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ORIGINAL ARTICLE

Antipsychotic treatment patterns and predictors of polypharmacy in psychotic disorders: 20-year real-world data from a tertiary center

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Abstract

Background Antipsychotics are the cornerstone of psychotic disorder treatment, often used in combination with other psychotropics. However, real-world data on inpatient treatment in Türkiye remain scarce.

Aim This study aims to investigate the clinical characteristics, hospitalization features, and psychotropic treatment patterns of inpatients diagnosed with psychotic disorders.

Methods This retrospective, cross-sectional pharmacoepidemiological study examined treatment patterns and predictors of antipsychotic polypharmacy (APP) among 934 patients (1241 hospitalizations) diagnosed with psychotic disorders at a university psychiatry clinic in Eastern Türkiye between 2001 and 2021.

Results The sample included 35.8% females and had a mean age of 34.03 ± 11.01 years. APP (use of ≥ 2 antipsychotics) was identified in 37.7% of cases, being significantly more frequent in males, those aged 55–65, schizophrenia (SCH) patients, and post-2012 hospitalizations. Atypical antipsychotics were prescribed in 95.25% of cases, and the most common APP pattern was atypical–atypical combinations (52.5%). Olanzapine (33.04%), risperidone (27.88%), and quetiapine (19.58%) were the most frequently prescribed agents. Mood stabilizers and antidepressants were used in 25.22% and 14.5% of cases, respectively. Multinomial regression showed that schizoaffective disorder (SAD) was strongly associated with both APP (OR = 3.05) and combined therapy (OR = 20.0), while delusional disorder also predicted combined therapy (OR = 2.4). Longer hospitalization duration and post-2012 admissions predicted APP, whereas outpatient follow-up and medical comorbidities predicted combined treatment. Linear regression revealed that higher PANSS scores predicted longer hospital stays, while hospitalizations in later years were associated with shorter stays.

Conclusions This study provides one of the most comprehensive longitudinal evaluations of inpatient psychosis treatment in Türkiye and offers valuable insights into prescribing trends, informing future clinical and policy approaches.

Keywords Antipsychotic polypharmacy · Inpatient psychiatry · Prescribing trends · Schizophrenia spectrum disorders · Treatment patterns

Introduction

Schizophrenia (SCH) and related psychotic disorders are defined as severe and chronic mental disorders that typically emerge in early adulthood and persist throughout the lifespan, with pervasive effects on cognition, functioning, and quality of life [1]. Versions of the World Health Organization's (WHO) International Classification of Diseases (ICD) and Diagnostic and Statistical Manuals of Mental Disorders classify psychotic disorders based on symptom duration, type, association with mood episodes, and etiological factors [2].

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People with psychotic disorders are at a high risk of cognitive decline, poor social functioning, substance abuse, suicidality, homelessness, victimization, and violence if they do not receive effective, appropriately dosed, and ongoing treatment [3]. Establishing a conclusive diagnosis, treating acute episodes, addressing medication nonadherence, and assessing aggression or suicide frequently call for inpatient care.

According to international guidelines, the first-line treatment for SCH and other psychotic disorders should be antipsychotic monotherapy [2, 4]. Antipsychotic polypharmacy (APP), which is the concurrent use of two or more antipsychotics, is one alternative strategy that is necessary because up to 20% of patients do not respond well to monotherapy [5]. There are notable regional differences in the reported prevalence rates of APP, which range from 10% to 30%, 16% in North America, 23% in Europe, and up to 32% in Asia [6–8].Interestingly, APP regimens frequently include atypical antipsychotics [9].

Although results on the effectiveness of combination strategies involving other psychotropic classes—such as mood stabilizers (MS), anxiolytics, or antidepressants (AD)—remain mixed, they are commonly used in addition to APP [10]. In addition to more general systemic and cultural variations across healthcare settings, patient-specific factors (such as symptom profile, comorbidities, and side effects) also contribute to the variability in combination practices [11].

Pharmacoepidemiology, the discipline that examines drug use and its effects across populations, is increasingly relevant in psychiatric research [12]. Recent pharmacoepidemiology has shown to change prescribing patterns with increased use of medications such as clozapine, aripiprazole, and paliperidone, and decreased use of risperidone and haloperidol [9]. Long-acting injectable (LAI) antipsychotics also gained popularity since they aid in the management of adherence-related relapse [13].

This study adopts a descriptive, cross-sectional, and retrospective pharmacoepidemiological approach to examine antipsychotic prescribing practices among inpatients with psychotic disorders in a tertiary psychiatric clinic of a university. By analyzing demographic and clinical correlates of polypharmacy and combination, and by assessing longitudinal trends in psychotropic use, this study aims to identify vulnerable subgroups and inform targeted, evidence-based prescribing practices. In doing so, it contributes to the growing body of research on real-world antipsychotic utilization.

Materials and methods

Ethical approval and study design

This retrospective cross-sectional study was approved by the Local University Ethics and Research Committee (Approval No: B.30.2.ATA.0.01.00/433). It examined psychotropic prescribing patterns in adult inpatients with psychotic disorders hospitalized between 2001 and 2021 at the Department of Psychiatry, University. In line with institutional policy, no additional consent was required beyond the general consent obtained at admission.

Study sample

Files of patients aged 18–65 years hospitalized with a primary diagnosis within the Schizophrenia Spectrum and Other Psychotic Disorders (ICD-9/10) were reviewed. During the transition from ICD-9 to ICD-10, our clinic applied structured diagnostic reassessment for all new admissions. All diagnoses were based on the contemporaneous ICD criteria, and documentation included symptom descriptions enabling cross-period comparability. Additionally, senior attending psychiatrists supervised all diagnostic decisions throughout the two decades to ensure consistency. Diagnoses included Schizophrenia (SCH), Schizoaffective Disorder (SAD), Delusional Disorder (DD), Brief Psychotic Disorder (BPD), Schizophreniform Disorder (SFD), and Non-Organic Psychotic Disorder (NOPD).

Data collection

Three senior psychiatry residents reviewed 1609 patient records, used a standardized data-entry form, and performed periodic cross-checks. To enhance reliability, 10% of the files were independently reviewed by two raters. The inter-rater agreement was high (Cohen's $\kappa = 0.87$). The inclusion criteria (age 18–65, hospitalization with ICD-9/10 psychotic disorder diagnosis, complete clinical records) and exclusion criteria (organic brain syndromes, primary substance-induced psychoses, severe intellectual disability, incomplete files or primary substance-induced psychotic disorder.) Of these, 368 were excluded. Cases with primary substance-induced psychotic disorder were excluded based on ICD diagnostic criteria and urine toxicology screening when available. For patients with psychotic disorders who also had comorbid personality disorders, the primary diagnosis determined by the attending psychiatrist at admission was used. These cases were not excluded, as personality

disorders were considered comorbidities rather than exclusionary conditions unless they were the primary reason for hospitalization.

