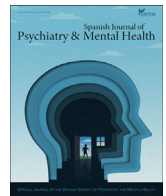




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Spanish Journal of Psychiatry and Mental Health

journal homepage: <http://http://www.elsevier.es/sjpmh>



Original

Use of antipsychotics in children and adolescents in Spain, 2015–2023: A real-world, population-based study

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ARTICLE INFO

Article history:

Received 10 April 2025

Accepted 14 January 2026

Available online xxx

Keywords:

Antipsychotic agents

Children

Adolescent

Pharmacoepidemiology

Drug use

ABSTRACT

Introduction: Antipsychotic (AP) prescription has risen across Europe, but updated data on prescribing trends and treatment intensity in youth remain limited. This study describes AP prescription patterns among children and adolescents in the region of Valencia, Spain, with 5 million inhabitants.

Methods: Population-based, cross-sectional study using the Valencia Health System's Integrated Database (VID) including all AP drugs prescribed to individuals aged 0–19 years from 2015 through 2023. APs were categorized by active substance, and yearly trends in prescription volume, patient numbers, and chlorpromazine equivalent doses (CED) per patient were presented. Results were stratified by age and sex.

Results: A total of 570,238 AP prescriptions were dispensed to 30,704 patients, increasing 1.61-fold over the study period. Risperidone and aripiprazole accounted for 60.5% of all prescriptions, while lurasidone experienced the highest growth (13-fold increase), followed by olanzapine (3.1-fold), aripiprazole (2.3-fold), and quetiapine (2.1-fold). The number of treated patients increased by 50%, with the highest relative increase in young children (0–4 years old) and adolescents (15–19 years old). AP use was higher in males but rose more sharply among females (1.4-fold vs 2.1-fold). Overall, CED per patient slightly declined.

Conclusions: AP prescriptions and patients treated among Spanish youth increased significantly between 2015 and 2023, with notable differences by age and sex. While total CED rose, treatment intensity per patient remained relatively stable. Future studies should investigate the clinical indications for these prescriptions as well as the outcomes associated with AP use in children and adolescents.

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Introduction

Child and adolescent mental-health problems have risen sharply in recent years. Since 2017, reported cases have increased across Europe, a trend further intensified by the COVID-19

pandemic,¹ resulting in almost one in five young people suffering from a mental-health disorder, with rates being higher in boys up to age 14 and in girls aged 14–19.² In Spain, 20.8% of 10–19-year-olds (21.4% of girls and 20.4% of boys) are diagnosed with a mental-health condition, the highest prevalence among European countries.¹ Since most mental disorders emerge during childhood or adolescence, early intervention is crucial, as underscored by the World Health Organization.³ Recommended care is multi-modal, combining psychosocial and pharmacological strategies.

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<https://doi.org/10.1016/j.sjpmh.2026.01.002>

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Please cite this article as: I. Hurtado, C. Robles-Cabaniñas, A. García-Sempere et al., Use of antipsychotics in children and adolescents in Spain, 2015–2023: A real-world, population-based study, *Spanish Journal of Psychiatry and Mental Health*, <https://doi.org/10.1016/j.sjpmh.2026.01.002>

Although among pharmacological options, antipsychotics (APs) are indispensable for severe illnesses such as schizophrenia and bipolar disorder, their use has expanded to conditions such as anxiety, depression, attention-deficit/hyperactivity disorder (ADHD), or behavioral disorders.^{4–6} This broader pattern of AP prescribing mirrors the growing mental health burden and raises new concerns about their safety when used in children and adolescents. Evidence from national and international studies highlights a high prevalence of off-label prescribing in this population,^{7–10} which poses questions about the appropriateness of these practices, the benefit–risk balance and the long-term safety of AP. These concerns are heightened by the fact that young patients are often excluded from clinical trials that assess the safety and efficacy profile of APs.

International evidence indicates an increase in antipsychotic prescribing among young people across Europe,^{11–13} but most available studies are outdated and primarily report prescription prevalence, with limited evaluation of changes in treatment intensity. In Spain, AP dispensing through the public system has grown by 29% per year in terms of defined daily doses (DDD) over the past 12 years,¹⁴ but youth-specific, granular data are scarce. In this context, it is crucial to better understand current AP prescribing practices in youth. To inform both clinical practice and policy, we analyzed population-based data from a Spanish region of five million inhabitants, quantifying time trends in AP prescribing and characterizing changes in treatment intensity among children and adolescents.

