Urbanicity, parental social deprivation, and risk of early psychosis in Chile: a national cohort study

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Summary

Background In Northern Europe, several studies have indicated that people born and raised in urban areas have an increased risk of psychosis. Emerging research in the Global South has produced more heterogeneous and inconsistent findings, suggesting that the impact of urban environments on psychosis risk may depend on social context and broader environmental factors at multiple levels.

Methods We constructed a cohort of 5,137,561 individuals born in Chile (1992–2012) using the national first episode psychosis (FEP) and Birth and Death registries. We identified 14,410 individuals with nonaffective FEP (ICD-10 F20–F29) recorded between 2005 and 2022. Urbanicity at birth (urban vs rural) was our main exposure. We estimated incidence rate ratios (IRRs) via Poisson regression, adjusting for year of birth and region to account for birth-cohort effects. We also examined whether parental education and employment—two indicators of social deprivation—modified this association.

Findings Over ~92 million person-years, the crude incidence rate was 15.67 per 100,000 person-years (95% CI: 15.42, 15.93). No overall association between urbanicity at birth and non-affective FEP was found after accounting for social factors (adjusted IRR = 0.96, 95% CI: 0.91, 1.01). However, parental low education appeared to modify the association between urbanicity and psychosis on both multiplicative and additive scales, with an additive interaction (RERI = 0.33, 95% CI: 0.18, 0.47), supporting a model where urbanicity increases psychosis risk primarily in the presence of social deprivation.

Interpretation Urban birth alone was not associated with higher FEP incidence in Chile, but an elevated risk was seen among families with lower educational attainment in urban areas. This suggests a causal interplay between urbanicity and social deprivation, underscoring the importance of multilevel frameworks for understanding psychosis risk, especially in rapidly urbanizing societies.

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Keywords: Psychosis; First episode psychosis; Incidence; Urbanicity; Social deprivation; Epidemiology; Cohort study; Chile

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Research in context

Evidence before this study

Most studies from Northern Europe and other high-income regions report a strong association between urban upbringing and risk of psychosis, with odds ratios typically >2. In contrast, evidence from Latin America and other Global South regions has been limited and inconsistent.

Added value of this study

This is the first national study in Chile to link birth registry data to a validated FEP registry and to examine urbanicity at birth and social deprivation in relation to psychosis risk. By leveraging a national, representative cohort, the study addresses previous methodological limitations and investigates effect modification by parental education and employment.

Implications of all the available evidence

Urbanicity per se may not increase psychosis risk universally, especially in middle-income countries. Instead, social deprivation—particularly low parental education—amplifies the risk among those born in urban settings, highlighting the need for targeted interventions and multilevel causal frameworks in global mental health research.

Introduction

Since the early 1900s, urban–rural differences in the distribution of psychosis have prompted extensive discussion in psychiatric and social epidemiology. One of the earliest large-scale ecological investigations by Faris and Dunham[1] documented that most people with schizophrenia in Chicago clustered in densely populated and socioeconomically deprived areas. This finding sparked decades of research into whether aspects of city life—such as social disorganization, environmental stress, or demographic heterogeneity—might contribute causally to psychosis risk.

In Northern Europe, a series of robust registry-based studies revealed that birth or upbringing in urban areas is associated with increased risk of schizophrenia and related psychoses.[2–7] These investigations leveraged national population registries in countries like Denmark and Sweden, enabling thorough control for confounders such as parental history of mental conditions.[5,8] A meta-analysis pooling results from these studies estimated that the odds of developing schizophrenia are more than twice as high for people from urban backgrounds compared with those from rural ones.[7] Authors have proposed multiple pathways to explain these findings, ranging from social stress (e.g., discrimination, neighborhood fragmentation) to potential environmental exposures.

Despite the consistency of results in Scandinavia and parts of Western Europe, research from other global regions—including the Global South—has been inconclusive. For instance, studies in Brazil,[9] China,[10] and Chile[11] have reported minimal or null urban–rural differences in psychosis incidence, although no study has assessed urbanicity (i.e., the extent to which a given area or environment exhibits characteristics typically associated with urban settings), at birth previously. A recent global study in low- and middle-income settings similarly showed that the urbanicity–psychosis association can vary greatly by local context.[12] Moreover, even in western Europe, the large EU-GEI study did not find increased psychosis risk in urban areas in the South of western Europe such as Spain and Italy.[13] These divergent findings have cast doubt on the existence of a universal, context-independent causal effect of urban living on psychosis.

