

ORIGINAL RESEARCH

Smoking Behavior and its Effect on Psychiatric Symptoms of Patients with Stable Schizophrenia

Botao Ma, MD; Qing Zhao, MD; Jiaqi Song, MD; Yu Li, MD;
Yun Bian, MD; Zhiren Wang, PhD; Fude Yang, MD

ABSTRACT

Context • Schizophrenia is a common and clinically disabling mental disorder. Many patients with schizophrenia smoke. Research on the effects of smoking on schizophrenia's symptoms are inconsistent.

Objective • The study intended to investigate the smoking status of patients with stable schizophrenia to determine the effects of smoking on schizophrenia-related symptoms.

Design • The research team performed a case-control study.

Setting • The study took place at Beijing Huilongguan Hospital in Beijing, Changping District, China.

Participants • Participants were 160 patients at the hospital who had been diagnosed with stable schizophrenia between April 2018 and March 2020.

Groups • The research team divided participants into two groups based on their current smoking status: (1) a smoking group with 72 participants and (2) a nonsmoking group with 88 participants.

Outcome Measures • The research team: (1) examined the types of antipsychotic drugs that participants received; (2) used a schizophrenia-related scale, the Positive and Negative Syndrome Scale (PANSS), to examine participants' status; (3) examined the smoking habits of the smoking group; and (4) analyzed the correlation between the PANSS score and

the smoking group's smoking index.

Results • No significant difference existed between the groups in the type of medicine used ($P > .05$). The smoking group's PANSS total ($P = .014$), positive symptom ($P = .039$), and negative symptom ($P = .003$) scores were significantly lower than those of the nonsmoking group ($P < .05$). No significant difference existed between the groups in the general psychopathological symptom score ($P > .05$). The smoking group started smoking between 13 and 24 years of age, with a mean age of 19.11 ± 4.10 years. The group smoked 10-30 cigarettes/d, with a mean smoking amount of 18.4 ± 3.1 cigarettes/d, and the smoking index was 344.7 ± 48.0 . The smoking group's smoking index was significantly negatively correlated with the positive symptom, negative symptom, and total PANSS scores (all $P = .000$). No correlation existed between the smoking index and the general psychopathological symptom score ($P > .05$).

Conclusions • Smoking patients with stable schizophrenia generally exhibit fewer symptoms than nonsmoking patients, which relate to the alleviation of mental tension that smoking can provide. (*Altern Ther Health Med*. [E-pub ahead of print.]

Botao Ma, MD, Attending Physician, Department of Clinical 3; Beijing Huilongguan Hospital. **Qing Zhao, MD**, Attending Physician, Department of Psychiatry; Beijing Children's Hospital; Capital Medical University; National Center for Children's Health, Beijing; China. **Jiaqi Song, MD**, Attending Physician, Department of Clinical 5; Beijing Huilongguan Hospital; China. **Yu Li, MD**, Attending Physician, Department of Psychiatry; Beijing Tongzhou District Psychiatric Hospital; China. **Yun Bian, MD**, Deputy Chief Physician, Department of Psychosomatic Medicine; Beijing Huilongguan Hospital; China. **Zhiren Wang, PhD**, Chief Physician, Department of Technology; Beijing Huilongguan Hospital; China. **Fude Yang, MD**, Chief Physician, Hospital Office; Beijing Huilongguan Hospital; China.

Corresponding author: Fude Yang, MD
E-mail: yangfd2002@163.com

Schizophrenia is a common and clinically disabling mental disorder that often develops in adolescents and young adults and that can cause great harm. Schizophrenia's clinical manifestations include disordered thinking, perception, behavior, and emotion. Patients are unable to integrate their mental activities and environments. Most patients have impaired social functions and can't maintain normal social activities or work, which places a heavy burden on their families and society.¹

Psychotropic drugs are the main clinical treatment for schizophrenia and can effectively control most patients' symptoms, allowing them to maintain a stable state. However, many factors influence the activities of schizophrenia, and the illness often recurs.² Identifying the influencing factors could be helpful for guiding clinical treatment.

Smoking

The harmful effects of tobacco on public health are well documented. People with schizophrenia are more prone to substance dependence and abuse than other people, with tobacco dependence being the most common.³ Phan, et al found that the smoking rate of patients with schizophrenia is 70-80%, which is 2-4 times that of the general population worldwide.⁴ Fond, et al and Chen, et al found that individuals with a smoking index of >400 are a high-risk population for lung cancer.^{5,6} Currently, the reasons for that high smoking rate aren't fully understood.

