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# Gender-specific correlates for suicide mortality in people with schizophrenia: a 9-year population-based study

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## Abstract

**Background** Schizophrenia is associated with a high mortality rate due to the high risk of suicide. However, there is still a lack of evidence on the gender-specific risk factors for suicide among people with schizophrenia. In this study, we aimed to measure the sociodemographic and clinical correlates of suicide deaths in different genders among people with schizophrenia.

**Methods** Data on patients with schizophrenia from 2013 to 2021 in Guangzhou, China were obtained from the National Information System for Psychosis (NISP), involving a total of 33,080 patients. Cox regression and Fine-Gray models were used to explore the sociodemographic and clinical risk factors for suicide mortality in different genders.

**Results** The overall age-standardized mortality rates due to suicide were 133.89 (95% CI: 124.31-143.47) per 100,000 person-years for females and 163.25 (95% CI: 152.92-173.59) per 100,000 person-years for males. To be specific, lack of medical insurance, history of non-treatment, and history of suicidal behavior was associated with a higher risk for suicide mortality for females, while an age of 35–54, being hospitalized once, and the age of onset being > 28 years were linked to lower risk for suicide mortality for males. For both genders, a lower risk for suicide mortality was observed in patients at an older age ( $\geq 55$  years) and with a history of hospitalization more than once, and a higher suicide mortality risk was found in married patients and those residing in rural areas.

**Conclusion** The present study found that gender differences should be taken into account in the development of suicide prevention programs for people with schizophrenia, and future research is still required to verify our preliminary results.

**Keywords** Schizophrenia, Suicide, Gender difference, Risk factors

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## Introduction

Schizophrenia is a severe and chronic mental illness, with patients estimated to lose 13–15 years of potential life compared to the general population [1]. Schizophrenia is also associated with high direct medical costs and overuse of medical resources [2], accounting for 1.3% of the total burden of disease in China [3]. The association between increased risk of suicide and schizophrenia has been well documented in prior studies. Suicidal behavior is common among people with schizophrenia worldwide [4], and it was reported that the pooled lifetime prevalence of suicide ideation and suicide attempts in China was 25.8% and 14.6%, respectively [5]. Approximately half of suicide cases occur in the first two years following diagnosis [6]. It has been found that schizophrenia is associated with a 9.76 times higher risk of suicide mortality than that of the general population, indicating that suicide may be a major cause of decline in the life expectancy of patients with schizophrenia [7]. Therefore, identifying risk factors for suicide mortality is essential for reducing suicide mortality in people with schizophrenia.

Common clinical risk factors for suicide in schizophrenia include prior attempted suicide, concurrent depression, substance abuse, and younger ages [8]. Many previous studies have identified gender differences in suicide mortality risks among people with schizophrenia [9–11]. It has been well documented that males with schizophrenia have a higher risk of suicide [12] and greater suicide mortality than their female counterparts [9, 11], which may be related to different pathological mechanisms in different genders. Gender-specific features have also been reported in people with schizophrenia. For example, a study indicated that up to 61% of the illness-related genes were gender-specific [13]. Furthermore, gender-specific risk factors mainly affect the symptoms, use of antipsychotic medications, and clinical care of people with schizophrenia [14]. Some studies reported that elderly patients were at a higher risk of suicidal ideation and suicidal attempts than younger patients [5]. Compared with patients who have never received antipsychotic treatment and those with poor treatment compliance, patients who received antipsychotic treatment and those compliant with treatment are at a lower risk of suicidal death [15]. However, due to different research methods and different studied populations, there are inconsistencies among some studies. Gender-specific risk factors for suicide mortality in schizophrenia have been rarely explored in developing countries, where there are limited mental health resources.

Therefore, more studies concerning gender-specific sociodemographic and clinical risk factors for suicide mortality in schizophrenia are needed. The present study aimed to examine the gender differences concerning sociodemographic and clinical characteristics in patients

with schizophrenia and to explore how these risk factors differ between different genders.

## Materials and methods

### Data source and study design

The present study was a retrospective observational study. Data on patients with schizophrenia registered between 2013 and 2021 in Guangzhou, China were obtained from the National Information System for Psychosis (NISP, established in 2011), which included detailed sociodemographic information and clinical data including follow-up records and survival time. The follow-up duration refers to the time of registration in NISP to the end of observation (December 31, 2021 for living patients and the date of death for deceased patients). The study protocol was approved by the Institutional Ethical Board of the Affiliated Brain Hospital, Guangzhou Medical University. As this study was observational and retrospective, informed consent was waived by the Institutional Ethical Board of the Affiliated Brain Hospital, Guangzhou Medical University.

