The Incidence of Psychotic Disorders and Area-level Marginalization in Ontario, Canada: A Population-based Retrospective Cohort Study

L’incidence des troubles psychotiques et de la marginalisation au niveau régional en Ontario, Canada: une étude de cohorte rétrospective dans la population

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Abstract

Background: There is limited Canadian evidence on the impact of socio-environmental factors on psychosis risk. We sought to examine the relationship between area-level indicators of marginalization and the incidence of psychotic disorders in Ontario.

Methods: We conducted a retrospective cohort study of all people aged 14 to 40 years living in Ontario in 1999 using health administrative data and identified incident cases of psychotic disorders over a 10-year follow-up period. Age-standardized incidence rates were estimated for census metropolitan areas (CMAs). Poisson regression models adjusting for age and sex were used to calculate incidence rate ratios (IRRs) based on CMA and area-level marginalization indices.

Results: There is variation in the incidence of psychotic disorders across the CMAs. Our findings suggest a higher rate of psychotic disorders in areas with the highest levels of residential instability (IRR = 1.26, 95% confidence interval [CI], 1.18 to 1.35), material deprivation (IRR = 1.30, 95% CI, 1.16 to 1.45), ethnic concentration (IRR = 1.61, 95% CI, 1.38 to 1.89), and dependency (IRR = 1.35, 95% CI, 1.18 to 1.54) when compared to areas with the lowest levels of marginalization. Marginalization attenuates the risk in some CMAs.

Conclusions: There is geographic variation in the incidence of psychotic disorders across the province of Ontario. Areas with greater levels of marginalization have a higher incidence of psychotic disorders, and marginalization attenuates the differences in risk across geographic location. With further study, replication, and the use of the most up-to-date data, a case may be made to consider social policy interventions as preventative measures and to direct services to areas with the highest risk. Future research should examine how marginalization may interact with other social factors including ethnicity and immigration.

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Introduction

The seminal work of Faris and Dunham conducted in Chicago in the 1930s provided empirical evidence that the incidence of non-affective psychotic disorders varied based on geographical and neighbourhood-level sociodemographic factors. It was observed that in neighbourhoods with increasing levels of social disorganization, there was a higher incidence of schizophrenia. In the intervening years since this early work, and with the advent of improved epidemiological methods, many studies have examined this association and similarly found area-level social factors to be associated with the risk of developing a psychotic disorder. Most of the research examining the social causes of psychotic disorders have been conducted in Europe. The international research has highlighted that people living in the most deprived neighbourhoods are at higher risk of having a psychotic disorder. The most recent epidemiological work from several European countries has also highlighted large differences in the incidence of psychotic disorders between different cities and urban contexts.

In Canada, there is a small but growing body of research on the role of social factors which may influence both the incidence and course of psychotic disorders. This is an important area of study considering prior work conducted in Ontario has found people with schizophrenia have a 3-fold increase in all-cause mortality when compared to the general population and high levels of ongoing health service use. In Ontario, the largest province in Canada, we know that where people live impacts how they use services. People who live in more deprived areas use more mental health services. In Toronto, the largest and most diverse city in the province, presentation to emergency mental health services for psychosis differs based on the level of marginalization of the neighbourhood in which people reside. Although there is prior Canadian research on health service use in this clinical population, there has been limited study of the role of social factors in the risk of developing a psychotic disorder in the Canadian context. One study in Ontario has looked at the risk of developing a psychotic disorder in immigrant and refugee groups, finding that some migrant groups have an elevated risk whereas others have a lower risk.

In Quebec, the second largest province, health administrative data have been used to examine the role of socio-environmental and geographical factors in the risk of developing first-episode psychosis. Similar to international work on this topic, there was a higher incidence of psychosis in the most deprived areas in Montreal. Differences in the incidence rates of schizophrenia between Quebec City and Montréal, 2 of the main metropolitan centres in the province, and between urban and rural areas have also been found.

The aim of the study was to examine the geographical distribution and the role of area-level marginalization indicators on the incidence of schizophrenia spectrum psychotic disorders in Ontario. We hypothesize that (i) there will be
variation in incidence between major metropolitan centres and (ii) there will be a higher incidence in areas with the highest levels of marginalization.

Methods
Study Design, Setting, and Population
We constructed a retrospective cohort that included all Ontario residents aged 14 to 40 years as of April 1, 1999, using data from the universal public health insurance plan, which has been described in detail previously. The cohort was followed for 10 years to ascertain incident cases of psychotic disorders. These ages were used as it would allow for a 10-year follow-up period beyond the maximum age of some of the early psychosis intervention programme in Ontario. The cohort was constructed from the administrative data holdings at ICES (formerly known as the Institute for Clinical Evaluative Sciences), which enables linkage of individual records from multiple health administrative databases across the province of Ontario.

