

Association Between Nonmedical Use of Prescription Drugs and Suicidal Behavior Among Adolescents

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IMPORTANCE Suicidal behavior is a leading cause of injury and death worldwide, and previous cross-sectional studies have demonstrated that nonmedical use of prescription drugs (NMUPD) was associated with suicidality. However, there is not any study in China having examined the longitudinal relationships between NMUPD, suicidal ideation, and suicidal attempts, as well as explored the potential mediating effects of depressive symptoms.

OBJECTIVE To determine whether baseline NMUPD was associated with subsequent suicidal ideation and attempts while controlling for depressive symptoms and to determine whether the increased risks were mediated by depressive symptoms.


DESIGN, SETTING, AND PARTICIPANTS In this longitudinal study, a total of 3273 students in randomly selected schools in Guangzhou were surveyed from 2009 to 2010 (response rate, 96.8%) and followed up at 1 year (2011-2012; retention rate, 96.1%). The dates of data analysis were October 9, 2015, to October 15, 2015; additional data analysis occurred March 23, 2016, to March 29, 2016.

MAIN OUTCOMES AND MEASURES Suicidal ideation, suicidal attempts, NMUPD, depressive symptoms, and alcohol-related problems.

RESULTS Overall, 3273 adolescents (mean [SD] age, 13.7 [1.0] years) were recruited for this study. The final results showed that after controlling for sociodemographic information (including sex, age, household socioeconomic status, and living arrangements), baseline depressive symptoms, baseline alcohol-related problems, baseline suicidal ideation, and baseline suicidal attempts, baseline opioids misuse (adjusted odds ratio [AOR], 2.31; 95% CI, 1.30-4.11), sedatives misuse (AOR, 4.46; 95% CI, 1.54-7.94), and nonmedical use of any prescription drug (AOR, 1.97; 95% CI, 1.21-3.23) were positively associated with suicidal ideation at follow-up. Additionally, baseline opioid misuse (AOR, 3.39; 95% CI, 1.33-5.63) and nonmedical use of any prescription drug (AOR, 2.91; 95% CI, 1.26-3.71) were also associated with subsequent suicidal attempts after controlling for sex, age, household socioeconomic status, living arrangements, depressive symptoms, alcohol-related problems, suicidal ideation, and suicidal attempts at baseline. There were significant standardized indirect effects of baseline opioids misuse on subsequent suicidal ideation (standardized β estimate = 0.020; 95% CI, 0.010-0.030) and suicidal attempts (standardized β estimate = 0.009; 95% CI, 0.004-0.015) through depressive symptoms; the standardized indirect effect of baseline sedatives misuse on subsequent suicidal ideation through depressive symptoms was also significant (standardized β estimate = 0.016; 95% CI, 0.005-0.026).

CONCLUSIONS AND RELEVANCE In this study, NMUPD at baseline was associated with subsequent suicidal ideation and attempts. These findings support that proper surveillance systems with the potential to reduce adolescent suicidality should be established to control and supervise suicidality and NMUPD among Chinese adolescents.

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Suicidal behavior is a range of behaviors that include suicidal ideation, suicidal attempts, and suicide itself and is a leading cause of injury and death worldwide.^{1,2} Moreover, suicidal ideation and suicidal attempts have shown an increased risk of recurrence.^{3,4} Although the overall rate of suicide in China has been significantly reduced from the rate in the 1990s,⁵ suicidal ideation and attempts are still currently serious problems among adolescents in China.⁶ Liu et al⁷ reported that 19% of Chinese rural adolescents reported having had suicidal ideation, and 7% reported having made a suicidal attempt during the past 6 months. Cui et al⁶ showed that 16.9% of adolescents reported having had suicidal ideation, and 8.0% reported having actually attempted suicide during the past 12 months. Additionally, suicidal ideation and suicidal attempts among youth can lead to a substantial economic, social, and psychological burden for the individuals, families, and communities.⁸ In China, most families have only 1 child as a result of the government's previous 1-child policy⁹; however, suicidal ideation and attempts in Chinese youth have rarely been studied.