A total of 1241 records were analyzed (Fig. 1). Extracted data included sociodemographic and clinical characteristics, prescriptions at admission and discharge, and psychotropic use during hospitalization. Antipsychotic polypharmacy (APP) was defined as concurrent prescription of ≥2 antipsychotics. Combination referred to adding another psychotropic (antidepressant, mood stabilizer, benzodiazepine) to an antipsychotic regimen. Only scheduled medications were considered; as needed prescriptions were excluded.

Statistical analysis

Analyses were conducted with IBM SPSS Statistics 25.0 (licensed 2017). Normality was assessed via histograms and the Kolmogorov–Smirnov test. Descriptive statistics were presented as means ± SD, medians (IQR), and percentages. Pearson's Chi-square was used for categorical comparisons; Mann–Whitney U for two-group comparisons; Kruskal–Wallis for ≥3 groups. Multinomial logistic regression examined predictors of treatment modality (monotherapy, combination, polypharmacy), with monotherapy as reference. Variables consistently shown in the psychosis pharmacoepidemiology literature to influence treatment modality (e.g., age, gender, hospitalization history, symptom severity) were included a priori regardless of univariate significance. Severity Odds ratios (OR) with 95% confidence intervals (CI) were reported. Linear regression assessed predictors of length of hospital stay using variables such as year of hospitalization, age at first symptom, duration of untreated psychosis (DUP), number of stays, illness duration, exacerbations, PANSS at admission, and number of discharge medications. To avoid overfitting, additional variables were included only if their univariate relationship with length of stay reached a threshold of $p<0.10$. A p-value <0.05 was considered significant. All variance inflation factors (VIF) values were below 2.5, indicating no concerning multicollinearity.

Results

Socio-demographic and clinical characteristics

A total of 1241 hospitalizations of 934 patients with psychotic spectrum disorders were analyzed. Females comprised 35.8% ($n=334$). The most common age group was 25–34 years (34.8%). Half of patients were single (52.1%), one quarter employed (26.9%), and two-thirds (62.3%) had pre-secondary education. Winter birth rate was 32.5%.

Schizophrenia (SCH) was the most frequent diagnosis (48.2%), followed by schizoaffective disorder (SAD, 18.4%). Urgent presentations and younger age (18–24 years) were more common in BPD & SFD. Male proportion was lower in BPD & SFD and NOPD. DD patients had higher winter births and marriage rates. SCH patients had the highest rate of work disability, while SAD patients more often reported a family history of psychotic/bipolar disorders or intellectual disability. Age of onset and diagnosis were highest in DD; BPD & SFD had the shortest DUP and illness duration. SAD patients had the highest hospitalization frequency and shortest remission. Length of stay was longer in SCH and SAD than in BPD & SFD or NOPD (Table 1).

Treatment approaches

At discharge, 34.6% received monotherapy ($n=430$), 27.7% combination ($n=344$), and 37.7% polypharmacy

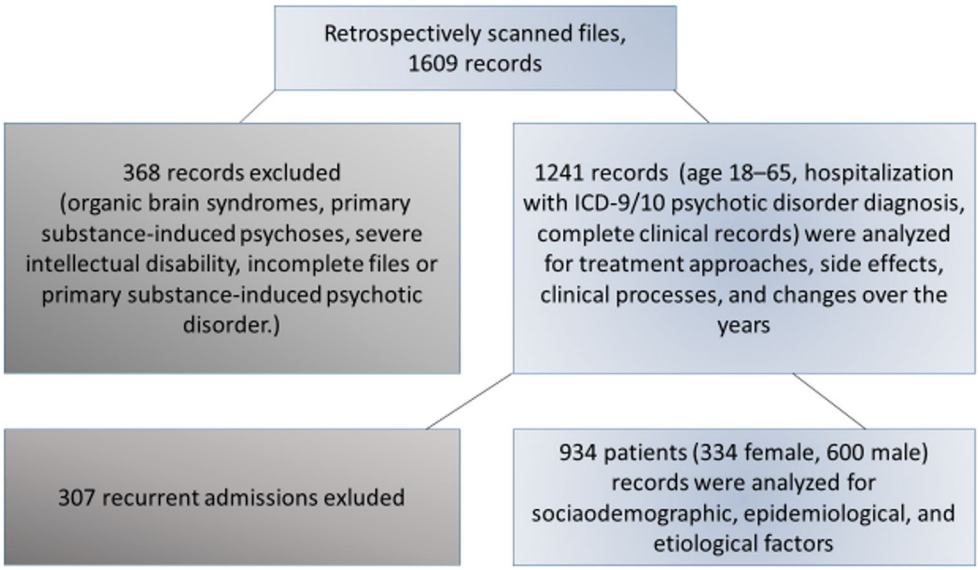


Fig. 1 Flow chart

Table 1 Sociodemographic and Clinical-related characteristics of the patients ($n=934$)