Various explanations have been posited for why urbanicity shows a strong effect in some settings but not others. The nature of social adversity may differ, with urban environments in certain regions offering better healthcare access, closer-knit familial networks, or different types of migration patterns that mitigate risk.[12,14] Demographic factors—such as rates of internal migration, population turnover, or ethnic density—could also moderate any urban effect.[2,14] Furthermore, methodological limitations, including how "urbanicity" is defined, the timing and length of the exposure (birth vs adolescence, birth vs upbringing), and how cases are ascertained, can drive heterogeneity in results.[13,15]

Independent of urbanicity, there is a well-documented association between social deprivation and psychosis. Indicators such as low parental education, unemployment, and neighborhood poverty have each been associated with elevated risk.[16,17] While these factors often serve as confounders in urbanicity research, they could also act as moderators, amplifying the causal impact of features of urban environments on vulnerable subgroups. Indeed, some families in urban environments may be better positioned to access healthcare or avoid social stress, while others may be trapped in overcrowded, under-resourced neighborhoods.[5,13,17]

Furthermore, urban birth occurs within a broader landscape of early-life exposures that shape psychosis risk. A recent meta-analysis identified multiple prenatal and perinatal factors—obstetric complications, extreme parental ages, maternal infections (e.g., HSV-2), birthweight deviations, and prenatal stress—that raise risk, alongside protective factors like optimal birthweight and maternal age of 20–29 years.[18] Embedding urbanicity within this developmental context underscores how its impact may emerge through interactions with underlying biological vulnerabilities.

Eco-epidemiological theory[19,20] proposes that disease distributions are best understood by tracing how exposures become embodied across nested ecological layers—genes, individuals, families, neighborhoods, and broader political–economic systems. March et al.[21,22] applied this perspective to psychosis, framing urbanicity as a "reservoir" that modulates multiple risk domains rather than as a single upstream cause. Evidence from the Global North supports this view: high social fragmentation has been associated with higher psychosis incidence.[23] Such studies imply that any urban effect is contingent on concomitant social or environmental stressors, reinforcing the need to analyze urbanicity jointly with markers of deprivation, segregation, and physical exposures.

Despite sustained economic growth, Chile remains one of the most unequal OECD countries, with a persistently high Gini coefficient and steep educational gradients in health.[24,25] These persistent disparities may shape how social context influences mental health outcomes. Notably, the incidence of nonaffective FEP has shown modest declines in more recent cohorts, a trend reported in Chilean studies, particularly among women.[11,26] Possible drivers include demographic shifts (lower fertility, higher parental education), maternal-child health gains, and improved early detection through the GES/AUGE program. While speculative, these changes may have reduced prenatal and perinatal risks, warranting continued surveillance.

Chile has high urban residence (88–90%), but regional differences in density, development, and healthcare remain.[11,26,27] Its public health system provides universal nonaffective FEP coverage through FONASA and GES/AUGE, entitling suspected cases since 2005 to free assessment and standardized treatment; the system covers nearly 88% of the population.[27] This framework reduces treatment gaps, improves detection, and ensures the FEP registry captures most incident cases. Chile also maintains robust administrative registries for births, deaths, and psychosis, offering a rare opportunity to study population-level determinants in a middle-income country that differs substantially from Northern Europe.

One previous study in Chile, focusing on regional density, did not detect an association between living in the most populous regions and higher psychosis incidence.[11] However, that study did not examine urbanicity at birth specifically (instead measuring urban exposure at the time of first episode), and it did not exclude unconfirmed cases of nonaffective FEP. Because it assessed urbanicity only at illness onset (a common approach in prior Global South studies),[12] a temporal link between early-life urban exposure and psychosis risk could not be established. Moreover, it did not address whether social deprivation might influence the effect of urbanicity. Considering Chile's pronounced socioeconomic disparities—particularly in education and labor markets—disentangling the role of parental social conditions is vital.[22,24] Notably, "deprivation" may have different implications in urban versus rural settings. In rural communities, limited formal education is more normative and may not confer the same disadvantage or stress as in urban settings. This context difference could help explain why low parental education appears unassociated with psychosis in rural areas yet elevates risk in cities.

We aimed to examine two main questions in a large Chilean cohort. First, is being born in an urban area, defined by national census criteria, independently associated with increased incidence of nonaffective FEP? Second, do markers of parental social deprivation—particularly low education (parents who did not complete high school) and unemployment—modify any observed relationship between urbanicity and psychosis risk? We hypothesized that urbanicity alone might show a null or weak association overall, but it would be stronger among children whose parents were less educated or unemployed.

Following an eco-epidemiological approach,[19] we conceptualized urbanicity not as a direct cause but as a context that modulates the expression of other risk factors at multiple ecological levels (individual, familial, environmental). Addressing these questions not only clarifies the urbanicity–psychosis association in Chile, but also enriches our broader understanding of how context shapes psychosis risk worldwide. This approach is essential in rapidly urbanizing societies, where health resources, education, and economic opportunities can differ dramatically across regions and population subgroups.[4,12,28]

Methods

Study design and data sources

This was a registry-based cohort study in Chile, using data from two primary sources. First, we obtained records from the national Birth and Death registry (1992–present), which includes virtually all births in Chile and provides individual-level information on sex, parental education, parental employment, and municipality of birth.[11,26] Second, we used the Fondo Nacional de Salud (FONASA) FEP registry (2005–2022), which systematically records cases of nonaffective FEP in public facilities.[26,27] All cases require a psychiatrist-led diagnostic process after at least six months of follow-up after psychosis onset.[26] Both data sources employ a unique national identifier assigned at birth, allowing for reliable linkage.