### Subjects

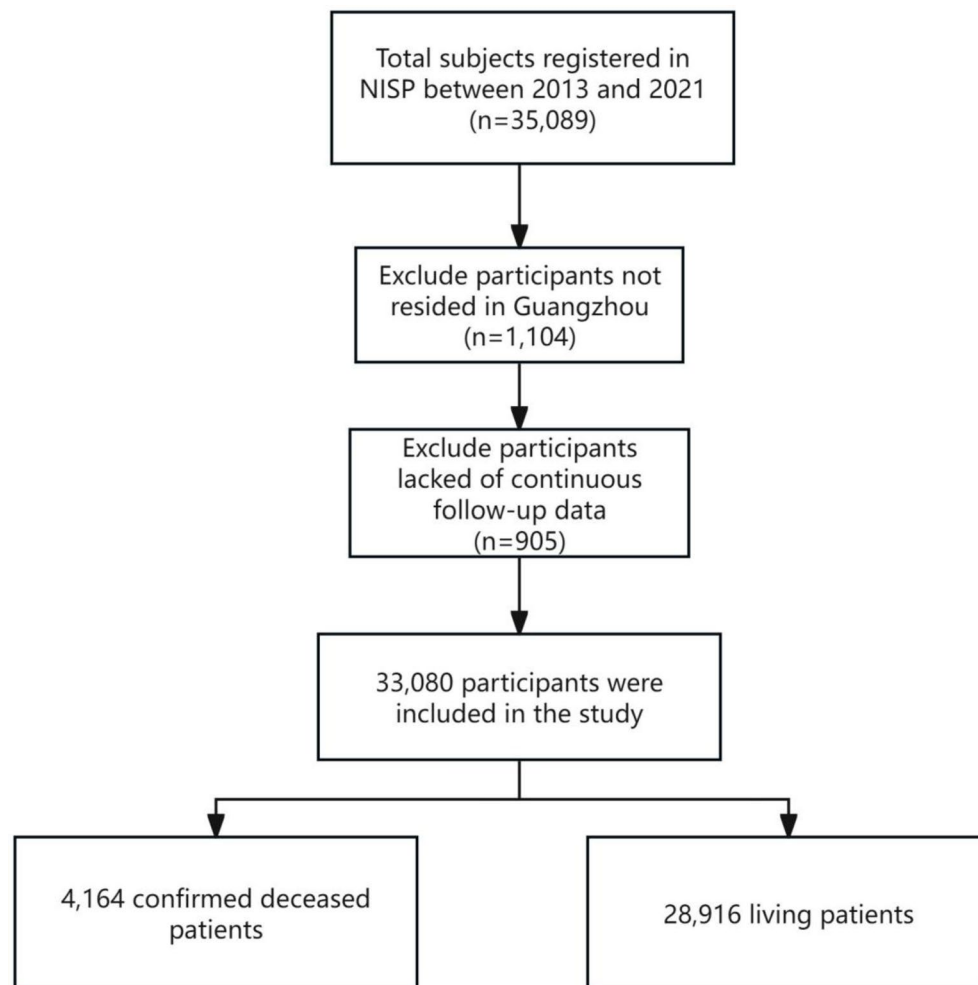
Patients with schizophrenia registered in Guangzhou, China between 2013 and 2021 were included as study subjects. Inclusion criteria were as follows: (1) patients aged  $\geq 10$  years, (2) patients diagnosed with schizophrenia according to the International Classification of Diseases 10th coding system (ICD-10): F20-21, F25, and (3) patients residing in Guangzhou, China. Patients with any of the following conditions were excluded: (1) with two or more missed items in the sociodemographic and clinical data and (2) lack of continuous follow-up records. A total of 33,080 subjects were involved in this study, including 28,916 living patients and 4,164 deceased patients, as confirmed by the Guangzhou Center for Disease Control and Prevention and Guangzhou Public Security Bureau between 2013 and 2021 (Fig. 1). The dropout rate of the total cohort was 5.53%.

### Categorization of causes of death

Causes of death for all the subjects were labeled using the ICD-10. The data on death were extracted from the NISP and linked to the monitoring system for causes of death in the Guangzhou Center for Disease Control and Prevention and Guangzhou Public Security Bureau to accurately identify the causes and dates of death. The subjects were divided into three groups based on their survival status during the follow-up period: alive, deceased due to suicide, and deceased due to non-suicidal causes.

### Risk factors

The following data were collected for each enrolled subject: age ( $\leq 34/35$ – $54/\geq 55$  years), gender (female/male),



**Fig. 1** Flowchart for inclusion of study participants

education level (high school and above/middle school/primary school and below), employment status (unemployed/employed), marital status (single/married), residence (urban/rural areas), costs covered by medical insurance (yes/no), frequency of hospitalization (none/once/more than once), duration of disease ( $\leq 11.5$ / $> 11.5$  years, based on the median duration of schizophrenia), family history of mental illness (no/yes), disease stability in the last follow-up period (stable/unstable), the continuity of treatment (continuous/non-continuous/non-treatment), follow-up duration (months), age of onset ( $\leq 28$ / $> 28$  years, based on the median age), age of diagnosis ( $\leq 34$ / $> 34$  years, based on the median age), financial status (non-poverty/poverty), history of violent behavior (no/yes), and history of suicide behavior (no/yes).

According to the Chinese Management and Treatment Regulations for Severe Mental Disordered Patients [16], the disease status and the continuity of treatment were categorized based on the following criteria: “stable disease” was defined as risk behavior at levels 0, with

disappearance of psychotic symptoms, basic recovery of insight, average or good social function, no serious adverse drug reactions, and no severe physical disease; “unstable disease” was defined as risk behavior at levels 1 to 5, with at least one of the psychotic symptoms and poorer insight and social function; “continuous treatment” was defined as regular treatment with prescribed medications; “discontinuous treatment” was defined as intermittent treatment without a psychiatric prescription; “non-treatment” was defined as the refusal to take psychiatric medications prescribed or no need to take psychiatric medications prescribed. The patients’ status of disease and the continuity of treatment during the follow-up period were determined by community mental health professionals based on the above criteria.

#### Statistical analysis

Categorical variables were presented as frequencies and percentages, and continuous variables were presented as means and standard deviations. The Chi-square ( $\chi^2$ )

test or continuity correction  $\chi^2$  test was used to compare the categorical variables between living patients with schizophrenia and patients deceased due to suicide. Continuous variables were analyzed using an independent t-test. The *cmprsk* and *survival* packages in R were used to establish Fine-gray models for univariate and multivariate analyses. The *cuminc* function was used for intergroup comparison and visual estimation of cumulative incidence function (CIF). Nelson-Aalen cumulative risk curves were then generated, and the outcome of patients was compared between the two groups using the Gray test. Hazard ratios (HRs) for potential predictors and the corresponding 95% confidence intervals (CIs) were computed. The R software (version 4.3.1) and SPSS 26.0 were used for all analyses in this study. All tests were two-sided, with  $P < 0.05$  indicating statistical significance.

The crude mortality rate was defined as the number of deaths per 100,000 person-years and calculated as the total number of observed deaths divided by the average size of the population per year. The age-standardized mortality rate was calculated as the observed number of deceased patients with schizophrenia in a certain period divided by the standardized size of the general Chinese population [17], which referred to China's population in 2017 (China Statistical Yearbook-2017) in this study [18].

## Results

### Sociodemographic and clinical characteristics of the cohort

The sociodemographic and clinical data of the subjects are shown in Table 1. Of the 33,080 patients with schizophrenia, most were males ( $n=17,021$ , 51.45%), were aged  $52.75 \pm 14.56$  years, and had a follow-up duration of  $69.73 \pm 39.62$  months. Among all included patients, 185 (0.56%) died from suicide, while 3,979 (12.03%) died from other causes. The mortality rates of the cohort are shown in Supplementary Table 1. The crude mortality rate of suicide in all the included subjects was 94.94/100,000 (82.72/100,000 for females, 105.85/100,000 for males). The overall age-standardized mortality rate related to suicide was 163.68/100,000 (95% CI: 156.28-171.09), and the age-standardized mortality rates for females and males were 133.89/100,000 (95% CI: 124.31-143.47) and 163.25/100,000 (95% CI: 152.92-173.59), respectively.

