Research

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Active Psychotropic Medication Use and Clinical Correlates in Children and Adolescents with Autism Spectrum Disorder

Otizm Spektrum Bozukluğu Tanılı Çocuk ve Ergenlerde Aktif Psikotrop İlaç Kullanımı ve İlişkili Klinik Özellikler

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ABSTRACT

Objective: The aim of this study was to describe active psychotropic medication records and agent-level patterns in children and adolescents with autism spectrum disorder (ASD), estimate psychotropic polypharmacy, and identify characteristics associated with an active psychotropic medication record.

Method: This single-centre retrospective cross-sectional study included patients with ASD aged 36–216 months who attended a tertiary child and adolescent psychiatry clinic during 2025. Of 172 records assessed, five patients with cognitive impairment attributable to an identified cause other than ASD were excluded; 167 were analysed. Current medications not documented as discontinued were classified as active. Polypharmacy was defined as at least two active psychotropic medications at the same visit.

Results: At least one active psychotropic medication was recorded for 123 patients (73.7%; 95% CI 66.5%–79.7%), and polypharmacy for 94 (56.3%; 95% CI 48.7%–63.6%); among the 123 patients with an active record, the polypharmacy proportion was 76.4%. At least one antipsychotic was recorded for 112 patients (67.1%) and at least two for 30 (18.0%). ADHD (aPR = 2.51; 95% CI 1.77–3.55) and irritability (aPR = 1.55; 95% CI 1.28–1.89) were independently associated with an active medication record.

Conclusion: Active psychotropic medication records and record-based polypharmacy were frequent in this tertiary-care sample, reflecting electronic health record documentation rather than confirmed medication intake.

Keywords: Autism spectrum disorder, psychotropic medication, attention-deficit/hyperactivity disorder

ÖZ

Amaç: Otizm spektrum bozukluğu (OSB) olan çocuk ve ergenlerde aktif psikotrop ilaç kayıtlarını ve etken madde örüntülerini tanımlamak, çoklu psikotrop ilaç kullanımını belirlemek ve aktif ilaç kaydıyla ilişkili klinik özellikleri incelemek amaçlandı.

Yöntem: Bu tek merkezli retrospektif kesitsel çalışmada, 2025 yılında üçüncü basamak çocuk ve ergen psikiyatrisi kliniğine başvuran 36–216 aylık OSB hastalarının elektronik kayıtları incelendi. Değerlendirilen 172 kayıttan beş hasta dışlandı ve 167 hasta analiz edildi. Çoklu kullanım, aynı başvuruda en az iki aktif psikotrop ilaç kaydı olarak tanımlandı.

Bulgular: En az bir aktif psikotrop ilaç 123 hastada (%73,7; %95 GA %66,5–%79,7), çoklu kullanım 94 hastada (%56,3; %95 GA %48,7–%63,6) kayıtlıydı; aktif ilaç kaydı bulunanlarda çoklu kullanım oranı %76,4'tü. En az bir antipsikotik 112 hastada (%67,1), en az iki antipsikotik 30 hastada (%18,0) kayıtlıydı. DEHB (aPR = 2,51; %95 GA 1,77–3,55) ve irritabilite (aPR = 1,55; %95 GA 1,28–1,89) aktif ilaç kaydıyla bağımsız ilişkiliydi.

Sonuç: Bu üçüncü basamak sağlık hizmeti örnekleminde, aktif psikotrop ilaç kullanım kayıtları ve kayıtlara dayalı çoklu ilaç kullanımı sıkça görülmekteydi; bu durum, teyit edilmiş ilaç alımından ziyade elektronik sağlık kayıtlarındaki belgelemeyi yansıtmaktadır.

Anahtar sözcükler: Otizm spektrum bozukluğu, psikotrop ilaç, dikkat eksikliği hiperaktivite bozukluğu

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Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterised by persistent differences in social communication and interaction and by restricted or repetitive patterns of behaviour. Children and adolescents with ASD frequently have co-occurring psychiatric and behavioural conditions, including attention-deficit/hyperactivity disorder (ADHD), anxiety, sleep problems, irritability, aggression, and self-injurious behaviour. These conditions contribute to clinical complexity and may prompt consideration of pharmacological treatment (Mutluer et al. 2022).

Pharmacotherapy does not treat the core features of ASD and is generally directed towards co-occurring psychiatric disorders or behavioural symptoms that substantially impair functioning (Hyman et al. 2020). Risperidone and aripiprazole have the strongest evidence among antipsychotics for ASD-associated irritability, although potential benefits must be balanced against metabolic, neurological, and other adverse effects (Solmi et al. 2020, Deb et al. 2023, Meza et al. 2025). ADHD symptoms may be treated with methylphenidate, atomoxetine, or guanfacine, but response and tolerability vary (Hyman et al. 2020, Rodrigues et al. 2021).

Estimates of psychotropic medication use in paediatric ASD populations vary considerably. A systematic review of 47 studies found rates ranging from 2.7% to 80%, with a median of 41.9% among children (Jobski et al. 2017). Differences in age, clinical setting, comorbidity burden, intellectual disability criteria, data source, medication coverage, and observation period probably contribute to this variation. Polypharmacy estimates are additionally affected by the number of medications required, the denominator used, and whether concurrent exposure must be sustained over time (Ritter et al. 2021). Consequently, estimates based on same-visit active medication lists, prescription or dispensing claims requiring a specified duration of overlap, and annual medication exposure quantify different constructs and should not be treated as directly comparable prevalence measures. This methodological heterogeneity underscores the importance of explicitly reporting the data source, observation window, concurrency requirement, medication threshold, and denominator used to calculate psychotropic polypharmacy.

