

Paper

Urbanicity and risk of first-episode psychosis: incidence study in Brazil

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We estimated the incidence of first-episode psychosis over a 3-year period in a Brazilian catchment area comprising the region's main city, Ribeirão Preto (1 425 306 persons-years at risk), and 25 other municipalities with a total of 1 646 556 persons-years at risk. The incidence rates were estimated and adjusted by gender and age, using the direct standardisation method to the world population as reference. The incidence of psychosis was higher in the younger groups, men, and among Black and minority ethnic Brazilians. Psychosis incidence was lower in Ribeirão Preto (16.69/100 000 person-years at risk; 95% CI 15.68–17.70) compared with the average incidence in the remaining municipalities (21.25/100 000 person-years at risk; 95% CI 20.20–22.31), which have lower population density, suggesting a distinct

role for urbanicity in the incidence of first-episode psychosis in low- and middle-income countries.

Declaration of interest

None.

Keywords

Schizophrenia spectrum and other psychotic disorders; urban and rural populations; incidence.

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Evidence on the epidemiology of psychosis has shown a wide variation in incidence rates between and within populations, with higher rates among men, in urban centres, and among migrants and minority ethnic groups.¹ The very few studies conducted so far in low- and middle-income countries (LMICs) indicate that social adversities can increase the risk of psychosis.² In Brazil, the incidence of first-episode psychosis (FEP) in São Paulo city was estimated at 15.8/100 000 person-years at risk (95% CI 14.3–17.6),³ a rate that was much lower than expected for a metropolis. It suggests that some of the aetiological mechanisms and environmental risk factors may not equally operate as in some European countries.

Brazil is a middle-income country with a large rate of urbanisation and one of the highest socially and economically unequal societies, where Black and minority ethnic people and those living in smaller towns have fewer educational, economic and health opportunities, which may operate as risk factors for psychosis. In the Schizophrenia and Other Psychoses Translational Research: Environment and Molecular Biology study, which is part of the international consortium European Network of National Schizophrenia Networks Studying Gene-Environment Interactions,⁴ we estimated the incidence of FEP in the catchment area of Ribeirão Preto, São Paulo State, Brazil. In this exploratory study, we aimed to describe the clinical profile of Brazilian patients with FEP and to estimate incidence rates according to some core demographic characteristics (age, gender, reported skin colour and municipality). We hypothesised that the FEP incidence rates in this Brazilian catchment area would vary depending on individual characteristics and municipality, but probably in directions other than those described in wealthy regions worldwide.

Method

Ribeirão Preto catchment area

In 2010 (Brazilian Census; <https://cidades.ibge.gov.br/>), the catchment area under study had a population of 1 327 989 inhabitants, distributed in 26 municipalities in a territorial area of 10 852 km². Ribeirão Preto is the main city of the region, with 604 682 inhabitants, a population density of 929.8 inhabitants/km², per capita Gross Intern Product of US\$9,143,20 and a Human Development

Index (HDI) score of 0.800, ranked 40th among 5570 Brazilian municipalities (<http://www.atlasbrasil.org.br/2013/pt/ranking>). The population of the remaining 25 towns varied from 1953 to 110 074 inhabitants (median, 23 862), with a median population density of 75.0 inhabitants/km² (13.2–308.4 inhabitants/km²), median Gross Intern Product of US\$5,254,80 (US\$2,234,80–US\$20,747,40) and HDI rankings varying from 145th to 2282nd nationally (<http://www.atlasbrasil.org.br/2013/pt/ranking>).

Inclusion criteria and recruitment

All individuals aged 16–64 years old, living in the Ribeirão Preto catchment area, with a first contact with mental health services due to primary psychotic disorders from 1 April 2012 to 31 March 2015 were eligible for the study. A surveillance strategy was established for all mental health services in the region that could be sought by patients with FEP, including all in-patient and community-based mental health services, through weekly personal and/or phone contacts of the assistant researchers with the personnel of all the services.

Trained researchers determined the psychiatric diagnoses by the Structured Clinical Interview for DSM-IV (SCID) translated into Portuguese, with good reliability indexes.⁵ The research assistants, nurses and psychologists with experience in mental health were trained in the use of the SCID at the beginning of the study. During all the study period (including the leakage study described below), weekly meetings were held by assistant researchers and the senior staff, comprising a psychiatric nurse, two psychologists and three senior psychiatrists, to check for inconsistent data, revision of the protocols and ratification of all the diagnoses.

Leakage study

The leakage study was carried out in the 12 months following the end of the inclusion period. This process involved visits to all mental health services of the catchment area by six trained psychologists in the use of the SCID. In total, they reviewed 65 469 medical records. Possible cases were initially discussed with senior researchers, a psychiatry nurse and a psychologist, and subsequently, a senior psychiatrist reviewed the data. The final diagnosis and the decision about the inclusion of the cases in the study were established by consensus.