We identified 6,977,202 live births between 1992 and 2012 (see Fig. 1). Individuals were excluded if they died prior to 2005 (n = 40,631) or were diagnosed with nonaffective FEP before 2005 (n = 37). The remaining 5,137,561 individuals constituted our cohort, observed from 1 January 2005 until the earliest of a confirmed

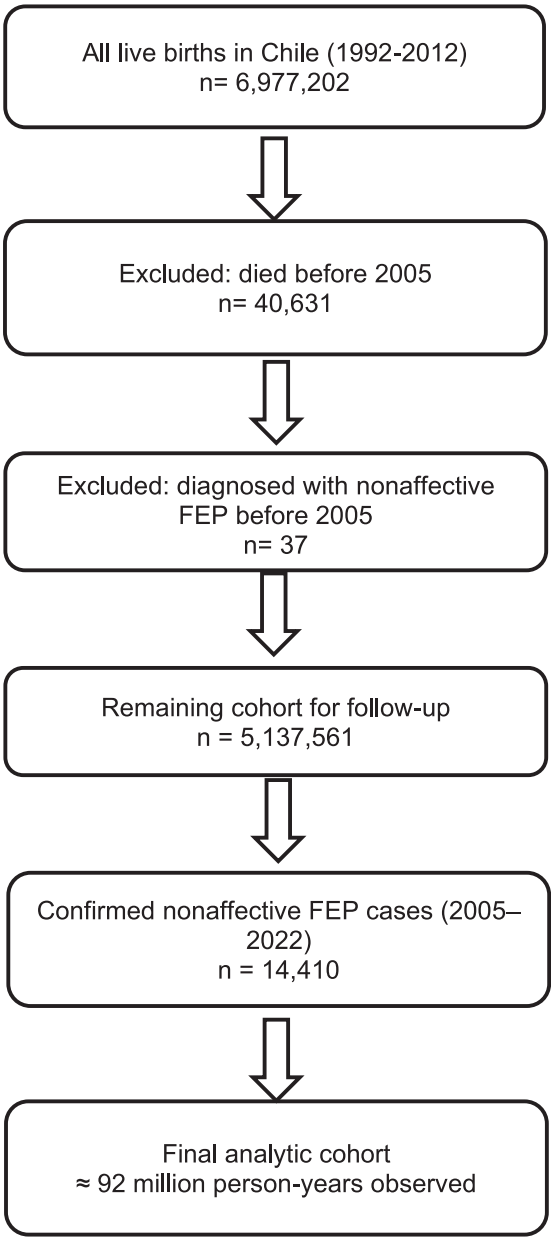

Fig. 1: **Assembly of the analytic cohort in Chile (1992–2012 births, 2005–2022 nonaffective FEP cases).**

nonaffective FEP diagnosis (ICD-10 F20–F29), death, or 31 December 2022.

Measures

Outcome (nonaffective FEP)

Our primary outcome comprised confirmed diagnoses of non-affective psychotic disorders (ICD-10 F20–F29), including schizophrenia, schizoaffective disorder, delusional disorder, acute and transient psychosis, and other non-affective psychoses. To reduce misclassification, we excluded cases initially recorded as "suspected" nonaffective FEP; these undergo psychiatrist-led re-evaluation after at least six months of follow-up and are either confirmed or rejected.[27] Prior evidence from Chile indicates that approximately 20% of suspected cases are ultimately not confirmed as nonaffective FEP, and diagnostic thresholds may vary regionally, which could introduce systematic bias.[26] Throughout the manuscript, we refer to these cases as "schizophrenia and other non-affective psychoses" or, more generally, "non-affective psychosis."

Exposure (urbanicity at birth)

We adopted the national census criterion from the National Institute of Statistics,[29] which classifies localities as "urban" if they exceed 2000 inhabitants, or if they have 1001–2000 inhabitants with <50% involved in primary activities (e.g., agriculture). All other localities are "rural." Urbanicity at birth was conceptualized as a contextual exposure that could causally interact with social deprivation.

Potential confounders

We considered year of birth and region. We followed the standard taxonomy of the National Institute of Statistics, which groups these regions into five larger areas: Northern Area (Arica y Parinacota, Tarapacá, Antofagasta, Atacama), Central Area (Coquimbo, Valparaíso, Metropolitan Santiago), Central South Area (O'Higgins, Maule, Ñuble, Biobío), Southern Area (La Araucanía, Los Lagos, Los Ríos), and Southernmost Area (Aysén, Magallanes, Chilean Antarctica). We treated region as a confounder because it was related to both urbanicity (the exposure) and psychosis incidence (the outcome), whereas year of birth was treated as a precision variable that improved model stability by accounting for secular trends in incidence.[11]

Effect modifiers (parental social deprivation)

Two indicators were explored:

1. Parental Education: categorized as "low" if the parent completed ≤8 years of schooling (did not finish compulsory basic education) and "high" if the parent completed ≥12 years of schooling (graduated from high school or beyond).
2. Parental Employment: categorized as "active" versus "inactive." The latter included those reported as unemployed, economically inactive (e.g., homemakers, students), or retired, because all three groups indicated the parent was not working for pay at the time of childbirth.

Parental education level (years of schooling completed) and employment status were recorded at the time of the participant's birth. Each variable was measured for mother and father separately.