Studies from Türkiye have also reported heterogeneous medication patterns across outpatient, tertiary-care, and adolescent samples (Uygun et al. 2020, Göknar et al. 2022, Özaydın et al. 2024, Cevher Binici et al. 2026). However, past medication history, annual prescribing, and medications documented as active at a particular visit represent different exposure measures and cannot be compared without qualification.

Evidence from Türkiye remains limited on the combined assessment of visit-based active medication records, agent-level distributions, psychotropic polypharmacy defined by a single explicit criterion, and associated clinical characteristics within the same ASD sample. Combining these elements allows the overall frequency of active medication records, the individual agents contributing to same-visit polypharmacy, and the associated clinical characteristics to be interpreted within a single denominator and exposure framework. This approach provides a transparent and clinically recognisable description of documented medication complexity and a reproducible reference point for future studies from Türkiye using clearly specified polypharmacy definitions. However, same-visit active co-listing does not establish dispensing, actual concurrent intake, treatment duration, or clinical appropriateness.

This study therefore aimed to determine the frequency and agent-level distribution of active psychotropic medications among children and adolescents with ASD attending a tertiary child and adolescent psychiatry clinic; estimate the proportion with at least two active psychotropic medications at the same visit; and identify sociodemographic and clinical characteristics associated with an active psychotropic medication record. Medication dispensing, adherence, treatment duration, effectiveness, and clinical appropriateness were outside the scope of the study.

Method

The study was approved by the Adana City Training and Research Hospital Scientific Research Ethics Committee on 25 June 2026 (Decision No. 1433). Access to the data for research purposes and all analyses

occurred after ethics approval. The ethics committee waived the requirement for individual informed consent because de-identified retrospective records were used. The study was conducted in accordance with the Declaration of Helsinki.

Sample

This single-centre retrospective cross-sectional study was conducted in the Child and Adolescent Psychiatry Clinic of Adana City Training and Research Hospital. Electronic health records were reviewed retrospectively for 1 January–31 December 2025. When a patient had more than one eligible visit during the study period, the first eligible visit was used. No new clinical interview, scale administration, or laboratory assessment was performed. Reporting was prepared with reference to the RECORD recommendations for observational studies using routinely collected health data (Benchimol et al. 2015).

Patients were eligible if they were aged 36–216 months and had received a diagnosis of childhood autism (F84.0), atypical autism (F84.1), or Asperger syndrome (F84.5) according to ICD-10 from a child and adolescent psychiatrist. These historical ICD-10 categories reflect the diagnostic coding recorded in the institutional electronic health records during the study period; for the purposes of this study, they were collectively analysed as ASD. Exclusion criteria were a chronic neurological condition other than epilepsy; metabolic, systemic, or genetic disease; continuous non-psychotropic treatment for a chronic condition; duplicate records; or missing core data.

For the purposes of eligibility, an identified cause of cognitive impairment was defined as a genetic, metabolic, neurological, syndromic, or other medical aetiology that was explicitly documented in the electronic health record and considered by the treating clinician to account for the cognitive impairment. Cognitive impairment or low cognitive-test performance without a documented aetiological diagnosis was not, by itself, considered an identified cause.

Of 172 records assessed, five patients with cognitive impairment attributable to an identified cause other than ASD were excluded; two of these patients also had syndromic ASD. No additional patient met another exclusion criterion, and the final sample comprised 167 patients. Because all records meeting the eligibility criteria during the prespecified 12-month period were included, no a priori sample-size calculation was performed.

Procedure

Data were extracted with a standardised form and included age, sex, ICD-10 ASD subtype, CARS severity, developmental characteristics, epilepsy, psychiatric comorbidities, behavioural characteristics, and active medications. Age was grouped as 36–71, 72–131, and 132–216 months for descriptive presentation only. ASD severity was evaluated with the Childhood Autism Rating Scale (CARS) (Schopler et al. 1980), for which the Turkish version has established validity and reliability (İncekaş Gassaloğlu et al. 2016). Scores were classified as mild-to-moderate (30–36.5) or severe (37–60). For each patient, the CARS score recorded closest in time to the selected study visit was used in the analyses. The interval between the CARS assessment and the selected visit, as well as its timing relative to psychotropic treatment initiation or continuation, was not standardised. Accordingly, recorded CARS severity should be interpreted as a routinely documented clinical measure rather than as ASD severity assessed at a uniform pretreatment time point.

Psychiatric comorbidities were obtained from diagnoses documented during routine clinical assessments. Structured diagnostic interviews were not systematically administered or documented, and the recorded diagnoses were not independently re-evaluated for the purposes of this retrospective study. Consequently, comorbidity variables reflected routine clinical diagnostic judgement, and the extent of possible diagnostic misclassification could not be quantified. At least one psychiatric comorbidity was defined as at least one documented psychiatric disorder other than ASD. The composite disruptive behaviour disorder variable comprised oppositional defiant disorder, conduct disorder, or both. Irritability, aggression, and self-injurious behaviour were examined as clinical characteristics rather than diagnostic

categories and were considered present only when explicitly documented. Blank fields were not interpreted as confirmed absence. There was one missing observation for sleep disorder, three for aggression, and two for self-injurious behaviour; irritability data were complete. Missing observations were excluded using variable-specific valid denominators, without imputation.

Active Psychotropic Medication Records and Definition of Polypharmacy

Medication exposure was determined from the current medication list and the clinical note for the selected visit. A medication was classified as active when it was listed as current and was not documented as discontinued in the same note. Medications documented as previously discontinued, prescribed only when required, or reduced to zero during discontinuation were not classified as active. This definition did not establish dispensing, adherence, regular use, or duration of exposure. Active medication status was not independently verified against pharmacy dispensing or claims data or through a structured contemporaneous caregiver medication reconciliation.

