

Association between nonmedical use of opioids or sedatives and suicidal behavior among Chinese adolescents: An analysis of sex differences

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Abstract

Objective: The rising rate of suicidal behavior among adolescents is a growing concern, and sex differences may induce differential exposure to prescription drug misuse or suicidal behavior. We estimated, among Chinese adolescents, (1) the prevalence of nonmedical use of prescription drugs, suicidal ideation and suicide attempts; (2) whether nonmedical use of prescription drugs was independently associated with suicidal ideation and suicide attempts; and (3) whether there were sex differences in the associations.

Methods: This was a secondary analysis of the data drawn from the 2015 National School-based Chinese Adolescents Health Survey. A total of 94,911 students completed questionnaires and qualified for our survey (response rate: 93.7%). All analyses were conducted separately for boys and girls.

Results: There were significant sex differences in the prevalence of opioid or sedative misuse, and the sources and reasons for nonmedical use of prescription drugs ($p < 0.05$). The prevalence of suicidal ideation or suicide attempts was significantly higher in girls than in boys (suicidal ideation: 17.9% among girls vs 14.1% among boys; suicide attempts: 3.5% among girls vs 2.7% among boys). Among girls, frequent use of opioids was associated with an increased risk of suicidal ideation (adjusted odds ratio = 1.84, 95% confidence interval = [1.57, 2.17]) and suicide attempts (adjusted odds ratio = 2.96, 95% confidence interval = [2.34, 3.74]), and frequent use of sedatives was also positively associated with suicidal ideation (adjusted odds ratio = 2.23, 95% confidence interval = [1.91, 2.60]) and suicide attempts (adjusted odds ratio = 4.02, 95% confidence interval = [3.25, 4.99]). These associations were also statistically significant in boys, but the magnitudes of adjusted odds ratios for the associations between frequent use of opioids and sedatives and suicidal behavior were greater in girls than boys.

Conclusion: There exist significant sex differences in the prevalence rates of nonmedical use of prescription drugs and suicidal behavior, and the child's sex plays a role in the association between nonmedical use of prescription drugs and suicidal behavior. The significant sex differences found above may provide a basis for early identification of adolescents at high risk of suicidal behavior.

Keywords

Nonmedical use of prescription drug, suicidal ideation, suicide attempts, sex differences, adolescents

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Introduction

Approximately 800,000 people die due to suicidal behavior (including suicidal ideation, suicidal attempts or completed suicide) worldwide every year (World Health Organization (WHO), 2014b), and the rising rate of suicidal behavior among adolescents is a growing concern. Suicidal behaviors among adolescents are significantly associated with disability and various physical disorders, and can cause a heavy economic, social and psychological burdens for the individuals, families and communities (Meltzer et al., 2012). Although the Chinese suicide rates have significantly declined in the past decade, Chinese adolescents are among the particularly vulnerable groups for suicidal ideation and suicide attempts (Zhang et al., 2014). Suicidal ideation and suicide attempts have shown an elevated risk of recurrence and are predictive of future completed suicide in adolescence (Cluver et al., 2015). Most Chinese families have only one child as a result of the government's prior one-child policy (Falbo and Poston, 1994); however, suicidal ideation and suicide attempts in Chinese adolescents have scarcely been studied. Although suicidal behavior is multifactorial, most people who die from suicide suffer from substance misuse (Mościcki, 2001). However, individuals with substance use disorders are infrequently identified as one of the most at-risk groups of suicidal behavior (Witt and Lubman, 2018). Over the last two decades, increased attention has been focused on the nonmedical use of prescription drugs (NMUPD) among adolescents, which is defined as taking medications without a doctor's prescription or solely for the feeling or experience caused by the drug. The 2014 National Survey on Drug Use and Health (NSDUH) in the United States reported that prescription drugs were the second most popular drug among adolescents (Hedden et al., 2015). Our prior study also showed that NMUPD was also prevalent among Chinese adolescents, and the prevalence of past-month opioid use and sedative use were 1.6% and 2.0%, respectively (Guo et al., 2018). Previous studies have indicated that individuals who report misusing a prescription drug are more likely to admit to having seriously thought about or attempted suicide (Ford and Perna, 2015). Sex differences may induce differential exposure to prescription drug misuse or suicidal behavior. Boys may have a stronger need for sensation-seeking than girls (Cross et al., 2013), and sensation-seeking is a vital personality trait related to drug misuse (Dubey and Arora, 2008). Girls are reported to be more sensitive to social stress (e.g. unequal chore burdens or exclusion from education) and thus may have higher levels of negative emotions (e.g. depression or suicidal ideation) (WHO, 2014a). In addition, girls are more prone to have suicidal ideation or suicide attempts as a response to stress, but boys are more inclined to die by suicide (e.g. use of more violent methods) (Amitai and Apter, 2012). The prevalence of NMUPD in boys is reportedly greater than girls (Wang et

