diagnosis (index date).

2.3 Study Measures and Outcomes

We described the baseline characteristics including patient age, sex, geographic region, insurance plan type, place of diagnosis, provider type at diagnosis, Elixhauser comorbidity score, and Diagnostic and Statistical Manual of Mental Disorders (DSM-5) comorbidity score were collected. Elixhauser is a tool which is used to evaluate overall severity of comorbidities.[10] DSM-5 index is a measure of comorbid psychiatric disorders.[11] We calculated a modified Elixhauser and DSM-5 Comorbidity Index, which excluded depressive and bipolar disorders, using ICD-10 diagnosis codes on medical claims collected during the 12-month pre-index period.

The primary outcomes of interest were treatment patterns observed during misdiagnosis and assessing the association between treatment type and time until BP-I diagnosis. We considered seven psychotropic drug classes: (1) antidepressants; (2) anxiolytics; (3) mood stabilizer/anticonvulsants; (4) psychostimulants; (5) atypical antipsychotics; (6) sedative/hypnotics; and (7) typical antipsychotics. We

grouped anticonvulsants with mood stabilizers because they are frequently used as mood stabilizers[10]. We provided the list of medications and corresponding GPI codes under each class in **Table 9.2**.

The secondary outcome of interest was to assess the association between patient characteristics, provider type, and clinical manifestations with the first treatment received after MDD diagnosis. We defined 'the first treatment' after MDD diagnosis to be all treatments given within 14 days of diagnosis, with at least one subsequent refill taken for ≥30 days. We also investigated the association between the first treatment with the time until BP-1 diagnosis. We defined the time until BP-1 diagnosis to be the difference between MDD diagnosis (first index) and BP-I diagnosis (second index) in the misdiagnosed group. Lastly, we compared the first treatment after BP-I between the misdiagnosed and non-misdiagnosed groups.

2.4 Statistical Analysis

Baseline characteristics and treatment patterns were calculated using means and standard deviations for continuous variables and frequency (n,%) for all categorical variables.

We calculated the average time until BP-I diagnosis based on the first treatment regimen after misdiagnosis of MDD. We employed Cox proportional hazards regression analysis to calculate the differential hazard rate ratio of BP-I diagnosis based on the first treatment regimen while adjusting for patient and provider characteristics. The outcome variable is the diagnosis of BP-1 (binary). The first treatment regimen is a categorical variable which included the five most common psychotropic drug class combinations in the misdiagnosed patients and an 'Others' category: (1) Antidepressant monotherapy, (2) Antidepressant + Anxiolytics, (3) Anxiolytics monotherapy, (4) Antidepressant + Mood Stabilizer/Anticonvulsant, (5) Mood stabilizer/Anticonvulsants monotherapy, and (6) Others. Patients and provider covariates include age, sex, place of diagnosis, provider type, DSM-5 comorbidity index score, and Elixhauser comorbidity index score.

Multinomial logistic regression analysis was used to calculate the odds of the first treatment regimen while adjusting for patient and provider characteristics. This method was chosen to account for our

multi-level categorical outcome of the first treatment type received after MDD diagnosis. Patients and provider covariates include age, sex, place of diagnosis, provider type, DSM-5 comorbidity index score, and Elixhauser comorbidity index score.

We performed cohort selection and descriptive statistics using SAS version 9.4 (SAS Institute, Cary, NC), and all statistical analyses in R 4.4.0 (R Core Team, 2024).

3. Results

3.1 Baseline Characteristics

Misdiagnosed Cohort

We identified 21,771 eligible BP-I patients who were misdiagnosed with MDD **(Figure 7.3)**. The average age at MDD diagnosis was 34.8 years old and the average age at BP-I diagnosis was 36.3 years old (**Table 6.1**). Females comprised 68.1% of the misdiagnosed cohort. Nearly half (45.8%) of the patients in this cohort were from the southern region of the U.S. The most common insurance plan type was Preferred Provider Organization (PPO) at 50.7%, followed by California Department of Public Health (CDHP) at 14.6%. In this cohort, 78.0% of the MDD diagnosis prior to BP-I diagnosis were in an outpatient setting though that number dropped to 64.9% at BP-I diagnosis (**Figure 7.4**). Contrarily, diagnosing via telehealth and inpatient went up from 4.4% and 5.9% at MDD diagnosis to 11.1% and 13.1% at BP-I diagnosis, respectively. Acute care providers were the most frequent to diagnose MDD (18.4%), followed by family practice (15.4%), and psychiatrists (14.8%)(**Figure 7.5**). At BP-I diagnosis provider type frequencies were acute care (15.2%), family practice (10.1%), and psychiatrist (21.3%). After excluding depressive disorders from the Elixhauser comorbidity index average score was 0.34, with 27% of patients having at least one comorbidity and 6.1% having 2 or more. After excluding depressive and bipolar disorders from the DSM-5 comorbidity index, the average score was 0.60, with 43.6% having at least one comorbidity and 14.3% having 2 or more.

Non-misdiagnosed Cohort

We identified 50,667 eligible BP-I patients who were never misdiagnosed with MDD (**Figure 7.3**). The average age in this cohort was 37.1 years old and females made up 65% of this population (**Table 6.1**). A majority of patients (45.6%) in this cohort were from the southern region of the U.S. The most common insurance plan type was PPO (50.4%) followed by CDHP (13.5%). Psychiatrists were the most frequent to diagnose BP-I (25.4%), followed by acute care providers (12.4%), and family practice (10.5%). After excluding depressive disorders from the Elixhauser comorbidity index average score was 0.29, with 23.3% of patients having at least one comorbidity and 4.8% having 2 or more. After excluding depressive and bipolar disorders from the DSM-5 comorbidity index, the average score was 0.51, with 37.5% having at least one comorbidity and 11.4% having 2 or more.

3.2 Primary Outcomes

Treatment patterns

In our misdiagnosed cohort, 28.5% of patients were started on an antidepressant monotherapy at MDD diagnosis (**Table 7.6**). Contrarily, in our non-misdiagnosed cohort, 11.2% of patients started on antidepressant monotherapy at BP-I diagnosis. Interestingly, polypharmacy became more common as misdiagnosed patients progressed from MDD to BP-I diagnosis. More specifically, 34.1% of patients were taking medications from 2+ unique psychotropic drug classes, and by the end of misdiagnosis that number went up to 37.3%, and after BP-I diagnosis 43.8% (**Table 6.2**). The five most common treatment regimens in both of our cohorts were Antidepressant monotherapy, Antidepressant + Anxiolytic, Antidepressant + Mood Stabilizer/Anticonvulsant, Mood Stabilizer/Anticonvulsant monotherapy, and Anxiolytic monotherapy. Patients went on to take a variety of psychotropic drug class combinations as the last line after being initially prescribed either an antidepressant monotherapy or antidepressant and anxiolytic combination therapy (**Table 7.7**, **Table 7.8**).

Time until BP-I Diagnosis

After the diagnosis of MDD, individuals initiated on different treatment regimens exhibited varying durations until the subsequent diagnosis of BP-I (**Figure 7.9**). Antidepressant monotherapy was associated with the longest duration until BP-I diagnosis (374 days), followed by combination therapy of antidepressants and anxiolytics (334 days), anxiolytic monotherapy (330 days), combination therapy with antidepressants and mood stabilizers/anticonvulsants (317 days), and the shortest duration was observed with mood stabilizer/anticonvulsant monotherapy (290 days)(**Table 6.3**). Mood stabilizer/anticonvulsant monotherapy was associated with the highest hazard compared to antidepressant monotherapy (1.26, 95% CI: 1.19-1.34, $p<0.001$), implying that mood stabilizer/anticonvulsant monotherapy as the first post-MDD diagnosis treatment is associated with an earlier BP-I diagnosis (**Table 6.4**). Notably, telehealth as a place of diagnosis exhibited higher hazard ratios across all treatment regimens compared to outpatient diagnosis (1.60, 95% CI: 1.50-1.71, $p<0.001$), implying that telehealth may have led to an earlier BP-I diagnosis. Nurse practitioners exhibited significantly higher hazards across all treatment regimens compared to psychiatrists, indicating potential differences in treatment selection and outcomes based on provider type (1.22, 95% CI: 1.12-1.31, $p<0.001$).

