Association of Urbanicity with Schizophrenia and Related Mortality in China

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Association de l'urbanité avec la schizophrénie et la mortalité qui y est reliée en Chine

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Abstract

Objective: Although higher prevalence of schizophrenia in Chinese urban areas was observed, studies focused on the association between schizophrenia and urbanicity were less in China. Using a national representative population-based data set, this study aimed to investigate the relationship between urbanicity and schizophrenia and its related mortality among adults aged 18 years old and above in China.

Methods: Data were obtained from the Second China National Sample Survey on Disability in 2006 and follow-up studies from 2007 to 2010 each year. We restricted our analysis to 1,909,205 participants aged 18 years or older and the 2,071 schizophrenia patients with information of survival and all-caused mortality of the follow-up surveys from 2007 to 2010. Schizophrenia was ascertained according to the *International Statistical Classification of Diseases, 10th Revision*. The degree of urbanicity and the region of residence were used to be the proxies of urbanicity. Of these, the degree of urbanicity measured by the ratio of nonagricultural population to total population and the region of residence measured by six categorical variables (first-tier cities, first-tier city suburbs, second-tier cities, second-tier city suburbs, other city areas, and rural areas). Logistics regression models and restricted polynomial splines were used to examine the linear/nonlinear relationship between urbanicity and the risk of schizophrenia. Cox proportional hazards regression models were used to test the role of urbanicity on mortality risk of schizophrenia patients.

Results: 10% increase in the degree of urbanicity was associated with increased risk of schizophrenia ($OR = 1.44$; 95% CI, 1.32 to 1.57). The nonlinear model further confirmed the association between the degree of urbanicity and the risk of schizophrenia. This association existed sex difference, as the level of urbanicity increased, schizophrenia risk of males grew faster than the risk of females. The hazard ratio (HR) of mortality in schizophrenia patients decreased with the elevated of urbanicity level, with a HR of 0.42 (95% CI, 0.21 to 0.84).

Conclusions: This research suggested that incremental changes in the degree of urbanicity linked to higher risk of schizophrenia, and as the degree of urbanicity elevated, the risk of schizophrenia increased more for men than for women. Additionally, we found that schizophrenia patients in higher degree of urbanicity areas had lower risk of mortality. These findings contributed to the literature on schizophrenia in developing nations under a non-Western context and indicates that strategies to improve mental health conditions are needed in the progress of urbanicity.

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Abrégé

Objectif : Bien qu'une prévalence plus élevée de la schizophrénie ait été observée dans les secteurs urbains de Chine, les études axées sur l'association entre la schizophrénie et l'urbanité étaient moins nombreuses en Chine. À l'aide d'un ensemble de données nationales représentatives dans la population, la présente étude visait à rechercher la relation entre l'urbanité et la schizophrénie, et la mortalité qui y est reliée chez les adultes de 18 ans et plus en Chine.

Méthodes : Les données ont été obtenues de la deuxième enquête nationale par sondage sur le handicap en Chine de 2006 ainsi que d'études de suivi chaque année de 2007 à 2010. Nous avons restreint notre analyse à 1 909 205 participants âgés de 18 ans et plus et aux 2 071 patients souffrant de schizophrénie ainsi qu'à l'information sur la survie et toutes les causes de la mortalité tirée des études de suivi de 2007 à 2010. La schizophrénie était déterminée selon la Classification statistique internationale des maladies, 10^e révision. Le degré d'urbanité et la région de résidence servaient de mandataires de l'urbanité. À cet égard, le degré d'urbanité était mesuré par le rapport de la population non agricole sur la population totale, et la région de résidence était mesurée par six variables catégorielles (villes de premier rang, banlieues de villes de premier rang, villes de deuxième rang, banlieues de villes de deuxième rang, autres régions urbaines et régions rurales). Des modèles de régression logistique et des splines polynomiales restreintes ont servi à examiner la relation linéaire/non linéaire entre l'urbanité et le risque de schizophrénie. Les modèles de régression aléatoire proportionnelle de Cox ont servi de test du rôle de l'urbanité dans le risque de mortalité des patients souffrant de schizophrénie.

