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Neighborhood-Level Predictors of Age-at-First-Diagnosis of Psychotic Disorders: A Swedish Register-Based Cohort Study

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The relationship between neighborhood-level factors and the incidence of psychotic disorders is well established. However, it is unclear whether neighborhood characteristics are also associated with age-at-first-diagnosis of these disorders. We used linked Swedish register data to identify a cohort of persons first diagnosed with an ICD-10 non-affective or affective psychotic disorder (F20-33) between 1997 and 2016. Using multilevel mixed-effect linear modelling, we investigated whether neighborhood deprivation and population density at birth were associated with age-at-first diagnosis of a psychotic disorder. Our final cohort included 13,440 individuals, with a median age-at-first-diagnosis of 21.8 years for women (interquartile range [IQR]: 19.0–25.5) and 22.9 years for men (IQR: 20.1–26.1; $P < .0001$). In an unadjusted model, we found no evidence of an association between neighborhood deprivation and age-at-first-diagnosis of psychotic disorder ($P = .07$). However, after multivariable adjustment, age-at-first-diagnosis increased by .13 years (95% CI: .05 to .21; $P = .002$) for a one standard deviation increase in neighborhood deprivation. This was equivalent to a later diagnosis of 47 days (95% CI: 18 to 77). We found no evidence of a different relationship for non-affective versus affective psychoses [LRT $\chi^2(1) = .14$; $P = .71$]. Population density was not associated with age-at-first-diagnosis in unadjusted ($P = .81$) or adjusted ($P = .85$) models. Later age-at-first-diagnosis for individuals born in more deprived neighborhoods suggests structural barriers in accessing equitable psychiatric care.

Key words: epidemiology/longitudinal/age-at-onset/deprivation/population density/schizophrenia

Introduction

The incidence of non-affective psychotic disorders varies geographically[1,2] and is associated with neighborhood characteristics,[3-5] as first observed by Faris and Dunham over 80 years ago.[6] They investigated the distribution of mental disorders in Chicago, and identified that rates of schizophrenia were higher in more socially disorganized neighborhoods; in contrast, this variation was not observed for affective psychoses, mirroring patterns replicated elsewhere since, including in nationwide register data in Denmark.[7]

These findings have been observed in numerous studies in high-income countries since, including in the United States and Europe, showing that there is a concentration of non-affective psychotic disorders in neighborhoods characterized by higher urbanicity,[8] deprivation,[9] income inequality, population density,[10] and lower social capital.[11] Moreover, longitudinal studies from Denmark found that there is a dose-response relationship between urbanicity at birth and during upbringing and later risk of schizophrenia.[12–14]

While the relationship between neighborhoods and the incidence of psychotic disorders is well established, little research has investigated whether the age-at-onset of psychosis—a key clinical epidemiological variable—also varies across neighborhoods. Age-at-onset typically refers to the age at which positive symptoms of psychosis first emerge, but other definitions have been used in the literature, including age-at-first-presentation or diagnosis.[15] Notwithstanding known variation in the duration of untreated psychosis (DUP),[16,17] most patients first

present to services close to the age-of-onset of psychotic symptoms.[16]

Age-at-onset of psychosis is a key predictor of disease outcomes.[15] Earlier age-at-onset is associated with poorer prognosis for schizophrenia, such as more negative symptoms, greater symptom severity, more hospitalizations, decreased likelihood of remission, more frequent relapses, and poorer social and occupational functioning.[15,18] Accordingly, minimizing the delay between age-at-onset of first symptoms and first treatment for psychosis can substantially improve the course and outcomes of the disorder.[19,20]

Factors that influence the age-at-onset of psychosis can also provide valuable insight into the complex etiology and origin of psychotic disorders.[21] To date, several demographic and clinical characteristics have been associated with an earlier age-at-onset, including male sex,[22] single marital status, poor premorbid occupational functioning,[23] cannabis use, obstetric complications,[24] and family history of psychosis.[25] Nevertheless, the influence of neighborhood-level risk factors of psychosis on the age-at-onset is largely unknown. To the best of our knowledge, only two studies have examined this relationship. One study of 555 FEP participants in Ireland reported no urban-rural birth differences in age-at-onset,[24] although a smaller study in the United States found that neighborhood residential instability was associated with an earlier age-at-onset in a sample of 143 patients with a first-episode of psychosis.[26]