Data analysis plan

We began by computing frequencies and proportions for all variables—exposure, outcome, covariates, and parental indicators of social deprivation. We then calculated crude incidence rates of nonaffective FEP (cases per 100,000 person-years) overall and stratified by key variables (sex, year of birth, region, urbanicity). Person-years were computed from 1 January 2005 (the first date of valid FEP case ascertainment) until diagnosis, death, or the end of 2022. Missing data were minimal for all core variables, with maternal education recorded in >99% of births and slightly lower completeness for paternal information. We treated missing paternal education as a separate "unknown" category; given the very low proportion of missingness, multiple imputation was not undertaken as it was unlikely to affect results.

We fitted Poisson regression models to estimate IRRs, using the log of person-years as an offset. First, we assessed the crude association between urbanicity at birth (urban vs rural) and nonaffective FEP risk. Our primary model simultaneously adjusted for region and year of birth. Intermediate models including only year of birth or only region were fitted solely to assess the incremental change in precision. In our final model, we simultaneously adjusted for both covariates, providing an IRR that captures the association between urban birth and psychosis independently of birth cohort and regional variations.

We opted for Poisson models because they directly estimate incidence rate ratios, are widely used in incidence studies, and provide results that are easily interpretable in public health terms. This approach is analogous to a piecewise exponential survival model and is appropriate for cohort data with events per person-year as the outcome.[11] Furthermore, we checked for over-dispersion in the Poisson models; none was detected (Pearson chi-square/df $\approx$ 1.0), so a Poisson was deemed appropriate. Consequently, a negative binomial model was not necessary, and results were essentially unchanged when we tested one.

To evaluate whether parental social deprivation modified any association with urbanicity, each parental indicator (education, employment) was examined in a separate interaction model. We introduced a product term with urbanicity and assessed statistical significance on the multiplicative scale via a likelihood-ratio test (LRT). Where interaction was detected, we also assessed additive interaction using the Relative Excess Risk due to Interaction (RERI) and Attributable Proportion (AP). A RERI >0 suggests that the combined effect of urbanicity and social deprivation exceeds the sum of their individual effects. All interaction estimates assume no unmeasured confounding of either the urbanicity–psychosis or deprivation–psychosis relationship. Analyses were conducted in R 4.3.1 (packages "tidyverse," "janitor," "data.table," "gtsummary," "broom," "lubridate").

Ethics approval

The study was reviewed and approved by the Columbia University Human Research Protection Office (Protocol #: IRB-AAAT6370).

Lived experience statement

No people with lived experience of psychosis were involved in the design or conduct of this study.

Role of the funding source

None.

Results

The study population comprised 5,137,561 individuals (Table 1). Of those, we identified 14,410 with confirmed nonaffective FEP between 2005 and 2022. Among those with confirmed FEP, 66.25% were male, 33.75% were females. People with FEP were diagnosed most frequently when they were between 15 and 24 years (25.91%). When comparing people with vs without FEP, there were more males (66.25% vs. 51.01%) and people living in the Metropolitan Santiago Area (46.45% vs. 40.65%); differences on urbanicity were minimal between the two groups (88.33% vs. 88.60%) (Table 2). Participants' fathers in urban areas had higher levels of education compared to those in rural areas ("high school or more": 74.1% vs. 38.8%, respectively), but both groups had a similar employment rate ("active": 84.9% vs. 88.4%). Participants' mothers in urban areas were significantly more educated ("high school or more": 80.9% vs. 47.3%) and had a higher likelihood of being employed ("active": 30.3% vs. 11.0%).

Table 3 shows the crude nonaffective FEP incidence rates by the variables of interest. Over a total of 91.96 million person-years, we observed a crude incidence rate of 15.67 cases per 100,000 person-years (95% CI: 15.42, 15.93). The incidence rate for males was higher than that for females, with 20.36 cases per 100,000 person-years (95% CI: 19.95, 20.77) compared to 10.79 cases per 100,000 person-years (95% CI: 10.49, 11.10) for females. The rates varied across different regions, ranging from 13.3 to 17.6 cases per 100,000 person-years. Among these regions, the Central Region (Coquimbo, Valparaíso, Metropolitan Santiago) had the highest incidence rate at 17.6 cases per 100,000 person-years (95% CI: 17.25, 17.98). Psychosis rates were higher in rural compared to urban areas in Northern, Central South, and Southern regions.

In unadjusted models (see Table 4), there was no significant association between urban birth and psychosis (IRR = 0.97, 95% CI: 0.92, 1.02). Adjusting for year of birth and region yielded a similar null finding (IRR = 0.96, 95% CI: 0.91, 1.01). Subgroup analyses showed a modest effect for males (IRR = 1.13, 95% CI: 1.06, 1.21) but no association for females (IRR = 0.93, 95% CI: 0.85, 1.01).