Résultats : Une hausse de 10% du degré d'urbanité était associée à un risque accru de schizophrénie ($RC = 1,44$; IC à 95% 1,32 à 1,57). Le modèle non linéaire a confirmé en outre l'association entre le degré d'urbanité et le risque de schizophrénie. Cette association existait dans la différence entre les sexes, comme le degré d'urbanité s'accroissait, le risque de schizophrénie chez les hommes grandissait plus rapidement que le risque chez les femmes. Le rapport de risque (RR) de mortalité chez les patients de la schizophrénie diminuait à mesure qu'augmentait le degré d'urbanité, avec un RR de 0,42 (IC à 95% 0,21 à 0,84).

Conclusions : Cette recherche a suggéré que des changements progressifs du degré d'urbanité étaient liés à un risque plus élevé de schizophrénie, et qu'à mesure que s'élevait le degré d'urbanité, le risque de schizophrénie augmentait davantage pour les hommes que pour les femmes. En outre, nous avons observé que les patients de la schizophrénie présentant un degré plus élevé d'urbanité étaient à moindre risque de mortalité. Ces résultats ont contribué à la littérature sur la schizophrénie dans les pays en développement, dans un contexte non occidental, et ils indiquent que les stratégies pour améliorer les conditions de santé mentale sont nécessaires pour le progrès de l'urbanité.

Keywords

schizophrenia, mortality, urbanicity, sex difference

Introduction

As one of the most severe mental disorders, schizophrenia has become a public health concern worldwide.^{1,2} Studies have widely cited that genetic predispositions and environmental risk factors are the established risk factors for schizophrenia. Urbanicity, the degree to which a given geographical area is urban, is one of the well-established environmental risk factors for mental health problems, especially strongly implicated in schizophrenia and their related mortality.³⁻⁵ Some hypothesis, such as considerable disparities in service delivery and economic resources, increasing living stress, greater pollution exposures, and ethnic minority status in urban areas, proposed to be the possible explanation of this urbanicity effect on schizophrenia.⁶

An increased interest in urbanicity effect on schizophrenia has raised in developed countries. Previous studies confirmed that schizophrenia and its mortality associated with the degree of exposure to urban environment despite the different methodologies used for the measurement of urban exposure (population size or density or rural-urban setting).^{7,8} Meta-analysis study presented that dwellers in urban had 2.37 times greater to be have schizophrenia than in rural

settings; 1.33 times of high risk of psychiatric morbidity has been found in urban living inhabitants than in rural residents.⁸ Considering that around 68% of the world's population are predicted to live in cities by 2050, urbanicity is a key area for psychosis research.⁹

China underwent an unprecedented scale of urbanicity since the initiation of the reform and opening policy in 1978, leading to almost a 5-fold rise in urban population in the past 4 decades.^{10,11} Urbanicity generated opportunities to obtain improved sanitary conditions and high-quality health care, but it resulted in substantial health risks, such as stressful social environment, greater social disparities, and serious pollution as well.¹²⁻¹⁴ In China, extremely rapid urbanicity also brings to rapid increases in city size, crowded living conditions, migration and population scale related problems of disparities in health care delivery and economic resources, considerable acculturative stress in working environment, and serious air and water pollution in urban areas,¹¹ which may lead to high risk of mental health problems to city dwellers.⁶

Although previous studies have observed that prevalence of schizophrenia was high in Chinese urban areas,^{15,16}

studies focused on the association between schizophrenia and urbanicity in China were less. Among the few, most were at the regional level with small size,¹⁷ and evidence investigating effects of urbanicity on mortality of schizophrenia is missing. In developed countries, although the link between urbanicity and schizophrenia has been suggested by a series of evidence,^{7,8} most of them only provided the linear association between urbanicity and schizophrenia, and no study reported the nonlinear exposure–response relationship.

By using a large nationally representative and population-based data set, this study aimed to investigate the linear and nonlinear relationship between urbanicity and schizophrenia among adults aged 18 years old and above in China. Further, this research examined the association between urbanicity and the mortality schizophrenia. This study may help to detect the high-risk populations of schizophrenia for early intervention in the progress of rapid urbanicity.

