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Recent trends in hospital admission due to bipolar disorder in 10–19-year-olds in Spain: A nationwide population-based study

Teresa López-Cuadrado[1] | Ezra Susser[2,3] | Gonzalo Martínez-Alés[4,5,6,7]

[1]Department of Chronic Diseases Epidemiology, National Center for Epidemiology, Carlos III Health Institute, Madrid, Spain

[2]Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, New York, USA

[3]New York State Psychiatric Institute, New York, New York, USA

[4]Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, New York, USA

[5]CAUSALab, Harvard TH Chan School of Public Health, Boston, Massachusetts, USA

[6]Hospital La Paz Institute for Health Research (IDIPaz), Madrid, Spain

[7]Mental Health Network Biomedical Research Center (CIBERSAM), Madrid, Spain

Correspondence
Teresa López-Cuadrado, Department of Chronic Diseases Epidemiology, National Centre for Epidemiology, Carlos III Health Institute, Monforte de Lemos 5, 28029 Madrid, Spain.
Email: teresalc@isciii.es

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Abstract

Introduction: Bipolar disorder (BD) hospitalization rates in children and adolescents vary greatly across place and over time. There are no population-based studies on youth BD hospitalizations in Spain.

Methods: We identified all patients aged 10–19 hospitalized due to BD in Spain between 2000 and 2021, examined their demographic and clinical characteristics, and assessed temporal trends in hospitalizations – overall and stratified by age and presence of additional psychiatric comorbidity. We used Joinpoint regressions to identify inflection points and quantify whole-period and annual percentage changes (APCs) in trends.

Results: Of 4770 BD hospitalizations in 10–19-year-olds between 2000 and 2021 (average annual rate: 4.8 per 100,000), over half indicated an additional psychiatric comorbidity, most frequently substance abuse (62.2%), mostly due to cannabis (72.4%). During the study period, admissions increased twofold with an inflection point: Rates increased annually only between 2000 and 2008, for APCs 34.0% (95% confidence interval: 20.0%, 71.1%) among 10–14-year-olds, 10.3% (6.4%, 14.3%) among 15–19-year-olds, and 15.5% (11.5%, 22.7%) among patients with additional psychiatric comorbidity. Between 2009 and 2021, rates decreased moderately among 10–14-year-olds – APC: −8.3% (−14.1%, −4.4%) and slightly among 15–19-year-olds without additional psychiatric comorbidity – APC: −2.6(−5.7, −1.0), remaining largely stable among 15–19-year-olds overall.

Conclusions: Recent trends in hospitalization due to BD in 10–19-year-olds in Spain indicate salient increases in the early 2000s – especially among (i) patients aged 10–14 (decreasing moderately after 2009 among 10–14-year-olds and plateauing among 15–19-year-olds) and (ii) patients with additional psychiatric comorbidity (i.e., cannabis use disorder). These findings suggest links with recent changes in clinical practices for children and recent trends in substance use among Spanish youth.

KEYWORDS
bipolar disorder, children and adolescents, hospital admissions, trends

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1 | INTRODUCTION

Bipolar disorder (BD) is a chronic psychiatric disorder characterized by altered mood including episodes of mania or hypomania and depression.[1] In a significant proportion of cases, BD onset occurs before adulthood and can significantly impair development, behavior, and functioning, increasing risk of disability due to academic and legal problems.[2] In addition, BD is associated with a 50-fold increase in juvenile suicide attempt rates and a 40-fold increase in juvenile suicide mortality risk.[3] Understanding mental healthcare resource use among children and adolescents diagnosed with BD is critical to guide resource allocation and for appropriate access to care and recovery.

Examining hospitalizations due to BD among children and adolescents and monitoring their temporal trends can support healthcare planning and enhance understanding of population-level determinants of BD incidence and severity. Population-based studies of hospital admissions due to BD in this age group indicate marked between-country variation: studies examining BD hospitalizations among children and adolescents have found rates in the United States to be around 10-fold higher than in Australia and New Zealand[4] and around 100-fold higher than in England and Germany,[4,5] with particularly diverging rates in very young children (i.e., aged 5–9). Cross-country variations in prevalence and admissions due to BD among children and adolescents probably reflect differences in the distribution of population determinants of BD incidence and hospitalization as well as, perhaps more importantly, in diagnostic practices.[4,6] While it is generally accepted that BD onset can occur during adolescence, there is scientific debate regarding validity of *pediatric* BD diagnoses among pre-pubertal patients.[7] Changes in diagnostic practices over the last three decades, such as adoption of BD diagnosis for children presenting with chronic irritability, aggressive outbursts, or ultradian mood cycles, may have led to an artificial inflation of the prevalence of BD in children.[8–11] Of note, recent changes in conceptualization of BD in children were initially proposed in the United States in the mid-1990s and have since expanded unevenly across the globe.[12] Accordingly, country-specific studies of BD admissions among children and adolescents are required for healthcare planning and causal hypothesis generation.

Recent increases in hospitalizations due to BD among children and adolescents have been described in population-based studies from the United States, where several reports indicate steady increases in admissions since the mid-90s,[13–16] and Europe, where increases have been noted in Denmark (fourfold increase between 1995 and 2010),[17] Germany (18% increase between 2008 and 2013),[18] and Portugal (fourfold increase between 2000 and 2015).[19] Importantly, interpretation of trends in admissions due to BD in this age group is also challenging, as temporal variations may reflect a combination of changes over time in diagnostic practices, true prevalence or severity of the disorder, and its population-level causes. An additional question with implications for healthcare planning and causal hypothesis generation is whether the average age at BD diagnosis among children and adolescents has decreased over recent years.

