Original Research

Time Trends in Lifetime Incidence Rates of First-Time Diagnosed Bipolar and Depressive Disorders Across 16 Years in Danish Psychiatric Hospitals:
A Nationwide Study

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ABSTRACT

Objective: There is conflicting evidence as to whether or not the incidences of affective disorders are on the rise. The aim of the present study was to identify time trends across 16 years in the incidences of affective disorders in a nationwide sample.

Methods: Using the Danish Psychiatric Central Research Registry, age- and sex-adjusted incidence rates of diagnosed affective disorders in Danish psychiatric hospitals using *ICD-10* classification were calculated per 100,000 person-years for the population aged 4–65 years during the period 1995–2010.

Results: Incidence rates of diagnosed bipolar disorder increased from 11.5 to 24.5, and there was an increase from 86.2 to 189.7 per 100,000 person-years for depression. Time trends were most pronounced for individuals up to 29 years of age. A sizeable part of the increase in incidence rates could be attributed to an increase in the total number of persons diagnosed in psychiatry.

Conclusions: Time trends in incidence rates showed an increase for bipolar disorder and depressive disorders across 16 years, but found that some of the observed increase in incidence rates was related to a more widespread trend in Danish society of seeking and receiving psychiatric assistance.

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Affective disorders represent a major contributor to the global burden of disease.[1,2] Whereas depressive disorders vary in duration by subtype, bipolar disorders often take a severe and chronic course.[3,4] These differences in the course of affective disorders limit the comparability of their prevalence rates. Based on various international studies published between 1980 and 2000, an incidence rate of 2.900 per 100,000 person-years (PY) has been estimated for mood disorders in adults.[5]

For depression, both increasing and decreasing trends have been observed in various international studies in adults[4,6,7] and in youth.[2] Data collected from general practitioners (GPs) in the United Kingdom from 1996 to 2006 reflected a decreasing trend in the incidence of the diagnosis of depression from 2,250 to 1,400 per 100,000 PY, but an increasing registration of depressive symptoms from 510 to 1,550 per 100,000 PY in adults was observed.[8] Historically, a trend for increasing incidence rates has also been found in the Lundby study in Sweden, where 2 cohorts from 1947 and 1957 were followed up in 1975. In this study, incidence rates had increased 2-fold for the youngest cohort.[6] However, at the 50 years follow-up in 1997, the incidence rates had decreased slightly.[9] The early findings of the Lundby study have been challenged by another large historical study from Sterling County, Canada, which demonstrated a steady annual incidence rate of around 370–450 per 100,000 PY.[7] It has been demonstrated with some consistency that the risk of developing depression is 2 times higher for females.[8–10]

Similarly, for bipolar disorders, there are both studies showing increasing incidence rates[11–13] and studies showing stable incidence rates.[14–16] Sex effects were found in 1 study,[14] but no sex differences were found in other studies.[12,13,17] More recently, the construct of prepubertal bipolar disorder has become an issue of major controversy,[18–24] especially because there are no internationally accepted criteria for bipolar disorders in children.[23] All studies have revealed rather low prevalence rates for bipolar disorders in children and youth.[25–28] However, retrospective interview studies of adult patients with bipolar disorder suggest that bipolar disorders often originate in childhood.[29] A recent Danish register-based study identified an increase in the diagnosis of bipolar disorder and mania from 1.0 to 2–4 per 100,000 PY in the time period 1995–2012 in youth below the age of 19 years.[30]

Most of the previous studies on incidence rates of affective disorders have not covered a large part of the lifespan, and there are only few studies investigating time trends. Thus, it is not sufficiently clear whether or not incidence rates are stable or on the rise. The aim of this study was to analyze time trends and contributing factors over 16 years in incidence rates of diagnosed bipolar disorders and depressive disorders from age 4 years to age 65 years in a nationwide register.

MATERIALS AND METHODS

Materials

The Danish Psychiatric Central Research Registry (DPCRR) provides nationwide coverage of information about discharge diagnoses in all inpatient

Clinical Points

- From 1995 to 2010, there was an increase in the number of psychiatric patients diagnosed with bipolar disorder and depression in Denmark as shown in this nationwide study.