Variables	All participants (n = 5,137,561)		Urban (n = 4,552,194)		Rural (n = 585,560)	
	N	%	N	%	N	%
Gender						
Male	2,623,047	51.06	2,325,555	51.09	297,399	50.79
Female	2,514,365	48.94	2,226,317	48.91	287,948	49.17
Undetermined	149	<0.01	129	<0.01	20	<0.01
Year of birth						
Before 1997	1,582,833	30.81	1,375,666	30.22	207,150	35.38
1998~2002	1,165,424	22.68	1,023,974	22.49	141,274	24.13
2003~2007	1,154,263	22.47	1,036,751	22.77	117,512	20.07
2008~2012	1,235,041	24.04	1,115,610	24.51	119,431	20.40
Region at birth						
Northern Region	454,461	8.85	441,113	9.69	13,328	2.28
Central Region	2,794,980	54.40	2,662,983	58.50	131,913	22.53
Central South Region	1,161,450	22.61	918,313	20.17	243,074	41.51
Southern Region	646,641	12.59	454,942	9.99	191,675	32.73
Southernmost Region	80,029	1.56	74,650	1.64	5377	0.92
Paternal characteristics						
Education						
Basic, primary, or none	963,237	18.75	682,763	15.00	280,441	47.89
High school or more	3,602,674	70.12	3,375,208	74.14	227,351	38.83
Missing	571,650	11.13	494,223	10.86	77,768	13.28
Employment[a]						
Inactive, unemployed, or retired	521,094	10.14	479,156	10.53	41,923	7.16
Active	4,382,214	85.30	3,864,584	84.89	517,452	88.37
Missing	234,253	4.56	208,454	4.58	26,185	4.47
Maternal characteristics						
Education						
Basic, primary, or none	1,178,603	22.94	869,996	19.11	308,535	52.69
High school or more	3,958,894	77.06	3,681,953	80.88	276,820	47.27
Missing			245	<0.01	205	<0.01
Employment[a]						
Inactive, unemployed, or retired	3,693,013	71.88	3,172,068	69.68	520,807	88.94
Active	1,444,537	28.12	1,379,923	30.31	64,559	11.03
Missing			203	<0.01	194	<0.01

[a]Active = employed; Inactive = students, retired, pensioners.

Table 1: **Characteristics of the study population.**

Table 5 shows that low paternal education significantly interacted with urbanicity on the multiplicative scale (IRR = 1.32; 95% CI: 1.17, 1.48; p < 0.001). This IRR compares individuals exposed to *both* urban birth and paternal low education with those exposed to *neither*. The additive-scale RERI was 0.23 (95% CI: 0.04, 0.42) and the AP was 0.17, indicating that 17% of incidence among the doubly exposed was attributable to their joint effect. An even stronger interaction emerged for maternal education (IRR = 1.34; 95% CI: 1.21, 1.49; p < 0.001). Here, the RERI was 0.33 (95% CI 0.18, 0.47) and the AP 0.24. To aid interpretation, we also plotted the observed incidence rates by urbanicity and parental education, which show that the urban + low education group had the highest risk compared with the other categories (Fig. 2).

We found no evidence for interaction between paternal employment and urbanicity (Table 6). However, a multiplicative interaction did appear between maternal employment and urbanicity (IRR = 1.30; 95% CI: 1.07–1.58; p < 0.011). On the additive scale, the RERI of 0.18 (95% CI: –0.14, 0.51) was inconclusive. Finally, the AP was 0.14, suggesting that 14% of the incidence among those doubly exposed was due to their combined effect.

Discussion

In this national registry–based cohort study, we found: (1) no overall association between being born in an urban area and the incidence of non-affective psychosis, and (2) a significant increase in psychosis risk among those born in urban areas who also had low parental education, suggesting an interaction between urbanicity and early-life social deprivation. The crude incidence of non-affective psychosis was 15.7 per 100,000 person-

Variables	All participants (n = 5,137,561)		With FEP (n = 14,410)		Without FEP (n = 5,123,151)	
	N	%	N	%	N	%
Sex						
Male	2,623,047	51.06	9547	66.25	2,613,500	51.01
Female	2,514,365	48.94	4863	33.75	2,509,502	48.98
Undetermined	149	<0.01		<0.01	149	<0.01
Rural/Urban						
Urban	4,552,001	88.60	12,729	88.33	4,539,272	88.60
Rural	585,367	11.39	1681	11.67	583,686	11.39
Region at birth						
Northern	454,461	8.85	1085	7.53	453,376	8.85
Central	2,794,980	54.40	8825	61.24	2,786,155	54.38
Central South	1,161,450	22.61	2562	17.78	1,158,888	22.62
Southern	646,641	12.59	1758	12.20	644,883	12.59
Southernmost	80,029	1.56	180	1.25	79,849	1.55
Paternal characteristics						
Education						
Low	963,237	21.09	3632	29.77	959,605	21.07
High	3,602,674	78.90	8570	70.23	3,594,104	78.93
Employment[a]						
Inactive	521,081	10.63	1132	8.00	519,949	10.64
Active	4,382,214	89.37	13,012	92.00	4,369,202	89.37
Maternal characteristics						
Education						
Low	1,172,180	22.85	4952	34.42	1,167,228	22.81
High	3,958,894	77.16	9434	65.58	3,949,460	77.19
Employment[a]						
Inactive	3,690,015	71.87	11,873	82.41	3,678,142	71.84
Active	1,444,537	28.13	2534	17.59	1,442,003	2816

[a]Active = employed; Inactive = students, retired, pensioners.

