Prevalence and Clinical Correlates of and Cognitive Function at the Time of Suicide Attempts in First-Episode and Drug-Naive Patients With Schizophrenia

Xiang Yang Zhang, MD, PhD[a,b,*]; Xiangdong Du, MD[c]; Guangzhong Yin, MD[c]; Yingyang Zhang, MS[c]; Dachun Chen, MD[d]; Meihong Xiu, PhD[d]; Changhong Wang, MD, PhD[e]; Ruilong Zhang, MD, PhD[e]; Ryan M. Cassidy, MD, PhD[b]; Yuping Ning, MD, PhD[f]; Xingbing Huang, MD, PhD[f]; and Jair C. Soares, MD, PhD[b]

ABSTRACT

Background: It is well established that patients with chronic schizophrenia have a substantially higher rate of attempted and completed suicide than the general population. However, the actual prevalence of suicide attempts at first-episode psychosis is relatively unknown. Previous studies showed that suicidal schizophrenia patients demonstrate higher cognitive function than nonsuicidal patients, though with inconsistent results. The aims of the study were to examine the prevalence of suicide attempts and the association of this prevalence with demographic and clinical variables and cognitive function in Chinese first-episode, drug-naive (FEDN) schizophrenia patients using a cross-sectional and case-control design.

Method: A total of 357 FEDN inpatients meeting *DSM-IV* criteria for schizophrenia and 380 healthy controls were enrolled and completed a detailed in-house questionnaire. The suicide attempt data were collected from medical records and interviews with the patients and their family members. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) was administered to measure cognition in the 28 patients with and 95 patients without a history of suicide attempt and 151 healthy controls. Also, patients were rated on the Positive and Negative Syndrome Scale (PANSS). This study was conducted from June 2013 to December 2015.

Results: A suicide attempt rate of 12.0% was found in inpatients with first-episode schizophrenia. The attempters were more likely to smoke (34.4% vs 17.9%; $\chi^2 = 5.49$, $P = .019$) and had lower severity of negative symptoms ($F_{1,354} = 4.12$, $P = .043$) as compared to FEDN patients without a suicide attempt. All 5 RBANS subscales (all $P < .001$) except for the Visuospatial/Constructional index ($P > .05$) showed significantly lower cognitive performance for FEDN patients than for healthy controls. Among the FEDN patients, the suicide attempters performed better than nonattempters on attention ($F_{1,121} = 5.12$, $P = .025$), with an effect size of 0.49. The following variables were independently associated with suicide attempt as shown by multivariate regression analysis: PANSS negative symptom subscale score (Wald $\chi^2_1 = 7.90$ $P = .005$; adjusted OR = 0.807, 95% CI, 0.696–0.936) and Attention (Wald $\chi^2_1 = 4.69$, $P = .03$; adjusted OR = 0.957, 95% CI, 0.918–0.997).

Conclusions: FEDN patients with schizophrenia attempt suicide more often than the general population. The suicidal patients were more likely to smoke, had lower severity of negative symptoms, and showed better attention than nonsuicidal patients.

J Clin Psychiatry 2018;79(4):17m11797

To cite: Zhang XY, Du X, Yin G, et al. Prevalence and clinical correlates of and cognitive function at the time of suicide attempts in first-episode and drug-naive patients with schizophrenia. *J Clin Psychiatry.* 2018;79(4):17m11797.

To share: https://doi.org/10.4088/JCP.17m11797

[a]Institute of Psychology, Chinese Academy of Sciences, Beijing, China
[b]Department of Psychiatry and Behavioral Sciences, The University of Texas Health Science Center at Houston, Houston, Texas
[c]Suzhou Psychiatric Hospital, The Affiliated Guangji Hospital of Soochow University, Suzhou, Jiangsu Province, China
[d]Beijing Hui-Long-Guan Hospital, Peking University, Beijing, China
[e]Xinxiang Medical University, The Second Affiliated Hospital, Xinxiang, Henan Province, China
[f]The Affiliated Brain Hospital of Guangzhou Medical University (Guangzhou Huiai Hospital), Guangzhou, China
**Corresponding author:* Xiang Yang Zhang, MD, PhD, 1941 East Rd, Houston, TX 77054 (xiang.y.zhang@uth.tmc.edu).

People with schizophrenia are more likely than those who do not to attempt suicide[1,2] and have early mortality.[3] The lifetime prevalence of suicide in individuals with schizophrenia ranges from 20% to 50%.[4–9] Schizophrenia is estimated to reduce life expectancy by 10 to 20 years, and suicide is the biggest single cause of premature death that contributes to this shortened life span.[2,10] Risk factors for suicide common to both schizophrenia patients and the general population include sex, higher levels of education, being single or divorced, living alone, lower socioeconomic status, symptoms of depression and anxiety, early-life adversities, history of previous suicide attempts, and family history of suicide.[11,12] It is unclear whether male or female schizophrenia patients are more likely to attempt suicide. A previous meta-analysis by Hawton et al[12] showed suicide risk was associated with male sex; however, a recent study showed that suicide attempts were associated with female sex among persons with schizophrenia.[11] Hopelessness, especially, has been widely recognized as an independent risk factor for suicide and suicidal behaviors in both patients with schizophrenia and the general population.[13,14] Also, hopelessness has been documented as an important risk factor for suicidality in patients with physical diseases.[15]

Risk factors for suicide specific to schizophrenia include younger age at onset, longer duration of untreated psychosis, increased positive and decreased negative symptoms, a greater level of insight,[3,16] noncompliance with antipsychotic medication,[17] higher premorbid IQ, and fewer cognitive deficits.[18,19] Further, substance use has been considered to be an important predictor for suicide and suicide-related behaviors.[20,21] Notably, the presence of cannabis use or dependence has been reported to enhance suicide risk in schizophrenia patients, especially in adolescence. Cannabis use or dependence may be critically involved in suicidal behavior among psychotic youths,

