Potential for prediction of psychosis and bipolar disorder in Child and Adolescent Mental Health Services: a longitudinal register study of all people born in Finland in 1987

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Current strategies to predict psychosis identify only a small proportion of individuals at risk. Additional strategies are needed to increase capacity for prediction and prevention of serious mental illness, ideally during childhood and adolescence. One possible approach would be to investigate systems in which psychosis risk factors are concentrated during childhood. One notable such system is represented by Child and Adolescent Mental Health Services (CAMHS). Although psychotic disorders are uncommon in CAMHS, many risk factors for psychosis are highly prevalent in young people who enter this system. We hypothesized, therefore, that youth attending CAMHS would be a high-risk group for psychosis if followed into adulthood and, furthermore, that CAMHS systems would capture a substantial proportion of future psychosis cases. We constructed a total population cohort study of all Finns born in 1987 (N=55,875), linking together extensive register data on health care contacts from birth through age 28 years. We identified all individuals diagnosed with a psychotic or bipolar disorder by age 28 (N=1,785). The risk of psychosis/bipolar disorder by age 28 years was 1.8% for individuals who had not attended CAMHS during childhood or adolescence, whereas it was 12.8% for those with a history of any outpatient CAMHS contact (odds ratio, OR=7.9, 95% CI: 7.2-8.7). Furthermore, the risk of psychosis/bipolar disorder by age 28 years was 2.3% for individuals without a history of inpatient CAMHS admission, whereas it was 24.0% for those with a history of inpatient CAMHS admission (OR=13.3, 95% CI: 11.9-14.9), and 36.5% for those with a history of inpatient CAMHS admission in adolescence (age 13-17 years) (OR=24.2, 95% CI: 21.2-27.6). Individuals who attended CAMHS but received no mental disorder diagnosis had an equally high risk of subsequently developing a psychosis/bipolar disorder as individuals who did receive a diagnosis (OR=0.9, 99.5% CI: 0.7-1.1). Compared to other CAMHS attendees, individuals who developed psychosis or bipolar disorder were more likely to have had an initial CAMHS diagnosis of depressive or other mood disorder (OR=2.3, 99.5% CI: 1.6-3.0) and disruptive behaviour disorder (OR=1.7, 99.5% CI: 1.2-2.5). Of all psychosis/bipolar diagnoses by age 28 years, 50.2% occurred in individuals who had, at some point in childhood or adolescence, attended CAMHS, indicating that CAMHS represent not only a high-risk but also a high-capacity system for prediction of psychosis/bipolar disorder. These findings suggest an enormous, untapped potential for large-scale psychosis/bipolar disorder prediction and prevention research within existing specialist CAMHS.

Key words: Psychosis, schizophrenia, bipolar disorder, prediction, prevention, Child and Adolescent Mental Health Services, high-risk groups

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The identification of individuals at risk for psychosis has been a major focus of psychiatric research in the past 25 years[1-8]. The dominant paradigm in this area has been the ultra-high risk or clinical high risk (CHR) approach[3,4,7,9], which involves structured assessments of attenuated psychotic symptoms or frank but brief psychotic symptoms, aiming to identify individuals at risk for psychotic disorder[1,3,10-12].

There have been thousands of papers published using the CHR paradigm[13], and such has been the impact of this work that CHR clinics are now considered a standard component of mental health services in many countries[14-18]. Building on this progress, research aimed at identifying individuals at elevated risk of (psychotic and non-psychotic) bipolar disorder has also grown in recent years[19-25].

An important challenge for the field, which has been recently highlighted, is that the CHR approach identifies only a small proportion of individuals who are at risk for psychosis, even at leading centres with well-established, free-access specialist CHR clinics[13,26-28]. In a 2-year review of South London mental health services, researchers found that only 4.4% of all psychosis cases received a CHR diagnosis prior to their first psychosis diagnosis[26], while the corresponding proportion was reported to be 13.7% in Melbourne[29]. These findings emphasize the need for additional, higher-capacity approaches to psychosis prediction. An alternative to the symptom-based approach of the CHR paradigm is to take a system-based approach, i.e. to investigate systems in which psychosis risk factors are concentrated during childhood.