Although suicidal behavior is multifactorial, approximately 90% of the individuals who die from suicide have substance use, depression or other mental disorders, or a combination of both.¹⁰ According to the 2014 National Survey on Drug Use and Health (NSDUH) in the United States, prescription drugs were the second most popular drug among adolescents, and 655 000 adolescents aged 12 to 17 years reported nonmedical use of prescription drugs (NMUPD).¹¹ A cross-sectional study using the 2012 NSDUH data showed that the respondents who admitted misusing prescription drugs in the past year were more likely to report having seriously thought about suicide.¹² Our 3 previous cross-sectional studies¹³⁻¹⁵ in Chongqing and Guangdong Provinces also demonstrated that NMUPD was prevalent among Chinese adolescents, and one of them¹⁵ illustrated that NMUPD was positively associated with suicidal ideation and suicidal attempts. Although drug use is a known correlate of suicidality, there is a relative dearth of studies on the relationships between NMUPD, suicidal ideation, and suicidal attempts. Furthermore, most prior studies on this topic used a cross-sectional design, and could not determine whether NMUPD preceded suicidality.

Depression is one of the risk factors that has been implicated in suicidal behavior. Previous cross-sectional studies and longitudinal investigations have demonstrated that depressive symptoms increase the risk of suicidal behavior among adolescents.¹⁶⁻¹⁸ Moreover, prior studies^{15,19} have also reported a significant association between NMUPD and depressive symptoms, and the association between depression and drug use may be related to similarities in the neurobiology.²⁰⁻²² Therefore, depressive symptoms may play a mediator role in the relationship between NMUPD and suicidality, but to our knowledge no study has examined the potential mediating effect.

We thus designed this prospective study among Chinese adolescents to examine the longitudinal relationships between NMUPD, suicidal ideation, and suicidal attempts while controlling for the effects of important covariates and to test for the potential mediating effects of depressive symptoms.

Key Points

Question Is nonmedical use of prescription drugs by adolescents associated with subsequent suicidal ideation and attempts while controlling for depressive symptoms?

Findings In this longitudinal study, adolescent baseline opioids misuse, sedatives misuse, and nonmedical use of any prescription drug were associated with suicidal ideation at follow-up. Additionally, baseline opioids misuse and any prescription drug misuse were also associated with subsequent suicide attempts.

Meaning Youths with nonmedical use of prescription drugs should be closely monitored for suicidal ideation and suicide attempts.

Methods

Participants and Procedures

This study analyzed data from a school-based survey that investigated adolescents NMUPD and suicidality in Guangzhou between 2009 and 2012. In 2009, all middle schools in Guangzhou (n = 121) were stratified by type (public and private). A random sample of 12 middle schools was selected with a probability proportional to size. All students grade 7 and 8 within the selected schools were invited to participate in this study voluntarily. The baseline sample included 3273 students (10-18 years of age) who were interviewed at baseline (2009-2010; response rate, 96.8%) and followed up at 1 year (2011-2012; retention rate, 96.1%); the follow-up sample included 3145 students. To protect the privacy of the students, the anonymity of the self-reported questionnaires was guaranteed, and the questionnaires were administered by research assistants in the classrooms without the presence of teachers (to avoid any potential information bias). After the procedure had been fully explained, written informed consent was obtained from each participating student who was at least 18 years of age. If the student was younger than 18 years of age, written informed consent was obtained from one of the student's parents (or legal guardian). The study was approved by the Sun Yat-Sen University School of Public Health institutional review board. All adolescents and their parents were provided with a list of resources in case of needing help.

Measures

Outcome

Suicidal ideation was defined as responding "1 or more times" to the question "During the past 12 months, how many times did you seriously consider attempting suicide?" Suicidal attempt was assessed by the question "During the past 12 months, how many times did you actually attempt suicide?" and asked that the student rate on a scale of zero or once or more.