Sociodemographic and clinical characteristics of the total cohort with schizophrenia between 2013 and 2021 are shown in Table 1. There were more males ( $n=109$ , 58.92%) in the suicide group, and the proportions of males and females differed significantly between living patients and the suicide group ( $P=0.027$ ). As shown in Table 2, the median follow-up duration of female and male patients who died from suicide was 36.43 and 39.22 months, respectively. For both females and males, the significant factors for the highest proportion of deaths

by suicide were the age of 35–54 years ( $n=53$ , 69.74%;  $n=73$ , 66.97%), an education level of primary school and below ( $n=38$ , 50.67%;  $n=59$ , 54.63%), being employed ( $n=45$ , 59.21%;  $n=55$ , 50.46%), being married ( $n=61$ , 80.26%;  $n=85$ , 77.98%), no history of hospitalization ( $n=46$ , 63.01%;  $n=73$ , 68.22%), and no history of violent behavior ( $n=72$ , 96.00%;  $n=102$ , 94.44%). In the female cohort, most patients who died of suicide had a history of continuous treatment ( $n=32$ , 42.11%) and a younger age of diagnosis ( $n=47$ , 61.84%). In addition, the variation of characteristics for male and female patients was not significantly different between living patients and those who died of suicide.

### Univariate analysis of gender-specific risk factors for suicide deaths

Univariate analysis showed that among the 18 studied sociodemographic and clinical factors, age, education level, employment status, marital status, residence, medical insurance, frequency of hospitalization, duration of disease, the continuity of treatment, age of diagnosis, history of violent behavior, and history of suicidal behavior were significant factors for suicide mortality (see details in Supplementary Table 2). The Nelson-Aalen cumulative incidence curves of cause-specific deaths by gender in the schizophrenia cohort are shown in Supplementary Fig. 1.

Furthermore, all sociodemographic and clinical factors except for disease stability showed significant impacts on non-suicide deaths, as compared to both female and male patients who were alive.

### Results from multivariable analysis

All sociodemographic and clinical variables were included in the Fine-Gray model. For female patients, being married (HR: 2.89, 95% CI: 1.54–5.43,  $P < 0.01$ ), residing in rural areas (HR: 2.10, 95% CI: 1.12–3.94,  $P < 0.05$ ), costs not covered by medical insurance (HR: 2.40, 95% CI: 1.05–5.48,  $P < 0.05$ ), history of non-treatment (HR: 2.96, 95% CI: 1.52–5.77,  $P < 0.01$ ), and history of suicide behavior (HR: 3.92, 95% CI: 1.30–11.77,  $P < 0.05$ ) were found to be risk factors for suicide mortality (Table 3), while for males, being married (HR: 10.20, 95% CI: 5.54–18.81,  $P < 0.001$ ) and residing in rural areas (HR: 2.29, 95% CI: 1.30–3.97,  $P < 0.01$ ) were found as risk factors for suicide mortality. In addition, older age ( $\geq 55$  years for females, 35–54 years and  $\geq 55$  years for males), history of hospitalization (more than once for females, once and more than once for males), and older age of onset ( $> 28$  years for males) were protective factors for suicide mortality. The interaction terms with gender and different characteristics in suicide and non-suicide deaths in people with schizophrenia are shown in Supplementary Table 3. It was indicated that there might

**Table 1** Sociodemographic and clinical characteristics of the total cohort group in people with schizophrenia between 2013 and 2021 in Guangzhou, China

Characteristics, n (%)	The total cohort group				P <sup>#</sup>
	Total (N=33080)	Alive (n=28916)	Suicide deceases (n=185)	Non-suicide deceases(n=3979)	
Age, mean ± SD, y	52.75 ± 14.56	51.32 ± 14.0	46.04 ± 12.37	63.45 ± 13.67	< 0.001 <sup>b</sup>
≤ 34	4118(12.45)	3985(13.78)	36(19.46)	97(2.44)	< 0.001 <sup>c</sup>
35–54	19,049(57.58)	17,399(60.17)	126(68.11)	1524(38.30)	
≥ 55	9913(29.97)	7532(26.05)	23(12.43)	2358(59.26)	
Gender					
Female	16,059(48.55)	14,232(49.22)	76(41.08)	1751(44.01)	0.027 <sup>c</sup>
Male	17,021(51.45)	14,684(50.78)	109(58.92)	2228(55.99)	
Educational level					
High school and above	9751(30.80)	8858(32.21)	50(27.32)	843(21.22)	< 0.001 <sup>c</sup>
Middle school	10,690(33.77)	9994(36.34)	36(19.67)	660(16.61)	
Primary School and below	11,218(35.43)	8651(31.45)	97(53.01)	2470(62.17)	
Missing	1421	1413	2	6	
Employment status					
Unemployed	19,583(59.20)	18,044(62.40)	85(45.95)	1454(36.54)	< 0.001 <sup>c</sup>
Employed	13,497(40.80)	10,872(37.60)	100(54.05)	2525(63.46)	
Marital status					
Single	16,024(49.46)	15,271(54.09)	39(21.08)	714(17.94)	< 0.001 <sup>c</sup>
Married	16,375(50.54)	12,964(45.91)	146(78.92)	3265(82.06)	
Missing	681	681	0	0	
Residence					
Urban areas	28,225(85.32)	25,034(86.57)	150(81.08)	3041(76.43)	0.029 <sup>c</sup>
Rural areas	4855(14.68)	3882(13.43)	35(18.92)	938(23.57)	
Costs covered by medical insurance					
Yes	30,743(94.51)	26,967(94.94)	169(92.35)	3607(91.48)	0.111 <sup>c</sup>
No	1786(5.49)	1436(5.06)	14(7.65)	336(8.52)	
Missing	551	513	2	36	
Frequency of hospitalization					
None	14,278(43.25)	11,539(39.91)	119(66.11)	2620(66.85)	< 0.001 <sup>c</sup>
Once	9930(30.08)	8987(31.08)	49(27.22)	894(22.81)	
More than once	8807(26.68)	8390(29.02)	12(6.67)	405(10.33)	
Missing	65	0	5	60	
Duration of disease, y					
≤ 11.5	16,414(49.62)	15,208(52.59)	93(50.27)	1113(27.97)	0.528 <sup>c</sup>
> 11.5	16,666(50.38)	13,708(47.41)	92(49.73)	2866(72.03)	
Family history of mental illness					
No	29,576(95.43)	25,770(95.08)	171(98.28)	3635(97.87)	0.052 <sup>c</sup>
Yes	1415(4.57)	1333(4.92)	3(1.72)	79(2.13)	
Missing	2089	1813	11	265	
Disease stability in the last follow-up period					
Stable	29,536(95.25)	26,056(95.39)	146(92.41)	3334(94.29)	0.074 <sup>c</sup>
Unstable	1472(4.75)	1258(4.61)	12(7.59)	202(5.71)	
Missing	2072	1602	27	443	
The continuity of treatment					
Continuous	18,239(55.36)	16,574(57.57)	83(44.86)	1582(39.83)	0.001 <sup>c</sup>
Non-continuous	9471(28.75)	7988(27.75)	60(32.43)	1423(35.83)	
Non-treatment	5236(15.89)	4227(14.68)	42(22.70)	967(24.35)	
Missing	134	127	0	7	
Follow-up duration, mean ± SD, m	69.73 ± 39.62	72.80 ± 39.74	38.08 ± 28.93	48.96 ± 31.46	< 0.001 <sup>b</sup>
Age of onset, y					
≤ 28	17,236(52.10)	15,455(53.45)	111(60.00)	1670(41.97)	0.075 <sup>c</sup>
> 28	15,844(47.90)	13,461(46.55)	74(40.00)	2309(58.03)	

