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Estimating the incidence of first-episode psychosis using population-based health administrative data to inform early psychosis intervention services

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Abstract

Background. Discrepancies between population-based estimates of the incidence of psychotic disorder and the treated incidence reported by early psychosis intervention (EPI) programs suggest additional cases may be receiving services elsewhere in the health system. Our objective was to estimate the incidence of non-affective psychotic disorder in the catchment area of an EPI program, and compare this to EPI-treated incidence estimates.

Methods. We constructed a retrospective cohort (1997–2015) of incident cases of non-affective psychosis aged 16–50 years in an EPI program catchment using population-based linked health administrative data. Cases were identified by either one hospitalization or two outpatient physician billings within a 12-month period with a diagnosis of non-affective psychosis. We estimated the cumulative incidence and EPI-treated incidence of non-affective psychosis using denominator data from the census. We also estimated the incidence of first-episode psychosis (people who would meet the case definition for an EPI program) using a novel approach.

Results. Our case definition identified 3245 cases of incident non-affective psychosis over the 17-year period. We estimate that the incidence of first-episode non-affective psychosis in the program catchment area is 33.3 per 100 000 per year (95% CI 31.4–35.1), which is more than twice as high as the EPI-treated incidence of 18.8 per 100 000 per year (95% CI 17.4–20.3).

Conclusions. Case ascertainment strategies limited to specialized psychiatric services may substantially underestimate the incidence of non-affective psychotic disorders, relative to population-based estimates. Accurate information on the epidemiology of first-episode psychosis will enable us to more effectively resource EPI services and evaluate their coverage.

Background

Accurate information on the epidemiology of first-episode psychosis is crucial for early psychosis intervention (EPI) services (Kirkbride *et al.*, 2017), both for programmatic and resource planning and to evaluate the proportion of potential cases who are detected and managed within a catchment area. There is a wide range in published incidence estimates (van der Werf *et al.*, 2014) that vary due to factors such as the age groups and diagnoses that are included (Castillejos *et al.*, 2018), the sampling frame for case identification (Hogerzeil *et al.*, 2014), and the inclusion of a range of inpatient and outpatient service providers in case finding strategies (Jörgensen *et al.*, 2010; Simon *et al.*, 2017). Furthermore, recent reports have found up to a 10-fold variation in the incidence of psychotic disorder across countries (Jongsma *et al.*, 2018), highlighting the need for local estimates to inform the planning and evaluation of EPI services.

The province of Ontario, Canada's largest province with a population of over 13.5 million people, has nearly 60 hospital- and community-based EPI programs. These programs estimate that the treated incidence of first-episode psychosis is in the range of 12–13 per 100 000 per year (Durbin *et al.*, 2016), which correspond to frequently cited estimates of the incidence of schizophrenia (McGrath *et al.*, 2008). However, the most recent incidence estimates from Ontario for schizophrenia spectrum psychoses suggest a population-based rate of 55.6 per 100 000 person-years among people between the ages of 14 and 40 (Anderson *et al.*, 2015). This discrepancy between broader population-based estimates of the incidence of psychotic disorder and the treated incidence reported by EPI programs suggests that there may be

additional cases receiving services elsewhere in the health care system, or not receiving treatment at all.

Conversely, not all incident cases of psychotic disorder detected by population-based case ascertainment strategies will meet the case definition for first-episode psychosis as defined by EPI programs (Anderson *et al.*, 2012). Many programs restrict admissions to first treatment contact, or by factors such as duration of psychotic symptoms or length of prior antipsychotic treatment (Breitborde *et al.*, 2009). Furthermore, people with intellectual and developmental disabilities, those with substantial contact with the criminal justice system, and those with complex medical or substance-related comorbidities are often excluded from these programs, and many programs have an upper age limit of 35–40 years (Greenfield *et al.*, 2018).

Few prior studies on the incidence of psychotic disorders have been conducted from the perspective of early intervention services (Cheng *et al.*, 2011), and those that have been done have typically limited case ascertainment to psychiatric services (Cheng *et al.*, 2011; Kirkbride *et al.*, 2017). The objectives of the current study were: (1) to use population-based health administrative data to estimate the cumulative incidence of non-affective psychosis in the catchment area of an EPI program; (2) to compare this estimate to the EPI-treated incidence of psychotic disorder; and (3) to use the proportion of referred cases confirmed by the EPI program to estimate the incidence of first-episode non-affective psychosis. The data used to estimate incidence were obtained from a larger project aimed at evaluating access to an EPI program (Anderson *et al.*, 2018*b*), and the effectiveness of EPI relative to treatment as usual (Anderson *et al.*, 2018*a*), using population-based health administrative data from a defined catchment area.