Understanding whether neighborhood-level factors influence the age-at-onset of psychotic disorders may not only provide evidence about the role of the social environment in the etiology of psychotic disorders but could also have public health implications. For example, such knowledge could inform the timing and resource allocation of early intervention in psychosis (EIP) services by identifying settings where the population may be at-risk of earlier (or later) diagnosis of psychotic disorders; targeting those at-risk before or around the most likely time of disease onset has the potential to improve both the course and outcomes of the disorder.[27,28]

Here, we used prospectively-collected register data on a nationwide cohort in Sweden to investigate whether neighborhood deprivation and population density at birth and during upbringing were associated with age-at-first-diagnosis of psychotic disorders after controlling for potential confounders, including sex, parental history of serious mental illness (SMI), obstetric complications, family disposable income at participants' birth, and parental migration status. In this study, we used age-at-first-diagnosis as a proxy for age-at-onset. We also investigated if there were differences in these associations between affective and non-affective psychoses.

We hypothesized that neighborhood deprivation and population density at birth and during upbringing would be negatively associated with age-at-first-diagnosis of psychotic disorders (i.e., people born in more deprived and densely populated areas would have a younger age-at-first-diagnosis of psychosis), even after adjusting for confounders. We also hypothesized that the association between neighborhood-level factors and age-at-first-diagnosis would be stronger for non-affective than for affective psychoses, given previous evidence that non-affective psychoses are more strongly related to the neighborhood characteristics than affective psychoses.[9,10]

Methods

Population and Study Design

We extracted nationwide data from Psychiatry Sweden, a comprehensive and anonymized database of linked Swedish national registers. Using the Register of the Total Population (RTP), we identified a cohort of individuals born in Sweden between January 1, 1982, and December 31, 2001, who were diagnosed with their first ICD-10 psychotic disorder in the National Patient Register (NPR) from their 15th birthday (earliest: January 1, 1997) until December 31, 2016. We defined age-at-first-diagnosis from age 15, as this corresponds with the age after which psychotic disorders can be reliably captured in the Swedish healthcare system.[29] We excluded individuals who received a diagnosis of a psychotic disorder before 15 years old, those born outside of Sweden, and those without permanent residency in Sweden.

Outcome

Our primary outcome was age-at-first-diagnosis of psychotic disorders, as recorded in the Swedish National Patient Register (NPR) with ICD-10 codes F20-29 (non-affective psychoses) and F30.2, F31.2, F32.3 and F33.3 (affective psychoses). Recording from psychiatric inpatient care across Sweden was 100% complete during the follow-up period, while recording from outpatient settings began in 2001 and has achieved complete national coverage since 2006.[30]

Exposures

Our exposures were neighborhood deprivation and population density at birth. Following similar studies in Sweden,[31,32] we defined neighborhoods according to the "Small Area for Market Statistics" (SAMS) classification system, which contains annual information on residential area characteristics. There are about 9,200 SAMS areas in Sweden, and their median population size in 2011 was 726 people (interquartile range [IQR]: 312–1,378). These administrative units are designed to maximize internal socioeconomic homogeneity, while preserving variance in characteristics of the social environment between SAMS.[31] Our cohort came from 4,896 SAMS areas.

We estimated population density as people per square kilometer in each participant's SAMS in their birth year. Likewise, we estimated neighborhood deprivation for each participant's SAMS in their birth year based on four factors: the proportion of people who: (1) received social benefit, (2) had a criminal conviction, (3) had income below the median national income, and (4) were unemployed. For deprivation, each item was *z*-standardized to have a mean of zero and standard deviation of one, which we aggregated into an overall *z*-score deprivation variable. For both deprivation and population density, we *z*-standardized these variables to have a mean of zero and standard deviation of one to align them to comparable scales, where greater scores indicated more deprived and densely populated areas. We also assigned participants to deprivation and population density quintiles at birth relative to all SAMS in Sweden in the participants' birth year for descriptive purposes.