Table 2: **Sociodemographic and clinical characteristics of the FEP versus non-FEP populations.**

years, consistent with prior Chilean estimates (18.9 per 100,000 in González-Valderrama et al.[11]; 15.9 per 100,000 in Larach et al.[26]). Minor differences likely reflect varying study periods and case definitions, but overall rates in Chile align with international figures and are slightly lower than some high-income countries.

The null overall association between urbanicity at birth and nonaffective FEP aligns with other reports

	All participants	Urban	Rural	p-value
Sex at birth				
Male	20.33 (19.92, 20.73)	20.40 (19.97, 20.84)	19.73 (18.53, 20.92)	0.302
Female	10.79 (10.48, 11.09)	10.60 (10.28, 10.92)	12.25 (11.29, 13.20)	0.001
Year of birth				
Before 1997	26.31 (25.71, 26.90)	26.62 (25.97, 27.26)	24.24 (22.66, 25.83)	0.006
1998–2002	22.91 (22.26, 23.56)	23.03 (22.34, 23.72)	22.05 (20.22, 23.88)	0.326
2003–2007	8.95 (8.55, 9.36)	8.95 (8.52, 9.38)	8.97 (7.68, 10.25)	0.977
2008–2012	1.35 (1.20, 1.50)	1.32 (1.16, 1.48)	1.59 (1.06, 2.13)	0.343
Region at birth				
Northern Region	13.33 (12.54, 14.12)	13.22 (12.42, 14.03)	16.80 (11.59, 22.00)	0.183
Central Region	17.62 (17.25, 17.98)	17.61 (17.23, 17.99)	17.78 (16.08, 19.48)	0.848
Central South Region	12.31 (11.84, 12.79)	11.80 (11.28, 12.33)	14.24 (13.12, 15.37)	<0.001
Southern Region	15.18 (14.47, 15.89)	14.34 (13.52, 15.17)	17.18 (15.79, 18.56)	<0.001
Southernmost Region	12.56 (10.73, 14.40)	12.57 (10.67, 14.47)	12.46 (5.41, 19.51)	0.976

[a]Cases per 100,000 person-years.

Table 3: **Crude incidence rates[a] with 95% Confidence Intervals (CI) and p values (urban vs rural).**

	IRR	2.5% CI	97.5% CI
Unadjusted model			
Urbanicity	0.97	0.92	1.02
Adjusted model 1[a]			
Urbanicity	1.06	1.01	1.11
Year of birth	0.89	0.89	0.89
Adjusted model 2[b]			
Urbanicity	0.96	0.91	1.01
Year of birth	0.89	0.89	0.89
Region at birth			
Central Region (Ref.)			
Northern Region	0.79	0.74	0.84
Central South Region	0.68	0.65	0.71
Southern Region	0.85	0.81	0.90
Southernmost Region	0.71	0.62	0.83

[a]Model 1: exposure: urbanicity; outcome: FEP diagnosis; adjusted for year of birth. [b]Model 2: exposure: urbanicity; outcome: FEP diagnosis; adjusted for year of birth and region.

Table 4: **Unadjusted and adjusted incidence rates ratios (IRR) for the urbanicity/psychosis association.**

from the Global South.[9–12] In contrast, robust evidence from Northern Europe has consistently shown an elevated incidence of psychosis among those born or raised in cities.[2–7] One explanation for this discrepancy may lie in the heterogeneous features of urban living, which differ significantly across geographic, cultural, and economic contexts.[8,14] Furthermore, the absence of an overall effect in Chile might indicate that city-specific stressors play a different role than in Northern Europe, where large immigrant populations, discrimination, or heightened social fragmentation can concentrate in certain urban areas.[14,16] In Chile, those same risk factors may be less prevalent or manifest differently, such that living in a city does not uniformly translate into higher psychosis risk. This pattern supports the "contingent urbanicity" hypothesis: city living increases psychosis risk primarily under conditions of social adversity.

Methodological variation may also explain divergent results. Prior Northern European studies often employed population density or continuous urbanicity gradients measured throughout childhood, whereas we used a dichotomous urban/rural definition at birth only.[2,6,7] Some studies in Denmark and Sweden have shown a dose–response effect of cumulative urban exposure from birth to adolescence.[5,8] Because our data only captured the location of birth (and not subsequent moves), we may have missed important later-life exposure to either rural or more densely urban settings. Moreover, access to timely diagnosis may also differ by setting. In rural areas and among families with lower education, barriers such as limited availability of psychiatric services and reduced mental health literacy could lead to under-ascertainment of cases. Such differential access may partly explain our null findings for urbanicity, reflecting diagnostic artifacts rather than absence of an effect.

Urbanicity exists on a continuum rather than a binary state,[30] but for this study we used Chile's official National Institute of Statistics definition to ensure comparability with registry data. This cut-off may mask variation across small towns and large metropolitan areas, and future research could apply graduated frameworks such as those proposed by UN-Habitat.[31] Regional variation in incidence may reflect higher population density, service availability, and local sociodemographic stressors; prior national registry studies have also reported elevated risk in central Chile, particularly in poorer areas near Santiago.[11]

Despite the null results, parental low education appeared to amplify the influence of urban birth on psychosis risk, with both multiplicative and additive interaction estimates reaching significance. Low parental education may reflect deeper socioeconomic disadvantage, such as constrained incomes and limited health literacy. As a result, families may face challenges in securing high-quality housing or consistent access to mental health services, especially in rapidly growing urban neighborhoods.[22,28] In this sense, rather than urban living itself being uniformly harmful, it may become detrimental when combined with low education and inadequate socioeconomic support.