At the time of cohort inception, approximately 11.5 million people resided in Ontario. All individuals included in the cohort were eligible for the Ontario Health Insurance Plan (OHIP), the provincially administered health insurance plan, in the 5 years prior to cohort inception. All long-term residents who primarily reside in Ontario are eligible for OHIP.

Person-time of follow-up was calculated for each person in the cohort from the time of cohort inception until an index episode of a psychotic disorder, death, or the end of the follow-up period. Those who had a history of contact with health services in Ontario for a psychotic disorder up to 20 years prior to the cohort start date, dependent on the databases, were removed to ensure incident cases were identified. This lookback window is in keeping with the optimal lookback period described in the literature. All covariates were defined at the time of cohort inception.

Data Sources
Sources of data included the Registered Persons Database which is a central population registry containing basic demographic information that enables linkage across administrative data by identifying all Ontario residents insured by OHIP; the Ontario Mental Health Reporting System containing data on hospitalizations to adult psychiatry beds; the Canadian Institute for Health Information Discharge Abstract Database containing data on all other acute care hospitalizations and inpatient psychiatric hospitalizations prior to 2005; the National Ambulatory Care Reporting System containing information on emergency department visits; data on outpatient physician billings from OHIP; and the Ontario Marginalization Index (ON-Marg) containing area-level deprivation indices based on census data.

Case Ascertainment
Incident cases of psychotic disorders were identified over the 10-year follow-up window of 1999 to 2008 inclusive. Incident cases of psychotic disorders were based on either (i) a primary discharge diagnosis from a general hospital bed with a diagnosis of schizophrenia or schizoaffective disorder based on International Classification of Diseases (ICD)-9 code 295.x, or ICD-10 code F20 or F25, (ii) a primary discharge diagnosis of schizophrenia or schizoaffective disorder from a psychiatric hospital bed based on Diagnostic and Statistical Manual of Mental Disorders, fourth edition code 295.x, or (iii) a minimum of 2 OHIP billing claims or emergency department visits with a diagnostic code for schizophrenia or schizoaffective disorder (ICD-9 code 295.x, or ICD-10 code F20 or F25) in a 12-month period. Previous research has validated a similar algorithm for case ascertainment against medical chart diagnoses and found high sensitivity (91.6%) and moderate specificity (67.4%).

Covariates and Exposure Classification
The socio-environmental exposures of interest included (i) where people in the cohort reside in the province based on census metropolitan area (CMA) and (ii) area-level indicators of marginalization.

(i) CMAs. The CMA of each cohort member was identified based on postal code linkage at the time of cohort entry. A CMA is a census geography that consists of 1 or more municipalities situated around a core urban area. All CMAs have a total population of at least 100,000 people, of which at least 50,000 live in an urban core. The areas surrounding the urban core have a high degree of integration with the core. Of note, some areas within the CMA that are outside the urban core may be classified as rural and described as the rural fringe; however, these areas have a high degree of integration and exposure to the urban population centre. For the purpose of this study, we are comparing people who reside in each of the province’s largest metropolitan population centres relative to those who reside in all other non-urban areas and smaller population centres.

(ii) Area-level indicators of marginalization. Exposure to area-level marginalization was captured by linking postal codes for all cohort members at the time of cohort entry to marginalization data from the ON-Marg. The ON-Marg is based on census data and is comprised of 4 factors (constructed from principal component factor analysis) and 18 census indicators presented in Table 1. The index is updated at regular intervals with the most recent census data available; for the current study, the 2006 indicators were used. The factors cover 4 distinct dimensions of marginalization: (i) material deprivation, an indicator of area levels of poverty and inability to access and attain basic material needs; (ii) residential instability, an indicator of housing or
family instability; (iii) dependency, an indicator of the concentration of people who do not have income from employment or may not be compensated for their work; and (iv) ethnic concentration, an indicator of the concentration of people who are immigrants and/or self-identify as belonging to a visible minority group. For each dimension, scores were divided into quintiles based on the provincial distribution, with the first quintile representing the least marginalized areas and the fifth quintile representing the most marginalized areas.

### Statistical Analyses

We summarized baseline characteristics of the cohort using descriptive statistics, specifically means and standard deviations (SD) for continuous data and proportions for categorical data. Age- and sex-standardized incidence rates were calculated per 100,000 person-years for the entire province and for the CMAs, using the 1996 population of Canada as the standard population to facilitate comparison across geographies by adjusting to the age structure of the standard population. The 1996 census was used as this was the last census prior to cohort entry. Sex-stratified age-standardized rates were also calculated, as the risk of psychotic disorders differs between males and females.

We used multivariable Poisson regression models to obtain adjusted incidence rate ratios (IRRs) with 95% confidence intervals (CIs). Complete case analyses were used for all regression models. We first fit a model for the incidence in each CMA, relative to people not living in a CMA, while adjusting for age and sex. We then proceeded to fit a model that accounted for exposure to area-level marginalization, in addition to CMA, while adjusting for age and sex.