Child and Adolescent Mental Health Services (CAMHS) are specialist psychiatric services for children and adolescents covering a distinct catchment area[30]. Psychotic and bipolar disorders are uncommon diagnoses in CAMHS; a large majority of these diagnoses occur in adult mental health services[31,32], and the reasons for presenting to CAMHS differ significantly from those leading to attendance of adult mental health services[33-36]. However, many of the risk factors associated with psychosis are heavily enriched in youth attending CAMHS, including not only mental disorders but also, for example, problems with motor coordination, cognitive function, language acquisition, social communi-

cation, and interpersonal relationships[37-42]. We hypothesized, therefore, that CAMHS could represent an important high-risk system for psychosis and bipolar disorder when attendees were followed into adulthood.

Using national register data, we carried out a longitudinal study of all individuals born in Finland in 1987. We calculated the absolute risk of psychosis and bipolar disorder in individuals who had one or more contacts with CAMHS in childhood or adolescence (age 0-17 years). We also assessed the proportion of psychosis and bipolar disorder cases that were preceded by a CAMHS contact (i.e., predictive capacity), the prospective risk of psychosis or bipolar disorder in individuals who had attended CAMHS, and the latency between the first CAMHS contact and the first psychosis or bipolar disorder diagnosis. As secondary analyses, we also investigated whether particular categories of index diagnoses were more predictive of psychosis and bipolar disorder than others.

METHODS

Study population

We used data from the nationwide 1987 Finnish Birth Cohort study[43], which includes all Finns born in the year 1987 (N=59,476), with official register data recorded from birth until December 31, 2015. The overall study is governed by the Finnish Institute of Health and Welfare and has been approved by its Research Ethics Committee (§28/2009).

The current study was approved by the Research Ethics Committee of the Royal College of Surgeons in Ireland (REC202006006). The data were pseudo-anonymized after linkage and before analysis, and were handled following Finnish data protection laws. The study was conducted following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Data from national registers

We used data linked from the Medical Birth Register (sex, date of birth), the Care Register for Health Care (dates and diagnoses of visits in public hospitals), Statistics Finland (deaths), and Digital and Population Data Services Agency (emigrations).

Information on exposures (having a CAMHS contact) and outcomes (psychotic and bipolar disorder diagnoses) were derived from the Care Register for Health Care[44,45]. This register covers all inpatient visits during the cohort members' lifetime, and all outpatient visits to secondary level health care from the year 1998 onwards. For each visit, the register records diagnoses assigned, medical specialty of treatment provided, and information on whether the visit was an inpatient or outpatient one. Diagnoses were coded using the ICD-9, Finnish modification (1987-1995) or the ICD-10 (1996 onwards). The Care Register for Health Care has been widely used for epidemiological research, and the diagnostic validity has been found to be good[44-50].

Youth who had one or more contacts with CAMHS in childhood or adolescence (age 0-17 years) were divided into two groups depending on whether or not they had had an inpatient admission. Those with an inpatient CAMHS admission were further divided into two groups based on whether their first admission occurred in childhood (<13 years) or adolescence (13-17 years).

Outcomes

Individuals who had been assigned a diagnosis of a non-organic psychotic disorder or bipolar disorder by age 28 years were identified from the Care Register for Health Care.

Non-organic psychotic disorders were categorized into three nested groups: schizophrenia (F20.x as in ICD-10; 295 as in ICD-9, Finnish modification); non-affective psychotic disorders (F20.x, F23.x, F28, F29, F22.x, F25.x and F24 as in ICD-10; 295, 297, 298 and 2999C as in ICD-9, Finnish modification); and all psychotic disorders (F20.x, F23.x, F28, F29, F22.x, F25.x, F24, F30.2, F31.2, F31.5, F32.3, F33.3 and F1x.5 as in ICD-10; 295, 297, 298, 2999C, 2691E, 2962E, 2963E and 2964E as in ICD-9, Finnish modification). Bipolar disorder included F31.x and F30.x as in ICD-10, and 2962, 2963, 2964 and 2967A as in ICD-9, Finnish modification.