al., 2014), and girls have had higher rates of suicidal ideation and suicide attempts than boys (Cash and Bridge, 2009). Although some studies reported NMUPD was associated with an elevated risk of suicidal behavior (Ashrafioun et al., 2017; Ford and Perna, 2015), little is known about sex differences in this association. Therefore, we hypothesized that the child's sex plays a role in the association of NMUPD with suicidal ideation and suicide attempts. Adolescent NMUPD and suicidal behavior has been well documented in Western or developed countries, but sporadic surveys have been performed in China. China has seen rapid social and economic changes in the past three decades, and those may have also affected the patterns of NMUPD and suicidal behavior among Chinese adolescents. Therefore, we conducted this large national study in China to estimate the prevalence of NMUPD, suicidal ideation and suicide attempts among Chinese adolescents, to test the independent associations of NMUPD with suicidal ideation and suicide attempts and to assess whether there are sex differences in the associations.

Methods

Sample and procedure

This study analyzed the data drawn from the 2015 National School-based Chinese Adolescents Health Survey (SCAHS). SCAHS is an ongoing study of risky health behaviors among Chinese adolescents (7th–12th grade) that collects large-scale cross-sectional data (conducted every 2 years since 2007) through questionnaires administered in classrooms (Guo et al., 2015). The 2015 SCAHS sampling is structured to obtain representative populations of Chinese adolescents. The procedures for data collection have been described in detail elsewhere (Guo et al., 2017b). Briefly, in stage 1, seven large provinces were selected according to geographic location. We divided each province into three economic stratifications by gross domestic product (GDP) per capita (high-level, middle-level and low-level), then randomly selected two representative cities from each stratus. In stage 2, four general high schools (focusing on educating students for entering university) and four vocational high schools (offering specific vocational training) were randomly selected from each representative city. In stage 3, two classes were randomly selected from each grade within the selected schools. All available students in the selected classes were invited to voluntarily participate in our study, and 94,911 students' questionnaires were completed and qualified for our survey (response rate: 93.7%). This study was approved by the Sun Yat-sen University School of Public Health Institutional Review Board. To protect the privacy of the students, a rigorously anonymous method was utilized to collect information from the self-report questionnaires, and the questionnaires were administered by research assistants in the classrooms

without the presence of teachers (to avoid any potential information bias).

Measures

Dependent variable

Suicidal ideation was assessed by the question ‘*During the past 12 months, how many times did you seriously consider attempting suicide?*’ Available responses were 0 and 1 or more times. Suicide attempt was defined as responding ‘one or more times’ to the question, ‘*During the past 12 months, how many times did you actually attempt suicide?*’ (Guo et al., 2016).

Independent variable

In this study, NMUPD included nonmedical use of opioids or sedatives. Opioids included compounded cough syrup with codeine (codeine), compounded licorice tablets (opium), tramadol hydrochloride and diphenoxylate. Sedatives included compounded aminopyrine phenacetin tablets (barbiturates), diazepam or triazolam (benzodiazepines) and scopolamine hydrobromide tablets (barbiturates) (Guo et al., 2017b). Nonmedical use of opioids or sedatives was assessed by the following questions: ‘*How many times have you ever used the abovementioned prescription drugs for a nonmedical purpose?*’ Students who answered ‘never’ were considered abstainers, those who reported once or twice were considered experimenters and those who admitted at least three times were considered frequent users.

Other variables

Demographic variables included age, sex (boy=1 and girl=2), living arrangement, household socioeconomic status (HSS), academic pressure, classmate relations and relationships with teachers. Students’ living arrangements (including ‘living with both parents’=1, ‘living with a single parent’=2 and ‘living with others’=3) was measured by asking students who lived in their primary home. HSS (categorized into ‘excellent or very good’=1, ‘good’=2 and ‘fair or poor’=3) was assessed by asking students about their perception of their family’s economic status. Academic pressure was assessed by the student’s self-rating of his or her academic pressure (responses were coded as ‘above average’=1, ‘average’=2 and ‘below average’=3). Classmate relations and relationships with teachers were measured by asking the student’s perception of their relationships with classmates and teachers (responses range from ‘good’=1 to ‘poor’=3).