- The increase was most pronounced among children, adolescents, and young adults but followed a general trend in psychiatry, as there appears to be an increase in the diagnosis of psychiatric disorders in general among these age groups.

- These findings do not necessarily mean that more members of the population become ill but may reflect changing societal attitudes toward mental illnesses.

and outpatient contacts made to Danish psychiatric departments.[31–33] Diagnoses were based on *ICD-8* criteria in the 1969–1994 period and on *ICD-10* diagnoses since 1995 whereas the *ICD-9* classification had never been in use in Denmark. In Danish psychiatry, assessment and diagnosis is carried out by specialists in psychiatry and in an interdisciplinary setting consisting of psychiatrists, psychologists, social workers, nurses, and others. Psychopathological and somatic assessment, psychological testing, and behavioral observations form the basis for diagnoses. Assessment and treatment is free within the public health care system in Denmark, and all contacts to the public psychiatric hospitals are recorded in the DPCRR. Only a very small number of private mental health services are not required to record to the DPCRR. The DPCRR is under the administration of the Danish government and can only be accessed by licensed research institutions by applying for data.

Definition of Sample

In the data set of the present study, an incidence was defined as the first-time registration of 1 of the following diagnoses: bipolar disorder (F30, F31 and F34.0) and depression (F32–33.9 and F34.1). Both primary and secondary diagnoses were counted, and each person was allowed to have a maximum of 1 registration per diagnostic entity. Patients were excluded from analysis if they had preceding incidences of the equivalent *ICD-8* disorders, namely, affective psychoses (296.X) and depressive neuroses (300.4). Furthermore, individuals were excluded from the analysis if they had only been diagnosed in the psychiatric emergency rooms, due to the low validity of these diagnoses. To calculate age and sex-standardized incidence rates, yearly census data for the calculation of incidence rates were available from Statistics Denmark.

Statistical Analyses

Besides the calculation of age- and sex-standardizing incidence rates, additional analyses were adjusted for any overall time trend in the number of patients diagnosed with any psychiatric disorders during the same time period. In the latter, the age and sex-standardized incidence rates were divided by a weight specifying either increases or decreases of incidence rates for any mental disorders for each year in the observation period. Incidence rates were calculated separately for the 2 sexes and the following age groups: children (4–12 years), adolescents (13–18 years), young adults (19–29 years), adults (30–39 years), and older adults (40–65 years). To identify time trends and allow for comparisons of various age and sex groups, data were fitted using the JoinPoint regression software.[34] This regression procedure fits observed time trend data to linear functions and calculates annual percent change (APC). In addition, we used Stata 11th ed software.[35]

Ethical Standards

The use of anonymized data was approved by the Danish Serum Institute, Statistics Denmark, and the Danish Data Protection Agency.

RESULTS

Sample Composition

In the time period from 1995 to 2010, a total of N = 96,185 individuals were newly diagnosed in Danish psychiatric inpatient and outpatient services with at least 1 affective disorder. In the observation period, a total of N = 249,607 individuals had a first-time contact with psychiatric inpatient or outpatient services.

Among the cases diagnosed with a bipolar disorder, n = 5,287 (43.9%) were males and n = 6,747 were females (56.1%). Significantly more females were diagnosed with bipolar disorders ($\chi^2_1 = 177.1$, $P < .001$). The mean age at first-time diagnosis was 41.4 years (SD = 13.1). Of these, 30% received their diagnosis before the age of 33 years, and the top 30% were above age 50 years. Males were older at first-time diagnosis of bipolar disorder (mean = 42.0, SD = 13.1) compared to females (mean = 40.8, SD = 13.1; $t_{12,032} = 4.8$, $P < .001$).

A total of 4,392 individuals had a diagnosis of depression preceding their first-time diagnosis of bipolar disorder. The group of individuals who had a diagnosis of depression preceding their first-time diagnosis of bipolar disorder accounted for only 3.7% of those individuals who had an incidence of first-time diagnosed depression. These 4,392 incidents of first-time diagnosed depression were also counted as first-time incidences of depression, as we treat the time trends for depressive disorders and bipolar disorders separately. This procedure also reflects the actual burden of new onsets of disease in the population for each year.

