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Original Article

Psychosis and bipolar disorder risk in child and adolescent mental health services in the UK: population cohort study

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Background

Current approaches to identifying individuals at risk for psychosis capture only a small proportion of future psychotic disorders. Recent Finnish research suggests a substantial proportion of individuals at risk of psychosis attend child and adolescent mental health services (CAMHS) earlier in life, creating important opportunities for prediction and prevention. To what extent this is true outside Finland is unknown.

Aims

To establish the proportion of psychotic and bipolar disorder diagnoses that occurred in individuals who had attended CAMHS in Wales, UK, and whether, within CAMHS, certain factors were associated with increased psychosis risk.

Method

We examined healthcare contacts for individuals born between 1991 and 1998 (N = 348 226), followed to age 25–32. Using linked administrative healthcare records, we identified all psychotic and bipolar disorder diagnoses in the population, then determined the proportion of cases where the individual had attended CAMHS. Regression analyses examined associations between sociodemographic and clinical risk markers with psychotic and bipolar disorder outcomes.

Results

Among individuals diagnosed with a psychotic or bipolar disorder, 44.78% had attended CAMHS (hazard ratio = 6.28, 95% CI = 5.92–6.65). Low birth weight (odds ratio = 1.33, 95% CI = 1.15–1.53), out-of-home care experience (odds ratio = 2.05, 95% CI = 1.77–2.38), in-patient CAMHS admission (odds ratio = 1.49, 95% CI = 1.29–1.72) and attending CAMHS in childhood (in addition to adolescence; odds ratio = 1.16, 95% CI = 1.02–1.30) were all within-CAMHS risk markers for psychotic and bipolar disorders.

Conclusions

A substantial proportion (45%) of future psychotic and bipolar disorder cases emerge in individuals who had attended CAMHS, demonstrating large-scale opportunities for early intervention and prevention within CAMHS.

Keywords

Child and adolescent psychiatry; bipolar type I or II disorders; psychotic disorders/schizophrenia; big data; epidemiology.

Severe mental illnesses, including psychotic and bipolar disorders, are major contributors to distress, disability and early mortality worldwide.[1] The prediction and prevention of these disorders is a public health priority.[2] Contemporary approaches to psychosis prediction have largely focused on either symptom-based approaches to detecting risk (i.e. clinical high-risk or ultra-high-risk strategies)[3,4] or identifying at-risk individuals based on genetic or familial risk (i.e. familial high-risk strategies).[5] Recent research, however, has shown that these approaches identify only a minority of future psychosis cases, with both clinical and familial high-risk strategies estimated to capture <7% of cases each.[6] Higher-capacity strategies for psychosis risk detection are therefore needed.

One alternative to focusing on symptoms or family history as indicators of risk is to concentrate on systems where risk factors for psychosis are naturally concentrated (i.e. a systems-based approach).[7] One such system is specialist child and adolescent mental health services (CAMHS). CAMHS provide specialist out- and in-patient services that assess, diagnose and treat mental health problems in young people aged up to 18 years.[8] Schizophrenia spectrum and bipolar disorders are uncommon diagnoses in CAMHS – only 8% of schizophrenia and 13% of bipolar disorder cases are diagnosed before age 18 years.[9] However, many of the risk factors for psychosis, such as developmental difficulties, early psychopathology, substance use, adversity, deprivation and cognitive and education difficulties, are present in those attending CAMHS.[10–12] Therefore, although psychosis may be uncommon in CAMHS, it may be the case that risk for later psychosis is elevated in this cohort, providing opportunities for prediction and, ultimately, prevention.