3.3 Secondary Outcome

Log Odds of Receiving First Treatment Regimen- Misdiagnosed Cohort

Younger patients are more likely to receive an antidepressant monotherapy ($p<0.001$) than all other psychotropic drug classes as a first treatment regimen (**Table 6.5**). Males had a 13.1% decrease in odds of receiving an antidepressant and mood stabilizer/anticonvulsant combination therapy instead of an antidepressant monotherapy compared to females ($p<0.05$). The odds of receiving a mood stabilizer/anticonvulsant monotherapy instead of antidepressant monotherapy are 61.0% lower when prescribed by family practice ($p<0.001$), 36.9% lower when prescribed by a nurse practitioner ($p<0.01$), and 45.1% lower when prescribed by an internal medicine provider ($p<0.001$) compared to when prescribed by a psychiatrist.

4. Discussion

We conducted a retrospective cohort study to describe patient characteristics, treatment patterns and assess time until BP-I diagnosis in patients who were initially misdiagnosed with MDD. We found that most patients were diagnosed with MDD in an outpatient setting (78.0%) though the number was lower (64.9%) at BP-I diagnosis. Consistent with that finding, we had seen over a 2-fold increase in BP-I diagnoses in an inpatient setting and through telehealth, which may be explained by a more severe event taking place that led to BP-I diagnosis (i.e., manic episode leading to a hospitalization).[12] Furthermore, there were higher hazards of BP-I diagnosis associated with inpatient (HR: 1.30, 95% CI: 1.22-1.39, p<0.001) and telehealth diagnoses (HR: 1.60, 95% CI: 1.50-1.71, p<0.001) compared to outpatient diagnosis. This shorter time to BP-I diagnosis may be partially explained by inpatient resources and time to gather collateral information as opposed to brief outpatient visits.[13]

Our findings also show that there were more initial diagnoses of MDD by acute care providers, internal medicine and family practice compared to greater subsequent diagnoses of BP-I by mental health facilities, psychiatrists, and nurse practitioners. This may be due to differences in diagnostic expertise, assuming that these specialized providers may be more familiar with nuanced diagnostic criteria and clinical presentation of BP-I.[14] Another possibility is that this pattern may also be due to referral patterns. Patients initially presenting with symptoms of depression may seek care from general medical providers who are more accessible in primary care settings. As symptoms progress, they may have later been referred to a specialty provider for a more comprehensive evaluation.

Bipolar I disorder presents a diagnostic conundrum in clinical practice, often masquerading as MDD during initial presentation. Previous literature has highlighted the danger of misdiagnosis, particularly the risk of initiating an antidepressant monotherapy in individuals with BP-I, which can induce a manic episode.[15] Our study underlines these findings, emphasizing the need for accurate identification of BP-I to mitigate risks associated with inappropriate treatments. BP-I can be extremely challenging due to there being no universally accepted diagnostic criteria, there are more common presentations of symptoms in BP-I patients.[16] For example, earlier onset of first depressive episode, shorter depressive

episodes, and family history of BP-I are all factors that can guide clinicians towards a correct diagnosis. Previous literature also reveals disparities in screening tools between MDD and BP-I. Most healthcare providers rely on tools to screen for depression but do not use any to assess BP-I.[17] There is a need for more frequent use of screening tools like the Mood Disorder Questionnaire (MDQ) or the Rapid Mood Screener (RMS) in patients suspected to have MDD to increase the likelihood of catching BP-I.

There are several limitations of our study. Firstly, diagnosis of BP-I is not possible until the first presence of manic or mixed symptoms, thus many patients first present with an acute depressive episode, without experiencing a manic episode.[18] This can be indicative that some patients were not misdiagnosed through poor assessment, but that they just have not presented as BP-I in its full form yet. Furthermore, patients may have experienced their first manic episode quicker due to antidepressant monotherapy which may have affected true time until BP-I diagnosis. Future research can aim to create a prognostic tool to detect BP-I in high-risk patients. Secondly, we characterized the first and last treatment regimens received, but we did not account for any medications that may have been taken in between. This leaves us with a gap in understanding treatment progression in our patient cohorts. Finally, this analysis was on full-time employees with employer sponsored private insurance which may not be generalizable to the full U.S. population. This is especially important in our population because low levels of household income are associated with several lifetime mental disorders including bipolar disorder.[19]

In summary, our study highlights the need of correctly diagnosing BP-I early and efficiently. By prioritizing initial correct diagnosis of BP-I, we can mitigate the risks associated with misdiagnosis, optimize treatment selection, and improve overall patient care.

5. Conclusion

We found that a significant proportion of misdiagnosed patients took antidepressant monotherapy at various stages of their diagnostic journey. Among patients who were ultimately diagnosed with BP-I after a prior misdiagnosis of MDD, 28.5% received an antidepressant monotherapy as their first treatment regimen. 18.8% of these patients received an antidepressant monotherapy as their last regimen before being diagnosed with BP-I and 13.3% continued to receive antidepressant monotherapy even after being correctly diagnosed. Furthermore, from patients who were initially correctly diagnosed with BP-I, 11.2% were initiated on antidepressant monotherapy. Notably, when taken as a first treatment regimen after misdiagnosis, mood stabilizer/anticonvulsant monotherapy had the highest hazard of BP-I diagnosis when compared to antidepressant monotherapy (1.26, 95% CI: 1.19-1.34, $p<0.001$).

6. Tables

6.1 Baseline Characteristics

		All Patients (n=72438)	Misdiagnosed Cohort (n=21771)		Correctly Diagnosed Cohort (n=50667)
		--	at MDD Dx	at BP-I Dx	at BP-I Dx
Demographic Characteristics					
Age, mean (SD)		36.5(14.2)	MDD dx: 34.8(14.1) BP-I dx: 36.3(14.0)		37.1(14.1)
Sex, male (%)		34.30%	31.9 %		35.00%
Elixhauser Comorbidity Index		0: 75.6% 1= 19.2% 2= 4.6% 3+ = 0.6% *Mean= 0.30(0.59)*	0: 73.0% 1= 20.9% 2=5.4% 3+ = 0.7% *Mean=0.34(0.61)*		0: 76.7% 1= 18.5% 2= 4.2% 3+ = 0.6% *Mean= 0.29(0.57)*
DSM-5 Comorbidity Index		0= 60.6% 1= 27.1% 2= 10.4% 3+ = 1.9% *Mean= 0.54(0.76)*	0: 56.4% 1: 29.4% 2: 12.0% 3+: 2.3% *Mean= 0.60(0.79)*		0= 62.5% 1= 26.0% 2 = 9.7% 3+ = 1.7% *Mean= 0.51(0.74)*
Geographic Region (%)	Northeast North Central South West	14.2% 21.1% 45.7% 18.8%	12.4% 22.0% 45.8% 19.4%		14.5% 20.1% 45.6% 18.7%
Plan Type (%)	PPO CDHP HMO HDHP POS Comprehensive EPO POS w/ capitation	50.5% 13.8% 13.0% 10.2% 8.0% 3.3% 0.7% 0.5%	50.7% 14.6% 12.9% 10.2% 7.0% 3.6% 0.6% 0.4%		50.4% 13.5% 13.1% 10.2% 8.4% 3.3% 0.7% 0.5%
	Telehealth	8.8%	4.4%	11.1%	8.1%

Setting of First Diagnosis	Outpatient	70.9%	78.0%	64.9%	72.7%
	Inpatient Hospital	9.9%	5.9%	13.1%	8.9%
	Emergency Room	1.2%	3.6%	1.3%	1.1%
	Other	9.2%	8.1%	9.6%	9.2%
Type of Provider to Initiate Diagnosis	Acute Care Hospital	13.0%	18.4%	15.2%	12.4%
	Mental Health Facility	3.7%	2.0%	4.6%	3.4%
	Internal Medicine	3.8%	5.5%	3.6%	3.9%
	Family Practice	10.4%	15.4%	10.1%	10.5%
	Psychiatrist	24.4%	14.8%	21.3%	25.4%
	Nurse Practitioner	7.4%	4.8%	8.7%	7.0%
	Therapist	10.4%	11.4%	10.4%	10.4%
	Other	26.9%	27.7%	26.1%	27.0%