	IRR	95% CI	p
Model 1			
Urbanicity	1.03	0.94, 1.12	0.59
Year of birth	0.89	0.89, 0.89	0.00
Paternal education	1.06	0.95, 1.19	0.27
Region at birth			
Central Region (Ref.)			
Northern Region	0.89	0.76	0.86
Central South Region	0.78	0.75	0.81
Southern Region	0.85	0.84	0.91
Southernmost Region	0.72	0.64	0.85
Urbanicity and paternal low education vs. rural location and paternal higher education	1.32	1.17, 1.48	0.00
Model 2			
Urbanicity	1.02	0.94, 1.11	0.67
Year of birth	0.89	0.89, 0.90	0.00
Maternal education	1.12	1.02, 1.24	0.02
Region at birth			
Central Region (Ref.)			
Northern Region	0.81	0.75	0.83
Central South Region	0.70	0.64	0.73
Southern Region	0.82	0.80	0.85
Southernmost Region	0.72	0.67	0.79
Urbanicity and maternal low education vs. rural location and maternal higher education	1.34	1.21, 1.49	0.00

Model 1: FEP + urbanicity at birth + year of birth + region + paternal education + combined effect (urbanicity + paternal education). Model 2: FEP + urbanicity at birth + year of birth + region + maternal education + combined effect (urbanicity + maternal education).

Table 5: **Parental education as a moderator on the multiplicative scale.**

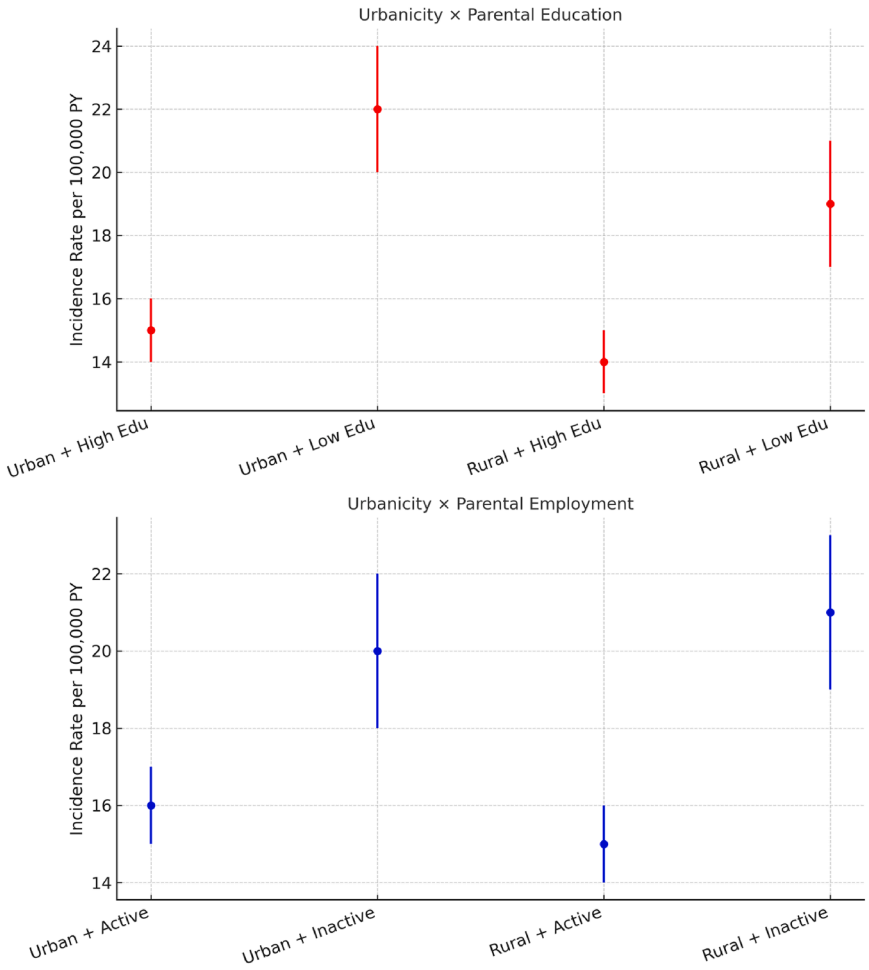

Fig. 2: **Incidence of non-affective psychosis by urbanicity and parental education/employment**.

Conversely, families with higher education might leverage the better healthcare and social opportunities typically available in metropolitan areas, thereby offsetting potential urban stressors.[28]

We also examined parental employment, finding some indication of interaction with maternal unemployment but not paternal. The weaker effects may arise from potential misclassification (e.g., homemakers or family caregivers might be coded as unemployed). Another possibility is that in the Chilean context, education is a more stable and salient indicator of social position than current employment. Indeed, national surveys show that short-term job fluctuations are common, whereas education is relatively fixed and highly stratified.[24,25] Future research could delve deeper into household income, job stability, and other markers of social deprivation in urban contexts.