Methods

Design

We conducted a population-based, cross-sectional study to analyze all AP prescriptions for patients aged 0–19 years from January 1st, 2015 through December 31st, 2023. All APs classified under code N05A of the Anatomical Therapeutic Chemical (ATC) classification system, and prescribed at least once during the study period, were included. They were categorized by their International Nonproprietary Names and relative prescription volume in 2023: aripiprazole, lurasidone, olanzapine, paliperidone, quetiapine, risperidone, and others.

Setting and population

The study was conducted in the region of Valencia, Spain, focusing on individuals covered by the public Valencia Health System (VHS), which serves approximately 97% of the region's inhabitants. We included all patients aged 0–19 years who received at least 1 AP prescription during the study period. Given the high population coverage of the VHS, population denominators were derived from census data. The reference population declined slightly over the study period, from approximately 990,000–970,000 children and adolescents per year (Supplementary data 1).

Data sources

Data were obtained from the VHS Integrated Databases (VID), which link multiple population-based health care, clinical, and administrative electronic databases via a single personal identification no. The VID has provided comprehensive information on the region's 5 million inhabitants since 2008. It includes sociodemographic and administrative data (e.g., sex, age, nationality), as well as health care-related information such as diagnoses, procedures, laboratory results, pharmaceutical prescriptions and dispensing (including drug brand, generic name, formulation, strength, and dosing schedule), hospital admissions, mortality, health care utilization, and public health data. Additionally, the VID integrates

specialized databases on key care areas, including cancer, rare diseases, vaccines, and imaging data.¹⁵

Outcome measures

The primary outcome measures were estimated annually and included: the number of prescriptions and prescriptions per 100 inhabitants aged 0–19; the number of patients receiving at least 1 AP prescription and the corresponding proportion of patients treated over 100 inhabitants 0–19 years old; and the yearly chlorpromazine equivalent doses (CED) per patient treated to assess treatment intensity. All outcomes were analyzed in total and separately for the most widely prescribed APs.

Analysis

We conducted a descriptive analysis to evaluate yearly trends in AP prescription volume, the number of patients treated, and CED per patient from 2015 through 2023. Trends were assessed both overall and for specific APs of major interest (e.g., those with the highest prescription levels or the greatest growth during the study period). All analyses were stratified by age groups (0–4, 5–9, 10–14, 15–19) and sex assigned at birth. All analyses were performed using R version 3.6.0., and CED were estimated with the chlorpromazineR package¹⁶; Supplementary data S2 for conversion equivalents employed.

Results

Prescriptions

A total of 570,238 AP prescriptions were dispensed between 2015 and 2023, with the annual number of prescriptions increasing 1.61-fold over the study period (Table 1 and Supplementary data S3 for detail of drugs included in the “Others” category). Risperidone and aripiprazole accounted for 60.5% of all prescriptions (Table 1). Among APs, lurasidone, introduced in 2019, showed the highest growth in prescription per 100 inhabitants (13-fold increase), followed by olanzapine (3.1-fold), aripiprazole (2.3-fold), and quetiapine (2.1-fold; Fig. 1a and Supplementary data S4). Yearly prescription increased across all age groups, with the most pronounced growth in adolescents aged 15–19 years (from 9.57 prescriptions per 100 inhabitants 15–19 years old in 2015 to 17.11 in 2023) and young children aged 0–4 years (from 0.25 to 0.52 per 100 inhabitants 0–4 years old; Fig. 1b and Supplementary data S5). Males received more prescriptions than females did, peaking at 10.49 prescriptions per 100 inhabitants. However, the relative increase in AP use was higher in females, rising from 2.75 prescriptions per 100 inhabitants in 2015 to 5.85 in 2023 (2.1-fold increase) vs a 1.4-fold increase in male (Fig. 1c and Supplementary data S6).