Statistical analyses

Analyses were conducted using Stata version 16.0. We excluded individuals who had died (N=756; 1.3%), emigrated (N=2,788; 4.7%) or were diagnosed with moderate to profound intellectual disability (N=79; 0.1%) by the end of the follow-up (December 31, 2015), resulting in a final study cohort of 55,875 individuals. We assessed the lifetime prevalence of CAMHS contacts and outcome disorders in percentages and Kaplan-Meier failure functions with Greenwood 95% confidence bands.

We calculated the risk of a psychotic or bipolar disorder up to age 28 years in individuals who had attended CAMHS (separately for each CAMHS contact type and each outcome disorder). We used unadjusted odds ratios (ORs) to compare the risk of first outcome disorder diagnosis among individuals with a CAMHS contact as compared to individuals who had not presented to CAMHS. For individuals who were not diagnosed with a psychotic or bipolar disorder within 3 months of their first outpatient CAMHS contact or in their first inpatient admission, we calculated the median time (with interquartile range, IQR) from first CAMHS contact/inpatient admission to ultimate diagnosis of psychotic or bipolar disorder.

We then calculated the total proportion of all psychosis and bipolar disorder cases who, at some point in childhood, had attended a CAMHS, and of those who had had an inpatient CAMHS admission (before or after age 13 years). To study the predictive capacity of focusing on individuals attending CAMHS, we assessed the proportion of first recorded outcome disorder diagnoses that were preceded by different types of CAMHS contacts.

For our secondary analyses, we investigated the relationship between the index CAMHS diagnoses and the risk of outcome disorders. Confidence levels were Bonferroni corrected for multiple testing. Index diagnosis was defined as a mental disorder diagnosis given within 3 months of the first CAMHS contact or, where the first CAMHS contact was an inpatient admission, a mental disorder diagnosis given during that admission.

RESULTS

The sample included 55,875 individuals (48.5% females). Of these, 7,011 (12.5%) had one or more contacts with CAMHS in childhood or adolescence (age 0-17 years), and 2,261 (4.0%) had at least one inpatient CAMHS admission (first admission when aged <13 years: 1,131, 2.0%; first admission when aged 13-17 years: 1,130, 2.0%).

Within the overall sample, 1,785 individuals (3.2%) had a lifetime diagnosis of any psychosis or bipolar disorder; 1,369 (2.5%) had a lifetime diagnosis of any psychosis; 1,032 (1.8%) had a lifetime diagnosis of non-affective psychoses, whereas the lifetime prevalence of schizophrenia was 0.5% (N=307) and that of bipolar disorder was 1.2% (N=673) (see Table 1). The percentage of individuals receiving their first diagnosis after age 18 years was 80.6% for any psychosis or bipolar disorder; 77.8% for any psychosis; 79.4% for non-affective psychoses; 85.3% for schizophrenia; and 90.6% for bipolar disorder.

Among the individuals who had not attended CAMHS during childhood or adolescence (N=48,864; 87.5%), those who were diagnosed with any psychosis or bipolar disorder by age 28 years were 889 (1.8%). Among the individuals who had one or more contacts with CAMHS in childhood or adolescence (N=7,011; 12.5%), the percentage of those who received a diagnosis of any psychosis or bipolar disorder by age 28 years was 12.8% (N=896) (OR=7.9, 95% CI: 7.2-8.7) (see Table 1).