**Table 1** (continued)

Characteristics, n (%)	The total cohort group				P <sup>#</sup>
	Total (N = 33080)	Alive (n = 28916)	Suicide deceases (n = 185)	Non-suicide deceases(n = 3979)	
Age of diagnosis, y					
≤ 34	16,866(50.99)	14,962(51.74)	114(61.62)	1790(44.99)	0.007 <sup>c</sup>
> 34	16,214(49.01)	13,954(48.26)	71(38.38)	2189(55.01)	
Financial status					
Non-poverty	29,281(88.79)	25,486(88.45)	170(91.89)	3625(91.10)	0.144 <sup>c</sup>
Poverty	3696(11.21)	3327(11.55)	15(8.11)	354(8.90)	
Missing	103	103	0	0	
History of violent behavior					
No	27,789(85.11)	23,941(83.77)	174(95.08)	3674(94.47)	< 0.001 <sup>c</sup>
Yes	4862(14.89)	4638(16.23)	9(4.92)	215(5.53)	
Missing	429	337	2	90	
History of suicide behavior					
No	31,969(97.91)	27,931(97.73)	175(95.63)	3863(99.33)	0.098 <sup>d</sup>
Yes	682(2.09)	648(2.27)	8(4.37)	26(0.67)	
Missing	429	337	2	90	

Note: <sup>#</sup> P value for comparison between alive and suicide deceases

<sup>a</sup> Data are expressed as No. (%) of patients. Percentages have been rounded and may not total 100

<sup>b</sup> Calculated using a 2-tail t test

<sup>c</sup> Calculated using a  $\chi^2$  test

be interactions between gender and the status of being married (HR: 2.51, 95% CI: 1.09–5.75,  $P < 0.05$ ) as well as the non-treatment status (HR: 0.32, 95% CI: 0.13–0.78,  $P < 0.05$ ) in the suicide group.

## Discussion

This retrospective cohort study suggested that gender differences were common in people with schizophrenia who died from suicide [19]. Our study indicated that males had a higher suicide mortality rate than females and that the risk decreased with age for both genders, which was consistent with previous findings [20–23]. This might be related to less positive social support and marginally more criticism received by males compared to females [24]; furthermore, male patients with schizophrenia also showed poorer long-term treatment outcomes than their female counterparts [25].

We found that for being female, costs not covered by medical insurance and no history of receiving treatment were associated with an increased risk of suicide mortality. The national medical security system in China is a multilevel system, with basic medical insurance (BMI) as the pillar. Approximately 95% of the Chinese population is covered by one of the BMI programs, including the employee basic medical insurance (EBMI) program for employed people and the residents' basic medical insurance (RBMI) program for non-working residents [26]. In the present study, the proportion of people with schizophrenia who had costs not paid by medical insurance was 5.4%, and uninsured medical services were more common among unemployed and impoverished people,

which might have resulted in their reduced access to health care services and resources. Evidence has shown that poverty is related to an increased risk of death resulting from a lack of health resources and poor quality of care [27]. With no medical insurance, patients with low incomes are more likely to be in despair due to their inability to afford healthcare costs [28], which accounts for the majority of out-of-pocket payments by patients [29]. The expenses of long-term treatment may also lead to non-adherence, which was found to be associated with a history of suicide attempts, especially for females [30]. Concerning treatment, antipsychotic treatment was associated with lower suicide mortality among individuals with schizophrenia [31], while no history of antipsychotic drug use was associated with an increased risk of mortality, with suicide being a major cause [23]. Evidence suggests that treatment-naive patients with schizophrenia may have a poorer outcome (e.g., higher mortality) than those who have received treatment with antipsychotic medications [32]. Poor adherence has also been found to be related to death by suicide in patients with schizophrenia [33]. A large follow-up study showed that nonuse of antipsychotic drugs led to a 37-fold rise in suicide mortality [34]. However, such an outcome was not observed in male patients; this might be related to that female patients with schizophrenia showed more depressive symptoms and males showed more negative symptoms [35], while depressive symptoms responded more quickly and more completely to antipsychotic treatments [36]. Moreover, evidence showed that female patients tended to have more frequent episodes of comorbid