CDHP = consumer driven health plan; DSM-5 = Diagnostic and Statistical Manual of Mental Disorders EPO = exclusive provider organization; HDHP = high deductible health plan; HMO = health maintenance organization; POS = point of service plan; PPO = preferred provider organization; SD = standard deviation

6.2 Treatment Patterns	Misdiagnosed (n=21771)			Control (n=50667)
	1st Regimen after MDD(%)	Final Regimen of MDD(%)	1st Regimen after BP-I(%)	1st Regimen after BP-I(%)
# of Drug Classes				
1	44.7	41.0	31.6	38.4
2	25.4	26.4	27.2	26.4
3+	8.7	10.9	16.6	12.4
Non-drugs of interest	21.2	21.7	24.6	22.8
Treatment Regimen				
Antidepressant	28.5	18.8	13.3	11.2
Antidepressant + Anxiolytic	9.4	6.6	5.6	3.8
Antidepressant + Mood Stabilizer/Anticonvulsant	6.8	8.9	10.1	9.0
Mood stabilizer/Anticonvulsant	6.3	5.8	9.7	15.0
Anxiolytic	5.5	6.6	4.3	5.6
Antidepressant + Anxiolytic + Mood Stabilizer/Anticonvulsant	3.0	4.1	5.4	3.8
Psychostimulant	2.7	2.7	2.7	3.2
Antidepressant +Psychostimulant	2.3	1.7	2.0	1.3
Anxiolytic + Mood Stabilizer/Anticonvulsant	2.1	3.3	3.3	4.0
Atypical Antipsychotic	0.8	1.4	1.2	2.5

Sedative/Hypnotic	0.7	0.6	0.5	0.7
Atypical Antipsychotic + Mood Stabilizer/Anticonvulsant	0.2	0.7	1.3	2.1
Typical Antipsychotic	0.0	0.0	0.1	0.1
Other	31.7	38.8	40.5	37.7

6.3 Time until BP-I Diagnosis Based on Initial Treatment Regimen

	Mean estimate	Median estimate
Antidepressant (n=6213)	374	282
Antidepressant + Anxiolytic (n=2050)	334	233
Anxiolytic (n=1207)	330	229
Antidepressant + Mood Stabilizer/Anticonvulsant (n=1492)	317	196
Mood Stabilizer/Anticonvulsant (n=1377)	290	153
Other (n=9435)	317	204

6.4 Cox Proportional Hazards Regression

	First Regimen post MDD Dx		Last Regimen of MDD Dx	
	Crude Model	**Adjusted Model**	**Crude Model**	**Adjusted Model**
	Hazard ratio (95% CI) P value	Hazard ratio (95% CI) P value	Hazard ratio (95% CI) P value	Hazard ratio (95% CI) P value
Tx Regimen (Reference: Antidepressant)				
Antidepressant + Anxiolytic	1.13 (1.08-1.19)***	1.13 (1.08-1.19)***	1.03 (0.98-1.09)	1.04 (0.99-1.10)
Anxiolytic	1.15 (1.08-1.22)***	1.17 (1.10-1.24)***	1.05 (1.00-1.10)	0.97 (0.92-1.03)
Antidepressant + Mood Stabilizer/Anticonvulsant	1.16 (1.10-1.23)***	1.17 (1.10-1.24)***	0.95 (0.90-1.00)	1.05 (1.00-1.10)
Mood Stabilizer/Anticonvulsant	1.27 (1.20-1.34)***	1.26 (1.19-1.34)***	1.01 (0.97-1.06)	1.01 (0.97-1.06)
Other	1.09 (1.06-1.13)***	1.10 (1.06-1.13)***	1.07 (1.03-1.11)***	1.09 (1.05-1.12)***
Age		1.00 (1.00-1.00)***		1.00 (1.00-1.00)**
Sex male		1.09 (1.06-1.12)***		1.08 (1.05-1.12)***
BP-I diagnosis setting (Reference: Outpatient)				
Inpatient		1.30 (1.22-1.39)***		1.31 (1.22-1.40)***
Telehealth		1.60 (1.50-1.71)***		1.60 (1.50-1.71)***
Emergency Room		1.24 (1.14-1.35)***		1.24 (1.14-1.35)***
Other		1.04 (0.98-1.10)		1.04 (0.98-1.09)
Provider Type (Reference: Psychiatrist)				
Family Practice		1.05 (1.00-1.10)*		1.04 (0.99-1.09)
Nurse Practitioner		1.23 (1.14-1.32)***		1.22 (1.12-1.31)***
Therapist		1.08 (1.02-1.13)**		1.08 (1.02-1.14)**
Internal Medicine		1.13 (1.06-1.21)***		1.12 (1.05-1.19)**
Mental Health Facility		1.18 (1.06-1.32)**		1.19 (1.07-1.32)**
Acute Care Hospital		1.18 (1.12-1.24)***		1.18 (1.12-1.24)***
Other		1.10 (1.05-1.15)***		1.10 (1.05-1.14)***
DSM-5 comorbidity score		0.95 (0.93-0.97)***		0.94 (0.93-0.95)***
Elixhauser comorbidity score		0.98 (0.95-1.00)*		0.98 (0.96-1.00)***

P-Value: <0.05*, <0.01**, <0.001*

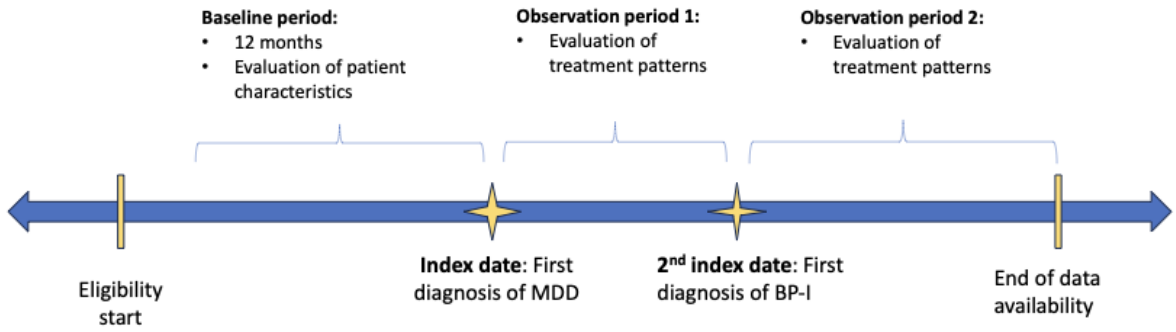
6.5 Multinomial Regression model (log-model)