Methods

Study Population

Data from the Second National Sample Survey on Disability (SNSSD) in 2006 and its follow-up surveys from 2007 to 2010 were used in this study. From April 1 to 31 May 2006, China State Council implemented this national sample survey. The SNSSD database was consisted of the recodes of prevalence, causes, severities of disability and socioeconomic status, living conditions, and the health services demand and utilization of disabled persons. A multistage, stratified random-cluster sampling strategy was used to select noninstitutionalized individuals in mainland China. Among each provincial-level administrative division, sampling strata were defined according to subordinate administrative areas, local geographical characteristics, and local gross domestic product, where appropriate, to allow for anticipated regional variability.¹⁸ Within each stratum, a 4-stage sampling strategy was used in this survey, and sampling was conducted with probability proportional to cluster size.¹⁸ First of the sampling stage was to select counties from 31 provincial-level administrative divisions in China. The investigators randomly selected counties from each stratum for the next stage sampling. The following stages were to randomly select towns from counties, villages/districts from towns, and finally communities from villages/districts. This survey comprised a total of 734 counties, 2,980 towns, and 5,964 communities. All households in each selected community were investigated. Ultimately, 771,797 households and 2,526,145 individuals were selected for this survey, with the response rate 99.8%, which have national representative of Chinese population. More details of SNSSD design and sample processing could be found elsewhere.¹⁸

A subsample of people with schizophrenia was selected for follow-up studies from 2007 to 2010 each year followed by the 2006 SNSSD. From 2007 to 2008, 734 study sites

randomly selected in 734 counties of 2006 SNSSD (1 study site for each county). After 2009, the follow-up surveys doubled to the study sites into 1,468. These 1,468 sites were also randomly selected in 734 counties of 2006 SNSSD. The follow-up surveys of SNSSD database were consisted of the information of living conditions, medical and rehabilitation demand and using information, community environment and information about household. For those who were deceased in each follow-up survey, the information of date of death and cause of death were recorded via the linkage to the public security bureau official register system.

Because the typical age of onset for schizophrenia is in late adolescence or early 20s,¹⁹ we restricted our analysis to adults aged 18 years or older and finally included 1,909,205 participants at baseline in 2006, and the 2,071 schizophrenia patients with information of survival and all-caused mortality of the follow-up surveys from 2007 to 2010. More details about the sample selection in the follow-up surveys could find in the other publication.²⁰

Ethics Approval

The survey was conducted in all provinces by the Leading Group of the National Sample Survey on Disability and the National Bureau of Statistics. It was approved by the China State Council (No. 20051104) and was implemented within the legal framework governed by the Statistical Law of the People's Republic of China.

Measures

Schizophrenia. The outcome variable was a binary measure (i.e., whether having schizophrenia). This survey identified schizophrenia by using a 3-step approach as following: First, mental illness with social function limitations was identified by the screening questionnaire with 5 items during the household face-to-face interview process. This questionnaire was developed for the survey according to the “Guidelines and Principles for the Development of Disability Statistics,” which had been demonstrated high reliability.²¹ Persons who answered a positive response was labeled as likely to be meeting thresholds of mental illness with social function limitations. Second, psychiatrists who have more than 5 years of clinical experience identified the mental illness with disability by using The World Health Organization Disability Assessment Schedule, Version II (WHO DAS II) in persons with possible mental illness with social function limitations.²² If persons who received a score of 52 or higher were diagnosed as mental illness with disability. Third, persons who have schizophrenia were diagnosed by experienced psychiatrists using the *International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10)* Symptom Checklist for Mental Disorders (ICD-10 code F20).²³ This instrument presented satisfactory reliability (overall $\kappa = 0.72$),²⁴ and over 95% cases could be confirmed through this Symptom Checklist.²⁵

