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The PADRIS-PRESTO cohort: A comprehensive population-based study on mental health in Catalonia

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Abstract

Background. Mental disorders affect nearly 970 million people worldwide, impacting individuals and healthcare systems. Large population databases offer insights often unattainable in smaller studies, but their findings may not always generalize across diverse regions. To address this, we introduce a European cohort from Catalonia, Spain, allowing for comparisons between individuals with mental disorders and the general population.

Methods. Data were obtained from the "Programa d'analítica de dades per a la recerca i la innovació en salut" (PADRIS). The cohort included all individuals who accessed public specialized mental health services between 2015 and 2019, with retrospective follow-up extending to 2010. These individuals, referred to as cases, were matched by age, sex, and health region with controls, individuals who had no interactions with mental health services during the same period. Sociodemographic and clinical characteristics, including psychiatric diagnoses, comorbidities, smoking status, healthcare utilization, and prescribed treatments, were analyzed.

Results. The study included 1,421,510 individuals (mean age: 41.6±22.1; 53.6% female), with 473,812 cases and 947,698 controls. Cases were more likely to be exempt from income reporting, be ever-smokers, and have musculoskeletal comorbidities. A total of 1,547,374 psychiatric diagnoses were recorded, with anxiety (31.38%) and mood disorders (18.83%) being the most frequent. Over the follow-up, 76.2 million primary care visits and 67.1 million prescriptions were recorded.

Conclusions. This cohort enhances our understanding of mental health service use, diagnostic trends, and treatment patterns in Catalonia. The insights derived from this cohort have the potential to inform mental health policies, improving outcomes within and beyond the region.

Introduction

Mental health has emerged as a fundamental component of public health, influencing individual well-being, quality of life, and societal functioning [1]. The scale of this challenge is extensive, and in 2019 nearly 970 million people worldwide were affected by mental health conditions [2], with

most cases first manifesting during mid-adolescence [3]. Understanding the prevalence, distribution, and contributing factors of mental health disorders is crucial for developing targeted public health initiatives [4], as their burden extends beyond individuals, affecting families, communities, and healthcare systems [5]. Conditions such as depression, anxiety, and schizophrenia consistently rank among the leading causes of disability and economic loss globally [2]. Addressing this public health challenge requires a deep understanding of the interrelated factors that shape mental health outcomes [6]. The emergence of large-scale population-based databases has created new opportunities for mental health research. These databases, characterized by their longitudinal design [7] and large representative sample sizes [8], provide robust data that enable researchers to identify trends, risk factors, and potential interventions that can inform both public health policies and clinical practices [9]. Large population databases have provided valuable insights into mental health outcomes across different healthcare systems. For example, the Swedish National Patient Register, including information on both inpatient and outpatient psychiatric care, has been used to identify mortality patterns among individuals with mental illnesses [10, 11]. Similarly, Denmark's nationwide register has been analyzed to explore the complex relationships between physical and mental health conditions [12]. In the United States, the Nationwide Inpatient Sample has helped researchers understand how psychiatric comorbidities affect both mental health outcomes and illness severity [13]. While these cohorts provide valuable insights, their findings may not apply uniformly across different regions and countries. Mental health outcomes can vary significantly based on local socioeconomic conditions [14], climate [15], and healthcare accessibility [16], highlighting the importance of region-specific data collection and analysis.

To address this need, we present a newly established cohort from Catalonia, Spain, that includes all individuals who accessed public specialized mental healthcare between 2015 and 2019, with retrospective follow-up extending to 2010. This cohort enables comparison with a representative sample from the general population. We describe its key features and explore its potential to advance our understanding of mental health patterns, risk factors, and effective interventions. This resource will contribute to improving our understanding of mental disorders and developing evidence-based public health strategies.

Methods

Data for this study were obtained from the "Programa d'analítica de dades per a la recerca i la innovació en salut" ("Public Data Analysis for Health Research and Innovation Programme", PADRIS) managed by the Agency for Health Quality and Assessment of Catalonia (AQuAS). PADRIS provides the scientific community with access to healthcare data to promote research, innovation, and health evaluation. This is achieved by enabling the reuse and integration of health data generated by the comprehensive public health system of Catalonia (SISCAT), in alignment with legal and regulatory frameworks, ethical principles, and a commitment to transparency with citizens [17]. The use of this data is part of the "PRimary carE digital Support ToOl in mental health" (PRESTO) project [18], which aims to develop an advanced machine learning-driven digital support platform for efficiently screening, assessing, triaging, and delivering personalized treatments for anxiety and depressive symptoms in primary care. This study was approved by the Hospital Clínic Ethics Committee (HCB/2020/0735).