Predictor Variables

Nonmedical use of prescription drugs was defined as taking medications without a physician's prescription or solely for the feeling or experience caused by the drug (0 = no and

1 = yes). In this study, 4 measures of NMUPD included non-medical use of opioids, sedatives, and stimulants separately, as well as nonmedical use of any of the above-mentioned prescription drugs in the past 12 months. Opioids included compound cough syrup with codeine (codeine), compound liquorice tablets (opium), tramadol hydrochloride, and diphenoxylate. Sedatives included compound aminopyrine phenacetin tablets (barbiturates), diazepam or triazolam (benzodiazepines), and phenobarbital and scopolamine hydrobromide tablets (barbiturates). Stimulants included paracetamol caffeine aspirin powder (caffeine).

Other Covariates

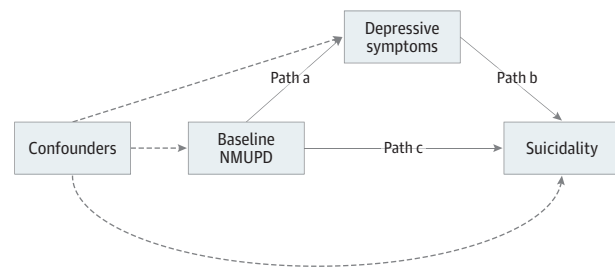
Factors that have previously been reported to be associated with suicidal behavior or NMUPD were taken into account.²³⁻²⁵ The 20-item Chinese version of the Center for Epidemiology Scale for Depression (CES-D) was used to identify whether individuals had depressive symptoms; the Chinese version of this scale has been previously validated among Chinese adolescents.^{26,27} Higher scores indicated more severe depressive symptoms, with a maximum score of 60.²⁸ Alcohol-related problems were measured by asking students one question, "How often did you experience the following problems in the past 12 months due to drinking alcohol: got into trouble with your parents, had problems at school, had problems with friends, and got into a physical fight?" The responses included "never," "once," "twice," "3-4 times," or "5 or more times." Data from all 5 responses were later recorded into a dichotomous variable, alcohol-related problems (0 = no, 1 = yes).

Sociodemographic information included age, sex (0 = male, 1 = female), household socioeconomic status (HSS), and living arrangement. Household socioeconomic status was measured by asking about the student's perceptions of his or her household's current socioeconomic status (responses were coded as excellent or very good = 1, good = 2, and fair or poor = 3). Living arrangement was assessed by asking who lived in the student's primary home (responses were coded as living with both parents = 1, living with father only = 2, living with mother only = 3, living with others = 4).

Statistical Analysis

First, descriptive analyses stratified by baseline NMUPD were used to describe the sample characteristics at baseline. Second, logistic regression analyses were conducted that accounted for the stratified cluster survey design and were weighted for nonresponse. For the outcome with low event rate, logistic regression models used the Firth penalized likelihood approach.^{29,30} Univariable logistic analyses were performed to explore the potential factors associated with suicidal ideation and attempts at follow-up. The variables that were significant at .10 level in univariable analyses or widely reported in the literature (eg, sex and age) were entered in the multivariable logistic regression models simultaneously to examine the independent longitudinal relationships between NMUPD, suicidal ideation, and suicidal attempts. Third, the interactions between NMUPD and depressive symptoms were tested using univariable logistic regression models before the mediation analyses. Structural equation modeling (SEM) analy-

Figure. Hypothesized Mediating Effects of Depressive Symptoms on the Association Between Baseline Nonmedical Use of Prescription Drugs (NMUPD) and Subsequent Suicidality



Suicidality included suicidal ideation and suicidal attempts. Depressive symptoms were measured using the Center for Epidemiology Scale for Depression.

ses using the robust maximum likelihood method were performed to measure the mediating effects of depressive symptoms on the relationships between NMUPD and suicidal behaviors (Figure). As the depressive symptoms score was a continuous variable and the measure of NMUPD were dichotomized, standardized probit coefficients, standardized indirect effects, and standardized total effects were reported, and the bias-corrected 95% CIs were estimated using 1000 bootstrap samples.³¹⁻³³ All data were analyzed using SAS 9.2 (SAS Institute Inc) and Mplus version 7.0 (Muthén and Muthén). *P* values less than .05 were considered statistically significant (tested 2-sided).