Urbanicity. China is a large country with a population of 1.395 billion people and a total area of land of 9,634,057 km². The mainland in China has a total of 4 municipalities and 293 prefectural-level cities. We used both the degree of urbanicity and region of residence to measure urbanicity. Of these, the degree of urbanicity measured by the ratio of nonagricultural population to total population (%). To establish this measure, data of the size of nonagricultural population and total population were obtained from 734 counties in 2000 China census, which subsequently linked to participants' addresses of this study. Additionally, the region of residence measured by 6 categorical variables: first-tier cities, first-tier city suburbs, second-tier cities, second-tier city suburbs, other city areas, and rural areas, which based on Chinese city tier system classification. This hierarchical classification of Chinese cities released by *CBN* magazine, including 19 first-tier cities, 30 second-tier cities, 70 third-tier cities, 90 fourth-tier cities, and 129 fifth-tier cities. These cities assessed based on 5 indicators: concentration of commercial resources, city's pivotability, citizen vitality, variety of lifestyle, and flexibility in the future.

Covariates. According to previous findings,^{26,27} we considered demographic characteristics and socioeconomic conditions as covariates in this study. Demographic characteristics included sex, age, marital status, residence, and household size. Of these, sex (male/female) and residence (urban/ rural) were dummy variables. Age was defined by 5 categories due to the onset age of schizophrenia around early adulthood and also menopause of women: 18 to 29, 30 to 39, 40 to 49, 50 to 59, and 60 years old and above. Given that the effect of family may associate with the risk of schizophrenia,²⁸ we added the family size as our potential confounder, which was classified into 4 categories: 1, 2, 3, 4, and above. Socioeconomic conditions were evaluated by education, household income per capita, and employment status.²⁹ Education was classified into 3 categories: primary school and below, junior high school, and senior high school and above. Employment status was defined by 2 categories: employment and unemployment. Household income per capita were divided into 3 groups based on tertiles, with the first tertile being the lowest group and the third tertile being the highest group.

Analytic strategy. To present the distribution of population, descriptive statistics were undertaken to present the prevalence of schizophrenia and mortality of schizophrenia patients in this study. By using cross-sectional data in 2006, logistic regression models were used to examine the relationship between urbanicity (measured by the degree of urbanicity and region of residence respectively) and schizophrenia allowing for multiple demographic and socioeconomic covariates. Besides that, the major results also presented the nonlinear associations between the degree of urbanicity and schizophrenia. To check for the nonlinear associations, we plotted restricted polynomial splines with knots at the 20th, 45th, 60th, and 80th percentiles for

exposure (measured by the degree of urbanicity) and replaced the linear terms of the degree of urbanicity with the spline terms in the regression model.

Additionally, in order to investigate the role of the degree of urbanicity at the baseline on the survival risk of schizophrenia, Cox proportional hazards regression models and the longitudinal data in 2007 to 2010 were used. We calculated the follow-up time as the time elapsed from the date of baseline interview to either the date of death or the date of the last SNSSD interview in which the individual participated.

A *P* value less than 0.05 was considered statistically significant. The software Stata version 13.0 for Windows (Stata Corp, College Station, TX, USA) was utilized for statistical analysis.

Results

Characteristics of Participants

Participants with schizophrenia were more likely to be female, single, living alone than those without schizophrenia. Compared with people without schizophrenia, schizophrenia individuals had lower level of education and income and were more likely to be unemployment (Online Appendix Table 1).

Compared with participants without schizophrenia, schizophrenia patients more often lived in areas with higher degree of urbanicity (mean = 46.02%, *SD* = 14.25%); 28% (*n* = 2,136) schizophrenia patients in this survey were in first-tier city and second-tier city areas, while around half of them lived in other city areas (*n* = 3,890, 51%) and 21% (*n* = 1,602) were in rural areas. Among the participants, first-tier city suburbs and second-tier city suburbs residents had the highest prevalence of schizophrenia (prevalence = 0.42%; Online Appendix Table 1).