Participants

Participants, referred to hereafter as "cases," included all individuals who accessed public specialized mental health services (i.e., outpatient clinics, inpatient units, or emergency departments) under SISCAT between January 1, 2015, and December 31, 2019. These individuals were individually matched 1:2 by age, sex, and health region with a comparison group, referred to hereafter as "controls," comprising individuals who sought primary care attention but had no interactions with public mental health services during the same period. Both cases and controls were retrospectively followed up to January 1, 2010, and data were extracted from public health service records for the entire study period. Information was anonymized and de-identified in strict adherence to the applicable legal and regulatory frameworks, ethical guidelines, and principles of transparency [17].

Measures

For each participant, sociodemographic and clinical characteristics were provided.

Sociodemographic characteristics included: age group, sex, country of birth, socioeconomic level, healthcare territorial unit, and date of death.

To ensure anonymization and de-identification, the exact age of the participants was not provided; instead, their age was reported within a five-year range. Based on this information, we estimated each participant's age by calculating the average of the lower and upper limits of the range.

The date of death was available only for the cases, as the controls were selected from individuals who were alive during the period considered.

Clinical characteristics included: psychiatric diagnosis, medical comorbidities, smoking status, body mass index (BMI), adjusted morbidity groups, number of visits to public specialized mental health services, general medicine services, primary care services, and pharmacological interventions prescribed.

Psychiatric diagnoses were recorded based on both specialized mental health services and primary care services, and were reported using International Classification of Diseases (ICD) codes, either the 9th edition [19] or the 10th edition [20]. To ensure consistency, we converted all ICD-9 diagnoses to ICD-10 using a conversion table. In addition to the specific diagnosis, we also reported the main ICD diagnostic category to which it belonged.

Medical comorbidities were determined based on the physical diagnoses participants received during the last two years of follow-up. These diagnoses were provided by PADRIS and were grouped into broader categories, including acquired immunodeficiency syndrome, arthritis, arthrosis, asthma, chronic kidney disease, cirrhosis, chronic obstructive pulmonary disease, dementia, diabetes, heart failure, hypertension, ischemic stroke, musculoskeletal disorders, neoplasms, and osteoporosis.

Regarding smoking status, individuals who were classified as smokers at least once during the study period were considered "ever smokers," while those who were never classified as smokers during the same period were considered "never smokers."

BMI data were available only for the final year of the follow-up period. In cases where multiple measurements were collected during the same year, we averaged them to obtain a single value. Additionally, since some values appeared unusually low or high, suggesting potential reporting errors, we decided to remove these outliers based on clinical judgment, excluding values greater than 65 or less than 10.

Adjusted morbidity groups were assigned to each participant to classify their health conditions based on the severity of their morbidity. These groups were designed to reflect the complexity of individuals' health conditions, accounting for multimorbidity and the level of medical intervention required [21]. This data was available from 2014 to 2019, with participants categorized into five risk groups, ranging from "Very Low Risk" to "Very High Risk".

Statistical analyses

Data cleaning, data harmonization, and all statistical analyses were conducted using RStudio, R version 4.3.1 [22]. Due to the large sample size, we assumed normality of the data based on the Central Limit Theorem, which states that, for sufficiently large sample sizes, the distribution of the sample mean approaches normality [23]. Continuous variables were reported as means and standard deviations, and categorical variables were presented as counts and percentages. Group comparisons for specific continuous variables (i.e., mean age and BMI) were conducted using independent samples t-tests. The magnitude of the effect for continuous variables was assessed using Cohen's d, with interpretations as follows: small (d = 0.2), moderate (d = 0.5), and large (d = 0.8) [24]. Group comparisons for specific categorical variables (i.e., age group, sex, country of birth, socioeconomic level, medical comorbidities, and smoking status) were made using the chi-square test. Cramer's V was used to assess the strength of the association, with interpretations as follows: small (V =0.1), moderate (V = 0.3), and large (V = 0.5) [25]. For each variable, we reported information based on all available data (available-case analysis). Specifically, individuals with missing values were excluded only from descriptions and analyses involving the corresponding measure, while being retained in all others where data were complete. No imputation procedures were applied. Statistical significance was set at p<0.05. To account for multiple comparisons, Bonferroni correction was applied, and adjusted p-values are reported.