Results

Baseline Sample Characteristics Stratified by NMUPD

The sample characteristics at baseline are shown in Table 1. Of the total sample, 48.9% (1599 of 3273) were boys, and 51.1% (1674 of 3273) were girls. The mean (SD) age of the total students was 13.7 (1.0) years. The proportion of students who reported nonmedical use of opioids, sedatives, stimulants, and any prescription drug was 1.8% (60 of 3273), 0.8% (26 of 3273), 1.8% (58 of 3273), and 2.8% (91 of 3273), respectively.

Univariable Analyses of Suicidal Ideation and Suicidal Attempts at Follow-up

Overall, 17.0% (534 of 3145) and 3.0% (94 of 3145) students reported suicidal ideation and attempts at follow-up, respectively. Without adjusting for other variables, baseline non-medical use of opioids (odds ratio [OR], 3.03; 95% CI, 1.47-6.22), sedatives misuse (OR, 4.60; 95% CI, 2.09-10.15), stimulants misuse (OR, 2.38; 95% CI, 1.07-5.84), and nonmedical use of any prescription drug (OR, 1.93; 95% CI, 1.19-3.11) were significantly associated with suicidal ideation at follow-up. Additionally, without adjusting for other variables, subsequent suicidal attempts were more common in students who reported baseline opioids misuse (OR, 5.96; 95% CI, 2.78-9.53), sedatives misuse (OR, 4.68; 95% CI, 1.86-10.83), stimulants misuse (OR, 2.67; 95% CI, 1.76-10.82), and any prescription drug

Table 1. Baseline Sample Characteristics of 3273 Patients Stratified by NMUPD

Variable	No. (%)												
	Total	Opioids Use			Sedatives Use			Stimulants Use			APDU		
		Yes	No	P Value ^a	Yes	No	P Value ^a	Yes	No	P Value ^a	Yes	No	P Value ^a
Total	3273 (100)	3010 (100)	3213 (100)		26 (100)	3247 (100)		58 (100)	3215 (100)		91 (100)	3182 (100)	
Sex				.94						.356			.59
Male	1599 (48.9)	1511 (48.3)	1570 (48.9)		13 (50.0)	1586 (48.9)	.91	32 (55.2)	1567 (48.7)		47 (51.6)	1552 (48.8)	
Female	1674 (51.1)	1511 (51.7)	1643 (51.1)		13 (50.0)	1661 (51.2)		26 (44.8)	1648 (51.3)		44 (48.4)	1630 (51.2)	
Age, mean (SD)	13.7 (1.0)	13.5 (0.9)	13.7 (1.0)	.4	13.7 (1.0)	13.7 (1.0)	.71	13.5 (0.9)	13.7 (1.0)	.26	13.6 (0.9)	13.7 (1.0)	.08
HSS				.01			.004			.079			.06
Excellent	1549 (47.3)	1511 (56.7)	1515 (47.2)		17 (65.4)	1532 (47.2)		31 (53.4)	1518 (47.2)		47 (51.6)	1502 (47.2)	
Good	1529 (46.7)	1317 (31.7)	1510 (46.9)		5 (19.2)	1524 (46.9)		20 (34.5)	1509 (46.9)		34 (37.3)	1495 (47.0)	
Fair	177 (5.4)	7 (11.7)	170 (5.3)		4 (15.4)	173 (5.3)		6 (10.3)	171 (5.3)		9 (9.9)	168 (5.3)	
Missing data	18 (0.5)	NA	NA		NA	NA		NA	NA		NA	NA	
Living arrangement				.01			.01			.001			<.001
With parents	2662 (81.3)	2611 (56.7)	2628 (81.7)		11 (42.0)	2651 (81.6)		32 (55.2)	2630 (92.1)		61 (67.0)	2601 (81.7)	
With father	336 (10.3)	316 (26.7)	320 (10.0)		11 (42.0)	325 (10.0)		18 (31.0)	318 (9.9)		20 (22.0)	316 (9.9)	
With mother	208 (6.4)	3 (5.0)	205 (6.3)		1 (3.8)	207 (6.4)		2 (3.4)	206 (6.4)		5 (5.5)	203 (6.4)	
Living with others	56 (1.7)	7 (11.7)	49 (1.5)		3 (11.5)	53 (1.6)		6 (10.3)	50 (1.6)		5 (5.5)	51 (1.6)	
Missing data	11 (0.3)	NA	NA		NA	NA		NA	NA		NA	NA	
CES-D scores, median (IQR)	13.0 (10.0-15.0)	13.0 (11.0-15.0)	13.0 (9.8-15.0)	.01	15.5 (12.8-18.0)	13.0 (10.0-15.0)	.03	9.5 (8.7-10.0)	13.0 (9.0-15.0)	.04	12.0 (17.0)	13.0 (9.0-15.0)	.02
Suicidal ideation				.005			.001			.080			.004
Yes	565 (17.3)	317 (31.7)	546 (17.0)		12 (46.1)	523 (16.1)		15 (25.9)	550 (17.1)		26 (28.6)	539 (16.9)	
No	2708 (82.7)	2683 (68.3)	2667 (83.0)		14 (53.9)	2694 (83.9)		43 (74.1)	2665 (82.9)		65 (71.4)	2643 (83.1)	
Suicidal attempts				.003			.001			<.001			<.001
Yes	154 (4.7)	11 (18.3)	143 (4.5)		6 (23.1)	148 (4.6)		8 (13.8)	146 (4.5)		13 (14.3)	141 (4.4)	
No	3119 (95.3)	3179 (81.7)	3070 (95.5)		20 (76.9)	3099 (95.4)		50 (86.2)	3069 (95.5)		78 (85.7)	3041 (95.6)	
Alcohol-related problems				.004			<.001			<.001			<.001
Yes	199 (6.1)	9 (15.0)	190 (5.9)		8 (30.8)	191 (5.9)		13 (22.4)	186 (5.8)		14 (15.4)	185 (5.8)	
No	3074 (93.9)	3181 (85.0)	3023 (94.1)		18 (69.2)	3056 (94.1)		45 (77.6)	3029 (94.2)		77 (84.6)	2997 (94.2)	