Current clinical reports on the effects of smoking on schizophrenia symptoms are inconsistent.^{7,8} Caponnetto, et al found that smoking can increase the degree of residual negative mental symptoms that remain after clinical treatment.⁹ On the other hand, Murphy, et al found that the psychiatric symptoms of stable schizophrenia patients who smoke were milder than those of nonsmoking patients.¹⁰

Smoking and Dopamine

Because nicotine in tobacco helps upregulate nicotine receptors, promotes the release of dopamine in patients' prefrontal cortexes, and improves positive and negative psychopathological symptoms, smoking tobacco may help overcome the deficits that patients with schizophrenia have.¹¹⁻¹³ McCutcheon, et al found that smoking may improve patients' basic perceptual processing ability.¹⁴

Smith, et al and Coustals, et al found that the nicotine in tobacco can diffuse into the brain through the blood-brain barrier; increase the number of nicotine receptors in the thalamus, striatum, and hippocampus; and regulate dopamine synthesis in the midbrain limbic system.^{15,16} Murphy et al found that that tobacco use was helpful in increasing the level of serum, brain-derived neurotrophic factor in patients with first-episode schizophrenia and can decrease their negative mental symptoms.¹⁰

McCutcheon et al found that smoking may be a self-treatment behavior that patients use to meet the internal needs that the disease causes.¹⁴ Kotz et al suggested that the smoking behavior of patients with schizophrenia may be related to the alleviation of clinical symptoms and that dysfunction of the nicotinic acetylcholine neurotransmitter system plays an important role.¹⁷

Current Study

The current study intended to investigate the smoking status of patients with stable schizophrenia to determine the effects of smoking on schizophrenia-related symptoms.

METHODS

Participants

The research team performed an observational case-control study, which took place at Beijing Huilongguan Hospital in Beijing, Changping District, China. Potential participants were patients who had been diagnosed with stable schizophrenia at the hospital between April 2018 and March 2020.

The study included potential participants if they: (1) were 19-65 years old, (2) had received a diagnosis of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders,¹⁸ (3) were in a stable condition and able to complete the relevant examinations, (4) had normal vision and hearing, and (5) were male.

The study excluded potential participants if they had: (1) fewer than 5 years of education, (2) severe anxiety or depression, (3) received a cancer diagnosis, (4) a history of cerebrovascular disease or recent acute myocardial infarction, (5) a history of epilepsy, or (6) a history of drug use or addiction.

The research team obtained informed consent from participants and their families. The Medical Ethics Committee at hospital approved the study's protocols and related materials [House(Lun) lot 07]. This study complied with the Helsinki Declaration.

Procedures

Groups. The research team divided participants into two groups based on their current smoking status: (1) a smoking group and (2) a nonsmoking group. The team defined smoking as ≥ 1 cigarette/d for ≥ 5 days/week.

Data collection. The research team recorded participants' ages, weights, heights, years of education, family history of psychosis, course of schizophrenia, age of onset, marital status, and residence from the medical records. All participants in the smoking group completed a smoking survey.

Outcome Measures. The research team: (1) examined the types of antipsychotic drugs that participants received; (2) used a schizophrenia-related scale, the Positive and Negative Syndrome Scale (PANSS),¹⁹ to examine participants' status; (3) examined the smoking habits of the smoking group; and (4) analyzed the correlation between the PANSS score and the smoking group's smoking index.

Outcome Measures

Use of anti-schizophrenia-related drugs. The research team identified the types of drugs that participants used, including clozapine, sulpiride, risperidone, quetiapine, olanzapine, aripiprazole, haloperidol, and combined medications.

PANSS. Medical practitioners use the positive and negative syndrome scale (PANSS) primarily to evaluate the severity of patients' schizophrenia symptoms. The questionnaire has 30 items that cover the severity of positive symptoms, negative symptoms, and general psychopathological symptoms. The total score ranges from 30 to 210 points, and the higher the score, the more severe the condition is. A higher total score indicates a more serious condition.¹⁹

Smoking habits. The smoking survey determined the age at which participants in the smoking group began smoking, the number and frequency of cigarettes smoked, and the smoking index. Smoking index = the number of cigarettes smoked per day x the number of years smoking.

Correlation between PANSS score and smoking index.

The research team performed a simple linear correlation analysis.