Results

Cohort description and sample characteristics

Data from a total of 1,421,510 individuals (age: 41.6 ± 22.1 , females: n =762,558; 53.6%) were obtained from the PADRIS. Data on sociodemographic characteristics was complete. Most individuals were born in Europe (90.5%), followed by America (4%), Africa (3.6%), Asia (1.9%), and Oceania (<0.1%). Most individuals had an annual income below €18,000 (50.9%), followed by those with an income between €18,000 and €100,000 (32.3%), and those earning more than €100,000 (0.9%); the remaining group was exempt from income reporting (15.9%). Data on clinical characteristics was incomplete, with medical comorbidities, smoking status, and BMI reported for 98.7% (n = 1,403,566), 54.3% (n = 772,093), and 10.6% (n = 150,636) of the sample, respectively. Additional details are presented in Table 1. Among the individuals included in the whole sample, 473,812 (mean age: 41.6 ± 22.1 , females: n = 254,133; 53.6%) were identified as cases, and 947,698 (mean age: 41.6 ± 22.1 , females: n = 508,425; 53.7%) as controls. Within the cases, 19,917 individuals died during the followup period, while 453,895 individuals (mean age: 40.2±21.3, females: n = 243,877; 53.8%) remained alive until the end of the follow-up.

Comparative analysis of sociodemographic and clinical variables

When comparing these surviving **cases** to the **control group**, significant differences were observed across all sociodemographic and

Table 1. Overall characteristics of the whole sample

	Mean ± SD/n (%)
Age, mean (<i>n</i> = 1,421,510)	41.58 ± 22.06
Age, class (n = 1,421,510)	
Adults (20–64 years old)	841,527 (59.20%)
Children/adolescents (0–19 years old)	342,679 (24.11%)
Older adults (>65 years old)	237,304 (16.69%)
Sex (n = 1,421,510)	
Females	762,558 (53.64%)
Geographic region (n = 1421,510)	
Europe	1,285,881 (90.46%
Americas	57,182 (4.02%)
Africa	50,698 (3.57%)
Asia	26,942 (1.90%)
Oceania	78 (0.01%)
Unspecified	729 (0.05%)
Economic status (n = 1,421,510)	
Exempted	226,208 (15.91%)
< 18,000	723,314 (50.88%)
18,001 – 100,000	458,684 (32.27%)
> 100,000	13,304 (0.94%)
BMI (n = 150,636)	26.96 ± 6.72
Smoker (n = 772,093)	320,503 (41.51%)
Comorbidities (<i>n</i> = 1,403,566)	
Musculoskeletal Disorders	601,843 (42.88%)
Hypertension	261,633 (18.64%)
Arthrosis	185,634 (13.23%)
Asthma	125,401 (8.93%)
Diabetes	103,281 (7.36%)
Neoplasms	91,566 (6.52%)
Arthritis	90,673 (6.46%)
COPD	69,378 (4.94%)
Osteoporosis	61,346 (4.37%)
Chronic kidney disease	46,747 (3.33%)
Ischemic stroke	38,569 (2.75%)
Heart failure	33,696 (2.40%)
Dementia	32,712 (2.33%)
Cirrhosis	7505 (0.53%)
AIDS	7123 (0.51%)

Abbreviations: AIDS, acquired immunodeficiency syndrome; BMI, body mass index; COPD, chronic obstructive pulmonary disease; SD, Standard deviation.

clinical characteristics, except for sex (p = 0.37; Bonferroni-corrected p = 1). Variables reaching at least a small effect size in the comparison between cases and controls included cases being more likely to be born in Europe (94.7% vs. 88.3%; p<0.001; V = 0.10), being exempt from income reporting (25.2% vs. 11.6%; p<0.001; V = 0.17), and were less likely in the €18,000 to €100,000 income range (22.9% vs. 37.1%; p<0.001; V = 0.14). Cases were also more frequently eversmokers (48.6% vs. 37.2%; p<0.001; V = 0.11) and had a higher

prevalence of musculoskeletal disorders as a comorbidity (51.4% vs. 38.1%; p<0.001; V = 0.13), compared to controls. Additional details are presented in Table 2. When deceased individuals were included, no differences were observed between cases and controls in

terms of age mean, age groups, or sex. However, comparisons of other sociodemographic and clinical characteristics showed differences of similar magnitude to those previously described. Further details can be found in the Supplementary Materials, eTable 1.