Over half of the patients were females (*n* = 4,195, 54.99%) who were more often diagnosed as schizophrenia (prevalence = 0.44%) than males. Compared with individuals without schizophrenia, the absence of marital bonding was more often observed among those with the diagnosis of schizophrenia. A higher proportion of patients with schizophrenia (51.68%) were in the lowest household income per capita group compared with participants without schizophrenia (29.63%), and the schizophrenia prevalence decreased with the increased of household income per capita. Primary school and below was reported by 28.89% of the patients compared with participants without schizophrenia (15.80%). More details could be found in Online Appendix Table 1.

The geographical distribution of the degree of urbanicity and prevalence of schizophrenia were presented in Figure 1. As suggested by the significant correlative value (*r* = 0.2220, *P* < 0.0001), there was an uphill linear relationship between the degree of urbanicity and schizophrenia prevalence's distribution.

Table 1. Logistic Regressions of the Association between Urbanization Rate and Schizophrenia.

Characteristics	Model 1	Model 2
Urbanization rate (10%)	1.44 (1.32 to 1.57)***	1.72 (1.53 to 1.93)***
Sex		
Male	Reference	Reference
Female	1.23 (1.18 to 1.29)***	1.40 (1.30 to 1.51)***
Urbanization rate $\times$ Sex		
Urbanization rate $\times$ Male		Reference
Urbanization rate $\times$ Female		0.72 (0.62 to 0.84)***
Age, year		
18 to 29	Reference	Reference
30 to 39	3.62 (3.33 to 3.95)***	3.64 (3.34 to 3.96)***
40 to 49	3.86 (3.54 to 4.22)***	3.88 (3.55 to 4.24)***
50 to 59	3.36 (3.06 to 3.68)***	3.37 (3.07 to 3.70)***
60+	1.15 (1.05 to 1.27)***	1.16 (1.05 to 1.28)***
Family size		
1	Reference	Reference
2	1.04 (0.95 to 1.14)	1.04 (0.95 to 1.14)
3	0.85 (0.77 to 0.93)***	0.85 (0.77 to 0.93)***
4+	0.67 (0.62 to 0.74)***	0.67 (0.61 to 0.74)***
Married status		
Married	Reference	Reference
Single	4.75 (4.50 to 5.01)***	4.78 (4.52 to 5.05)***
Household income per capita		
Tertile 1 (lowest)	Reference	Reference
Tertile 2	0.53 (0.50 to 0.56)***	0.53 (0.50 to 0.56)***
Tertile 3 (highest)	0.30 (0.28 to 0.32)***	0.30 (0.28 to 0.32)***
Education		
Primary school and below	Reference	Reference
Junior high school	0.74 (0.70 to 0.79)***	0.75 (0.70 to 0.80)***
Senior high school and above	0.56 (0.52 to 0.60)***	0.57 (0.53 to 0.61)***
Employment		
Yes	Reference	Reference
No	2.50 (2.30 to 2.72)***	2.47 (2.27 to 2.69)***

* $P < 0.05$. ** $P < 0.01$. *** $P < 0.001$. **Figure 1.** Geographical distributions of the degree of urbanicity and prevalence of schizophrenia at city level in China (327 cities). The geographical distribution of the degree of urbanicity and prevalence of schizophrenia was similar as suggested by their significant correlative value ($r = 0.2220$, $P < 0.0001$).

Table 2. Logistic Regressions of the Association between Region of Residence and Schizophrenia.