Patients

Between 2015 and 2023, the annual number of patients on at least 1 AP prescription increased from 7791 to 11,895, a 1.5-fold rise (Table 2). When examining trends by active substance, the number of patients treated with olanzapine more than tripled, while those receiving aripiprazole and quetiapine more than doubled over the study period (Table 2, Fig. 2a, Supplementary data S7). Regarding age groups, the highest relative increase in treated patients per 100 inhabitants occurred among children aged 0–4 years old, rising from 0.06 in 2015 to 0.14 in 2023 (a 2.3-fold increase). Adolescents aged 15–19 showed the next highest increase, from 1.2 to 1.7 per 100 inhabitants (Fig. 2b, Supplementary data S8). In terms of sex assigned at birth, the number of treated females patients per 100 inhabitants rose from 0.44 in 2015 to 0.73 in 2023, with a notable

Table 1
Evolution of antipsychotic prescriptions in the region of Valencia, Spain, by year and active substance, period 2015–2023, n (%).

	2015	2016	2017	2018	2019	2020	2021	2022	2023
Aripiprazole	9,372 (18.67%)	11,422 (20.83%)	12,866 (22.46%)	13,795 (22.82%)	14,908 (24.31%)	15,272 (24.97%)	18,206 (26.46%)	20,119 (26.65%)	21,684 (26.87%)
Lurasidone	0	0	0	0	35 (0.06%)	200 (0.33%)	901 (1.31%)	2,216 (2.94%)	2,593 (3.21%)
Olanzapine	3,307 (6.59%)	3,474 (6.34%)	3,913 (6.83%)	4,799 (7.94%)	5,774 (9.42%)	6,372 (10.42%)	8,178 (11.89%)	9,584 (12.70%)	10,232 (12.68%)
Paliperidone	5,256 (10.47%)	5,336 (9.73%)	5,427 (9.47%)	4,996 (8.26%)	5,370 (8.76%)	4,906 (8.02%)	4,709 (6.84%)	4,422 (5.86%)	4,101 (5.08%)
Quetiapine	3,891 (7.75%)	4,442 (8.10%)	4,500 (7.85%)	4,564 (7.55%)	4,291 (7.00%)	4,487 (7.34%)	5,565 (8.09%)	7,067 (9.36%)	7,802 (9.67%)
Risperidone	21,034 (41.90%)	22,714 (41.42%)	23,416 (40.87%)	24,537 (40.59%)	23,212 (37.85%)	22,083 (36.10%)	22,822 (33.17%)	23,205 (30.74%)	24,768 (30.70%)
Others	7,344 (14.63%)	7,445 (13.58%)	7,167 (12.51%)	7,763 (12.84%)	7,731 (12.61%)	7,851 (12.83%)	8,426 (12.25%)	8,877 (11.76%)	9,509 (11.78%)
Total	50,204	54,833	57,289	60,454	61,321	61,171	68,807	75,490	80,689

Table 2
No. of patients treated in the region of Valencia, Spain, by year and active substance, period 2015–2023.

	2015	2016	2017	2018	2019	2020	2021	2022	2023
Aripiprazole	1,165	1,407	1,600	1,710	1,867	1,877	2,402	2,667	2,839
Lurasidone	0	0	0	0	13	43	164	362	402
Olanzapine	479	520	589	716	841	928	1,265	1,504	1,558
Paliperidone	672	656	675	639	653	570	575	533	495
Quetiapine	457	539	554	566	583	625	870	1,034	1,127
Risperidone	3,350	3,493	3,466	3,409	3,491	3,253	3,419	3,609	3,663
Others	1,668	1,499	1,444	1,496	1,643	1,372	1,620	1,816	1,811
Total	7,791	8,114	8,328	8,536	9,091	8,668	10,315	11,525	11,895

increase between 2020 and 2022 (Fig. 2c, Supplementary data S9). Overall, a total of 30,704 individuals aged 0–19 years old received at least one AP prescription during the study period.

Chlorpromazine equivalent doses (CED)

Total yearly CED increased 1.4-fold during the period (Supplementary data S10), while overall CED per patient treated decreased over time (Fig. 3a and Supplementary data S11). Lurasidone CED per patient grew 2.1-fold, followed by the “others” category (1.4-fold, led by the growth of total CED of cariprazine, aripiprazole, risperidone, olanzapine, zuclophenthixol, Supplementary data S10) and paliperidone (1.3-fold, Fig. 3a and Supplementary data S11). CED per patient showed a slight decrease in 5–15 years old, and remained stable for 0–4 years old and 15–19 years old groups (Fig. 3b and Supplementary data S12). Overall, CED per patients was 39.3% higher for males but remained stable over the study period, whereas it showed a slight increase for females (1.2-fold between 2014 and 2023; Fig. 3c and Supplementary data S13).