Table 2. Comparison between people affected by mental disorders and general population, excluding deceased individuals

Total sample (<i>n</i> = 1,401,593)	Patients (<i>n</i> = 453,895)	Controls (n = 947,698)	p value*	Statistical test (df)	Effect size
Age, mean	40.21 ± 21.30	41.59 ± 22.07	<0.001	t = 35.36 (923723)	<i>d</i> = 0.06
Age, class					
Children/adolescents (0–19 years old)	114204 (25.16%)	228436 (24.10%)	<0.001	$\chi^2 = 185.44 (1)$	V = 0.01
Adults (20–64 years old)	274848 (60.55%)	560974 (59.19%)	<0.001	$\chi^2 = 235.72 (1)$	V = 0.01
Older adults (65–104 years old)	64843 (14.29%)	158288 (16.70%)	<0.001	$\chi^2 = 1338.67 (1)$	V = 0.03
Sex					
Female	243877 (53.73%)	508425 (53.65%)	1	$\chi^2 = 0.81 (1)$	V = 0.000
Geographical region					
Europe	429595 (94.65%)	836629 (88.28%)	<0.001	$\chi^2 = 14254.68 (1)$	V = 0.10
Americas	11263 (2.48%)	45,810 (4.83%)	<0.001	$\chi^2 = 4347.25 (1)$	V = 0.06
Africa	10163 (2.24%)	40,420 (4.27%)	<0.001	$\chi^2 = 3620.73 (1)$	V = 0.05
Asia	2674 (0.59%)	24,238 (2.56%)	<0.001	$\chi^2 = 6313.54 (1)$	V = 0.07
Unspecified	186 (0.04%)	537 (0.06%)	0.005	$\chi^2 = 14.34 (1)$	V = 0.003
Oceania	14 (0.00%)	64 (0.01%)	0.31	$\chi^2 = 6.78 (1)$	V = 0.002
Socioeconomical status					
Exempted	114,224 (25.17%)	109,608 (11.57%)	<0.001	χ^2 = 42,296.91 (1)	V = 0.17
< 18,000	233,991 (51.55%)	474,902 (50.11%)	<0.001	$\chi^2 = 254.78 (1)$	V = 0.01
18,001 – 100,000	104,007 (22.91%)	351,614 (37.10%)	<0.001	$\chi^2 = 28156.04 (1)$	V = 0.14
> 100,000	1673 (0.37%)	11,574 (1.22%)	<0.001	$\chi^2 = 2382.57 (1)$	V = 0.04
BMI (n = 149871)	27.42 ± 7.10 (n = 57038)	26.67 ± 6.46 (n = 92,833)	<0.001	t = -20.44 (112068)	<i>d</i> = −0.11
Smoking status (<i>n</i> = 757,479)	n = 276950	n = 480,529			
Ever smoker	134700 (48.64%)	178,608 (37.17%)	<0.001	$\chi^2 = 9526.12 (1)$	V = 0.11
Medical comorbidities (n = 1383649)	n = 453894	n = 929755			
Musculoskeletal Disorders	233474 (51.44%)	354583 (38.14%)	<0.001	$\chi^2 = 22079.06 (1)$	V = 0.13
Hypertension	87061 (19.18%)	161525 (17.37%)	<0.001	$\chi^2 = 676.39 (1)$	V = 0.02
Arthrosis	69385 (15.29%)	107785 (11.59%)	<0.001	$\chi^2 = 3726.83 (1)$	V = 0.05
Asthma	52412 (11.55%)	70826 (7.62%)	<0.001	$\chi^2 = 5803.99 (1)$	V = 0.06
Diabetes	37392 (8.24%)	58930 (6.34%)	<0.001	$\chi^2 = 1699.35 (1)$	V = 0.04
Arthritis	37341 (8.23%)	51021 (5.49%)	<0.001	$\chi^2 = 3827.58 (1)$	V = 0.05
Neoplasms	30415 (6.70%)	53919 (5.80%)	<0.001	$\chi^2 = 433.05 (1)$	V = 0.02
COPD	29241 (6.44%)	34259 (3.68%)	<0.001	$\chi^2 = 5295.87 (1)$	V = 0.06
Osteoporosis	20333 (4.48%)	37659 (4.05%)	<0.001	$\chi^2 = 139.85 (1)$	V = 0.01
Dementia	15476 (3.41%)	10428 (1.12%)	<0.001	$\chi^2 = 8690.04 (1)$	V = 0.08
Chronic kidney disease	15121 (3.33%)	26231 (2.82%)	<0.001	$\chi^2 = 273.56 (1)$	V = 0.01
Ischemic stroke	13347 (2.94%)	21673 (2.33%)	<0.001	$\chi^2 = 459.06 (1)$	V = 0.02
Heart failure	11106 (2.45%)	17028 (1.83%)	<0.001	$\chi^2 = 579.51 (1)$	V = 0.02
AIDS	3952 (0.87%)	2771 (0.30%)	<0.001	$\chi^2 = 2067.32 (1)$	V = 0.04
Cirrhosis	3224 (0.71%)	3172 (0.34%)	<0.001	$\chi^2 = 902.41 (1)$	V = 0.03