Methods

Study setting

The *Prevention and Early Intervention Program for Psychoses* (PEPP) in London, Ontario is the only EPI program serving a well-defined catchment area of nearly 425 000 people, 50% of whom fall within the age range for the program (approximately 213 000 people). The catchment area includes a mix of both urban and rural communities, and 10% of the population is living below the low-income cut-off. Migrant groups comprise 20% of the population, and approximately 12% self-identify as a visible minority (Statistics Canada, 2007). The program accepts clients who met the following criteria: (i) primary diagnosis of a first-episode non-affective psychotic disorder, defined as <30 days of prior antipsychotic treatment; (ii) aged 16–50 years; (iii) absence of a developmental disability or organic psychosis; and (iv) no outstanding major criminal charges. Eligibility for the program is based on a clinical assessment by a program psychiatrist, and the program has been described in detail elsewhere (Norman and Manchanda, 2016).

Cohort creation

We constructed a retrospective cohort of incident cases of non-affective psychotic disorder in the EPI catchment area over a 17-year period (1997–2013, inclusive), defined based on six-digit postal codes. The cohort was constructed using linked population-based health administrative data arising from the Ontario Health Insurance Plan (OHIP), which is the publicly funded universal health system that covers medically necessary services for nearly the entire population (>96%) (OHIP for All: Healthier Together, 2018). These data are held by the Institute for Clinical Evaluative Sciences (ICES) and include information on physician billings, hospitalizations, emergency department (ED) visits, and basic demographic data, as well as linkages to other databases, such as immigration data (Table 1).

We identified cases aged 16–50 years in the health administrative data by the presence of at least one of the following:

- an inpatient hospitalization with a primary discharge diagnosis of a non-affective psychotic disorder from a general hospital bed [International Classification of Diseases (ICD), 9th Revision code 295.X, 297.X, 298.X; ICD-10 code F20 or F25]; or
- an Axis 1 diagnosis of non-affective psychotic disorder from a designated psychiatric hospital bed [Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) code 295.X, 297.X, 298.X]; or
- at least two outpatient billing claims or ED visits within a 12-month period with a diagnostic code for non-affective psychotic disorder (ICD-9 code 295.X, 297.X, 298.X; ICD-10 code F20 or F25).

This algorithm has been previously validated in ICES data against medical charts and found to have moderate positive predictive value (proportion of true positives among all people meeting case definition = 62%) and high negative predictive value (proportion of true negatives among all people who do not meet the case definition = 90%) for a diagnosis of non-affective psychotic disorder (Kurdyak *et al.*, 2015). Cases were excluded as prevalent if there was evidence of contact with mental health services for non-affective psychosis prior to the study window – this exclusion period ranged from 9 to 25 years depending on the database and year of diagnosis. People with a prior history of diagnosis for affective psychotic disorder were not excluded, and were counted as an incident case at the point where the diagnosis changed to non-affective psychosis. We did not apply any additional exclusions to the study cohort on factors such as duration of prior antipsychotic use or presence of a substance use disorder. For all people included in the cohort, we extracted available sociodemographic information, including age at index date, gender, neighborhood-level income quintile, migrant status, and rurality of residence.

We obtained data on all clients admitted to the EPI program since its inception, and we linked this to the study cohort using unique identifiers, which allowed us to identify EPI clients within the health administrative data. We also linked the physician registration number and dates of tenure for all PEPP program psychiatrists, which allowed us to identify people who may have had contact with an EPI-psychiatrist for screening but were ultimately found to be ineligible for the program. Cohort members were divided into the following groups:

(i) Confirmed cases – people admitted to the EPI program;
(ii) Confirmed non-cases – people screened by an EPI psychiatrist but not admitted to the program; and
(iii) Suspected cases – people not in the EPI database who had never seen an EPI psychiatrist.

The Research Ethics Board at the University of Western Ontario and Sunnybrook Health Sciences Centre granted approval for the linkage of the primary data to the ICES data

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Table 1. Description of the linked health administrative databases used to construct the cohort of incident cases of non-affective psychotic disorder

Source of data	Description	Variables of interest	Years
Registered Persons Database (RPDB)	Socio-demographic and mortality information	Age at index diagnosis, gender, rural residence, income quintile	1990–2014
Immigration, Refugees, and Citizenship Canada (IRCC)	Information on all permanent residents who land in Ontario	Migrant status	1985–2014
Ontario Health Insurance Plan (OHIP)	Information on all physician services and outpatient visits	Case definition, index diagnosis, diagnosing physician, prior alcohol-related disorder, prior substance-related disorder, family physician contact in previous 6 months, psychiatrist contact in previous 6 months	1991–2014
Discharge Abstracts Database (DAD)	Data on acute hospitalizations	Case definition, index diagnosis, inpatient status, prior alcohol-related disorder, prior substance-related disorder, hospitalization in previous 6 months	1988–2014
Ontario Mental Health Reporting System (OMHRS)	Information on inpatient mental health hospitalizations to designated psychiatry beds. *Note: data on psychiatric hospitalization prior to 2005 available in DAD*	Case definition, index diagnosis, inpatient status, prior alcohol-related disorder, prior substance-related disorder, hospitalization in previous 6 months	2005–2014
National Ambulatory Care Reporting System (NACRS)	Information on visits to the emergency department	Case definition, index diagnosis, prior alcohol-related disorder, prior substance-related disorder, emergency department visit in previous 6 months	2000–2014

holdings. Patient-level data were linked using coded identifiers, and the de-identified datasets were analyzed on site at ICES. We followed the RECORD guidelines for observational studies using routinely collected data (online Supplementary Table S1), and a description of all codes and algorithms used to create study variables is presented in online Supplementary Table S2.