Among the individuals diagnosed with depressive disorders, n = 34,366 (37.6%) were males and n = 56,928 (62.4%) were females. Females were more frequently diagnosed with depressive disorders compared to males ($\chi^2_1 = 5575.9$, $P > .001$). The mean age at diagnosis for depressive disorders was 38.1 (SD = 13.9) years. Males were older (mean = 39.7, SD = 13.6) than females (mean = 37.2 SD = 14.0) at the first-time diagnosis of depressive disorders ($t_{91,292} = 26.4$, $P < .001$). Among these individuals with depressive disorders, 30% received their diagnosis before the age of 29 years, and the top 30% were above age 47 years.

Table 1. Sex-Specific and Total Incidence Rates and Annual Percent Changes in Incidence Rates of Affective Disorders

Disorder	Sex	Nonadjusted Incidence Rate per 100,000 PY				APC (1995–2010)	Adjusted Incidence Rate per 100,000 PY				APC (1995–2010)
		1995	2000	2005	2010		1995	2000	2005	2010	
Bipolar disorders	Male	10.1	12.9	16.5	21.1	5.2	11.0	12.9	15.1	17.7	3.3
	Female	13.2	17.0	21.9	28.3	5.3	14.8	17.8	21.5	26.0	4.1
	Total	11.5	14.8	19.1	24.5	5.4	12.7	15.2	18.1	21.6	3.5
Depression	Male	63.9	83.1	108.4	141.2	5.6	69.5	81.9	96.4	113.5	3.5
	Female	110.6	143.4	185.9	241.0	5.7	120.9	143.5	170.3	202.0	3.3
	Total	86.2	112.1	145.9	189.7	5.7	94.1	111.2	131.5	155.5	3.7
Affective disorders	Male	67.7	89.1	117.3	154.4	5.5	73.7	87.6	104.3	124.2	3.3
	Female	111.2	146.8	193.9	256.0	5.3	121.2	146.7	177.6	215.1	3.5
	Total	88.4	116.8	154.2	203.7	5.4	96.3	115.8	139.2	167.3	3.4

Abbreviations: APC = annual percent change, PY = person-years.

Table 2. Incidence Rates and Annual Percent Changes in Affective Disorders by Age

Disorder	Age Group (y)	Nonadjusted Incidence Rate per 100,000 PY				APC (1995–2010)	Adjusted Incidence Rate per 100,000 PY				APC (1995–2010)
		1995	2000	2005	2010		1995	2000	2005	2010	
Bipolar disorders	4–12	0.1	0.2	0.4	0.7	13.0	0.2	0.02	0.2	0.3	3.4
	13–18	3.0	4.5	6.6	10.7	8.1	3.3	3.3	3.3	3.4	0.1
	19–29	8.0	13.0	21.0	33.8	10.1	8.5	11.2	14.8	19.4	5.7
	30–39	12.0	17.0	24.0	34.0	7.2	13.0	17.4	23.1	30.8	5.9
	40–65	18.6	21.2	24.1	27.4	2.6	20.4	22.9	25.8	29.0	2.4
Depression	4–12	2.1	4.1	8.1	16.0	14.6	2.8	4.0	5.7	8.2	7.5
	13–18	36.4	66.7	122.0	223.3	12.9	29.3	42.2	60.8	87.7	7.6
	19–29	79.6	128.0	205.8	330.9	10.0	75.3	104.1	143.7	198.6	6.7
	30–39	102.4	137.4	184.2	247.1	6.1	110.1	139.9	177.6	225.5	4.9
	40–65	161.3	165.4	169.6	173.9	0.5	141.0	149.4	158.3	167.7	1.2
Affective disorders	4–12	2.7	4.2	8.4	16.6	14.5	3.0	4.2	6.0	8.5	7.3
	13–18	38.6	70.1	127.3	231.1	12.7	31.6	44.8	63.6	90.3	7.3
	19–29	85.6	136.9	219.1	350.6	9.9	81.6	111.8	153.2	209.9	6.5
	30–39	108.4	146.2	197.1	265.6	6.2	116.7	148.9	189.9	242.3	5.0
	40–65	127.4	140.9	155.8	172.3	2.0	139.1	152.4	166.9	182.9	1.8

Abbreviations: APC = annual percent change, PY = person-years.