Discussion

We identified a notable increase in AP prescriptions among children and adolescents in the region of Valencia between 2015 and 2023. Over this period, the total number of prescriptions increased by 61%, and the number of patients receiving at least one AP prescription grew by 50%, with the most pronounced relative increases observed in female and older adolescents. Aripiprazole and risperidone accounted for almost two-thirds of total prescriptions, while lurasidone, olanzapine, aripiprazole, and quetiapine showed the highest growth. Overall, treatment intensity per patient declined slightly over the study period, with males receiving notably higher CEDs per treated patient than females.

Our findings are consistent with former studies from various European countries, confirming a general upward trend in AP use among children and adolescents. However, our study provides more recent data and includes treatment intensity metrics, which are lacking in many earlier publications. Cross-country differences remain notable: while countries like the United Kingdom,¹⁷ the Netherlands, Denmark or the Nordic countries have reported marked increases in pediatric AP prescriptions,^{8,18} others such as

Germany and Italy have shown more moderate trends.⁷ The sharp rise in aripiprazole and quetiapine use in our study echoes similar patterns in Germany and Belgium,^{9,19} and our observation of a substantial increase in lurasidone prescriptions since its introduction in 2019 adds a novel finding, scarcely documented in the literature.

Several studies have examined the impact of the COVID-19 pandemic on antipsychotic prescribing in youth and have consistently reported a post-pandemic increase in use, particularly among adolescent females.^{19–25} Although the present study is descriptive, we observed a potential acceleration after 2020 in both prescription rates and the number of treated patients. This trend may reflect increased mental health needs among young people following the pandemic or shifts in care delivery, such as reduced access to nonpharmacological interventions. However, further research is required to confirm and explain these findings.

Our results suggest that the overall exposure to APs in children and adolescents in our setting is higher than in most European countries, with rates approximately three times those reported in the United Kingdom.¹⁷ This raises concerns about potential overuse or reliance on pharmacological interventions in contexts where non-pharmacological options may be less accessible, even in presence of specific policies such as the implementation of early psychosis prevention services. Several factors could contribute to this pattern, including higher prevalence of mental health disorders in Spanish youth,¹ the historical lack of a specific training pathway in child and adolescent psychiatry in Spain, differences in clinical guidelines or diagnostic practices, or the structure of the Spanish health care system, which may offer fewer resources for psychotherapy or community-based interventions. These findings highlight the importance of health system-level approaches to ensure balanced and appropriate mental health care pathways for young patients.

The steeper increase in prescriptions among adolescents and, notably, among very young children (0–4 years, despite their low absolute numbers), a trend also observed in countries such as Germany, France, United Kingdom, or Belgium,^{19,20,26,27} warrants attention. In the case of younger children, while some of this increase may reflect earlier recognition and diagnosis of behavioral or neurodevelopmental disorders, it also raises concerns about the appropriateness and safety of early pharmacological intervention. Similarly, the faster relative increase in AP prescribing