	Antidepressant + Anxiolytic	Anxiolytic	Antidepressant + Mood Stabilizer/Anticonvulsant	Mood stabilizer/Anticonvulsant	Other
Intercept	-1.44 (-1.64, -1.25)***	-2.67 (-2.92, -2.42)***	-1.8 (-2.02, -1.58)***	-1.80 (-2.02, -1.57)***	-0.13 (-0.26, 0.00)*
Age	0.014 (0.01, 0.02)***	0.03 (0.03, 0.04)***	0.02 (0.02, 0.03)***	0.02 (0.01, 0.02)***	0.02 (0.02, 0.02)***
Sex Male	-0.16 (-0.27, -0.05)**	-0.21 (-0.35, -0.07)**	-0.14 (-0.27, -0.02)*	0.03 (-0.15, 0.10)	-0.09 (-0.16, -0.02)*
Setting of Diagnosis (Ref: Outpatient)					
Inpatient	0.63 (0.40, 0.86)***	0.02 (-0.31, 0.35)	0.28 (0.01, 0.56)*	0.03 (-0.28, 0.33)	0.27 (0.11, 0.44)**
Telehealth	-0.08 (-0.32, 0.17)	-0.14 (-0.46, 0.18)	-0.05 (-0.35, 0.22)	-0.05 (-0.33, 0.23)	-0.18 (-0.34, -0.03)*
Emergency Room	0.32 (0.00, 0.65)*	0.24 (-0.15, 0.63)	0.28 (-0.08, 0.64)	0.2 (-0.17, 0.57)	0.25 (0.04, 0.47)*
Other	-0.18 (-0.38, 0.03)	-0.07 (-0.32, 0.17)	-0.03 (-0.24, 0.19)	-0.21 (-0.44, 0.02)	-0.05 (-0.17, 0.07)
Provider Type (Ref: Psychiatrist)					
Family Practice	-0.40 (-0.57, -0.23)***	-0.43 (-0.65, -0.21)***	-0.72 (-0.92, -0.52)***	-0.94 (-1.06, -0.61)***	-0.57 (-0.69, -0.46)***
Nurse Practitioner	-0.06 (-0.30, 0.18)	-0.13 (-0.45, -0.18)	-0.45 (-0.75, -0.16)**	-0.46 (-0.78, -0.14)**	-0.40 (-0.57, -0.23)***
Therapist	-0.25 (-0.47, -0.03)*	0.28 (0.03, 0.53)*	-0.00 (-0.23, 0.22)	0.44 (0.22, 0.67)***	0.43 (0.29, 0.56)***
Internal Medicine	-0.51 (-0.76-0.26)***	-0.33 (-0.62, -0.03)*	-0.75 (-1.04, -0.46)***	-0.60 (-0.90, -0.29)***	-0.44 (-0.60, -0.28)***
Mental Health Facility	0.20 (-0.17, 0.57)	-0.48 (-1.11, 0.16)	0.25 (-0.16, 0.65)	0.03 (-0.45, 0.51)	0.06 (-0.21, 0.33)
Acute Care Hospital	-0.19 (-0.38, 0.01)	0.12 (-0.11, 0.36)	-0.17 (-0.38, 0.05)	0.01 (-0.21, 0.23)	0.18 (0.05, 0.31)**
Other	-0.27 (-0.43, -0.11)***	-0.27 (-0.36, 0.04)	-0.25 (-0.43, -0.08)**	-0.03 (-0.22, 0.15)	-0.06 (-0.17, 0.04)
DSM-5 Score	0.12 (0.06, 0.18)***	0.11(0.04, 0.19)**	-0.08 (-0.15, -0.00)*	-0.14 (-0.22, -0.06)***	0.05 (0.00, 0.09)*
Elixhauser Score	0.07 (-0.01, 0.16)	0.15 (0.05, 0.25)**	0.01 (-0.08, 0.11)	-0.03 (-0.13, 0.07)	0.07 (0.01, 0.12)*

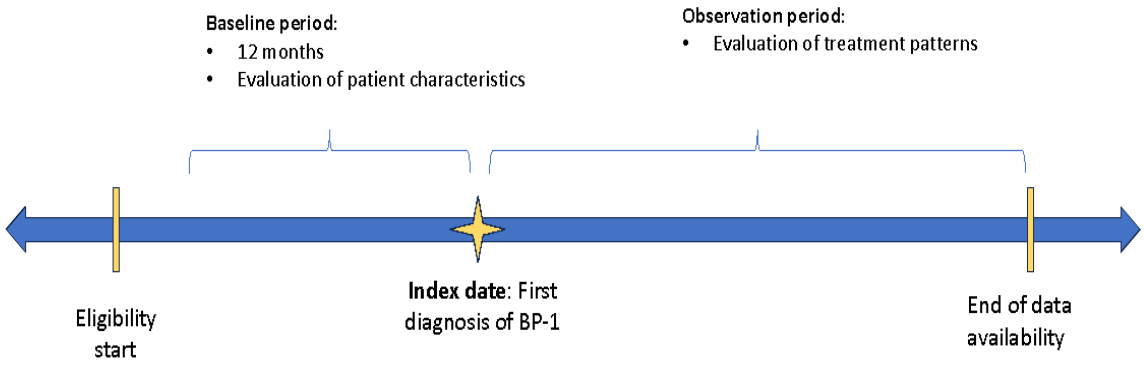
P-Value: <0.05*, <0.01**, <0.001*

7. Figures

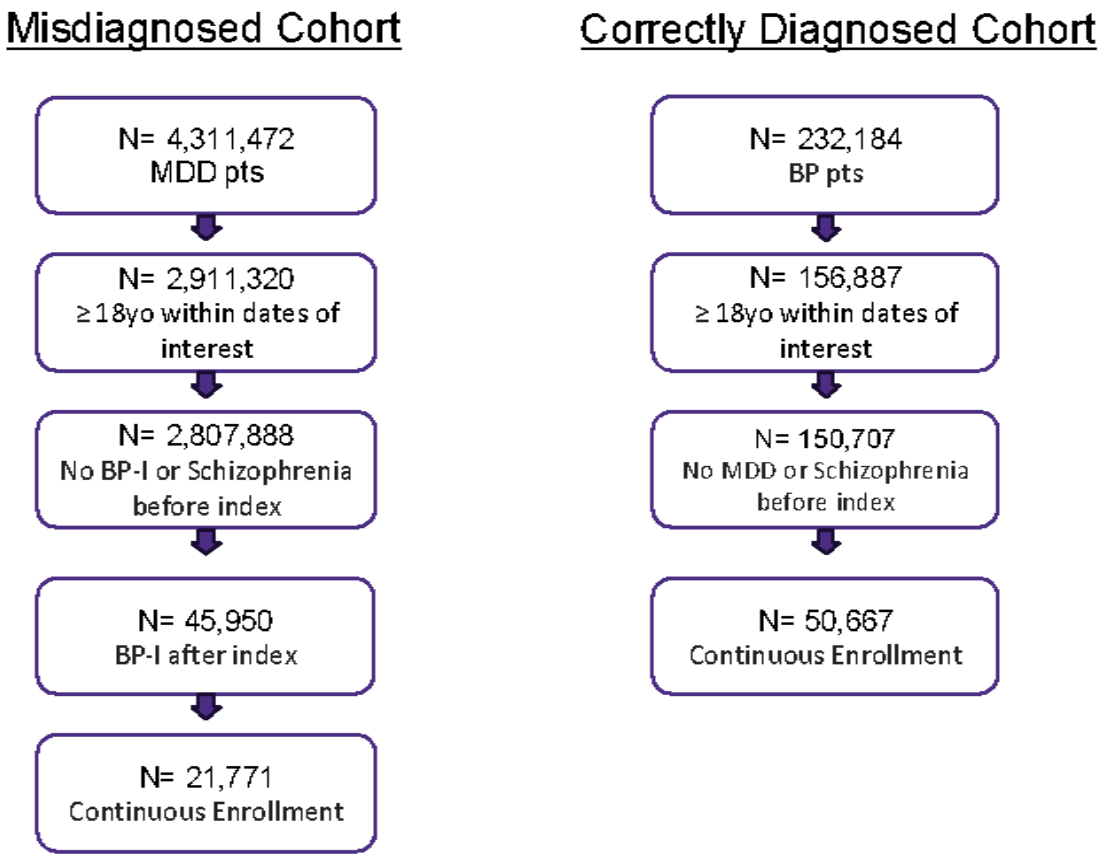
7.1 Study Design- Misdiagnosed Cohort



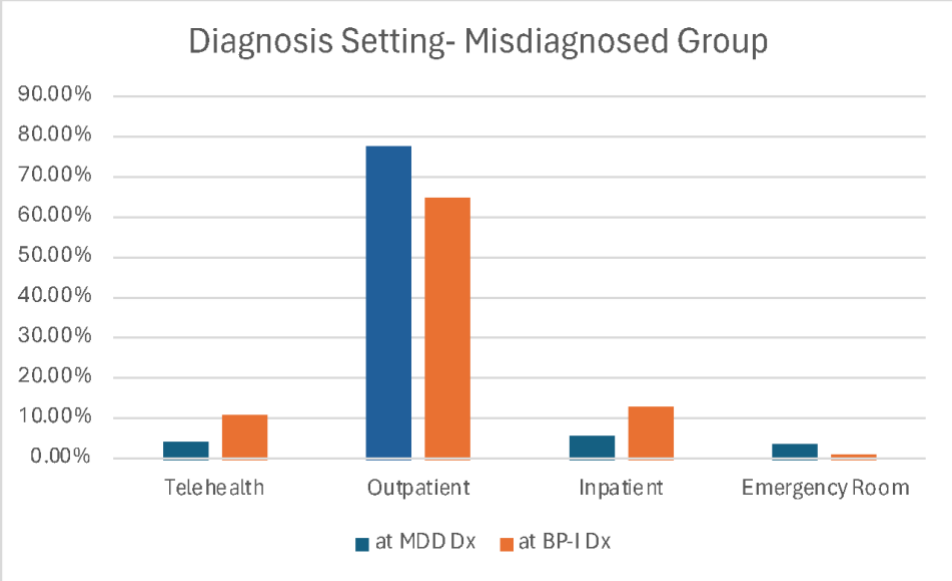
7.2 Study Design- Non-misdiagnosed Cohort