In the combined group of first-time diagnosed affective disorders, n = 37,096 (38.6%) were males and n = 59,089 (61.4%) were females, with a significantly higher proportion of females than males (χ^2_1 = 5028.8, P > .001). The mean age at first-time diagnosis of any affective disorder was 37.9 (SD = 13.8) years. Again, females were younger (mean = 36.9, SD = 13.8) compared to males (mean = 39.5, SD = 13.6; $t_{96.193}$ = 28.4, P < .001). Although the differences in age at first diagnosis for the 2 sexes were significant in all 3 diagnostic groups due to the large sample size, they were relatively small in magnitude.

Time Trends in the Total Sample and for the 2 Sexes

The time trends in incidence rates of diagnosed bipolar disorder, depressive disorders, and the composite category of affective disorder are displayed in Table 1 for every fifth year in the observation period. For bipolar disorder, the incidence rates per 100,000 PY were similar for males and females. Furthermore, the APCs estimated for the entire observation period were also similar for the 2 sexes, suggesting similar increases in incidence rates across the observation period. In depressive disorders, incidence rates were almost 2 times higher in females than in males. For bipolar disorders, similar time trends of APC were observed for males and females. The incidence rates and time trends

for the composite category of affective disorders were similar to those observed for depressive disorders, because most cases of affective disorders were cases of depression.

Adjusting for the time trends in the total number of persons diagnosed in psychiatric inpatient and outpatient services reduced the annual percent changes. The reduction of the incidence rate for affective disorders for the combined sample in 2010 amounted to 17.9%. The percent reduction in incidence rates of affective disorders was larger for males (19.6%) than for females (16.0%). Obviously, a sizeable part of the increasing incidence rates for affective disorders was due to a general trend of more individuals seeking assistance from the in- and outpatient psychiatric services.

Time Trends by Age Groups

Table 2 presents findings coming from the analyses of time trends by age. For bipolar disorders, different time trends were observed in the various age groups. The APCs were largest in the 4- to 12-year-olds, but only because incidence rates rose from zero to 0.7 per 100,000 PY in 2010. Large APCs were seen in the 3 age groups covering the ages from 13 to 39 years. For the 40- to 65-year-olds, the incidence rates were rather stable across the entire observation period.

Similar time trends were observed for depressive disorders, although the incidence rates of depressive

disorders were much larger than those observed for bipolar disorders. However, the largest incidence rates in diagnosed depressive disorders were observed in young adulthood, and the incidences of depression were almost equally frequent among adolescents and older adults. Due to the majority of cases in the study having diagnoses of depressive disorders, similar trends were observed for the major category of affective disorders.

For the data on affective disorders in 2010, adjustment resulted in large reductions in incidence rates for the younger age groups, namely, by 48.8% for children, by 60.1% for adolescents, and by 40.9% in young adults. Adjustment affected the incidence rates for adults to a lesser extent (8.8% reduction) and even increased the incidence rates for the older adults (+6.2%).

Due to these different time trends in the various age groups, the mean age at first-time diagnosis decreased during the observation period. From 1995 to 2010, the mean age at first diagnosis of bipolar disorder decreased from 43.5 to 39.6 years ($t_{1,594} = 6.3$, $P < .001$); for depression, from 43.9 to 35.2 years ($t_{11,641} = 32.2$, $P < .001$); and for affective disorders combined, from 43.0 to 35.3 years ($t_{12,193} = 28.6$, $P < .001$) .

DISCUSSION

This study on incidence rates of affective disorders had some unique characteristics. With a wide age range between 4 and 65 years, it covered a rather large span of the lifetime in a nationwide and representative sample over an extended period of 16 years. Furthermore, by analyzing both crude and adjusted incidence rates, this study extended the analytic approach of preceding studies. For bipolar disorders, the incidence rates of 11.5 to 24.5 per 100,000 PY in the total population of the present study were similar to findings from other studies[11,13] but in contrast to studies suggesting stable incidence rates.[14,15] In addition and in line with other studies,[12,13,17] there were significant sex differences in the rates of diagnosed bipolar disorder with a preponderance of females, but there were no sex differences in time-trends with a rather stable male:female ratio around 0.8:1 during the entire observation period of 16 years.