Estimation of incidence

We estimated the annual cumulative incidence proportion of non-affective psychoses for the total sample meeting our case definition (total incidence) and the sample admitted to EPI services (EPI-treated incidence). We also attempted to estimate the incidence of first-episode psychosis – specifically, new cases of non-affective psychosis who would meet the case definition for an EPI program – using the following approach. Firstly, we estimated the proportion of confirmed cases among all cases referred to the program [confirmed cases/(confirmed cases + confirmed non-cases)] for each age and gender strata. Assuming our sample of suspected cases would be comprised of a similar mix of true cases and false positives, we applied these proportions to the sample of suspected cases to estimate the number of people with first-episode psychosis potentially missed by the EPI program. Finally, we added this number to the number of confirmed cases to correct our treated incidence estimate, yielding an estimated incidence of first-episode non-affective psychosis for the EPI program catchment area.

Age- and gender-stratified denominator data were obtained from the 2006 census for the county of Middlesex-London (Statistics Canada, 2007), which represents the mid-point of our study period. Incidence estimates were adjusted for age and gender using direct standardization to the 2011 Canadian population, which is the standard population used by Statistics Canada. We computed crude and adjusted risk ratios (RRs) using Poisson regression to adjust for age and gender; however, detailed denominator data were not available for migrant status or income quintile so we computed crude RRs only. The crude and adjusted estimates, where available, were highly similar; therefore, we discuss the crude RRs throughout the manuscript for consistency, although both estimates are available in the summary table.

All analyses were conducted in Stata Version 15, and results are reported as cumulative incidence proportions or RRs with corresponding 95% confidence intervals (CI).

Results

Our algorithm identified 3245 cases of incident non-affective psychotic disorder presenting to services in the EPI catchment area over the 17-year period, of whom 21% were confirmed cases, 28% were confirmed non-cases, and 51% were suspected cases (Table 2). This yields an age- and gender-standardized total cumulative incidence of 90.0 per 100 000 per year (95% CI 87.0–93.1). Men had a higher incidence than women (RR = 1.46, 95% CI 1.36–1.57), and there was a decline in incidence across age groups (age 46–50 *v.* 16–20 years: RR = 0.61, 95% CI 0.54–0.69). The incidence of non-affective psychosis peaked among men aged 16–20 years, and declined steeply thereafter (Fig. 1), whereas women showed a steadier trajectory across the age groups (Fig. 2). Incidence estimates were higher in the low-income areas of the catchment area (lowest *v.* highest: RR = 2.55, 95% CI 2.28–2.85) and among migrant groups (RR = 1.41, 95% CI 1.26–1.59) (Table 3).

Over this same period, 683 people were admitted to the EPI program, yielding an age- and gender-standardized EPI-treated incidence of 18.8 per 100 000 per year (95% CI 17.4–20.3). The trends in effect estimates across subgroups were similar to those found for the total incidence (Table 2), but showed a greater magnitude of effect for gender, age and migrant status (men *v.* women: RR = 3.01, 95% CI 2.53–3.57; age 46–50 *v.* 16–20 years: RR = 0.04, 95% CI 0.02–0.07; migrants *v.* non-migrants: RR = 1.81, 95% CI

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Table 2. Sociodemographic and clinical characteristics of confirmed cases, confirmed non-cases, and suspected cases of incident non-affective psychotic disorder

	Confirmed cases	Confirmed non-cases	Suspected cases	Total cases
	n = 683	*n* = 909	*n* = 1653	*n* = 3245
Variable	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Age at index date				
16–20 years	277 (40.6)	193 (21.2)	158 (9.6)	628 (19.4)
21–25 years	184 (26.9)	142 (15.6)	220 (13.3)	546 (16.8)
26–30 years	88 (12.9)	120 (13.2)	199 (12.0)	407 (12.5)
31–35 years	63 (9.2)	127 (14.0)	236 (14.3)	426 (13.1)
36–40 years	38 (5.6)	117 (12.9)	258 (15.6)	413 (12.7)
41–45 years	22 (3.2)	100 (11.0)	284 (17.2)	406 (12.5)
46–50 years	11 (1.6)	110 (12.1)	298 (18.0)	419 (12.9)
Men	508 (74.4)	492 (54.1)	900 (54.4)	1900 (58.6)
Rural residence	23 (3.4)	24 (2.6)	43 (2.6)	90 (2.8)
Income quintile				
Highest (5)	118 (17.3)	105 (11.6)	195 (11.8)	418 (12.9)
4	94 (13.8)	109 (12.0)	204 (12.3)	407 (12.5)
3	130 (19.0)	149 (16.4)	297 (18.0)	576 (17.8)
2	170 (24.9)	207 (22.8)	386 (23.4)	763 (23.5)
Lowest (1)	169 (24.7)	334 (36.7)	562 (34.0)	1065 (32.8)
Migrant status				
Non-migrants	601 (88.0)	837 (92.1)	1495 (90.4)	2933 (90.4)
Immigrant	45 (6.6)	38 (4.2)	82 (5.0)	165 (5.1)
Refugee	37 (5.4)	34 (3.7)	76 (4.6)	147 (4.5)
Index diagnosis				
Schizophrenia	263 (38.5)	357 (39.3)	780 (47.2)	1400 (43.1)
Delusional disorder	55 (8.1)	83 (9.1)	149 (9.0)	287 (8.8)
Other psychoses	365 (53.4)	469 (51.6)	724 (43.8)	1558 (48.0)
Diagnosing physician				
Family physician	30 (4.4)	131 (14.4)	749 (45.3)	910 (28.0)
Psychiatrist	552 (80.8)	624 (68.6)	542 (32.8)	1718 (52.9)
Family physician + psychiatrist	53 (7.8)	72 (7.9)	75 (4.5)	200 (6.2)
Other	48 (7.0)	82 (9.0)	287 (17.4)	417 (12.9)
Inpatient at index diagnosis	160 (23.4)	164 (18.0)	133 (8.0)	457 (14.1)