Depressive symptoms were measured with the Chinese version of the Center for Epidemiology Scale for Depression (CES-D), and the Chinese version of this scale has been validated and extensively utilized in Chinese studies and exhibits a satisfactory reliability (total Cronbach’s $\alpha=0.88$) in Chinese adolescents (Chen et al., 2009). The respondents

were asked to rate the frequencies of 20 symptoms of depression by choosing one of the four response options that ranged from ‘rarely or none of the time’ to ‘most or all of the time’. Higher scores were indicative of more severe depressive symptomatology, with a maximum score of 60.

Weight status was categorized into normal=1 and overweight or obese=2. According to the standardized growth charts from the Working Group on Obesity for Children (WGOC) in China, body mass index (BMI) z scores (standard deviation [SD]) for each student were calculated to represent the deviation compared with an average child of the same sex and age (Li et al., 2009). Students with a BMI z score less than the 85th percentile were deemed normal, students with a BMI z score between the 85th and 95th percentile were considered overweight and those with a BMI z score above the 95th percentile were thought obese (Mei et al., 2008).

Smoking or alcohol drinking was assessed by asking students the following question: ‘*Have you smoked or drunk alcohol at least once during your lifetime?*’ Responses were coded as ‘yes’=1 and ‘no’=2.

Statistical analysis

All statistical analyses were conducted using SAS 9.2 (SAS Institute, Inc., Cary, NC, USA). Given sex differences in the sample characteristics and the prevalence of NMUPD observed in previous work (Wang et al., 2014), analyses were conducted separately for boys and girls. First, descriptive analyses stratified by sex were used to describe the sample characteristics; the chi-square test for categorical variables and t test for continuous variables were used to assess whether there were any statistically significant differences between boys and girls. Second, univariable logistic regression models were performed to explore the potential factors associated with nonmedical use of opioids or sedatives. Multivariable logistic regression models were conducted to investigate the independent associations of NMUPD with suicidal ideation and suicide attempts, and the variables that were significant at the 0.10 level in univariable analyses (Table 1) or widely reported in the literature were entered simultaneously as control variables. Firth’s penalized likelihood approach for the outcomes with low event rates was utilized in the logistic regression models (Wang, 2014). For all relevant variables, the percentage of missing data was less than 0.6. Regarding logistic regression analyses, observations with missing data were eliminated (less than 6.0%). Statistical significance was evaluated at the <0.05 level using two-sided tests.

Results

Sample characteristics stratified by sex

Basic demographic information is shown in Table 1. Of the total sample, 47.3% (44,906) were boys, and 52.7%

Table 1. Sample characteristics stratified by sex (N=94,911).