Abbreviations: APDU, any prescription drug use; CES-D, Center for Epidemiology Scale for Depression; HSS, household socioeconomic status; IQR, interquartile range; NMUPD, nonmedical use of prescription drugs; NA, not applicable or no data available.

^a χ^2 Tests were used for categorical variables, t tests were used for age data, and Wilcoxon rank-sum tests were used for CES-D scores.

misuse (OR, 4.20; 95% CI, 2.07-8.56). Moreover, female students were more likely to be involved in subsequent suicidal ideation than male students (OR, 1.58; 95% CI, 1.31-1.91). Other baseline characteristics including HSS, living arrangement, depressive symptoms, alcohol-related problems, suicidal ideation, and suicidal attempt were also associated with suicidal ideation and attempts at follow-up (eTable in the Supplement).

Longitudinal Relationships Between NMUPD and Suicidality: Multivariable Analyses

As shown in Table 2, our final multivariable logistic regression models demonstrated that baseline opioids misuse (adjusted odds ratio [AOR], 2.31; 95% CI, 1.30-4.11), sedatives misuse (AOR, 4.46; 95% CI, 1.54-7.94), and nonmedical use of any prescription drug (AOR, 1.97; 95% CI, 1.21-3.23) were positively associated with suicidal ideation at follow-up after con-

trolling for sociodemographic information (including sex, age, HSS, and living arrangement), baseline depressive symptoms, baseline alcohol-related problems, baseline suicidal ideation, and baseline suicidal attempts.

Additionally, after controlling for sex, age, HSS, living arrangement, depressive symptoms, alcohol-related problems, suicidal ideation, and suicidal attempts at baseline, the final results showed that students who reported baseline misuse of opioids (AOR, 3.39; 95% CI, 1.33-5.63) and nonmedical use of any prescription drug (AOR, 2.91; 95% CI, 1.26-3.71) were more likely to be involved in suicidal attempts 1 year later.