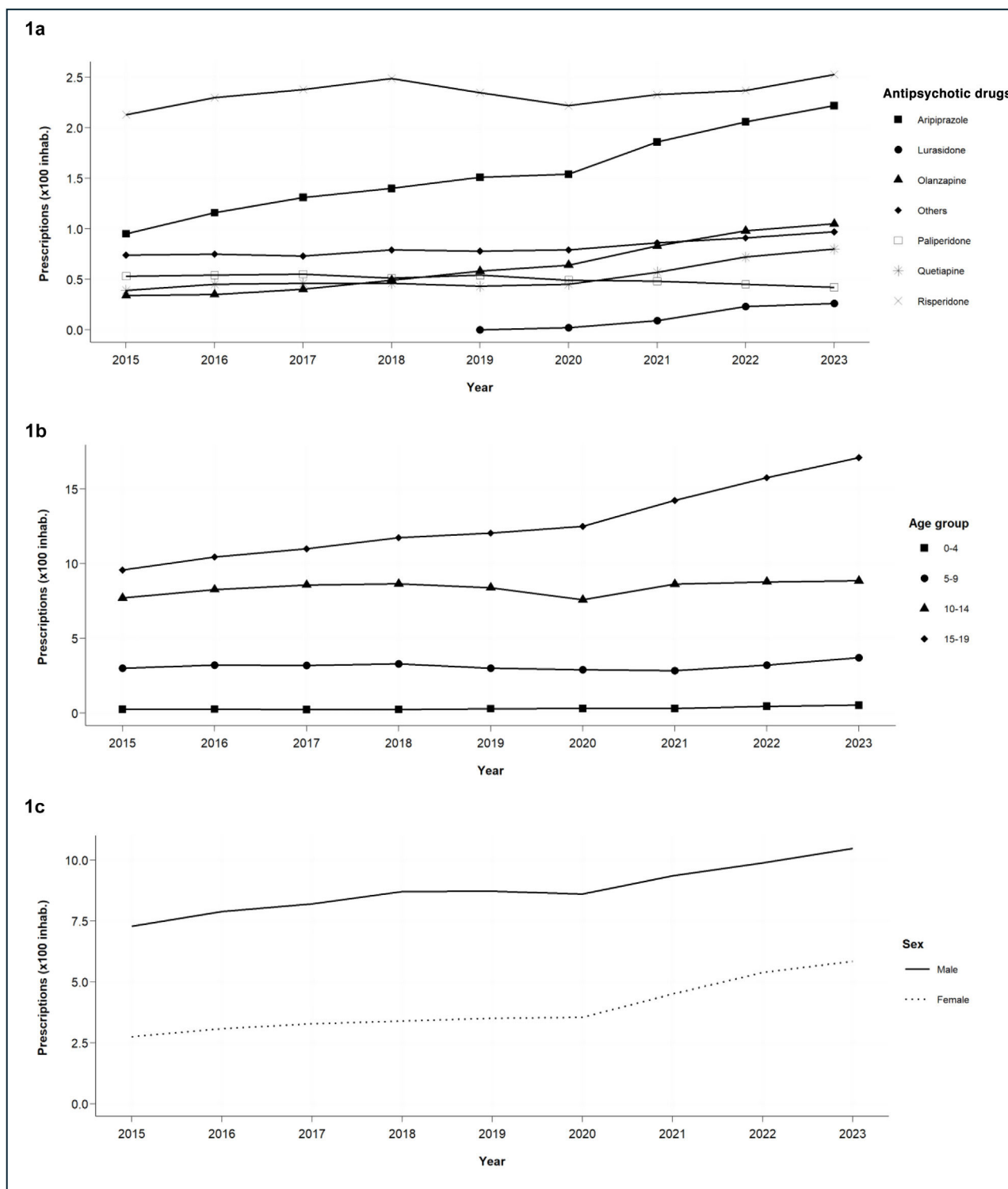


Fig. 1. Yearly number of antipsychotic prescription per 100 inhabitants, per substance (a), age group (b) and sex assigned at birth (c).

among females (despite consistently higher rates in males) points to changing patterns in mental health service use or diagnostic trends among girls, as also observed in Scandinavian and Finland data.^{27,28} These sex and age-specific patterns deserve further investigation to assess potential mismatches between clinical needs and treatment approaches.

The observed increase in cumulative yearly CED alongside a slight decline in per-patient CED over time may suggest a shift toward the use of APs in less severe, off-label indications. This

hypothesis is supported by the growing use of agents such as quetiapine and aripiprazole, which are often prescribed at lower doses for conditions like anxiety or behavioral issues. Only one previous study in Scandinavia has addressed this topic, reporting similar trends, where an increase in overall AP use was accompanied by relatively stable dosing patterns.²³ These patterns underline the importance of closely monitoring prescribing practices assessing their safety and efficacy in clinical practice. The consistently higher dosing in males may reflect differences in body weight or indication