Of all diagnoses of any psychosis or bipolar disorder by age 28 years, 50.2% (N=896) occurred among individuals who had attended CAMHS during childhood or adolescence (Table 1). Of these individuals, 83.4% received their diagnosis of any psychosis or bipolar disorder later than 3 months after the first CAMHS contact, with a median latency from first CAMHS contact to diagnosis of psychosis or bipolar disorder of 6.5 years (IQR=2.7-10.1) (see Table 2).

Of individuals with at least one inpatient CAMHS admission, 24.0% were diagnosed with psychosis or bipolar disorder by age 28 years, versus 2.3% of those without an inpatient CAMHS admission (OR=13.3, 95% CI: 11.9-14.9) (see Table 3). The percentage of individuals diagnosed with a psychotic or bipolar disorder by age 28 years was 11.5% among those with a first inpatient CAMHS admission before age 13 years (OR=5.5, 95% CI: 4.5-6.6), and 36.5% among those with a first inpatient CAMHS admission when aged 13-17 years (OR=24.2, 95% CI: 21.2-27.6) (see supplementary information).

Of all diagnoses of psychosis or bipolar disorder by age 28 years, 7.3% (N=130) occurred among individuals with first inpatient CAMHS admission before age 13 years. Of these 130 individuals, 0.8% had been diagnosed with psychosis or bipolar disorder as an outpatient prior to first inpatient admission, 5.4% had received this diagnosis on their first inpatient admission, and 93.8% after their first inpatient CAMHS admission. The median latency from first CAMHS inpatient admission to diagnosis of psychosis or bipolar disorder in the latter group was 12.0 years (IQR=8.7-16.2 years) (see supplementary information).

Of all diagnoses of psychosis or bipolar disorder by age 28 years, 23.1% (N=412) occurred among individuals with first inpatient CAMHS admission between ages 13 and 17 years. Of these 412 individuals, 5.3% had been diagnosed with psychosis or bipolar disorder as an outpatient prior to their first inpatient admission, 37.1% had received this diagnosis on their first inpatient admission, and 57.5% after their first inpatient CAMHS admission. The median latency from first CAMHS inpatient admission to diagnosis of psychosis/bipolar disorder in the latter

Table 1 CAMHS contacts and diagnoses of psychosis and bipolar disorder by age 28 years

		Total	No CAMHS contact			CAMHS contact				
Outcome diagnosis		**N**	**N**	**% column**	**% row**	**N**	**% column**	**% row**	**OR**	**95% CI**
Psychosis and/or bipolar disorder	Yes	1,785	889	1.8	49.8	896	12.8	50.2	7.9	7.2-8.7
	No	54,090	47,975	98.2	88.7	6,115	87.2	11.3		
All psychoses	Yes	1,369	684	1.4	50.0	685	9.8	50.0	7.6	6.8-8.5
	No	54,506	48,180	98.6	88.4	6,326	90.2	11.6		
Non-affective psychoses	Yes	1,032	512	1.0	49.6	520	7.4	50.4	7.6	6.7-8.6
	No	54,843	48,352	99.0	88.2	6,491	92.6	11.8		
Schizophrenia	Yes	307	140	0.3	45.6	167	2.4	54.4	8.5	6.8-10.6
	No	55,568	48,724	99.7	87.7	6,844	97.6	12.3		
Bipolar disorder	Yes	673	323	0.7	48.0	350	5.0	52.0	7.9	6.8-9.2
	No	55,202	48,541	99.3	87.9	6,661	95.0	12.1		

CAMHS – Child and Adolescent Mental Health Services, OR – odds ratio

Table 2 CAMHS attendance among individuals diagnosed with psychosis or bipolar disorder by age 28 years