The local research ethics committee approved the study (process number 12606/2012). Informed written consent was obtained from all participants with the exception of those identified by the leakage study, for which the sample inclusion was based only on medical records. This procedure was predicted in the original project, which was also approved by the local mental health services.

Variable definition and statistical analysis

Patients were classified as either non-affective psychosis (NAP; DSM-IV⁶ codes 295.xx, 297.1 and 298.8) or affective psychosis (AP; DSM-IV codes 296.04, 296.44, 296.64). The duration of untreated psychosis (DUP) was defined as the difference, in weeks, between the date of onset of clinically significant positive or catatonic psychotic symptoms, which last at least 1 week, and the start date of effective pharmacological treatment, based on the Nottingham Onset Schedule, which was built specifically for this purpose.⁷

For descriptive analyses, tests for statistical associations were calculated with Stata software version 13 for Windows. We used the projected population during the 3-year study period based on the 2015 Brazilian Census to calculate person-years at risk. Considering that this is an exploratory study, we initially included only basic demographic variables to calculate the incidence rates, which were estimated by gender, age band, self-reported skin colour and place of living (Ribeirão Preto versus remaining cities). We considered the population density as an indicator of urbanicity. The incidence rates were adjusted by gender and age, using the direct standardisation method to the world population as reference (<https://esa.un.org/unpd/wpp/Download/Standard/Population/>). The 95% CI of the rates were calculated based on the s.e. for proportions in stratified samples. In the case of skin colour partitioned by gender and age, we used the proportions observed in the last census of 2010 over the 2015 population, since it was not available in the archives of the Brazilian Census official bureau (<https://www.ibge.gov.br/>).

Results

We identified 588 participants over the 3-year period: 309 (52.5%) by direct contact with mental health services and 279 (47.5%) by the leakage study. The leakage study participants were older (median, 34.0 v. 28.0; $Z = 6.41$; $P < 0.001$) and with longer DUP (median, 17.0 v. 9.0; $Z = 5.43$; $P < 0.001$) than those identified by mental health services. First contact was mainly with mental health community-based services (62.4%), followed by psychiatric emergency services (27.2%). Three patients were found without prior contact with mental health services during the recruitment of population-based controls for a case-control study.

Table 1 shows the demographic and clinical features of the sample. More patients were men ($n = 318$, 54.1%), who were more often diagnosed as NAP (62.5%) than women ($P < 0.001$). Over half of the patients classified themselves as White (52.4%), without significant differences between diagnoses ($P = 0.359$). The absence of marital bonding was more often observed among those with the diagnosis of NAP (56.9%, $P = 0.005$), particularly among men (66.5%) compared with women ($P = 0.024$). A higher proportion of patients with NAP (42.1%) reported occupational inactivity compared with patients with AP (34.2%), although without statistically significant differences ($P = 0.621$). Up to 9 years of schooling was reported by 37.8% of the patients, without differences between the diagnoses ($P = 0.393$).

Patients with NAP had a lower age of illness onset than those with AP (median, 27.0 v. 31.0; $P = 0.001$), which was significant among men only (24.0 v. 29.0, $P = 0.002$). Men with NAP were

younger than their AP counterparts at first contact with mental health services (27.0 v. 31.0, $P = 0.015$); however, among women, those with NAP were older than those with AP at the moment of first contact (36.5 v. 33.0; $P = 0.048$). The median DUP was 14.0 weeks (interval from <1 to 1292.4 weeks). The DUP was lower in those with AP (median, 9.0) than those with NAP (median, 21; $P < 0.001$), for both genders.

The total population at risk during 3-year period was 3071 862 person-years. The overall incidence rate of FEP, adjusted by gender and age, was 19.46/100 000 person-years at risk (95% CI 18.71–20.20; crude incidence 19.14/100 000 person-years at risk, 95% CI 17.59–20.68). The incidence of FEP declined with age and was higher in men and Black and minority ethnic individuals (Table 2). Compared with the incidence among those living in the main city, the incidence among those living in the other 25 municipalities was almost 26% higher (incidence rate ratio, 1.27; 95% CI 1.08–1.51). We carried out a sensitivity analysis calculating incidence rates only with the patients identified through direct contact and results remained consistent for all the variables, except for the difference between Ribeirão Preto and the other 25 municipalities, which became statistically non-significant.

Discussion

This is one of very few studies generating estimates of the incidence of psychosis in South America in recent decades. The incidence was higher in men, who had younger age of illness onset than women and among Black and minority ethnic individuals, which is in line with results from previous studies.⁸ However, our results showed a higher incidence of psychosis in areas with lower population density compared with the incidence in the main town of the catchment area.