Statistical Analysis

The research team analyzed the data using the SPSS 21.0 (IBM, Armonk, New York, USA). The team: (1) tested variables such as age, weight, height, and years of education for normal distribution by normality test, (2) expressed continuous data with normal distribution as means ± standard deviations (SDs) and compared the groups using the Student's *t* test, and for data with not normal distribution, the nonparametric test was used. (3) expressed categorical data as numbers (N) and percentages (%) and compared the groups using the Chi-square (χ^2) test, and (4) used Pearson's correlation coefficient for the correlation analysis. *P* < .05 indicated statistical significance.

RESULTS

Participants

The research team included and analyzed the data of 160 participants, 72 in the smoking group and 88 in the nonsmoking group (Table 1). In the smoking group, the mean: (1) age was 36.9 ± 7.0 y, (2) height was 165.2 ± 4.1 cm, (3) weight was 63.2 ± 4.6 kg, (4) education was 8.95 ± 2.67 y, (5) course of disease was 6.93 ± 2.40 y, and (6) age of first onset was 23.8 ± 4.0 y.

In the nonsmoking group, the mean: (1) age was 35.0 ± 7.8 y, (2) height was 164.2 ± 3.8 cm, (3) weight was 64.1 ± 6.1 kg, (4) education was 9.62 ± 2.44 y, (5) course of disease was 7.12 ± 2.90 y, and (6) age of first onset was 24.2 ± 4.5 y.

In the smoking group: (1) nine participants had a family history of mental illness (12.50%) and 63 participants did not (87.50%); (2) 34 were married (47.22%), 22 were unmarried (30.56%), and 16 were divorced or widowed (22.22%), and (3) 38 lived in a city (52.78%) and 34 lived in a rural area (47.22%).

In the nonsmoking group: (1) 16 participants had a family history of mental illness (18.18%) and 72 participants did not (81.82%); (2) 38 were married (43.18%), 27 were unmarried (30.68%), and 23 were divorced or widowed (26.14%), and (3) 55 lived in a city (62.50%) and 33 lived in a rural area (37.50%).

No significant difference in characteristics existed between the groups (*P* > .05).

Anti-schizophrenia Drugs

In the smoking group (Table 2 and Figure 1): (1) 10 participants used clozapine (13.89%), (2) four used sulpiride (5.56%), (3) 28 used risperidone (38.89%), (4) six used quetiapine (8.33%), (5) 11 used olanzapine (15.28%), (6) six used aripiprazole (8.33%), (7) three used haloperidol (4.17%), and (8) four used combined medications (5.56%).

In the nonsmoking group: (1) 18 participants used clozapine (20.45%), (2) two used sulpiride (2.27%), (3) 34 used risperidone (38.64%), (4) three used quetiapine (3.41%),

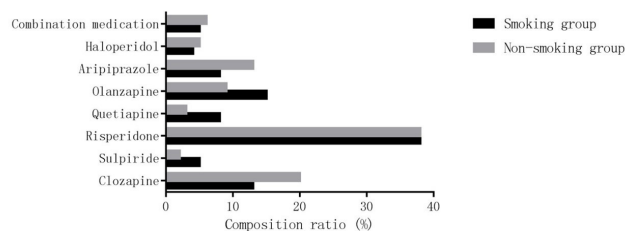
Table 1. Participants' Demographic and Clinical Characteristics (N=160)

Characteristics	Smoking Group n=72 Mean ± SD n (%)	Nonsmoking Group n=88 Mean ± SD n (%)	t/ χ^2 value	P value
Age, y	36.9 ± 7.0	35.0 ± 7.8	1.605	.111
Height, cm	165.2 ± 4.1	164.2 ± 3.8	1.598	.112
Weight, kg	63.2 ± 4.6	64.1 ± 6.1	-1.034	.303
Education, y	8.95 ± 2.67	9.62 ± 2.44	-1.656	.100
Course of Disease, y	6.93 ± 2.40	7.12 ± 2.90	-0.445	.657
Age of First Onset, y	23.8 ± 4.0	24.2 ± 4.5	-0.588	.558
Family History of Mental Illness, %			0.970	.325
Yes	9 (12.50)	16 (18.18)		
No	63 (87.50)	72 (81.82)		
Marital status, %			0.393	.822
Married	34 (47.22)	38 (43.18)		
Unmarried	22 (30.56)	27 (30.68)		
Divorced/widowed	16 (22.22)	23 (26.14)		
Place of residence, %			1.538	.215
City	38 (52.78)	55 (62.50)		
Rural area	34 (47.22)	33 (37.50)		