		All patients		SCH		DD		BPD&SFD		SAD		NOPD		p*
		%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	
The mode of arrival	Polyclinic	68.8	643	67.6	304	78.9	75	55.9	62	68.6	118	79.2	84	**<0.001**
	ER	31.2	291	32.4	146	21.1	20	44.1	49	31.4	54	20.8	22	
Gender	Female	35.8	334	31.1	140	38.9	37	46.8	52	34.9	60	42.5	45	**0.013**
	Male	64.2	600	68.9	310	61.1	58	53.2	59	65.1	112	57.5	61	
Marital status	Married	37.4	349	28.0	126	71.6	68	41.4	46	40.1	69	37.7	40	**<0.001**
	Single	60.9	569	71.9	324	28.4	27	58.6	64	59.9	103	62.3	66	
Education year groups	0–8	62.3	582	57.6	259	70.5	67	73.0	81	61.6	106	65.1	69	0.239
	9–12	25.1	234	28.0	126	21.1	20	18.9	21	25.0	43	22.6	24	
	13–16	12.1	113	13.8	62	7.4	7	8.1	9	12.8	22	12.3	13	
	>16	0.5	5	0.7	3	1.1	1	0.0	0	0.6	1	0.0	0	
Employment status	Working	26.9	251	21.8	98	38.9	37	36.0	40	26.7	46	28.3	30	**<0.001**
	Unable	35.2	329	44.7	201	13.7	13	7.2	8	43.1	75	31.1	33	
	Not	37.9	354	33.6	151	47.4	45	56.8	63	30.2	52	40.6	43	
Residential location	Village	20.7	193	20.9	94	12.6	12	28.8	32	24.4	42	12.3	13	**0.025**
	Country	26.1	244	26.2	118	28.4	27	22.5	25	26.2	45	27.4	29	
	City	53.2	497	52.9	238	57.9	55	48.6	54	49.4	85	60.4	64	
Tobacco users	Yes	45.6	426	48.9	220	41.1	39	32.4	36	52.9	91	37.7	40	**0.002**
Developmental Retardation	Yes	2.8	26	2.7	12	0.0	0	0.9	1	1.2	2	10.4	11	**<0.001**
Season of birth	Winter	32.5	304	38.0	153	39.8	33	30.1	28	38.4	58	30.5	32	0.652
	Spring	22.7	212	25.3	102	24.1	20	32.3	30	19.9	30	28.6	30	
	Summer	16.7	156	17.4	70	15.7	13	20.4	19	19.9	30	22.9	24	
	Fall	17.5	163	19.4	78	20.5	17	17.2	16	21.9	33	18.1	19	
Family history[a]	No	59.4	738	58.4	263	64.2	61	77.5	86	48.8	84	60.4	64	**<0.001**
	Unknown	10.3	128	9.1	41	12.6	12	7.2	8	9.9	17	14.2	15	
	Group 1	5.5	69	6.2	28	6.3	6	6.3	7	7.6	13	1.9	2	
	Group 2	24.6	306	26.2	118	16.8	16	9.0	10	33.7	58	23.6	25	
Medical Comorbidity	Yes	14.5	153	10.8	36	26.7	27	10.8	12	9.5	19	17.2	17	**0.011**
Suicide	Yes	14.7	183	16.4	100	10	12	7	8	16.6	39	13.4	19	**0.037**
Homoside	Yes	20.7	257	21.8	133	17.4	21	24.6	28	18.3	43	19.7	28	0.666
		mean ± SD		mean ± SD		mean ± SD		mean ± SD		mean ± SD		mean ± SD		
Age		34.4 ± 11.2		34.3 ± 10.9		44 ± 12.4		28.1 ± 9.8		34.5 ± 9.2		32.7 ± 10.6		**<0.001**
Age of First Psychotic Symptoms		25 ± 9.2		23.5 ± 7.7		35.5 ± 12.7		26.4 ± 9.5		22.6 ± 6.8		25.0 ± 8.8		**<0.001**
Age at Diagnosis		26.9 ± 9.7		25.8 ± 8.1		38.3 ± 12.9		26.9 ± 9.5		24.3 ± 7.4		26.6 ± 9.7		**<0.001**
DUP		24.5 ± 44.3		28.3 ± 43.7		32.8 ± 57.9		7.8 ± 24.5		21.8 ± 40.0		21.5 ± 50.4		**<0.001**
Number of Hospitalizations		3.4 ± 3.6		3.5 ± 3.3		1.94 ± 1.4		1.4 ± 0.9		5.6 ± 5		2.7 ± 2.6		**<0.001**
Last Hospitalization (days)		37.2 ± 25.4		39.1 ± 25.4		35.9 ± 24.3		29.7 ± 22.4		40.2 ± 26.2		32.3 ± 26.3		**<0.001**
Longest Remission Period (month)		24.7 ± 37.5		28.1 ± 36.0		18.3 ± 47.7		8.8 ± 23.7		31.0 ± 37.7		19.6 ± 38.8		**<0.001**
Total Disease Duration (months)		109 ± 103		129 ± 105		78 ± 94		24 ± 46		137 ± 100		80 ± 94		**<0.001**
Baseline CGI (severity)		5.1 ± 0.7		5.1 ± 0.7		5 ± 0.5		5.2 ± 1.1		5.2 ± 0.7		4.8 ± 0.7		0.285

Table 1 (continued)

	All patients		SCH		DD		BPD&SFD		SAD		NOPD		p^*
	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	
Total PANSS score	83.9 ± 20.5		86.9 ± 21.1		71.9 ± 17.4		85.6 ± 20.5		82.2 ± 20.6		82.4 ± 18.2		**< 0.001**
Positive PANSS score	29.7 ± 16.8		29.7 ± 16.7		23.8 ± 12.2		28.2 ± 16.7		32.4 ± 18.7		24.6 ± 16.9		**0.006**
Negative PANSS score	35.6 ± 26.3		40.2 ± 25.9		25.4 ± 24.3		36.9 ± 27.4		25.1 ± 24.1		47.5 ± 23.7		**< 0.001**
Total BPRS score	46.7 ± 16.9		48.4 ± 16.9		45.6 ± 14.9		46.6 ± 16.1		44.4 ± 18.3		41.2 ± 14.5		**0.012**
GAF score	32.4 ± 12.6		31.1 ± 12.7		38.6 ± 13.4		32.6 ± 13.7		35.1 ± 12.4		35.1 ± 11.3		**0.033**

Abbreviations: SCH: Schizophrenia. DD: Delusional disorder. BPD&SFD: Brief psychotic disorder&Schizophreniform disorder. SAD: Schizoaffective disorder. NOPD: non-organic psychotic disorder. p*: Chi-Square Test. *$p < 0.05$. **$p < 0.01$. ***$p < 0.001$

[a]: Group 1 – patients who have a family member who has a neurotic disorder such as anxiety, or depression. OCD. conversion. etc. Group 2 – patients who have a family member who has a psychotic disorder, bipolar affective disorder, and mental retardation

($n = 467$). Most patients used atypical APs (95.3%), while 23.6% received typical APs. Typical AP use ($p = 0.006$) and polypharmacy ($p = 0.004$) were higher in men. The most common APP pattern was atypical–atypical (52.5%).

LAI use was more frequent in males ($p < 0.001$) and SCH ($p = 0.018$), but lower in younger (18–24 years) and BPD & SFD groups (both $p < 0.001$). Combination therapy was most common in SAD, particularly with mood stabilizers/antiepileptics ($p < 0.001$). AD use was highest in NOPD ($p < 0.001$), while BZD use was lowest in DD ($p = 0.007$). Details of psychotropic utilization are provided in Table 2.