The frequency of patients reporting themselves as White was lower than that described for the catchment area under study (66.3%; Brazilian Census), suggesting a higher risk of FEP among Black or minority ethnic individuals, following findings from minority groups in Europe.¹ This association may be explained by the lower socioeconomic status among Black Brazilians compared with White Brazilians.

The median age of first contact with mental health service was higher than previously assumed, but resembling that observed in European cities, as formerly reported.¹ The median DUP found in our sample was lower when compared with those described previously,⁹ but it is similar to that found in São Paulo city.³ However, more recent data have shown a reduction of the DUP in European countries,¹ which could be related to the implementation of early intervention services,¹⁰ which have not yet been established in Brazil.

The incidence of FEP observed in the Ribeirão Preto catchment area is similar to that reported in São Paulo city³ and in Southern Italy,¹¹ but lower than rates described for large urban centres in European countries,¹² adding to the evidence of heterogeneity of the incidence of psychosis worldwide. Interestingly, the incidence estimated for the main town, where about 40% of the population at risk resides (i.e. those aged between 16 and 64 years old and living in the catchment area according to the national census), was lower than the average incidence in the remaining municipalities of the region, which have much lower population densities. This finding is opposite to the association between urbanicity and risk of psychosis consistently described in some European populations, but is similar to results recently reported in Italy,¹ and is also in agreement with a recent published data showing no association between urbanicity and psychosis in LMICs.¹³ In Brazil, municipalities with lower population density tend to show worse socioeconomic indicators, which is confirmed by the discrepancy

Table 1 Demographic and clinical features of patients with first-episode psychosis from the Ribeirão Preto catchment area, Brazil, according to the type of psychosis (affective and non-affective) and the gender of the participant

Characteristic	Affective psychosis (n = 284)	Non-affective psychosis (n = 304)	Total (n = 588)	Statistic test	P value
Men ^a	128 (45.1)	190 (62.5)	318 (62.5)	17.96	<0.001*
White ^a	146 (51.4)	162 (53.3)	308 (52.4) ^d	2.05 ^c	0.359
Men	70 (47.9)	95 (58.6)	165 (53.6)	3.53 ^c	0.060
Women	76 (52.1)	67 (41.4)	143 (46.4)		
Single/divorced/widow ^a	125 (44.0)	173 (56.9)	298 (50.7) ^e	10.56 ^c	0.005*
Men	67 (53.6)	115 (66.5)	182 (61.1)	5.06 ^c	0.024*
Women	58 (46.4)	58 (33.5)	116 (38.9)		
Occupational inactivity ^a	97 (34.2)	128 (42.1)	225 (38.3) ^f	0.95 ^c	0.621
Men	41 (37.3)	80 (52.6)	121 (46.2)	0.23 ^{a,c}	0.634
Women	56 (47.5)	48 (49.5)	104 (48.4)		
Up to 9 years of study ^a	106 (37.3)	116 (38.2)	222 (37.8) ^g	1.87 ^c	0.393
Men	53 (50.0)	68 (58.6)	121 (54.5)	0.80 ^c	0.372
Women	53 (50.0)	48 (41.4)	101 (45.5)		
Onset age of psychosis ^b	31.0 (23.0–41.0)	27.0 (20.0–37.0)	29.0 (21.0–39.0) ^h	2.78 ^j	0.001*
Men	29.0 (22.0–41.0)	24.0 (19.0–33.0)	26.0 (20.0–36.0)	3.12 ^j	0.002*
Women	31.0 (24.0–41.0)	32.0 (24.5–45.0)	31.0 (24.0–42.0)	0.45 ^j	0.654
Age at first contact ^b	32.0 (25.0–44.0)	31.0 (22.0–41.0)	31.0 (23.0–42.0)	1.58 ^j	0.114
Men	31.0 (22.3–44.0)	27.0 (21.0–37.0)	28.0 (21.0–39.0)	2.43 ^j	0.015*
Women	33.0 (26.3–43.0)	36.5 (27.8–48.0)	34.0 (27.0–45.3)	1.98 ^j	0.048*
Duration of untreated psychosis, weeks ^b	9.0 (4.0–22.0)	21.0 (8.0–59.5)	14.0 (4.0–41.0) ⁱ	6.02 ^j	<0.001*
Men	9.0 (3.3–22.0)	18.0 (8.0–77.8)	15.0 (4.0–46.0)	4.32 ^j	<0.001*
Women	10.0 (4.0–21.0)	21.0 (8.0–53.5)	13.0 (4.0–38.0)	4.08 ^j	<0.001*

a. n (%) and differences between genders.
b. Median (interquartile range) within genders.
c. Pearson χ^2 -test.
d–i. Missing data: d. n = 73; e. n = 94; f. n = 111; g. n = 186; h. n = 2; i. n = 6.
j. Mann-Whitney U test (Z).
*P < 0.05.

between the HDI rankings of Ribeirão Preto (40th position) and the remaining 25 municipalities (ranked 145th to 2282nd positions; <http://www.atlasbrasil.org.br/2013/pt/ranking>). Therefore, the observed association between urbanicity and risk of FEP in the region of Ribeirão Preto suggests a possible effect of socioeconomically deprived contexts in the incidence of psychosis.¹⁰ It is important to highlight that this is an initial and exploratory study where we considered population density as a proxy of urbanicity; we did not include more direct measures of urbanicity. Further studies with the identification of environmental variables that could be

more explanatory of urbanicity as a risk factor to psychosis in the socioeconomic context of our region and other LMICs are needed.