The mean age at first-time diagnosis of bipolar disorders and depression was higher than found in other studies looking at the age at onset for these disorders. Several reasons may account for this difference. First of all, it is important to distinguish between the mean age at onset and the mean age of first-time diagnosis, which typically will be later than the onset. Second, the present study based on data from ages 4 to 65 years covered a much wider age range than all preceding studies. In particular, the older ages with a higher load of affective disorders had not been covered sufficiently in previous studies. Third, all incidences were recorded in psychiatric hospitals and not in primary care settings. Finally, the age at incidence could to some extent have been inflated due to changes in the registry over time and our decision to exclude first-time diagnoses recorded in the *ICD-8* period. The DPCRR included only data on inpatient contacts prior to 1995 in the *ICD-8* period. If individuals with affective disorders were seen as outpatients only without a recording in the DPCRR prior to 1995 and then recontacted psychiatry in the *ICD-10* period, these subjects would have been wrongly classified as first-time diagnosed cases with the consequence of an inflated age at first-time diagnosis.

Furthermore and quite importantly, the present study found that the increase in incidence rates of diagnosed bipolar disorders could largely be attributed to increases in diagnosed adolescents and young adults. Several explanations might apply to this finding. First, the increase in incidence rates in these age groups could be the result of an earlier identification of true patients with bipolar disorders. Retrospective assessments of patients with bipolar disorder found that for most individuals there is a large time gap between onset of the disorder and first-time diagnosis.[21,29] The more recent international debate in child and adolescent psychiatry on early symptoms of bipolar disorders might have also contributed to giving Danish clinicians a greater clinical awareness of the early manifestation of bipolar disorders.

Second, and related to this debate, the extension of the psychopathological features of early onset bipolar disorders[18–24] might have also directed the awareness of clinicians to the lesser known characteristic features of bipolar disorders in young people, such as irritability or less pronounced mood swings. In addition, given the fact that the psychopathological phenomena of early-onset bipolar disorder are somewhat different from those of classical adult-onset bipolar disorder, there is more room for clinical interpretation. Finally, one may not rule out the possibility that the incidence rates of bipolar disorder were truly on the rise in younger cohorts.

Furthermore, the present findings show that the incidence rates of diagnosed depression have risen in Denmark during the last 16 years, which is in accordance with a comparable study investigating time trends in dispensed antidepressants.[36] However, the increase in incidence rates of diagnosed depression (from 86.2 to 189.7 per 100,000 PY) was lower than found in other studies (from 719 to 2.900 per 100,000 PY).[5,8,37] Since most incidence studies of diagnosed depression so far had been carried out in primary care facilities, and since only the more severe and complicated cases of depression are referred to psychiatry, the difference in findings between the present and previous studies had to be expected. Furthermore, in contrast to preceding studies, the present study also included children in the calculation of the total incidence rates.

Increasing incidence rates for depressive disorders were also observed in the study of a primary care population in the United Kingdom[8] and in the earlier follow-up assessments of the Swedish Lundby studies.[6] As for bipolar disorders, this increase in first-time depression diagnoses could be due to an increasing awareness of depression in the public realm leading to higher rates of help-seeking in the medical sector.[38] As a consequence and in parallel, general

practitioners as gatekeepers for the access to psychiatry might have lowered the threshold for referral and diagnosis. In addition, the increasing numbers might also reflect changes in the diagnostic practice in Danish psychiatry by providing more attention to diagnosing depressive disorders both as single and coexisting disorders.

This interpretation of attitudinal and clinical practice changes is supported by the finding that a large part of the increase in the time trends of diagnosed incidence rates could be explained by a more general population trend of increasing numbers of individuals seen in the psychiatric inpatient and outpatient services. However, the present findings are most likely not a consequence of expanding services attracting more individuals to enter the services. Data from the Danish Health Authority indicated that the number of hospital beds in psychiatry had decreased significantly during the study period.[39] In adult psychiatry, the number of inpatient beds decreased from 4.121 to 3.078 in the time period 1996 to 2007 but increased slightly from 151 to 209 from 1994 to 2007 in child and adolescent psychiatry. While there was a decrease in the number of beds in psychiatry, outpatient services were expanded.