**Table 2** (continued)

Characteristics, n (%)	Female				Male			
	Alive	Suicide deceases	Non-suicide	P <sup>#</sup>	Alive	Suicide deceases	Non-suicide	P <sup>#</sup>
≤ 34	6577(46.21)	47(61.84)	674(38.49)	0.006 <sup>c</sup>	8385(57.10)	67(61.47)	1116(50.09)	0.359 <sup>c</sup>
> 34	7655(53.79)	29(38.16)	1077(61.51)		6299(42.90)	42(38.53)	1112(49.91)	
Financial status								
Non-poverty	12,781(90.08)	71(93.42)	1608(91.83)	0.331 <sup>d</sup>	12,705(86.87)	99(90.83)	2017(90.53)	0.223 <sup>c</sup>
Poverty	1407(9.92)	5(6.58)	143(8.17)		1920(13.13)	10(9.17)	211(9.47)	
Missing	44	0	0		59	0	0	
History of violent behavior								
No	12,076(85.92)	72(96.00)	1626(95.09)	0.012 <sup>d</sup>	11,865(81.69)	102(94.44)	2048(93.99)	0.001 <sup>c</sup>
Yes	1979(14.08)	3(4.00)	84(4.91)		2659(18.31)	6(5.56)	131(6.01)	
Missing	177	1	41		160	1	49	
History of suicide behavior								
No	13,693(97.42)	70(93.33)	1699(99.36)	0.063 <sup>d</sup>	14,238(98.03)	105(97.22)	2164(99.31)	0.799 <sup>d</sup>
Yes	362(2.58)	5(6.67)	11(0.64)		286(1.97)	3(2.78)	15(0.69)	
Missing	177	1	41		160	1	49	

Note: <sup>#</sup> P value for comparison between alive and suicide deceases

<sup>a</sup> Data are expressed as No. (%) of patients. Percentages have been rounded and may not total 100

<sup>b</sup> Calculated using a 2-tail t test

<sup>c</sup> Calculated using a  $\chi^2$  test

<sup>d</sup> Calculated using a calibration  $\chi^2$  test

depression and mania, more self-harm, and more suicide attempts [37], which contributed to more frequent use of antidepressants, mood stabilizers, benzodiazepines, and other sedatives by females as compared to males [9].

This study also found that a history of suicide behavior was a risk factor for suicide deaths in female patients, which is supported by numerous studies [38]. Suicide attempts are among the most important predictors of suicidal behaviors in the early stage of schizophrenia [39]. It has been reported that 25-50% of patients with schizophrenia had attempted suicide in their lifetime [40]. Female patients with schizophrenia usually have more non-lethal suicide acts than male patients, while males are more likely to use lethal means and less likely to engage in suicide attempts [41].

In the present study, the mean follow-up duration of the suicide group was 38.08 months, which was longer than the usually used 2-year follow-up in prior studies [6]. However, it has been noted that the majority of suicides in people with schizophrenia occur within the first 10 years of the illness [6], and a median time to suicide was found to be 5.6 years from the first episode of psychosis [42]. Consistent with our findings, the mortality due to suicide is remarkably high in the first 4 years of follow-up [43]. We also found that the mean age of the total cohort was 52.75 years. A study [44] has shown that among the 6,430,587 patients registered in the NISP across China, more than 60% were aged 45 and above. The present study also revealed that residing in rural areas was a risk factor for suicide deaths in both female and male patients with schizophrenia [45]. It has been

well documented that rural communities lack mental health resources, including mental health services, community resources, human resources, and funding [46]. Moreover, patients with schizophrenia in rural communities experience more stigma and discrimination than those in urban communities [47], where patients may be more socially accepted and receive more interventions to reduce their stigma and improve their clinical symptoms and social function [48].

Although it is believed that marriage is helpful for patients with schizophrenia to get better social support [49] and achieve better clinical, social, and occupational functions [50], the impact of marriage on the long-term outcomes of the patients is debatable [51, 52]. Although a 14-year follow-up study based in rural China indicated that the rate of death by suicide was more common among unmarried patients with schizophrenia [51], being married was not found to be a risk factor for suicide mortality in schizophrenia [21]. The present study found that married men with schizophrenia were at a higher risk for suicide deaths than married women, which might be attributed to the following reasons. Firstly, females experienced acute stress more frequently than males during the year before onset; as most women had been married before the occurrence of psychosis [53], they tended to get more support from their partners and children. Secondly, evidence showed that female patients had longer and more stable remission periods and less frequent relapses [35], while males preferred to get married more frequently to improve their social status throughout the illness [25]. However, further studies are still needed