In Spain, no studies have obtained population-based estimates of rates of admission due to BD among children and adolescents nor have hospitalization trends over time been examined. Here, we describe characteristics and hospital resource use of BD admissions in 10–19-year-olds in Spain between 2000 and 2021 and analyze temporal trends overall and by age.

2 | METHODS

2.1 | Data source

We conducted a population-based study based on Spain's Hospital Minimum Basic Data Set (CMBD-H), a nationwide mandatory registry of all acute hospital admissions maintained by Spain's Ministry of Health. CMBD-H includes data on >90% of hospital admissions and is thus considered nationally representative. For each hospitalization, CMBD-H includes the following information: date and type of admission (i.e., elective vs. non-elective), demographic characteristics (age and sex), date of and destination after discharge (e.g., in-hospital death), cost of stay in euros (calculated based on diagnostic-related groups), and clinical information consisting of a primary diagnosis and up to 19 additional diagnoses and up to 20 clinical procedures. All information is coded in hospitals prior to discharge according to the International Classification of Diseases, 9th (before 2016) or 10th revision (from 2016 onwards), Clinical Modification (i.e., ICD-9-CM or ICD-10-CM). Denominator data, used for the calculation of rates, come from Spain's ongoing census and were obtained from Spain's National Institute of Statistics. As these data are de-identified, informed consent was not required.

2.2 | Study population and variables

We selected all hospital admissions due to BD of individuals aged 10–19 years in Spain between 2000 and 2021. Selection was based on presence of the following ICD-9-CM codes as primary reason for admission: 296.0 (bipolar I disorder, single manic episode), 296.1 (Manic disorder recurrent episode), 296.4 (bipolar I disorder, most recent episode [or current] manic), 296.5 (bipolar I disorder, most recent episode [or current] depressed), 296.6 (bipolar I disorder, most recent episode [or current] mixed), 296.7 (bipolar I disorder, most recent episode [or current] unspecified), or 296.8 (Other and unspecified BDs); or of ICD-10-CM codes F30 (Manic episode) or F31 (BD). Additional variables retrieved included sex and age in years at admission, type of admission, BD episode polarity (i.e., mania, depression, mixed, or unspecified, as detailed in Table S1); additional psychiatric diagnoses (as detailed in Table S2); presence of suicidal ideation at admission; presence of recorded family psychiatric history; in-hospital mortality; and hospital resource use (length and cost of stay).

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2.3 | Analyses

We first performed descriptive analyses of the demographic and clinical characteristics of the study population, overall and by age group (10–14 and 15–19 years) – using mean and standard deviation or median and interquartile range for continuous variables and absolute and relative frequency for categorical variables. We conducted stratified descriptive analyses to examine differences in average hospital stay duration and direct medical costs per admission across age group and between individuals admitted due to BD with and without additional psychiatric disorders.

Then, we obtained annual admission rates due to BD between 2000 and 2021 per 100,000 individuals aged 10–19 years. To examine temporal trends, we implemented Joinpoint regression models – a class of generalized linear models that assumes a Poisson distribution. This method allows for the identification of inflection points (year) where there is a significant trend change via a series of Monte Carlo permutation tests as well as for the quantification of the annual percentage change (APC) between consecutive years and the average annual percentage change (AAPC) over the whole period, with 95% confidence intervals (95% CIs). Trends were assessed for the overall study population and for subgroups defined by age group and presence of additional psychiatric diagnoses.

Last, linear regression models were used to quantify potential variations over time in the average age at discharge controlling for sex, calculating coefficients (β) and 95% CIs. Analyses were conducted using Stata version 17 and Joinpoint Regression Program, Version 5.0.2.

3 | RESULTS

Between 2000 and 2021, there were 4770 hospital admissions due to BD among individuals aged 10–19 years – accounting for 4% of child and adolescent psychiatric admissions. There were an average annual 218 hospital admissions due to BD in individuals aged 10–19 years – 30 among individuals aged 10–14 years and 188 among individuals aged 15–19 years, for an annual hospitalization rate of 4.8 BD admissions per 100,000 population aged 10–19 years – 1.33 BD admissions per 100,000 population aged 10–14 years, and 8.08 BD admissions per 100,000 population aged 15–19 years.

Table 1 shows the demographic and clinical characteristics of hospitalizations due to BD in 10–19-year-olds in Spain, between 2000 and 2021 (overall and by age group). Most hospitalizations corresponded with male children and adolescents (mean age 16 years), admitted following emergency room visits, and diagnosed with acute manic episode. Notably, younger patients were less likely to be admitted due to manic episode and to have comorbidity due to substance use disorders, and more likely to be admitted due to unspecified BD and to have comorbidity due to ADHD, conduct disorder, or intellectual disability. Figure S1 represents the proportion of admissions indicating acute manic episode by age: mania cases were relatively uncommon in patients aged <15, and thereafter increased with age. Importantly, one in two hospitalized BD patients aged 10–19 had an additional psychiatric diagnosis (i.e., comorbidity). Figure S2 represents the distribution of psychiatric comorbidities in the study population. Substance abuse was the most diagnosed comorbid psychiatric disorder (62.6%), and cannabis was the most frequently reported substance. Around 11% of hospitalized BD patients aged 10–19 had a diagnosis of personality disorder, an additional 11% had intellectual disability, and roughly 6% had both diagnoses of substance abuse and personality disorder.

TABLE 1 General characteristics of hospital admissions for bipolar disorder in children and youth (10–19 years).