	Schizophrenia (N=307)		Non-affective psychoses (N=1,032)		All psychoses (N=1,369)		Bipolar disorder (N=673)		Psychosis/bipolar disorder (N=1,785)	
	N (%)	Time (yrs.) to diagnosis, median (IQR)	N (%)	Time (yrs.) to diagnosis, median (IQR)	N (%)	Time (yrs.) to diagnosis, median (IQR)	N (%)	Time (yrs.) to diagnosis, median (IQR)	N (%)	Time (yrs.) to diagnosis, median (IQR)
CAMHS attendance	167 (54.4)		520 (50.4)		685 (50.0)		350 (52.0)		896 (50.2)	
Diagnosed in the 3 months after first CAMHS contact	11 (6.6)		95 (18.3)		135 (19.7)		19 (5.4)		149 (16.6)	
Diagnosed >3 months after first CAMHS contact	156 (93.4)	6.8 (3.2-10.7)	425 (81.7)	7.0 (3.0-10.9)	550 (80.3)	6.5 (2.4-10.1)	331 (94.6)	7.3 (3.7-10.7)	747 (83.4)	6.5 (2.7-10.1)
Inpatient CAMHS admission	115 (37.5)		339 (32.8)		449 (32.8)		178 (26.4)		542 (30.4)	
Diagnosed before first admission	1 (0.9)		17 (5.0)		19 (4.2)		4 (2.2)		23 (4.2)	
Diagnosed on first admission	11 (9.6)		98 (28.9)		148 (33.0)		17 (9.6)		160 (29.5)	
Diagnosed after first admission	103 (89.6)	5.8 (1.5-10.6)	224 (66.1)	7.4 (2.3-11.6)	282 (62.8)	6.9 (1.5-11.1)	157 (88.2)	5.6 (2.0-10.3)	359 (66.2)	6.3 (1.5-11)

CAMHS – Child and Adolescent Mental Health Services, IQR – interquartile range

Table 3 Inpatient CAMHS admissions and diagnoses of psychosis and bipolar disorder by age 28 years

		Total	No inpatient CAMHS admission			Inpatient CAMHS admission				
Outcome diagnosis		**N**	**N**	**% column**	**% row**	**N**	**% column**	**% row**	**OR**	**95% CI**
Psychosis and/or bipolar disorder	Yes	1,785	1,243	2.3	69.6	542	24.0	30.4	13.3	11.9-14.9
	No	54,090	52,371	97.7	96.8	1,719	76.0	3.2		
All psychoses	Yes	1369	920	1.7	67.2	449	19.9	32.8	14.2	12.6-16.0
	No	54,506	52,694	98.3	96.7	1,812	80.1	3.3		
Non-affective psychoses	Yes	1,032	693	1.3	67.2	339	15.0	32.9	13.5	11.8-15.5
	No	54,843	52,921	98.7	96.5	1,922	85.0	3.5		
Schizophrenia	Yes	307	192	0.4	62.5	115	5.1	37.5	14.9	11.8-18.9
	No	55,568	53,422	99.6	96.1	2,146	94.9	3.9		
Bipolar disorder	Yes	673	495	0.9	73.6	178	7.9	26.5	9.2	7.7-10.9
	No	55,202	53,119	99.1	96.2	2,083	92.1	3.8		

CAMHS – Child and Adolescent Mental Health Services, OR – odds ratio

group was 3.0 years (IQR=0.9-7.3 years) (see supplementary information).

In order to assess whether certain mental disorder diagnoses were more predictive of psychosis or bipolar disorder than others, we looked at index diagnoses made on initial CAMHS contact (see Table 4). Overall, there was a broad spread of index diagnoses among individuals attending CAMHS who went on to be diagnosed with psychosis or bipolar disorder. Individuals who attended CAMHS but received no mental disorder diagnosis had an equally high risk of psychosis and bipolar disorder as individuals who did receive a diagnosis (OR=0.9, 99.5% CI: 0.7-1.1). The most common diagnoses among individuals subsequently diagnosed with psychosis or bipolar disorder were depressive or other mood disorders (non-psychotic) (24.4%); anxiety, stress-related or somatoform disorders (12.4%); and neurodevelopmental disorders (12.3%).