Current study

In a recent study using longitudinal register data in Finland, approximately 50% of all psychotic disorders diagnosed in the population by age 28 years were in individuals who had, at some point in childhood or adolescence, attended CAMHS.[13] This demonstrates important opportunities for prediction and prevention within CAMHS. Given the unique features of Scandinavian health and social care services,[8] however, it is not clear to what extent this would be true in other parts of the world, including in the UK. We therefore wished to assess what proportion of psychotic and bipolar disorder diagnoses emerged in individuals who had, at some point up to 18 years of age, attended CAMHS in Wales, UK. In addition, we wished to assess whether particular population risk factors for psychosis also identified an increased risk for psychosis among these CAMHS patients. In order to do this, we used linked longitudinal administrative data for a population cohort in Wales

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followed up to a maximum age of 32 years. Our primary aim was to calculate the proportion of all psychotic and bipolar disorder diagnoses in the population by age 32 that occurred in individuals who had attended CAMHS. We also calculated the cumulative risk of psychotic and bipolar disorder diagnoses among individuals who attend CAMHS, and examined associations between sociodemographic and clinical risk markers and psychotic and bipolar disorder outcomes in adolescent patients.

Method

Study design

This study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[14] Participants were identified from linked data hosted in the Secure Anonymised Information Linkage (SAIL) databank.[15–19] SAIL contains anonymised, routinely collected data from a variety of health, social care and administrative data-sets in Wales. Data-sets are linked using an established and validated split-file approach, which has a sensitivity of >99.8%.[17] SAIL's Information Governance Review Panel (IGRP) granted approval to conducting this research (IGRP no. 1635).

Information on exposures and outcomes was identified from a range of data-sets in the SAIL Databank: (a) the Welsh Demographic Service Data-set (WDSD), containing anonymised demographic and general practitioner practice registration history for all individuals in Wales that use NHS services; (b) the Patient Episode Data-set for Wales (PEDW), containing records of all in-patient hospital admissions to Welsh hospitals (available from 1995 to study end); (c) the Out-patient Database for Wales (OPDW), containing records of all hospital out-patient appointments in Wales (available from 2004 to study end); and (d) the Welsh Longitudinal General Practice Data-set (WLGP), containing electronic health records from ~80% of general practitioner practices in Wales, covering ~83% of the population. The start date for availability of WLGP records varies for each general practitioner practice, depending on when coded electronic records were implemented.[20] In addition, information on risk markers was identified in the National Community Child Health Database (NCCHD), the Education Wales (EDUW) data-set, the Emergency Department Data-set (EDDS) and the Looked After Children Wales (LACW) data-set.

Cohort

Participants were included if they were born between 1991 and 1998 (inclusive) and were registered with a Welsh general practice before the age of 13 years.

Exposure

Child and adolescent mental health service contacts in Wales were identified from in-patient (PEDW), out-patient (OPDW) and general practitioner (WLGP) records. Wales is one of four nations in the UK. Child and adolescent mental health services are broadly similar across the four nations, in that these are publicly funded, specialist mental health services for youth aged up to 18 years and are free at the point of access. We created indicators for any CAMHS contact, and for in-patient CAMHS admission. In-patient CAMHS contact was defined as any admission beginning before age 18 years where the primary diagnosis was of a mental disorder (any ICD-10 F code), or where the specialty code for the admission was for a relevant psychiatry specialty (see Supplementary Table 1). Out-patient CAMHS contacts were defined as appointments that occurred before the individual was 18 years old and that had a relevant psychiatry specialty code (as above). CAMHS contacts in general practitioner records were identified using Read codes denoting specialist mental health service contact for events that occurred before the individual was 18 years old (Supplementary Table 1), adapted from Joseph et al[21] and reviewed by a consultant child and adolescent psychiatrist on the study team (I. Kelleher). We derived indicators for having both a CAMHS contact at any point (<18 years) and a CAMHS contact in adolescence (13–18 years [inclusive]). Due to the different start dates of the three health data-sets, complete data on childhood (<13 years) CAMHS contacts were not available for all individuals, but complete data were available for adolescent (13–18 years) CAMHS contacts.

Outcome

Diagnosis of psychotic and bipolar disorder at any time during the study period was identified from clinical codes in in-patient (PEDW) and general practitioner (WLGP) records (see Supplementary Table 2 for codes). Psychotic disorder diagnoses recorded in administrative data are generally accurate, with a systematic review finding that such diagnoses had a relatively high positive predictive value (>80%) when externally validated.[22] An overall indicator of any psychotic and/or bipolar disorder was calculated, as well as indicators for the subcategories of: (a) non-affective psychotic disorders (ICD 10 codes F20–9 and Read codes adapted from Abel et al[23]); (b) bipolar affective disorders (ICD 10 codes F30–1 and Read codes adapted from Carr et al[24] and Kuan et al[25]); and (c) depressive disorders with psychotic features (ICD 10 codes F32.3 and F33.3 and Read codes adapted from John et al[26]). Subcategories were not mutually exclusive.