Poisson regression models were compared to negative binomial models—given that the model estimates were similar, the data were not overdispersed, and the results of the Poisson regression were presented.

All statistical analyses were conducted using Stata version 16.1 and presented as incidence rates or IRRs with 95% CIs, and confidence intervals that do not include unity are considered statistically significant. Mapping of incidence estimates was conducted using QGIS version 3.6.

### Ethics Approval

Ethics approval for this study was obtained from the research ethics board at the Centre for Addiction and Mental Health, Toronto, Ontario, Canada.

### Results

The cohort included 4,284,694 people, of whom 50% (n = 2,158,166) were male. Of the total cohort, 0.7% (n = 32,017) people were unable to be linked to the ON-Marg database due to missing postal code information and were excluded from the analyses. Baseline characteristics of the cohort are presented in Table 2. There were 25,686 incident cases of psychotic disorder, of whom 62% (n = 15,809) were male and 38% (n = 9,877) were female. The mean age at the time of cohort entry was 28.0 years (SD = 7.9), and the mean age at the time of index diagnosis was 32.5 years (SD = 8.6).

The age- and sex-standardized incidence rate of psychotic disorders among the entire cohort was 54.9 (95% CI, 53.6 to 56.3) per 100,000 person-years. Incidence rates by CMA are visualized in Figure 1 and presented in Online
Table 2. Sociodemographic Characteristics of the Cohort Aged 14 to 40 Years Living in Ontario as of April 1, 1999.