The psychotropic medication count included antipsychotics, ADHD medications, antidepressants, mood stabilisers used for psychiatric indications, melatonin, and sedative-hypnotics. Antiepileptic medications used solely for epilepsy were excluded.

Psychotropic polypharmacy was defined as at least two active psychotropic medications at the same visit. Its frequency was calculated using the entire analysis sample (n = 167) as the denominator. As a complementary denominator-specific estimate, the proportion meeting the same polypharmacy definition was also calculated among patients with at least one active psychotropic medication record. The presence of at least two active antipsychotics at the same visit was retained as a separate secondary measure and was not treated as an alternative definition of psychotropic polypharmacy.

Statistical Analysis

Categorical variables are presented as counts and percentages; valid denominators are reported for variables with missing observations. Continuous age is presented as median and interquartile range, whereas clinically meaningful age categories are additionally provided for descriptive purposes in Table 1. Wilson score 95% confidence intervals were calculated for the principal patient-level proportions. Patients with (n = 123) and without (n = 44) an active psychotropic medication record were compared across 19 prespecified sociodemographic, developmental, and clinical variables using the Mann–Whitney U test for continuous age and Pearson's chi-square test or Fisher's exact test for categorical variables, as appropriate. To control the family-wise type I error rate, Bonferroni-adjusted p values were calculated as min(19 × unadjusted p, 1). Statistical significance was defined as a Bonferroni-adjusted $p < 0.05$, equivalent to an unadjusted $p < 0.05/19$ (0.00263).

Clinical characteristics independently associated with an active psychotropic medication record were examined using modified Poisson regression with a log link and robust standard errors (Zou 2004). Age in months, sex, recorded CARS severity, ADHD, and irritability were entered simultaneously on the basis of clinical relevance and model parsimony. Age was retained as a continuous variable to avoid the information loss associated with categorisation. For clinical interpretability, its coefficient is presented per 12-month increase. No data-driven variable-selection procedure was applied. Associations are reported as adjusted prevalence ratios (aPRs) with 95% confidence intervals (CIs) and p values.

Because ADHD and irritability were uncommon among patients without an active psychotropic medication record, two sensitivity analyses were conducted to assess the robustness of the multivariable findings. First, the modified Poisson model was repeated after omitting each participant in turn to assess the influence of individual observations on the adjusted prevalence ratios. Second, a Firth bias-reduced logistic regression model using the same covariate set was fitted to reduce potential finite-sample bias. Because the outcome was common, odds ratios from the Firth model were used only to assess the direction and robustness of the associations and were not interpreted as effect estimates directly comparable in magnitude to prevalence ratios. A formal separation diagnostic for complete or quasi-complete separation was also performed.

Analyses were conducted in Python 3.12.3 using pandas 3.0.2, NumPy 2.4.4, SciPy 1.17.1, and statsmodels 0.14.6. The additional sensitivity analyses were conducted in Python 3.12.13. Leave-one-out modified Poisson analyses were performed using statsmodels version 0.15.0 with the same covariate set and HC3 robust variance estimator as in the primary model. Firth bias-reduced logistic regression, profile-likelihood confidence intervals, and formal assessment of complete or quasi-complete separation were performed using firthmodels version 0.8.2. The Firth coefficient estimates were independently reproduced using pyfirth version 0.0.6.

Results

The analysis included 167 patients, of whom 124 (74.3%) were male. Median age was 74.0 months (IQR 57.0–106.0). Seventy-six patients (45.5%) were aged 36–71 months, 68 (40.7%) were aged 72–131 months, and 23 (13.8%) were aged 132–216 months. Atypical autism was recorded in 126 patients (75.4%), childhood autism in 35 (21.0%), and Asperger syndrome in six (3.6%). CARS severity was mild-to-moderate in 118 patients (70.7%) and severe in 49 (29.3%).

Table 1. Sociodemographic, developmental, and clinical characteristics of the patients (n = 167)

Variable	Category	n (%) or median (IQR)
Age (months), median (IQR)	—	74.0 (57.0–106.0)
Age group	36–71 months	76 (45.5)
	72–131 months	68 (40.7)
	132–216 months	23 (13.8)
Sex	Male	124 (74.3)
	Female	43 (25.7)
ASD diagnosis	Childhood autism	35 (21.0)
	Atypical autism	126 (75.4)
	Asperger syndrome	6 (3.6)
CARS severity	Mild-to-moderate	118 (70.7)
	Severe	49 (29.3)
Epilepsy	Present	13 (7.8)
Sentence formation	Present	85 (50.9)
Toilet training	Present	98 (58.7)
Reading and writing	Present	27 (16.2)
ADHD	Present	105 (62.9)
Oppositional defiant disorder	Present	64 (38.3)
Conduct disorder	Present	25 (15.0)
Disruptive behaviour disorder	Present	75 (44.9)
Anxiety disorder	Present	9 (5.4)
Tic disorder	Present	7 (4.2)
Obsessive-compulsive disorder	Present	2 (1.2)
Sleep disorder	Present	39/166 (23.5)
Autism-related irritability	Present	92 (55.1)
Aggression	Present	47/164 (28.7)
Self-injurious behaviour	Present	23/165 (13.9)
At least one psychiatric comorbidity	Present	120 (71.9)

Continuous age is presented as median (IQR); age categories are retained for descriptive clinical context. Denominators are shown separately for variables with missing observations. ADHD = attention-deficit/hyperactivity disorder; CARS = Childhood Autism Rating Scale

Epilepsy was recorded in 13 patients (7.8%) and at least one psychiatric comorbidity in 120 (71.9%). ADHD was the most frequent comorbidity (105/167, 62.9%), followed by oppositional defiant disorder (64/167, 38.3%) and conduct disorder (25/167, 15.0%). Disruptive behaviour disorder was recorded in 75 patients (44.9%) and irritability in 92 (55.1%). Aggression was documented in 47 of 164 patients with valid data (28.7%) and self-injurious behaviour in 23 of 165 (13.9%) (Table 1).