1.44–2.28), and were attenuated for neighborhood income quintile (lowest *v.* highest income: RR = 1.43, 95% CI 1.13–1.81) (Table 3).

Among people referred to the program for screening (*n* = 1592), 43% were admitted (men = 51%; women = 30%), with substantial variation by age and gender in the proportion admitted: among men, the admission proportion ranged from 6% for men aged 46–50 years, to 64% for men aged 16–20 years; among women, the admission proportions ranged from 13% for women aged 46–50 years, to 45% for women aged 16–20 years (Figs 1 and 2). If we assume that similar age- and gender-stratified proportions of suspected cases would have been admitted to the EPI program, had they presented for screening, we estimate that the standardized cumulative incidence of first-episode non-affective psychosis in the program catchment area is 33.3 per 100 000 per year (95% CI 31.4–35.1), with a cumulative incidence of 46.3 per 100 000 per year (95% CI 43.1–49.4) for men (Fig. 1), and a cumulative incidence of 20.1 per 100 000 per year (95% CI 18.0–22.1) for women (Fig. 2). Based on these data, we estimate that 38% of men with first-episode psychosis, and 52% of women, are not captured by the EPI sample.

Discussion

Our corrected estimates of the incidence of first-episode non-affective psychotic disorder in the EPI catchment area suggest that the true incidence may be nearly twice as high as the

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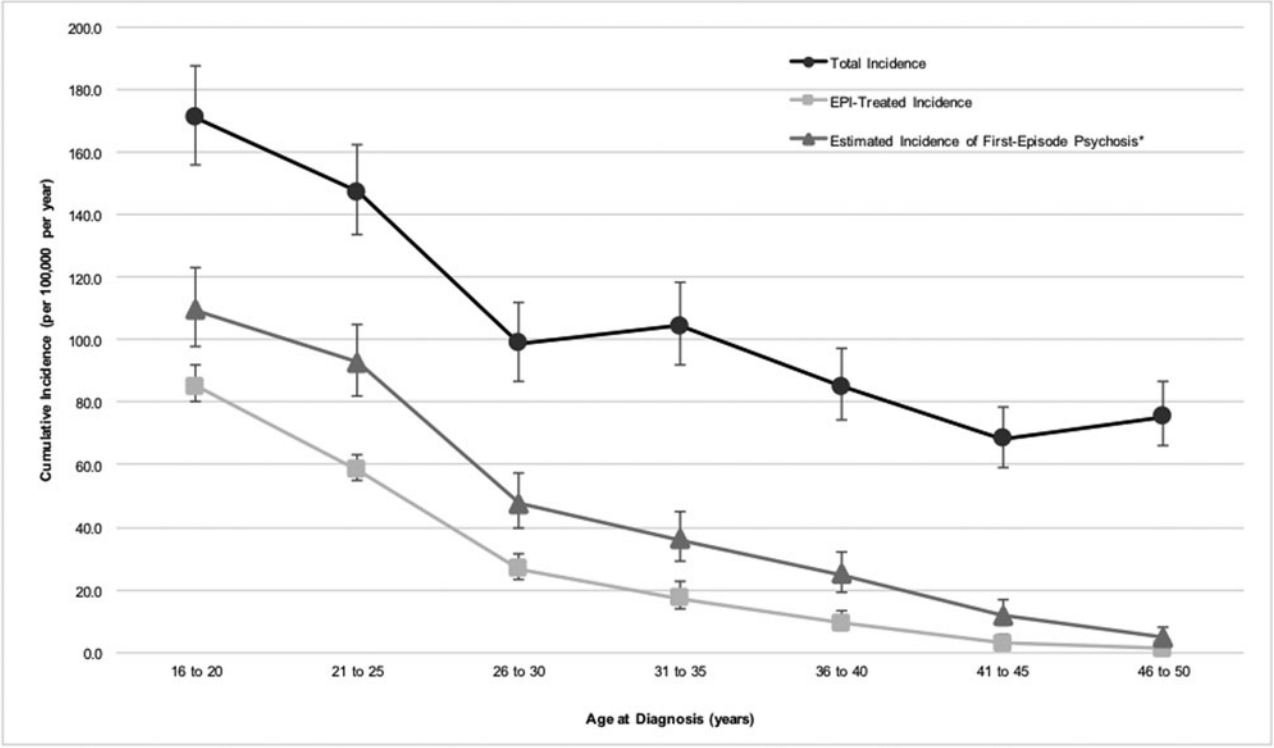