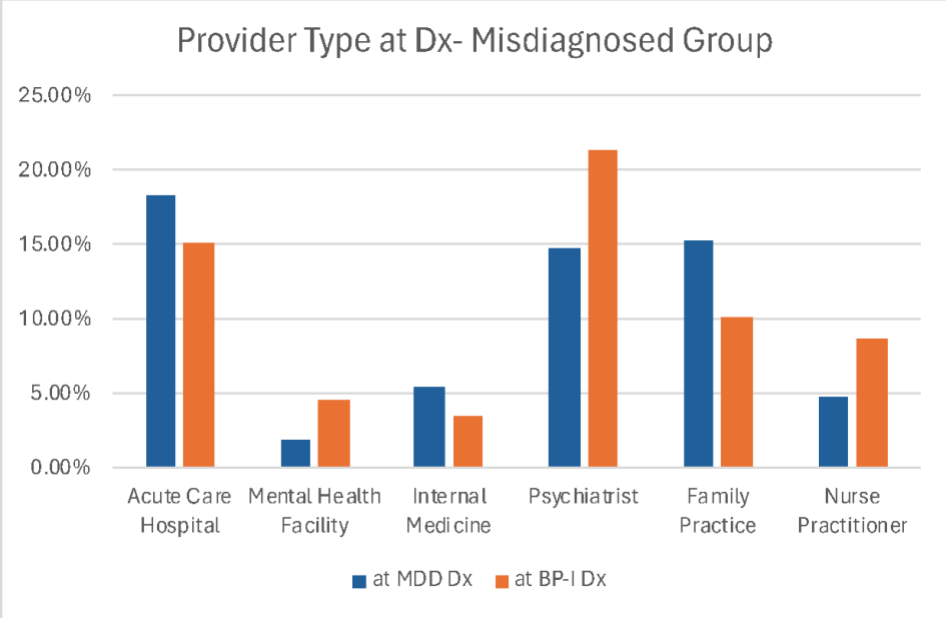
7.3 Cohort Selection Process



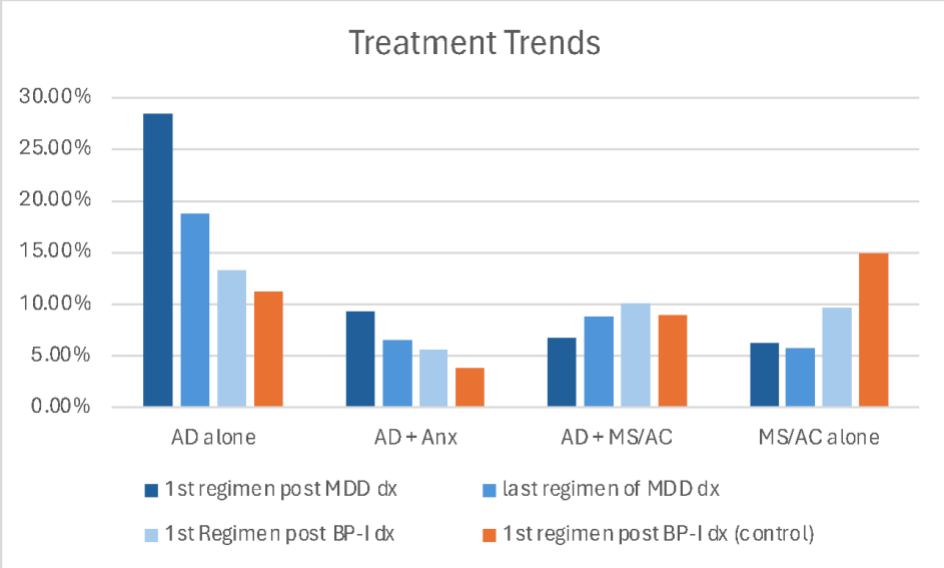
7.4 Place of Diagnosis



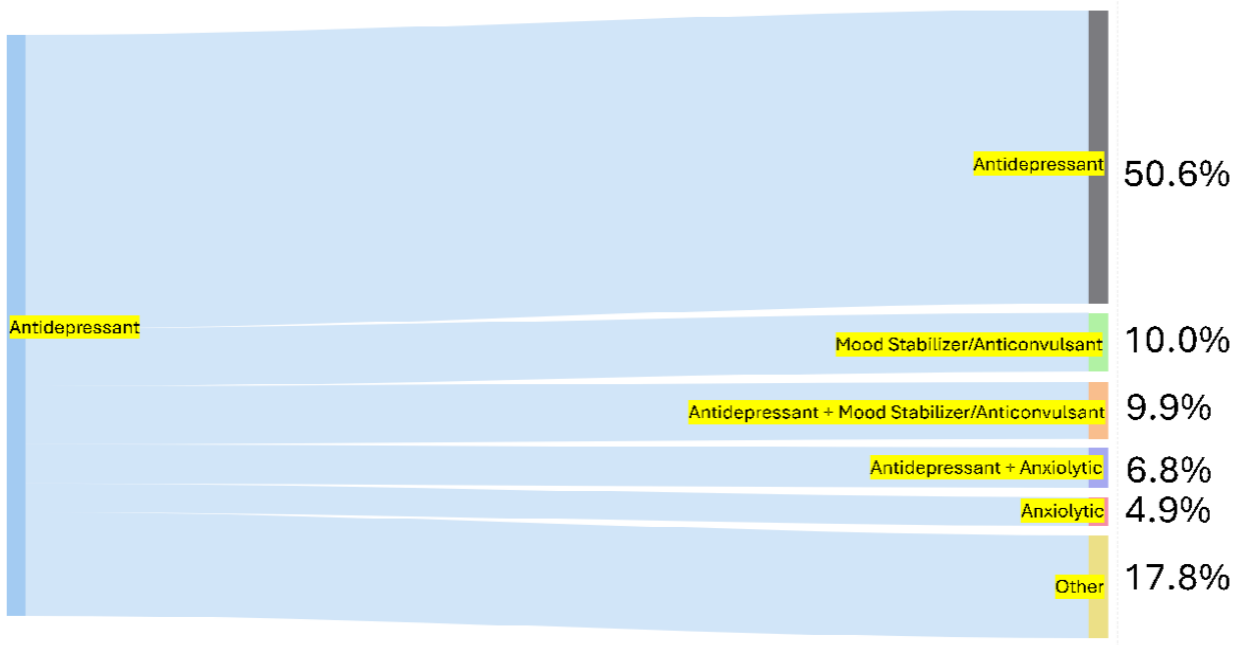
7.5 Provider Type at Diagnosis



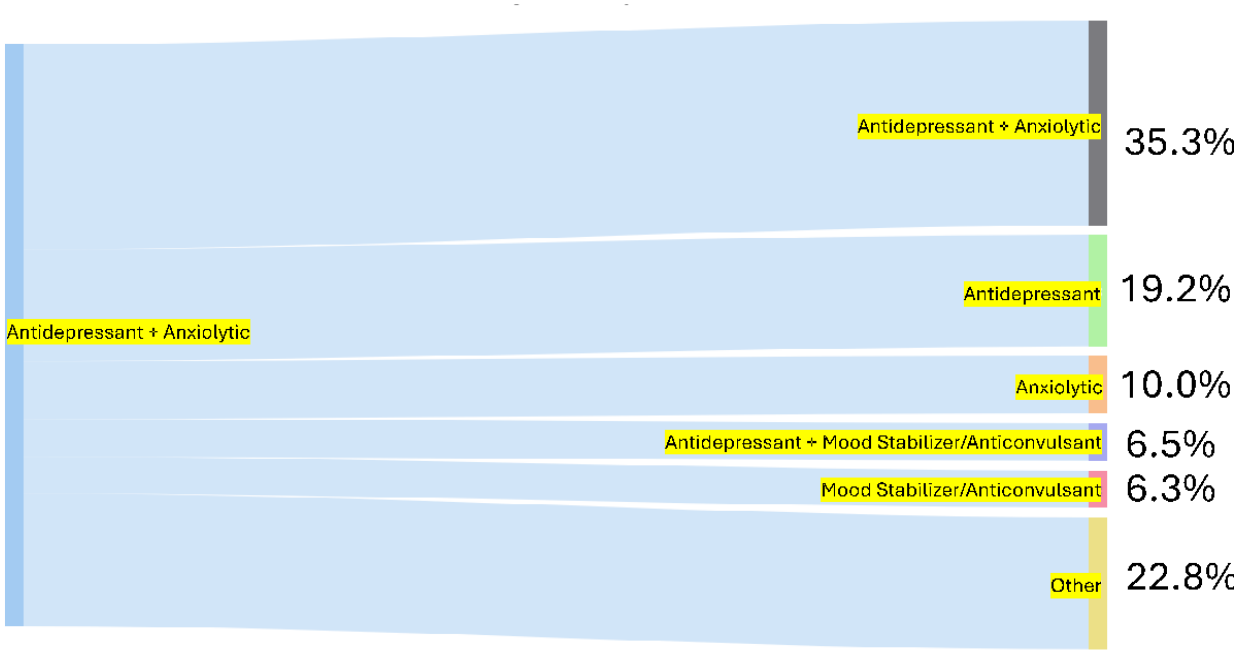
7.6 Treatment Patterns



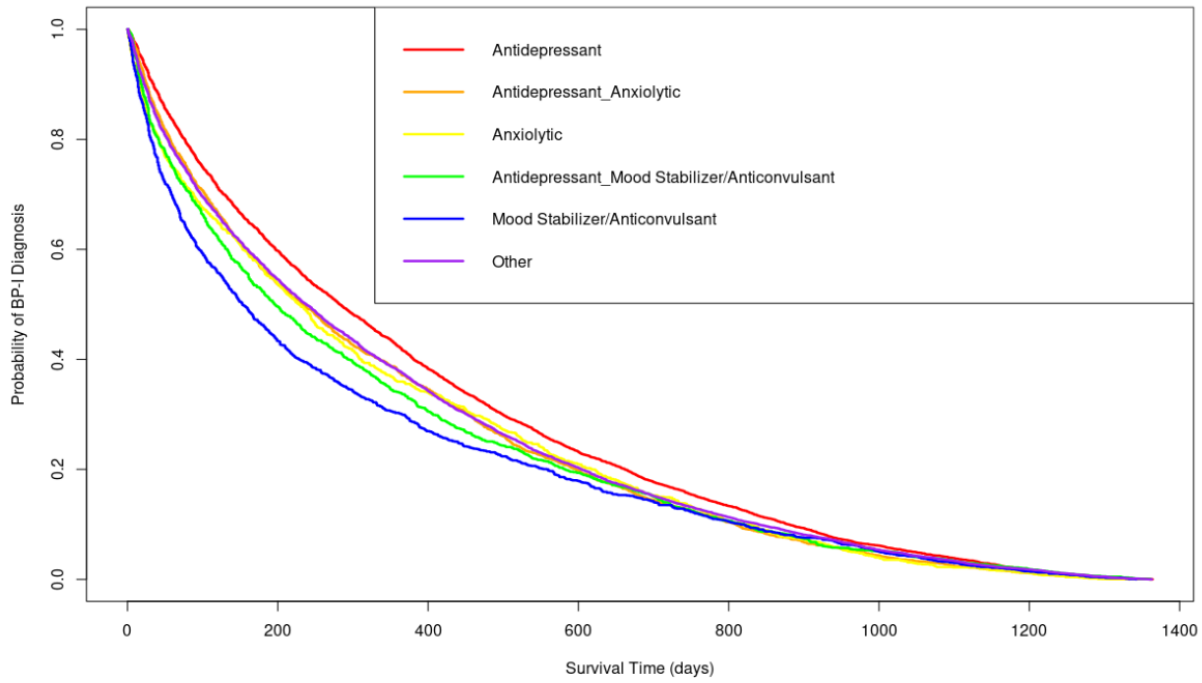
7.7 Sankey Graph- From Antidepressant Monotherapy as First Tx Regimen During Misdiagnosis



7.8 Sankey Graph- From Antidepressant _ Anxiolytic Combination therapy as First Tx Regimen During Misdiagnosis



7.9 Kaplan-Meier Curve- Time Until BP-I Diagnosis Based on First Tx Regimen



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9. APPENDIX

9.1 ICD-10 Diagnosis Codes

ICD-10-CM Code	Code Description
BP-I Disorder	
F30	*Manic episode*
F30.1	*Manic episode without psychotic symptoms*
F30.10	Manic episode without psychotic symptoms, unspecified
F30.11	Manic episode without psychotic symptoms, mild
F30.12	Manic episode without psychotic symptoms, moderate
F30.13	Manic episode, severe, without psychotic symptoms
F30.2	Manic episode, severe with psychotic symptoms
F30.3	Manic episode in partial remission
F30.4	Manic episode in full remission
F31	*Bipolar disorder*
F31.0	Bipolar disorder, current episode hypomanic
F31.1	*Bipolar disorder, current episode manic without psychotic features*
F31.10	Bipolar disorder, current episode manic without psychotic features, unspecified
F31.11	Bipolar disorder, current episode manic without psychotic features, mild