Compared to other CAMHS attendees, individuals who developed psychosis or bipolar disorder were more likely to have had an initial CAMHS diagnosis of depressive or other mood disorder (24.4% vs. 12.4%; OR=2.3, 99.5% CI: 1.6-3.0) and disruptive behaviour disorder (9.2% vs. 5.6%; OR=1.7, 99.5% CI: 1.2-2.5), and less likely to have been diagnosed with neurodevelopmental disorders (12.3% vs. 19.9%; OR=0.6, 99.5% CI: 0.4-0.8).

Table 4 Diagnoses assigned during the first 3 months after first CAMHS contact and subsequent diagnosis of psychosis or bipolar disorder

		All	No subsequent diagnosis of psychosis/bipolar disorder (N=6,115)			Subsequent diagnosis of psychosis/bipolar disorder (N=747)				
Index CAMHS diagnoses		**N (%)**	**N**	**% row**	**% column**	**N**	**% row**	**% column**	**OR**	**99.5% CI**
Substance use disorders	Yes	236 (3.4)	213	90.3	3.5	23	9.7	3.1	0.9	0.5-1.6
	No	6,626 (96.6)	5,902	89.1	96.5	724	10.9	96.9		
Depressive or other mood disorders (non-psychotic)	Yes	878 (13.7)	758	80.6	12.4	182	19.4	24.4	**2.3**	**1.6-3.0**
	No	5,922 (86.3)	5,357	90.5	87.6	565	9.5	75.6		
Anxiety, stress-related or somatoform disorders	Yes	810 (11.8)	717	88.5	11.7	93	11.5	12.4	1.1	0.8-1.5
	No	6,052 (88.2)	5,398	89.2	88.3	654	10.8	87.6		
Eating disorders	Yes	279 (4.1)	246	88.2	4.0	33	11.8	4.4	1.1	0.6-1.9
	No	6,583 (95.9)	5,869	89.2	96.0	714	10.8	95.6		
Personality disorders	Yes	21 (0.3)	17	81.0	0.3	4	19.0	0.5	1.9	0.4-9.2
	No	6,841 (99.7)	6,098	89.1	99.7	743	10.9	99.5		
Neurodevelopmental disorders	Yes	1,310 (19.1)	1,218	93.0	19.9	92	7.0	12.3	**0.6**	**0.4-0.8**
	No	5,552 (80.9)	4,897	88.2	80.1	655	11.8	87.7		
Disruptive behaviour disorders	Yes	410 (6.0)	341	83.2	5.6	69	16.8	9.2	**1.7**	**1.2-2.5**
	No	6,452 (94.0)	5,774	89.5	94.4	678	10.5	90.8		
Other and unspecified emotional or social interaction disorders	Yes	483 (7.0)	430	89.0	7.0	53	11.0	7.1	1.0	0.7-1.5
	No	6,379 (93.0)	5,685	89.1	93.0	694	10.9	92.9		
Other disorders	Yes	163 (2.4)	150	92.0	2.5	13	8.0	1.7	0.7	0.3-1.6
	No	6,699 (97.6)	5,965	89.0	97.5	734	11.0	98.3		
No mental disorder diagnosis	Yes	2,623 (38.2)	2,351	89.6	38.4	272	10.4	36.4	0.9	0.7-1.1
	No	4,239 (61.8)	3,764	88.8	61.6	475	11.2	63.6		

CAMHS – Child and Adolescent Mental Health Services, OR – odds ratio. Significant values are highlighted in bold prints

DISCUSSION

In a total population study of all individuals born in Finland in 1987 and followed to age 28 years, we assessed the risk of psychotic and bipolar disorders among those who had, at some point in childhood or adolescence, attended specialist CAMHS. In terms of absolute risk, 12.8% of individuals who attended CAMHS received a diagnosis of a psychotic or bipolar disorder, compared to 1.8% of the rest of the population (OR=7.9, 95% CI: 7.2-8.7). This elevated risk is similar to the level of psychosis risk associated with a formal CHR diagnosis in childhood or adolescence: in a recent systematic review of all CHR studies, we found a transition rate to psychosis of 9.5% at 1 year, 12.1% at 2 years, and 16.1% at 5 or more years[51].