Risk markers

We examined the following risk markers: (a) sex, identified from WDSD and categorised as male or female; (b) ethnicity, identified as the most common ethnicity code reported across PEDW, NCCH, EDUW and EDDS data-sets; due to low numbers of individuals in many ethnic groups, an indicator was derived for belonging to a minoritised ethnic group (defined as belonging to an Asian, Black, mixed or other ethnic group versus belonging to a White ethnic group); (c) socioeconomic deprivation in childhood, measured using the 2014 version of the Welsh Index of Multiple Deprivation (WIMD)[27] identified from the individual's earliest available record in the WDSD, with an indicator calculated for belonging to the most deprived quintile of the WIMD (versus the other four quintiles); (d) urbanicity in childhood, indexed using the 2011 rural–urban classification[28] of each individual's earliest available area code record in the WDSD. An indicator was calculated for living in an urban (versus rural) area; (e) winter birth, defined as month of birth (as reported in WDSD) that occurred in December, January or February; (f) low birth weight, classified as <2500 g; (g) out-of-home care experience, identified from the presence of any record in the LACW data-set; (h) in-patient CAMHS admission, excluding those that occurred prior to or during a diagnosis of psychotic or bipolar disorder; and (i) childhood (<13 years) CAMHS attendance, in addition to adolescent attendance.

Statistical analyses

We calculated the total proportion of psychotic and bipolar disorder cases by the study end-point (age 25–32 years) where the individual had, at some point in childhood or adolescence, attended CAMHS. We also calculated cumulative risk and hazard ratio with 95% CI for psychotic and bipolar disorder outcomes (diagnosed at any age before the study end-point) among individuals who had attended CAMHS. Hazard ratios were calculated using a Cox

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proportional hazards model, with date of entry set as either the date of the individual's birth (for any CAMHS contact) or 13th birthday (for CAMHS contacts in adolescence), and date of exit set as the earliest of the date of the outcome, death, last available general practitioner registration (indicating emigration) or administrative censoring at the end of the study period (November 2023). Cumulative risk of psychosis or bipolar disorder onset (by age 32 years) was described using the Kaplan–Meier failure function (1 – survival).[29] Descriptive statistics (median and interquartile range) of the time between psychosis and bipolar disorder outcomes and CAMHS attendance in adolescence were calculated for outcome diagnoses that occurred more than 3 months following the individual's first CAMHS contact, or after their initial in-patient admission, in keeping with Lång et al.[13]

We used univariable and multivariable logistic regression to estimate associations between sociodemographic and clinical risk markers and psychotic and bipolar disorder outcomes in individuals who had a record of CAMHS attendance in adolescence. In these analyses, individuals were excluded if they had died or were no longer registered with a Welsh general practitioner at the end of the study period (indicating that they were not living in Wales throughout the entire duration of the study period). We first estimated unadjusted associations between each risk marker and psychotic and bipolar disorder diagnosis. Risk markers that had significant associations in univariable models were then included in a multivariable model, again examining the relationship with psychotic and bipolar disorder outcomes. Analyses resulted in odds ratios with 95% CIs as measures of effect size, with odds ratios of 1.00–1.49 interpreted as small, 1.50–2.49 as medium and 2.50 or more as large.[30] We also calculated the absolute risk of psychotic/bipolar disorder for subgroups of adolescent patients, stratified by the presence of each risk marker, using the number of individuals with both the risk marker and psychotic/bipolar disorder diagnosis as the numerator, and total number of individuals with the risk marker as the denominator.

SQL Db2 was used to interrogate data in the SAIL Databank, and analyses were conducted using R version 4.3.1.