Temporal changes

Hospitalizations increased from 490 (39%) in 2001–2011 to 751 (61%) in 2012–2021, peaking in 2018 and reaching a low in 2003 (Fig. 2a–b).

Between 2012 and 2021, there were significant increases in polypharmacy ($p < 0.001$), atypical AP use ($p < 0.001$), combined atypical–atypical use ($p < 0.001$), LAI use ($p < 0.001$), AD ($p = 0.031$), and BZD use ($p < 0.001$) (Fig. 3a–b). Use of aripiprazole, paliperidone, and clozapine increased (all $p < 0.001$), while risperidone, chlorpromazine, and zuclopenthixol decreased (all $p < 0.001$) (Fig. 3c). LAI formulations of aripiprazole, haloperidol, and monthly paliperidone rose (all $p < 0.001$), whereas risperidone LAI declined ($p < 0.001$).

Specific APs' changing utilization rates over the years are illustrated below [Figure 4].

Predictors of treatment approaches

Multinomial regression showed significant model fit ($\chi^2 = 395.1$, df = 54, $p < 0.001$, Nagelkerke $R^2 = 0.33$). Compared with monotherapy, combined treatment was predicted by outpatient rather than emergency admissions, medical comorbidity, longer hospital stay and later hospitalization decade. Relative to BPD & SFD, combined treatment was 2.4 times more likely (95% CI = 1.06–5.57) in DD and 20 times more (95% CI = 8.51–46.95) in SAD.

Polypharmacy was associated with longer hospital stay (OR = 1.019, 95% CI = 1.012–1.026, $p < 0.001$) and later hospitalization decade (OR = 0.308, 95% CI = 0.218–0.434, $p < 0.001$). SCH and SAD diagnoses had 2.05- and 3.15-fold higher APP risk relative to BPD & SFD, respectively (Table 3). Other factors (age, sex, illness duration, family history, smoking, suicidality) were not predictive.

Table 2 Patterns of the most commonly used psychotropic drugs

				n	%
AP	Olanzapine			410	33.04
	Risperidone			346	27.88
	Quetiapine			243	19.58
	Paliperidone			229	18.45
	Aripiprazole			227	18.29
	Clozapine			180	14.50
	Amisülpiride			103	8.30
	Haloperidol			202	16.28
LAI (38.84%. *n* = 482)	Paliperidone monthly			217	17.49
	Risperidone			139	11.20
	Aripiprazole			61	4.92
MS (25.22%. *n* = 313)	Valproic Acid (VA)			184	14.83
	Lithium			120	9.67
AD (14.50%. *n* = 180)	SSRI (9.11%. *n* = 113)		Sertraline	48	3.87
			Fluoxetine	28	2.26
			Escitalopram	23	1.85
	SNRI (1.45%. *n* = 118)		Venlafaxine	16	1.29
BZD (64.38%. *n* = 799)	Lorazepam			677	54.55
	Clonazepam			95	7.66
APP (≥2 antipsychotics)					
		FGA + FGA		112	9
	SGA + SGA			652	52.6
	FGA + SGA			226	18.2

AP = antipsychotics, LAI = long-acting injectable antipsychotics, MS = mood stabilizers, AD = antidepressant, BZD = benzodiazepine APP = antipsychotic polypharmacy

Duration of hospitalization

Linear regression (Adj. R^2=0.082, $p < 0.001$, Durbin-Watson = 1.968) identified year of hospitalization (negative predictor) and PANSS admission score (positive predictor) as significant factors for length of stay. Other variables (age at first symptom, DUP, number of hospitalizations, illness duration, exacerbations, discharge medications) were included but less influential (Fig. 5).

Discussion

The demographic profile of our sample was consistent with prior psychosis research: male predominance (two-thirds) and mean age of 34 years paralleled findings from both large and small-scale studies on schizophrenia (SCH) spectrum disorders [14]. One-third of patients were winter-born, supporting evidence linking winter birth with increased SCH risk—possibly via seasonal viral or environmental exposures [15]. Although well described in SCH, our results suggest this association may extend across the broader psychosis spectrum. Family history of psychiatric illness was most frequent in schizoaffective disorder (SAD), followed by SCH, reflecting shared genetic vulnerability between psychotic and affective disorders [16].

Diagnostic distinctions were evident. Patients with delusional disorder (DD) had later onset and higher marriage rates, indicating a more insidious course and preserved social functioning [17]. Conversely, brief psychotic disorder (BPD) and schizophreniform disorder (SFD) cases presented younger with shorter illness durations, consistent with their reactive and self-limiting nature [18]. These contrasts underscore the prognostic value of diagnostic specificity.

The results of this study broadly align with existing research characterizing the demographic and clinical heterogeneity of psychotic disorders, while also highlighting distinctive treatment patterns across diagnostic subgroups. Consistent with prior observations, male patients were more frequently prescribed typical antipsychotics and long-acting injectable (LAI) formulations, possibly reflecting greater concerns about adherence, more severe symptomatology, or cultural perceptions influencing prescribing decisions [19]. This underscores the potential benefits of gender-informed treatment planning to address higher relapse risk and functional impairment among men with psychosis.

The differences in the incidence of polypharmacy in psychotic conditions in different areas of the world are due to several non-medical factors in addition to the clinical aspects, pracs of the health care system, availability of medications, culture of the prescribers, and reimbursement