	N (%)	10–14 years	15–19 years
Number of admissions	4770	654 (13.7)	4116 (86.3)
Female sex	2051 (43.0)	290 (44.3)	1761 (42.8)
Age, median (P25, P75)	17 (16, 18)	13 (12, 14)	18 (16, 19)
Type of admission			
Non-elective	3725 (78.2)	379 (58.1)	3346 (81.4)
Elective	1039 (21.8)	273 (41.9)	766 (18.6)
Bipolar index diagnosis			
Manic episode	3298 (69.1)	357 (54.6)	2941 (71.4)
Depressive episode	280 (5.9)	26 (4.0)	254 (6.2)
Mixed episode	457 (9.6)	106 (16.2)	351 (8.5)
Unspecified	735 (15.4)	165 (25.2)	570 (13.9)
Psychiatric comorbidity present	2642 (55.4)	341 (52.1)	2301 (55.9)
Substance abuse	1655 (62.6)	37 (10.9)	1618 (70.3)
Cannabis	1198 (72.4)	17 (46.0)	1181 (51.3)
Personality disorders	306 (11.6)	12 (3.5)	294 (12.8)
Intellectual disability	292 (11.0)	77 (22.6)	215 (9.3)
Attention deficit hyperactivity disorder	240 (9.1)	103 (30.2)	137 (6.0)
Conduct disorders	198 (7.5)	74 (21.7)	124 (5.4)
Generalized developmental disorder	162 (6.1)	66 (19.4)	96 (4.2)
Suicidal ideation	107 (2.2)	19 (2.9)	88 (2.1)
Family history of mental health problems	941 (19.7)	172 (26.3)	769 (18.7)
In-hospital mortality	4 (0.1)	0	4 (0.1)
Stay of lengths, median(P25, P75)	15 (8, 25)	13 (5, 22)	15 (8, 25)
Average cost per discharge (€)	6670	6828	6645
Average annual cost (€)	1,446,218	202,968	1,243,250

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During the study period, admissions due to any psychiatric disorder (i.e., ICD-9-CM and ICD-10-ES Chapter 5 codes) increased in Spain from 78 per 100,000 population aged 10–19 years in 2000 to 186 in 2021, which represents an average annual 2.6% (95% CI: 2.0%, 3.3%) increase (Figure 1). BD admission rates increased from 2.64 to 5.05 cases per 100,000 population aged 10–19 years, for an average annual 3.2% (1.4%, 4.9%) change. The Joinpoint method identified one inflection point in the trend in 2008: BD admission rates in 10–19-year-olds increased between 2000 and 2008 – for an annual percent change (APC) of 12.2% (7.8%, 16.8%), and subsequently decreased unsteadily between 2008 and 2021 – for an APC of −2.0% (−3.6%, −0.4%).

Temporal variations were particularly remarkable for BD patients aged 10–14 years. In this age group, BD admissions increased threefold between 2000 and 2021, from 0.23 to 0.79 per 100,000 population; for an average annual 5.9 (2.0%, 12.6%) change, the APC for the 2000–2008 period was 34.0% (13.0%, 58.9%), and the APC for the 2008–2021 period was −8.3% (−13.2%, −3.2%). Among BD patients aged 15–19 years, BD admissions doubled between 2000 and 2021, from 4.61 to 9.44 per 100,000 population – for an average annual 3.5% (2.5%, 5.0%) change. In this age group, the APC for the 2000–2008 period was 10.3% (6.4%, 14.3%), and the APC for the 2008–2021 was −0.5% (−1.9%, 1.0%; Figure 1).

Trends over time in BD admissions in 10–19-year-olds were different between patients with and without additional psychiatric comorbidity, as depicted in Figures 2 and 3. Among patients with BD and at least one additional psychiatric disorder, admission rates went up from 1.00 to 3.17 cases per 100,000 population aged 10–19 between 2000 and 2021, for an average annual 5.6% (4.4%, 7.5%) increase. The Joinpoint method identified one inflection point in the trend in 2008: rates increased between 2000 and 2008, for an APC of 15.5% (11.5%, 22.7%), and subsequently stabilized between 2008 and 2021, for an APC of −1.2% (−3.4%, 0.7%; Figure 2).

Among patients with BD and no additional psychiatric comorbidity, on the contrary, admission rates were roughly similar in 2000 and 2021 (1.63 and 1.88 per 100,000 population aged ≤19, respectively), for an annual average 0.2% (−1.4%, 1.9%) change. Rates were not stable, however, and the Joinpoint method identified one inflection point in the trend in 2008: rates increased between 2000 and 2008, for an APC of 7.7% (3.0%, 21.9%), and subsequently decreased between 2008 and 2021 for an APC of −4.2% (−8.0%, −2.2%; Figure 3).

Stratification by both age group and presence of psychiatric comorbidity revealed further differences across subgroups, as also shown in Figures 2 and 3 – with largest increases driven by trends in patients with BD and comorbidity. In BD patients aged 15–19 without comorbidity, admission rates were roughly similar in 2000 and 2021 (2.78 and 3.58 per 100,000, respectively). Rates were not stable over time: there was an initial increase, for a 2000–2007 APC of 7.5% (2.8%, 23.1%), and a mild subsequent decrease, for a 2007–2021 APC of −2.6% (−5.7%, −1.0%; Figure 3). In BD patients aged 15–19 with comorbidity, however, rates went up threefold between

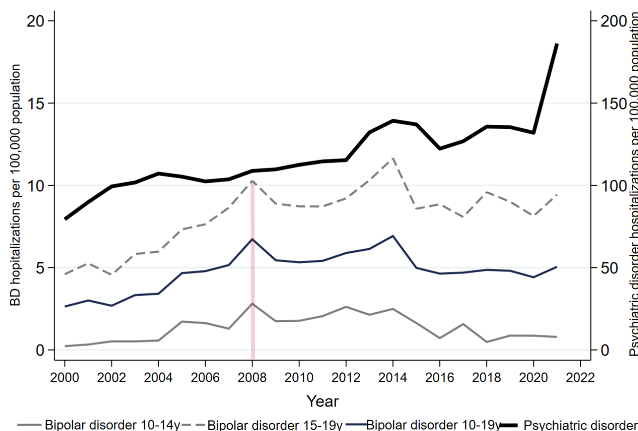

FIGURE 1 Trends in prevalence of hospital admissions due to any psychiatric disorder and to bipolar disorder among individuals aged 10–19 years between 2000 and 2021 in Spain. One inflection point was identified in 2008 via the Joinpoint method.