Table 2. Use of Anti-schizophrenia Drugs in Smoking and Nonsmoking Groups (N=160)

Types of Medicine	Smoking Group n=72 n (%)	Nonsmoking Group n=88 n (%)	χ^2 value	P value
Clozapine	10 (13.89)	18 (20.45)	1.182	.277
Sulpiride	4 (5.56)	2 (2.27)	1.182	.277
Risperidone	28 (38.89)	34 (38.64)	0.001	.974
Quetiapine	6 (8.33)	3 (3.41)	1.809	.179
Olanzapine	11 (15.28)	8 (9.09)	1.448	.229
Aripiprazole	6 (8.33)	12 (13.64)	1.115	.291
Haloperidol	3 (4.17)	5 (5.68)	0.191	.662
Combination medication	4 (5.56)	6 (6.82)	0.108	.743

Figure 1. Use of Anti-schizophrenia Drugs in the Smoking and Nonsmoking Groups



(5) 8 used olanzapine (9.09%), (6) 12 used aripiprazole (13.64%), (7) five used haloperidol (5.68%), and (8) six used combined medications (6.82%).

No significant differences in types of medication existed between the groups (*P* > .05).

PANSS Scores

In the smoking group (Table 3 and Figure 2), the mean positive symptom score was 15.84 ± 3.30, the mean negative symptom score was 19.43 ± 3.52, the mean general psychiatric pathology score was 29.86 ± 4.74, and the mean PANSS total score was 63.58 ± 8.19.

In the nonsmoking group, the mean positive symptom score was 16.90 ± 3.14, the mean negative symptom score was 19.43 ± 3.52, the mean general psychiatric pathology score was 30.73 ± 4.90, and the mean PANSS total score was 67.06 ± 9.22.

The smoking group's mean positive symptom (*P* = .039), negative symptom (*P* = .003), and PANSS total (*P* = .014)

Table 3. PANSS Scores for Smoking and Nonsmoking Groups (N=160)

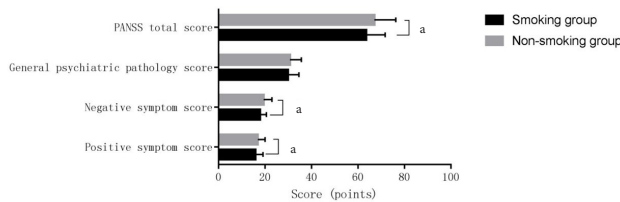
PANSS Scores	Smoking Group n=72	Nonsmoking Group n=88	t value	P value
Positive symptom score	15.84 ± 3.30	16.90 ± 3.14	-2.076	.039 ^a
Negative symptom score	17.88 ± 2.70	19.43 ± 3.52	-3.069	.003 ^b
General psychiatric pathology score	29.86 ± 4.74	30.73 ± 4.90	-1.134	.259
Total score	63.58 ± 8.19	67.06 ± 9.22	-2.496	.014 ^a

^a*P* < .05, indicating that the smoking group's PANSS total and positive symptom scores were significantly lower than those of the nonsmoking group

^b*P* < .01, indicating that the smoking group's negative symptom score was significantly lower than those of the nonsmoking group

Abbreviations: PANSS, Positive and Negative Syndrome Scale

Figure 2. Histogram of PANSS Scores of Smoking and Nonsmoking Groups



^a*P* < .05, indicating that the smoking group's PANSS total and positive symptom scores were significantly lower than those of the nonsmoking group

Abbreviations: PANSS, Positive and Negative Syndrome Scale

Table 4. Smoking Habits of the Smoking Group

Variable	Smoking Group n=72 Mean ± SD n (%)
Smoking Start	
Age, y	19.11 ± 4.10
Range, y	13-24
Cigarettes Per Day	
Number	18.4 ± 3.1
Range	10-30
Smoking Index	344.7 ± 48.0

Table 5. Linear Correlation Analysis

PANSS Score	Smoking Index	
	R value	P value
Positive symptom score	-0.438	.000 ^a
Negative symptom score	-0.519	.000 ^a
General psychiatric pathology score	0.112	.326
Total score	-0.5481	.000 ^a

^a*P* < .001, indicating that the smoking group's PANSS total, positive symptom, and negative symptom scores were significantly correlated with smoking