Mediating Effects of Depressive Symptoms on the Relationship Between NMUPD and Suicidality

First, univariable regression models were conducted to test the associations between the interaction items (between non-medical use opioids/sedatives/any prescription drugs and de-

Table 2. Longitudinal Relationships Between NMUPD, Suicidal Ideation, and Suicidal Attempts: Multivariable Logistic Regression Analyses in 3145 Patients

Variable (Baseline)	Suicidal, AOR (95% CI)	
	Ideation at Follow-up ^a	Attempts at Follow-up ^b
Opioids use (yes vs no)	2.31 (1.30-4.11) ^c	3.39 (1.33-5.63) ^c
Sedatives use (yes vs no)	4.46 (1.54-7.94) ^c	1.77 (0.53-4.88)
Stimulants use (yes vs no)	2.08 (0.60-7.12)	2.10 (0.64-4.87)
APDU (yes vs no)	1.97 (1.21-3.23) ^c	2.91 (1.26-3.71) ^c

Abbreviations: AOR, adjusted odds ratio; APDU, any prescription drug use; NMUPD, nonmedical use of prescription drugs.

^a The 4 multivariable logistic regression models for suicidal ideation at follow-up used the maximum likelihood approach and were adjusted for sex, age, household socioeconomic status, living arrangement, Center for Epidemiology Scale for Depression scores, alcohol-related problems, suicidal ideation, and suicidal attempts at baseline.

^b The 4 multivariable logistic regression models for suicidal attempts at follow-up used the Firth penalized likelihood approach for the low event rate and were adjusted for sex, age, household socioeconomic status, living arrangement, Center for Epidemiology Scale for Depression scores, alcohol-related problems, suicidal ideation, and suicidal attempts at baseline.

^c $P < .05$.

pressive symptoms) and suicidality; these interaction items were not statistically significant in the models (Table 3).

Next, Table 4 shows that the standardized indirect effects of baseline opioids misuse on subsequent suicidal ideation and attempts through depressive symptoms were significant (suicidal ideation at follow-up: standardized β estimate = 0.020; 95% CI, 0.010-0.030; suicidal attempts at follow-up: standardized β estimate = 0.009, 95% CI, 0.004-0.015), indicating that depressive symptoms partially mediated the associations between baseline nonmedical use of opioids and suicidal ideation and attempts at follow-up. Additionally, there was a significant standardized indirect effect of baseline sedatives misuse on subsequent suicidal ideation through depressive symptoms (standardized β estimate = 0.016; 95% CI, 0.005-0.026), suggesting that the association between baseline sedatives misuse and subsequent suicidal ideation was partially mediated by depressive symptoms.

Discussion

To our knowledge, this is the first large-scale, prospective longitudinal study to investigate the relationships between NMUPD, suicidal ideation, and suicidal attempts and to test the potential mediating effects of depressive symptoms.

Consistent with previous studies,^{16,23,34,35} our univariable analyses first reported that female students were at a higher risk of suicidal ideation and that those having alcohol-related problems were more likely to be involved in suicidality. For the adolescents who reported previous suicidal attempts, the likelihood of future attempts was greatly increased. These findings are useful for identifying adolescents who may be at risk of suicidality, and we should focus on high-risk students who present with the adverse characteristics mentioned above.

Table 3. Associations of Interaction Items With Suicidal Ideation and Suicidal Attempts: Univariable Logistic Regression Analyses in 3145 Patients

Interaction Item (Baseline)	P Value for Interaction	
	Suicidal Ideation at Follow-up	Suicidal Attempts at Follow-up ^a
CES-D scores ^a		
Opioids use	.26	.70
Sedatives use	.13	NA
APDU	.15	.76

Abbreviations: APDU, any prescription drug use; CES-D, Center for Epidemiology Scale for Depression; NA, not applicable or no data available.

^a The univariable logistic regression models used the Firth penalized likelihood approach for the low rate of suicidal attempts.