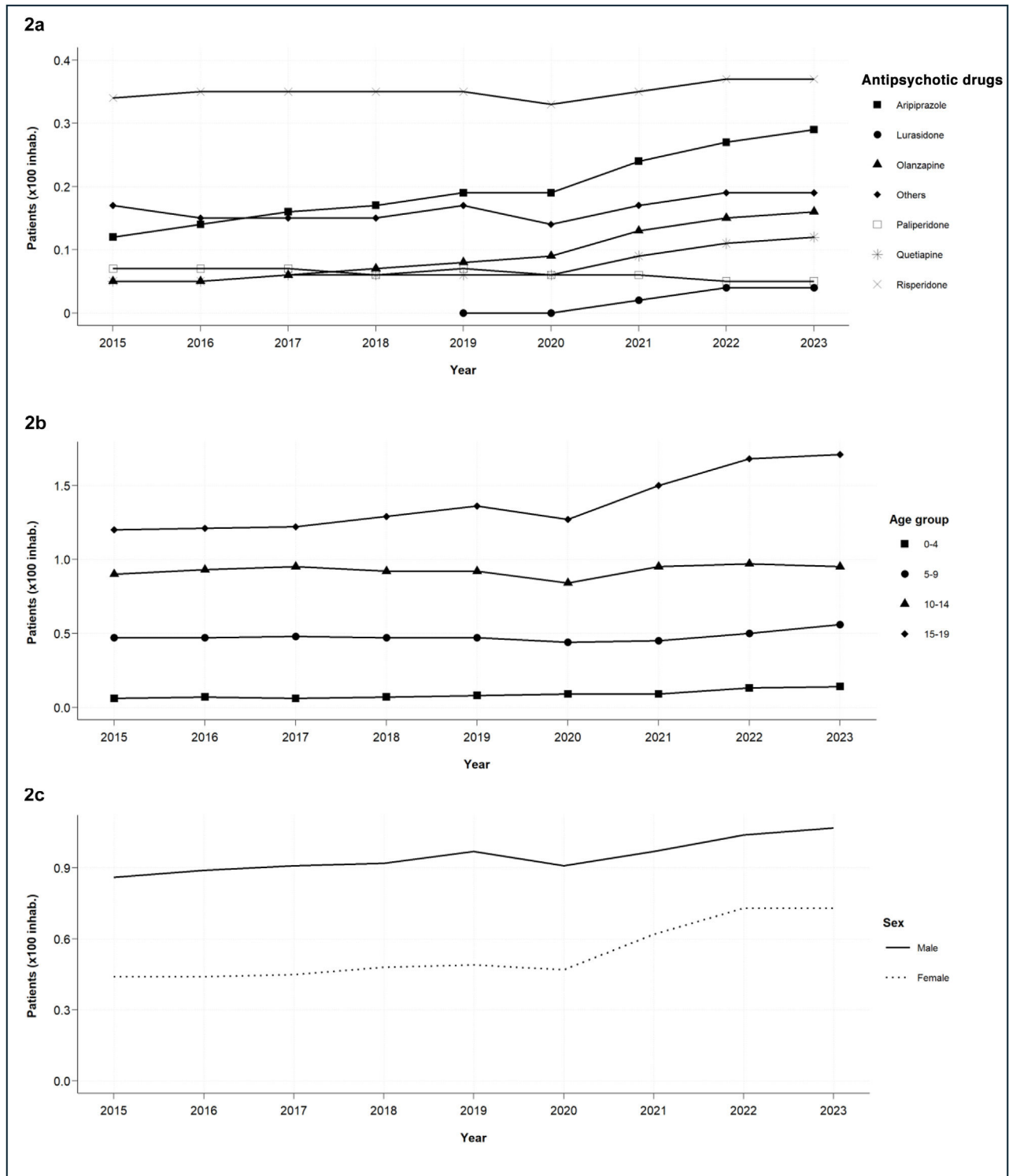


Fig. 2. Yearly number of patients with at least 1 antipsychotic prescription per 100 inhabitants, per substance (a), age group (b) and sex assigned at birth (c).

profiles, but the relatively faster increase in CED among females further supports the need to understand emerging sex differences in treatment patterns and outcomes. A key strength of our study is its large sample size, covering a source population of almost a million individuals aged 0–19 and identifying 570,238 prescriptions and 30,704 patients over an eight-year period, allowing for a robust analysis of trends over time. Additionally, our study provides the most recent update available and incorporates treatment intensity

data using CED, which offers a more precise assessment of dosing trends vs former studies.