Confounders

We selected the following variables from linked registers as potential a priori confounders based on theory and previous evidence: sex,[22] parental history of SMI,[25] obstetric complications,[24] family disposable income at participants' birth,[33] and parental migration status.[34]

We defined parental history of SMI as either biological parent ever having been diagnosed with an ICD-8, -9, or -10 psychotic disorder or bipolar disorder with or without psychotic symptoms between 1973, when the NPR began, until 2016, to gather data regarding psychiatric admissions. We obtained family disposable income at birth from the Population and Housing Census (FOB) in 1980, 1985, and 1990 for participants born between 1982 and 1989, and from the Longitudinal Integration Database for Health Insurance and Labour Market Studies (LISA) for participants born from 1990 onwards when the LISA superseded the FOB. From each source, we created annual quintiles of family disposable income relative to all adults in Sweden in that year to account for inflation over the birth cohort, and assigned participants their family income quintile in the year of birth, as the highest of either the biological or adopted father's or mother's income quintile. Full methods are provided in the Supplementary Methods and Supplementary Table 1. We used Apgar scores at 5 min after birth to define obstetric complications, as recorded in the Maternal Birth Register. Apgar scores are an accepted and convenient method for reporting vital signs in newborn infants and any response to resuscitation that may be required.[35] We categorized this according to the definitions used by the American College of Obstetricians and Gynecologists as "reassuring" (scores of 7–10), "moderately abnormal" (scores of 4–6) and "low" (scores of 0–3).[35] We defined parental migration status as both parents being Swedish-born or at least one parent being foreign-born, by linking data from the RTP and the Multi-Generational Register.

Statistical Analysis

We conducted a complete-case analysis since the proportion of missing data was low (6.9%), and was not expected to produce biased results.[36] We used multilevel linear regression with random intercepts at the neighborhood (SAMS) level to take into account the hierarchical structure of the data and to quantify variation in age-at-first-diagnosis attributable to neighborhood-level effects in null and fully-adjusted models. Modeling proceeded as follows. First, we ran null models to quantify this variation. Second, we ran unadjusted analyses to determine univariable associations between neighborhood-level deprivation and population density at-birth and age-at-first-diagnosis of psychotic disorder. Third, we adjusted for all a priori confounders in a multivariable model. Fourth, we tested whether the effect of deprivation or population density at-birth on age-at-first-diagnosis differed for non-affective and affective psychoses by testing for multiplicative interaction between these variables and performing a likelihood ratio test (LRT) against a model without the interaction term. Finally, we performed secondary analyses to investigate whether cumulative exposure to deprivation or population density during childhood (from birth to age 14) was associated with age-at-first-diagnosis of psychosis. For all models, we reported the change in age-at-first-diagnosis for a one standard deviation increase in deprivation or population density. Modelling was conducted in Stata, version 15.

Ethical Approval

This study was approved by the Stockholm Regional Ethical Review Board (2010/1185-31/5) and the UCL Research Ethics Committee (21019/001).

Results

Sample Characteristics

Our cohort included 14,438 individuals born in Sweden between 1982 and 2001, and diagnosed with a psychotic disorder after their 15th birthday, of whom 998 (6.9% of cohort) were missing data (Table 1). Compared with the complete case sample, participants with missing data were more likely to be older (median age-at-first-diagnosis: 23.7 vs. 22.5 years; $P < .0001$), children of migrants (40.3% vs. 25.9%: $P < .0001$), from either the lowest or highest income quintile at birth ($P < .0001$), from more densely populated ($P = .01$) and deprived neighborhoods ($P = .02$) at birth, and to have a parental history of SMI ($P = .02$) and a personal history of non-affective (vs. affective) psychotic disorder ($P = .01$). There were no differences between the complete case sample and those with missing data by sex or 5-min Apgar score.

Our complete case sample included 13,440 individuals (93.1% of cohort) nested within 4,896 SAMS neighborhoods at birth. The sample was predominantly