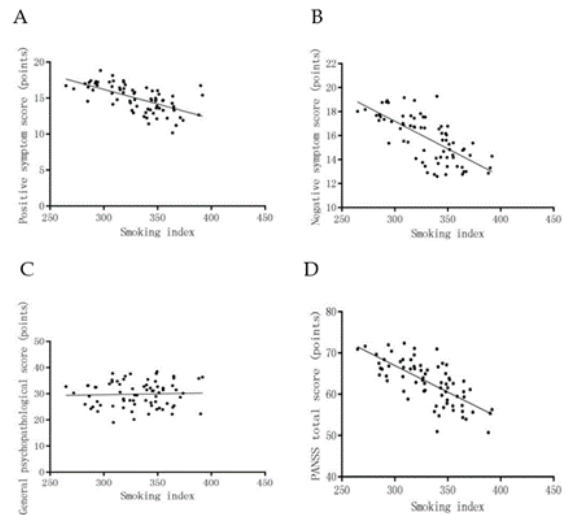
Abbreviations: PANSS, Positive and Negative Syndrome Scale

scores were significantly lower than those of the nonsmoking group. No significant difference existed between the groups for the general psychiatric pathology score (*P* > .05).

Smoking Habits

In the smoking group, the mean age for starting smoking was 19.11 ± 4.10 y, with a ranges of 13 to 24 years old; the mean number of cigarettes consumed was 18.4 ± 3.1

Figure 3. Scatter Diagram of Smoking Index and PANSS Score for the Smoking Group. Figures 3A, 3B, and 3D are the scatter diagrams for the smoking index showing patients' positive symptom, negative symptom, and PANSS total scores, respectively. Figure 3C is the scatter plot for the smoking index showing patients' general psychopathological symptom score.



cigarettes/d, with a range of 10 to 30 cigarettes/d; and the smoking index was 344.7 ± 48.0.

Smoking Index and PANSS Score

Table 5 shows that the smoking group's smoking index was significantly negatively correlated with the positive symptom score (*P* = .000), negative symptom score (*P* = .000), and PANSS total score (*P* = .000). No correlation existed between the smoking index and the general psychopathological symptom score (*P* > .05). Figure 3 shows the scatter diagrams for the scores.

DISCUSSION

The current study's findings suggest that the psychiatric symptoms of stable schizophrenia patients who smoke are milder than those of nonsmoking patients. This may be due to an increase in the number of nicotine receptors in the thalamus, striatum, and hippocampus of patients with schizophrenia.

A smoking index > 400 is considered a high-risk population for lung cancer.^{5,6} In the current study, the smoking group's smoking index was 344.7 ± 48.0, which was close to this critical value.

The correlation analyses revealed that the smoking index of stable patients with schizophrenia was significantly negatively correlated with the positive symptom, negative symptom, and PANSS total scores, but no correlation existed between the smoking index and the general psychopathological symptom score, suggesting that the greater the smoking index, the lighter the psychopathological symptoms may be.

The current study had some limitations. Due to the limitation of sample size, the results may be biased, requiring

further study. Also due to the limited sample size, the current study didn't conduct a detailed analysis of the influence of smoking on patients with different types of schizophrenia.

Future studies with an improved experimental designs, larger sample sizes, and longer observation times that analyze the relationship between smoking and different types of schizophrenia would provide a strong basis for guiding the treatment of schizophrenia.

CONCLUSIONS

In summary, smoking patients with stable schizophrenia generally exhibit fewer symptoms than nonsmoking patients, which may relate to the alleviation of mental tension that smoking can provide.

FUNDING

Beijing Municipal Administration of Hospitals Incubating Program, No.PX2020077.

AUTHOR CONTRIBUTIONS

Botao Ma and Qing Zhao contributed equally to this work.