The Danish Regions who are responsible for the provision of health care in Denmark concluded in a recent report[40] that despite working toward increasing the outpatient capacities in psychiatry these developments have not been able to match the faster growing service demands resulting in increasing waiting lists. In the light of these recent developments, one may not definitively rule out the possibility that the increase in outpatient facilities that occurred since the 1990s contributed to an increase in the number of diagnosed patients. However, based on the report from the Danish Regions, it seems more likely that services have expanded due to an increase in the demands for such services.

There were no major differences between the 2 sexes in the time trends as measured by the estimated APC. In contrast, there were different time trends in the various age groups, with large APCs for bipolar disorders in the younger cohorts of the 4–12, 13–19, and 20–29 years age groups ranging from 10.1% to 13.6% change per annum. The APCs showed even stronger increases for the incidence rates of depression in children and adolescents. However, after adjusting for the trends for any mental disorder, the increases in incidence rates were modified substantially, indicating that they were not specific to affective disorders. In fact, parallel trends in first-time diagnosed ADHD[41] and autism spectrum disorder (ASD)[42] have been documented, with incidence rates of diagnosed ADHD increasing from 7.3 to 91.2 per 100,000 PY and incidence rates of diagnosed ASD increasing from 9.0 to 38.6 per 100,000 PY for the same population and time period under investigation as in the present study. These trends were mainly driven by an increased number of children, adolescents, and young adults receiving diagnoses.

It is uncertain whether children, adolescents, or young adults really are experiencing an increased risk of mental disorders, or whether the large increases in incidence rates observed in these age groups are the result of better recognition of psychiatric disorders earlier in life. Improved knowledge about mental illness in the general population and among general practitioners, school psychologists, and others who in Denmark are responsible for referral to the psychiatric inpatient and outpatient services and improved knowledge and the availability of better diagnostic assessment tools could have helped with identifying disorders such as depression earlier in life. Alternatively, the observed increase in incidence rates in the young population might be the result of increased stress levels in society. Additional data on stressors and observations over extended periods would be needed for a test of this hypothesis.

The definite causes of these general increases in incidence rates of both affective disorders and other mental disorders are not yet fully understood. These trends may not be independent of major changes in the attitude of the general population toward psychiatric diagnoses and treatment. However, there is also reason for societal concern in terms of burden and costs if the increase in diagnosed mental disorders is on the rise. It is up to the community of psychiatry experts to reflect whether or not changes in the nosology of mental disorders are leading not only to a refinement of diagnostic entities in terms of the characteristic psychopathology but also to a narrowing of the construct of normality.

Limitations

With data coming from a large number of clinicians from various services, the validity of the diagnoses may be questioned. However, DPCRR data on *ICD-8* defined manic-depressive psychoses have previously been validated in adults seen in psychiatric departments in 1971–1993 in a random sample of 100 patients with 95% of the individuals fulfilling lifetime *ICD-10* diagnostic criteria for an affective disorder.[43] Although these results indicate that at least data on bipolar disorders have good validity in the DPCRR, further validation studies of more recent patient populations need to be conducted. It may be added that further studies using the DCPRR have validated other disorders such as schizophrenia[44] and childhood autism[45] and, thus, have highlighted the overall quality of the registry data.

Furthermore, and as in all registry-based studies, the reported incidence rates were based only on individuals who came into contact with the public psychiatric health care system. Limitations in terms of incomplete coverage might apply more to the study of early and less severe manifestations. This might be true in particular for diagnosed bipolar disorders because the DPCRR, with its reference to the *ICD-10* classification, most likely covers mainly individuals with *DSM-5* bipolar I disorder.[30] Unfortunately, the extent of underestimation of bipolar II disorder cannot be assessed, since the *ICD-10* does not operate with this distinction.

CONCLUSION

Based on the present findings, one may conclude that there had been an increase in the number of individuals

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diagnosed with affective disorders in Denmark during the 16 years of observation and that these trends are not gender-specific. Incidence rates were lowest in children and adolescents, but these age groups were those who showed the largest time trends with annual percent changes in the 12.7% to 14.5% range during the years 1995 to 2010. The APC for young adults was also pronounced (9.9%). The present study found that at least some of the observed increase in incidence rates was related to a more widespread trend in Danish society of seeking and receiving more assistance by psychiatric inpatient and outpatient services across time, especially for children, adolescents, and young adults.

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