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The incidence, psychiatric co-morbidity and pharmacological treatment of severe mental disorders in children and adolescents

Ragnar Nesvåg[a,*], Jørgen G. Bramness[b], Marte Handal[c], Ingeborg Hartz[c,d], Vidar Hjellvik[c], Svetlana Skurtveit[c,e]

[a] Nydalen DPS, Department of Mental Health and Addiction, Oslo University Hospital, P.O. Box 4950, Nydalen, N-0424 Oslo, Norway
[b] Norwegian National Advisory Unit on Concurrent Substance Abuse and Mental Health Disorders, Innlandet Hospital Trust, P.O. Box 104, N-2381 Brumunddal, Norway
[c] Norwegian Institute of Public Health, P.O. Box 4404 Nydalen, N-0403 Oslo, Norway
[d] Department of Research, Innlandet Hospital Trust, P.O. Box 104, N-2381 Brumunddal, Norway
[e] Norwegian Center for Addiction Research, University of Oslo, P.O. Box 1171 Blindern, N-0318 Oslo, Norway

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ABSTRACT

Background: Antipsychotic drug use among children and adolescents is increasing, and there is growing concern about off-label use and adverse effects. The present study aims to investigate the incidence, psychiatric co-morbidity and pharmacological treatment of severe mental disorder in Norwegian children and adolescents.
Methods: We obtained data on mental disorders from the Norwegian Patient Registry on 0–18 year olds who during 2009–2011 were diagnosed for the first time with schizophrenia-like disorder (International Classification of Diseases, 10th revision codes F20-F29), bipolar disorder (F30-F31), or severe depressive episode with psychotic symptoms (F32.3 or F33.3). Data on filled prescriptions for psychotropic drugs were obtained from the Norwegian Prescription Database.
Results: A total of 884 children and adolescents (25.1 per 100 000 person years) were first time diagnosed with schizophrenia-like disorder (12.6 per 100 000 person years), bipolar disorder (9.2 per 100 000 person years), or severe depressive episode with psychotic symptoms (3.3 per 100 000 person years) during 2009–2011. The most common co-morbid mental disorders were depressive (38.1%) and anxiety disorders (31.2%). Antipsychotic drugs were prescribed to 62.4% of the patients, 72.0% of the schizophrenia-like disorder patients, 51.7% of the bipolar disorder patients, and 55.4% of the patients with psychotic depression. The most commonly prescribed drugs were quetiapine (29.5%), aripiprazole (19.6%), olanzapine (17.3%), and risperidone (16.6%).
Conclusions: When a severe mental disorder was diagnosed in children and adolescents, the patient was usually also prescribed antipsychotic medication. Clinicians must be aware of the high prevalence of depressive and anxiety disorders among early psychosis patients.

1. Introduction

The onset of schizophrenia or bipolar disorder usually occurs in early adult life, but a number of patients have their first episode of psychosis, mania or depression in adolescence or even in childhood [1,2]. Among all adults with schizophrenia, about 1% experienced onset of disease prior to 13 years of age and 12–33% had an onset prior to 18 years [3]. A registry-based nationwide study from specialist health care in Denmark demonstrated that 0.3% of the population were diagnosed with a schizophrenia-like disorder by 20 years of age [4]. Schizophrenia with onset prior to 18 years of age has a poorer psychosocial outcome than adult-onset schizophrenia [5], with a particularly poor outcome for onset before 13 years of age [6].

Bipolar disorder has traditionally been regarded as an adult-onset disorder, but recent nationwide studies from UK and US have demonstrated that bipolar disorder is often diagnosed in paediatric populations as well [7,8]. In a multi-center study from US, Germany and the Netherlands, the proportion of adult bipolar disorder patients with onset prior to age 19 was 61% in the US and 30% in Europe, indicating substantial geographical difference in prevalence of paediatric bipolar disorder [9]. In the US National

* Corresponding author. Present address: The Norwegian Medical Association, P. O. Box 1152, Sentrum, N-0107 Oslo, Norway.
E-mail address: ragnar.nesvag@legeforeningen.no (R. Nesvåg).