| Characteristic                  | Provincial Population (n = 4,284,699); Mean ± SD and no. (%) | Male (n = 2,158,166); Mean ± SD and no. (%) | Female (n = 2,126,533); Mean ± SD and no. (%) | All Incident Cases (n = 25,686); Mean ± SD and no. (%) | Incident Male Cases (n = 15,809); Mean ± SD and no. (%) | Incident Female Cases (n = 9,877); Mean ± SD and no. (%) |
|--------------------------------|---------------------------------------------------------------|------------------------------------------------|-----------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------|
| Age at cohort entry (years)    | 28.0 ± 7.9                                                    | 27.9 ± 7.9                                      | 28.1 ± 7.9                                     | 26.8 ± 8.1                                                | 25.8 ± 8.1                                                | 28.6 ± 7.8                                                |
| Age at index diagnosis (years) | —                                                             | —                                              | —                                             | —                                                        | —                                                        | —                                                        |
| Marginalization (quintiles)    |                                                               |                                                |                                               |                                                          |                                                          |                                                          |
| Instability                    |                                                               |                                                |                                               |                                                          |                                                          |                                                          |
| 1 (lowest)                     | 545,443 (12.9)                                                | 272,007 (12.7)                                 | 274,436 (13)                                  | 2,560 (10)                                                | 1,516 (10)                                                | 944 (10)                                                  |
| 2                              | 423,759 (10)                                                  | 211,337 (9.9)                                  | 212,422 (10.1)                                | 1,771 (7)                                                 | 1,067 (7)                                                 | 704 (7)                                                   |
| 3                              | 454,368 (10.7)                                                | 228,856 (10.7)                                 | 225,512 (10.7)                                | 2,326 (9)                                                 | 1,423 (9)                                                 | 903 (9)                                                   |
| 4                              | 355,123 (8.4)                                                 | 179,128 (8.4)                                  | 175,995 (8.3)                                 | 2,005 (8)                                                 | 1,254 (8)                                                 | 751 (8)                                                   |
| 5 (highest)                    | 2,472,989 (58.2)                                             | 1,250,386 (58.4)                               | 1,222,603 (57.9)                               | 16,902 (66)                                               | 10,398 (66)                                               | 6,504 (66)                                                |
| Deprivation                    |                                                               |                                                |                                               |                                                          |                                                          |                                                          |
| 1 (lowest)                     | 740,094 (17.4)                                               | 267,284 (17.2)                                 | 372,810 (17.7)                                | 3,238 (13)                                                | 1,960 (13)                                                | 1,278 (13)                                                |
| 2                              | 1,129,498 (26.6)                                             | 567,188 (26.5)                                 | 562,310 (26.6)                                | 6,118 (24)                                                | 3,749 (24)                                                | 2,369 (24)                                                |
| 3                              | 522,792 (12.3)                                               | 262,463 (12.3)                                 | 260,329 (12.3)                                | 3,191 (13)                                                | 1,959 (13)                                                | 1,232 (13)                                                |
| 4                              | 1,761,747 (41.4)                                             | 894,342 (41.8)                                 | 867,405 (41.1)                                | 12,259 (48)                                               | 7,574 (48)                                                | 4,685 (48)                                                |
| 5 (highest)                    | 98,551 (2.3)                                                 | 50,437 (2.4)                                   | 48,114 (2.3)                                  | 658 (3)                                                   | 416 (3)                                                   | 242 (2)                                                   |
| Ethnic concentration           |                                                               |                                                |                                               |                                                          |                                                          |                                                          |
| 1 (lowest)                     | 47,971 (1.1)                                                 | 24,922 (1.2)                                   | 23,049 (1.1)                                  | 217 (1)                                                   | 144 (1)                                                   | 73 (1)                                                    |
| 2                              | 114,704 (2.7)                                                | 58,899 (2.8)                                   | 55,805 (2.6)                                  | 565 (2)                                                   | 346 (2)                                                   | 219 (2)                                                   |
| 3                              | 294,643 (6.9)                                                | 149,759 (7)                                    | 144,884 (6.9)                                 | 1,397 (5)                                                 | 910 (6)                                                   | 487 (5)                                                   |
| 4                              | 510,910 (12)                                                 | 258,404 (12.1)                                 | 252,506 (12)                                  | 2,749 (11)                                                | 1,743 (11)                                                | 1,006 (10)                                                |
| 5 (highest)                    | 3,284,454 (77.2)                                             | 1,649,730 (77)                                 | 1,634,724 (77.4)                               | 20,536 (81)                                               | 12,515 (80)                                               | 8,021 (82)                                                |
| Dependency                     |                                                               |                                                |                                               |                                                          |                                                          |                                                          |
| 1 (lowest)                     | 1,501,595 (35.3)                                             | 748,266 (34.9)                                 | 753,329 (35.7)                                 | 7,682 (30)                                                | 4,649 (30)                                                | 3,033 (31)                                                |
| 2                              | 1,903,934 (44.8)                                             | 964,903 (45.1)                                 | 939,031 (44.5)                                | 12,793 (50)                                               | 7,900 (50)                                                | 4,893 (50)                                                |
| 3                              | 455,330 (10.7)                                               | 229,770 (10.7)                                 | 225,560 (10.7)                                | 2,657 (10)                                                | 1,677 (11)                                                | 980 (10)                                                   |
| 4                              | 301,056 (7.1)                                                | 152,460 (7.1)                                  | 148,596 (7)                                   | 1,765 (7)                                                 | 1,082 (7)                                                 | 683 (7)                                                   |
| 5 (highest)                    | 90,767 (2.1)                                                 | 46,315 (2.2)                                   | 44,452 (2.1)                                  | 567 (2)                                                   | 350 (2)                                                   | 217 (2)                                                   |
Appendix 1. Across the province, there was a higher incidence among males, with an age-standardized incidence rate of 67.4 (95% CI, 65.4 to 69.6) per 100,000 person-years, compared to an age-standardized incidence rate of 42.4 (95% CI, 40.8 to 44.1) per 100,000 person-years in females. Incidence rates varied between CMAs across the province. For the entire cohort, standardized incidence rates ranged from 51.4 (95% CI, 50.1 to 52.7) per 100,000 person-years in people residing outside of CMAs to 74.5 (95% CI, 73.0 to 76.1) per 100,000 person-years in Kingston.

We found the risk of developing a psychotic disorder was higher in specific CMAs and was associated with area-level marginalization (Table 3). The rates of psychotic disorder were significantly elevated in Kingston, Belleville, Peterborough, Toronto, Hamilton, St. Catharines, Brantford, Guelph, London, Windsor, Sarnia, and Sudbury, when compared to those who were not residing in a CMA and without area-level marginalization being taken into account. The highest risk was observed in Kingston (IRR = 1.48, 95% CI, 1.27 to 1.62) when compared to non-CMAs.

Marginalization attenuated the IRR when added to the model, whereby previously significant IRRs in many of the CMAs are no longer statistically significant when compared to non-CMA areas. When area-level marginalization is taken into account, the elevated risk persists in Kingston (IRR = 1.20, 95% CI, 1.05 to 1.37), Guelph (IRR = 1.23, 95% CI, 1.06 to 1.41), Sarnia (IRR = 1.24, 95% CI, 1.05 to 1.46), and a marginally elevated risk in Toronto (IRR = 1.04, 95% CI, 1.00 to 1.08). With these additional factors accounted for, we found a lower risk of developing a psychotic disorder in Hamilton (IRR = 0.86, 95% CI, 0.80 to 0.92) and Windsor (IRR = 0.90, 95% CI, 0.82 to 0.99) when compared to non-CMA areas.