Clinical Points

- The suicide attempt data were collected from 357 Chinese inpatients with first-episode, drug-naive schizophrenia and 380 healthy controls. Cognition was measured in some individuals.
- The patients showed a higher suicide attempt rate (12.0%) and excessive cognitive impairments compared with controls.
- Among patients, suicide attempters were more likely to smoke and had lower severity of negative symptoms and better attention.

with those who attempted or completed suicide reporting additional risk factors for suicide such as mood disorders, stressful life events, interpersonal problems, poor social support, loneliness, and feelings of hopelessness.[20] In addition, a history of prior suicide attempt is strongly predictive of future completed suicide, and the majority of schizophrenia patients who commit suicide have at least one previous attempt.[22] However, the ability to appropriately screen for and prevent suicidality in schizophrenia patients is difficult because of the incomplete knowledge about its phenomenology in this special patient population.

Until recently, most studies reporting an elevated prevalence of suicide were conducted with chronically ill and medicated schizophrenia patients.[23] In a recent study by our group, Zhang and colleagues[24] found that chronic and medicated patients with schizophrenia had a 9.2% prevalence of suicide attempts in a Chinese Han population. Only a few studies[9,25] have reported suicide in the first episode of psychosis. This is a critical period in the disease, as the rate of suicide-related mortality is higher among subjects recently diagnosed with schizophrenia[9,26] and suicide risk peaks in the first few years after onset.[7] The suicide risk is 2-fold higher at the onset of psychotic illness than later on in the course of the illness.[8] Thus, it is of great importance to investigate the relevant risk factors in this population, particularly since early intervention and therapy may reduce suicidality among first-episode psychosis patients.[9,27]

Schizophrenia patients display cognitive impairments across a number of domains, including learning, memory, attention, working memory, information processing, social cognition, and executive function.[28,29] Previous studies[18,30] showed that suicidal schizophrenia patients demonstrate higher cognitive function than nonsuicidal patients. A recent study showed that patients with schizophrenia or schizoaffective disorder who had lifetime history of suicide attempt had better executive functioning and good insight.[31] However, other studies reported that suicidal intent in patients with schizophrenia and schizoaffective disorder was not correlated with cognition[22,32,33] or with lower cognitive function.[34] Thus, there is some controversy regarding this issue, and further investigation that more closely identifies the cognitive function at the time of suicide attempt may provide resolution. Interestingly, neurocognitive dysfunctions are usually present even in the prodromal phases of schizophrenia patients. A recent study[35] has suggested that neurocognitive impairments, especially in attention and working memory abilities and declarative memory abilities, may be considered a robust characteristic of the clinical high-risk state of psychosis, especially in individuals who later develop psychosis. Thus, interventions targeting the enhancement of neurocognitive functioning are warranted even in the prodromal phases of the illness for prevention of suicidal behaviors in this population.

Only a few systematic studies have investigated the sociodemographic and clinical correlates of suicide attempts in Chinese schizophrenia patients. Those that evaluated the prevalence of suicide attempt and demographic and clinical risk factors in chronic patients with schizophrenia have mixed results.[22,24,36,37] None of these, however, have evaluated first-episode psychosis in drug-naive patients, who, as we discussed, represent a particularly high risk population. On the other hand, there exist the complex interrelationships between antipsychotic medication, clinical symptoms, cognitive deficits, and suicidality in patients with chronic schizophrenia. For example, more negative symptoms were found to be associated with suicide[7]; however, another study[38] had the opposite finding, and others[39–41] had conflicting results. Also, the literature has reported mixed results regarding the association between antipsychotic treatment and suicide-related behavior in schizophrenia.[42] For example, some antipsychotics—especially those classified as second-generation agents, such as clozapine—were reported to have an antisuicidal effect[43]; however, others[44] found a higher suicide risk among patients who were on treatment with antipsychotics, possibly due to side effects such as extrapyramidal symptoms and tardive dyskinesia. Thus, studying suicide in first-episode and unmedicated patients can potentially disentangle an antisuicidal effect due to antipsychotic medication from an antisuicidal effect characteristic of the disease itself and also minimize the potential impact of other confounders, such as illness duration and the psychiatric and medical comorbidities that are associated with chronic illness. In this study, we recruited a large sample of first-episode, drug-naive (FEDN) patients with schizophrenia in a Han Chinese population (N = 357) to investigate the prevalence of suicide attempts among FEDN Chinese schizophrenia patients and to determine the sociodemographic and clinical correlates of and cognition at the time of suicide attempts.

METHODS

Subjects

Three hundred fifty-seven (173 male and 184 female) FEDN inpatients were recruited in the Beijing Hui-Long-Guan Hospital, a city-owned psychiatric hospital, from June 2013 to December 2015. All hospital admissions were screened for patients who met the following 6 criteria: (1) patients had an acute episode that met *DSM-IV* criteria for schizophrenia, as assessed by 2 independent, experienced psychiatrists using the Structured Clinical Interview for

DSM-IV (SCID) at study intake; (2) these patients were followed for 3 months as inpatients after admission and were included only if the second 3-month evaluation was consistent in diagnosing schizophrenia; (3) the duration of symptoms was not longer than 60 months at admission; (4) patients had no prior treatment with antipsychotic medication; (5) patients were Han Chinese and between 18 and 45 years of age; (6) the current psychotic symptoms were of moderate or greater severity as determined by a Clinical Global Impressions–Severity of Illness scale (CGI-S) score ≥ 4. Exclusion criteria for the first-episode schizophrenia patients were (1) current major medical problems; (2) history of any brain diseases; (3) family history of neurologic disorder; (4) lifetime history of alcohol or substance dependence except tobacco, or having alcohol or substance abuse within the 6 months preceding the study; (5) refusal to provide written informed consent and take part in cognitive assessment. In addition, *first episode* was defined in this study as first symptom onset.