Characteristics	Model 1	Model 2
Region of residence		
Rural areas	Reference	Reference
First-tier cities	1.74 (1.60 to 1.90)***	1.98 (1.75 to 2.24)***
First-tier city suburbs	1.40 (1.24 to 1.57)***	1.40 (1.17 to 1.69)***
Second-tier cities	1.57 (1.37 to 1.79)***	1.92 (1.59 to 2.32)***
Second-tier city suburbs	1.52 (1.36 to 1.69)***	1.78 (1.52 to 2.09)***
Other city areas	1.19 (1.12 to 1.26)***	1.34 (1.23 to 1.47)***
Region of residence		
Rural areas × Male		Reference
First-tier cities × Female		0.79 (0.68 to 0.93)***
First-tier city suburbs × Female		0.99 (0.78 to 1.26)*
Second-tier cities × Female		0.69 (0.54 to 0.89)***
Second-tier city suburbs × Female		0.75 (0.6 to 0.93)
Other city areas × Female		0.80 (0.71 to 0.9)***
Age, year		
18 to 29	Reference	Reference
30 to 39	3.63 (3.33 to 3.96)***	3.65 (3.34 to 3.97)***
40 to 49	3.86 (3.54 to 4.22)***	3.87 (3.55 to 4.23)***
50 to 59	3.33 (3.03 to 3.65)***	3.34 (3.04 to 3.66)***
60+	1.13 (1.03 to 1.25)*	1.14 (1.03 to 1.26)*
Family size		
1	Reference	Reference
2	1.05 (0.96 to 1.16)	1.05 (0.96 to 1.16)
3	0.86 (0.78 to 0.94)***	0.86 (0.78 to 0.94)***
4+	0.69 (0.63 to 0.75)***	0.69 (0.63 to 0.75)***
Sex		
Male	Reference	Reference
Female	1.23 (1.18 to 1.29)***	1.47 (1.33 to 1.63)***
Married status		
Married	Reference	Reference
Single	4.76 (4.51 to 5.03)***	4.78 (4.53 to 5.05)***
Household income per capita		
Tertile 1 (lowest)	Reference	Reference
Tertile 2	0.52 (0.49 to 0.55)***	0.52 (0.49 to 0.55)***
Tertile 3 (highest)	0.29 (0.27 to 0.31)***	0.29 (0.27 to 0.31)***
Education		
Primary school and below	Reference	Reference
Junior high school	0.73 (0.69 to 0.78)***	0.74 (0.69 to 0.79)***
Senior high school and above	0.56 (0.52 to 0.60)***	0.56 (0.52 to 0.6)***
Employment		
Yes	Reference	Reference
No	2.51 (2.31 to 2.72)***	2.49 (2.29 to 2.71)***

* $P < 0.05$. ** $P < 0.01$. *** $P < 0.001$.

Among all adults, the mortality rates of schizophrenia for adults decreased with the increased of degree of urbanicity. The mortality rate for patients with schizophrenia in tertile 1(lowest), tertile 2, and tertile 3(highest) degree of urbanicity areas was 1.81%, 1.72%, and 1.00%, respectively. The patterning of mortality rates in females was similar to that among all children by areas with various degree of urbanicity. However, males reported different variation in these parallel analyses. Among male adults, the highest mortality rates group lived in areas with highest degree of urbanicity (2.91%), while the lowest resided in tertile 2 degree of urbanicity areas (0.76%). More details could be found in Online Appendix Table 2.

The Association between Urbanicity and the Risk of Schizophrenia

Table 1 shows the results of the association between the degree of urbanicity and schizophrenia. Model 1 shows that 10% increase in the degree of urbanicity was associated with increased risk of schizophrenia ($OR = 1.44$; 95% CI, 1.32 to 1.57) after controlling for age, gender, marital status, household income per capita, education, and employment. The non-linear model further confirmed the association between the degree of urbanicity and the risk of schizophrenia (Figure 2). Incremental changes in the degree of urbanicity tended to be strongly linked to higher risk of schizophrenia. Also, we found

Figure 2. Restricted splines of the ORs with 95% CI for the relation of the degree of urbanicity to the occurrence of schizophrenia in adults aged 18 years old and above.

an effect threshold of 9% for every increment in the degree of urbanicity. Stratified analyses found that the level of degree of urbanicity increased, schizophrenia risk of males (OR = 1.59; 95% CI, 1.40 to 1.82) grew faster than the risk of females (OR = 1.40; 95% CI, 1.24 to 1.58) (Online Appendix Table 3). Model 2 (Table 1) adds the interaction between sex and the degree of urbanicity; this interaction was statistically significant (OR = 0.72; 95% CI, 0.62 to 0.84), indicating that there was a significant sex difference of the association between degree of urbanicity and the risk of schizophrenia.