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Comorbidity Survey of nationally representative adolescents, 2.9% of the 13–18 year olds met diagnostic criteria for bipolar disorder type I or II [8]. This is higher than European figures, but a recent study from Germany demonstrated an 18% increase in the rate of discharge diagnosis for bipolar disorder among 0–19 year olds between 2000 and 2013 [10]. In the above mentioned registry-based study from specialist health care in Denmark, 0.1% of the population were diagnosed with bipolar disorder by the age of 20 years [4].

The range of prevalence estimates for paediatric psychosis illustrates the need for investigations of diagnostic practice in a variety of settings. The incidence rates for diagnosed schizophrenia, bipolar or depressive disorder with psychotic features among children and adolescents in Norway are presently unknown.

If depressive or anxiety disorders are diagnosed prior to the first-episode of psychosis, they may serve as early signs and prognostic markers of the emerging severe mental disorder [11]. For about 20% of patients with adult-onset psychosis clinical depressive symptoms are present even 10 years after onset of psychosis [12]. Depressive or anxiety disorders may also be co-morbid disorders, present in about half of adult first-episode psychosis patients [13,14]. Good prevalence data on co-morbid mental disorders in adolescent-onset psychosis are, however, lacking.

Early adequate treatment of first-episode psychosis in young adults may improve long-term outcome and most often involves the use of antipsychotic drugs [15]. The use of antipsychotic drugs in children and adolescents is, however, controversial due to a scarcity of clinical evidence from randomized controlled studies [16]. Also, a recent meta-analysis has demonstrated that antipsychotics had only modest symptomatic effect in younger patients [17]. A Danish randomized controlled trial of quetiapine vs aripiprazole among 12–17 year old first-episode psychosis patients demonstrated that both drugs had moderate effect on alleviating positive symptoms, but most patients experienced unwanted adverse effects like sedation, weight gain or tremor [18]. There is a substantial discontinuation rate due to weight gain and other adverse side effects [19] and there is generally a growing concern about long-term consequences of antipsychotic drugs on somatic and mental health [20,21]. In a recent study we showed that the majority of children and adolescents using antipsychotic drugs were diagnosed with non-psychotic disorders like hyperkinetic, anxiety or depressive disorder [22]. The extent to which younger patients diagnosed with psychotic disorders is treated with antipsychotic drugs in Norway is unknown.

Data from national health registries have the advantage that they cover all individuals who have been in contact with the health care system, but there is concern regarding validity of diagnostic information and completeness of data [23]. For severe mental disorders like schizophrenia and bipolar disorder, the national clinical guidelines recommend assessment and start of treatment in specialized mental health care [24]. Thus, the prevalence estimates of severe mental disorders based on national health care registry data will be representative of the general population.

1.1. Aims of the study

Based on linked individual-level data from national health registries we aimed to estimate 1) incidence rates of severe mental disorders, here defined as schizophrenia-like disorder, bipolar disorder, or severe depressive episode with psychotic symptoms, among 0–18 year old children and adolescents diagnosed in specialist health care in Norway during 2009–2011, 2) investigate the prevalence of co-morbid mental disorders, and 3) explore use of antipsychotics and other psychotropic drugs in this patient group.

2. Material and methods

The present study is based on linked data from the Norwegian Patient Registry (NPR) and the Norwegian Prescription Database (NorPD). Individual-level registry data were linked using the unique 11-digit personal identity number assigned to all individuals living in Norway.

2.1. Data sources

2.1.1. The Norwegian Patient Registry (NPR)

The NPR is an administrative database of records reported by the specialist health care, i.e. all hospitals and outpatient clinics owned or financed by the government, including most private practitioners in child and adolescent psychiatry. Thus, the NPR

Table 1
Classification of psychotropic drugs.