Three hundred eighty (179 male and 201 female) healthy controls with ages ranging from 18 to 45 years were recruited randomly from the local community in Beijing during the same period. All participants were recruited without any selection, and they were interviewed by trained investigators supervised by a research psychiatrist. Current mental status and personal or family history of any mental disorder were assessed. No controls had either a personal or a family history of a psychiatric disorder.

We obtained a complete medical history and results of physical examination and laboratory tests from all subjects. They were in good physical health, and any subjects with medical illnesses or drug and alcohol abuse or dependence except related to tobacco were excluded. The Institutional Review Board for the Beijing Hui-Long-Guan Hospital approved the research protocol, and all subjects provided informed consent.

Sociodemographic Characteristics

Research staff administered a detailed questionnaire that asked for general information, sociodemographic characteristics, smoking and alcohol drinking behavior, and history of suicide attempts. In our current study, we used the following definitions for smoking behavior[45]: *current smokers:* adults who have smoked 100 cigarettes in their lifetime and currently smoke cigarettes every day (daily) or some days (nondaily); *former or ex-smokers*: adults who have smoked at least 100 cigarettes in their lifetime, but currently do not smoke; and *never smokers*: adults who have never smoked a cigarette or who smoked fewer than 100 cigarettes in their entire lifetime. In our present study, former smokers were excluded, and only never smokers were included as nonsmokers.

According to the report of the World Health Organization, the outcome-based term *fatal suicidal behavior* or *completed suicide* has been proposed for suicidal acts that result in death and similarly, *nonfatal suicidal behavior* for suicidal actions that do not result in death. The latter actions are also often called *attempted suicide*.[46] Hence, in this study, we defined a suicide attempt as an intentionally self-destructive act performed with at least some intent to die,[47] but not resulting in death. During the research interview, all subjects were asked about previous suicide attempts with the following details: the number of attempts, the exact date for each suicide attempt, and the methods. The screening question was, "In your entire lifetime did you ever attempt suicide?" Responses were coded as yes or no. History of suicide attempts was confirmed by a review of medical records supplemented by a clinical diagnostic interview of patients and, whenever possible, their relatives by a qualified psychiatrist. Additional visits to their family members, relatives, or even friends and coworkers were requested for subjects with missing or ambiguous suicide-related data, such as the number of suicide attempts, the date for suicide attempt and the exact methods. Since our study design was retrospective and the information for suicide attempt was collected from medical case notes and interviews with the patients and their family members, a possible recall bias could not be ruled out completely. To reduce the recall bias, we specifically collected these data related to the aforementioned suicidal behaviors.

Clinical Assessment

Two experienced psychiatrists assessed the psychopathology and symptom severity of the patients using the Positive and Negative Syndrome Scale (PANSS)[48] and CGI.[49] To ensure consistent and reliable ratings, the 2 psychiatrists simultaneously attended a training session in the use of the PANSS and CGI prior to the start of the study. After training, they maintained an intraclass correlation coefficient of greater than 0.8 on both the PANSS and the CGI total scores at repeated assessments during the course of this study.

In addition, the Chinese translation of the standardized Fagerstrom Test for Nicotine Dependence was employed to measure the degree of nicotine dependence.[50]

Cognitive Performance

We utilized the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)[51] for cognitive performance testing. The RBANS comprises 12 subtests that are used to calculate 5 age-adjusted index scores and a total score. The mean score of the general population is 100 with a standard deviation of 15. Test indices include Immediate Memory (comprising List Learning and Story Memory tasks), Visuospatial/Constructional (comprising Figure Copy and Line Orientation tasks), Language (comprising Picture Naming and Semantic Fluency tasks), Attention (comprising Digit Span and Coding tasks), and Delayed Memory (comprising List Recall, Story Recall, Figure Recall, and List Recognition tasks). Our group previously translated the RBANS into Chinese and established the translated version's clinical validity and test-retest reliability among patients with schizophrenia.[52]

Statistical Analysis

Group differences were compared using 1-way analysis of variance (ANOVA) for continuous variables and χ^2 test for

categorical variables. The prevalence of suicide attempt was analyzed by χ^2 test. The odds ratio (OR) for suicide attempt risk in schizophrenia as compared to healthy controls was derived from logistic regression analysis after controlling for sociodemographic factors. We compared RBANS scores among the 3 groups (suicide attempters vs nonattempters vs controls) using ANOVA. The Fisher least significant difference test was used to perform post hoc pairwise between-group comparisons. Bonferroni correction was used to adjust for multiple testing. When significance was found in ANOVA, the effects of the relevant variables were added to the logistic regression analysis model as covariates. Effect sizes were calculated for the 2-way comparisons. In addition, a binary logistic regression analysis was conducted to assess which factors were most strongly associated with suicide attempts. All statistical analysis used SPSS version 15.0 (2006; SPSS Inc; Chicago, Illinois) with significance defined by 2-tailed *P* values < .05.

RESULTS

Prevalence of Suicide Attempts in FEDN Patients

Table 1 shows that the patients did not differ from healthy controls with respect to demographic characteristics except that schizophrenia patients had lower body mass index (BMI) ($P < .001$). The frequency of suicide attempt was 12.0% (43/357) for patients and 0.79% (3/380) for controls, with an OR of 17.21 (95% confidence interval [CI], 5.29–56.00; $\chi^2 = 39.8$, $P < .001$). This difference remained significant after using logistic regression to control for the sociodemographic confounders, including sex, age, education, smoking status, and BMI ($\chi^2 = 21.31$, $P < .001$, adjusted OR = 16.39; 95% CI, 4.98–53.26). Within the schizophrenia group, there was no significant difference in the frequency of suicide attempt between male and female patients (11.6% male vs 12.5% female) ($\chi^2 = 0.07$, $P = .79$).