Results

The overall sample included 348 198 individuals, of whom 2912 (0.8%) died during the study period and a further 91 588 (26.3%) were no longer registered with a Welsh general practitioner at the end of follow-up (i.e. had probably emigrated; see Supplementary Fig. 1 for flow diagram). Among the overall sample, 37 140 (10.7%) individuals had a record of CAMHS attendance and 4513 (1.30%) had a diagnosis of a psychotic or bipolar disorder by the end of follow-up. Sample characteristics are described in Table 1.

Our main finding was that, of all individuals with a psychotic or bipolar disorder among the total population, 44.78% had attended CAMHS at some point up to age 18 years (Table 2). In total, 41.41% of psychotic or bipolar disorder cases had attended CAMHS in their adolescence and 10.64% had had an in-patient CAMHS admission (Table 2). For schizophrenia specifically, 49.28% of cases had attended CAMHS prior to age 18. The proportion of bipolar disorder cases where the individual had attended CAMHS was 43.70% (Table 2 and Supplementary Table 3). When analyses were stratified by sex, a greater proportion of female psychotic and bipolar disorder cases had attended CAMHS in adolescence compared with males – 45.93 and 36.59%, respectively (Supplementary Table 4).

The cumulative risk of psychotic or bipolar disorder among CAMHS attenders was 6.99%, compared with 1.30% among the total population (hazard ratio = 6.28, 95% CI = 5.92, 6.65; Table 2 and Supplementary Fig. 2). Among adolescent patients the cumulative risk was 7.92% (hazard ratio = 6.92, 95% CI = 6.52, 7.34). CAMHS attenders had elevated risk of all three types of disorder compared with the total population. When analyses were stratified by sex, female adolescent patients had a higher cumulative risk of bipolar disorders and depression with psychotic features when compared with males, but males had a higher cumulative risk of non-affective psychotic disorders compared with females (Supplementary Table 4 and Supplementary Fig. 2).

Time between CAMHS contact and psychosis outcomes: for the majority (88.01%) of cases, a psychotic or bipolar disorder was not the index diagnosis on attending CAMHS, defined as a diagnosis occurring within 3 months following initial CAMHS contact (Table 3). For those individuals, the median time to diagnosis was 6.05 years. Across the various disorder types the median length of time from CAMHS contact to diagnosis ranged from 4.71 years (depression with psychotic features) to 6.44 years

Table 1 Sample characteristics

Sample characteristics	Uncensored cohort		Censored cohort[a]	
	N	%	*N*	%
Total, *N*	348 198		253 687	
Died before end of follow-up	2912	0.8	–	–
Not registered with general practitioner by end of follow-up	91 588	26.3	–	–
CAMHS contact				
Any CAMHS contact	37 140	10.67	31 909	12.58
Adolescent first CAMHS contact	29 968	8.61	25 950	10.23
In-patient CAMHS admission	4017	1.15	3375	1.33
Adolescent first in-patient CAMHS	3172	0.91	2670	1.05
Psychotic disorder diagnoses				
Any psychosis/bipolar	4513	1.30	4034	1.59
Non-affective psychotic disorders	2527	0.73	2232	0.88
Bipolar disorder	2293	0.66	2077	0.82
Depression with psychotic features	196	0.06	179	0.07
Demographic factors				
Sex				
Female	169 889	48.79	123 267	48.59
Male	178 297	51.21	130 415	51.41
Missing	6	<0.01	5	<0.01
Ethnicity				
Minoritised ethnic group	2988	0.86	2077	0.82
White ethnic group	112 738	32.38	91 857	36.21
Missing	232 472	66.76	159 753	62.97
Welsh Index Multiple Deprivation				
Quintile 1 (most deprived)	87 664	25.18	71 116	28.03
2	70 799	20.33	55 074	21.71
3	68 063	19.55	49 631	19.56
4	63 459	18.22	41 849	16.50
5 (least deprived)	58 084	16.68	36 016	14.20
Missing	129	0.04	1	<0.01
Urbanicity				
Rural location	109 358	31.41	75 215	29.65
Urban location	238 711	68.56	178 471	70.35
Missing	129	0.04	1	<0.01
Season of birth				
Winter	84 085	24.15	61 473	24.23
Summer/spring/autumn	264 113	75.85	192 214	75.77
Birth weight				
Low	42 898	12.32	24 951	9.84
Normal/high	297 198	85.35	226 862	89.43
Missing	8102	2.33	1874	0.74
Out-of-home care				
Out-of-home care record	5353	1.54	4582	1.81
No out-of-home care	342 845	98.46	249 105	98.19

CAMHS, child and adolescent mental health services.
a. Excluding individuals who died/were no longer registered with general practitioner before end of follow-up.