Abbreviations: AIDS, acquired immunodeficiency syndrome; BMI, body mass index; COPD, chronic obstructive pulmonary disease; d, Cohen's d; df, degrees of freedom; SD, standard deviation; V, Cramer's V.

^{*}p-value after Bonferroni correction for multiple comparisons.

Distribution of psychiatric diagnoses

A total of 1,547,374 psychiatric diagnoses were recorded during the follow-up period across various settings, including outpatient clinics, inpatient units, emergency departments, and primary care services, encompassing 716 unique ICD-10 codes. The most common diagnosis was "Anxiety disorder, unspecified" (F41.9; 10.46%), followed by "Major depressive disorder, single episode, unspecified" (F32.9; 5.63%), "Nicotine dependence, unspecified, uncomplicated" (F17.200; 3.86%), "Adjustment disorder with mixed anxiety and depressed mood" (F43.23; 3.76%), and "Dysthymic disorder" (F34.1; 3.29%). The complete list is provided in the Supplementary Materials, eTable 2. When considering the main diagnostic categories, "Anxiety, dissociative, stress-related, somatoform, and other nonpsychotic mental disorders" (F40-F48) accounted for the highest percentage of diagnoses at 31.38%, followed by "Mood disorders" (F30-F39; 18.83%), "Mental and behavioral disorders due to psychoactive substance use" (F10-F19: 13.59%), "Behavioral and emotional disorders with onset usually occurring in childhood and adolescence" (F90-F98; 11.07%), "Disorders of adult personality and behavior" (F60-F69; 6.51%), "Schizophrenia, schizotypal, delusional, and other nonmood psychotic disorders" (F20-F29; 6.09%), "Behavioral syndromes associated with physiological disturbances and physical factors" (F50-F59; 5.23%), "Pervasive and specific developmental disorders" (F80-F89; 4.26%), "Mental disorders due to known physiological conditions" (F01–F09; 1.81%), and "Intellectual disabilities" (F70–F79; 1.09%). Lastly, "Unspecified mental disorder" (F99) made up 0.14% of the diagnoses. The distribution of main diagnostic categories is represented in Figure 1, and the top five categories for each year between 2010 and 2019 are shown in the Supplementary Materials, eFigure 2.

Patterns of healthcare service use

A total of 687,051 individuals (48.3%) received at least one psychiatric diagnosis in either specialized mental health services or primary care services (mean: 5.33±6.57; range: 1–361), and 492,866 individuals (34.7%) received more than one psychiatric diagnosis.

Regarding the number of visits, a total of 76,241,239 visits (mean: 6.3 ± 8.57 ; range: 0-1,227; 5.36 visits/person/year) were conducted in primary care services during the follow-up period, and 9,318,815 visits to specialized mental health outpatient services (mean: 0.78 ± 2.93 ; range: 0-427) were recorded. Emergency visits amounted to 5,113,577 (mean: 0.43 ± 1.21 ; range: 0-358), while psychiatric hospitalizations reached 158,972 (mean: 0.01 ± 0.19 ; range: 0-51). Day hospital services accounted for 440,771 visits (mean: 0.16 ± 1.54 ; range: 0-179). A total of 1,068,470 hospitalizations (mean: 0.09 ± 0.39 ; range: 0-42) were conducted in general medical settings, while visits to emergency departments specifically for general medical issues totaled 1,410,515