As mentioned in the Introduction section, the previous study by our group[24] showed that the prevalence of suicide attempts was 9.2% (48/520) in the chronically ill, medicated patients with schizophrenia.[24] Although the prevalence of suicide attempts appears to be higher in FEDN than chronically ill, medicated patients (12.0% vs 9.2%), there was no significant difference between these datasets ($\chi^2_1 = 1.80$, $P = .18$), possibly due to limited sample size.

Clinical Characteristics Between the Patients With and Without History of Suicide Attempt

Table 2 shows that smoking was more common in attempters (34.4%) than in nonattempters (17.9%; χ^2=5.49, $P = .019$). This difference remained significant after using logistic regression to adjust for clinical characteristics including sex, age, education, BMI, and age at onset ($\chi^2 = 5.79$, $P = .016$; adjusted OR = 3.33; 95% CI, 1.25–8.86). Compared to nonattempters, attempters had a significantly lower PANSS negative symptom subscale score ($F_{1,354} = 4.12$, $P = .043$; Bonferroni-corrected $P > .05$). In stepwise multiple logistic regression analysis for associations with suicide attempts, we added the demographic and clinical data including sex, age, education, smoking status, BMI, age at onset, and PANSS positive, negative, and general psychopathology subscale scores together into the model and found that the PANSS negative symptom subscale score (Wald $\chi^2_1 = 6.32$ $P = .012$; adjusted OR = 0.836; 95% CI, 0.742–0.943) and smoking status (Wald $\chi^2_1 = 5.31$, $P = .021$; adjusted OR = 0.887; 95% CI, 0.797–0.986) remained significant.

Cognitive Functioning in Suicide Attempters and Nonattempters in FEDN Patients

The RBANS total and index scores for the 28 patients with and 95 without a history of suicide attempt and 151 healthy controls are shown in Table 3. The subjects from these 3 subgroups were matched for demographics including sex, age, education, smoking status, and BMI (all $P > .05$). When schizophrenia patients were compared with healthy controls,

Table 1. Clinical and Demographic Data for Patients With First-Episode Schizophrenia Versus Controls[a]

Characteristic	Schizophrenia (n = 357)	Controls (n = 380)	F/χ^2	*P* Value
Male/female, n	173/184	179/201	0.14	.71
Age, y	27.6 ± 9.4	27.3 ± 7.4	0.09	.76
Education, y	11.2 ± 5.8	11.4 ± 8.2	0.08	.78
Smoking, %	28.3	29.9	0.26	.61
BMI, kg/m^2	21.6 ± 3.6	24.5 ± 5.0	49.4	.000
Suicide attempters/ nonattempters, n	43/314	3/377	39.8	.000

[a]Values shown as mean ± SD unless otherwise noted.
Abbreviation: BMI = body mass index.

Table 2. Demographic and Clinical Characteristics of Suicide Attempters Versus Nonattempters Among Drug-Naive Patients With First-Episode Schizophrenia[a]

Characteristic	Suicide Attempters (n = 43)	Suicide Nonattempters (n = 314)	F/χ^2	*df*	*P*[b]
Male/female, n	20/23	153/161	0.07	1	.79
Age, y	29.3 ± 10.6	27.3 ± 9.3	1.63	1,354	.20
Education, y	10.6 ± 3.2	11.0 ± 4.1	0.48	1,353	.49
Marriage status, n			1.56	2	.46
Single	25	214			
Married	15	83			
Divorced	2	15			
Smoker/nonsmoker, n	13/25	47/215	5.49	1	**.019**
Age at onset, y	27.2 ± 10.3	25.6 ± 9.0	1.16	1,346	.28
BMI, kg/m^2	21.7 ± 3.7	21.5 ± 3.6	0.06	1,349	.81
PANSS score					
Positive symptom subscale	23.6 ± 7.6	24.0 ± 6.7	0.02	1,354	.90
Negative symptom subscale	17.1 ± 8.1	19.6 ± 7.6	4.12	1,354	**.043**
General psychopathology subscale	41.4 ± 14.3	38.3 ± 10.2	3.11	1,354	.08
Total	82.3 ± 25.0	81.7 ± 18.5	0.02	1,354	.90

[a]Values shown as mean ± SD unless otherwise noted. Since some subjects did not complete the questionnaire or clinical measures fully, numbers vary slightly in different categories.
[b]Statistically significant values are shown in boldface.
Abbreviations: BMI = body mass index, PANSS = Positive and Negative Syndrome Scale.

Table 3. Comparison of RBANS Scores Between First-Episode Schizophrenia Patients With or Without a History of Suicide Attempt and Healthy Controls[a]

Index	Suicide Attempters (n = 28)	Suicide Nonattempters (n = 95)	Healthy Controls (n = 151)	F^b	*df*	P^b
Immediate Memory	66.3 ± 13.2	61.9 ± 15.2	78.8 ± 15.8	30.33	7,266	.001
Attention	77.9 ± 17.6	69.4 ± 17.1[c]	93.8 ± 18.9	6.17	7,266	< .001
Language	69.7 ± 17.7	69.3 ± 17.0	95.4 ± 13.5	70.65	7,266	.002
Visuospatial/ Constructional	75.2 ± 13.5	72.8 ± 12.5	80.5 ± 15.8	54.29	7,266	.15
Delayed Memory	71.5 ± 19.3	67.9 ± 18.8	86.3 ± 13.6	33.85	7,266	< .001
Total	65.8 ± 13.4	61.8 ± 12.0	82.9 ± 13.9	65.07	7,266	< .001

[a]RBANS scores shown as mean ± SD values.
[b]Adjusted *F* value controlling for gender, age, education, smoking status, and BMI among attempters, nonattempters, and healthy controls.
[c]Among patients, suicide attempters performed better than nonattempters on attention ($P < .05$).
Abbreviations: BMI = body mass index, RBANS = Repeatable Battery for the Assessment of Neuropsychological Status.