Group	Type	ATC code
Antipsychotic drugs	Any	N05A except N05AN01 (lithium)
First generation antipsychotics	Perphenazine	N05AB03
	Haloperidol	N05AD01
	Zuclopentixole	N05AF05
Second generation antipsychotics	Ziprasidone	N05AE04
	Olanzapine	N05AH03
	Quetiapine	N05AH04
	Risperidone	N05AX08
	Aripiprazole	N05AX12
	Paliperidone	N05AX13
	Clozapine	N05AH02
Auxiliary antipsychotic drugs	Chlorpromazine	N05AA01
	Levomepromazine	N05AA02
Lithium	n.a.	N05AN01
Antidepressant	Any	N06A
Antiepileptic drugs used for treatment of bipolar disorder	Carbamazepine	N03AF01
	Valproic acid	N03AG01
	Lamotrigine	N03AX09
	Topiramat	N03AX11
Anxiolytic drugs	Any	N05B
Psychostimulant	Any	N06BA

Abbreviations: ATC: Anatomic Therapeutic Classification; n.a.: not applicable.

includes information on patients that have been referred by a general practitioner (GP) because of a need of specialist health care. All Norwegian citizens are enrolled in the patient list of a dedicated GP who represents the lowest level of public health care. If a patient requires treatment at a higher level, the GP may refer to a specialist health care facility, i.e. a hospital, outpatient clinic or private practitioner. All referrals and registered contacts with specialist health care are included in the NPR. In Norway, government-funded mental health clinics for children and adolescents are available throughout the country, serving the entire population. Mental health care for children and adolescents is free of charge. The NPR contains nationwide individual-level specialist health care data from 2008 and onwards, and diagnoses are recorded according to the International Classification of Diseases, 10th revision (ICD-10) [25].

For the present study we retrieved data reported by the specialist health care during 2008–12 for all individuals who were 0–18 years of age at first registration in the NPR with an ICD-10 diagnosis of either schizophrenia-like disorder (F20-F29), bipolar disorder (F30-F31), or severe depressive episode with psychotic symptoms (F32.3, F33.3) during 2009–2011.

To investigate prevalence of co-morbid mental disorders, all registered contacts with the following ICD-10 diagnoses were noted: Substance use disorders (SUD, F10-F19), depressive disorder (F32-F34), anxiety disorder (F40-F48), mental retardation (F70-F79), autism-spectrum disorder (F84), hyperkinetic disorder (F90), and conduct disorder (F91).

2.1.2. The Norwegian Prescription Database (NorPD)

Data on psychotropic drug use were obtained from the NorPD, which covers all dispensed prescriptions at pharmacies in Norway. Since January 2004 all Norwegian pharmacies have been obliged to send data electronically to the Norwegian Institute of Public Health on all prescribed drugs (irrespective of reimbursement or not) dispensed to individuals in ambulatory care. Drugs administered to patients while in hospital are not reported to the NorPD. The drugs in the NorPD are classified according to the Anatomical Therapeutic Chemical (ATC) classification system [26].

For the present study we included the patients' unique identity number (encrypted), sex, age, date of dispensing and generic drug information (ATC code). Information about all prescriptions of psychotropic drugs in the period 2008–2012 was obtained. The ATC codes included in each psychotropic drug category are presented in Table 1.

2.2. Analytical approach

Incidence rates of each of the specified severe mental disorders (schizophrenia-like disorder, bipolar disorder, and severe depressive episode with psychotic symptoms) were calculated as the number of boys and girls per 100 000 person years who were registered with the disorder between January 1, 2009 and December 31, 2011, following a minimum washout period of one year, i.e. no registration with any of the three types of disorders from the start of 2008. Number of person years (3 521 950) was calculated as the sum of boys and girls aged 0–18 years living in Norway as per January 1, 2009 (1 168 235), 2010 (1 174 347) and 2011 (1 179 368) according to data obtained from Statistics Norway.