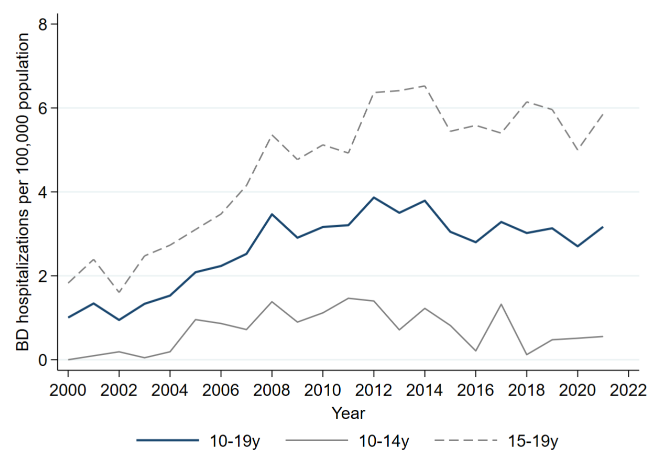

FIGURE 2 Trends in prevalence of hospital admissions due to bipolar disorder including at least one additional psychiatric comorbidity among individuals aged 10–19 between 2000 and 2021 in Spain.

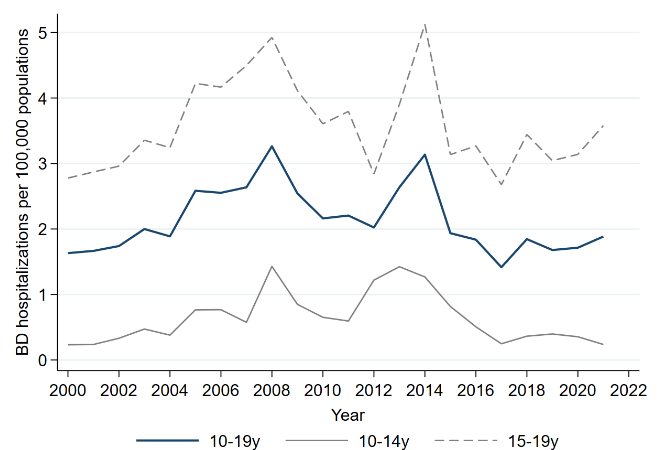

FIGURE 3 Trends in prevalence of hospital admissions due to bipolar disorder without additional psychiatric comorbidity among individuals aged 10–19 between 2000 and 2021 in Spain.

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2000 and 2021, from 1.83 to 5.86 admissions per 100,000, respectively, for an average annual 5.2% (4.1%, 6.6%) increase. An initial increasing trend between 2000 and 2012, for an APC of 10.6% (8.4%, 14.4%), was followed by relative stability of annual admissions between 2012 and 2021 – APC: −1.7% (−5.3%, 1.0%; Figure 2).

In BD patients aged 10–14 without comorbidity, admission rates were also similar in 2000 and 2021 (0.23 and 0.24 per 100,000, respectively). The 2000–2013 initial increase – APC of 11.3% (6.2%, 22.3%) was followed by a marked 2013–2021 decrease – APC of −20.8% (−35.8%, −13.1%; Figure 3). In BD patients aged 10–14 with comorbidity, on the contrary, rates went up 10-fold between 2000 and 2021, from 0.05 to 0.55 admissions per 100,000, respectively, for an average annual 8.6% (2.0%, 23.9%) increase. There was a remarkable increase in admissions between 2000 and 2008, for an APC of 39.6% (16.7%, 164.4%), followed by a 2008–2021 decline – APC: −6.9% (−15.3%, −1.7%; Figure 2). Table 2 includes rates of BD admission per 100,000 population aged 10–19 years for years 2000 and 2021, the resulting AAPC, as well as APC for the temporal trends identified via the Joinpoint method, overall, by age group, and by presence of comorbidity.

Mean age of patients aged 10–19 years admitted due to BD in Spain decreased over the last two decades; while in 2000 the average age at discharge was 17.6, by 2021 the average age at discharge 17.0 years – non-linear $\beta=-0.009$ [−0.019, 0.001]. This phenomenon was particularly salient for patients with an additional psychiatric disorder, among whom the average age at discharge decreased from 17.9 years in 2000 to 16.9 years in 2021.

Table 3 summarizes the distribution of hospital stay in days and direct medical costs for BD patients aged 10–19 admitted in Spain between 2000 and 2021. Hospital stays were somewhat shorter in patients aged 10–14 than in older counterparts, and the median stay of 15 days was similar in patients with and without psychiatric comorbidity, although, in the younger age group, presence of comorbidity was associated with longer hospital stay. Each admission due to BD in 10–19-year-olds incurred an average €6670 in direct medical costs, with slightly higher costs for younger versus older patients and for patients with versus without comorbidity.

4 | DISCUSSION

This nationwide population-based study included all hospital admissions due to BD among individuals aged 10–19 years between 2000 and 2021 in Spain. Hospitalizations due to BD in this age group doubled over the last two decades in Spain, largely due to increases in admissions between 2000 and 2008 that were mostly driven by particularly salient increases in admissions among individuals aged 10–14 years and among patients with BD and at least one additional psychiatric disorder. These results enhance our understanding of recent variations in prevalence of and treatment for BD in 10–19-year-olds and should help guide healthcare planning as well as causal hypothesis generation to enhance treatment and prevention of BD among youth.