Table 1. Baseline characteristics of sample with complete and missing data

Characteristic	Complete Data[a] (*N* = 13,440; 93.1%)	Missing Data[b] (*N* = 998; 6.9%)	χ^2-test (df); *P* value[c]
	n (%)	*n* (%)	
Sex			0.8 (1); .38
Male	7,785 (57.9)	564 (56.5)	
Female	5,655 (42.1)	434 (43.5)	
Age-at-first-diagnosis (median and IQR)	22.5 (19.6–25.9)	23.7 (20.3–27.2)	47.2 (14,434); <.0001
Missing	—	2 (0.01%)	
Migrant status			98.3 (1); <.0001
Children of migrants	3,476 (25.9)	402 (40.3)	
Swedish-born	9,964 (74.1)	596 (59.7)	
Parental region-of-origin			134.3 (6); <.0001
Swedish	9,964 (74.1)	594 (59.6)	
Other Europe	1,417 (10.5)	159 (16.0)	
Asia	71 (0.5)	8 (0.8)	
North Africa & Middle East	395 (2.9)	63 (6.3)	
Sub-Saharan Africa	145 (1.1)	23 (2.3)	
Mixed	1,378 (10.3)	130 (14.0)	
Other	70 (0.5)	19 (1.9)	
Missing	—	2 (0.01%)	
Population density quintiles (at birth)[d]			12.5 (4); .01
Quintile 1 (lowest)	1,033 (7.7)	57 (6.5)	
Quintile 2	1,500 (11.2)	79 (9.0)	
Quintile 3	2,186 (16.3)	123 (14)	
Quintile 4	3,355 (25.0)	230 (26.1)	
Quintile 5 (highest)	5,366 (39.9)	391 (44.4)	
Missing	—	118 (0.8%)	
Neighborhood deprivation quintiles (at birth)[d]			11.4 (4); .02
Quintile 1 (lowest)	1,921 (14.3)	144 (16.4)	
Quintile 2	2,341 (17.4)	143 (16.3)	
Quintile 3	2,646 (19.7)	154 (17.5)	
Quintile 4	2,797 (20.8)	162 (18.4)	
Quintile 5 (highest)	3,735 (27.8)	277 (31.5)	
Missing	—	118 (0.8%)	
Diagnosis			6.4 (1);.01
Non-affective psychosis	10,047 (74.8)	782 (78.4)	
Schizophrenia or Schizoaffective (F20, F25)	3,033 (25.6)	287 (28.8)	
Other non-affective psychosis	7,014 (52.2)	495 (49.6)	
Affective psychosis	3,393 (25.2)	216 (21.6)	
Bipolar psychosis	1,166 (8.7)	89 (8.9)	
Depressive psychosis	2,227 (16.6)	127 (12.7)	
Parental history of SMI			5.2 (1); .02
No	11,830 (88.0)	854 (85.6)	
Yes	1,610 (12.0)	144 (14.4)	
Obstetric complications (5-min Apgar score)			1.1 (2); 0.58
Reassuring (7–10)	13,272 (98.8)	290 (99.3)	
Moderately abnormal (4–6)	128 (0.9)	2 (0.7)	
Low (0–3)	40 (0.3)	0 (0.0)	
Missing	—	658 (4.6%)	
Family disposable income (at birth)[d]			56.4 (4); <.0001
Quintile 1 (lowest)	530 (3.9)	57 (7.7)	
Quintile 2	1,610 (12.0)	119 (16.1)	
Quintile 3	3,274 (24.4)	136 (18.4)	
Quintile 4	4,248 (31.6)	189 (25.6)	
Quintile 5 (highest)	3,778 (28.1)	238 (32.2)	
Missing	—	218 (1.5)	

Note: IQR = Interquartile range, df = degrees of freedom.
[a] Sample used for the analyses and containing complete data on all variables.
[b] Excluded from analysis because of missing data on parental income (1.51%), neighborhood exposures at birth (0.82%), age-at-first-diagnosis (0.01%), region (0.01%), and obstetric complications (4.56%).
[c] *P*-values compare those with missing data and those without; chi-square tests for categorical characteristics and linear regression for continuous characteristics.
[d] Measured at each participant's birth year.

Table 2. Unadjusted and adjusted analyses for the association of neighborhood deprivation and population density with the age-at-first-diagnosis of psychosis

	Age-at-first-diagnosis of psychosis (N = 13,440)			
	Unadjusted		Adjusted[b]	
Exposure	Effect estimate (95% CI)	P value	Effect estimate (95% CI)	P value
Neighborhood deprivation[a]	−.07 (−.14 to .00)	.07	.13 (.05 to.21)	.002
Population density[a]	−.01 (−.08 to .07)	.81	.01 (-.07 to.08)	.85

Note: CI = Confidence intervals.
[a] Scores were z-standardized.
[b] Adjusted for family disposable income at birth, sex, obstetric complications, parental history of SMI, and parental migration status.