Variable	Total, n (%)	Boys, n (%)	Girls, n (%)	p value ^a
Total	94,911 (100.0)	44,906 (47.3)	50,005 (52.7)	
Age, mean (SD)	15.18 (1.76)	15.14 (1.74)	15.22 (1.77)	<0.001
Weight status				
Normal	80,670 (85.0)	37,267 (83.0)	43,403 (86.8)	<0.001
Overweight or obese	14,241 (15.0)	7639 (17.0)	6602 (13.2)	
Living arrangement				
Living with two parents	73,794 (77.8)	34,295 (76.6)	39,499 (79.2)	<0.001
Living with a single parent	9579 (10.1)	4864 (10.9)	4715 (9.5)	
Living with others	11,287 (11.9)	5615 (12.5)	5672 (11.4)	
Missing data	251 (0.3)			
HSS				
Excellent or very good	21,001 (22.1)	10,495 (23.4)	10,506 (21.1)	<0.001
Good	57,640 (60.7)	26,416 (59.0)	31,224 (62.6)	
Fair or poor	15,981 (16.8)	7855 (17.5)	8126 (16.3)	
Missing data	289 (0.3)			
Academic pressure				
Above average	15,496 (16.3)	8270 (18.4)	7226 (14.5)	<0.001
Average	43,942 (46.3)	19,821 (44.2)	24,121 (48.3)	
Below average	35,387 (37.3)	16,766 (37.4)	18,621 (37.3)	
Missing data	86 (0.1)			
Classmate relations				
Good	70,442 (74.2)	36,631 (73.4)	33,811 (75.5)	<0.001
Average	22,765 (24.0)	12,704 (25.5)	10,061 (22.5)	
Poor	1484 (1.6)	568 (1.1)	916 (2.0)	
Missing data	220 (0.2)			
Teacher–classmate relationships				
Good	53,142 (56.0)	25,639 (57.3)	27,503 (55.1)	<0.001
Average	38,561 (40.6)	17,076 (38.1)	21,485 (43.1)	
Poor	2965 (3.1)	2048 (4.6)	917 (1.8)	
Missing data	243 (0.3)			
Smoking				
Yes	5455 (5.7)	4566 (10.2)	889 (1.8)	<0.001
No	89,456 (94.3)	40,340 (89.8)	49,116 (98.2)	
Drinking				
Yes	44,318 (46.7)	24,576 (54.7)	19,742 (39.5)	<0.001
No	50,593 (53.3)	20,330 (45.3)	30,263 (60.5)	
CES-D score, mean (SD)	20.5 (7.1)	20.4 (7.4)	20.5 (6.9)	<0.001
Opioid misuse				
Abstainers	88,842 (93.6)	41,719 (92.9)	47,123 (94.2)	<0.001
Experimenters	4160 (4.4)	2111 (4.7)	2049 (4.1)	
Frequent users	1909 (2.0)	1076 (2.4)	833 (1.7)	
Sedative misuse				
Abstainers	87,825 (92.5)	40,179 (89.5)	47,646 (95.3)	<0.001
Experimenters	5415 (5.7)	3955 (8.8)	1460 (2.9)	

(continued)

Table 1. (Continued)

Variable	Total, n (%)	Boys, n (%)	Girls, n (%)	p value ^a
Frequent users	1671 (1.8)	772 (1.7)	899 (1.8)	
Suicidal ideation				
No	79,632 (83.9)	38,577 (85.9)	41,055 (82.1)	<0.001
Yes	15,279 (16.1)	6329 (14.1)	8950 (17.9)	
Suicide attempts				
No	91,934 (96.9)	43,678 (97.3)	48,256 (96.5)	<0.001
Yes	2977 (3.1)	1228 (2.7)	1749 (3.5)	

HSS: household socioeconomic status; CES-D: Center for Epidemiology Scale for Depression.

^aThe chi-square test was used for categorical variables, and the t test was used for age data and CES-D scores.

Table 2. Sources and reasons for NMUPD.

Variable	Total, n (%)	Boys, n (%)	Girls, n (%)	p value ^a
Source of prescription drugs				
Home	1277 (45.0)	597 (46.7)	680 (53.2)	0.007
Drugstore	186 (6.6)	95 (51.1)	91 (48.9)	
Peers	734 (25.9)	314 (42.8)	420 (57.2)	
Nightclub/Pub	22 (0.8)	9 (40.9)	13 (59.1)	
Others	619 (21.8)	314 (50.7)	305 (49.3)	
Reason for NMUPD				
To relax or relieve tension	910 (32.1)	433 (47.6)	477 (52.4)	<0.001
To experiment	753 (26.5)	440 (58.4)	313 (41.6)	
To feel good or get high	352 (12.4)	208 (59.0)	144 (41.0)	
To yield to peer pressure	280 (9.9)	132 (47.1)	148 (52.9)	
Other	543 (19.1)	289 (53.2)	254 (46.8)	

NMUPD: nonmedical use of prescription drugs.

^aThe chi-square test was used to examine the differences between boys and girls.

(50,005) were girls. The proportion of students who were overweight or obese was 15.0%. Approximately 5.7% students admitted smoking during their lifetime, and 46.7% students reported drinking alcohol. The mean CES-D score of the students was 20.5 (SD: ± 7.1). The proportion of students who frequently used opioids was 2.0%, and the proportion of those who frequently used sedatives was 1.8%. A total of 16.1% students reported having suicidal ideation, and those who admitted having suicide attempts accounted for 3.1%. There were statistically significant differences in the sex distribution of age, weight status, living arrangement, HSS, academic pressure, classmate relations, relationships with teachers, smoking, drinking, depressive symptoms, opioid misuse and sedative misuse ($p < 0.05$).