TABLE 2 Hospital admissions due to BD among individuals aged 10–19 years between 2000 and 2021 in Spain: admission rates at the beginning and end of the study period, average annual percentage change for the 2000–2021 period, and annual percentage change for trends identified via the Joinpoint method.

	Rate per 100,000				Trend 1		Trend 2	
	Rate for 2000	Rate for inflection year (year: rate)	Rate for 2021	AAPC 2000–21	Period	APC	Period	APC
Overall (10–19 years) BD	2.64	2008: 6.73	5.05	3.2 (1.9, 5.0)[a]	2000–08	12.2 (7.9, 21.5)[a]	2008–21	−2.0 (−4.5, −0.3)[a]
With comorbidity	1.00	2009: 2.91	3.17	5.6 (4.4, 7.5)[a]	2000–09	15.5 (11.5, 22.7)[a]	2009–21	−1.2 (−3.4, 0.7)
Without comorbidity	1.63	2008: 3.26	1.88	0.2 (−1.4, 1.9)	2000–08	7.7 (3.1, 21.3)[a]	2008–21	−4.2 (−8.0, −2.2)[a]
10–14 years BD	0.23	2008: 2.81	0.79	5.9 (2.0, 12.6)[a]	2000–08	34.0 (20.0, 71.1)[a]	2008–21	−8.3 (−14.1, −4.4)[a]
With comorbidity	0.05	2008: 1.38	0.55	8.6 (2.0, 23.9)[a]	2000–08	39.6 (16.7, 164.4)[a]	2008–21	−6.9 (−15.3, −1.7)[a]
Without comorbidity	0.23	2013: 1.42	0.24	−2.2 (−6.4, 2.2)	2000–13	11.3 (6.2, 22.3)[a]	2013–21	−20.8 (−35.8, −13.1)[a]
15–19 years BD	4.61	2008: 10.28	9.44	3.5 (2.5, 5.0)[a]	2000–08	10.3 (6.8, 18.4)[a]	2008–21	−0.5 (−2.7, 1.0)
With comorbidity	1.83	2012: 6.37	5.86	5.2 (4.1, 6.6)[a]	2000–12	10.6 (8.4, 14.4)[a]	2012–21	−1.7 (−5.3, 1.0)
Without comorbidity	2.78	2007: 4.5	3.58	0.7 (−0.7, 2.1)	2000–07	7.5 (2.8, 23.1)[a]	2007–21	−2.6 (−5.7, −1.0)[a]

[a]p-value < .05.

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TABLE 3 Impact of comorbidity on utilization of hospital resources.

	Length of stay (days)[a]			Costs[b], €		
	Overall	With Comorbidities	Without comorbidities	Overall	With Comorbidities	Without comorbidities
Overall	15 (8, 25)	15 (8, 25)	15 (7, 24)	6670 ± 1501	6836 ± 1532	6465 ± 1436
10–14 years	13 (5, 22)	14 (5, 24)	11 (4, 20)	6828 ± 1504	6876 ± 1486	6775 ± 1524
15–19 years	15 (8, 25)	15 (8, 25)	15 (8, 25)	6645 ± 1500	6830 ± 1539	6411 ± 1414

[a]Median (IQR).

[b]Mean ± standard deviation.

Overall, between 2000 and 2021, there were 4.6 admissions due to BD per 100,000 population aged 10–19 in Spain. Similarly designed studies conducted in other European countries found somewhat lower estimates, for example, in Germany between 2000 and 2007 (2.5 admissions per 100,000),[18] Portugal between 2000 and 2015 (1.2 admissions per 100,000),[19] or England between 2000 and 2010 (0.9 admissions per 100,000).[5] These studies, however, used 0–19 years as age range to define BD admissions and population denominators: Inclusion of patients aged 0–10, among whom BD is extremely rare, could explain overall lower admission rates. In fact, in Germany in 2007 there were 6.33 admissions due to BD per 100,000 population aged 15–19, a figure roughly in line with our results in this age group (studies examining youth BD admissions in Portugal and England did not provide estimates specific to the 15–19 years age group). On the contrary, our results revealed markedly lower BD admission rates in children and adolescents than studies from the United States, with estimates ranging between 73 and 100.9 admissions due to child and adolescent BD per 100,000 population[4,5,13] – in line with prior research highlighting differences between American and European diagnostic and clinical practices regarding BD in youth. We found a median hospital stay of 15 days per BD admission in 10–19-year-olds – similar to studies from Germany and Portugal. Reported median admission stays for child and adolescent BD in the United Kingdom and the United States, however, were 34 and 6 days, respectively. It seems plausible that differences in decision to hospitalize patients and in access to alternatives to hospitalized treatment may partially explain between-country differences in admission rates – that is, one possible explanation to this incongruence is that admission for BD patients in the younger age groups is reserved for more severe patients in the United Kingdom than in Spain, Germany, or Portugal, while the severity threshold to admit a patient may be lower in the United States. All in all, differences between countries in admissions due to child and adolescent BD are difficult to interpret given the potential mixture of previously mentioned cross-country differences in diagnostic practices, disease prevalence, and healthcare planning and delivery.