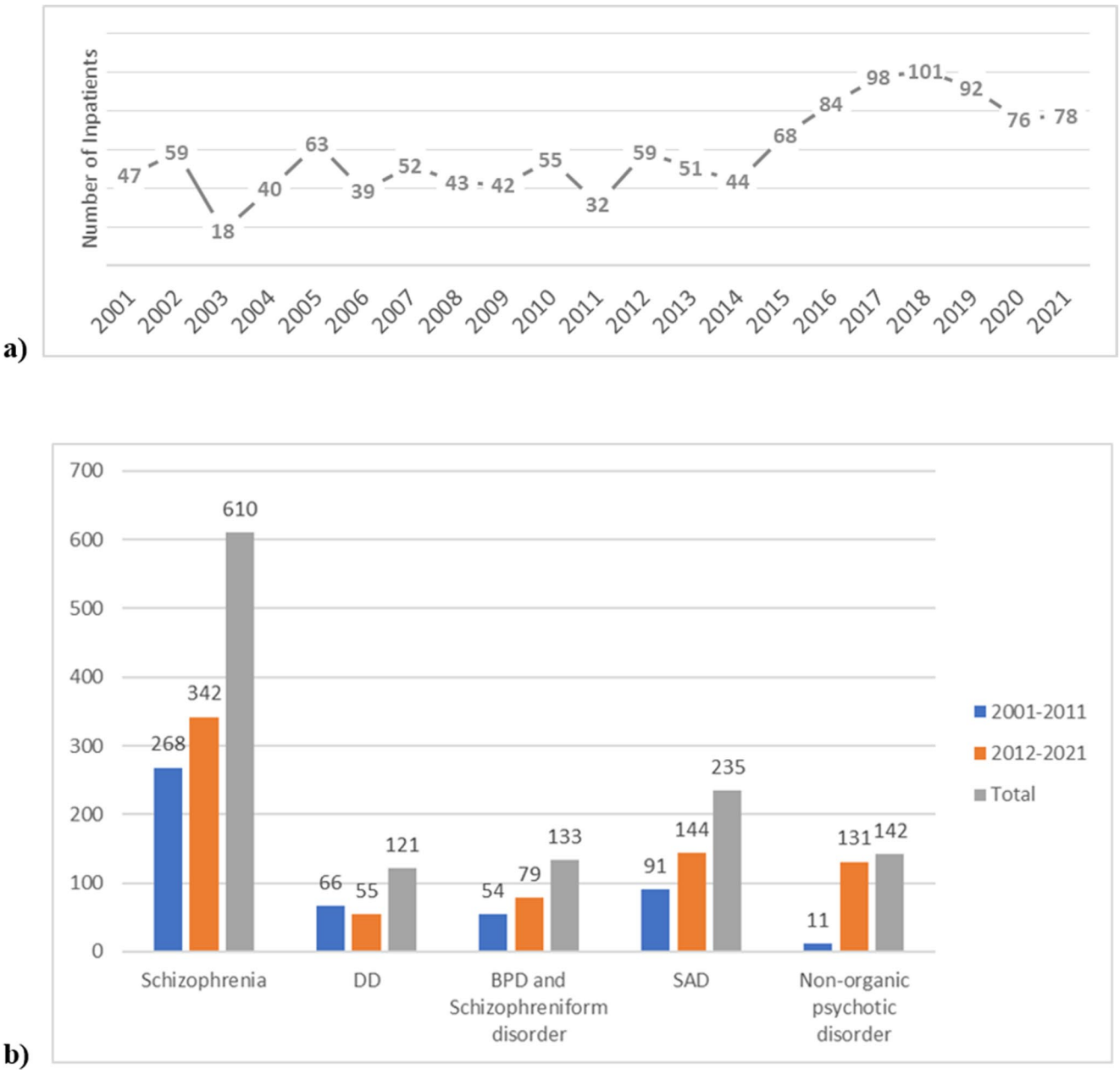
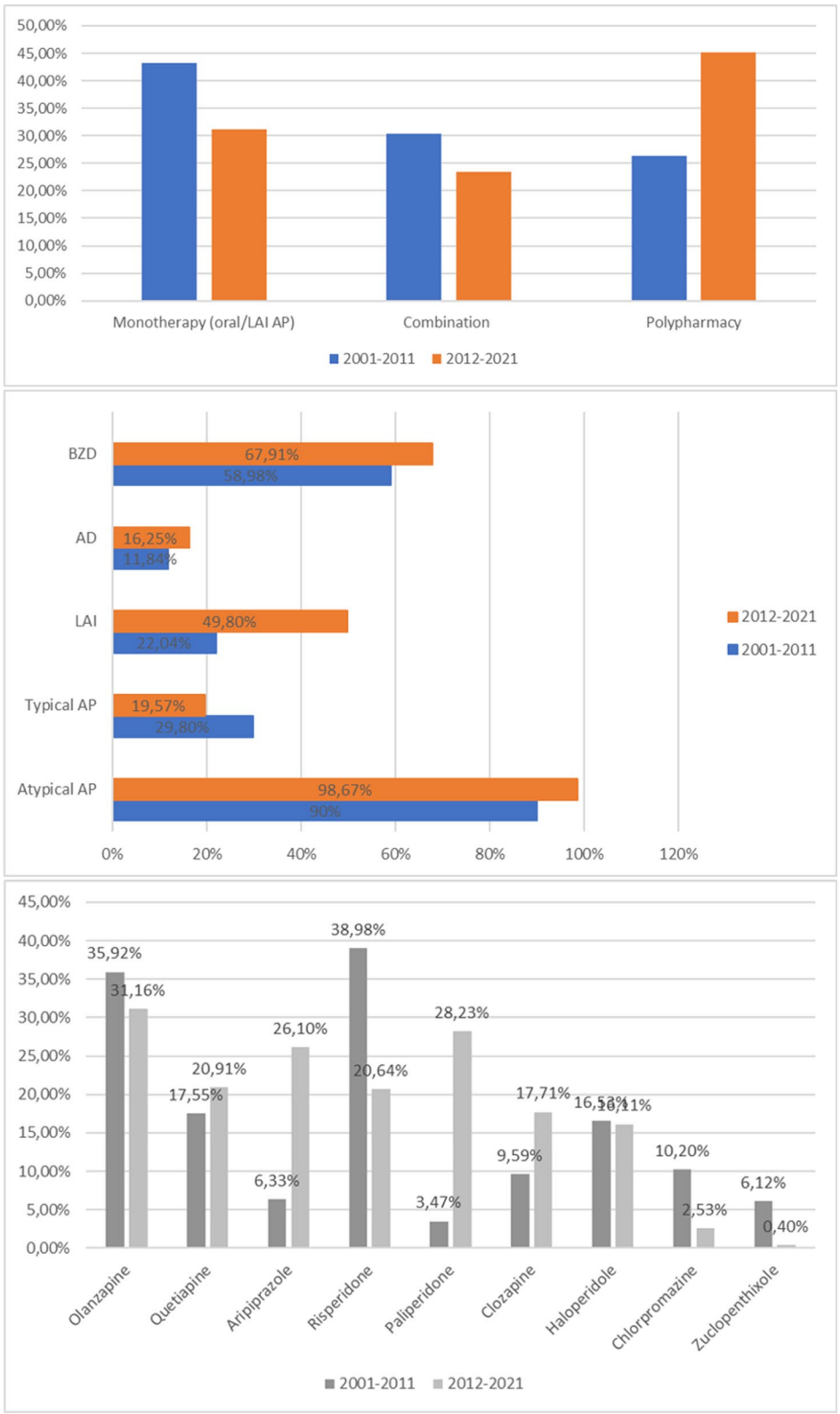