At least one active psychotropic medication was recorded for 123 patients (73.7%; 95% CI 66.5%–79.7%); 44 patients (26.3%) had no active psychotropic medication record. Ninety-four patients had at least two

active psychotropic medications at the same visit, yielding a psychotropic polypharmacy estimate of 56.3% for the entire sample (95% CI 48.7%–63.6%). Among the 123 patients with at least one active psychotropic medication record, 94 met the same polypharmacy definition, corresponding to 76.4% (95% CI 68.2%–83.1%).

Table 2. Active psychotropic medication records and record-based psychotropic polypharmacy

Active medication measure or agent	n (%)
At least one active psychotropic medication	123 (73.7)
Record-based psychotropic polypharmacy (≥2)	94 (56.3)
At least one antipsychotic	112 (67.1)
At least two antipsychotics	30 (18.0)
Risperidone	74 (44.3)
Atomoxetine	74 (44.3)
Aripiprazole	56 (33.5)
Methylphenidate	28 (16.8)
Olanzapine	11 (6.6)
Guanfacine	10 (6.0)
Melatonin	7 (4.2)
Lithium	4 (2.4)
Haloperidol	4 (2.4)
Sertraline	2 (1.2)
Other single psychotropic agents*	5 medication records

Percentages were calculated using the entire analysis sample (n = 167) unless otherwise specified. Among patients with at least one active psychotropic medication record, 94/123 (76.4%) met the same polypharmacy definition. The first four summary measures are patient-level estimates; agent counts represent active psychotropic medication records. The dataset contained 286 active medication records when psychotropic medications and antiepileptics used solely for epilepsy were considered together. Psychotropic polypharmacy was defined as ≥2 active psychotropic medications. Eleven antiepileptic records used solely for epilepsy were excluded from the psychotropic medication count. *Amisulpride, fluoxetine, clonazepam, trazodone, and zuclopenthixol each accounted for one medication record.

Table 3. Comparisons according to active psychotropic medication record

Variable	Category	No active record (n=44)	Active record (n=123)	p	Adjusted p
Age (months), median (IQR)	—	58.0 (47.0–72.3)	83.0 (61.5–115.0)	<0.001	<0.001
CARS severity	Severe	2 (4.5)	47 (38.2)	<0.001	<0.001
Sex	Female	15 (34.1)	28 (22.8)	0.140	>0.999
Epilepsy*	Present	1 (2.3)	12 (9.8)	0.188	>0.999
Sentence formation	Present	29 (65.9)	56 (45.5)	0.020	0.386
Toilet training	Present	29 (65.9)	69 (56.1)	0.257	>0.999
Reading and writing	Present	4 (9.1)	23 (18.7)	0.137	>0.999
ADHD	Present	2 (4.5)	103 (83.7)	<0.001	<0.001
Oppositional defiant disorder	Present	1 (2.3)	63 (51.2)	<0.001	<0.001
Conduct disorder	Present	0 (0.0)	25 (20.3)	0.001	0.022
Disruptive behaviour disorder	Present	1 (2.3)	74 (60.2)	<0.001	<0.001
Anxiety disorder*	Present	1 (2.3)	8 (6.5)	0.448	>0.999
Tic disorder*	Present	0 (0.0)	7 (5.7)	0.191	>0.999
Obsessive-compulsive disorder*	Present	0 (0.0)	2 (1.6)	1.000	>0.999
Sleep disorder	Present	0/44 (0.0)	39/122 (32.0)	<0.001	<0.001
Autism-related irritability	Present	3 (6.8)	89 (72.4)	<0.001	<0.001
Aggression	Present	1/42 (2.4)	46/122 (37.7)	<0.001	<0.001
Self-injurious behaviour	Present	0/44 (0.0)	23/121 (19.0)	0.002	0.035
At least one psychiatric comorbidity	Present	3 (6.8)	117 (95.1)	<0.001	<0.001

Continuous age is presented as median (IQR) and was compared using the Mann–Whitney U test; categorical variables are presented as n (%) and were compared using Pearson's chi-square test or Fisher's exact test, as appropriate. Adjusted p values were calculated as min(19 × p, 1). Bonferroni-adjusted p values were calculated across the 19 prespecified comparisons. *Variables analysed using Fisher's exact test. Valid denominators are shown separately for variables with missing data

At least one active antipsychotic was recorded for 112 patients (67.1%), and at least two active antipsychotics for 30 (18.0%). Risperidone and atomoxetine were each recorded for 74 patients (44.3%), followed by aripiprazole in 56 (33.5%) and methylphenidate in 28 (16.8%). The complete agent-level distribution is presented in Table 2, and the most frequently recorded active psychotropic medications are shown in Figure 1. The frequency of an active psychotropic medication record increased across age groups: 44/76 (57.9%) at 36–71 months, 58/68 (85.3%) at 72–131 months, and 21/23 (91.3%) at 132–216 months. These category-specific frequencies are presented descriptively.

Eleven of the 19 prespecified comparisons remained statistically significant after Bonferroni correction. Median age was higher among patients with an active psychotropic medication record than among those without an active record [83.0 months (IQR 61.5–115.0) vs 58.0 months (IQR 47.0–72.3); Mann–Whitney U = 1415.5; unadjusted and Bonferroni-adjusted $p < 0.001$]. Severe CARS classification was recorded in 38.2% of patients with an active medication record and in 4.5% of those without one.