F31.12	Bipolar disorder, current episode manic without psychotic features, moderate
F31.13	Bipolar disorder, current episode manic without psychotic features, severe
F31.2	Bipolar disorder, current episode manic severe with psychotic features
F31.3	*Bipolar disorder, current episode depressed, mild or moderate severity*
F31.30	Bipolar disorder, current episode depressed, mild or moderate severity, unspecified
F31.31	Bipolar disorder, current episode depressed, mild
F31.32	Bipolar disorder, current episode depressed, moderate
F31.4	Bipolar disorder, current episode depressed, severe, without psychotic features
F31.5	Bipolar disorder, current episode depressed, severe, with psychotic features
F31.6	*Bipolar disorder, current episode mixed*
F31.60	Bipolar disorder, current episode mixed, unspecified
F31.61	Bipolar disorder, current episode mixed, mild
F31.62	Bipolar disorder, current episode mixed, moderate
F31.63	Bipolar disorder, current episode mixed, severe, without psychotic features
F31.64	Bipolar disorder, current episode mixed, severe, with psychotic features
F31.7	*Bipolar disorder, currently in remission*
F31.71	Bipolar disorder, in partial remission, most recent episode hypomanic
F31.72	Bipolar disorder, in full remission, most recent episode hypomanic
F31.73	Bipolar disorder, in partial remission, most recent episode manic
F31.74	Bipolar disorder, in full remission, most recent episode manic