However, our work has some limitations. First, the VID databases contain real-world clinical practice data recorded by health care professionals during routine care, but they are not specifically designed for research. Studies based on real-world data like VID are susceptible to biases such as differential recording, misclassification, or missing data. Nevertheless, prescription and

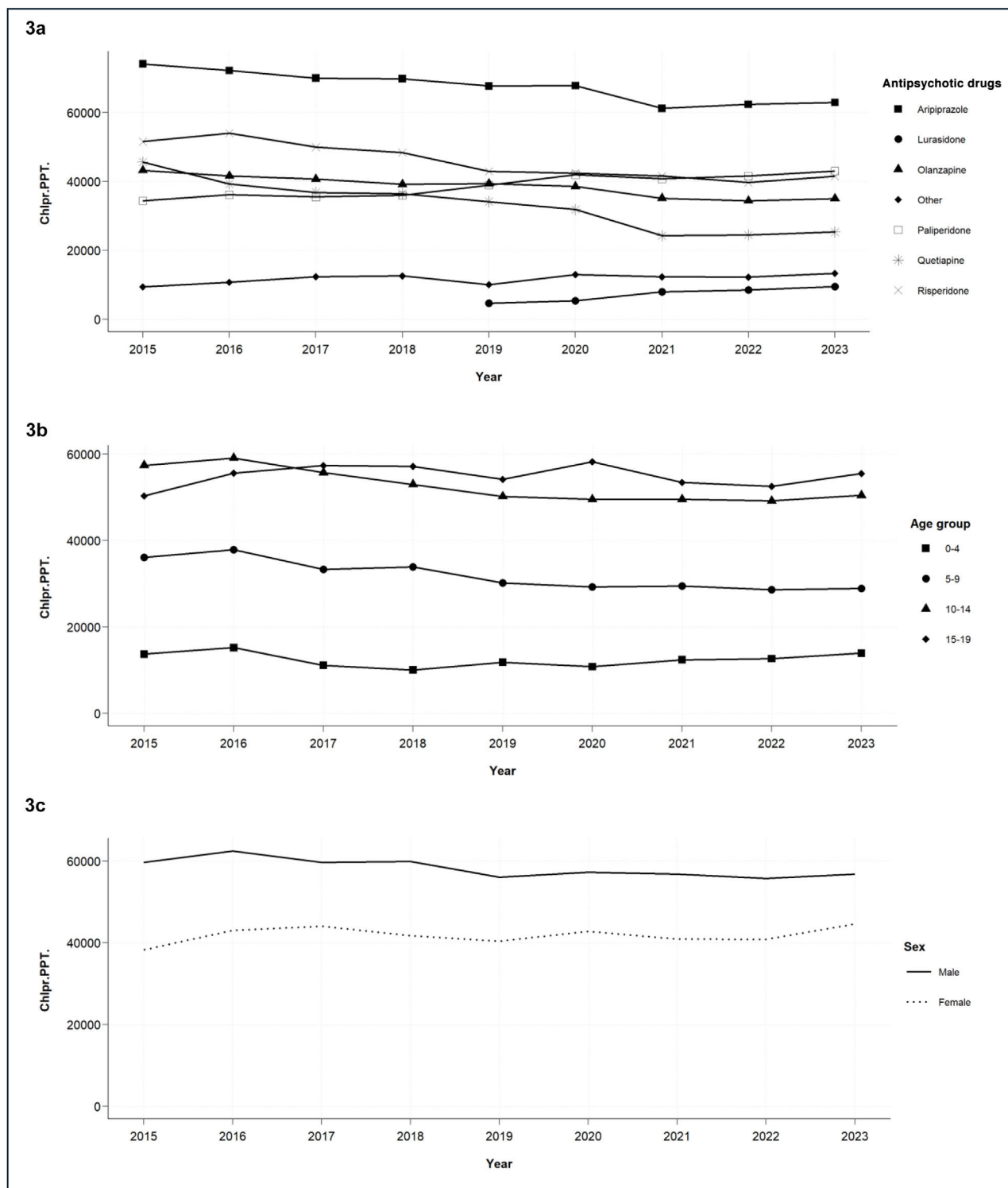


Fig. 3. Yearly number of chlorpromazine equivalent doses per patient treated, per substance (a), age group (b) and sex assigned at birth (c).