ADHD (83.7% vs 4.5%), irritability (72.4% vs 6.8%), disruptive behaviour disorder (60.2% vs 2.3%), and at least one psychiatric comorbidity (95.1% vs 6.8%) showed the largest between-group differences. Oppositional defiant disorder, conduct disorder, sleep disorder, aggression, and self-injurious behaviour were also more frequently documented among patients with an active medication record. After correction, no significant difference was demonstrated for sex, epilepsy, developmental characteristics, anxiety, tic disorder, or obsessive-compulsive disorder. Table 3 provides all comparisons, p values, and valid denominators.

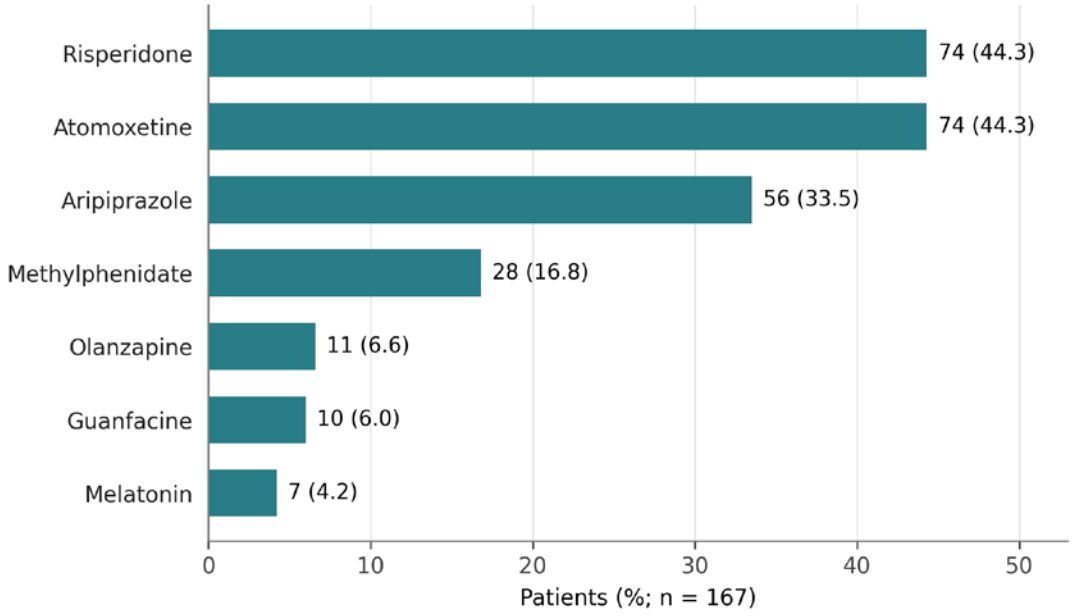


Figure 1. Distribution of the most frequently recorded active psychotropic medications

Percentages were calculated using the entire analysis sample (n = 167) as the denominator

Table 4. Characteristics related with an active psychotropic medication record: modified Poisson regression

Variable	B	SE	aPR	95% CI	p
Age (per 12-month increase)	0.002	0.009	1.002	0.986–1.019	0.777
Sex: Female (ref. Male)	-0.076	0.077	0.927	0.797–1.077	0.323
Severe CARS (ref. Mild-to-moderate)	0.009	0.056	1.009	0.905–1.126	0.868
ADHD: Present (ref. Absent)	0.919	0.178	2.506	1.768–3.552	<0.001
Irritability: Present (ref. Absent)	0.441	0.100	1.554	1.276–1.892	<0.001

Poisson regression with a log link and robust standard errors was used. The model simultaneously included age, sex, CARS, ADHD, and irritability; no variable-selection procedure was applied. The coefficient for age represents a 12-month increase. Overall robust Wald test: $\chi^2 = 83.56$; df = 5; $p < 0.001$.
B = regression coefficient; SE = robust standard error; aPR = adjusted prevalence ratio; CI = confidence interval

The modified Poisson model was significant overall (robust Wald χ^2 = 83.56; df = 5; p < 0.001). ADHD (aPR = 2.51; 95% CI 1.77–3.55; p < 0.001) and autism-related irritability (aPR = 1.55; 95% CI 1.28–1.89; p < 0.001) were independently associated with an active psychotropic medication record. Age was not independently associated with an active psychotropic medication record (aPR per 12-month increase = 1.002, 95% CI 0.986–1.019; p = 0.777). Sex and recorded CARS severity were also not independently associated with the outcome (Table 4, Figure 2).

Variance inflation factors ranged from 1.018 to 1.347. Only two of the 44 patients without an active psychotropic medication record had ADHD, and only three had irritability. A formal separation diagnostic did not identify complete or quasi-complete separation. Nevertheless, these sparse subgroup counts indicated limited covariate overlap and raised concern regarding finite-sample bias and the precision of the corresponding population effect estimates. In leave-one-out analyses, the aPR ranged from 2.44 to 2.61 for ADHD and from 1.51 to 1.58 for irritability, indicating that no single observation materially changed the point estimates. The Firth bias-reduced logistic model converged after 22 iterations, and the directions of both associations were retained (ADHD: aOR = 65.80, 95% profile-likelihood CI 16.18–412.13; irritability: aOR = 27.47, 95% profile-likelihood CI 7.29–139.94). Because the outcome was common, these odds ratios were not considered directly comparable in magnitude to the prevalence ratios. Although the sensitivity analyses supported the direction of the associations, the sparse subgroup counts and wide profile-likelihood confidence intervals indicate that their magnitudes should be interpreted cautiously.