An inpatient CAMHS admission during adolescence was associated with a particularly high risk of psychosis and bipolar disorder. More than one third of young people with a first CAMHS inpatient admission when aged 13 to 17 years were diagnosed with psychosis or bipolar disorder by age 28 years. In 37.1% of these cases, the psychosis or bipolar disorder diagnosis occurred during their initial adolescent admission. In nearly 60% of cases, however, the diagnosis was first made later in life, and the median time to psychosis/bipolar disorder in this group was 3.0 years. These findings highlight the importance of a new sharp focus on psychosis and bipolar disorder risk in adolescents who are admitted to inpatient CAMHS, regardless of their reason for admission at that time.

A key finding of our study was that, in contrast to the small proportion of psychosis cases identified by current high risk strategies[26,29], at least half of all individuals diagnosed with psychosis or bipolar disorder by age 28 years had, at some point in their childhood or adolescence, attended specialist CAMHS. Just 16.6% of these psychosis or bipolar disorder cases were diagnosed within 3 months of first attending outpatient CAMHS or on first inpatient CAMHS admission. For the remaining 83.4%, the median time from first CAMHS contact to psychosis or bipolar diagnosis was >6 years. Overall, these findings highlight an enormous untapped potential for prediction of psychosis and bipolar disorder within already existing specialist paediatric mental health services.

Our secondary analyses involved identifying index CAMHS diagnoses of individuals who went on to be diagnosed with psychosis or bipolar disorder, in order to explore whether certain clinical diagnoses were more predictive of later psychosis and bipolar disorder. Previous research has shown that mental disorders in childhood and adolescence are risk factors for later psychosis[37-42,52-55], although it is important to note that only a small proportion of all young people with a mental disorder present to specialist CAMHS. We found that there was a broad spread of index diagnoses among individuals who went on to be diagnosed with psychosis or bipolar disorder. However, importantly, we found that psychosis and bipolar disorder risk was similarly elevated in young people who attended CAMHS but who were not diagnosed with any mental disorder. This finding, together with the fact that only a small proportion of young people with mental disorders attend specialist CAMHS[30], highlights that the psychosis/bipolar disorder risk indexed by CAMHS contact is best considered a system-related rather than a diagnosis-related risk.

Our findings can help guide and advance psychosis research in several important ways. First, and fundamentally, our findings show that specialist CAMHS represent a high-capacity system for future psychosis and bipolar disorder prediction research. Our findings also suggest that ongoing research aimed at refining risk prediction within high-risk groups, such as neuroimaging, cognitive and proteomic work aimed at predicting psychosis in CHR samples[56-59], should also be applied to and tested in (higher-capacity) CAMHS patient samples.

Beyond that, our findings provide guidance on optimal strategies for different types of psychosis and bipolar disorder prediction and prevention research. In studies, for example, where the overall goal is to improve psychosis outcomes, our findings suggest that a total outpatient CAMHS sample would represent the optimal sampling approach, since it has the potential to reach a large proportion of all psychosis and bipolar disorder cases. In studies, on the other hand, where the research approach seeks a very high-risk group – for instance, for a proof of principle study or for targeted intervention studies where adverse treatment effects might be more significant – our findings suggest that recruitment of an adolescent inpatient sample might be optimal.

Our findings also point to the value of preventive intervention research in CAMHS. There is intense interest in pharmacological and psychosocial treatments that might help to prevent psychosis and bipolar disorder[60]. CAMHS patients represent an ideal group for this research, since this population already receives a wide variety of interventions. As exposure to treatment in CAMHS is not random, future preventive research could include the conduction of randomized controlled trials within CAMHS but also the application of causal inference research methods to existing clinical data.