Age Group (years)	Denominator	Confirmed Cases	Confirmed Non-Cases	Suspected Cases	Total	% of Screened Confirmed	Estimated Missed Cases	Proportion Missed	Estimated Incidence of First-Episode Psychosis* (95% CI)
16 to 20	15201	220	124	98	442	64%	63	22%	109.4 (97.6 - 122.9)
21 to 25	15439	153	90	143	386	63%	90	37%	92.6 (81.7 - 104.9)
26 to 30	13714	62	67	101	230	48%	49	44%	47.4 (39.6 - 57.3)
31 to 35	13205	39	74	121	234	35%	42	52%	36.0 (29.0 - 44.8)
36 to 40	14601	23	55	133	211	29%	39	63%	25.1 (19.5 - 32.0)
41 to 45	16650	8	38	147	193	17%	26	76%	11.9 (8.6 - 16.8)
46 to 50	15897	3	44	157	204	6%	10	77%	4.8 (2.8 - 8.2)
TOTAL:	104707	508	492	900	1900	51%	318	38%	46.3 (43.1 - 49.4)**

** Incidence of first-episode psychosis calculated based on confirmed cases and estimated missed cases. The latter was estimated by applying the proportion of referrals who meet criteria for an early psychosis intervention program ($^{\text{confirmed cases}}/_{\text{confirmed cases + confirmed non-cases}}$) applied to the suspected cases.*
*** Age-standardized estimate*

Fig. 1. Age-stratified estimates of the average annual cumulative incidence of non-affective psychotic disorder among men in the catchment area. Incidence estimates reflect the total incidence in the health administrative data, the early psychosis intervention (EPI)-treated incidence, and our adjusted estimates of the incidence of first-episode psychosis.

EPI-treated incidence, leading to a substantial number of missed cases of first-episode psychosis each year. Our various incidence estimates are in line with other reports – ranging from high incidence estimates obtained from population-based health administrative data (69–126 per 100 000 per year/person-years) (Jörgensen *et al.*, 2010; Anderson *et al.*, 2012; Vanasse *et al.*, 2012; Hogerzeil *et al.*, 2014; Kühl *et al.*, 2016; Simon *et al.*, 2017), to the lower estimates of treated incidence obtained in the context of EPI services (21–28 per 100 000 person-years) (Hogerzeil *et al.*, 2014; Kirkbride *et al.*, 2017). However, it is difficult to compare absolute numbers to those obtained in other jurisdictions given that recent evidence suggests up to a 10-fold difference in estimates across countries (Jongsma *et al.*, 2018). Over half of all cases identified by our algorithm had their first presentation to services after age 30, which is similar to previous reports (Simon *et al.*, 2017) and has important implications for the delivery of EPI services, which typically have an upper age limit of 30–35 years (Lappin *et al.*, 2016; Anderson *et al.*, 2018*b*).

There are several potential explanations for the large discrepancy that we observed between incidence estimates obtained from health administrative data and the treated incidence within EPI services. First, not all incident cases of psychotic disorder would meet the case definition for first-episode psychosis as defined by EPI programs, with the latter using a more restrictive criterion for inclusion (Anderson *et al.*, 2012). The operational definition of first-episode psychosis may exclude potential clients based on the duration of psychotic symptoms, duration of antipsychotic medication, or prior help-seeking contacts (Breitborde *et al.*, 2009), and in the case of the EPI program in the current study, exclusions are also made if there is an affective presentation at first onset. Our findings suggest that only 40% of people identified by our case-finding algorithm who were screened by the EPI program were ultimately admitted, which is in line with reported estimates from some programs (O'Donoghue *et al.*, 2012; Clay *et al.*, 2018), but much lower than others (Kirkbride *et al.*, 2017). A recent study used electronic medical records to 'confirm' whether