We found higher risk of psychotic disorders in areas with higher levels of marginalization for each of the 4 indicators, when compared to areas with the lowest levels of
Table 3. Age- and Sex-adjusted Incidence Rate Ratios by Census Metropolitan Areas (CMAs) Compared to Non-CMAs in Ontario and Model with Marginalization Factors.

| Variable                      | Model 1 Adjusted IRR (95% CI) | Model 2 Adjusted IRR (95% CI) |
|-------------------------------|-------------------------------|-------------------------------|
| CMAs                          | Ref.                          | Ref.                          |
| Ottawa–Gatineau               | 1.01 (0.94 to 1.07)           | 0.93 (0.86 to 1.01)           |
| Kingston                      | 1.48 (1.27 to 1.62)           | 1.20 (1.05 to 1.37)           |
| Belleville                    | 1.37 (1.12 to 1.68)           | 1.14 (0.92 to 1.42)           |
| Peterborough                  | 1.36 (1.16 to 1.58)           | 1.01 (0.85 to 1.20)           |
| Oshawa                        | 1.08 (0.99 to 1.18)           | 1.01 (0.92 to 1.12)           |
| Toronto                       | 1.36 (1.10 to 1.17)           | 1.04 (1.00 to 1.08)           |
| Hamilton                      | 1.06 (1.00 to 1.12)           | 0.86 (0.80 to 0.92)           |
| St. Catharines                 | 1.15 (1.11 to 1.47)           | 0.99 (0.91 to 1.09)           |
| Niagara                       |                               |                               |
| Kitchener                     | 1.06 (0.98 to 1.14)           | 1.02 (0.93 to 1.11)           |
| Brantford                     | 1.28 (1.11 to 1.47)           | 0.98 (0.85 to 1.14)           |
| Guelph                        | 1.33 (1.16 to 1.53)           | 1.23 (1.06 to 1.41)           |
| London                        | 1.16 (1.08 to 1.25)           | 0.97 (0.88 to 1.06)           |
| Windsor                       | 1.17 (1.07 to 1.28)           | 0.90 (0.82 to 0.99)           |
| Sarnia                        | 1.18 (1.02 to 1.37)           | 1.24 (1.05 to 1.46)           |
| North Bay                     | 1.12 (0.94 to 1.34)           | 0.87 (0.72 to 1.04)           |
| Greater Sudbury               | 1.19 (1.03 to 1.37)           | 1.14 (0.98 to 1.33)           |
| Sault Ste. Marie              | 0.94 (0.80 to 1.10)           | 0.88 (0.73 to 1.05)           |
| Thunder Bay                   | 1.13 (0.99 to 1.29)           | 1.09 (0.94 to 1.26)           |

Marginalization

| Instability (quintiles)       | Ref.                          |
|-------------------------------|-------------------------------|
| 1                             | —                             |
| 2                             | 0.97 (0.91 to 1.04)           |
| 3                             | 1.09 (1.02 to 1.16)           |
| 4                             | 1.23 (1.15 to 1.32)           |
| 5                             | 1.26 (1.18 to 1.35)           |

| Deprivation (quintiles)       | Ref.                          |
|-------------------------------|-------------------------------|
| 1                             | —                             |
| 2                             | 1.13 (1.07 to 1.19)           |
| 3                             | 1.11 (1.02 to 1.19)           |
| 4                             | 1.20 (1.11 to 1.29)           |
| 5                             | 1.30 (1.16 to 1.45)           |

| Ethnic Concentration (quintiles) | Ref.                          |
|----------------------------------|-------------------------------|
| 1                                | —                             |
| 2                                | 1.21 (1.03 to 1.42)           |
| 3                                | 1.22 (1.04 to 1.42)           |
| 4                                | 1.29 (1.11 to 1.51)           |
| 5                                | 1.61 (1.38 to 1.89)           |

| Dependency (quintiles)          | Ref.                          |
|---------------------------------|-------------------------------|
| 1                                | —                             |
| 2                                | 1.13 (1.06 to 1.20)           |
| 3                                | 1.13 (1.03 to 1.23)           |
| 4                                | 1.17 (1.06 to 1.28)           |
| 5                                | 1.35 (1.18 to 1.54)           |

Notes. IRR = incidence rate ratio. CI = confidence interval. Ref. = reference category. *Unless otherwise indicated; statistically significant results bolded.

dependency (IRR = 1.35, 95% CI, 1.18 to 1.54) when compared to areas with the lowest levels of marginalization on these indicators.

Discussion

In this study, we found differences in the incidence rates of psychotic disorders across geographic areas in the province of Ontario. There are differences in incidence rates between males and females, and differences between major metropolitan areas, when compared to areas outside of metropolitan areas. Approximately 40% of incident cases occurred outside of the major metropolitan areas in the province. Some geographical differences remain when area-level marginalization is considered, although the effects are attenuated. Greater levels of marginalization on each of the 4 factors were associated with a higher incidence of psychotic disorders.