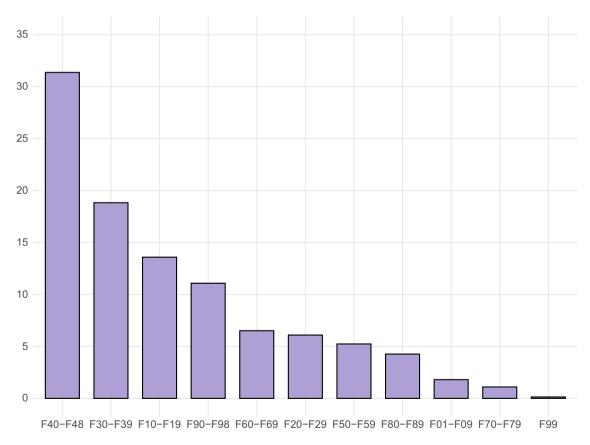


Figure 1. Distribution of the 1,547,374 psychiatric diagnoses recorded during the follow-up period and grouped according to the ICD-10 categories. F01–F09, Mental disorders due to known physiological conditions, F10–F19, Mental and behavioral disorders due to psychoactive substance use, F20–F29, Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders, F30–F39, Mood Disorders, F40–F48, Anxiety, dissociative, stress-related, somatoform, and other nonpsychotic mental disorders, F50–F59, Behavioral syndromes associated with physiological disturbances and physical factors, F60–F69, Disorders of adult personality and behavior, F70–F79, Intellectual disabilities, F80–F89, Pervasive and specific developmental disorders, F90–F98, Behavioral and emotional disorders with onset usually occurring in childhood and adolescence, F99, Unspecified mental disorder.

(mean: 0.51 ± 1.35 ; range: 0-318). Regarding inpatient care, the total number of days spent in psychiatric inpatient care was 1,025,679 (mean: 0.37 ± 6.60 ; range: 0-366), in general medical units was 1,064,758 (mean: 0.38 ± 3.42 ; range: 0-366), and in emergency-related general hospitalizations was 781,279 (mean: 0.28 ± 2.76 ; range: 0-366). Additionally, 330,819 days (mean: 0.12 ± 4.11 ; range: 0-366) were spent in long-term sociosanitary facilities and 431,144 days (mean: 0.15 ± 3.52 ; range: 0-366) in medium-term sociosanitary facilities.

Pharmacological treatment profiles

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Regarding pharmacological interventions, a total of 67,086,050 prescriptions were recorded during the follow-up period (4.72 prescriptions/person/year), covering 217 unique interventions. Figure 2 illustrates the distribution of interventions that account for at least 1% of the total prescriptions. Of these, 45,995,358 prescriptions (68.6%) were for medications with Anatomical Therapeutic Chemical (ATC) codes starting with N03 (antiepileptics), N05 (psycholeptics), and N06 (psychoanaleptics), corresponding to 89 unique interventions. A total of 368,217 individuals received at least one prescription for these interventions (mean: 124.91±137.68; range: 1–1309), with 356,671 individuals receiving more than one prescription. Further details on the medications can be found in the Supplementary Materials, eTable n.3.

Adjusted morbidity groups and risk stratification

Regarding the adjusted morbidity groups, data from six years were considered. The full population distribution for each year is provided in the Supplementary Materials, eTable 4, and graphically represented in eFigure n.1.

Discussion

This paper provides a comprehensive overview of the PADRIS-PRESTO cohort, which contains sociodemographic and clinical information for all individuals who accessed specialized mental health services in Catalonia during the period from 2010 to 2019, along with a representative sample of matched individuals from the general population. With 1,421,510 individuals, including 473,812 cases and 947,698 controls, this represents the largest population-based cohort focused on mental health in Catalonia and, more broadly, in Spain. This resource will enable researchers to study patterns of access to public health facilities, medication prescription patterns, diagnostic practices across different mental health settings, and other important aspects such as the role of psychiatric and physical comorbidities in the progression of primary disorders.

The descriptive analysis revealed disparities between cases and controls, and differences that reached at least small magnitude are discussed. Individuals accessing specialized mental health services

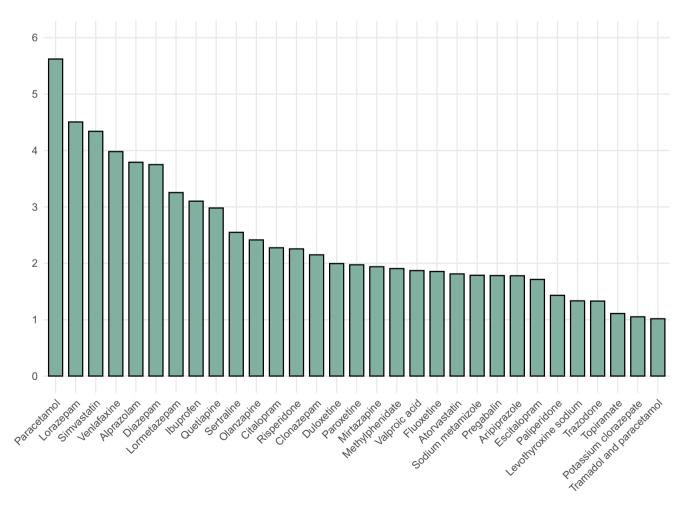


Figure 2. Distribution of interventions that account for at least 1% of the total number of prescriptions.