Table 3. Interaction term for diagnosis (non-affective/affective psychosis)

Neighborhood Deprivation on Age-at-First-Diagnosis, by Psychotic Disorder[a]	Adjusted Effect Size[b] (95% CI)
Affective psychosis	.10 (−.06 to .25)
Non-affective psychosis	.13 (.04 to .22)
Population density on age-at-first-diagnosis, by psychotic disorder[c]	Adjusted effect size[d] (95% CI)
Affective psychosis	−.07 (−.21 to .07)
Non-affective psychosis	.04 (−.05 to .12)

Note: CI = Confidence intervals.
[a] Likelihood ratio test of interaction between deprivation and psychotic disorder category on 1 degree of freedom: χ^2 = .14; P = .71.
[b] Change in age-at-first-diagnosis of 1-SD change in deprivation (z-standardized). Adjusted for family disposable income at birth, sex, obstetric complications, and parental migration status.
[c] Likelihood ratio test of interaction between population density and psychotic disorder category on 1 degree of freedom: χ^2 = 1.61; P = .21.
[d] Change in age-at-first-diagnosis of 1-SD change in population density (z-standardized). Adjusted for family disposable income at birth, sex, obstetric complications, and parental migration status.

male (57.9%), Swedish-born to two Swedish-born parents (74.1%) and diagnosed with a non-affective psychosis (74.8%). Median age-at-first-diagnosis was 22.5 years (IQR, 19.6–25.9), although this was younger for women (21.8; IQR, 19.0–25.5) than men (22.9; IQR, 20.1–26.1; Mann–Whitney U = 12.4; P < .0001). Participants were over-represented in the most deprived (27.8%) and densely populated (39.9%) quintiles at birth. Twelve percent of participants had at least one biological parent diagnosed with SMI.

Multilevel Modeling

A null multilevel linear model showed that only 0.01% (95% CI: 0.00 to 0.03; P = .07; Supplementary Table 2) of variance in age-at-first-diagnosis of psychotic disorders could be attributed to the neighborhood level; this remained unaltered in the fully adjusted model (0.01%; 95% CI: 0.00 to 0.03; P = .04).

In unadjusted analyses, we found no evidence of an association between neighborhood deprivation (−.07; 95% CI: −.14 to .00; P = .07; Table 2) or population density (−.01; 95% CI: −.08 to .07; P = .81) at birth and age-at-first-diagnosis of psychosis. However, after multivariable control for a priori covariates (see Supplementary Table 3 for full results), we observed that a one standard deviation increase in neighborhood deprivation became associated with an increase in age-at-first-diagnosis of .13 years (95% CI: .05 to .21; P = .002). This was equivalent to a later diagnosis of 47 days (95% CI: 18 to 77); population density remained unassociated with age-at-first-diagnosis (.01; 95% CI: −.07 to .08; P = .85).

We found no evidence that the association between neighborhood deprivation and the age-at-first-diagnosis differed for people diagnosed with either non-affective or affective psychosis [LRT for interaction: $\chi^2(1)$ = .14; P = .71; Table 3]. Likewise, we did not observe any effect modification between population density and age-at-first-diagnosis by diagnosis [LRT: $\chi^2(1)$ = 1.61; P = .21].

Secondary Analyses

We repeated our modeling for cases on whom continuous SAMS data from birth to 14 years old was available (N = 13,089; 97.4% of the complete case sample). Our findings showed similar trends: in an unadjusted model, cumulative exposure to neighborhood deprivation in childhood was not associated with age-at-first-diagnosis of psychosis (−.05; 95% CI: −.13 to .02; P = .15) (Table 4). However, after multivariable adjustment, a one standard deviation increase in cumulative exposure to neighborhood deprivation was associated with an increased age-at-first-diagnosis of .15 years (95% CI: .08 to .23; P < .0001), equivalent to 55 days (95% CI: 29 to 84). We found no evidence that cumulative exposure to population density was associated with age-at-first-diagnosis of psychosis in unadjusted (−.06; 95% CI: −.13 to .02; P = .14) or adjusted analyses (.00; 95% CI: −.07 to .08; P = .99).