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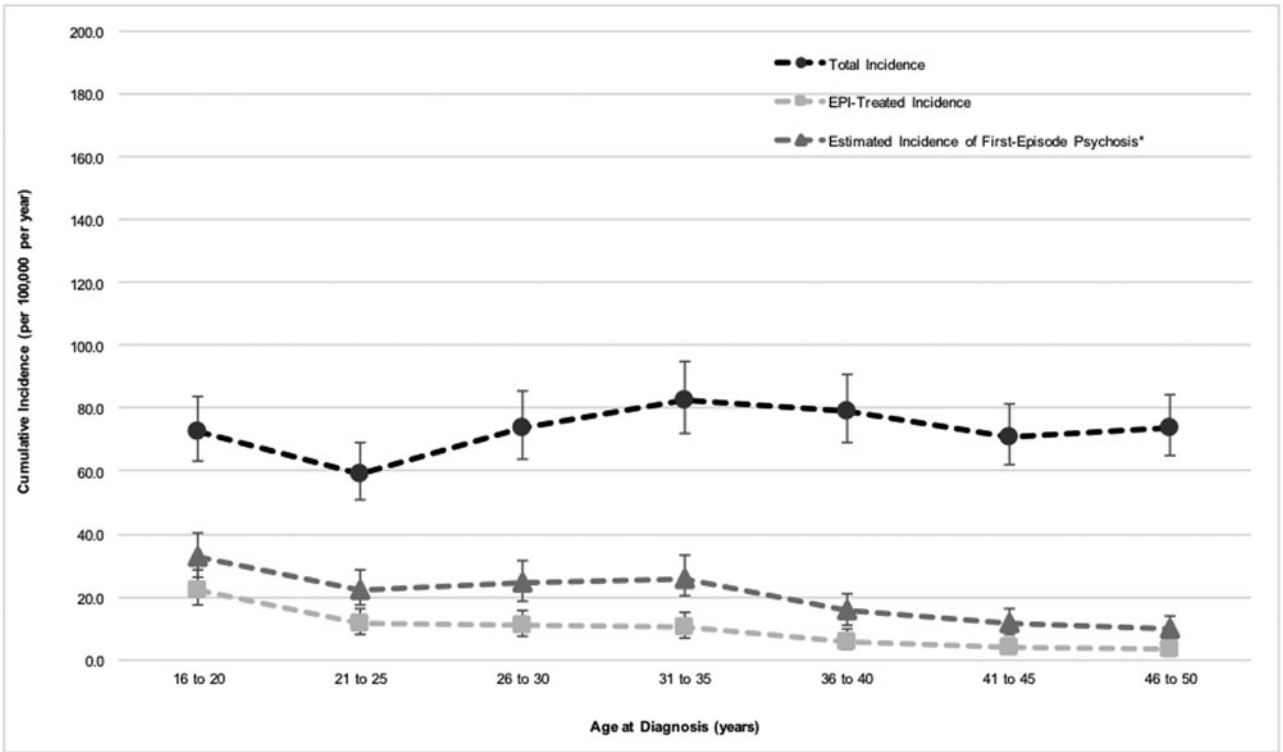

Age Group (years)	Denominator	Confirmed Cases	Confirmed Non-Cases	Suspected Cases	Total	% of Screened Confirmed	Estimated Missed Cases	Proportion Missed	Estimated Incidence of First-Episode Psychosis* (95% CI)
16 to 20	15057	57	69	60	186	45%	27	32%	32.9 (26.5 - 40.6)
21 to 25	15861	31	52	77	160	37%	29	48%	22.2 (17.3 - 28.6)
26 to 30	14091	26	53	98	177	33%	32	55%	24.3 (18.7 - 31.3)
31 to 35	13663	24	53	115	192	31%	36	60%	25.8 (20.1 - 33.2)
36 to 40	15023	15	62	125	202	19%	24	62%	15.4 (11.2 - 20.9)
41 to 45	17492	12	62	137	211	16%	22	65%	11.5 (8.2 - 16.0)
46 to 50	17244	10	66	141	217	13%	19	65%	9.7 (6.9 - 14.2)
TOTAL:	108431	175	417	753	1345	30%	189	52%	20.1 (18.0 - 22.1)**

** Incidence of first-episode psychosis was calculated based on confirmed cases and estimated missed cases. The latter was estimated by applying the proportion of referrals who meet criteria for an early psychosis intervention program ($^{\text{confirmed cases}}/_{\text{confirmed cases + confirmed non-cases}}$) applied to the suspected cases.*
*** Age-standardized estimate*

Fig. 2. Age-stratified estimates of the average annual cumulative incidence of non-affective psychotic disorder among women in the catchment area. Incidence estimates reflect the total incidence in the health administrative data, the early psychosis intervention (EPI)-treated incidence, and our adjusted estimates of the incidence of first-episode psychosis.

cases identified in health administrative data would meet the case definition for first-episode psychosis. These findings suggest that the proportion of confirmed cases varies by age and care setting of initial presentation, ranging from 19–47% for cases identified in non-mental health outpatient settings, to 66–84% for cases diagnosed in an inpatient setting (Simon *et al.*, 2017). This same study also found that the most frequent reasons for not meeting the case definition for first-episode psychosis were a lack of criterion A symptoms required for diagnosis and prior treatment for psychotic disorder, particularly among the older age groups (Simon *et al.*, 2017). We applied the confirmation proportions from this study to our suspected cases group – when combined with the confirmed cases group, this approach yields numbers consistent with our incidence estimates for first-episode non-affective psychosis (38.4 per 100 000 per year – data available on request).