A washout period of one year may have resulted in some prevalent cases being misidentified as incident ones (cf. Section 4.1 Strengths and limitations). To enable comparison with previous incidence studies, one-year incidence rates were calculated for the year 2011, allowing for a washout period of at least three years. The incidence rates were calculated as number of boys and girls per 100 000 person years who were diagnosed with schizophrenia-like disorder, bipolar disorder, or severe depressive episode with psychotic symptoms in 2011, but not in 2008–2010. Number of person years was calculated as the sum of boys and girls aged 0–18 years living in Norway as per January 1, 2011 (605 201 boys and 574 167 girls) according to data obtained from Statistics Norway.

The prevalence of co-morbid mental disorders was calculated as the proportion of patients who were registered with SUD, depressive illness, anxiety disorders, mental retardation, autism-spectrum disorder, hyperkinetic disorder or conduct disorder between one year prior to and one year after the incident severe mental disorder diagnosis in the NPR. In search of early diagnostic markers of psychotic disorder, the proportion of patients diagnosed with SUD, depressive illness, anxiety disorder or hyperkinetic disorder within one year prior to the incident severe mental disorder diagnosis was calculated separately.

The proportion of patients using antipsychotic medication and other types of psychotropic drugs between one year prior to and one year after the incident severe mental disorder diagnosis was determined from registrations of dispensed prescriptions in the NorPD. Having at least one prescription dispensed during this period was defined as use of the specific drug. The proportion of patients filling more than one antipsychotic medication prescription was calculated as a proxy for regular use.

All analyses were performed using SPSS 22.0 for Windows.

2.3. Ethical considerations

The study has been approved by the Regional Committee for Medical Research Ethics (2010/131–REK Sør-Øst) and by the Norwegian Data Protection Authority.

3. Results

3.1. Incidence of severe mental disorders in children and adolescents

During 2009–2011 a total of 884 children and adolescents 18 years or younger (incidence rate 25.1 per 100 000 person years)

Table 2
Incidence of severe mental disorders in children and adolescents. Data from the Norwegian Patient Registry on all 0–18 year olds registered with a first diagnosis of schizophrenia-like disorder, bipolar disorder, or depressive episode with psychotic symptoms during 2009–2011.

	SCZ (n = 443)		BIP (n = 323)		DEP w/psych (n = 118)		Total (n = 884)	
Incidence (per 100 000 person years)	12.6		9.2		3.3		25.1	
Boys (n, %)	239	54.0	119	36.8	31	26.3	389	44.0
Age at 1st diagnosis (mean, SD)	16.1	2.5	16.2	2.4	16.1	1.7	16.1	2.3
Age 0–11 at 1st diagnosis (n, %)	18	4.1	13	4.0	<5	n.a.	33	3.7
Age 12–15 at 1st diagnosis (n, %)	106	23.9	73	22.6	32	27.1	211	23.9
Age 16–18 at 1st diagnosis (n, %)	319	72.0	237	73.4	84	71.2	640	72.4

Abbreviations: SCZ: schizophrenia-like disorder (International Classification of Diseases, 10th revision code F20-F29), BIP: bipolar disorder (F30-F31), DEP w/psych: severe depressive episode with psychotic symptoms (F32.3 or F33.3), n.a.: not applicable.

were registered with a first-episode of severe mental disorder in specialist health care in Norway, of whom 12.6, 9.2, and 3.3 per 100 000 person years were diagnosed with schizophrenia-like disorder, bipolar disorder or severe depressive episode with psychotic symptoms, respectively (Table 2). Overall more girls (n = 495) than boys (n = 389) were diagnosed with a first-episode of severe mental disorder, due to a higher number of girls being diagnosed with bipolar disorder or severe depressive episode with psychotic symptoms. However, more boys than girls were diagnosed with schizophrenia-like disorder. Mean age at first registered severe mental disorder was 16 years. Only 3.7% of the 884 patients had their first registered psychotic disorder diagnosis prior to the age of 12, while 23.9% were first diagnosed between 12 and 15 years of age, and 72.4% were first diagnosed between 16 and 18 years of age.

In 2011, 113 boys and 160 girls were diagnosed with a severe mental disorder with no prior registrations in the period 2008–2010, yielding an incidence rate of 18.6 per 100 000 person years for boys and 27.9 per 100 000 person years for girls. Corresponding rates were for schizophrenia-like disorder 12.4 for boys and 11.0 for girls, for bipolar disorder 4.6 for boys and 11.5 for girls, and for severe depressive episode with psychotic symptoms 1.7 for boys and 5.6 for girls.