Furthermore, our findings can help advance important aetiology research aimed at understanding the potentially multiple pathways to psychosis. It has long been posited that psychosis may be a shared outcome for a heterogeneous group of diseases[61,62]. Given the relatively low incidence of psychosis in the population, however, this theory has been difficult to test empirically. Imaging studies have shown that core structural brain abnormalities of psychosis are present at the time of diagnosis[61,63], as are many core cognitive deficits[64], meaning that research on developmental aetiology needs to begin earlier in the disease process. However, identifying a suitable (risk-enriched) sample earlier in the disease course in which to carry out this research has been a major challenge. Our findings suggest that children and adolescents attending specialist CAMHS can be an important target in developmental research on psychosis and bipolar disorder aetiology, given the high incidence of these illness outcomes in this population and considering that the median time to diagnosis from first CAMHS contact is >6 years. Identifying pathways to psychosis-related brain abnormalities will, in turn, lead to further opportunities for treatment research.

Our findings also highlight the importance of transition between adolescent and adult mental health services. The reasons for presenting to CAMHS differ from those for presenting to adult mental health services, and only a small minority of CAMHS patients are subsequently referred to the latter services[33-36]. Even in cases where onward referral occurs, transition is often associated with poor planning, disrupted care and very high non-attendance or once-off attendance only[30,65,66]. Our findings highlight the importance of a careful coordination of the above transition.

A key strength of this study was the use of total population, official service-use data, which means that our findings are not just generalizable to, but directly reflect the total population. Replication of our analyses in other countries will be valuable, but it is important to note that the structure, function and attendance at Finnish CAMHS is similar to other Western countries. In a review of CAMHS across 19 European countries, the median proportion of all children and adolescents attending CAMHS per year was 2.0%, while for Finland it was 1.8%[30]. It will also be important to routinely re-assess our findings over time to monitor for changes in the relationship between CAMHS attendance and risk of psychosis and bipolar disorder: this type of routine re-assessment should be considered good practice for any high-risk approach and will be facilitated by the routine collection of necessary data in Finnish health care registers.

A CAMHS focus for psychosis and bipolar disorder prediction is, of course, only possible in countries where these services exist. These include most World Bank category 1 countries, but CAMHS are less common in other countries[30]. The possibility of prediction and prevention of serious mental health disorders adds to the reasons to support the development and/or expansion of CAMHS where they are lacking.

Because our study used clinical data, it only included individuals presenting to specialist mental health services and did not identify all psychopathology in the general population. This, however, was precisely the point of this approach: our aim was not to investigate childhood mental disorders as a risk factor for psychosis or bipolar disorder, but to assess psychosis and bipolar disorder risk associated with contact with a specific system, CAMHS, where these data are available with high validity[30]. It is also important to highlight that our findings are system-specific: they apply to specialist CAMHS and should not be extrapolated to

other (e.g., primary care) mental health services for children and adolescents.

The dataset included information on outpatient visits only from the year 1998 onwards (when the cohort was 11 years old). This could, in theory, lower the prevalence estimate of outcome disorders. However, psychosis or bipolar disorder before age 11 years is extremely rare. Although the follow-up covers a substantial portion of the high-risk age for onset of psychoses and bipolar disorders, their prevalence among the cohort members will continue to rise over time. For this reason, our risk figures should be considered as lower estimates and the true level of risk may be even higher.

CONCLUSIONS

In a total population study of all individuals born in Finland in 1987 and followed up to 28 years, half of all psychosis and bipolar diagnoses occurred in individuals who had attended CAMHS during childhood or adolescence. There was a large window of opportunity for intervention in terms of the time from initial CAMHS attendance to a diagnosis of psychosis or bipolar disorder: >6 years median latency.

These findings highlight an enormous, untapped potential for the prediction of psychosis and bipolar disorder within already existing structures providing specialist paediatric mental health care. They support a new focus for psychosis and bipolar disorder prediction efforts on specialist community and inpatient CAMHS and present exciting new opportunities for psychosis and bipolar disorder prevention research.

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