**Table 3** Multivariate analysis of socio-economic and clinical factors in male and female patients with schizophrenia

Characteristics	Total		Female		Male	
	Suicide	Non-suicide deceases	Suicide	Non-suicide deceases	Suicide	Non-suicide deceases
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Age, y						
≤ 34	Ref	Ref	Ref	Ref	Ref	Ref
35–54	0.31(0.17–0.58)**	1.14(0.88–1.47)	0.57(0.20–1.61)	0.85(0.56–1.28)	0.19(0.08–0.41)***	1.38(1.00–1.89)
≥ 55	0.06(0.03–0.14)***	2.05(1.58–2.67)***	0.13(0.04–0.50)**	1.83(1.20–2.80)**	0.03(0.01–0.10)***	2.23(1.60–3.10)***
Gender						
Female	Ref	Ref	/	/	/	/
Male	1.38(0.97–1.97)	1.59(1.48–1.72)***	/	/	/	/
Educational level						
High school and above	Ref	Ref	Ref	Ref	Ref	Ref
Middle school	0.62(0.38–1.02)	0.69(0.62–0.78)***	0.67(0.32–1.39)	0.50(0.42–0.61)***	0.61(0.31–1.18)	0.87(0.75–1.01)
Primary School and below	1.27(0.83–1.97)	1.57(1.42–1.73)***	0.95(0.47–1.93)	1.02(0.88–1.18)	1.64(0.95–2.83)	2.18(1.92–2.47)***
Employment status						
Unemployed	Ref	Ref	Ref	Ref	Ref	Ref
Employed	1.23(0.89–1.69)	1.63(1.52–1.75)***	1.41(0.88–2.26)	1.73(1.55–1.93)***	1.07(0.69–1.64)	1.53(1.39–1.68)***
Marital status						
Single	Ref	Ref	Ref	Ref	Ref	Ref
Married	5.73(3.62–9.09)***	3.29(3.00–3.60)***	2.89(1.54–5.43)**	2.43(2.12–2.78)***	10.20(5.54–18.81)***	4.12(3.67–4.64)***
Residence						
Urban areas	Ref	Ref	Ref	Ref	Ref	Ref
Rural areas	2.23(1.47–3.39)***	2.71(2.49–2.94)***	2.10(1.12–3.94)*	3.09(2.72–3.50)***	2.27(1.30–3.97)**	2.44(2.18–2.72)***
Costs covered by medical insurance						
Yes	Ref	Ref	Ref	Ref	Ref	Ref
No	1.38(0.71–2.68)	3.29(2.87–3.78)***	2.40(1.05–5.48)*	3.11(2.55–3.80)***	0.74(0.23–2.37)	3.40(2.81–4.11)***
Frequency of hospitalization						
None	Ref	Ref	Ref	Ref	Ref	Ref
Once	0.51(0.34–0.76)**	0.56(0.51–0.62)***	0.73(0.39–1.36)	0.56(0.48–0.65)***	0.39(0.23–0.68)***	0.57(0.50–0.64)***
More than once	0.17(0.09–0.35)***	0.34(0.30–0.38)***	0.20(0.07–0.62)**	0.34(0.28–0.42)***	0.17(0.07–0.41)***	0.34(0.29–0.40)***
Duration of disease, y						
≤ 11.5	Ref	Ref	Ref	Ref	Ref	Ref
> 11.5	0.70(0.45–1.08)	1.00(0.92–1.10)	0.75(0.39–1.44)	1.12(0.98–1.28)	0.68(0.37–1.25)	0.90(0.80–1.02)
Family history of mental illness						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	0.49(0.16–1.56)	0.60(0.47–0.75)***	0.38(0.05–2.78)	0.39(0.25–0.59)***	0.67(0.16–2.78)	0.80(0.60–1.06)
Disease stability in the last follow-up period						
Stable	Ref	Ref	Ref	Ref	Ref	Ref
Unstable	1.78(0.96–3.33)	1.29(1.11–1.50)***	1.97(0.76–5.11)	1.35(1.08–1.68)**	1.62(0.72–3.65)	1.24(1.01–1.52)*
The continuity of treatment						
Continuous	Ref	Ref	Ref	Ref	Ref	Ref
Non-continuous	1.02(0.70–1.50)	1.33(1.23–1.45)***	1.13(0.60–2.14)	1.33(1.18–1.51)***	0.97(0.59–1.57)	1.31(1.18–1.46)***
Non-treatment	1.50(0.94–2.39)	1.34(1.21–1.48)***	2.96(1.52–5.77)**	1.37(1.18–1.59)***	0.84(0.42–1.70)	1.30(1.14–1.48)***
Age of onset, y						

**Table 3** (continued)

Characteristics	Total		Female		Male	
	Suicide	Non-suicide deceases	Suicide	Non-suicide deceases	Suicide	Non-suicide deceases
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
≤ 28	Ref	Ref	Ref	Ref	Ref	Ref
> 28	0.75(0.49–1.14)	0.99(0.91–1.08)	1.03(0.54–1.93)	1.03(0.89–1.18)	0.55(0.30–0.99)*	0.96(0.85–1.07)
Age of diagnosis, y						
≤ 34	Ref	Ref	Ref	Ref	Ref	Ref
> 34	0.90(0.55–1.48)	0.94(0.85–1.03)	0.67(0.33–1.35)	1.06(0.91–1.22)	1.19(0.59–2.39)	0.85(0.75–0.96)*
Financial status						
Non-poverty	Ref	Ref	Ref	Ref	Ref	Ref
Poverty	0.71(0.39–1.29)	0.86(0.75–0.97)*	0.56(0.19–1.67)	0.94(0.77–1.16)	0.90(0.44–1.82)	0.82(0.70–0.97)*
History of violent behavior						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	0.39(0.19–0.80)*	0.40(0.34–0.46)***	0.37(0.11–1.21)	0.38(0.30–0.48)***	0.40(0.16–1.00)	0.42(0.35–0.51)***
History of suicide behavior						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	2.36(0.99–5.63)	0.51(0.33–0.80)**	3.92(1.30–11.77)*	0.38(0.17–0.83)*	1.38(0.33–5.74)	0.61(0.36–1.05)

Note: Ref: Reference

\* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$

to explore the association between suicide mortality and marital status or quality of marriage in people with schizophrenia.

Studies have found that schizophrenia is associated with an increased rate of violent crime when comorbid with substance abuse [54], as well as an increased risk of suicide and premature mortality. The present study found no significant association between a history of violent behavior and increased suicide mortality, which might be related to that a history of violent behavior might only indicate a behavioral pattern of deliberate attacks rather than attempts to end their own life [55].

For both female and male patients with schizophrenia, older age and a history of hospitalization were found to be protective factors for suicide mortality. We also found that the age of onset of more than 28 years was a protective factor for suicide mortality in male patients. Studies suggest that the risk of suicide decreases with age [56–58] and that younger patients of both genders have a high rate of suicide mortality [59]. However, this association may be more related to the onset of schizophrenia than to the age per se [12]. In the present study, we found that female patients who survived during the 9-year follow-up period had an older age of onset (31.50 years for females vs. 27.98 years for males), and female patients also had an older age of suicide death (27.92 years for females vs. 27.26 years for males) by the end of the follow-up. Overall, the global peak age of onset of schizophrenia is 20.5 years, and almost half of all cases (47.4%) occur by the age of 25 years, with males accounting for a larger proportion

[60]. Prior research showed that an older age of onset was associated with a better outcome in patients with schizophrenia, and evidence indicates that a younger age of onset was associated with more frequent hospitalizations, more negative symptoms, more relapses, poorer social/occupational functions, and poorer global outcomes [61]. Consistent with previous research, we found that people with schizophrenia who had no history of hospitalization had a higher rate of suicide mortality [21], which might be attributed to the fact that patients with a history of hospitalization tended to receive better anti-psychotic treatment.

#### Limitations

The present study benefited from a large sample size extracted from a population-based database. However, this study also has several limitations. First, detection bias was inevitable given the retrospective observational nature of this study. Second, the suicide rates in this study might have been underestimated due to the loss to follow-up. Third, due to the retrospective study design, we were unable to evaluate some important risk factors, such as comorbid substance abuse and depression. Fourth, the lack of data on the means of suicide further limited further exploration, and this factor may be explored in future prospective studies. Fifth, the mean age of patients with schizophrenia was 53 years in the present study, which is higher than what is generally expected for schizophrenia patients, who usually have the disease onset in adolescence or young adulthood

[61]. This limitation may affect the generalizability of our findings, suggesting the need for future studies involving a younger population with schizophrenia. In addition, given the nature of this study, establishing a causal link between the identified risk factors and suicide mortality is still challenging. Thus, further prospective studies are needed to verify our preliminary results.