Table 2 displays the similar trend in the other way with urbanicity measured by region of residence. Compared to residents in rural areas, living at higher levels of urbanicity was associated with greater risk of schizophrenia. We observed the highest OR of schizophrenia for adults who lived in first-tier inner cities areas (OR = 1.74; 95% CI, 1.60 to 1.90). Subsequent adjustment for the interaction between sex and region of residence presented a sex difference in the association between urbanicity and schizophrenia (Table 2, model 2, Online Appendix Table 4), which further confirmed the trend in the way of urbanicity measured by the degree of urbanicity.

The Association between Urbanicity and the Mortality Risk of Schizophrenia

Table 3 illustrates the Cox proportional hazards regressions on the role of urbanicity on the mortality of schizophrenia patients. The hazard ratio (HR) of mortality in schizophrenia patients decreased with the increased of the degree of urbanicity, with a HR of 0.42 (95%CI, 0.21 to 0.84) in model 1. Additionally, there was no significant sex difference in the association between urbanicity and the mortality risk of schizophrenia (model 2).

Discussion

This study examined the association of urbanicity on schizophrenia and its mortality in China. To the best of our knowledge, this is the first study using a large nationally representative and population-based data set to estimate the relationship between the degree of urbanicity and schizophrenia and to consider the urbanicity effect on mortality of schizophrenia patients to date. The current study demonstrated an association between the degree of urbanicity and schizophrenia and its mortality among Chinese adults.

Our results showed that incremental changes in the degree of urbanicity were strongly linked to higher risk of schizophrenia, which were consistent with previous studies.^{13,30} Several hypotheses have been put forward to explain this association. First, living environments in modern urban areas are very mixed in terms of poverty and wealthy.³¹ Despite urban populations becoming generally wealthier, residents in deprived neighborhood are more likely to have higher risk of psychosis by increasing the likelihood of exposing to higher social stressors, lower social cohesion and crime victimization.³⁰ These increased exposures may rise the risk of schizophrenia. Second, green space decreased with the rapid increased degree of urbanicity, which was associated with the descended of mental health level.⁴ The mechanisms explaining this association including space as a means for stress reducing and social cohesion increasing.⁴ Third, city living has negative impacts on social stress processing of humans. Biological hypotheses regard that living in urban areas associates with increased amygdala activity, the key region for regulation of negative affect, social stress and cognitive processing, which was negative for mental health.¹³

In contrast, our finding showed that higher mortality risk of schizophrenia patients decreased with the incremental

Table 3. Hazard Ratio of the Role of Urbanicity on the Mortality of Schizophrenia Patients.

Characteristics	Model 1	Model 2
Urbanization rate (10%)	0.42 (0.21 to 0.84)**	0.63 (0.25 to 1.58)
Sex		
Male	Reference	Reference
Female	0.86 (0.60 to 1.24)	1.12 (0.65 to 1.95)
Urbanization rate × Sex		
Urbanization rate × Male		Reference
Urbanization rate × Female		0.45 (0.13 to 1.59)
Age, year		
18 to 29	Reference	Reference
30 to 39	1.18 (0.82 to 1.70)	1.18 (0.82 to 1.70)
40 to 49	1.10 (0.78 to 1.54)	1.10 (0.78 to 1.54)
50 to 59	1.13 (0.82 to 1.55)	1.13 (0.82 to 1.55)
60+	1.17 (0.86 to 1.58)	1.17 (0.86 to 1.58)
Family size		
1	Reference	Reference
2	1.02 (0.91 to 1.14)	1.02 (0.91 to 1.14)
3	1.00 (0.89 to 1.13)	1.00 (0.89 to 1.13)
4+	0.98 (0.89 to 1.09)	0.98 (0.89 to 1.09)
Married status		
Married	Reference	Reference
Single	1.98 (1.39 to 2.82)***	2.00 (1.40 to 2.85)***
Household income per capita		
Tertile 1 (lowest)	Reference	Reference
Tertile 2	0.95 (0.64 to 1.43)	1.27 (0.84 to 1.92)
Tertile 3 (highest)	1.06 (0.66 to 1.72)	0.95 (0.58 to 1.57)
Education		
Primary school and below	Reference	Reference
Junior high school	1.23 (0.82 to 1.85)	0.95 (0.64 to 1.43)
Senior high school and above	0.94 (0.57 to 1.55)	1.07 (0.66 to 1.74)
Employment		
Yes	Reference	Reference
No	1.06 (0.56 to 2.02)	1.05 (0.55 to 2.00)