1-way ANOVA showed significantly lower cognitive scores on the RBANS total and all of its 5 subscale scores (all $P < .001$; Bonferroni-corrected $P < .01$) except for the Visuospatial/ Constructional index ($P > .05$), with effect sizes ranging from 0.74 to 1.13.

In addition, we made clinical and demographic comparisons between patients who had the cognitive evaluation versus the ones who did not, to check for a selection bias that could have increased the protective role of poor cognition. However, there was no significant difference in demographic variables including sex, age, education, smoking status, BMI, age at onset, PANSS total score and its 3 subscale scores, and the rate of suicide attempt (all $P > .05$). Further, both the suicide attempters and nonattempters showed significantly lower cognitive scores on the RBANS total and all domain scores (all $P < .001$; Bonferroni-corrected $P < .01$) except for the Visuospatial/Constructional index (both tasks, $P > .05$) (Table 3). When suicide attempters were compared with to nonattempters within the schizophrenia group, attempters performed better on the Attention domain ($F_{1,121} = 5.12$, $P = .025$; Bonferroni-corrected $P > .05$), with an effect size of 0.49. However, there were no significant differences in the RBANS total and any other domain scores between the attempters and nonattempters (all $P > .05$). When adding these data including sex, age, education, smoking status, BMI, age at onset, and the PANSS positive, negative and general psychopathology subscale scores together into a single stepwise multiple logistic regression analysis of all risk factors evaluated, the PANSS negative symptom subscale score (Wald $\chi^2_1 = 7.90$ $P = .005$; adjusted OR = 0.807; 95% CI, 0.696–0.936) and Attention (Wald $\chi^2_1 = 4.69$, $P = .03$; adjusted OR = 0.957; 95% CI, 0.918–0.997) remained significant for suicide attempt.

DISCUSSION

In our present study, the frequency of suicide attempts in schizophrenia was 12%, which was exactly the same as in the recent report of the Chinese community-dwelling schizophrenia patients in Beijing,[37] close to the 10.6% attempted suicide rate in patients with first-episode psychosis in Hong Kong,[53] and close to the 7.5% rate of suicide attempts in Chinese schizophrenia outpatients of a rural community in a recent report.[22] A recent epidemiologic survey showed that the overall prevalences of suicidal ideation, plans, and attempts were 2.8%, 1.6%, and 1.3%, respectively, in a rural sample and 1.8%, 1.3%, and 0.9%, respectively in an urban sample in the Beijing Municipality.[54] Thus, our results showed that the prevalence of lifetime suicide attempt in the FEDN patients with schizophrenia was appropriately 11 times greater than in the general population in Beijing (12.0% vs 1.1%), suggesting a marked increased prevalence of suicide attempts in both FEDN and chronically ill, medicated patients (9.2%) with schizophrenia in the Chinese population. However, most reports on suicide attempts in FEDN or chronically ill, medicated Chinese schizophrenia patients show lower prevalence as compared to the 20%–50% prevalence estimated in Western countries.[6,7]

Interestingly, suicide-related mortality is higher among subjects recently diagnosed with schizophrenia (≤ 5 years from diagnosis).[26] This risk appears to peak in the first year of illness and then steadily decline over the following years.[9] Recently, a Norwegian study[33] showed that in the early phases of the first episode of psychosis, 38.8% of patients reported suicidal ideation and 25.9% attempted suicide before receiving any treatment. In our present study, although we found a higher prevalence of suicide attempts in FEDN than in chronically ill, medicated patients (12.0% vs 9.2%), there was no significant difference between the groups, suggesting that there is no significant change in suicide attempt rate over the progression of the illness course and that most attempts occur early in the disease.

In our present study, we found that smoking and reduced negative symptoms were associated with suicide attempt in FEDN patients. This finding corroborates the previous study by our group[24] in which nicotine dependence severity was associated with suicide attempts in chronically ill, medicated schizophrenia patients, suggesting that smoking is a risk factor in both categories. Several epidemiologic studies have reported an association between smoking and suicidal behaviors, but the results are inconsistent.[55] However, a recent meta-analysis[56] has demonstrated that smoking is associated with an increased risk of suicidal behaviors in general. In chronically ill patients with schizophrenia, several studies (eg, Kao et al[47]) also showed increased suicidal risk among smoking schizophrenia patients. Taken together, these studies suggest that smoking may be a contributing factor for suicide in schizophrenia.

Further, our study found that lower negative symptom severity correlated with an increased risk of suicide attempt and that positive symptoms had no association. Many studies[39–41] found that the negative symptoms of schizophrenia may increase suicidal experience in

psychotic individuals; however, the results have been inconsistent. For example, earlier studies (eg, McGirr et al[38]) found that individuals with chronic schizophrenia and other psychotic disorders at risk for suicide exhibited fewer negative symptoms. Further, a recent study[7] showed that more negative symptoms trended toward significantly lower suicide risk in recent-onset psychosis. On the other hand, increased negative symptoms significantly correlate with severity and intensity of recent suicidal ideation even after adjustment for depression scores.[57] Our current study showed that negative symptom severity was significantly lower in suicide attempters, suggesting that negative symptoms may be a protective factor for suicide attempt risk in FEDN patients with schizophrenia. It is hard to provide a reasonable explanation for the lower negative symptom severity in suicide attempters in first-episode schizophrenia patients found in our current study. We speculate that higher negative symptom severity is associated with the progressive loss of social drive, the diminished capacity to experience affect, and the indifference toward the future,[57] which are markedly disabling, but may decrease or even eliminate the painful hopelessness, self-awareness, and stigma that are associated with suicide-related behaviors. Finally, there was no effect for positive symptoms in our current study, which is consistent with previous findings for positive symptoms.[7,58,59] A few studies[18,60] have reported a significant association, but this does not to appear to be a strong relationship.