## Conclusion

In summary, this study suggests that there are gender differences in suicide risk factors among patients with schizophrenia. It should be noted that a higher suicide mortality risk was found in married patients and those residing in rural areas. Costs not covered by medical insurance, no history of antipsychotic treatment, and a history of suicide behavior were associated with an increased risk of suicide death in females, whereas these factors seemed less significant in males. Thus, taking the role of gender into account in the assessment of suicide mortality risk may facilitate the development of strategies for suicide prevention for people with schizophrenia.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12888-024-06089-0>.

Supplementary Material 1

Supplementary Material 2

## Author contributions

PZ, ZS, and ZL conceived and designed the study. PZ performed data analysis and wrote the first draft of the manuscript. ZS and ZL revised the manuscript and interpreted the results. CY, SJ, and DX collected the data and assisted in the analyses. ZS and ZL managed and supported the project. PZ, ZS, and ZL fully assessed all the data in the study. All authors approved the final version of the manuscript.

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## Data availability

The datasets generated and analyzed in the present study are not publicly available to protect the privacy of subjects; however, they are available from the corresponding author (Shaoling Zhong) upon reasonable request.

## Declarations

### Ethics approval and consent to participate

The study protocol was approved by the Institutional Ethical Board of the Affiliated Brain Hospital, Guangzhou Medical University. As this study was observational and retrospective, informed consent was waived by the Institutional Ethical Board of the Affiliated Brain Hospital, Guangzhou Medical University. All the participants were anonymized during data processing. Prior to data analysis, all researchers committed to an agreement to ensure patient privacy and confidentiality.

### Consent for publication

Not applicable.

## Competing interests

The authors declare no competing interests.

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## References

- Hjorthoj C, et al. Years of potential life lost and life expectancy in schizophrenia: a systematic review and meta-analysis. *Lancet Psychiatry*. 2017;4(4):295–301.
- Zhang H, et al. Direct medical costs for patients with schizophrenia: a 4-year cohort study from health insurance claims data in Guangzhou city, Southern China. *Int J Ment Health Syst*. 2018;12:72.
- Montgomery W, et al. The personal, societal, and economic burden of schizophrenia in the People's Republic of China: implications for antipsychotic therapy. *Clinicoecon Outcomes Res*. 2013;5:407–18.
- Bai W, et al. Worldwide prevalence of suicidal ideation and suicide plan among people with schizophrenia: a meta-analysis and systematic review of epidemiological surveys. *Transl Psychiatry*. 2021;11(1):552.
- Dong M, et al. Suicide-related behaviours in schizophrenia in China: a comprehensive meta-analysis. *Epidemiol Psychiatr Sci*. 2019;28(3):290–9.
- Montross LP, Zisook S, Kasckow J. Suicide among patients with schizophrenia: a consideration of risk and protective factors. *Ann Clin Psychiatry*. 2005;17(3):173–82.
- Correll CU, et al. Mortality in people with schizophrenia: a systematic review and meta-analysis of relative risk and aggravating or attenuating factors. *World Psychiatry*. 2022;21(2):248–71.
- Carlborg A, et al. Suicide in schizophrenia. *Expert Rev Neurother*. 2010;10(7):1153–64.
- Sommer IE, et al. The clinical course of schizophrenia in women and men: a nation-wide cohort study. *NPJ Schizophr*. 2020;6(1):12.
- Qin P. The impact of psychiatric illness on suicide: differences by diagnosis of disorders and by sex and age of subjects. *J Psychiatr Res*. 2011;45(11):1445–52.
- Lester D. Sex differences in completed suicide by schizophrenic patients: a meta-analysis. *Suicide Life Threat Behav*. 2006;36(1):50–6.
- Sher L, Kahn RS. Suicide in Schizophrenia: an Educational Overview. *Med (Kaunas)*. 2019. 55(7).
- Tiihonen J, et al. Sex-specific transcriptional and proteomic signatures in schizophrenia. *Nat Commun*. 2019;10(1):3933.
- Seeman MV. Sex differences in schizophrenia relevant to clinical care. *Expert Rev Neurother*. 2021;21(4):443–53.
- Li S, et al. Factors influencing suicide deaths in patients with Schizophrenia based on Cohort Data: an empirical study of a sample of 170006 patients in Sichuan Province]. *Sichuan Da Xue Xue Bao Yi Xue Ban*. 2023;54(1):142–7.
- Commission NH. Chinese management and treatment regulations for severe mental disordered patients[in Chinese]. 2018.
- Anderson RN, Rosenberg HM. Age standardization of death rates: implementation of the year 2000 standard. *Natl Vital Stat Rep*. 1998;47(3):1–16.
- China N. B.o.S.o., China Statistical Yearbook-2017. China State Statistical; 2018.
- Hor K, Taylor M. Suicide and schizophrenia: a systematic review of rates and risk factors. *J Psychopharmacol*. 2010;24(4 Suppl):81–90.
- Ran MS, et al. Gender differences in outcomes in people with schizophrenia in rural China: 14-year follow-up study. *Br J Psychiatry*. 2015;206(4):283–8.
- Ran MS, et al. Mortality and suicide in schizophrenia: 21-year follow-up in rural China. *BJPsych Open*. 2020;6(6):e121.
- Olfson M, et al. Premature mortality among adults with Schizophrenia in the United States. *JAMA Psychiatry*. 2015;72(12):1172–81.
- Stromme MF, et al. Mortality and non-use of antipsychotic drugs after acute admission in schizophrenia: a prospective total-cohort study. *Schizophr Res*. 2021;235:29–35.
- Willhite RK, et al. Gender differences in symptoms, functioning and social support in patients at ultra-high risk for developing a psychotic disorder. *Schizophr Res*. 2008;104(1–3):237–45.
- Cechnicki A, et al. Comparison of the long-term treatment outcomes of women and men diagnosed with schizophrenia over a period of 20 years. A prospective study. *Compr Psychiatry*. 2018;84:62–7.
- Yi B. An overview of the Chinese healthcare system. *Hepatobiliary Surg Nutr*. 2021;10(1):93–5.