Table 4. Subgroup analysis for the association of cumulative neighborhood deprivation and population density (0-14 years) with the age-at-first-diagnosis

	Age-at-first-diagnosis of psychosis (N = 13,089)			
	Unadjusted		Adjusted[b]	
Exposure	Effect estimate (95% CI)	P value	Effect estimate (95% CI)	P value
Cumulative neighborhood deprivation (0–14 years)[a]	−.05 (−.13 to .02)	.15	.15 (.08 to .23)	<.0001
Cumulative population density (0–14 years)[a]	−.06 (−.13 to .02)	.14	.00 (−.07 to .08)	.99

Note: CI = Confidence intervals.
[a]Scores were z-standardized.
[b]Adjusted for family disposable income at birth, sex, obstetric complications, parental history of SMI, and parental migration status.

Discussion

Main Findings

In this large, population-based study of people diagnosed with a psychotic disorder throughout Sweden aged up to 34 years old, neighborhood deprivation at birth and during upbringing were longitudinally associated with older age-at-first-diagnosis of psychosis after multivariable adjustment, in contrast to our hypothesis. This pattern did not differ by diagnosis. We found no evidence that population density-at-birth or during upbringing was associated with age-at-first-diagnosis of psychotic disorder, despite being associated with the incidence of psychotic disorders in the general population.[12,32]

Strengths and Limitations

Strengths of our study included a large sample followed for up to 20 years with only a small amount of missing data. Swedish register data are also reliable for research purposes,[37] and diagnoses of psychotic disorders in the NPR have good validity.[29,30] The longitudinal design (exposure measured at birth) excludes the possibility that individual social drift could have accounted for our findings. We could not exclude the possibility that other forms of reverse causation accounted for our findings, including inter-generational social drift or selection of families at genetically higher risk of psychosis moving into more deprived areas before participant birth. People at genetically high risk of psychosis have been shown to be born in more deprived areas,[38] and family history of psychosis has also been linked to earlier age-at-onset.[25] Nonetheless, in our study, parental history of SMI was not associated with age-at-first-diagnosis (Supplementary Table 2), and deprivation at-birth was independently associated with a later age-at-first-diagnosis in our study after controlling for parental history of SMI. These findings suggest that genetic selection is an unlikely explanation of our findings as they pertain to age-at-first-diagnosis. We controlled for several potential confounders in our analyses, informed by a priori knowledge, though we recognize that unobserved or residual confounding remain possible; unobserved confounding may include familial genetic risk not captured via our parental history of SMI variable. We did not control for cannabis use, previously found to be associated with age-at-onset of psychosis,[24] since this was on the causal pathway between our exposures (measured at birth) and outcome.

Our findings should be interpreted in the context of several limitations. First, previous research has defined age-at-onset of psychosis in numerous ways, including age at first positive psychotic symptoms, age at first admission, or age at first diagnosis by healthcare professionals.[15] Although the onset of positive symptoms lies closest to the true endophenotype we are seeking to study, this information can only be subjectively obtained by the patient or close relatives and is usually retrospectively ascertained and subject to recall. Our definition was based on the availability of register data, and we used age-at-first-diagnosis as a proxy for age-at-onset. Prior to conducting this study, we assumed this to be a reasonable assumption, given evidence that age-at-onset of positive symptoms and age-at-first-diagnosis are highly correlated, typically occurring within 6–18 months of each other;[15] we explore the validity of this assumption in more detail below in interpreting our findings.

Second, our results may not generalize to people with psychosis older than 34 years old, the maximum observed age at the end of follow-up in our cohort. The median age-at-first diagnosis in our sample of people aged up to 34 years old was 22.5 years (IQR, 19.6–25.9), but this figure should not be compared with summary estimates based on samples which cover the typical adult-onset age range up to 64 years old, where median ages are likely to be older.[27] Our median estimate compares with evidence from samples based on similar age ranges, such as data from the Social Epidemiology of Psychoses in East Anglia [SEPEA] first onset study in people aged 16–35 years old, which reported an almost identical median age-at-first diagnosis.[39] Our results may also not generalize to other countries with different levels of deprivation and population density. Future research could also investigate if there are different patterns in countries where access to healthcare is not universal, or where the effects of income

inequalities on health may be more pronounced, such as in the United States.[40]

Third, the Swedish registers had complete coverage of psychiatric contacts from in-patient settings for the whole duration of the study, but out-patient coverage began in 2001 and was complete from 2006 onwards.[29] We might have missed some participants as outpatients from 1997 to 2005, though this effect on our results is likely to have been small, unless the rollout of outpatient coverage in Sweden was differential by population density and deprivation; data were unavailable to investigate this possibility.