dispensation records (the core data in this study) are of the highest quality, as they are used for billing purposes. Second, we described prescription trends for all APs by active substance, regardless of formulation. Third, we did not analyze the indications for prescriptions or examine prescribing patterns of interest, such as appropriateness of prescription, off-label use or deviations from clinical guidelines, which warrants further investigation. Instead, our study highlights potential areas of concern that should be prioritized for future research and intervention. Fourth, certain APs included in the

“Other” category, such as tiapride and levomepromazine, warrant further attention, as they accounted for a non-negligible volume of prescriptions throughout the study period, but were not analyzed individually in this study. Fifth, yearly CED per patient figures should be interpreted with caution, especially in absence of indication data. Sixth, 2023 population data from the National Institute of Statistics was still unavailable at this time and we used 2022 data, which could result in imprecise estimates for the last observation year. Finally, the generalization of our results to other regions

within or outside Spain should be approached with caution, as contextual factors may significantly influence prescribing patterns. Our study confirms a growing trend in AP prescriptions and the number of treated patients among children and adolescents in Spain, with notable differences by age and sex. Future research should explore the clinical indications driving these prescriptions and assess the outcomes associated with increased AP use in young populations.

CRediT authorship contribution statement

IH, AG, GS, RT and IB were responsible for the study concept, design and data acquisition. IH and CR carried out the data preparation and the statistical analysis and AG drafted the manuscript. All authors participated in the analysis and interpretation of data as well as the critical revision of the manuscript for important intellectual content. They approved the final version submitted for publication and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics statement

The study was reviewed and approved by the Ethics Committee for Drug Research of the *Hospital Clínico-Universitario de Valencia* (Order 2025/042, Resolution 434, March 3rd, 2025). Written informed consent for participation was deemed unnecessary for this study in full compliance with the national legislation and the institutional requirements.

Funding

This study was funded by the Spanish Foundation for Science and Technology (FECYT), the Spanish Ministry of Science, Innovation and Universities, grant FCT-24-20488, “Children and Adolescents Antipsychotic Research for Evidence-based Strategies – CARES project”, and by grants RD21/0016/0006 and RD24/0005/0009, from *Instituto de Salud Carlos III* (ISCIII), the Spanish Ministry of Science, Innovation and Universities, and the Recovery, Transformation and Resilience Plan through NextGenerationEU European funds. IB was partially funded by a Pons Bartran grant (FCRB.IPB 2-2023). RT was partially funded by grant PID2021-129099OB-I00 from the Ministry of Science, Innovation and Universities, and by the Ministry of Education of the Valencian Regional Government (grant CIPROM/2022/58). The funders had no role in considering the study design or in the collection, analysis, interpretation of data, writing of the report, or decision to submit the article for publication. The views presented here are those of the authors and not necessarily those of the FISABIO Foundation, the Valencia Ministry of Health, or the study funders.

Conflicts of interest

IB declared to have received honoraria or funding to attend conferences from Angelini and Lundbeck. The remaining authors declared that the research was conducted in the absence of any additional commercial or financial relationships that could be construed as a potential conflict of interest.

Isabel Hurtado reports financial support from the *Instituto de Salud Carlos III* and the Spanish Foundation for Science and Technology. Inmaculada Baeza reports receiving speaker and lecture fees from Lundbeck LLC and Angelini Holding SpA. No other disclosures were reported. The remaining authors declare no known competing financial interests or personal relationships that could have influenced the work reported in this article.

Data availability

The data sets generated and/or analyzed in this study are not publicly available because of legal restrictions on data sharing imposed by the Valencia regional government. Specifically, dissemination of these data to third parties is prohibited under the legal resolution of the Valencia Health Agency (2009/13312) (available at: <http://www.san.gva.es/documents/152919/157920/resolucionesolicituddatos.pdf>). Upon reasonable request, authors can allow access to the databases to verify the accuracy of the analysis or the reproducibility of the study. Requests to access the datasets should be directed to Management Office of the Data Commission in the Valencia Health Agency (E-mail address: solicitud_datos@gva.es; Tel.: +34 961 928207; +34 961 928198). Requests to access the datasets should be directed to solicitud_datos@gva.es.

Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version available at <https://doi.org/10.1016/j.sjpmh.2026.01.002>.

Declaration of competing interest

None declared.

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