Sources and reasons for nonmedical use of opioids or sedatives

As shown in Table 2, the nonmedically used prescription opioids or sedatives among adolescents were most commonly obtained from home (45.0%), followed by from peers (25.9%) and others (21.8%). The most prevalent reason for NMUPD was 'to relax or relieve tension' (32.1%), followed by 'to experiment' (26.5%) and 'to feel good or get high' (12.4%). In addition, the differences in the sex distribution of sources and reasons for nonmedical use of opioids or sedatives were statistically significant ($p < 0.05$). Girls had a higher proportion of taking prescription drugs 'to relax or relieve tension' than boys (52.4% among girls vs 47.6% among boys). In contrast, boys had a greater

proportion of taking opioids or sedatives ‘to feel good or get high’ than girls (59.0% among boys vs 41.0% among girls).

Prevalence and characteristics of suicidal ideation and suicide attempts

The prevalence of suicidal ideation was 14.1% among boys and 17.9% among girls, and the prevalence of suicide attempts was 2.7% among boys and 3.5% among girls. Without adjusting for other variables, suicidal ideation and suicide attempts were more prevalent among students who were frequent users of opioids (suicidal ideation: 25.7% among boys vs 34.2% among girls; suicide attempts: 8.7% among boys vs 12.7% among girls) and those with frequent use of sedatives (suicidal ideation: 29.9% among boys vs 35.9% among girls; suicide attempts: 12.3% among boys vs 14.0% among girls). Among both boys and girls, nonmedical use of opioids or sedatives, weight status, living arrangement, HSS, academic pressure, classmate relations, relationships with teachers, depressive symptoms, smoking and drinking were correlated with suicidal ideation. However, there were sex differences in the correlates of suicide attempts, and age and weight status were only associated with suicide attempts among girls (Table 3).

Association between nonmedical use of opioids or sedatives and suicidal behavior

The final multivariable logistic regression models for suicidal ideation and suicide attempts are shown in Table 4 and Figure 1. After adjusting for age, weight status, living arrangement, HSS, academic pressure, classmate relations, relationships with teachers, smoking, drinking, and depressive symptoms, experimental and frequent use of opioids were positively associated with suicidal ideation and suicide attempts among both boys and girls. Moreover, girls who were frequent users of opioids were at a higher risk of suicidal ideation, (adjusted odds ratio [aOR]=1.84, 95% confidence interval [CI]=[1.57, 2.17]) and suicide attempts (aOR=2.96, 95% CI=[2.34, 3.74]). Among girls, frequent use of sedatives was also positively associated with suicidal ideation (aOR=2.23, 95% CI=[1.91, 2.60]) and suicide attempts (aOR=4.02, 95% CI=[3.25, 4.99]). These associations were also statistically significant in boys, but the magnitudes of aORs for the associations between frequent use of opioids and sedatives and suicidal behavior were greater in girls than boys. In addition, the magnitudes of aORs for the significant associations between frequent use of opioids and sedatives and suicidal behavior were greater than those between experimental use and suicidal behavior.

Discussion

Summary of the findings

Our findings demonstrate that 16.1% of the sampled students reported having suicidal ideation and 3.1% admitted having suicide attempts. These results were aligned with our prior study in Fujian province of China (Guo et al., 2017b) and were lower than those described in a study conducted by the Centers for Disease Control and Prevention (CDC) of the United States, which illustrated that 19.6% of the adolescents reported suicidal ideation and 8.2% reported suicide attempts in the preceding 12 months (Zwald et al., 2018). This study also found that nonmedical use of opioids or sedatives was prevalent among Chinese adolescents. Several studies have suggested that sex differences may exist in NMUPD and suicidal behavior among adolescents. However, there is no agreement on whether NMUPD or suicidal behavior is higher, lower or similar in boys than girls. In this study, we first found that girls had higher prevalence rates of suicidal ideation and suicide attempts compared to boys. WHO has also reported that adolescent girls are more prone to suicidal behaviors, notably due to sex norms and discrimination (e.g. unequal chore burdens or exclusion from education) (WHO, 2014a). In addition, in this study, boys were found to have higher prevalence rates of experimental and frequent use of opioids, but girls were found to have greater prevalence rates of frequent use of sedatives. Wang et al. reported that nonmedical use of opioids was more prevalent in male adolescents (Juan et al., 2015); Cotto et al. (2010) illustrated that although males generally reported more substance use than females, this pattern did not hold for all drugs (e.g. sedatives and tranquilizers) in the youths. One possible explanation might be related to the potential sex differences in vulnerability to use specific drugs. Girls are more likely to use sedatives to decrease anxiety or relieve pain, whereas boys are more likely to non-medically use opioids to get high (McCabe et al., 2007). In this study, boys had a higher proportion of taking opioids or sedatives ‘to feel good or get high’, but girls were more likely to do so ‘to relax or relieve tension’. Several lines of evidence have also suggested that different drugs are chemically different and have various physical and psychological effects, as well as different users (Dubey and Arora, 2008). Considering the implications of sex differences in vulnerability to different types of prescription drug use, taking the child’s sex into account may be helpful to prevent and treat different pattern of NMUPD.