REFERENCES

1. Uptegrove R, Khandaker GM. Cytokines, Oxidative Stress and Cellular Markers of Inflammation in Schizophrenia. *Curr Top Behav Neurosci*. 2020;44:49-66. doi:10.1007/7854_2018_88
2. Tanzer T, Shah S, Benson C, et al. Varenicline for cognitive impairment in people with schizophrenia: systematic review and meta-analysis. *Psychopharmacology (Berl)*. 2020;237(1):11-19. doi:10.1007/s00213-019-05396-9
3. Cuoco F, Agostoni G, Lesmo S, et al. Get up! Functional mobility and metabolic syndrome in chronic schizophrenia: Effects on cognition and quality of life. *Schizophr Res Cogn*. 2022;28:100245. Published 2022 Mar 2. doi:10.1016/j.scog.2022.100245
4. Phan PT, Vu GV, Ngo CQ, et al. Tobacco smoking and nicotine dependence among patients with respiratory diseases in Vietnam: status and correlated factors. *J Subst Abuse Treat*. 2022;135:108562. doi:10.1016/j.jsat.2021.108562
5. Fond GB, Lagier JC, Honore S, et al. Microbiota-Orientated Treatments for Major Depression and Schizophrenia. *Nutrients*. 2020;12(4):1024. Published 2020 Apr 8. doi:10.3390/nu12041024
6. Chen J, Chen R, Xiang S, et al. Cigarette smoking and schizophrenia: mendelian randomisation study. *Br J Psychiatry*. 2021;218(2):98-103. doi:10.1192/bjp.2020.116
7. Gakkhar A, Mehendale A, Mehendale S. Tobacco Cessation Intervention for Young People. *Cureus*. 2022;14(10):e30308. Published 2022 Oct 14. doi:10.7759/cureus.30308
8. Ohi K, Nishizawa D, Muto Y, et al. Polygenic risk scores for late smoking initiation associated with the risk of schizophrenia. *NPJ Schizophr*. 2020;6(1):36. Published 2020 Nov 23. doi:10.1038/s41537-020-00126-z
9. Caponnetto P, DiPiazza J, Kim J, Maglia M, Polosa R. A Single-Arm, Open-Label, Pilot, and Feasibility Study of a High Nicotine Strength E-Cigarette Intervention for Smoking Cessation or Reduction for People With Schizophrenia Spectrum Disorders Who Smoke Cigarettes. *Nicotine Tob Res*. 2021;23(7):1113-1122. doi:10.1093/ntr/ntab005
10. Murphy CM, Onu MC, Goodwin C, Williams DM, Tidey JW. Acute effects of exercise among individuals with schizophrenia who smoke cigarettes. *Addict Behav*. 2023;144:107749. doi:10.1016/j.addbeh.2023.107749
11. Chen J, Chen R, Xiang S, et al. Cigarette smoking and schizophrenia: mendelian randomisation study. *Br J Psychiatry*. 2021;218(2):98-103. doi:10.1192/bjp.2020.116
12. Peterson RE, Bigdeli TB, Ripke S, et al; Schizophrenia Working Group of the Psychiatric Genomics Consortium. Genome-wide analyses of smoking behaviors in schizophrenia: Findings from the Psychiatric Genomics Consortium. *J Psychiatr Res*. 2021;137:215-224. doi:10.1016/j.jpsychires.2021.02.027
13. Coustals N, Martelli C, Brunet-Lecomte M, Petillion A, Romeo B, Benyamina A. Chronic smoking and cognition in patients with schizophrenia: A meta-analysis. *Schizophr Res*. 2020;222:113-121. doi:10.1016/j.schres.2020.03.071
14. McCutcheon RA, Reis Marques T, Howes OD. Schizophrenia-An Overview. *JAMA Psychiatry*. 2020;77(2):201-210. doi:10.1001/jamapsychiatry.2019.3360
15. Smith RL, O'Connell K, Athanasu L, et al. Identification of a novel polymorphism associated with reduced clozapine concentration in schizophrenia patients—a genome-wide association study adjusting for smoking habits [published correction appears in *Transl Psychiatry*. 2020 Nov 2;10(1):366]. *Transl Psychiatry*. 2020;10(1):198. Published 2020 Jun 19. doi:10.1038/s41398-020-00888-1
16. Coustals N, Martelli C, Brunet-Lecomte M, Petillion A, Romeo B, Benyamina A. Chronic smoking and cognition in patients with schizophrenia: A meta-analysis. *Schizophr Res*. 2020;222:113-121. doi:10.1016/j.schres.2020.03.071
17. Kotz D, Batra A, Kastaun S. Smoking Cessation Attempts and Common Strategies Employed. *Dtsch Arztebl Int*. 2020;117(1-2):7-13. doi:10.3238/arztebl.2020.0007
18. American Society of Psychiatry. *Handbook on Diagnosis and Statistics of Mental Disorders*. Zhang D, trans. Peking University Press; 2016:146.
19. Jaaro-Peled H, Sawa A. Neurodevelopmental Factors in Schizophrenia. *Psychiatr Clin North Am*. 2020;43(2):263-274. doi:10.1016/j.psc.2020.02.010