27. Liu X, et al. Risk factors for mortality due to natural causes and suicide among people with severe mental illness in western China. *Psychiatry Res.* 2023;322:115108.
28. Kominski GF, Nonzee NJ, Sorensen A. The affordable Care Act's impacts on Access to Insurance and Health Care for low-income populations. *Annu Rev Public Health.* 2017;38:489–505.
29. Center CNHDR. China National Health Accounts Report, C. National Health and Family Planning Commission. Editor: Beijing; 2014.
30. Lieslehto J, et al. Primary nonadherence to antipsychotic treatment among persons with Schizophrenia. *Schizophr Bull.* 2022;48(3):655–63.
31. Haukka J, et al. Association between medication and risk of suicide, attempted suicide and death in nationwide cohort of suicidal patients with schizophrenia. *Pharmacoepidemiol Drug Saf.* 2008;17(7):686–96.
32. Tiihonen J, et al. 11-year follow-up of mortality in patients with schizophrenia: a population-based cohort study (FIN11 study). *Lancet.* 2009;374(9690):620–7.
33. Pompili M, et al. Completed suicide in schizophrenia: evidence from a case-control study. *Psychiatry Res.* 2009;167(3):251–7.
34. Tiihonen J, et al. Effectiveness of antipsychotic treatments in a nationwide cohort of patients in community care after first hospitalisation due to schizophrenia and schizoaffective disorder: observational follow-up study. *BMJ.* 2006;333(7561):224.
35. Ochoa S et al. Gender differences in schizophrenia and first-episode psychosis: a comprehensive literature review. *Schizophr Res Treatment*, 2012. 2012:916198.
36. Seeman MV, Does Gender Influence Outcome in Schizophrenia?, *Psychiatr Q* 2019;90(1):173–184.
37. Hou CL et al. Comorbid moderate-severe depressive symptoms and their association with quality of life in Chinese patients with schizophrenia treated in primary care. *Community Ment Health J* 2016;52(8):921–926.
38. Hettige NC, et al. A biopsychosocial evaluation of the risk for suicide in schizophrenia. *CNS Spectr.* 2018;23(4):253–63.
39. Bertelsen M, et al. Suicidal behaviour and mortality in first-episode psychosis: the OPUS trial. *Br J Psychiatry Suppl.* 2007;51:s140–6.
40. Meltzer H.Y. Treatment of suicidality in schizophrenia. *Ann N Y Acad Sci.* 2001;932:44–58. discussion 58–60.
41. Cassidy RM, et al. Risk factors for suicidality in patients with Schizophrenia: a systematic review, Meta-analysis, and Meta-regression of 96 studies. *Schizophr Bull.* 2018;44(4):787–97.
42. Dutta R, Reassessing the long-term risk of suicide after a first episode of psychosis. *Arch Gen Psychiatry.* 2010;67(12):1230–7.
43. Limosin F et al. Ten-year prospective follow-up study of the mortality by suicide in schizophrenic patients. *Schizophr Res.* 2007;94(1–3):23–8.
44. Zhang WF, et al. Management and services for psychosis in the People's Republic of China in 2020 [in Chinese]. *Chin J Psychiatry.* 2022;55(2):122–8.
45. Phillips MR, et al. Suicide and the unique prevalence pattern of schizophrenia in mainland China: a retrospective observational study. *Lancet.* 2004;364(9439):1062–8.
46. Saxena S, et al. Resources for mental health: scarcity, inequity, and inefficiency. *Lancet.* 2007;370(9590):878–89.
47. Loganathan S, Murthy SR. Experiences of stigma and discrimination endured by people suffering from schizophrenia. *Indian J Psychiatry.* 2008;50(1):39–46.
48. Li J, et al. Community-based comprehensive intervention for people with schizophrenia in Guangzhou, China: effects on clinical symptoms, social functioning, internalized stigma and discrimination. *Asian J Psychiatr.* 2018;34:21–30.
49. Yang LH, et al. What matters most: a cultural mechanism moderating structural vulnerability and moral experience of mental illness stigma. *Soc Sci Med.* 2014;103:84–93.
50. Thara R, Srinivasan TN. Outcome of marriage in schizophrenia. *Soc Psychiatry Psychiatr Epidemiol.* 1997;32(7):416–20.
51. Ran MS, et al. Marriage and outcomes of people with schizophrenia in rural China: 14-year follow-up study. *Schizophr Res.* 2017;182:49–54.
52. Ponnudurai R, Jayakar J, Sathiya Sekaran BW. Assessment of mortality and marital status of schizophrenic patients over a period of 13 years. *Indian J Psychiatry.* 2006;48(2):84–7.
53. Segarra R, et al. Similarities in early course among men and women with a first episode of schizophrenia and schizophreniform disorder. *Eur Arch Psychiatry Clin Neurosci.* 2012;262(2):95–105.
54. Fazel S, et al. Schizophrenia, substance abuse, and violent crime. *JAMA.* 2009;301(19):2016–23.
55. Skogman K, Alsn M, jehagen A. Sex differences in risk factors for suicide after attempted suicide. *Soc Psychiatry Psychiatr Epidemiol.* 2004;39(2):113–20.
56. Caldwell CB, Gottesman II. Schizophrenia—a high-risk factor for suicide: clues to risk reduction. *Suicide Life Threat Behav.* 1992;22(4):479–93.
57. Olsson M, et al. Suicide risk in medicare patients with Schizophrenia across the life span. *JAMA Psychiatry.* 2021;78(8):876–85.
58. Nordentoft M, et al. Change in suicide rates for patients with schizophrenia in Denmark, 1981–97: nested case-control study. *BMJ.* 2004;329(7460):261.
59. Ko YS, et al. Higher mortality and years of potential life lost of suicide in patients with schizophrenia. *Psychiatry Res.* 2018;270:531–7.
60. Solmi M, et al. Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. *Mol Psychiatry.* 2022;27(1):281–95.
61. Immonen J, et al. Age at onset and the outcomes of schizophrenia: a systematic review and meta-analysis. *Early Interv Psychiatry.* 2017;11(6):453–60.

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