Meaning of Findings

Greater deprivation at birth and during upbringing were associated with older age-first-diagnosis, corresponding to point estimates of 47 and 55 days (or 6.7 and 7.9 weeks), for a one standard deviation increase in deprivation at-birth and cumulative deprivation during upbringing, respectively.

Contrary to our hypothesis, we observed a delay in the first diagnosis of psychotic disorder of around 47–55 days (6.7–7.9 weeks) for a one standard deviation increase in deprivation at-birth and during upbringing, respectively. We originally hypothesized that greater deprivation (and population density) would hasten the onset of psychotic disorders because enduring exposure to systemic disadvantage would accelerate disruption to stress mechanisms implicated in increasing psychosis risk,[41] consistent with etiological theory.[42] By contrast, our results suggest either (1) that exposure to wider social adversities increases psychosis *risk* in a manner that is unrelated to age at first *onset* of symptoms; (2) that the social environment is not causally related to age at psychosis *onset* or *risk* of psychosis; or (3) that age-at-first-diagnosis was a poor proxy for age-at-first-onset in our dataset, and may, in fact, be related to duration of untreated psychosis (DUP).

We suggest that our results are most parsimoniously explained by the latter explanation, with age-at-first-diagnosis influenced by help-seeking behavior in different environments, and perhaps more weakly correlated to age-at-first-onset in our dataset than assumed a priori. Although Sweden has a universal healthcare system which should reduce the DUP between age at symptom onset and first diagnosis, we do not know whether this acted differentially by exposure status (i.e., deprivation or population density). Previous cross-sectional studies have found no association between deprivation and DUP,[16,17,43,44] but evidence from longitudinal studies or register-based data on this issue are missing. Ongoing, chronic exposure to more social disadvantage may lead to longer delays in seeking help for psychosis, given enduring barriers to accessing care including consistent under-investment in appropriately-resourced mental health services in deprived communities, reductions in education and public awareness of the initial signs and symptoms of psychosis, less familiarity with the availability of mental health services, fewer personal, social or community resources to help signpost or support people in the initial phases of psychosis, reduced forms of other measures of informal social control (such as greater tolerance of unusual behaviors in more deprived neighborhoods), a greater likelihood of competing priorities for individuals in resource-poor environments from seeking access to care (such as maintaining a job or caring for family), and greater mistrust of institutions (particularly those concerned with mental health care).[45-49] All such factors could explain the association between deprivation and age-at-first-diagnosis observed in our study.

There is only limited direct evidence on the relationship between psychosis age-at-onset and the wider social environment. For example, a small study ($N = 143$) in the United States observed that earlier age-at-onset of psychotic symptoms was associated with residential instability, even when controlling for known predictors of an early age-at-onset, but not with socioeconomic status, employability, or household value.[26] The authors suggested that more residentially unstable neighborhoods may be less socially integrated, making it difficult to maintain social contacts with others, leading those predisposed to psychosis to manifest symptoms earlier. Nonetheless, a larger study in Ireland found no urban-rural birth differences in age-at-onset. Further longitudinal research which directly measures age-at-onset in relation to the wider social environment could further elucidate these findings.

Implications

Knowledge that neighborhood-level factors—here, specifically deprivation—could influence the age-at-first-diagnosis of psychosis could help inform the allocation of resources to support timely access to early intervention programs for people in their first episode of psychosis. Given our research has also shown that a disproportionate burden of new cases will present in more deprived areas,[32,50] mental health policymakers should prioritize resourcing appropriate psychosis services in these areas. Our data suggest this should include provision of early detection and outreach strategies in more deprived communities to minimize delays to care, and maximize positive functional, symptomatic, and social outcomes for people in their first episode of psychosis.

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin Open* online.

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Conflicts of Interest

J.B.K. reports consultancy fees from Roche and the Health Services Executive, Ireland. All authors declare they have no other conflicts of interest to report.

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