Before accounting for marginalization, we observed significantly elevated rates of psychotic disorder in smaller metropolitan areas in Southeastern Ontario, specifically in Kingston, Belleville, and Peterborough. There were also elevated rates in South Western Ontario in Guelph, London, Windsor, and Sarnia. In Northern Ontario, there were elevated rates in Sudbury. Toronto, the largest city in Ontario, also has an elevated rate of psychotic disorders, compared to non-metropolitan areas.

Marginalization attenuates differences in risk across metropolitan areas. We found lower rates in Windsor and Hamilton when area-level marginalization was accounted for. The rates in Kingston, Guelph, and Sarnia remain elevated, albeit with attenuated effects. This suggests that area-level marginalization may play an important role in explaining geographic differences in the risk of developing a psychotic illness.

Previous literature has highlighted elevated rates of psychotic illness in urban areas. In the current study, we looked at rates among people residing in major metropolitan areas, which include urban areas and surrounding areas that are integrated with the urban core. This suggests that contextual factors associated with geography are important to consider. Some of the marginalization factors examined in this study may be present at different levels in metropolitan and non-metropolitan areas, which can increase the risk of developing a psychotic disorder. Therefore, there may be marginalized areas in both metropolitan and non-metropolitan areas which may have elevated risk. Although greater levels of ethnic concentration may be largely located in urban environments, areas with high levels of material deprivation and dependency are present in rural regions of the province.

In the current study, areas with the highest levels of ethnic concentration had the highest risk of psychotic disorders. Previous work looking at the risk of developing psychotic disorders among immigrant and refugee populations in Ontario has found that there are elevated rates of psychosis in some immigrant groups and lower rates in others. The current study does not account for individual-level immigration.
status, which would be important to further understand the role of area-level ethnic concentration, which takes into account both visible minority status and immigrant concentration. Previous work in Europe has found that ethnic density, which looks at the concentration of people of a similar ethnic background in an area, moderates risk of psychosis in ethnic minority groups, who may have an elevated baseline risk compared to the general population.\textsuperscript{30,31} Although there may be some similarities between ethnic concentration and ethnic density, it is not the same measure, as the latter implies same-group ethnic density, and we do not know the ethnic backgrounds of people in the current study nor the specific ethnic breakdown in the areas in which they reside. There has yet to be work conducted in Ontario that looks at the incidence of psychotic disorder in relation to ethnic minority status or racialized identity.

\textbf{Limitations}

This study is limited by the fact that exposure to area-level marginalization was defined at the time of cohort entry, and we did not account for changes in exposure during the follow-up period. Furthermore, any movement between geographical areas was not accounted for and may have influenced exposure and risk. Prior research suggests that following the first episode of psychosis, people may move to both areas of higher and lower marginalization.\textsuperscript{32,33} This study only accounts for marginalization at the area level, and it is important to highlight that individual-level data on sociodemographic factors were not available, including individual-level immigration history. Previous research has found that neighbourhood-level factors moderate the role of individual-level social factors in relation to psychosis risk.\textsuperscript{29,30}

This study used administrative health data that were not collected to specifically answer the research questions we posed. To reduce potential misclassification, we used a validated algorithm to identify incident cases.\textsuperscript{21} The algorithm was created to identify cases of chronic schizophrenia; however, in this study, we are using it to identify incident cases of psychotic disorder, and it may therefore have different psychometric properties. The algorithm has a positive predictive value of 67.4\%, which suggests that some cases identified in this cohort may be false positives.

Furthermore, the data used for the current study and the previous validation study are over 10 years old and warrant replication. Beyond replication, there is also an opportunity to use up-to-date socio-environmental and clinical data for predictive modelling to forecast service use and resource allocation as recently been done in the United Kingdom.\textsuperscript{34,35}

This study was not designed to make causal inferences and does not account for all factors that may be part of a causal pathway. Given that environmental factors only explain a portion of the risk, it is also important to consider genetic and other individual biological factors that impact a person’s risk of developing psychosis.\textsuperscript{36} Both family history, genetic factors\textsuperscript{37} and unobservable familial selections factors (e.g., relatives who also have an increased risk of developing a psychotic disorder who may be more likely to reside in marginalized or urban areas)\textsuperscript{38} as well as patterns of substance use may be associated with socio-environmental and geographical factors that are examined in this study. Due to limitations of the data sources used, we were not able to account for substance-use patterns at the individual and area levels nor genetic and familial factors in this study. Future research should build on these limitations and further examine how the socio-environmental factors examined in this study are impacted by known biological risk factors and substance use patterns\textsuperscript{39} using spatial approaches that explore synergistic risk. Beyond biological factors, further attention should also be given to the role of other socio-environmental factors including immigration, ethnicity, and additional contextual factors including social capital, which may have important roles in moderating risk. These factors, in addition to geography and socio-environmental factors, should be examined in relation to the incidence of psychotic disorders as well as in relation to health service utilization and care outcomes.