The dataset contained 286 active medication records when psychotropic medications and antiepileptics used solely for epilepsy were considered together. Of these, 275 were included in the psychotropic medication count, whereas 11 epilepsy-only antiepileptic records were excluded. Treatment duration was documented for 48/286 active medication records (16.8%).

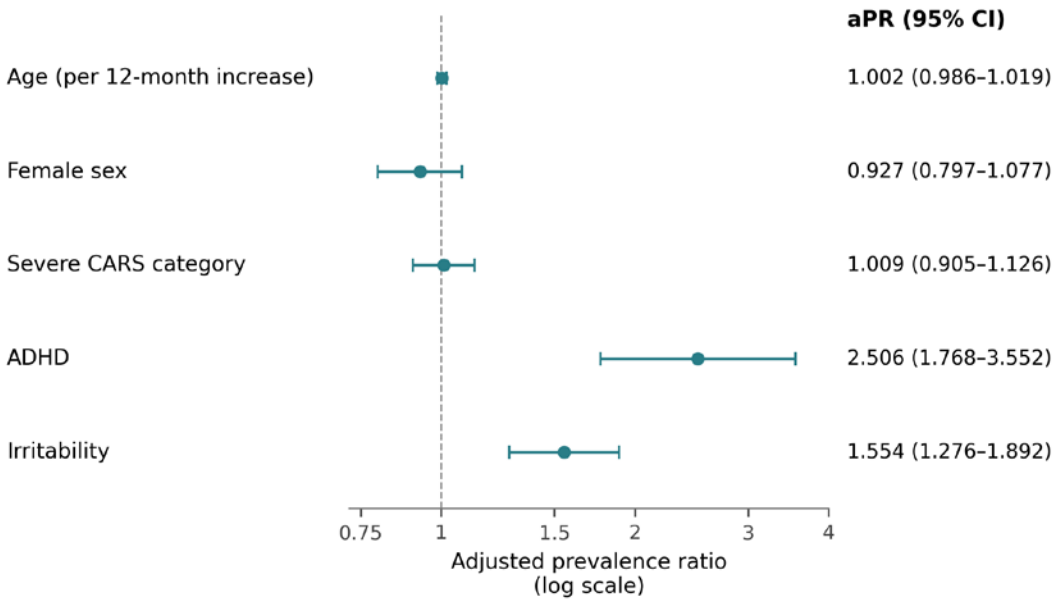


Figure 2. Adjusted prevalence ratios for characteristics associated with an active psychotropic medication record

aPR = adjusted prevalence ratio; CARS = Childhood Autism Rating Scale; CI = confidence interval; ADHD = attention-deficit/hyperactivity disorder.

Discussion

This study provides a visit-based description of active psychotropic medication use in a tertiary-care ASD sample. Approximately three-quarters of patients had at least one active psychotropic medication record, more than half met the single study definition of psychotropic polypharmacy, and antipsychotics were the dominant medication class. ADHD and irritability were independently associated with an active psychotropic medication record, whereas age, sex, and recorded CARS severity were not. These results

describe electronic medication records and should not be interpreted as confirmation of dispensing, adherence, sustained exposure, effectiveness, or appropriate prescribing.

The 73.7% frequency observed here was higher than the 34.3%–42.6% reported in earlier clinical series from Türkiye (Uygun et al. 2020, Göknar et al. 2022). More recent Turkish data also show variation according to age and psychiatric comorbidity (Cevher Binici et al. 2026). Recent nationwide Medicaid data from the United States likewise showed that psychotropic medication exposure was common among children and youth with ASD, although approximately half had at least one psychotropic prescription within a year (Rast et al. 2025). This claims-based annual measure is not directly equivalent to the visit-based active medication record used in the present study. The estimates are not directly interchangeable: the studies differed in setting, age distribution, comorbidity burden, reason for attendance, and method of medication ascertainment. Referral pathways, reasons for tertiary-care attendance, and whether the selected visit represented an initial assessment or a follow-up visit were not systematically available. These factors provide plausible mechanisms through which the observed frequencies could have been higher than those in community-based or less specialised samples. Tertiary referral pathways may preferentially select patients with greater psychiatric comorbidity, behavioural complexity, previous treatment exposure, or a need for specialist medication review. Similarly, if follow-up encounters constituted a substantial proportion of the selected visits, patients who had already been prescribed psychotropic medication would be more strongly represented than patients undergoing an initial assessment, some of whom might not yet have started pharmacotherapy. Medication lists carried forward across follow-up visits could further increase the frequency of medications recorded as active. However, because referral source, prior treatment history, and visit status were not systematically documented, the presence and magnitude of these potential selection and recording effects could not be determined. The higher estimate should therefore be interpreted as specific to this tertiary-care, visit-based sample and not as evidence of either population-level prevalence or a temporal increase in prescribing. Compared with previous studies from Türkiye, the present study extends the available evidence by combining visit-based active medication records, agent-level medication patterns, and psychotropic polypharmacy defined using a single explicit whole-sample criterion within the same tertiary-care ASD cohort. In addition, clinical characteristics associated with having an active psychotropic medication record were evaluated using prevalence ratios, which are directly interpretable for this common outcome. These features complement earlier Turkish studies by providing a more transparent description of medication-record patterns, polypharmacy, and associated clinical characteristics within a single visit-based framework.

The high frequency in older age groups also requires contextual interpretation. Özaydın et al. (2024) found a history of any medication use in 92.4% of an adolescent ASD sample and antipsychotic use in 83.9%. This direction is consistent with our unadjusted age pattern, but past exposure and medication recorded as active at one visit are distinct measures. In addition, age was not independently associated with the outcome after adjustment, and the adolescent subgroup in our study was small.