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Table 2 Child and adolescent mental health service contact and diagnoses of psychotic and bipolar disorders by age 25–32 years ($N = 348\,198$)

	Any (childhood or adolescent) CAMHS contact			Adolescent CAMHS contact		
Outcome diagnosis	Predictive capacity (%)	Cumulative risk (%)	Hazard ratio (95% CI)	Predictive capacity (%)	Cumulative risk (%)	Hazard ratio (95% CI)
Any CAMHS contact						
Any psychotic or bipolar disorder	44.78	6.99	6.28 (5.92–6.65)	41.41	7.91	6.93 (6.53–7.35)
Non-affective psychotic disorders	46.62	3.95	6.72 (6.21–7.26)	42.98	4.47	7.34 (6.78–7.94)
Bipolar disorder	43.70	3.63	6.03 (5.55–6.55)	40.60	4.13	6.73 (6.19–7.31)
Depression with psychotic features	47.96	0.29	6.94 (5.24–9.18)	47.45	0.35	8.59 (6.49–11.38)
In-patient CAMHS admission						
Any psychotic or bipolar disorder	10.64	14.05	9.72 (8.84–10.68)	9.68	15.90	11.14 (10.10–12.30)
Non-affective psychotic disorders	13.22	9.56	12.41 (11.06–13.93)	12.07	10.92	14.25 (12.64–16.06)
Bipolar disorder	8.55	6.32	7.64 (6.60–8.84)	7.76	7.16	8.75 (7.51–10.20)
Depression with psychotic features	22.45	1.19	23.49 (16.79–32.85)	21.94	1.47	29.09 (20.74–40.80)

CAMHS, child and adolescent mental health services. Predictive capacity is the proportion of all disorder cases in the population that occurred among CAMHS patients.

Table 3 Time to psychosis/bipolar disorder diagnosis following adolescent CAMHS attendance

	Any psychotic or bipolar disorder		Non-affective psychotic disorder		Bipolar disorder		Depression with psychotic features	
Time of psychosis/bipolar disorder diagnosis	*N* (%)	Time (years) to diagnosis, median (IQR)	*N* (%)	Time (years) to diagnosis, median (IQR)	*N* (%)	Time (years) to diagnosis, median (IQR)	*N* (%)	Time (years) to diagnosis, median (IQR)
Any CAMHS contact								
Diagnosed <3 months after first CAMHS contact	224 (11.99)		158 (14.55)		87 (9.34)		20 (21.51)	
Diagnosed >3 months after first CAMHS contact	1645 (88.01)	6.05 (3.32, 9.17)	928 (85.45)	5.48 (2.77, 8.62)	844 (90.66)	6.44 (3.72, 9.59)	73 (78.49)	4.71 (2.24, 6.07)
In-patient CAMHS admission								
Diagnosed before first admission	57 (13.04)		32 (10.49)		25 (14.04)		–	
Diagnosed during first admission	103 (23.57)		86 (28.20)		14 (7.87)		18 (41.86)[a]	
Diagnosed after first admission	277 (63.39)	4.47 (1.82, 8.96)	187 (61.31)	3.98 (1.79, 7.82)	139 (78.09)	5.84 (2.51, 9.80)	25 (58.14)	3.90 (1.13, 5.62)

CAMHS, child and adolescent mental health services; IQR, interquartile range.
a. Diagnosed during OR before first admission.

(bipolar disorder). For those with in-patient admissions, the majority (63.39%) of cases were also diagnosed following their first admission; the median length of time to being diagnosed with a psychotic or bipolar disorder in this group was 4.47 years.