In terms of temporal trends, our main finding was that, over the study period, admissions due to BD in Spain increased globally, from 2.64 to 5.05 admissions per 100,000 population aged 10–19. There was, notably, an inflection point in temporal trends in 2008 and a slight decrease in admissions between 2008 and 2021. Temporal variations in admissions due to BD were more salient among the youngest age group: while in individuals aged 10–14 admissions due to BD increased by 34% between 2000 and 2008 and decreased by 8% between 2008 and 2021, and in individuals aged 15–19, there was only a 10% increase in admissions between 2000 and 2008 and no variation over the rest of the study period. These results mirror population-based studies from the United States, where admissions due to BD among minors increased in the early 2000s and subsequently decreased after 2004,[20] and from Portugal, where there was a similar pattern with a 2006 inflection point and subsequent stabilization and decrease in admissions.[19]

Variations in diagnostic practices, with an initial uptake of the conceptualization of *pediatric* BD as defined in the late 1990s in the United States and a subsequent decline in its use in the late 2000s,[13] may partially explain our results. As mentioned, late 1990s changes in diagnosing practices of BD in early age mainly consisted of use of BD diagnosis for children presenting with chronic irritability, aggressive outbursts, or ultradian mood cycles.[8–11,21] This hypothesis is supported by the findings that 2000–2021 temporal variations in BD admissions (i.e., initial increases and subsequent declines) were particularly salient among patients aged 10–14 in Spain and that a large proportion of BD admissions among patients in this age group were defined as "unspecified" in terms of polarity and included comorbidities that can also describe chronic irritability and aggressiveness, such as ADHD or conduct disorders. In fact, the vast majority of admissions specifically indicating manic episode took place in older patients. Some authors link declines in use of *pediatric* BD diagnoses in the late 2000s to (i) emergence of critical literature emphasizing validity limitations in these diagnoses and (ii) the emergence of disruptive mood dysregulation disorder (DMDD), an entity first included in the 5th edition of the diagnostic and statistical manual of mental disorders (DSM-5) and partially designed to better describe chronically irritable children who may be incorrectly labeled with and treated for BD.[22]

Changes in psychotropic prescription patterns for children and adolescents might also have contributed to temporal variations in BD admissions in this age group. There is evidence that antidepressant use in individuals without BD increases risk of subsequent mania and BD diagnosis.[23] Data from the United Kingdom indicate that antidepressant (i.e., SSRIs) prescription for children and adolescents increased in the late 1990s and early 2000s. However, between 2003 and 2005, safety warnings due to concerns of a potential increase in suicide risk following antidepressant initiation

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in children and adolescents were issued by regulating agencies, leading to a temporary stabilization or decrease in antidepressant prescription in this age group between 2004 and 2010. Population-level antidepressant prescription for children and adolescents in the United Kingdom subsequently bounced back, reaching 2002 levels in 2014.[24] Comparable trends have been reported in Denmark and the Netherlands, but not Germany or the United States.[25] In Spain, where national data on antidepressant prescription for youth are not available, a 2005 guideline by the National Agency for Medications and Healthcare Products[26] recommended against use of antidepressants for children and adolescents based on limited therapeutic benefits and increased risks of suicidal and aggressive behaviors.

Increasing substance use, especially of cannabis, might also explain some of the variation specific to subgroups. We found larger temporal changes in admission rates for BD patients aged 10–19 with versus without psychiatric comorbidity. Of note, the most common psychiatric comorbidity recorded in our population were substance use disorders (62.2% of all psychiatric comorbidities – a vast majority diagnosed based on cannabis use), followed by personality disorders (11.6%) and intellectual disability (11.0%). Whether substance use and BD are causally associated is currently under debate. Importantly, substance use is associated with BD among children and adolescents in cross-sectional designs[27] and has been identified as a risk factor for subsequent development of BD in samples of adolescents diagnosed with other mental disorders (e.g., eating disorders,[28] anxiety,[29] and ADHD[30]). In addition, cannabis use predicts onset of BD among adults.[31,32] Accordingly, a potential role of substance use explaining recent trends in BD admissions among Spanish youth, and especially in adolescents given population patterns of substance use by age, seems intuitive. Representative data indicate that lifetime, last-year, and frequent uses of illicit substances (i.e., cannabis, cocaine, and stimulants) in this age group in Spain increased between 1994 and 2004, peaked between 2004 and 2008, and declined steadily.[33,34] For instance, while the prevalence of last-year use of cannabis, cocaine, and amphetamines among Spanish students aged 14–18 was, respectively, 36.6%, 7.2%, and 4.1% in 2004, by 2014 figures had declined to 25.4%, 2.8%, and 0.9%.[34] The distribution of psychiatric comorbidities we found is at odds with a recent systematic review of non-representative cohort studies of child and adolescent BD patients, where attention-deficit–hyperactivity disorder and oppositional defiant disorder were diagnosed in 60% and 47% of patients, respectively.[35] This systematic review, however, has been criticized because (i) included studies were not representative, but instead corresponded to highly specialized psychiatric centers and, as stated by authors, may be "prone to a selection bias" – yielding comparisons with our results difficult to interpret; and (ii) its authors did not include recent changes in BD diagnoses in children as a potential explanation to their findings.

Lastly, even though there was a slight spike in admissions due to BD in 10–19-year-olds following the initial onset of the COVID-19 pandemic, it is important to note that the pandemic seemingly had a larger impact on pediatric mental health admissions due to other reasons (i.e., suicidal ideation, non-suicidal self-injury, and suicidal behaviors).[36,37] According to our data source, annual admissions due to mental health disorders per 100,000 population aged 10–19 years increased from 132 in 2020 to 186 in 2021.

The main strength of our study is that data come from a nationwide population-based electronic health record. Because Spain's tax-funded national health system provides universal healthcare at no cost to everyone living in Spain, selection bias due to lack of access to hospital care is unlikely. This study also has limitations. First, data quality depends on the accuracy of clinical coding of clinical-administrative databases. The CMBD-H registry, however, is mandatory and subject to periodic audits of data quality. Second, because data are obtained at the hospital admission level, conclusions regarding population-level prevalence of BD should not be drawn – although variations in hospitalizations should somewhat reflect variations in population prevalence or severity – given the abovementioned focus of Spain's health system on ensuring equity in access to care. Notably, while there are no available data on population-level prevalence of BD among children and adolescents in Spain, data from Spain's National Health Survey indicate that prevalence of common mental disorders (i.e., depression or anxiety) in the population aged 0–14 years in Spain has followed a similar trend to that of BD admissions – increasing from 0.82 cases per 100,000 population in 2006 to 1.0 in 2010, and subsequently decreasing to 0.60 in 2017.