exhibited greater economic vulnerability, as indicated by their higher rates of exemption from healthcare copayments and lower representation in the 18,000–100,000-euro income bracket. This socioeconomic disparity reflects what previous literature has documented extensively: the relationship between financial difficulties and mental disorders is complex and bidirectional [6]. Mental health conditions may increase the risk of unemployment and subsequent financial strain [26], while economic instability simultaneously undermines mental well-being [27]. Additionally, previous research has linked lower economic status to suicidal ideation and behavior [28], increasing the public health significance of these findings. Health behavior assessments revealed a significantly higher prevalence of ever smoking among cases. Individuals with psychiatric conditions have high rates of nicotine dependence [29], and while cigarette smoking has declined in the general population over recent decades [30], those with severe psychiatric conditions may not have experienced the same reductions [31]. These differences are particularly concerning as tobacco use may amplify existing vulnerabilities, contributing to the increased susceptibility to physical disorders commonly observed in psychiatric populations, including cardiovascular diseases and neoplastic disorders [32]. The interaction between mental health conditions and physical comorbidities was further evidenced in our findings. Among medical comorbidities, musculoskeletal disorders showed the largest difference between cases and controls. Conditions such as low back pain are among the leading causes of disability worldwide [33], and prior research has documented associations between musculoskeletal disorders and mental health conditions [34]. Additionally, these conditions may be associated to increased BMI [35], a common side effect of many psychotropic drugs [36], as well as a result of sedentary lifestyle and unhealthy eating habits.

Examination of diagnostic distributions within the PADRIS-PRESTO cohort reveals anxiety disorders, mood disorders, and behavioral and emotional disorders with childhood and adolescent onset as the most prevalent diagnostic categories in the Catalan population. This pattern aligns with the latest Global Burden of Disease Study [2], where anxiety and depressive disorders showed the highest disability-adjusted life-years and years lived with disability across most age groups, while conduct and anxiety disorders ranked highest during childhood and early adolescence. This distribution highlights the significant challenges that mental disorders pose to both individuals and public health systems. In fact, anxiety disorders can significantly impair cognitive performances and reduce quality of life, leading to cascading consequences including academic underachievement, underemployment, and interpersonal difficulties [37]. These outcomes generate both direct and indirect healthcare costs [38]. Similarly, depressive disorders are associated with cognitive impairments, reduced quality of life, higher morbidity and mortality, and adverse functional outcomes through their effects on academic and vocational achievement, economic status, and relationships [39]. From a societal perspective, the economic burden of depressive disorders has been increasing in recent years, with workplace costs representing the largest growth component [40]. It is important to highlight that the diagnostic patterns observed in this cohort reflect routine clinical practice, where variability in ICD coding among providers and settings is shaped by both clinical practices and the complexity of mental health presentations. Factors such as clinician workload, time constraints, and the nature of the healthcare setting may lead clinicians to prioritize diagnoses with clearer or more acute symptoms, potentially resulting in the overrepresentation of certain conditions and the inadequate recognition of others requiring more detailed clinical assessment.

The substantial healthcare use and burden associated with these conditions is reflected in the more than 76 million clinical visits conducted and 67 million pharmacological interventions prescribed during the 10-year study period. This extensive prescription pattern warrants careful examination, as it may indicate changing clinical practices with significant public health implications. For instance, a previous analysis of the PADRIS-PRESTO cohort focusing solely on antidepressant prescriptions in primary care revealed an increasing prescription rate that outpaced the incidence of mental disorders with established antidepressant indications [41]. This phenomenon, observed in other countries as well [42, 43], carries additional implications beyond clinical outcomes. For example, the increased production and distribution of psychotropic drugs contributes a significant carbon footprint [44], with environmental consequences that could potentially exacerbate mental health conditions through ecological degradation and climate change effects [15], creating a concerning feedback loop between treatment approaches and environmental determinants of mental health. Additionally, the rising prevalence of anxiety and depressive symptoms may also be linked to systemic shortcomings in psychological care resources, highlighting the need for a more integrated approach [18].