Using the single definition of at least two active psychotropic medications at the same visit and the full sample as the denominator, psychotropic polypharmacy was present in 56.3% (94/167). When the denominator was restricted to the 123 patients with at least one active psychotropic medication record, 94 patients met the same definition, corresponding to 76.4%. Reporting both estimates illustrates the effect of denominator selection and facilitates comparison with studies that calculate polypharmacy only among patients with a medication record. This estimate was numerically higher than the 19.1% reported by Göknar et al. (2022) in their full clinical sample and the 35% reported by Spencer et al. (2013) for at least two medication classes with 30 or more days of overlapping pharmacy claims. Other studies have applied annual exposure without requiring chronological overlap or have restricted analyses to sustained treatment (Lohr et al. 2018, Taniguchi et al. 2022). Accordingly, the present estimate represents medications listed together as active at one visit, not sustained concurrent treatment. Variation in thresholds, denominators, observation periods, and medication coverage limits direct comparison of polypharmacy estimates (Ritter et al. 2021). Across this combined set of psychotropic medication records and antiepileptic records used solely for epilepsy, treatment duration was documented for only 48 of 286 records (16.8%). Consequently, same-visit active co-listing could not be reliably distinguished from

sustained concurrent treatment, temporary overlap during cross-tapering, or other transitional prescribing arrangements. The reported polypharmacy estimate should therefore be interpreted as a point-in-time record-based measure and not as evidence of prolonged concurrent medication exposure.

Antipsychotics were the most frequently recorded class, consistent with previous Turkish and international studies (Jobski et al. 2017, Uygun et al. 2020, Göknar et al. 2022). Their prominence may partly reflect treatment of severe irritability and related behaviours. However, frequency of recording is not evidence of effectiveness or appropriateness. Given established metabolic, neurological, and other safety concerns, treatment targets, adverse effects, and physical-health monitoring should be reviewed systematically (Solmi et al. 2020, Deb et al. 2023, Meza et al. 2025).

The association between irritability and active psychotropic medication records accords with observational evidence linking externalising behaviours with psychotropic treatment and polypharmacy in ASD (Logan et al. 2015, Geoffray et al. 2023). ADHD has likewise been associated with psychotropic treatment in ASD populations (Casseus et al. 2023). These associations should be interpreted in the context of confounding by indication. ADHD and irritability are common pharmacological treatment targets in paediatric ASD care, and the most frequently recorded agents in our sample included medications commonly used to address these clinical dimensions: atomoxetine and methylphenidate for ADHD symptoms, and risperidone and aripiprazole for irritability and associated behavioural symptoms. Moreover, because ADHD medications were included in the composite psychotropic outcome, an association between recorded ADHD and this outcome was partly expected. However, medication-specific indications were not systematically available, and we could not determine whether an individual agent had been prescribed for a particular recorded diagnosis or behavioural characteristic. Although the leave-one-out analyses indicated that no single observation materially influenced the findings and the Firth sensitivity analysis retained the direction of both associations, the limited covariate overlap and wide profile-likelihood confidence intervals indicate that the magnitudes of these associations remain uncertain. ADHD and irritability should therefore be interpreted as descriptive clinical correlates of medication recording rather than as causal determinants of treatment initiation. Neither association establishes temporal order, causality, treatment effectiveness, or clinical appropriateness at the individual-patient level.

At least two antipsychotics were listed as active for 18.0% of the sample. This secondary finding is clinically distinct from overall psychotropic polypharmacy. In a tertiary ASD clinic, Wink et al. (2017) identified sustained use of two or more antipsychotics across at least two visits in 6.4% of patients. However, their longitudinal exposure definition is not directly comparable with our same-visit active-record measure. The same duration-data limitation prevented differentiation of a brief, planned overlap during cross-tapering from intentional, sustained combination treatment. These scenarios have materially different clinical and safety implications because the duration and purpose of concurrent exposure affect how potential adverse-effect burden and monitoring requirements should be interpreted. As treatment intent, duration of overlap, adverse effects, and monitoring data were not systematically available, no safety inference regarding antipsychotic combination treatment can be drawn from the 18.0% same-visit estimate. This estimate must therefore not be interpreted as the prevalence of maintenance antipsychotic combination therapy.

Recorded CARS severity was not independently associated with the outcome despite a marked unadjusted difference. This does not show that ASD severity is clinically unimportant; rather, medication decisions may be more closely related to specific treatment targets and comorbidities than to a broad severity category. The study did not model the relationships among severity, age, comorbidities, and behavioural features, and residual confounding remains possible.

Atomoxetine was recorded more frequently than methylphenidate, whereas Özaydın et al. (2024) reported psychostimulants more often than atomoxetine in adolescents. Differences in age, previous treatment trials, access, tolerability, or local practice could contribute, but these factors were not systematically documented. This descriptive pattern warrants confirmation in other centres and does not imply that atomoxetine was more effective or appropriate.

The findings have several implications for routine clinical practice. ADHD and irritability were independently associated with an active psychotropic medication record, supporting careful assessment of these specific co-occurring clinical dimensions when pharmacotherapy is considered or reviewed. However, these associations should not be interpreted as demonstrating treatment indication, appropriateness, effectiveness, or causality at the individual-patient level. Given the high frequency of active medication records and same-visit psychotropic polypharmacy in this tertiary-care sample, regular medication reconciliation and structured review of each agent may be particularly important. For each psychotropic medication, the treatment target, review date, observed response, adverse effects, and continuing need should be documented clearly. When more than one antipsychotic is listed as active, the record should clarify whether this represents a transition or intended combination treatment and document relevant metabolic and neurological monitoring. Similar documentation gaps have been identified in large record-based studies of paediatric antipsychotic prescribing (Vinogradova et al. 2025). Prospective studies are required to determine whether such structured review improves treatment quality or patient outcomes. No formal local audit or quality-improvement initiative was under way at the time of this study. The findings will be shared within the department and may inform the feasibility and design of a future documentation audit.