Overall, whether positive or negative symptoms show a significant association with suicide-related behaviors is still unclear. The possible explanations related to this mixed finding may be due to the patients in different stage of disease progression (acute vs chronic or active phase vs remission), different age at onset or illness duration, different exposure to antipsychotic treatment (naive vs medicated), or different ethnic origin or genetic background of the patients studied. Therefore, the relationship between clinical symptoms and suicide in patients with schizophrenia deserves further investigation in a study with a large sample size of FEDN patients and a longitudinal design.

Interestingly, we found that patients who had a history of suicide attempt outperformed suicide nonattempters on the RBANS Attention domain, which was consistent with the findings of earlier studies.[18,30,31] For example, a previous study[30] found an association between suicidality and better performance for attention together with psychomotor speed, verbal working memory, and executive function in schizophrenia patients. A study by Nangle et al[18] similarly observed that schizophrenia patients who had previously attempted suicide performed better for attention and verbal fluency than nonattempters. Interestingly, the previous studies[18,30] also found an association between suicidality and better performance on tests of executive function. Two recent studies in this area[31,61] have affirmed the role of executive functioning in increased suicidality.

Although we did not measure executive functioning directly in our present study, attention is an important component of executive function and thus can be seen as a proxy for it. Executive function relates to the capacity to shift attention from one stimulus to another, initiate or cease engaging in a given behavior, evaluate risk, and develop plans of action and carry them out.[18] Impairment in this supervisory attentional system can result in difficulties with goal formulation and an inability to plan effectively.[18,51] Thus, those schizophrenia patients with relatively higher attention and executive functioning may have greater ability to formulate plans and initiate behavior directed toward suicide attempt.[18] However, other studies[19,32,33] failed to find significant relationship between cognitive performance and suicidal behavior in schizophrenia. This discrepancy may arise from differences in techniques of measuring cognitive performance; differences in sampling of patients in different stages of disease progression (acute vs chronic or active phase vs remission); different illness courses (first episode vs multiple episodes); exposure to different type, dosage, and length of antipsychotics; different definitions of suicidal categories; or sociocultural factors that have close relationship with suicidality. Taken together, these results show the complexity and difficulty in determining the relationship between suicidality and cognitive functioning in schizophrenia, which warrant further investigation in a large sample from the different ethnicities.

There are several limitations of this current study. First, although we found better attention in suicide attempters compared to the nonattempters among schizophrenia patients, the significance did not remain after the correction for multiple comparisons, suggesting a small effect or a limited sample size. This positive result warrants further investigation before the firm conclusion can be drawn. Second, this study has a cross-sectional, case-control design and cannot show direct causality between suicide attempts and the risk factors in patients with schizophrenia. Thus, the main findings of our study should be regarded as of an exploratory or preliminary nature. Third, we used the RBANS to investigate only Immediate Memory, Visuospatial/Constructional, Language, Attention, and Delayed Memory indices, but not additional neurocognitive features that have been explored elsewhere. While the RBANS has been validated as a reliable screening test for cognitive impairment, it is not designed to be sensitive for cognitive impairment specific to schizophrenia, particularly in domains such as executive functioning, which has been reported to be closely associated with suicide in schizophrenia.[30,31] Thus, there may be important differences in cognitive functioning that were not captured with the RBANS, which is one of the main methodological limitations of our current study. Fourth, premorbid IQ was not measured among the subjects in the study, which would have been prudent since premorbid IQ definitely has an impact on performance on cognitive tasks. Thus, the impact of premorbid IQ on cognitive performance should be adjusted for in the future studies. Fifth, the suicide attempt data were collected from medical case notes and interviews with the patients and their family members rather than measured by a structured instrument at the time of the suicide attempt. Moreover, we did not assess the severity of suicide attempts; doing so is important for examining the clinical correlates with lethality.

Submitted: July 8, 2017; accepted December 27, 2017.

Published online: July 24, 2018.

Potential conflicts of interest: None.

Funding/support: Funding for this study was provided by the National Natural Science Foundation of China (81371477), the Scientific and Technological Program of Suzhou (SYS201261), Key Diagnosis and treatment Program of Suzhou (LCZX201515), Suzhou Key Medical Center for Psychiatric Diseases (Szzx201509), and Suzhou Key Disciplines for Psychiatry (Szxk201515).

Role of the sponsor: These sources had no further role in this study design, in the data collection and analysis, in the writing of the report, and in the decision to submit the paper for publication.