3.2. Co-morbid mental disorders

The most prevalent co-morbid mental disorders diagnosed between one year prior to and one year after the incident severe mental disorder diagnosis were depressive disorder (38.1%), anxiety disorder (31.2%) and hyperkinetic disorder (16.6%) (Table 3). Analysis of early diagnostic markers revealed that within one year prior to the incident severe mental disorder diagnoses, 13.3% of schizophrenia patients had a depressive disorder diagnosis, 14.8% had an anxiety disorder diagnosis, and 10.2% had a hyperkinetic disorder diagnosis. The corresponding percentages for bipolar disorder patients were 21.1% (depressive disorder), 13.9% (anxiety disorder), and 14.6% (hyperkinetic disorder), and for patients with psychotic depression the percentages were 28.0% (depressive disorder), 16.9% (anxiety disorder), and 2.5% (hyperkinetic disorder). In the total group of patients, 10.1% were diagnosed with a SUD, and 5.7% were diagnosed with SUD during the year prior to the first diagnosis of a severe mental disorder.

3.3. Use of psychotropic drugs

Among the 884 children and adolescents first diagnosed with a severe mental disorder during 2009–2011, 552 (62.4%) were prescribed an antipsychotic drug between one year prior to and one year after the incident diagnosis of severe mental disorder, predominantly a second generation antipsychotic (Table 4). Among the patients using antipsychotic medication, 486 (88.0%) filled more than one prescription during the two years of observation, indicating regular use. The proportion of patients filling more than one prescription was higher among those diagnosed with schizophrenia-like disorder (90.9%), than among those diagnosed with bipolar disorder (85.6%) or severe depressive episode with psychotic symptoms (80.3%). The most commonly prescribed antipsychotic drug was quetiapine (29.5%), followed by aripiprazole (19.6%), olanzapine (17.3%) and risperidone (16.6%). In general, patients diagnosed with schizophrenia-like disorder were more likely to be prescribed an antipsychotic drug (72.0%) compared to patients diagnosed with bipolar disorder (51.7%) or severe depressive episode with psychotic symptoms (55.4%).

An antiepileptic drug was prescribed to 26.4% of the patients, predominantly to patients diagnosed with a bipolar disorder. Antidepressants were prescribed to 35.1%, and anxiolytic drugs to 13.2%. Lithium was prescribed to 8.0% of patients with bipolar disorder, and psychostimulants were prescribed to 19.2% of patients with schizophrenia-like disorder and 20.1% of patients with bipolar disorder.

4. Discussion

In the present study we report that 25 per 100 000 children and adolescents in Norway were diagnosed with a first episode of severe mental disorder each year during 2009–2011. Half of the patients were diagnosed with schizophrenia-like disorder, 37% with bipolar disorder, and 13% with psychotic depression. About one third of the patients were diagnosed with co-morbid depressive or anxiety disorder around the time of their incident

Table 3
Co-morbid mental disorders in children and adolescents with severe mental disorders. Data from the Norwegian Patient Registry on all 0–18 year old boys and girls registered with a first-episode of schizophrenia-like disorder, bipolar disorder, or depressive disorder with psychotic symptoms during 2009–2011. Co-morbid diagnoses are defined as any registered diagnosis with substance use disorder (ICD-10 codes F10-F19), depressive disorder (F32-F34), anxiety disorders (F40-F48), hyperkinetic disorder (F90), mental retardation (F70-F79), autism-spectrum disorder (F84), or conduct disorder (F91) between one year prior to and one year after the first registered diagnosis of a severe mental disorder.