The main limitation of our study is that almost half of patients with FEP were identified by a leakage study. This could be due to the organisation of community mental health services, such as the lack of early intervention protocols for psychoses, the non-existence of common databases for the records of clinical information and the unfamiliarity of health professionals with epidemiologic research. Also, patients identified through the leakage study tended to have longer DUP (suggesting that they might have milder symptoms),

Table 2 Incident rates of first-episode psychosis in the Ribeirão Preto catchment area, Brazil, according to demographic features (per 100 000 inhabitants)

	Cases, n (%)	Person-years at risk, n (%)	Crude incidence rate per 100 000 (95% CI)	Adjusted incidence rate per 100 000 (95% CI) ^a
Gender ^b				
Female	270 (45.9)	1 523 085 (49.6)	17.72 (15.61–19.84)	17.66 (16.66–18.67)
Male	318 (54.1)	1 548 777 (50.4)	20.53 (18.27–22.78)	21.21 (20.12–22.29)
Age, years ^c				
16–19	63 (10.7)	325 392 (10.6)	19.36 (14.58–24.14)	19.39 (17.33–21.45)
20–24	98 (16.7)	360 573 (11.7)	27.17 (21.79–32.55)	27.21 (24.83–29.59)
25–29	97 (16.5)	386 319 (12.6)	25.11 (20.11–30.10)	25.08 (22.68–27.47)
30–34	83 (14.1)	391 725 (12.8)	21.19 (16.63–25.74)	21.27 (18.94–23.58)
35–39	71 (12.0)	338 757 (11.0)	20.95 (16.08–25.83)	20.96 (18.62–23.28)
40–44	53 (9.0)	299 592 (9.7)	17.69 (12.92–22.45)	17.69 (15.48–19.89)
45–49	48 (8.2)	279 855 (9.1)	17.15 (12.29–22.00)	17.14 (14.84–19.45)
50–54	44 (7.5)	269 838 (8.8)	16.30 (11.48–21.12)	16.24 (13.82–18.67)
55–59	17 (2.9)	233 205 (7.6)	7.29 (3.82–10.75)	7.25 (5.53–8.98)
60–64	14 (2.4)	186 606 (6.1)	7.50 (3.57–11.43)	7.58 (5.55–9.59)
Skin colour ^d				
White	308 (52.4)	2 030 999 (66.1)	15.16 (12.79–17.53)	15.36 (14.70–16.02)
Black and minority ethnic	207 (35.2)	1 040 863 (33.9)	19.89 (17.95–21.83)	19.72 (20.46–18.97)
Missing	73 (12.4)			
Region of residence ^d				
Main town	238 (40.5)	1 425 306 (46.4)	16.69 (15.68–17.70)	17.05 (16.03–18.07)
Remaining towns	350 (59.5)	1 646 556 (53.6)	21.25 (20.20–22.31)	21.53 (20.47–22.59)

a. Standardised by global population (<https://esa.un.org/unpd/wpp/Download/Standard/Population/>).
b. Adjustment by age.
c. Adjustment by gender.
d. Adjustment by gender and age.

higher education level, be White and be from the remaining 25 municipalities, compared with patients included through direct assessment (data not shown). These differences may explain why the association between urbanicity and risk of FEP was no longer observed when we excluded patients identified in the leakage study from the incidence rates estimated.

A question that might also be raised is related to the accuracy of a national census carried out in a country with continental dimensions and huge socioeconomic inequalities. However, the latest Brazilian census conducted in 2010 had decentralised commissions and was operated totally in a digital format. From the total 67.5 million households registered by the official census bureau, interviews with at least one resident were done in 83.7% of them (<https://censo2010.ibge.gov.br/noticias-censo>). Therefore, we believe that the information available in the Brazilian census can be considered accurate.

In summary, we have shown that some risk factors for psychosis observed in wealthy countries, such as age, gender and ethnicity, can also be present in LMICs, but others, such as population density, may behave differently or even not be present in other socio-economic contexts. Our findings highlight the need for high-quality research on the epidemiology of FEP, particularly focusing on the peculiarities of the social and economic arrangements in LMICs, which can contribute to the development of effective prevention actions and policies, aiming to improve the lives of those who are direct or indirectly affected by psychosis.

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