Fig. 2 Number of Patients and Diagnosis by Years and Decades

schemes [9]. In Türkiye the incidence of anti antipsychotics polypharmacy is 37% in our cohort is therefore situated at the upper end of global reports. Several structural factors may explain this trend. First, tertiary psychiatric centers in Türkiye disproportionately receive patients with severe, treatment-resistant illness, contributing to higher use of combination and augmentation strategies. Second, the national reimbursement system (SGK) covers a broad range of both typical and atypical antipsychotics, including LAIs and clozapine, reducing economic barriers to multidrug regimens. Third, historical prescribing culture—similar to patterns observed in parts of Asia—has favored rapid symptom control in acute inpatient settings, which may inadvertently increase the use of overlapping antipsychotics, benzodiazepines, and mood stabilizers [20]. Finally, national formulary changes, generic availability of SGAs, and the growing presence of LAIs in clinical practice have influenced clinicians' preferences during the last decade [21].

Overall, these system-level factors help explain why polypharmacy rates in our setting are higher than those seen in Western Europe and more comparable to other high-severity tertiary centers worldwide [6, 7, 9]. Acknowledging these international differences is important for understanding

Fig. 3 Changes in Years



prescribing behavior and for guiding efforts to promote more rational antipsychotic use. Such efforts include reinforcing guideline-based practice, closely monitoring combination treatments, and increasing clinician training on when and how to safely reduce unnecessary medications.

Although atypical antipsychotics were preferred over typical antipsychotics in all diagnostic groups in this

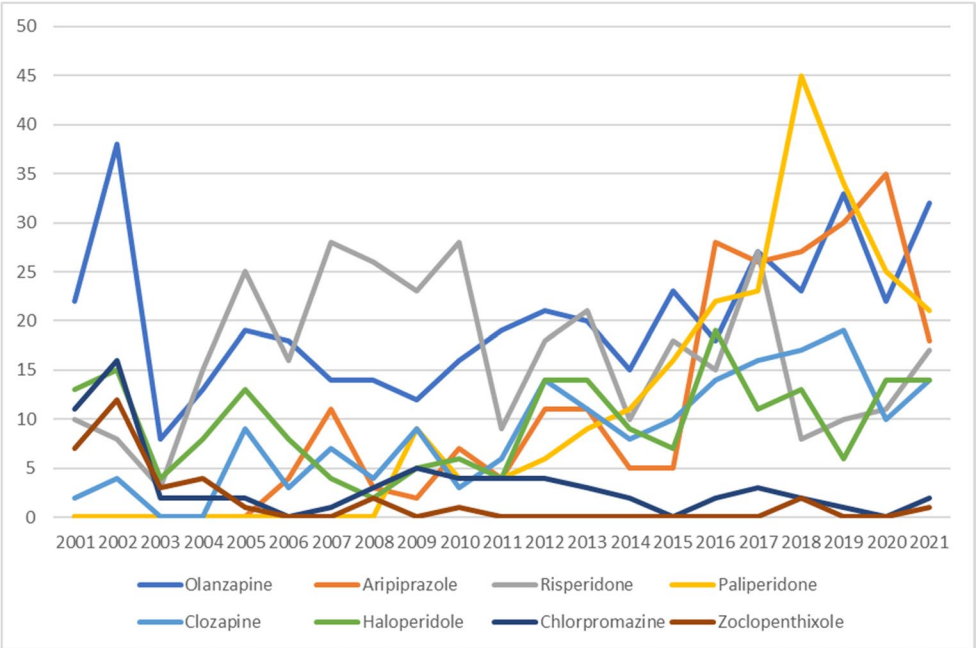


Fig. 4 Specific APs' changing utilization rates over the years are illustrated below

study, different patterns of pharmacotherapy were also evident across diagnostic categories. Reasons for APP use include increased focus by clinicians on targeting different receptor profiles (e.g., dopamine-serotonin modulation, α-adrenergic blockade, glutamatergic potentiation), newer atypical antipsychotics, management of partial response and treatment resistance in a tertiary care patient setting [4, 8]. When the literature was reviewed both in Türkiye and internationally, old and new atypical antipsychotics were preferred over typical ones in most studies, and atypical antipsychotic use rates were reported to be over 70% [10]. The higher prevalence of polypharmacy and mood stabilizer use in patients diagnosed with SAD supports the idea that SAD is a diagnostically hybrid condition that requires multidimensional pharmacological approaches [22]. In contrast, the more conservative use of antipsychotic combinations in patients with BPD & SFD is in line with clinical guidelines advocating minimum and duration treatment for acute, transient psychoses [23].

Second-generation antipsychotics (SGAs), especially olanzapine and risperidone, were most common, consistent with international trends favoring better tolerability [24]. Nevertheless, the widespread adoption of polypharmacy—despite guidelines generally recommending monotherapy highlights the pragmatic considerations clinicians face in managing persistent or treatment-resistant symptoms [12]. The frequent use of atypical–atypical combinations in the present study echoes previous reports documenting similar practices in Asia and Europe [11]. The increasing preference for atypical antipsychotics may be attributed to their lower risk of extrapyramidal side effects and their potential greater efficacy in addressing cognitive and negative symptoms. Aripiprazole has also been highlighted in several studies as a useful adjunct to relieve hyperprolactinemia without compromising antipsychotic efficacy [25]. Collectively, these findings suggest that the higher rates of atypical antipsychotic combinations observed in our study reflect both clinical necessity and evolving prescribing practices. Although this strategy may reflect attempts to optimize symptom control, it raises ongoing questions about cumulative side effects and long-term outcomes.

The higher rates of clozapine use observed in schizophrenia cases are notable and likely attributable to the referral of treatment-resistant patients to the tertiary care setting, aligning with recommendations favoring earlier clozapine initiation in such cases [5, 14]. Similarly, the predominance of paliperidone palmitate as the preferred LAI formulation supports previous findings highlighting its favorable adherence profile and clinical effectiveness in schizophrenia management [21]. In contrast, LAI use was lower in patients diagnosed with BPD or SFD, consistent with treatment guidelines recommending short-term oral antipsychotics [26].