F31.75	Bipolar disorder, in partial remission, most recent episode depressed
F31.76	Bipolar disorder, in full remission, most recent episode depressed
F31.77	Bipolar disorder, in partial remission, most recent episode mixed
F31.78	Bipolar disorder, in full remission, most recent episode mixed
Major Depressive Disorder	
F32	*Major depressive disorder, single episode*
F32.0	Major depressive disorder, single episode, mild
F32.1	Major depressive disorder, single episode, moderate
F32.2	Major depressive disorder, single episode, severe without psychotic features
F32.3	Major depressive disorder, single episode, severe with psychotic features
F32.4	Major depressive disorder, single episode, in partial remission
F32.5	Major depressive disorder, single episode, in full remission
F32.9	Major depressive disorder, single episode, unspecified
F33	*Major depressive disorder, recurrent*
F33.0	Major depressive disorder, recurrent, mild
F33.1	Major depressive disorder, recurrent, moderate
F33.2	Major depressive disorder, recurrent severe without psychotic features
F33.3	Major depressive disorder, recurrent, severe with psychotic symptoms
F33.4	*Major depressive disorder, recurrent, in remission*
F33.40	Major depressive disorder, recurrent, in remission, unspecified
F33.41	Major depressive disorder, recurrent, in partial remission
F33.42	Major depressive disorder, recurrent, in full remission
F33.9	Major depressive disorder, recurrent, unspecified
Schizophrenia	
F20	*Schizophrenia*
F20.0	Paranoid schizophrenia
F20.1	Disorganized schizophrenia
F20.2	Catatonic schizophrenia

F20.3	Undifferentiated schizophrenia
F20.5	Residual schizophrenia
F20.8	*Other schizophrenia*
F20.81	Schizophreniform disorder
F20.89	Other schizophrenia
F20.9	Schizophrenia, unspecified
F25	*Schizoaffective disorders*
F25.0	Schizoaffective disorder, bipolar type
F25.1	Schizoaffective disorder, depressive type
F25.8	Other schizoaffective disorders
F25.9	Schizoaffective disorder, unspecified

9.2 Medications and GPI Codes

Generic Name	GPI
Atypical Antipsychotic	
Cariprazine	5940001810
Quetiapine	5915307010
Aripiprazole	5925001500
Lurasidone	5940002310
Brexpiprazole	5925002000
Lumateperone	5940002240
Asenapine	5915501500, 5915501510
Clozapine	5915202000
Iloperidone	5907003500
Olanzapine	5915706000, 5915706010
Olanzapine-Fluoxetine	6299500250
Olanzapine-Samidorphan	6299480250
Paliperidone	5907005000, 5907005010
Risperidone	5907007000, 5907007010
Ziprasidone	5940008510, 5940008520
Antidepressant/Anxiolytics	
Citalopram	5816002010
Escitalopram	5816003410
Fluoxetine	5816004000, 9652646380, 6220604000
Paroxetine	5816006000, 5816006030
Sertraline	9678506010, 5816007010
Desvenlafaxine	5818002020
Duloxetine	5818002510
Venlafaxine	5818009010
Amitriptyline	5820001010

Amitriptyline/Chlordiazepoxide	6299200220
Amoxapine	5820002000
Clomipramine	5820002510, 9646644620
Desipramine	5820003010
Doxepin	5820004010, 6040003010
Imipramine	5820005010, 5820005020
Maprotiline	5830001010
Nortriptyline	5820006010
Protriptyline	5820007010
Trimipramine	5820008010
Isocarboxazid	5810001000
Phenelzine	5810002010, 9672561475
Selegiline	5810002700, 7330003010
Tranylcypromine	5810003010
Bupropion	5830004020, 5830004010, 9644824980
Fluvoxamine	5816004510
Ketamine HCL	9662500339, 7040002010
Mirtazapine	5803005000
Nefazodone	5812005010
Trazodone	5812008010
Vilazodone	5812008810
Psychostimulants	
Amphetamine	6110000000
Amphetamine mixtures (with Dextroamphetamine)	6110990210, 6110990000
Dextroamphetamine	9648507510, 6110002010
Dexmethylphenidate	6140001610
Methylphenidate	6140002000, 6140002010, 9666507010
Lisdexamfetamine	6110002510

Mood stabilizers/Anticonvulsants	
Lithium	5950001010
Divalproex	7250001010
Valproic Acid	7250003000, 9684423600
Valproate	7250002010, 9684423610
Carbamazepine	7260002000, 5940001500
Oxcarbazepine	7260004600
Lamotrigine	7260004000
Typical Antipsychotics	
Chlorpromazine	5920001510
Promazine	9672764370
Thioridazine	5920008010, 9680562810
Loxapine	5915402020, 9664709003
Molindone	5916005010
Perphenazine	9672505600, 5920004500
Thiothixene	5930002010, 9680562855
Droperidol	5720003000
Fluphenazine	9652646447, 9652646447, 5920002530, 5920002510, 9652646450
Haloperidol	5910001010, 5910001030, 9656423730, 5910001020
Pimozide	6200003000
Prochlorperazine	5920005500, 5920005520, 9672764310, 5920005510
Trifluoperazine	5920008510

9.3 Elixhauser Comorbidities

ICD-10-CM Code	Code Description
Congestive heart failure	I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5–I42.9, I43, I50, P29.0
Cardiac arrhythmias	A52.0, I05–I08, I09.1, I09.8, I34–I39, Q23.0–Q23.3, Z95.2–Z95.4
Valvular disease	A52.0, I05–I08, I09.1, I09.8, I34–I39, Q23.0–Q23.3, Z95.2–Z95.4
Pulmonary circulation disorders	I26, I27, I28.0, I28.8, I28.9
Peripheral vascular disease	I70, I81, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9
Hypertension (combine uncomplicated and complicated)	Hypertension, uncomplicated: I10 Hypertension, complicated: I11–I13, I15
Paralysis	G04.1, G11.4, G80.1, G80.2, G81, G82, G83.0–G83.4, G83.9
Other neurological disorders	G10–G13, G20–G22, G25.4, G25.5, G31.2, G31.8, G31.9, G32, G35–G37, G40, G41, G93.1, G93.4, R47.0, R56
Chronic pulmonary disease	I27.8, I27.9, J40–J47, J60–J67, J68.4, J70.1, J70.3
Diabetes without chronic complications	E10.0, E10.1, E10.9, E11.0, E11.1, E11.9, E12.0, E12.1, E12.9, E13.0, E13.1, E13.9, E14.0, E14.1, E14.9
Diabetes with chronic complications	E10.2–E10.8, E11.2–E11.8, E12.2–E12.8, E13.2–E13.8, E14.2–E14.8
Hypothyroidism	E00–E03, E89.0
Renal Failure	I12.0, I13.1, N18, N19, N25.0, Z49.0–Z49.2, Z94.0, Z99.2
Liver Disease	B18, I85, I86.4, I98.2, K70, K71.1, K71.3–K71.5, K71.7, K72–K74, K76.0, K76.2–K76.9, Z94.4

Chronic peptic ulcer disease	K25.7, K25.9, K26.7, K26.9, K27.7, K27.9, K28.7, K28.9
HIV and AIDS	B20–B22, B24
Lymphoma	C81–C85, C88, C96, C90.0, C90.2
Metastatic cancer	C77–C80
Solid tumor without metastasis	C00–C26, C30–C34, C37–C41, C43, C45–C58, C60–C76, C97
Rheumatoid arthritis/ collagen vascular diseases	L94.0, L94.1, L94.3, M05, M06, M08, M12, M12.3, M30, M31–M31.3, M32–M35, M45, M46, M46.8, M46.9
Coagulation deficiency	D65–D68, D69.1, D69.3–D69.6
Obesity	E66
Weight loss	E40–E46, R63.4, R64
Fluid and electrolyte disorders	E22.2, E86, E87
Blood loss anemia	D50.0
Deficiency anemias	D50.8, D50.9, D51–D53
Alcohol abuse	F10, E52, G62.1, I42.6, K29.2, K70.0, K70.3, K70.9, T51, Z50.2, Z71.4, Z72.1
drug abuse	F11–F16, F18, F19, Z71.5, Z72.2
psychoses	F20, F22–F25, F28, F29, F30.2, F31.2, F31.5
Depression	F20.4, F31.3–F31.5, F32, F33, F34.1, F41.2, F43.2