	SCZ (n = 443)		BIP (n = 323)		DEP w/psych (n = 118)		Total (n = 884)	
	n	%	n	%	n	%	n	%
Substance use disorder	41	9.3	37	11.5	11	9.3	89	10.1
Substance use disorder 1 year prior to incident severe mental disorder diagnosis	23	5.2	22	6.8	5	4.2	50	5.7
Substance use disorder 1 year after incident severe mental disorder diagnosis	34	7.7	23	7.1	8	6.8	65	7.4
Depressive disorder	123	27.8	96	29.7	118	100	337	38.1
Depressive disorder 1 year prior to incident severe mental disorder diagnosis	59	13.3	68	21.1	33	28.0	160	18.1
Depressive disorder 1 year after incident severe mental disorder diagnosis	104	23.5	68	21.1	111	94.1	283	32.0
Anxiety disorder	141	31.8	81	25.1	54	45.8	276	31.2
Anxiety disorder 1 year prior to incident severe mental disorder diagnosis	79	14.8	45	13.9	20	16.9	144	16.3
Anxiety disorder 1 year after incident severe mental disorder diagnosis	117	26.4	61	18.9	52	44.1	230	26.0
Hyperkinetic disorder	63	14.2	75	23.2	9	7.6	147	16.6
Hyperkinetic disorder 1 year prior to incident severe mental disorder diagnosis	45	10.2	47	14.6	<5	n.a.	95	10.7
Hyperkinetic disorder 1 year after incident severe mental disorder diagnosis	55	12.4	70	21.7	8	6.8	133	15.0
Mental retardation	36	8.1	12	3.7	<5	n.a.	50	5.7
Autism spectrum disorder	44	9.9	13	4.0	<5	n.a.	61	6.9
Conduct disorder	8	1.8	20	6.2	<5	n.a.	29	3.3

Abbreviations: SCZ: schizophrenia-like disorder (International Classification of Diseases, 10th revision code F20-F29), BIP: bipolar disorder (F30-F31), DEP w/psych: severe depressive episode with psychotic symptoms (F32.3 or F33.3), n.a.: not applicable.

Table 4
Psychotropic drug use among children and adolescents diagnosed with severe mental disorder. Data from the Norwegian Prescription Database on all dispensed prescriptions between one year prior to and one year after an incident diagnosis of schizophrenia-like disorder, bipolar disorder, or severe depressive episode with psychotic symptoms among 0–18 year olds as registered in the Norwegian Patient Registry for the period 2009–2011.

	SCZ (n = 443)		BIP (n = 323)		DEP w/psych (n = 118)		Total (n = 884)	
Drug type	n	%	N	%	n	%	n	%
Any antipsychotic	319	72.0	167	51.7	66	55.4	552	62.4
Second generation antipsychotic	307	69.3	158	48.9	59	50.0	524	59.3
Risperidone	99	22.3	28	6.3	20	16.9	147	16.6
Aripiprazole	115	26.0	47	14.6	11	9.3	173	19.6
Quetiapine	136	30.7	87	26.9	38	32.2	261	29.5
Olanzapine	100	22.6	41	12.7	12	10.2	153	17.3
Antiepileptic	37	8.4	187	57.9	9	7.6	233	26.4
Lithium	< 5	n.a.	26	8.0	0	0	29	3.3
Antidepressant	122	27.5	117	36.2	71	60.2	310	35.1
Anxiolytic	62	14.0	48	14.9	7	5.9	117	13.2
Psychostimulant	57	19.2	65	20.1	7	5.9	129	14.6

Abbreviations: SCZ: schizophrenia-like disorder (International Classification of Diseases, 10th revision code F20-F29), BIP: bipolar disorder (F30-F31), DEP w/psych: severe depressive episode with psychotic symptoms (F32.3 or F33.3), n.a.: not applicable.

severe mental disorder diagnosis. More than 60% of the patients filled prescriptions for antipsychotic medication, mostly second generation antipsychotics, and 88% of patients on antipsychotic medication filled more than one prescription which indicates regular use.