As depressive symptoms, alcohol-related problems, and prior suicidality are well-known risk factors for suicidal behavior,^{17,23,36} and as the associations of these factors with suicidality were significant in our univariable analyses, the final multivariable logistic regression models found that baseline opioids misuse, sedatives misuse, and nonmedical use of any prescription drug were significantly associated with suicidal ideation at follow-up after controlling for sociodemographic information (including sex, age, HSS, and living arrangement), baseline depressive symptoms, baseline alcohol-related problems, baseline suicidal ideation, and baseline suicidal attempts. Similarly, after controlling for sex, age, HSS, living arrangement, depressive symptoms, alcohol-related problems, suicidal ideation, and suicidal attempts at baseline, the relationships between baseline opioids misuse, baseline any prescription drug misuse, and subsequent suicidal attempts were statistically significant in our final logistic regression models. These results were consistent with some previous cross-sectional findings, suggesting that there are significant relationships between the misuse of any prescription drug and suicidal ideation^{12,19,37} and suicidal attempts.^{13,38-40} Therefore, NMUPD is an important risk factor for suicidal ideation and suicidal attempts in adolescence. This finding may be related to several possible explanations: (1) drug use (including NMUPD) may impair judgment through its intoxicating effects, (2) it may have acute and chronic mood-altering effects, or (3) it may facilitate the route to suicidal behavior through inhibitions loss, impulsiveness, and/or aggression.^{41,42} These findings suggest the following interventions to prevent adolescent suicidal behavior: (1) establishing a proper surveillance system to manage and oversee suicidality among adolescents, (2) promoting resilience among current nonmedical users of prescription drugs, and (3) strengthening regulations to limit sales of prescription drugs containing opioids, sedatives, or stimulants to adolescents.

In addition, our study also showed that the effect of baseline nonmedical use of opioids on suicidal ideation or suicidal attempts 1 year later was partially mediated by depressive symptoms. Moreover, the association between baseline sedatives misuse and subsequent suicidal ideation was also partially mediated by depressive symptoms. The neurobiological similarities between NMUPD and depressive disorder might

Table 4. Mediating Effects of Depressive Symptoms on the Relationships Between Baseline NMUPD and Suicidal Ideation and Attempts at Follow-up in 3145 Patients

Characteristic	Symbol	Standardized β Estimate (95% CI)	
		Model 1 (outcome = SI at follow-up) ^a	Model 2 (outcome = SA at follow-up) ^b
Baseline			
Opioids use	Predictor	0.033 (0.001 to 0.066) ^c	0.079 (0.019 to 0.148) ^c
CES-D scores	Mediator	0.071 (0.035 to 0.106) ^c	0.071 (0.008 to 0.137) ^c
Baseline opioids use \rightarrow baseline CES-D scores	Predictor \rightarrow mediator	0.280 (0.240 to 0.319) ^c	0.128 (0.070 to 0.186) ^c
Standardized effect			
Indirect		0.020 (0.010 to 0.030) ^c	0.009 (0.004 to 0.015) ^c
Total		0.053 (0.016 to 0.087) ^c	0.088 (0.054 to 0.122) ^c
Baseline			
Sedatives use	Predictor	0.046 (0.013 to 0.079) ^c	NA
CES-D scores	Mediator	0.056 (0.020 to 0.091) ^c	NA
Baseline sedatives use \rightarrow Baseline CES-D scores	Predictor \rightarrow mediator	0.280 (0.241 to 0.319) ^c	NA
Standardized effect			
Indirect		0.016 (0.005 to 0.026) ^c	NA
Total		0.062 (0.025 to 0.095) ^c	NA
Baseline			
APDU	Predictor	0.039 (0.007 to 0.072) ^c	0.069 (0.035 to 0.103) ^c
CES-D scores	Mediator	0.030 (-0.006 to 0.065)	0.030 (-0.006 to 0.065)
Baseline sedatives use \rightarrow baseline CES-D scores	Predictor \rightarrow mediator	0.281 (0.242 to 0.321) ^c	0.131 (0.069 to 0.190) ^c
Standardized effect			
Indirect		0.009 (-0.002 to 0.019)	0.004 (-0.001 to 0.009)
Total		0.048 (0.011 to 0.082) ^c	0.073 (0.038 to 0.107) ^c

Abbreviations: APDU, any prescription drug use; CES-D, Center for Epidemiology Scale for Depression; CFI, comparative fit analysis; NMUPD, nonmedical use of prescription drugs; RMSEA, root mean square error of approximation; SA, suicidal attempts; SI, suicidal ideation; SRMR, standardized root mean square residual; arrows, direction of effects; NA, not applicable or no data available.