Associations between risk markers and psychosis outcomes: among the 25 950 individuals who attended CAMHS in adolescence (and had not died or were no longer registered with a Welsh general practitioner before the end of the study period), several risk markers were associated with a psychotic or bipolar disorder outcome in univariate analyses (Table 4). Low birth weight, out-of-home care, having an in-patient CAMHS admission (for a reason other than psychosis) and having had a CAMHS visit in childhood (in addition to having had a CAMHS visit in adolescence) were all associated with increased odds of any type or psychotic or bipolar disorder. Sex was not a predictor of any type of psychotic or bipolar disorder. However, this was a result of the fact that male sex predicted later non-affective psychosis and female sex predicted later bipolar disorder; thus, looking at a combined non-affective psychosis, bipolar outcome results in sex effects ostensibly disappearing when there are, in fact, sex-specific differences (Table 4). Male sex, socioeconomic deprivation, low birth weight, out-of-home care, in-patient CAMHS admission and childhood CAMHS attendance (in addition to adolescent CAMHS attendance) were all associated with an increased risk of non-affective psychosis. Bipolar disorders were predicted by female sex, low birth weight, out-of-home care and in-patient CAMHS admission. Effect sizes for associations were all small to medium.

In multivariable analyses, the majority of risk markers retained significant associations with psychosis outcomes when adjusted for the other risk markers, with the exception of the associations of socioeconomic deprivation with non-affective psychosis and low birth weight with bipolar disorder (Table 4).

Discussion

In this population cohort of almost 350,000 individuals living in Wales, we assessed the proportion of all psychotic and bipolar disorders diagnosed in the population up to age 32 years that occurred in individuals who had, at some stage in childhood or adolescence, attended CAMHS. We found that 47% of all non-affective psychosis (including 49% of schizophrenia), 44% of bipolar disorder and 48% of psychotic depression cases in the population diagnosed by age 32 years) occurred in individuals who had attended CAMHS. Our results are in keeping with recent findings in a Finnish population sample, where 50% of psychotic

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Table 4 Associations between demographic factors and psychosis outcomes among individuals with CAMHS contact in adolescence ($N = 25\,950$)

Predictors	Any psychotic or bipolar disorder			Non-affective psychotic disorder			Bipolar disorders		
	uOR (95% CI)	aOR[d] (95% CI)	Absolute risk (%)	uOR (95% CI)	aOR[d] (95% CI)	Absolute risk (%)	uOR (95% CI)	aOR[d] (95% CI)	Absolute risk %
Whole population[a]	–	–	1.59	–	–	0.88	–	–	0.82
CAMHS population[a]	–	–	6.38	–	–	3.62	–	–	3.26
Sex[b]	1.06 (0.96–1.17)	–	6.54	**1.88 (1.65, 2.15)**	**1.82 (1.59–2.09)**	4.87	**2.50 (2.13–2.93)**	**2.56 (2.18–3.01)**	4.38
Minoritised ethnic group	1.46 (0.76–2.55)	–	8.11	2.03 (0.95–3.80)	–	6.08	0.65 (0.16–1.73)	–	2.03
Socioeconomic deprivation	1.05 (0.95–1.17)	–	6.59	**1.20 (1.05–1.38)**	1.12 (0.97–1.28)	4.05	0.89 (0.77–1.03)	–	3.03
Urban location	0.99 (0.89–1.11)	–	6.37	0.93 (0.80–1.08)	–	3.56	1.01 (0.87–1.19)	–	3.27
Winter birth	1.09 (0.97–1.22)	–	6.78	1.04 (0.89–1.21)	–	3.73	1.16 (0.99–1.36)	–	3.63
Low birth weight	**1.37 (1.18–1.57)**	**1.33 (1.15–1.53)**	8.20	**1.44 (1.20–1.73)**	**1.42 (1.18–1.70)**	4.92	**1.26 (1.03–1.54)**	1.19 (0.97–1.46)	3.94
Out-of-home care experience	**2.21 (1.91–2.55)**	**2.05 (1.77–2.38)**	12.18	**2.48 (2.07–2.96)**	**2.17 (1.80–2.60)**	7.77	**1.93 (1.57–2.36)**	**1.98 (1.60–2.43)**	5.74
CAMHS in-patient admission[c]	**1.57 (1.37–1.81)**	**1.49 (1.29–1.72)**	9.21	**1.81 (1.51–2.15)**	**1.75 (1.46–2.09)**	5.91	**1.33 (1.08–1.62)**	**1.23 (1.00–1.51)**	4.15
Childhood CAMHS attendance	**1.25 (1.11–1.41)**	**1.16 (1.02–1.30)**	7.52	**1.51 (1.30–1.76)**	**1.20 (1.03–1.40)**	4.94	0.93 (0.78–1.11)	–	3.07