\textbf{Conclusion}

We found geographic variation in the incidence of psychotic disorders across the province of Ontario, and incidence was associated with contextual socio-environmental factors. There were elevated rates of psychotic disorders in some of the major metropolitan areas in the province when compared to areas outside of these metropolitan areas. Area-level marginalization appears to attenuate the risk associated with geographical location. Future research should account for important individual-level factors and examine how they may influence the risk of developing a psychotic disorder, particularly in relation to area-level factors. With further replication, use of the most up-to-date data and further study of socio-environmental exposures future work may be useful in informing social policy interventions as preventative measures and planning delivery of services. It is particularly important to target services for people with the first episode of psychosis, to ensure adequate resource allocation across the province, and to direct services to areas with elevated rates of psychotic disorders.

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The dataset used for this study is held at ICES and may be accessible with appropriate permission via a DAS data request. The Ontario Marginalization Index is accessible online via https://www.publichealthontario.ca/en/data-and-analysis/health-equity/ontario-marginalization-index.

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References
1. Faris REL, Dunham HW. Mental disorders in urban areas: an ecological study of schizophrenia and other psychoses. Chicago: University of Chicago Press; 1939.
2. O’Donoghue B, Roche E, Lane A. Neighbourhood level social deprivation and the risk of psychiatric disorders: a systematic review. Soc Psychiatry Psychiatr Epidemiol. 2016;51(7):941-950.
3. Selten J-P, Van Der Ven E, Termorshuizen F. Migration and psychosis: a meta-analysis of incidence studies. Psychol Med. 2020;50(2):303-313. Epub ahead of print 2019. doi: 10.1017/S0033291719000035.
4. Jongsma HE, Turner C, Kirkbride JB, Jones PB. International incidence of psychotic disorders, 2002-17: a systematic review and meta-analysis. Lancet Public Health. 2019;4(5):e229-e244.
5. Jarvis GE. The social causes of psychosis in North American psychiatry: a review of a disappearing literature. Can J Psychiatry. 2007;52(5):287-294.
6. Jongsma HE, Gayer-Anderson C, Lasalvia A, et al. Treated incidence of psychotic disorders in the multinational EU-GEI study. JAMA Psychiatry. 2018;75(1):36-46.
7. Anderson KK, Fuhrer R, Abramowicz M, Malla AK. The incidence of first-episode schizophrenia-spectrum psychosis in adolescents and young adults in Montreal: an estimate from an administrative claims database. Can J Psychiatry. 2012;57(10):626-633.
8. Anderson KK, Cheng J, Susser E, McKenzie KJ, Kurdyak P. Incidence of psychotic disorders among first-generation immigrants and refugees in Ontario. CMAJ. 2015;187(9):E279-E286.
9. Anderson KK, Norman R, MacDougall AG, et al. Estimating the incidence of first-episode psychosis using population-based health administrative data to inform early psychosis intervention services. Psychol Med. 2019;49(12):2091-2099.
10. Rotenberg M, Tuck A, Pushny R, McKenzie K. The role of ethnicity in pathways to emergency psychiatric services for clients with psychosis. BMC Psychiatry. 2017;17(1):137.
11. Rotenberg M, Tuck A, McKenzie K. Psychosocial stressors contributing to emergency psychiatric service utilization in a sample of ethno-culturally diverse clients with psychosis in Toronto. BMC Psychiatry. 2017;17(1):324.
12. Gato E, Rosella L, Chiu M, Kurdyak PA. Trends in standardized mortality among individuals with schizophrenia, 1993-2012: a population-based, repeated cross-sectional study. CMAJ. 2017;189(37):E1177-E1187.
13. Kurdyak P, Vigod SN, Newman A, Giannakeas V, Mulsant BH, Stukel T. Impact of physician follow-up care on psychiatric readmission rates in a population-based sample of patients with Schizophrenia. Psychiatr Serv. 2018;69(1):61-68.
14. Durbin A, Moineeddin R, Lin E, Steele LS, Glazier RH. Examining the relationship between neighbourhood deprivation and mental health service use of immigrants in Ontario, Canada: a cross-sectional study. BMJ Open. 2015;5(3):e006690.
15. Anderson KK, Kurdyak P. Factors associated with timely physician follow-up after a first diagnosis of psychotic disorder. Can J Psychiatry. 2017;62(4):268-277.
16. Rodrigues R, MacDougall AG, Zou G, et al. Involuntary hospitalization among young people with early psychosis: a population-based study using health administrative data. Schizophr Res. 2019;208:276-284.
17. Rodrigues R, Beswick A, Anderson KK. Psychiatric hospitalization following psychosis onset: a retrospective cohort study using health administrative data. Early Interv Psychiatry. 2020;14(2):235-240.
18. Ngui AN, Apparicio P, Fleury M-J, et al. Spatio-temporal clustering of the incidence of schizophrenia in Quebec, Canada from 2004 to 2007. Spat Spatiotemporal Epidemiol. 2013;6:637-647.
19. Statistics Canada. The Daily, Thursday, October 7, 1999. Population estimates. [accessed 2020 Dec 16] https://www150.statcan.gc.ca/n1/daily-quotidien/991007/dq991007a-eng.htm.
20. Vanasse A, Courteau J, Fleury M-J, Grégoire J-P, Lesage A, Moisan J. Treatment prevalence and incidence of schizophrenia in Quebec using a population health services perspective: different algorithms, different estimates. Soc Psychiatry Psychiatr Epidemiol. 2012;47(4):533-543.
21. Kurdyak P, Lin E, Green D, Vigod S. Validation of a population-based algorithm to detect chronic psychotic illness. Can J Psychiatry. 2015;60(8):361-366.
22. Statistics Canada. Census metropolitan area and census agglomeration definitions: 2016 census metropolitan area and census agglomeration strategic review consultation guide; 2015 [accessed 2020 Jul 23]. https://www150.statcan.gc.ca/n1/pub/93-600-x/2010000/definitions-eng.htm.
23. Matheson FI, Dunn JR, Smith KLW, Moineddin R, Glazier RH. Development of the Canadian Marginalization Index: a new tool for the study of inequality. Can J Public Health. 2012;103(8 Suppl 2):S12-S16.