The present incidence rates from specialist health care settings are substantially lower than what was found in the US National Comorbidity Survey of mental disorders on a representative community sample of 13–18 year olds, finding that 2.9% met diagnostic criteria for bipolar disorder type I or II [8]. However, our findings are more in line with a Danish registry-based study from specialist health care, which demonstrated a 12-year cumulative incidence of 0.3% for schizophrenia-like disorder and about 0.1% for bipolar disorder by 20 years of age [4]. The current findings are also similar to incidence rates of bipolar disorder in children and adolescents found in health care settings in the UK [7] and Germany [10]. In a registry-based study from Denmark, the incidence of schizophrenia-like disorder (F20-F29) among 5–18 year olds increased significantly during the period 2000–2012 [27], demonstrating higher incidence rates of schizophrenia when outpatient contacts were included in the Danish Psychiatric Central Register [28]. In the present study, the incidence rate for schizophrenia-like disorder (F20-F29) in 2011 was 11–12 per 100 000 person years. In comparison, the mean age-standardized incidence rate for the more narrow diagnosis of schizophrenia (F20) among 0–18 year olds was 5.2 per 100 000 person years in the Danish study [28].

Prevalence estimates of severe mental disorders in European children and adolescents are scarce, since the paediatric population has been excluded in previous interview-based surveys of mental disorders in the general population in Norway [29], the Netherlands [30], and in the European Study of the Epidemiology of Mental Disorders [31], leaving the present figures valuable.

Co-morbid diagnoses of depressive, anxiety or hyperkinetic disorders were registered in 38.1%, 31.2%, and 16.6%, respectively, of patients with severe mental disorder. Anxiety disorders were most common in patients first diagnosed with schizophrenia-like disorder (31.8%) or severe depressive episode with psychotic symptoms (45.8%), while hyperkinetic disorder was most common among patients first diagnosed with bipolar disorder (23.2%). Depressive illness and anxiety disorders are commonly reported in clinical studies of adult first-episode psychosis patients [13,14], and the results of the present study further emphasize that symptoms of depressive illness or anxiety disorder may serve as early signs, albeit non-specific, of severe mental disorders also in children and adolescents. Data from the Avon Longitudinal Study of Parents and Children (ALSPAC) birth cohort have shown a considerable overlap in early risk factors for anxiety, depression and psychotic-like symptoms in adolescents, indicating a continuous underlying common factor of mental distress [32]. In the present study, 13–21% of the patients had either an anxiety or a depressive diagnosis during one year prior to having first-episode schizophrenia-like or bipolar disorder. Further, the fact that 23% of patients with first-episode bipolar disorder were also diagnosed with hyperkinetic disorder concurs with findings from clinical studies linking irritability or hyperactivity to bipolar disorder in young age [33].

Among children and adolescents diagnosed with severe mental disorders, 62.4% were prescribed antipsychotic medication, most commonly a second-generation antipsychotic. The proportion on antipsychotic drugs was higher in patients first diagnosed with schizophrenia-like disorder (72.0%) compared to patients first diagnosed with bipolar disorder (51.7%) or psychotic depression (55.4%). We have previously shown that children and adolescents who use antipsychotic medication are commonly diagnosed with non-psychotic disorders like hyperkinetic, anxiety or depressive disorder [22]. The findings of the present study demonstrate that children and adolescents diagnosed with schizophrenia, bipolar disorder or psychotic depression are usually also prescribed antipsychotic medication, and the great majority of patients treated with antipsychotic medication use it regularly.

To the best of our knowledge, there are no published studies from Norway linking information on diagnoses of severe mental disorders in children and adolescents to information on their psychotropic drug use, but a previous registry-based study indicated an increase in use of mood stabilizers among 0–17 year olds in general between 2004 and 2007 in Norway [34]. The most commonly used drugs among the patients in our study were quetiapine (29.5%), aripiprazole (19.6%), olanzapine (17.3%), and risperidone (16.6%). These four types of antipsychotic drugs also represent the most commonly prescribed antipsychotic drugs to Norwegian children and adolescents in the general population as described in our previous study [22]. In Norway, only risperidone, aripiprazole and ziprasidone are approved for use in children and adolescents, and use of quetiapine and olanzapine must therefore be regarded as off-label. These substances are, however, approved for paediatric use in USA, which may explain use elsewhere. During the later years there has been an increasing off-label use of especially quetiapine in children and adolescents in Norway [35]. One explanation to this may be that weight-gain seems to be a