uOR, unadjusted odds ratio; aOR, adjusted odds ratio. Bold font indicates statistically significant associations (i.e. 95% CI does not include 1).
a. Absolute risk calculated in censored cohort (i.e. excluding those that died/were no longer registered with general practitioner prior to study end).
b. Female sex for any psychotic or bipolar disorder/bipolar disorder outcomes; male sex for non-affective psychotic disorder outcomes.
c. Excluding admissions where a psychotic or bipolar disorder diagnosis was made during or before the admission.
d. Adjusted for other predictors significantly associated with the outcome of interest.

and bipolar disorder cases emerged in individuals who had attended CAMHS.[13] Our results demonstrate that this finding is not unique to Finnish healthcare systems and that UK CAMHS offers similar important opportunities for psychosis prediction and prevention.

The proportion of psychosis cases that emerged from CAMHS services was substantially higher than that shown to emerge from other high-risk approaches. Research on the clinical high-risk approach, for example, has found that <7% of psychosis cases are identified by clinical high-risk services,[6] and this approach appears to be even more limited in identifying at-risk children and adolescents.[31,32] Similarly, recent research suggests that only a small proportion (7%) of psychotic disorders is captured using the familial high-risk approach.[33] A new focus on CAMHS, therefore, would stand to substantially increase capacity for psychosis prediction and prevention.

The baseline absolute risk of a psychotic or bipolar disorder in patients who had attended CAMHS was 7% by the end of follow-up. Several sociodemographic and clinical risk markers predicted an increased risk beyond the baseline risk associated with CAMHS attendance, with small to medium effect sizes. This included (a) sex (male sex for non-affective psychosis; female sex for bipolar disorder), (b) low birthweight, (c) out-of-home care experience, (d) in-patient CAMHS admission (for reasons other than psychosis) and (e) having a childhood CAMHS visit (in addition to adolescence). Absolute risk differences associated with these factors were relatively small, and additional research will be necessary to identify higher-risk subgroups within this population, which may include genomic, proteomic, cognitive, neuroimaging, electrophysiological and other measures.

The baseline level of psychosis risk associated with CAMHS attendance was lower in Wales (7%) than in our previous Finnish research (13%).[13] This probably reflects a difference in the prevalence of psychotic and bipolar disorders in Welsh and Finnish healthcare registers (1.3 *v.* 3.2%). This could represent real differences in the population prevalence of psychotic disorders between countries, but probably also reflects differences in how psychosis is recognised, diagnosed and recorded by services, because methodological differences have previously been found to be a major contributor to variance in prevalence estimates across settings.[34] While Wales has publicly funded mental health services, challenges with staffing levels contribute to longer waiting times and uneven access, particularly in rural areas,[35] which may impact case finding and recording. In any case, these findings, based only on register-captured diagnoses, probably represent a conservative estimate of the true risk of psychosis in this population.

Most (88%) psychotic and bipolar disorder cases were diagnosed more than 3 months following an index CAMHS visit – the median time to diagnosis from the point of first CAMHS contact was, in fact, 6 years. This is also in keeping with findings from Finland,[13] where the median time to psychosis diagnosis was 6.5 years. This highlights that there is a wide window of opportunity in which to intervene prior to psychosis diagnosis, and suggests that CAMHS contact typically occurs far upstream of psychotic disorder, which is auspicious in terms of opportunities for intervention in the context of a disorder that typically has a slow, insidious onset.