The PADRIS-PRESTO cohort represents the largest population-based cohort in Catalonia dedicated to mental health research, providing an important resource for researchers and public health authorities to gather insights into regional mental health trends and challenges [45]. By including all individuals who accessed specialized mental health care facilities during the study period alongside a matched sample, the findings derived from this cohort may reasonably be generalized to the broader Catalan population and potentially extended to other regions in Spain and countries with similar demographic and healthcare characteristics. While this cohort is rooted in the Catalan healthcare system, which provides public access to healthcare services, the structure of this system is broadly aligned with models in other European countries such as Italy, Portugal, and the United Kingdom [46]. In terms of mental health services specifically, the Catalan system is characterized by a community-oriented approach, similar to those observed in other European contexts. It also shows parallels in how local decisionmakers implement protocols to guide system reforms, allocate resources, and promote collaboration between research teams and public health agencies [47]. Nevertheless, broader differences in local policies, resource availability, and population characteristics should be considered when extrapolating these findings to other settings. The PADRIS-PRESTO database opens unprecedented possibilities to explore in detail factors associated with the whole mental health spectrum and the need for specialized mental health care in each case. For policymakers, this cohort may offer evidence-based insights to inform resource allocation, service planning, and targeted intervention strategies [48]. The diagnostic distribution, for instance, highlights the predominance of anxiety and mood disorders, allowing authorities to prioritize interventions targeting these conditions that significantly impact quality of life and healthcare use [49]. The detailed prescription data can help monitor adherence to clinical guidelines, identify potential prescribing disparities across demographic groups, and evaluate the economic impact of various treatment approaches. As mental health continues to gain recognition as a global public health priority, population-based resources like the PADRIS-PRESTO cohort will be instrumental in advancing our understanding of

mental health conditions and developing effective interventions. The insights generated from this cohort will contribute to international comparative research, identifying both universal aspects of mental health challenges and the region-specific considerations necessary for developing more precise healthcare solutions. We already have and continuously work on each of these aspects as subprojects to enable the dissemination of these results toward these aims.

The present work has some limitations. First, our cases include individuals who had at least one contact with specialized public mental health services, but it is possible that some subjects, despite having psychiatric diagnoses provided by specialists, accessed private facilities only and therefore were not included in our cohort. As a result, our estimates may slightly underestimate the true prevalence of mental disorders or differ from patterns in populations with higher use of private services. Despite this limitation, Catalonia operates within a public healthcare system where care is provided free of charge, which minimizes the proportion of people exclusively using private services. Second, mortality data are available only for cases, while controls were selected among individuals who remained alive throughout the study period. Although this prevents us from making mortality comparisons between cases and controls, it remains possible to compare mortality outcomes across different subpopulations of cases. Third, not all data are available for the entire population, with missing values particularly common for smoking status and BMI. We addressed this by using an available-case analysis, which assumes that data are missing at random, which may not always hold true. As such, findings involving variables with high levels of missingness should be interpreted with caution. Nonetheless, these variables are still available for a substantial number of participants, and most other data, including number of visits, diagnoses, and prescription types, are available for each year of follow-up, allowing for detailed observation of longitudinal trends in this cohort. Fourth, to ensure anonymization of each participant, some data, such as age or income levels, were not provided precisely but rather as ranges. This approach, while limiting certain analyses, strengthens the ethical foundations of the database and ensures compliance with privacy regulations while still enabling meaningful population-level insights. Fifth, the nature of registry-based data collection means that clinical information was recorded in routine clinical practice by various healthcare professionals across different settings, rather than through standardized research protocols. This introduces several potential concerns, including variability in diagnostic practices, inconsistencies in the application of ICD coding, and the absence of structured or validated clinical assessment tools. Such heterogeneity may lead to classification bias and reduce the internal consistency of certain measures. These limitations are common to all large populationbased datasets but should be weighed against the ecological validity of our findings, which offer valuable insights into real-world clinical practices, treatment patterns, and outcomes that may not be captured in more controlled research environments.

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Data availability statement. The dataset used and analyzed in this study will be available upon reasonable request from the corresponding author, in accordance with the agreement between PADRIS-AQuAS and Hospital Clínic of Barcelona.

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All the other authors have no conflict to declare.

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