Our results add to a broader global debate: is the urban environment harmful only in tandem with certain vulnerabilities, such as migrant status or socioeconomic disadvantage? For example, some European research indicates that the higher psychosis risk among migrants concentrates in deprived urban areas.[12,23] Although our data did not address migration, we observed stronger effects among families with low parental education—suggesting a parallel mechanism. Regarding sex, we found a small positive association between urbanicity and psychosis for males but not females, aligning with earlier work suggesting sex-specific vulnerability to certain environmental stressors.[32] Sex differences in psychosis incidence have been observed consistently, with men consistently show higher psychosis risk (≈1.5–2 times) and earlier onset than women, a pattern also seen in our cohort and prior Chilean studies.[32] Explanations include biological (sex hormones, neurodevelopment) and social factors (substance use, delayed help-seeking).[33] While these may contribute, our conclusions do not rest on sex interactions, and subgroup findings should be interpreted cautiously given multiple comparisons.

	IRR	95% CI	p
Model 3			
Urbanicity	1.06	1.01, 1.12	0.03
Year of birth	0.89	0.89, 0.89	0.00
Paternal employment	1.11	0.89, 1.39	0.34
Region at birth			
Central Region (Ref.)			
Northern Region	0.87	0.80	0.90
Central South Region	0.70	0.66	0.72
Southern Region	0.80	0.76	0.91
Southernmost Region	0.76	0.72	0.80
Urbanicity and paternal unemployment vs. rural location and paternal employment	0.96	0.76, 1.21	0.72
Model 4			
Urbanicity	0.89	0.74, 1.07	0.22
Year of birth	0.89	0.89, 0.89	0.00
Maternal employment	1.23	1.01, 1.48	0.04
Region at birth			
Central Region (Ref.)			
Northern Region	0.73	0.69	0.78
Central South Region	0.65	0.62	0.72
Southern Region	0.82	0.79	0.88
Southernmost Region	0.70	0.68	0.75
Urbanicity and maternal unemployment vs. rural location and maternal employment	1.30	1.07, 1.58	0.01

Model 3: FEP + urbanicity at birth + year of birth + region + paternal employment + combined effect (urbanicity + paternal employment). Model 4: FEP + urbanicity at birth + year of birth + region + maternal employment + combined effect (urbanicity + maternal employment).

Table 6: **Parental employment as a moderator on the multiplicative scale.**

Key strengths include large sample size, near-complete national coverage, and the use of confirmed nonaffective FEP diagnoses rather than suspected cases. We also explicitly tested for both multiplicative and additive interaction, addressing calls for more nuanced epidemiologic analyses of psychosis risk factors.[8] That said, several limitations remain. First, we lacked fine-grained data on neighborhood variables such as crime rates or social cohesion and individual-level risk factors like family psychiatric history, cannabis or other substance use, which could shape risk in urban contexts.[7] Second, we only measured urbanicity at birth, not capturing childhood or adolescent relocations. We lacked detailed data on participants' residence at nonaffective FEP diagnosis, so we could not directly assess the impact of subsequent migration or duration of urban exposure.[4] Future studies could explore the influence of moving from rural to urban environments (or vice versa) on psychosis risk. Third, under-ascertainment of cases—particularly in remote or impoverished areas—cannot be ruled out, although universal coverage of mental healthcare in Chile partially mitigates this concern.[26]

Our findings suggest that urbanicity alone does not explain psychosis risk in Chile; rather, risk emerges from its interaction with socioeconomic conditions, healthcare access, and population density. Future studies should integrate residential histories, neighborhood deprivation, and protective factors such as family networks. Chile's experience highlights how universal coverage and national registries can enable robust surveillance, offering a model for other Global South countries to strengthen evidence and reduce epidemiological gaps.

In terms of policy, children from socioeconomically disadvantaged families in urban areas may require targeted early psychosis prevention. Clinicians should remain alert to early signs among youth in these settings, while policymakers can mitigate risks through investments in prenatal care, parental education, and early childhood programs in urban poor communities. Broader strategies to reduce urban poverty and expand educational and employment opportunities for young parents may also serve as indirect but powerful approaches to psychosis prevention.

Contributors

FM and ES conceived and designed the study, developed the methodology, supervised the project, and drafted the initial manuscript.

JB, VH, and RC curated the data, provided resources, and contributed to validation and visualization.

XY, ZL, KR, and JS conducted the formal analysis and contributed to data interpretation. LY, MTMQ, SRN, and PS critically reviewed and revised the manuscript.

All authors contributed to manuscript revisions and approved the final version for submission.

Data sharing statement

The registry linkage and data preparation were conducted exclusively by authorized personnel at the Chilean Ministry of Health using unique national identifiers. Once linkage was complete, all personal identifiers were removed or encrypted, and the research team received only a de-identified dataset containing study-specific IDs and variables such as commune of birth (coded numerically), parental education, and employment categories. No names, addresses, or national ID numbers were included. All analyses were performed on secure servers, and results are reported only in aggregate to prevent re-identification. Data were obtained under a formal data-sharing agreement with the Ministry of Health.

AI use statement

We used ChatGPT to increase readability and correct grammar issues.

Declaration of interests

All authors declare no competing interests.

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