The use of atypical antipsychotic combinations was found to be significantly lower in patients diagnosed with BPD & SFD compared to other diagnostic groups ($p < 0.001$). Although specific studies focusing exclusively on treatment patterns in these diagnostic categories are limited, clinical guidelines generally recommend using the lowest effective dose and the shortest treatment duration for such patients, due to the typically transient nature of their symptoms. Particularly for short-term psychotic conditions like BPD & SFD, monotherapy with atypical antipsychotics is advised. Supporting this approach, a study examining

Table 3 Multinomial logistic regression for polypharmacy and combine therapy treatments (with respect to monotheraphy)

Independent Variable		Combine therapy OR (95% CI)	Polypharmacy OR (95% CI)
Age		0.96 (0.88–1.04)	1.01 (0.94–1.08)
Age of First Psychotic Symptoms		1.01 (0.94–1.10)	1.00 (0.93–1.01)
DUP		1.00 (0.99–1.00)	1.00 (0.99–1.00)
Number of Hospitalizations		1.10 (0.98–1.23)	1.01 (1.01–1.25)
Last Hospitalization	(days)	**1.02**(1.01–1.03) ***	**1.27** (0.99–1.62) ***
Longest Remission Period	(months)	1.00 (0.99–1.01)	1.00 (0.99–1.01)
Total Disease Duration	(months)	1.00 (1.00–1.01)	1.01 (1.00–1.01)
Number of attacks		0.98 (0.88–1.10)	1.01 (0.90–1.12)
Admission Method	Polyclinic	**1.68** (1.13–2.48) **	0.89 (0.64–1.23)
	Emergency	0	0
Gender	Female	0.76(0.48–1.18)	0.68 (0.48–0.96)
	Male	0	0
Marital Status	Married	0.99(0.65–1.49)	0.95(0.67–1.35)
	Single	0	0
Tobacco users	Yes	0.98(0.66–1.44)	0.83(0.59–1.17)
	No	0	0
Family history	No	1.03 (0.68–1.56)	1.36 (0.94–1.97)
	Unknown	1.24 (0.67–2.33)	1.44 (0.82–2.51)
	Group 1	0.96 (0.43–1.44)	0.92 (0.45–1.88)
	Group 2	0	0
Medical Comorbidity	Yes	**1.87** (1.08–3.26) *	1.39 (0.85–2.28)
	No	0	0
Annual Periods	2001–2011	**1.68** (1.13–2.50) ***	**0.30** (0.22–0.43) **
	2012–2021	0	0
Employment status	Working	0.85 (0.56–1.28)	0.85 (0.56–1.28)
	Unable	1.47 (0.98–2.20)	1.47 (0.98–2.20)
	Disabled	0	0
Suicide	Yes	0.74(0.48–1.15)	0.74(0.48–1.15)
	No	0	0
Diagnosis groups	SCH	1.88 (0.89–3.98)	**2.05** (1.18–3.58) *
	SAD	**20.0** (8.51–46.95)***	**3.15** (1.51–6.56)**
	DD	**2.43** (1.06–5.57)*	1.15 (0.60–2.19)
	NOPD	2.43 (0.98–6.01)	1.82 (0.90–3.67)
	BPD&SFD	0	0
Clinical Severity	Groups Mild Moderate Significant	1.36 (0.21–1.06)	0.48 (0.21–1.06)
	Severe	1.86 (0.33–1.34)	0.66 (0.33–1.34)
		1.48 (0.55–4.02)	0.70 (0.34–1.45)
		0	0

OR: odds ratio; 95% CI: 95% Confidence Interval; * $p<0.05$; ** $p<0.01$; *** $p<0.001$

Goodness-of-Fit: Pearson = 0.11, Deviance = 0.98

Nagelkerke R^2 = 0.33

polypharmacy patterns in schizophrenia spectrum disorders found that patients with SAD had a higher likelihood of complex polypharmacy, whereas those grouped with diagnoses such as DD, BPD & SFD, and unspecified psychosis showed a lower probability of such regimens [27]. Similarly, a study by Zhu et al. involving hospitalized patients with first-episode psychosis—99 of whom were diagnosed with BPD or SFD—found no significant association between diagnosis and treatment modality, suggesting conservative pharmacological strategies may be sufficient in these cases [23]. Accordingly, the lower frequency of atypical antipsychotic combination use observed in our study among these diagnostic groups likely reflects this clinical preference for brief and focused pharmacotherapy in patients with transient psychotic presentations. Nonetheless, further research with larger and diagnostically diverse samples is warranted to substantiate these findings.

The rise in atypical antipsychotic use, SGA–SGA combinations, and LAI prescriptions observed during the second decade may also be shaped by several system-level influences. These include the wider availability of newer antipsychotic agents, expanded national formulary coverage and SGK reimbursement policies, evolving insurance regulations, increasing clinician familiarity with recently introduced medications, and the broader adoption of LAIs as they became more accessible across Türkiye. Hospital-level