Study strengths include inclusion of all eligible patients over a full year, a transparent definition of active medication exposure, one explicit whole-sample definition of psychotropic polypharmacy, agent-level reporting, correction for multiple univariable comparisons, and use of prevalence ratios for a common outcome. Several limitations should also be considered. The single-centre tertiary-care setting restricts generalisability to community and primary-care ASD populations and may have selected patients with greater clinical complexity. Electronic medication lists did not establish dispensing, adherence, or sustained concurrent use. Across the combined set of psychotropic medication records and antiepileptic records used solely for epilepsy, treatment duration was documented for only 48 of 286 records (16.8%). This substantial documentation gap prevented reliable differentiation of sustained concurrent treatment from short-term overlap during cross-tapering or other medication transitions. Accordingly, the record-based polypharmacy estimate may include both maintenance combinations and temporary same-visit overlap, but their respective contributions could not be determined. Active medication status was not independently cross-verified against pharmacy dispensing or claims data or through a structured contemporaneous caregiver medication reconciliation. Medication discrepancies, including medications remaining in electronic records despite not being taken by patients, have been documented even in integrated electronic health-record systems (Linsky and Simon 2013). Outdated records may have retained medications that had been discontinued or were no longer being taken, resulting in overestimation, whereas incomplete lists may have omitted medications prescribed elsewhere or not entered into the institutional record, resulting in underestimation. The direction and magnitude of this exposure misclassification could not be determined.

Indications, intended treatment targets, treatment response, adverse effects, body weight, metabolic monitoring, referral pathways, and reasons for tertiary-care attendance were not systematically available; consequently, the clinical rationale and appropriateness of individual medication combinations could not be evaluated. Whether the selected visit represented an initial assessment or a follow-up visit was not documented; therefore, differences in medication recording according to follow-up status could not be examined. Comorbidities were based on routine clinical assessment rather than systematically documented structured diagnostic interviews. Because no uniform reference-standard assessment or independent diagnostic re-evaluation was available, the sensitivity and specificity of the recorded diagnoses, and therefore the magnitude and direction of possible diagnostic misclassification, could not be estimated. Such misclassification may have biased the observed associations either towards or away from the null. Missing positive behavioural documentation could not be equated with confirmed absence. A uniform aetiological assessment for cognitive impairment was not documented for all patients. The exclusion criterion therefore depended on aetiologies already recognised and recorded in routine clinical care, and unrecognised or incompletely documented causes may have resulted in residual diagnostic or eligibility misclassification.

Data extraction was not independently duplicated. ADHD and irritability were recorded in only two and three, respectively, of the 44 patients without an active psychotropic medication record, resulting in limited covariate overlap and raising concern regarding finite-sample bias and the precision of the corresponding population effect estimates. A formal separation diagnostic did not identify complete or quasi-complete separation. Leave-one-out analyses showed limited variation in the adjusted prevalence ratios, and a Firth bias-reduced logistic sensitivity analysis retained the direction of both associations. Nevertheless, these analyses cannot eliminate the uncertainty arising from the sparse subgroup counts. The adjusted prevalence ratios, particularly their magnitudes, should therefore be interpreted cautiously rather than as precise population effect estimates. The adolescent subgroup was also small. The Bonferroni adjustment controlled the family-wise type I error rate across the 19 prespecified univariable comparisons but, given its conservative nature and the available sample size, may also have reduced statistical power and increased the possibility of false-negative findings. Accordingly, failure to meet the adjusted significance threshold should not be interpreted as excluding associations of smaller magnitude or potential clinical relevance. Both unadjusted and Bonferroni-adjusted p values are reported to allow readers to evaluate this trade-off. The interval between the CARS assessment and the selected study visit, and its timing relative to psychotropic treatment initiation, were not standardised. Although the CARS score recorded closest in time to the selected visit was used, ratings may have been obtained at different stages of clinical follow-up and cannot be assumed to represent ASD severity at a uniform pretreatment time point. This temporal uncertainty should be considered when interpreting the absence of an independent association between recorded CARS severity and an active psychotropic medication record. Finally, the cross-sectional design precluded assessment of temporal or causal relationships. Confounding by indication is particularly relevant because ADHD and irritability are themselves common pharmacological treatment targets, while medication-specific indications were not systematically documented.

Conclusion

In this tertiary-care ASD sample, active psychotropic medication records and same-visit record-based polypharmacy were frequent. ADHD and irritability were independently associated with having an active psychotropic medication record, whereas recorded CARS severity was not independently associated with the outcome in the multivariable model. These findings represent a cross-sectional description of electronic health-record entries and do not confirm dispensing, actual medication intake, sustained concurrent exposure, treatment effectiveness, safety, or clinical appropriateness. As a suggested next step, structured documentation of treatment targets, medication start, review, and stop dates, observed response, adverse effects, monitoring parameters, and continuing need may support more reliable longitudinal medication review. When multiple medications, particularly multiple antipsychotics, are listed as active, documentation should clarify whether this represents temporary overlap during a medication transition or intended combination treatment. Future multicentre prospective studies should evaluate medication trajectories, indications, adherence, effectiveness, adverse effects, monitoring, and patient and family perspectives.

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