^a The structural equation models for suicidal ideation at follow-up were adjusted for sex, age, household socioeconomic status, living arrangement, alcohol-related problems, suicidal ideation, and suicidal attempts at baseline. Model 1 (baseline opioids use: CFI = 0.930; RMSEA = 0.042, 95% CI, [0.030-0.055]; SRMR = 0.051; baseline sedatives use: CFI = 0.951;

RMSEA = 0.040, 95% CI, [0.024-0.063]; SRMR = 0.055; baseline APDU: CFI = 0.971; RMSEA = 0.040, 95% CI [0.033-0.074]; SRMR = 0.052).

^b The structural equation models for suicidal attempts at follow-up were adjusted for gender, age, household socioeconomic status, living arrangement, alcohol-related problems, suicidal ideation, and suicidal attempts at baseline. Model 2 (baseline opioids use: CFI = 0.987; RMSEA = 0.040, 95% CI, [0.024-0.073]; SRMR = 0.041; baseline APDU: CFI = 0.986; RMSEA = 0.041, 95% CI, [0.035-0.062]; SRMR = 0.042).

^c $P < .05$.

be a possible explanation for the mediating effects of depressive symptoms.²⁰⁻²² Furthermore, it has been well established that most suicidal behavior is associated with depressive symptoms among culturally diverse teens,^{16,18,40,43} and previous studies^{15,19} have also reported a significant association between NMUPD and depressive symptoms. Moreover, some prior studies have demonstrated mediating effects between adverse child experiences and suicide attempts through depressive symptoms²³ and between sleep problems and suicidal attempts through depressive symptoms.⁴⁴ To our knowledge, few studies have discussed the mediating effects of depressive symptoms on the relationship between NMUPD and suicidality. Our findings highlighted the importance of depressive mood and NMUPD on suicidality among adolescents. Furthermore, an accessible and effective adolescent mental health service and a suicidality monitoring system may be essential components in reducing Chinese youth suicidality.

Several limitations of the study should be noted when interpreting the results. First, our study sample included only

school students and did not include adolescents who had dropped out of school or were not present in school on the day the survey was administered; suicidality or depressive symptoms may be more common among adolescents who were absent. Second, we used a structured self-rating questionnaire to collect data; although self-reporting is a common and accepted method, we could not completely rule out the possibility of recall bias. Third, suicidal behavior was measured by single items. Although these items had face validity, the reliability of these measures is unknown. Future studies should use multiple items to measure suicidality. Fourth, we may lose some information by dichotomizing the variables of suicidal behavior and NMUPD. Fifth, although this is the first known Chinese study to collect prospective data to study the relationships between NMUPD and suicidality, the longitudinal sample was limited to 1 year.

Despite these limitations, the primary strengths of our study are that it provides the first known longitudinal evidence for the relationships between baseline NMUPD and sub-

sequent suicidal ideation and attempts among Chinese adolescents and is the first to report the mediating effects of depressive symptoms on the above-mentioned relationships.

Conclusions

Our study identified that baseline nonmedical use of opioids was significantly associated with suicidal ideation and suicidal attempts at follow-up, baseline nonmedical use of sedatives was related to suicidal ideation at follow-up, and baseline nonmedical use of any prescription drug was also associated with subsequent suicidal ideation and suicidal attempts. Moreover, depressive symptoms significantly par-

tially mediated those significant relationships. Suicide is a complex behavior, and further studies are needed to better understand the respective roles of these factors (ie, interactions and mediation). Based on the findings of our study, effective prevention and intervention programs should be established. First, educational campaigns directed at students are needed to improve their awareness of the serious consequences of NMUPD. Second, we should pay close attention to the adolescents who have depressive symptoms, are involved in NMUPD, or have suicidal thoughts or attempts. Third, a proper surveillance system needs to be developed by learning from the experiences of the NSDUH in the United States to control and oversee the NMUPD and suicidality among Chinese adolescents.

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