* $P < 0.05$. ** $P < 0.01$. *** $P < 0.001$.

degree of urbanicity. Compared with other health problems, schizophrenia patients suffering from behavioral disorders, which often led to a high incidence of unnatural deaths, such as suicide, homicide, and accident.³² Almost 51.9% schizophrenia patients died from the unnatural deaths according to the previous study.³³ Less access to emergency and limited emergency medical service capability in less urbanicity areas resulted in higher mortality rates for unnatural mortality.³⁴ Especially in China with major imbalanced development among different areas, less urbanicity areas related with poverty, shortage of health care resources, which may result in the inconsistency of the relationship between mortality and the degree of urbanicity in schizophrenia patients with the results in developed countries.

Further, our results found that as the level of degree of urbanicity increased, schizophrenia risk of males grew faster than the risk of females. In the progress of high-speed urbanicity in China, males may be at higher risk of exposure to adverse factors for poor mental health than females. Males with higher proportion of rural–urban labor migration and greater exposure to unhealthy lifestyles than in females may

interpret this sex difference. In China, rapid urbanicity brings a large number of rural–urban labor migration workers, and these migration workers have a higher sex ratio of male to female, reaching 160:100 (= males: females) in some parts of China.³⁵ This high sex ratio of the floating population in China may increase the likelihood of exposure to considerable acculturative stress, social marginalization, and unhealthy lifestyles for poor mental health⁷ in males than in females.

Limitations

This study used a very large sample, representing the 1.9 million Chinese people, to test the association of urbanicity with schizophrenia and related mortality in China. By using the WHO DAS II and the ICD-10 Symptom Checklist for Mental Disorders as diagnostic tools and the use of experienced clinical psychiatrists as interviewers, the information bias minimized and the comparability of the diagnostic process improved in this study. To our best knowledge, this is the first time to report the empirical

results of the relationship between schizophrenia and its mortality in mainland China.

However, this study also had limitations. First, despite different methodologies used for the measurement of urban exposure, we could not distinguish exposure duration and could not examine the role of urban birth or urban upbringing on schizophrenia. Second, the measurement of degree of urbanicity based on 2000 census data may result in bias to the findings, although using "region of residence" to measure urbanicity in this study may make up for the vulnerable of the degree of urbanicity measurement. Third, some schizophrenia patients without disabilities may not have been identified in this survey. Therefore, these findings may underestimate the overall prevalence of schizophrenia. Fourth, we were unable to control for individual-level substance misuse or family history of mental illness because these data were not available from denominator sources. Finally, this study should be interpreted with caution because of the lack of design weights used in the analysis stage.

Conclusions

This research suggested that incremental changes in the degree of urbanicity linked to higher risk of schizophrenia, and as the degree of urbanicity elevated, the risk of schizophrenia increased more for men than for women. Additionally, we found that schizophrenia patients in higher degree of urbanicity areas had lower risk of mortality. These findings contributed to the literature on schizophrenia in developing nations of a non-Western context and indicates that strategies to improve mental health conditions are needed in the progress of urbanicity.

Authors' Note

Yanan Luo and Lihua Pang contributed equally to this study. Yanan Luo contributed to study concept and design, drafting the manuscript, data analysis, and interpretation. Lihua Pang contributed to study concept, critical revision of article for important intellectual content. Chao Guo and Lei Zhang contributed to revision of article. Xiaoying Zheng contributed to study concept and design, critical revision of article for important intellectual content. All authors gave final approval of the version to be published. Data are available from <http://www.cdprf.org.cn/> with the permission of China Disabled Persons' Federation. Restrictions apply to the availability of these data, which were used under license for this study.

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Supplemental Material

The supplemental material for this article is available online.

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