There are a number of important clinical and research implications arising from our findings. Our results highlight that, although psychosis is an uncommon diagnosis in CAMHS, it is a common outcome for patients who have attended CAMHS when followed into adulthood. Clinicians in adult mental health services should be aware of the elevated risk of psychosis and bipolar disorder in patients who had previously attended CAMHS. Second, while the long median latency between CAMHS attendance and

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ultimate psychosis diagnosis in our cohort suggests that, in most cases, CAMHS patients were far upstream of psychosis, it is also likely that a minority of patients were, in fact, psychotic during their CAMHS presentation, and this was not identified. This highlights the importance of expertise in the recognition and management of psychosis within CAMHS. Third, the high proportion of psychosis and bipolar diagnoses that arose in former CAMHS patients highlights the need for an intense research focus on risk for severe, chronic and enduring mental illnesses within child and adolescent mental health services. Notably, our results demonstrate that a far higher proportion of psychosis cases emerge from child and adolescent mental health services than do from clinical high-risk services.[6] Fourth, precision medicine research that allows us to identify individuals or subgroups at particularly elevated risk will also be valuable, including through examination of the impact of combinations of different risk factors that tend to act cumulatively rather than independently.[36] Last, future research will need to examine ways to reduce risk for psychosis in patients who attend CAMHS. This clinical population holds promise for intervention, however, because (a) increased risk is identifiable based on routine administrative healthcare data (i.e. data that capture CAMHS attendance) and (b) risk is identified, by definition, while still in childhood, which may be a more opportune time to impact on neurobiological and psychosocial development, rather than the early adult stage typically associated with CHR diagnoses.

The strengths of this study include the use of a large population cohort covering approximately 83% of the Welsh population and the use of prospective administrative data that are not subject to interview or recall bias. That this study replicates and extends previous findings in Finland is also important given the 'replication crisis' in research.[37] Limitations include that complete information on CAMHS attendances before age 13 years was not available, meaning that we were likely to miss early childhood CAMHS contacts. However, young people attending CAMHS in adolescence appear to be at higher risk of psychotic and bipolar disorders than those attending in childhood,[13] so the period of highest risk was likely to have been fully captured. Second, the exclusion of individuals without continuing general practitioner registration through the study period may have introduced selection bias because this may disproportionally exclude specific populations, including unhoused people and those who had emigrated out of Wales. Severe mental illness is associated with increased likelihood of residential mobility and migration,[38] and of experiencing homelessness.[39] Thus, excluding these populations may have contributed to underestimating the prevalence of psychotic and bipolar disorders and, for the same reasons, our estimates are likely to be conservative. Third, given that self-harm and suicidal behaviours often precede a psychosis diagnosis,[40,41] it is also possible that, in some cases of suicide, there was an emerging (but hitherto undiagnosed) psychosis. This would also have led to an underestimation of psychosis risk in the CAMHS population in the current data. Fourth, it was not possible to investigate the relationship between specific adolescent mental disorder diagnoses and risk of psychosis and bipolar disorder, because information on CAMHS diagnoses is not, in most cases, captured in the register. This will be an important area for future research. Last, data on ethnicity were not available for a large proportion of the participants, as is common in electronic health records collected during earlier time periods in the UK.[42] Future research should investigate the relationship between ethnicity, CAMHS attendance and psychotic/bipolar disorder outcomes in data-sets where this information is more complete.

In conclusion, we found that child and adolescent mental health services in Wales, UK, capture risk for a substantial proportion of the total population incidences of psychotic and bipolar disorders. This highlights important opportunities for psychosis and bipolar disorder prediction and prevention within existing child and adolescent mental health services, at a scale far exceeding current high-risk approaches.

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Supplementary material

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Data availability

Access to SAIL data is available on application to the SAIL Databank via their usage governance process (www.saildatabank.com).

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Author contributions

K.O. performed the statistical analysis and drafted the manuscript. U.L. and C.H. interpreted data and critically reviewed and revised the manuscript. I. Kougianou and A.T. participated in data analysis and critically reviewed and revised the manuscript. R.M., S.M.L. and A.J. critically reviewed and revised the manuscript. I. Kelleher conceived the study, supervised the design and coordination of the study, supervised analysis and acquired funding. All authors read and approved the final manuscript.

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Declaration of interest

S.M.L. is a member of the *BJPsych* editorial board. He did not take part in the review or decision-making process of this paper. Declaration of interest for all other authors: none.

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