REFERENCES

1. Pompili M, Amador XF, Girardi P, et al. Suicide risk in schizophrenia: learning from the past to change the future. *Ann Gen Psychiatry*. 2007;6(1):10.
2. Balhara YP, Verma R. Schizophrenia and suicide. *East Asian Arch Psychiatry*. 2012;22(3):126–133.
3. Hor K, Taylor M. Suicide and schizophrenia: a systematic review of rates and risk factors. *J Psychopharmacol*. 2010;24(suppl):81–90.
4. Altamura AC, Bassetti R, Bignotti S, et al. Clinical variables related to suicide attempts in schizophrenic patients: a retrospective study. *Schizophr Res*. 2003;60(1):47–55.
5. Suokas JT, Perälä J, Suominen K, et al. Epidemiology of suicide attempts among persons with psychotic disorder in the general population. *Schizophr Res*. 2010;124(1–3):22–28.
6. Aleman A, Denys D. Mental health: a road map for suicide research and prevention. *Nature*. 2014;509(7501):421–423.
7. Castelein S, Liemburg EJ, de Lange JS, et al. Suicide in recent onset psychosis revisited: significant reduction of suicide rate over the last two decades—a replication study of a Dutch incidence cohort. *PLoS One*. 2015;10(6):e0129263.
8. Nordentoft M, Madsen T, Fedyszyn I. Suicidal behavior and mortality in first-episode psychosis. *J Nerv Ment Dis*. 2015;203(5):387–392.
9. Ventriglio A, Gentile A, Bonfitto I, et al. Suicide in the early stage of schizophrenia. *Front Psychiatry*. 2016;7:116.
10. Lopez-Morinigo JD, Ayesa-Arriola R, Torres-Romano B, et al. Risk assessment and suicide by patients with schizophrenia in secondary mental healthcare: a case-control study. *BMJ Open*. 2016;6(9):e011929.
11. Fuller-Thomson E, Hollister B. Schizophrenia and suicide attempts: findings from a representative community-based Canadian sample. *Schizophr Res Treatment*. 2016;2016:3165243.
12. Hawton K, Sutton L, Haw C, et al. Schizophrenia and suicide: systematic review of risk factors. *Br J Psychiatry*. 2005;187(1):9–20.
13. Aloba O, Esan O, Alimi T. Adaptation of the Beck Hopelessness Scale as a suicide risk screening tool among Nigerian patients with schizophrenia. *Int J Psychiatry Clin Pract*. 2018;22(1):19–24.
14. Cassidy RM, Yang F, Kapczinski F, 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):787–797.
15. Eskelinen M, Korhonen R, Selander T, et al. Suicidal ideation versus hopelessness/helplessness in healthy individuals and in patients with benign breast disease and breast cancer: a prospective case-control study in Finland. *Anticancer Res*. 2015;35(6):3543–3551.
16. Barrett EA, Mork E, Færden A, et al. The development of insight and its relationship with suicidality over one year follow-up in patients with first episode psychosis. *Schizophr Res*. 2015;162(1–3):97–102.
17. Tiihonen J, Lönnqvist J, Wahlbeck K, et al. Antidepressants and the risk of suicide, attempted suicide, and overall mortality in a nationwide cohort. *Arch Gen Psychiatry*. 2006;63(12):1358–1367.
18. Nangle JM, Clarke S, Morris DW, et al. Neurocognition and suicidal behaviour in an Irish population with major psychotic disorders. *Schizophr Res*. 2006;85(1–3):196–200.
19. Zoghbi AW, Al Jurdi RK, Deshmukh PR, et al. Cognitive function and suicide risk in Han Chinese inpatients with schizophrenia. *Psychiatry Res*. 2014;220(1–2):188–192.
20. Serafini G, Pompili M, Innamorati M, et al. Can cannabis increase the suicide risk in psychosis? a critical review. *Curr Pharm Des*. 2012;18(32):5165–5187.
21. Østergaard MLD, Nordentoft M, Hjorthøj C. Associations between substance use disorders and suicide or suicide attempts in people with mental illness: a Danish nation-wide, prospective, register-based study of patients diagnosed with schizophrenia, bipolar disorder, unipolar depression or personality disorder. *Addiction*. 2017;112(7):1250–1259.
22. Ran MS, Xiang MZ, Mao WJ, et al. Characteristics of suicide attempters and nonattempters with schizophrenia in a rural community. *Suicide Life Threat Behav*. 2005;35(6):694–701.
23. Reutfors J, Clapham E, Bahmanyar S, et al. Suicide risk and antipsychotic side effects in schizophrenia: nested case-control study. *Hum Psychopharmacol*. 2016;31(4):341–345.
24. Zhang XY, Al Jurdi RK, Zoghbi AW, et al. Prevalence, demographic and clinical correlates of suicide attempts in Chinese medicated chronic inpatients with schizophrenia. *J Psychiatr Res*. 2013;47(10):1370–1375.
25. Pompili M, Serafini G, Innamorati M, et al. Suicide risk in first episode psychosis: a selective review of the current literature. *Schizophr Res*. 2011;129(1):1–11.
26. Fleischhacker WW, Kane JM, Geier J, et al. Completed and attempted suicides among 18,154 subjects with schizophrenia included in a large simple trial. *J Clin Psychiatry*. 2014;75(3):e184–e190.
27. Pompili M, Serafini G, Innamorati M, et al. Unmet treatment needs in schizophrenia patients: is asenapine a potential therapeutic option? *Expert Rev Neurother*. 2011;11(7):989–1006.
28. Bora E. Differences in cognitive impairment between schizophrenia and bipolar disorder: considering the role of heterogeneity. *Psychiatry Clin Neurosci*. 2016;70(10):424–433.
29. Schulz SC, Murray A. Assessing cognitive impairment in patients with schizophrenia. *J Clin Psychiatry*. 2016;77(suppl 2):3–7.
30. Kim CH, Jayathilake K, Meltzer HY. Hopelessness, neurocognitive function, and insight in schizophrenia: relationship to suicidal behavior. *Schizophr Res*. 2003;60(1):71–80.
31. Verma D, Srivastava MK, Singh SK, et al. Lifetime suicide intent, executive function and insight in schizophrenia and schizoaffective disorders. *Schizophr Res*. 2016;178(1–3):12–16.
32. Potkin SG, Anand R, Alphs L, et al. Neurocognitive performance does not correlate with suicidality in schizophrenic and schizoaffective patients at risk for suicide. *Schizophr Res*. 2003;59(1):59–66.
33. Barrett EA, Sundet K, Simonsen C, et al. Neurocognitive functioning and suicidality in schizophrenia spectrum disorders. *Compr Psychiatry*. 2011;52(2):156–163.
34. Kosidou K, Dalman C, Fredlund P, et al. School performance and the risk of suicide attempts in young adults: a longitudinal population-based study. *Psychol Med*. 2014;44(6):1235–1243.
35. Seidman LJ, Shapiro DI, Stone WS, et al. Association of neurocognition with transition to psychosis: baseline functioning in the second phase of the North American Prodrome Longitudinal Study. *JAMA Psychiatry*. 2016;73(12):1239–1248.
36. Xiang YT, Weng YZ, Leung CM, et al. Socio-demographic and clinical correlates of lifetime suicide attempts and their impact on quality of life in Chinese schizophrenia patients. *J Psychiatr Res*. 2008;42(6):495–502.
37. Yan F, Xiang YT, Hou YZ, et al. Suicide attempt and suicidal ideation and their associations with demographic and clinical correlates and quality of life in Chinese schizophrenia patients. *Soc Psychiatry Psychiatr Epidemiol*. 2013;48(3):447–454.
38. McGirr A, Tousignant M, Routhier D, et al. Risk factors for completed suicide in schizophrenia and other chronic psychotic disorders: a case-control study. *Schizophr Res*. 2006;84(1):132–143.
39. Kelleher I, Corcoran P, Keeley H, et al. Psychotic symptoms and population risk for suicide attempt: a prospective cohort study. *JAMA Psychiatry*. 2013;70(9):940–948.
40. DeVylder JE, Hilimire MR. Suicide risk, stress sensitivity, and self-esteem among young adults reporting auditory hallucinations. *Health Soc Work*. 2015;40(3):175–181.
41. Koyanagi A, Stickley A, Haro JM. Subclinical psychosis and suicidal behavior in England: Findings from the 2007 Adult Psychiatric Morbidity Survey. *Schizophr Res*. 2015;168(1–2):62–67.
42. Leucht S, Cipriani A, Spineli L, et al. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. *Lancet*. 2013;382(9896):951–962.
43. Ernst CL, Goldberg JF. Antisuicide properties of psychotropic drugs: a critical review. *Harv Rev Psychiatry*. 2004;12(1):14–41.
44. Reutfors J, Bahmanyar S, Jönsson EG, et al. Medication and suicide risk in schizophrenia: a nested case-control study. *Schizophr Res*. 2013;150(2–3):416–420.
45. Schoenborn CA, Adams PE. Health behaviors of adults: United States, 2005–2007. *Vital Health Stat 10*. 2010;(245):1–132.
46. Krug EG, Dahlberg LL, Mercy JA, et al. *World Report on Violence and Health*. Vol. 1. Geneva, Switzerland: World Health Organization; 2002:185.
47. Kao YC, Liu YP, Cheng TH, et al. Cigarette smoking in outpatients with chronic schizophrenia in Taiwan: relationships to socio-demographic and clinical characteristics. *Psychiatry Res*. 2011;190(2–3):193–199.
48. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull*. 1987;13(2):261–276.
49. Guy W. *ECDEU Assessment Manual for Psychopharmacology*. Revised Edition. Washington, DC: US Department of Health, Education, and Welfare; 1976.
50. Fagerström KO. Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment.