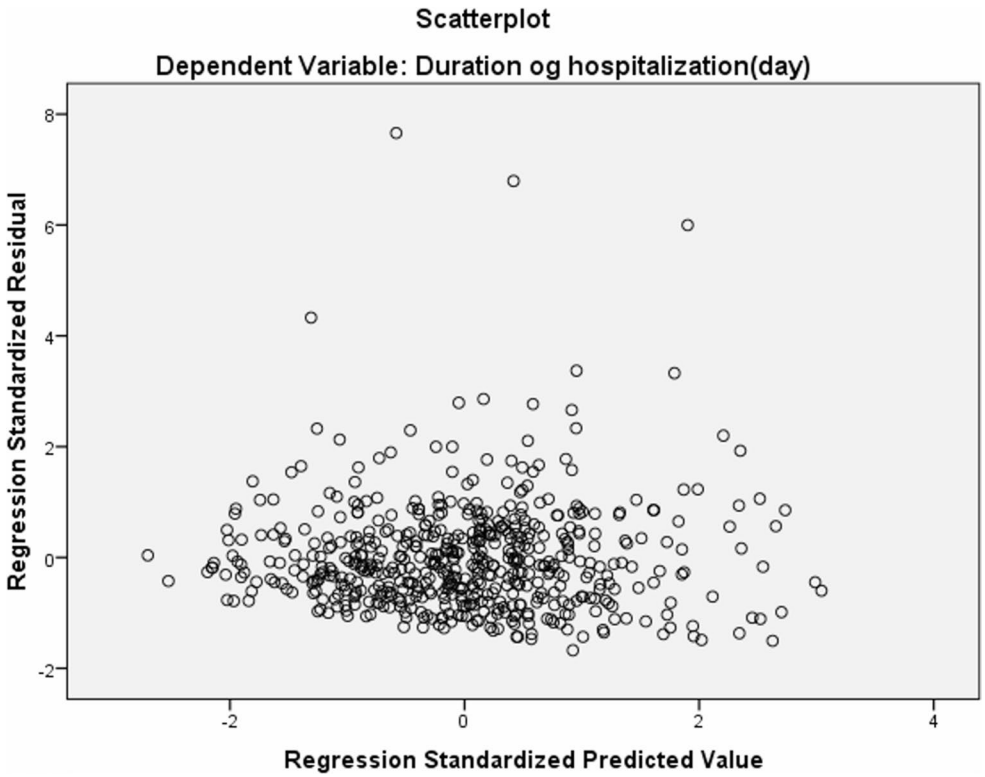


Fig. 5 Linear regression for duration of hospitalization

procurement and supply practices may have further contributed to these shifts. Taken together, these contextual factors likely influenced prescribing patterns over time and should be considered when interpreting the observed trends, as they limit the ability to draw causal inferences.

The frequent co-prescription of mood stabilizers, antidepressants, and benzodiazepines further reflects the complexity of real-world psychosis management, particularly in severe or treatment-resistant cases, comorbid affective or anxiety symptoms or prominent negative symptoms [28]. The high prevalence of benzodiazepine use in this inpatient sample exceeds rates typically reported in community settings and likely relates to the acute behavioral dysregulation and agitation commonly encountered during hospitalization. While such regimens may be necessary for short-term stabilization, they call for careful monitoring to mitigate risks of dependence and adverse effects.

Regression analyses supported these patterns: SAD diagnosis predicted both combination therapy and polypharmacy, consistent with its complex presentation [29]. Wide CIs reflect subgroup heterogeneity and variance inflation due to the relatively smaller size of the SAD group compared with schizophrenia. The broad CI (8.51–46.95) suggests that while the association is robust and statistically significant, the precise magnitude should be interpreted cautiously. The effect likely reflects the complex clinical presentation of SAD and its well-documented tendency toward multimodal pharmacotherapy, but we emphasize that the CI widens the uncertainty range around the effect size. We also highlight that, because this is a real-world inpatient sample with high clinical severity, effect sizes may naturally be larger and more variable than in randomized controlled settings.

Longer hospitalization was associated with both strategies, reflecting higher illness severity, poor response, or medication adjustment needs [30]. Conversely, declining hospitalization duration over time may relate to policy shifts, earlier intervention, or community-based care. Outpatient admissions predicted combination therapy, suggesting partial response to prior monotherapy. Comorbid medical conditions also increased polytherapy likelihood, consistent with studies showing complex prescribing in comorbid patients [31].

Collectively, findings highlight how diagnosis, illness course, comorbidities, and gender shape prescribing. Rising use of SGAs, LAIs, and polypharmacy reflects evolving practice driven by both necessity and guidelines [6]. These trends, while reflecting efforts to address persistent symptoms and adherence challenges, warrant continued evaluation of long- term safety and functional outcomes.

In our analysis of factors affecting length of stay, more recent years were associated with shorter hospital stays, which may reflect improvements in clinical care, earlier diagnosis and treatment, or changes in healthcare policies aimed at reducing length of stay. Conversely, higher symptom severity on admission was associated with longer hospital

stays, highlighting the practical impact of acute symptom burden on treatment needs and healthcare resources.

While the model only explains a modest portion of the variation in length of stay, these results are consistent with existing research suggesting that both clinical severity and systemic changes in healthcare delivery shape inpatient outcomes. Looking ahead, future studies would benefit from considering factors like institutional practices, family or community support, and access to outpatient care, all of which could play a role in safely reducing the need for prolonged hospitalization. Incorporating such insights into routine practice can help move toward more efficient, personalized, and recovery-oriented care for individuals with psychotic disorders.

Strengths and limitations

This study benefits from a large, diagnostically diverse inpatient sample, detailed sociodemographic and pharmacological data, and a 20-year observation period capturing prescribing shifts. Results of statistical analysis with both categorical and continuous predictors are considered in light of local and global prescribing trends. Limitations include its retrospective design, reliance on clinical records, and tertiary setting bias toward severe cases. Clinical variables such as illness duration and hospitalization frequency may share conceptual overlap and should be interpreted with this context in mind. Absence of standardized symptom ratings, psychosocial intervention data, and patient-reported outcomes limited assessment of clinical impact. Broader prospective studies incorporating psychosocial and functional measures are needed.

Conclusions

This study highlights considerable variability in antipsychotic prescribing practices among inpatients with psychotic disorders, emphasizing the frequent use of polypharmacy and mood stabilizer combinations, particularly in schizoaffective disorder. While atypical antipsychotics were predominant, treatment choices were influenced by diagnosis, illness severity, comorbidities, and hospitalization era. These findings underscore the need for individualized, evidence-based approaches that balance symptom control with minimizing treatment burden and long-term risks [32]. Future prospective research integrating standardized assessments and patient-centered outcomes will be essential to inform safer, more effective pharmacological strategies in psychosis care.

International guidelines from APA, NICE, and CANMAT consistently recommend antipsychotic monotherapy as first-line treatment, reserving combination strategies for cases with clear clinical justifications, such as inadequate response, intolerance, or cross-titration. The rate of polypharmacy we observed (37.7%) highlights the need to strengthen systematic medication review in inpatient care, document rationales, and conduct regular treatment discontinuation assessments. Strategies to reduce unnecessary polypharmacy include early initiation of clozapine when indicated, structured monitoring of treatment response, and use of LAIs instead of changing or adding oral medications in noncompliant patients. Multidisciplinary case discussions and the importance of improving medication adherence should be considered during discharge planning.

Antipsychotic polypharmacy has been associated in previous literature with higher metabolic risk, including weight gain, dyslipidemia, insulin resistance, and cardiovascular burden [33]. Polypharmacy may also increase cognitive load, sedation, and anticholinergic load, and reduce functional recovery; results are particularly pronounced in schizophrenia spectrum disorders, highlighting the need for careful prescribing and routine metabolic monitoring [34]. Future studies should include direct metabolic or neurocognitive measures in patients receiving multiple antipsychotic treatment.

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Declarations

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