9.4 DSM-5 Comorbidities

Sleep-wake disorders	G47.00, G47.09, G47.10, G47.19, G47.8, G47.9, G47.419, G47.411, G47.429, G47.33, G47.31, R06.3, G47.37, G47.34, G47.35, G47.36, G47.21, G47.22, G47.23, G47.24, G47.26, G47.20, F51.3, F51.4, F51.5, G47.52, G25.81
Anxiety disorders	F93.0, F94.0, F40.218, F40.228, F40.230, F40.231, F40.232, F40.233, F40.248, F40.298, F40.10, F41.0, F40.00, F41.1, F06.4, F41.8, F41.9
Trauma- and stressor-related disorders	F94.1, F94.2, F43.10, F43.0, F43.21, F43.22, F43.23, F43.24, F43.25, F43.20, F43.9, F43.8
Neurodevelopmental disorders	F70, F71, F72, F73, F79, F88, F80.9, F80.0, F80.89, F80.81, F80.9, F84.0, F90.2,F90.1, F90.8, F90.9, F90.0, F81.0, F81.81, F81.2, F82, F98.4, F95.2, F95.1, F95.0, F95.8, F95.9, F89
Medication-induced movement disorders and other adverse effects of medication	G21.11, G21.19, G21.0, G24.02, G24.09, G25.71, G25.79, G24.01, G25.1, T43.205A, T43.205D, T43.205S, T50.905A, T50.905D, T50.905S
Bipolar and related disorders	F31.11,F31.12, F31.13,F31.2, F31.73,F31.74, F31.9,F31.0, F31.31, F31.32,F31.4,F31.5, 31.75, F31.76, F31.9, , F31.81, F31.89, F34.0, F06.33, F06.34, F06.31, F06.32, F31.9
Neurocognitive disorders	F05, R41.0, G31.84, G31.9, F02.81, F02.80, F01.50, F01.51, R41.9
Obsessive-compulsive and related disorders	F42, F63.2, L98.1, F06.8
Sexual dysfunctions	F52.32, F52.21, F52.22, F52.31, F52.6, F52.0, F52.4, F52.8, F52.9
Schizophrenia spectrum and other psychotic disorders	F21, F22, F23, F20.81, F20.9, F25.0, F25.1, F06.2, F06.0, F06.1, F28, F29

Depressive disorders	F34.8, F32.0,F32.1,F32.2, F32.3,F32.4, F32.5,F32.9, F33.0,F33.1 F33.2, F33.3, F33.41, F33.42, F33.9, F34.1, N94.3, F32.8, F32.9
Elimination disorders	F98.0, F98.1, N39.498, R32, R15.9
Personality disorders	F60.0, F60.1, F60.3, F60.4, F60.81,F60.6, F60.7, F60.5, F07.0, F60.89, F60.9
Somatic symptom and related disorders	F45.1, F45.9, F45.21, F45.22, F44.4, F44.5, F44.6, F44.7, F54, F68.10, F45.8
Dissociative disorders	F44.81, F44.0, F44.1, F48.1, F44.89, F44.9
Feeding and eating disorders	F98.3, F50.8, F98.21, F50.01, F50.02, F50.2, F50.9
Disruptive, impulse-control, and conduct disorders	F91.3, F63.81, F91.1, F91.2, F63.3, F91.9, F91.8, F60.2, F63.1, F91.9
Gender dysphoria	F64.2, F64.8, F64.9, F64.1
Paraphilic disorders	F65.3, F65.2, F65.81, F65.89, F65.51, F65.52, F65.4, F65.0, F65.1, F65.9
Gambling disorder	F63.0
Other mental disorders	F09, F99
Other conditions that may be a focus of clinical attention	Z62.820, Z62.891, Z62.29, Z63.8, Z62.898, Z63.0, Z63.5, Z63.4, T74.12XA, T74.12XD, T76.12XA, T76.12XD, T74.22XA, T74.22XD, T76.22XA, T76.22XD, T74.02XA, T74.02XD, T76.02XA, T76.02XD, T74.32XA, T74.32XD, T76.32XA, T76.32XD, Z69.010, Z69.020, Z69.011, Z62.812, Z62.811, Z91.412, Z91.411, T74.11XA, T74.11XD, T76.11XA, T76.11XD, T74.31XA, T74.31XD, T76.31XA, T76.31XD, T74.21XA, T74.21XD, T76.21XA, T76.21XD, T74.01XA, T74.01XD, T76.01XA, T76.01XD, Z69.11, Z69.81, Z69.12, Z70.9, Z69.81, Z69.82, Z69.021, Z62.810, Z91.410, Z55.9, Z56.82, Z56.9, Z59.0, Z59.1, Z59.2, Z59.3, Z59.4, Z59.5, Z59.6, Z59.7, Z59.9, Z60.0, Z65.4, Z65.8, Z64.4, R41.83V, Z60.2, Z60.3, Z60.4, Z60.5,

	Z65.0, Z65.1, Z65.2, Z65.3, Z64.0, Z64.1, Z65.5, Z91.82, Z60.9, Z65.9, Z71.9, Z91.49, Z91.5, Z91.89, Z72.9, Z72.811, Z72.810, Z75.3, Z75.4, Z91.19, E66.9, Z76.5, Z91.83
Mental retardation	F70, F71, F72, F73, F74, F75, F76, F78, F79

9.5 Variables of Interest

Long Name	Name	Description
Clinical variable		
diagnosis principal	PDX	Principal diagnosis explains the main reason for an admission; usually the discharge diagnosis
Diagnosis 1 through diagnosis 3	DX1 through DX3	On the admission table, the principal diagnosis and up to fourteen secondary diagnosis codes as recorded on the service records. On the facility header table, up to nine diagnosis codes. On the inpatient services table and outpatient claims tables, up to four diagnosis codes.
Major Diagnostic Category	MDC	Body-system or disease related groupings of clinical conditions, based on diagnosis codes
length of stay	DAYS	Number of overnight stays for a hospital admission
Quantity of services	QTY	Number of services performed for an inpatient service or outpatient claim and number of prescriptions filled for prescription drug claims
Drug Variables		
Therapeutic Class	THERCLS	A 3-digit code that indicates the therapeutic/ pharmacologic category of the drug product. Based on an aggregation of THERDTL values (see below), though not related directly by numeric value (i.e. THERCLS=124 will not correspond to 10-digit THERDTL values beginning with 124).
Therapeutic group	THERGRP	Therapeutic Group is a further aggregation of THERCLS (Therapeutic Class) values. See THERCLS and THERDTL.
Generic product id	GENERID	
national drug code	NDENUM	
Demographic Variables		
Age of patient	AGE	

gender of patient	SEX	Gender of the patient on admissions, services, outpatient claims and prescription drug claims; of covered life on populations
employment status	EESTATU	
Data Type	DATATYPE	A value identifying whether the claim or eligible population is fee-for-service, encounter, Medicare, or Medicare encounter. This field was new in 1998 and was developed to identify claims formerly found in the Private Pay Fee-For-Service, Encounter, and Medicare databases.
data type month 1 through 12	DATTYP1 through DATTYP12	
date enrollment end	DTEND	End date of continuous enrollment period
date enrollment start	DTSTART	Start date of continuous enrollment period
geographic location employee	EGEOLOC	Geographic location (state, division, region) of primary beneficiary's residence
enrollment months	ENRMON	Total number of months during the year in which an individual was enrolled
member days	MEMDAYS	The number of member days an enrollee was enrolled
enrollee Id	ENROLID	A unique three to eleven digit number identifying each enrollee in the data file
Health plan indicator	HLTHPLAN	An indicator as to whether the data supplier of a record was a large US employer or a Health Plan
metropolitan statistical area	MSA	Metropolitan Statistical Area of primary beneficiary (mapped from zip code)
region	REGION	Geographic Region of employee residence (northeast, north central, south, west, unknown)
plan indicator	PLANTYP	Type of benefit plan

state hospital	STATE	The geographic state in which the admission occurred
place of service	STDPLAC	Setting where service occurred
provider type	STDPROV	001-099 Facility100-799 Physician 100-199 Non-admitting Physicians 200-499 Admitting Physicians 500-599 Surgeons800-899 Professionals (Non-Physician)900-999 Agencies
Enrollment indicator month 1 through 12	ENRIND1 through ENRIND12	
date service incurred	SYCDATE	Date of inpatient or outpatient service or date prescription was filled