24. Matheson FI, Ontario Agency for Health Protection and Promotion (Public Health Ontario). 2011 Ontario marginalization index: technical document. Toronto (ON): St. Michael’s Hospital; 2017. Joint publication with Public Health Ontario [accessed 2020 Apr 25]. https://www.publichealthontario.ca/-/media/documents/O/2017/on-marg-technical.pdf.

25. Statistics Canada. 1996 Census of population. Catalogue no. 93F0021XDB96001 [accessed 2020 Dec 16] https://www12.statcan.gc.ca/English/census96/data/tables/.

26. Aleman A, Kahn RS, Selten J-P. Sex differences in the risk of schizophrenia: evidence from meta-analysis. Arch Gen Psychiatry. 2003;60(6):565-571.

27. StataCorp. Stata Statistical Software: Release 16. College Station (TX): StataCorp LLC; 2019.

28. QGIS.org. QGIS Geographic Information System. QGIS Association; 2020. [accessed 2020 Dec 16] http://www.qgis.org.

29. Heinz A, Deserno L, Reininghaus U. Urbanicity, social adversity and psychosis. World Psychiatry. 2013;12(3):187-197.

30. Kirkbride JB, Jones PB, Ullrich S, Coid JW. Social deprivation, inequality, and the neighborhood-level incidence of psychotic syndromes in east London. Schizophr Bull. 2014;40(1):169-180.

31. Veling W, Susser E, van Os J, Mackenbach JP, Selten J-P, Hoek HW. Ethnic density of neighborhoods and incidence of psychotic disorders among immigrants. Am J Psychiatry. 2008;165(1):66-73.

32. Ngamini Ngui A, Cohen AA, Courteau J, et al. Does elapsed time between first diagnosis of schizophrenia and migration between health territories vary by place of residence? A survival analysis approach. Health Place. 2013;20:66-74.

33. Kirkbride JB. Hitting the floor: understanding migration patterns following the first episode of psychosis. Health Place. 2014;28(100):150-152.

34. Kirkbride JB. Epidemiology on demand: population-based approaches to mental health service commissioning. BJPsych Bull. 2015;39(5):242-247.

35. McDonald K, Ding T, Dliwayo R, et al. O1.3. Back to the future: predicting population need for psychosis care based on the epidemiology of psychotic disorders in England, an applied Bayesian methodology. Schizophr Bull. 2020;46(suppl 1):S1-S2.

36. Paksarian D, Trabjerg BB, Merikangas KR, et al. The role of genetic liability in the association of urbanicity at birth and during upbringing with schizophrenia in Denmark. Psychol Med. 2018;48(2):305-314.

37. Fan CC, McGrath JJ, Appadurai V, et al. Spatial fine-mapping for gene-by-environment effects identifies risk hot spots for schizophrenia. Nat Commun. 2018;9(1):5296. Epub ahead of print December 13, 2018. doi: 10.1038/s41467-018-07708-7.

38. Sariaslan A, Larsson H, D'Onofrio B, Långström N, Fazel S, Lichtenstein P. Does population density and neighborhood deprivation predict schizophrenia? A nationwide Swedish family-based study of 2.4 Million Individuals. Schizophr Bull. 2015;41(2):494-502.

39. Forti MD, Quattrone D, Freeman TP, et al. The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study. Lancet Psychiatry. 2019;6(5):427-436.