Addict Behav. 1978;3(3–4):235–241.
51. Randolph C, Tierney MC, Mohr E, et al. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS): preliminary clinical validity. *J Clin Exp Neuropsychol*. 1998;20(3):310–319.
52. Zhang BH, Tan YL, Zhang WF, et al. Repeatable battery for the assessment of neuropsychological status (RBANS) as a screening test in Chinese: reliability and validity. *Chin Ment Health J*. 2009;28:865–869.
53. Chang WC, Chen ESM, Hui CLM, et al. Prevalence and risk factors for suicidal behavior in young people presenting with first-episode psychosis in Hong Kong: a 3-year follow-up study. *Soc Psychiatry Psychiatr Epidemiol*. 2015;50(2):219–226.
54. Ma X, Xiang YT, Cai ZJ, et al. Lifetime prevalence of suicidal ideation, suicide plans and attempts in rural and urban regions of Beijing, China. *Aust N Z J Psychiatry*. 2009;43(2):158–166.
55. Li D, Yang X, Ge Z, et al. Cigarette smoking and risk of completed suicide: a meta-analysis of prospective cohort studies. *J Psychiatr Res*. 2012;46(10):1257–1266.
56. Poorolajal J, Darvishi N. Smoking and suicide: a meta-analysis. *PLoS One*. 2016;11(7):e0156348.
57. Gill KE, Quintero JM, Poe SL, et al. Assessing suicidal ideation in individuals at clinical high risk for psychosis. *Schizophr Res*. 2015;165(2-3):152–156.
58. Pratt D, Gooding P, Johnson J, et al. Suicide schemas in non-affective psychosis: an empirical investigation. *Behav Res Ther*. 2010;48(12):1211–1220.
59. Fedyszyn IE, Robinson J, Harris MG, et al. Predictors of suicide-related behaviors during treatment following a first episode of psychosis: the contribution of baseline, past, and recent factors. *Schizophr Res*. 2012;140(1–3):17–24.
60. Mitter N, Subramaniam M, Abdin E, et al. Predictors of suicide in Asian patients with first episode psychosis. *Schizophr Res*. 2013;151(1–3):274–278.
61. Delaney C, McGrane J, Cummings E, et al. Preserved cognitive function is associated with suicidal ideation and single suicide attempts in schizophrenia. *Schizophr Res*. 2012;140(1–3):232–236.

Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Suicide section. Please contact Philippe Courtet, MD, PhD, at pcourtet@psychiatrist.com.