lesser problem with quetiapine, compared to for example olanzapine among children and adolescents in general. However, a recently published randomized controlled trial demonstrated that adolescents using quetiapine for 12 weeks gained 3 kg more weight than adolescents on aripiprazole [18]. Thus the choice of antipsychotic drugs for children and adolescents strikes a fine balance between efficacy and adverse effects profile. Clinicians who treat young patients with antipsychotic drugs should carefully monitor body weight, blood lipids and subjective signs of adverse effects.

4.1. Strengths and limitations

The major strength of the present study was the use of data from mandatory health registries covering the entire country and all available specialist health care facilities. This ensured a close to complete coverage of patients in treatment for severe mental disorders with no selection bias. However, the results must be interpreted with the following limitations in mind. First, the data only include patients in specialist health service and not patients treated by their GP only. Mental health care for children and adolescents is free of charge and readily available throughout the country, presumably lowering the threshold for seeking treatment. National clinical guidelines stress that patients with suspected psychotic illness should be evaluated by a psychiatrist or psychologist within two weeks [24]. GPs are therefore strongly encouraged to refer children and adolescents with suspected psychosis to mental health care for evaluation by a specialist as soon as possible. Second, individual-level data in NPR have been available since 2008, and the short observation period limits the opportunity to obtain true incident cases. In the current study, patients were considered incident cases at the date of the first registered diagnosis of a severe mental disorder after 31 December 2008 if there were no previous registrations since beginning of 2008. However, less than 1% of patients diagnosed with F20-F31, F32.3 or F33.3 in 2011, but not in 2010, were diagnosed with any of the relevant diagnoses during 2008–2009, which indicates that more than 99% of our assumed incident cases were true incident cases. Nevertheless, we cannot exclude the possibility that some patients registered in the NPR for the first time in the period 2009–2011 could have been diagnosed with a severe mental disorder prior to 2008, when individual data from NPR were not available. Sensitivity analyses revealed that the prevalence of co-morbid disorders and psychotropic drug use was similar for patients registered for the first time in 2011 compared to the total group registered for the first time during 2009–2011 (data not shown). Third, diagnostic data registered in the NPR are reported by the treating psychiatrist or psychologist and not subjected to external quality assessment. However, a recent study demonstrated a high degree of agreement between the clinical diagnoses as reported to the NPR and diagnoses based on structured diagnostic interview in a clinical research setting for adult patients with severe mental disorder [36]. Fourth, a limitation with the NorPD is that it only includes data on filled prescriptions with no information on secondary compliance to treatment.

5. Conclusion

During 2009–2011, the incidence of severe mental disorders among children and adolescents in Norway was 25 per 100 000 person years. About half of the patients were diagnosed with schizophrenia-like disorder, and a third with bipolar disorder. More than 30% of the patients had co-morbid depressive illness or anxiety disorder, and 10% had SUD. Most of the diagnosed patients used antipsychotic medication, and about 90% of the patients on antipsychotic medication filled more than one prescription which indicates regular use. Secondgeneration antipsychotics were by far the most commonly prescribed types, and studies of the long-term efficacy and safety of antipsychotic drug treatment in young patients with psychotic disorders are needed.

Conflict of interest statement

The authors declare that they have no conflict of interest. Author SS had full access to the data and performed all statistical analyses. Data from the NPR and the NorPD have been used in this publication. The interpretation and reporting of these data are the sole responsibility of the authors, and no endorsement by the registry owners is intended nor should be inferred.

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Author contribution

RN conceptualized and designed the study, and wrote the first draft of the manuscript. JGB, MH, and IH conceptualized and designed the study. VH prepared the data for analysis. SS conceptualized and designed the study and carried out the initial analyses. All authors participated in interpretation of the data, critical review of the manuscript for scientific content, and all authors have approved of the final version of the manuscript.

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