In conclusion, between 2000 and 2021 in Spain, there was a twofold increase in the annual admission rate of individuals aged 10–19 years due to BD. This increase was largely circumscribed to the 2000–2008 period and more salient among individuals aged 10–14 and, most importantly, BD patients with at least one additional psychiatric diagnosis. These findings may be partially explained by recent changes in BD diagnostic practices, especially for younger patients, and trends in substance use among Spanish youth, as the most frequent comorbidity was substance use disorder, and the most frequent substance used was cannabis.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data come from anonymized registries. As a result of the confidentiality agreement signed with the Ministry of Health, the data from this study cannot be shared with third parties. The authors did

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not have special access privileges. Should any researcher wish to gain access to these data, they can do so by applying directly to the Ministry through the following link https://www.sanidad.gob.es/en/estadEstudios/estadisticas/estadisticas/estMinisterio/SolicitudCMBD.htm.

ETHICS STATEMENT

This study was approved by the Research Ethics Committee of the Spanish Institute of Health Carlos III.

ORCID

Teresa López-Cuadrado https://orcid.org/0000-0002-5542-9782

REFERENCES

1. García-Blanco AC, Sierra P, Livianos L. Nosología, epidemiología y etiopatogenia del trastorno bipolar: Últimas aproximaciones. *Psiquiatr Biológica*. 2014;21(3):89-94. doi:10.1016/j.psiq.2014.07.004
2. Birmaher B. Bipolar disorder in children and adolescents. *Child Adolesc Mental Health*. 2013;18(3):140-148. doi:10.1111/camh.12021
3. Tondo L, Vázquez GH, Baldessarini RJ. Prevention of suicidal behavior in bipolar disorder. *Bipolar Disord*. 2021;23(1):14-23. doi:10.1111/bdi.13017
4. Clacey J, Goldacre M, James A. Paediatric bipolar disorder: international comparisons of hospital discharge rates 2000–2010. *BJPsych Open*. 2015;1(2):166-171. doi:10.1192/bjpo.bp.115.001933
5. James A, Hoang U, Seagroatt V, Clacey J, Goldacre M, Leibenluft E. A comparison of American and English hospital discharge rates for pediatric bipolar disorder, 2000 to 2010. *J Am Acad Child Adolesc Psychiatry*. 2014;53(6):614-624. doi:10.1016/j.jaac.2014.02.008
6. Dubicka B, Carlson GA, Vail A, Harrington R. Prepubertal mania: diagnostic differences between US and UK clinicians. *Eur Child Adolesc Psychiatry*. 2008;17(3):153-161. doi:10.1007/s00787-007-0649-5
7. Duffy A, Vandeleur C, Heffer N, Preisig M. The clinical trajectory of emerging bipolar disorder among the high-risk offspring of bipolar parents: current understanding and future considerations. *Int J Bipolar Disord*. 2017;5(1):37. doi:10.1186/s40345-017-0106-4
8. Parry PI, Levin EC. Pediatric bipolar disorder in an era of "mindless psychiatry". *J Trauma Dissociation*. 2012;13(1):51-68. doi:10.1080/15299732.2011.597826
9. Malhi GS, Jadidi M, Bell E. Time to transition from paediatric to adolescent bipolar disorder. *Acta Neuropsychiatr*. 2023;16:1-2. doi:10.1017/neu.2023.26
10. Duffy A. Debate: pediatric bipolar disorder—the elephant in the room. *Child Adolesc Mental Health*. 2019;24(1):99-100. doi:10.1111/camh.12316
11. Connors MH. Paediatric bipolar disorder and its controversy. *Acta Neuropsychiatr*. 2023;35(2):96-103. doi:10.1017/neu.2022.28
12. Parry P, Allison S, Bastiampillai T. The geography of a controversial diagnosis: a bibliographic analysis of published academic perspectives on "paediatric bipolar disorder". *Clin Child Psychol Psychiatry*. 2019;24(3):529-545. doi:10.1177/1359104519836700
13. Blader JC, Carlson GA. Increased rates of bipolar disorder diagnoses among U.S. child, adolescent, and adult inpatients, 1996-2004. *Biol Psychiatry*. 2007;62(2):107-114. doi:10.1016/j.biopsych.2006.11.006
14. Lasky T, Krieger A, Elixhauser A, Vitiello B. Children's hospitalizations with a mood disorder diagnosis in general hospitals in the United States 2000-2006. *Child Adolesc Psychiatry Ment Health*. 2011;5(1):27. doi:10.1186/1753-2000-5-27
15. Holtmann M, Duketis E, Poustka L, Zepf FD, Poustka F, Bölte S. Bipolar disorder in children and adolescents in Germany: national trends in the rates of inpatients, 2000-2007. *Bipolar Disord*. 2010;12(2):155-163. doi:10.1111/j.1399-5618.2010.00794.x
16. Moreno C, Laje G, Blanco C, Jiang H, Schmidt AB, Olfson M. National Trends in the outpatient diagnosis and treatment of bipolar disorder in youth. *Arch Gen Psychiatry*. 2007;64(9):1032-1039.
17. Kessing LV, Vradi E, Andersen PK. Are rates of pediatric bipolar disorder increasing? Results from a nationwide register study. *Int J Bipolar Disord*. 2014;2(1):10. doi:10.1186/s40345-014-0010-0
18. Rao P, Moore JK, Stewart R, et al. Bipolar disorder in children and adolescents: diagnostic inpatient rates from 2000 to 2013 in Germany. *Int J Bipolar Disord*. 2016;4(1):23. doi:10.1186/s40345-016-0064-2
19. Campos A, Ferreira AR, Gonçalves-Pinho M, Freitas A, Fernandes L. Bipolar disorder in pediatric patients: a nationwide retrospective study from 2000 to 2015. *J Affect Disord*. 2022;298:277-283. doi:10.1016/j.jad.2021.10.113
20. Sherwood SN, Carlson GA, Freeman AJ. Decreasing rate of inpatient pediatric bipolar disorder diagnosis in the US between 2004 and 2010. *Bipolar Disord*. 2022;24(2):149-160. doi:10.1111/bdi.13145
21. Carlson GA, Meyer SE. Phenomenology and diagnosis of bipolar disorder in children, adolescents, and adults: complexities and developmental issues. *Dev Psychopathol*. 2006;18(4):939-969. doi:10.1017/S0954579406060470
22. Findling RL, Zhou X, George P, Chappell PB. Diagnostic trends and prescription patterns in disruptive mood dysregulation disorder and bipolar disorder. *J Am Acad Child Adolesc Psychiatry*. 2022;61(3):434-445. doi:10.1016/j.jaac.2021.05.016
23. Patel R, Reiss P, Shetty H, et al. Do antidepressants increase the risk of mania and bipolar disorder in people with depression? A retrospective electronic case register cohort study. *BMJ Open*. 2015;5(12):e008341. doi:10.1136/bmjopen-2015-008341
24. Sarginson J, Webb RT, Stocks SJ, Esmail A, Garg S, Ashcroft DM. Temporal trends in antidepressant prescribing to children in UK primary care, 2000-2015. *J Affect Disord*. 2017;210:312-318. doi:10.1016/j.jad.2016.12.047
25. Bachmann CJ, Aagaard L, Burcu M, et al. Trends and patterns of antidepressant use in children and adolescents from five western countries, 2005-2012. *Eur Neuropsychopharmacol*. 2016;26(3):411-419. doi:10.1016/j.euroneuro.2016.02.001
26. AEMPS. *Uso de Medicamentos* Inhibidores Selectivos de La Recaptación de Medicamentos Inhibidores Selectivos de La Seoronina (ISRS) y Otros Antidepresivos En Niños y Adolescentes. 2005. https://www.aemps.gob.es/informa/notasinformativas/medicamentosusohumano-3/seguridad-1/2005/ni_2005-09_isrs_antidepresivos/
27. Jerrell JM, McIntyre RS, Tripathi A. A cohort study of the prevalence and impact of comorbid medical conditions in pediatric bipolar disorder. *J Clin Psychiatry*. 2010;71(11):1518-1525. doi:10.4088/JCP.09m05585ora
28. Guarin MBR. Associated variables with bipolar disorder risk in a sample of Colombian women with eating disorders. *Eur Eat Disord Rev*. 2006;14(4):242-247. doi:10.1002/erv.727
29. Aguglia A, Di Stefano A, Maina G. A 10-year evaluation on adolescents with anxiety disorders: are they at risk of bipolarity? *Int J Psychiatry Clin Pract*. 2017;21(2):125-130. doi:10.1080/13651501.2016.1268163
30. Jerrell JM, McIntyre RS, Park YMM. Correlates of incident bipolar disorder in children and adolescents diagnosed with attention-deficit/hyperactivity disorder. *J Clin Psychiatry*. 2014;75(11):e1278-e1283. doi:10.4088/JCP.14m09046
31. Cougle JR, Hakes JK, Macatee RJ, Chavarria J, Zvolensky MJ. Quality of life and risk of psychiatric disorders among regular users of alcohol, nicotine, and cannabis: an analysis of the