Differences in methodology have also been highlighted as an explanation for discrepant incidence estimates across studies (van der Werf *et al.*, 2014; Moreno-Küstner *et al.*, 2018), and could explain the differences in estimates in the current study. Our estimate of the EPI-treated incidence loosely resembles a first contact incidence study, which has been considered to date as the 'gold standard' methodology for estimating incidence and used in many large-scale international epidemiological studies (Hogerzeil and Susser, 2017). This approach relies on the monitoring of 'entry points' to psychiatric services for case ascertainment, and cases who initially present with other mental disorders are screened out and censored for the remaining follow-up period. Conversely, our estimate of the total incidence obtained from health administrative data more closely resembles a longitudinal sampling frame (Hogerzeil and Susser, 2017), which allows for the presence of other psychiatric symptoms in the evolution of psychotic disorder. Analyses that use a longitudinal sampling frame to estimate the incidence of psychotic disorder find rates that are three times higher than estimates based on a first contact sampling frame (Hogerzeil *et al.*, 2014), largely due to changes in the clinical presentation over time.

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Table 3. Crude and adjusted risk ratios for the early psychosis intervention (EPI)-treated incidence and the total incidence of non-affective psychotic disorder in the program catchment area

	Total incidence		EPI-treated incidence	
Variable	Crude RR (95% CI)	Adjusted RR (95% CI)	Crude RR (95% CI)	Adjusted RR (95% CI)
Gender				
Women	*Ref.*	*Ref.*	*Ref.*	*Ref.*
Men	1.46 (1.36–1.57)	1.46 (1.36–1.56)	3.01 (2.53–3.57)	2.95 (2.48–3.50)
Age at diagnosis				
16–20 years	*Ref.*	*Ref.*	*Ref.*	*Ref.*
21–25 years	0.84 (0.75–0.94)	0.84 (0.75–0.95)	0.64 (0.53–0.77)	0.65 (0.54–0.78)
26–30 years	0.71 (0.62–0.80)	0.71 (0.62–0.80)	0.35 (0.27–0.44)	0.35 (0.27–0.44)
31–35 years	0.76 (0.68–0.86)	0.77 (0.68–0.87)	0.26 (0.19–0.34)	0.26 (0.20–0.34)
36–40 years	0.67 (0.59–0.76)	0.67 (0.60–0.76)	0.14 (0.10–0.20)	0.14 (0.10–0.20)
41–45 years	0.57 (0.50–0.65)	0.57 (0.51–0.65)	0.06 (0.04–0.10)	0.06 (0.04–0.10)
46–50 years	0.61 (0.54–0.69)	0.62 (0.55–0.70)	0.04 (0.02–0.07)	0.04 (0.03–0.08)
Income quintile				
Highest (5)	*Ref.*	–	*Ref.*	–
4	0.97 (0.85–1.12)		0.80 (0.61–1.04)	
3	1.38 (1.21–1.56)		1.10 (0.86–1.41)	
2	1.83 (1.62–2.06)		1.44 (1.14–1.82)	
Lowest (1)	2.55 (2.28–2.85)		1.43 (1.13–1.81)	
Migrant status				
Non-migrant	*Ref.*	–	*Ref.*	–
Migrant	1.41 (1.26–1.59)		1.81 (1.44–2.28)	

EPI, early psychosis intervention; RR, risk ratio; CI, confidence interval; Ref., reference category.

Similar to our findings, known risk factors for psychotic disorder, such as gender and ethnic minority status, are attenuated when using a longitudinal *v.* a first contact sampling frame (Hogerzeil *et al.*, 2014, 2017), although our findings suggest greater disparities by neighborhood income quintile for a longitudinal sampling frame, which has not been reported previously. This raises the question of the extent to which the evidence on these well-established risk factors for psychotic disorder may have been conflated with factors that impact on access to specialized psychiatric services. Given that most prior studies on risk factors for psychosis were based on a first contact sampling frame, which may have missed over half of incident cases, this prior knowledge on the etiology of psychotic disorders may have consequently been impacted by selection bias (Hogerzeil *et al.*, 2014). To address these issues, Hogerzeil and Susser (2017) have recently proposed a new 'hybrid design', which would combine the validity of a first contact sampling frame (e.g. standardized diagnoses) with the comprehensiveness of a longitudinal sampling frame as the new gold standard for incidence estimation (Hogerzeil and Susser, 2017).

Prior studies also vary widely in the type of data that are included, ranging from data from specialized services only (e.g. inpatient unit, EPI program) to data from all types of service providers. Estimates of the incidence and prevalence of psychotic disorder can vary widely depending on whether outpatient data are included in the case-finding algorithm (Jörgensen *et al.*, 2010; Vanasse *et al.*, 2012), and may also lead to a narrowing of the gender differential in incidence rates if men are more likely to be treated in an inpatient setting (Anderson, 2013). Commonly accepted estimates of the incidence of psychotic disorder obtained from meta-analyses are almost entirely based on first contact samples (van der Werf *et al.*, 2014), and only a third of included studies include primary care in case ascertainment (Castillejos *et al.*, 2018). As such, the use of these estimates for the planning and evaluation of EPI services may underestimate the program case load.

Another explanation for the discrepancy in incidence estimates could arise from the validity of the algorithm used to identify cases in health administrative data. In the current study, we used a slightly more conservative algorithm than one validated previously, which has a moderate positive predictive value (62%) and a high negative predictive value (90%), and was validated for chronic psychotic illness rather than first-episode cases (Kurdyak *et al.*, 2015). These numbers suggest that we have likely captured some false positives in our study sample, with relatively few missed cases. There is likely some degree of overascertainment across all studies using health administrative data, where diagnostic codes are assigned based on clinical records rather than a standardized diagnostic interview. However, prior reports suggest that physicians are typically cautious when assigning diagnoses of psychotic disorder (Goldner *et al.*, 2003), and sensitivity analyses of estimates obtained from

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health administrative data do not find evidence of overdiagnosis (Hogerzeil *et al.*, 2014). The case-finding algorithms also do not typically account for changes in diagnostic trajectories over time, such as from non-affective to affective psychosis (Fusar-Poli *et al.*, 2016b), or may have detected transient or self-limiting cases of psychosis that could resolve without intervention from an EPI program (Fusar-Poli *et al.*, 2016*a*).

Finally, it is highly likely that EPI services are missing a substantial number of cases of first-episode psychosis – our estimates suggest that as many as half of all cases are being missed, with increasing proportions in older age groups, which we have discussed in detail in other reports (Anderson *et al.*, 2018*b*). This is consistent with a recent multi-site first contact incidence project, where a leakage study found that up to half of cases at one site (Brazil) were missed by psychiatric services, with considerable variation (10–50%) across sites (Jongsma *et al.*, 2018). The extent of missed cases will likely vary across jurisdictions due to differences in the health system context and local availability of resources. Even if only a small fraction of our non-users group were true cases of first-episode psychosis, the EPI program would be missing a substantial number of people, thus highlighting the need to consider cases receiving care outside of the specialized mental health sector when computing incidence estimates. Furthermore, these findings also highlight the need to re-evaluate the inclusion criterion for EPI programs to ensure that people with newly diagnosed psychotic disorder who may not meet the operational definition of first-episode psychosis will still have the opportunity to benefit from early intervention.

Limitations

We do not know how many people in our suspected cases group would be eligible for EPI services. We have attempted to estimate this using available data on the proportion of referrals admitted; however, the suspected cases group might be expected to have a lower acceptance rate. Additionally, we do not have information on the reasons behind non-admission of the 'confirmed non-case' group – some of these people did not meet the diagnostic criteria for non-affective psychosis, whereas others would be a 'non-case' for reasons such as duration of prior antipsychotic use, involvement of the criminal justice system, or an unwillingness to engage with the program. The former group should be excluded from incidence estimates, and the latter included; however, the health administrative data did not contain sufficient information to allow us to make this distinction. Our estimates of the incidence of first-episode psychosis could have been further refined through the inclusion of data on prior antipsychotic medication use, which is an exclusion for many EPI programs, but the lack of a universal pharmacare program in Ontario precluded this. Our denominator data were obtained from the Canadian census, and we used the midpoint of the 17-year study period for the estimation of cumulative incidence – however, the size of population in the program catchment area increased by 13% over this period (Statistics Canada, 2007), and this change in denominator would impact our estimates. The incidence estimates that we computed reflect diagnosed incidence, and not the incidence in the community, and may therefore be underestimated. Prevalence estimates obtained using a general population sampling frame are higher than those using a health services sampling frame (Moreno-Küstner *et al.*, 2018), suggesting that we may have missed some cases who do not present to health services. Our case-finding algorithm excluded people who had only one outpatient visit for non-affective psychotic disorder, as inclusion of these people would have further increased the number of false-positive cases in our sample (positive predictive value = 57%). However, if some of these visits represented true cases of non-affective psychotic disorder, then this exclusion would underestimate the incidence to an even greater extent than we report. Further research is warranted to better understand this 'single visit' group and the implications for epidemiologic estimates and service delivery. Finally, our case definition was limited to non-affective psychotic disorders in keeping with the inclusion criteria for the EPI program, and our estimates do not include people with affective psychotic disorders or substance-induced psychosis, although the latter may have been coded as psychosis NOS and captured by our estimates.

Conclusions

Our findings suggest that incidence estimates limited to specialized psychiatric services may substantially underestimate the incidence of first-episode non-affective psychotic disorders, relative to population-based estimates. Conversely, not all incident cases of psychotic disorder would meet the case definition for first-episode psychosis. We need accurate information on the epidemiology of first-episode psychosis to allow service planners and administrators to more effectively resource EPI services and evaluate their coverage.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0033291718002933.

Data. The dataset from this study is held securely in coded form at ICES and the ICES analyst (CL) had full access to study data. While data sharing agreements prohibit ICES from making the dataset publicly available, access can be granted to those who meet pre-specified criteria for confidential access, available at http://www.ices.on.ca/DAS. The full dataset creation plan is available from the authors upon request.

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