13995618, 2024, 8, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/bdi.13500 by Readcube (Labtiva Inc.), Wiley Online Library on [23/12/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

National Epidemiological Survey on alcohol and related conditions (NESARC). *J Psychiatr Res*. 2015;66-67:135-141. doi:10.1016/j.jpsychires.2015.05.004
32. van Laar M, van Dorsselaer S, Monshouwer K, de Graaf R. Does cannabis use predict the first incidence of mood and anxiety disorders in the adult population? *Addiction*. 2007;102(8):1251-1260. doi:10.1111/j.1360-0443.2007.01875.x
33. Leal-López E, Sánchez-Queija I, Rivera F, Moreno C. Trends in cannabis use among adolescents in Spain 2006–2018. *J Child Adolesc Subst Abuse*. 2020;29(4–6):221-231. doi:10.1080/1067828X.2021.1988021
34. Arroyo A. Substance use among adolescents in Spain: a brief report. *J Addict Med Ther Sci*. 2017; 3(1):7-10. doi:10.17352/2455-3484.000019
35. Fahrendorff AM, Pagsberg AK, Kessing LV, Maigaard K. Psychiatric comorbidity in patients with pediatric bipolar disorder—a systematic review. *Acta Psychiatr Scand*. 2023;148(2):110-132. doi:10.1111/acps.13548
36. Vázquez López P, Armero Pedreira P, Martínez-Sánchez L, et al. Self-injury and suicidal behavior in children and youth population: learning from the pandemic. *An Pediatr (Engl Ed)*. 2023;98(3):204-212. doi:10.1016/j.anpede.2022.11.005
37. García-Fernández L, Romero-Ferreiro V, Izquierdo-Izquierdo M, et al. Dramatic increase of suicidality in children and adolescents after COVID-19 pandemic start: a two-year longitudinal study. *J Psychiatr Res*. 2023;163:63-67. doi:10.1016/j.jpsychires.2023.04.014

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