Our univariable analyses first reported that older girls were less likely to have suicidal behavior. A prior study also illustrated that young adolescents (aged 12–15 years) were more likely to make risky choice than other age groups (aged 16–18 and 25–35 years), and the age at which risk-taking was highest was 14.38 years (Burnett et al., 2010). In

Table 3. Lifetime prevalence, unadjusted odds ratios and 95% confidence interval of suicidal ideation and suicidal attempts among adolescents.

Variable	Suicidal ideation				Suicide attempts ^a							
	Total		Boys		Girls		Total		Boys		Girls	
	N (%)	OR [95% CI]	N (%)	OR [95% CI]	N (%)	OR [95% CI]	N (%)	OR [95% CI]	N (%)	OR [95% CI]	N (%)	OR [95% CI]
Total	15,279 (16.1)		6329 (14.1)		8950 (17.9)		2977 (3.1)		1228 (2.7)		1749 (3.5)	
Opioids use												
Abstainers	13,675 (15.4)		5614 (13.5)		8061 (17.1)		2476 (2.8)		1009 (2.4)		1467 (3.1)	
Experimenters	1042 (25.0)		438 (20.7)		604 (29.5)		301 (7.2)		125 (5.9)		176 (8.6)	
Frequent users	562 (29.4)		277 (25.7)		285 (34.2)		200 (10.5)		94 (8.7)		106 (12.7)	
Sedative use												
Abstainers	13,576 (15.5)		5408 (13.5)		8168 (17.1)		2443 (2.8)		976 (2.4)		1467 (3.1)	
Experimenters	1149 (21.2)		690 (17.4)		459 (31.4)		313 (5.8)		157 (4.0)		156 (10.7)	
Frequent users	554 (33.2)		231 (29.9)		323 (35.9)		221 (13.2)		95 (12.3)		126 (14.0)	
Age, mean (SD) [1, score increase]	15.09 (1.69)		15.11 (1.68)		15.08 (1.69)		15.01 (1.64)		15.13 (1.67)		14.93 (1.62)	
Weight status												
Normal	12,795 (15.9)		5156 (13.8)		7669 (17.6)		2490 (3.1)		1008 (2.7)		1487 (3.4)	
Overweight or obese	2484 (17.4)		1190 (15.6)		1306 (19.7)		487 (3.4)		222 (2.9)		270 (4.1)	
Living arrangement												
Living with two parents	11,072 (15.0)		4519 (13.2)		6582 (16.6)		2089 (2.8)		860 (2.5)		1235 (3.1)	
Living with a single parent	1934 (20.2)		843 (17.3)		1095 (23.2)		395 (4.1)		163 (3.4)		233 (4.9)	
Living with others	2231 (19.8)		963 (17.1)		1276 (22.5)		485 (4.3)		202 (3.6)		286 (5.0)	
HSS												
Excellent	3155 (15.0)		1318 (12.5)		1849 (17.6)		659 (3.1)		270 (2.6)		390 (3.7)	
Good	8837 (15.3)		3559 (13.5)		5294 (16.9)		1566 (2.7)		586 (2.2)		987 (3.2)	
Fair	3246 (20.3)		1449 (18.4)		1810 (22.2)		738 (4.6)		369 (4.7)		371 (4.6)	
Academic pressure												
Above average	1670 (10.8)		804 (9.7)		868 (12.0)		354 (2.3)		166 (2.0)		189 (2.6)	
Average	5375 (12.2)		2066 (10.4)		3321 (13.7)		961 (2.2)		323 (1.6)		642 (2.7)	
Below average	8227 (23.2)		3473 (20.7)		4782 (25.6)		1662 (4.7)		741 (4.4)		926 (5.0)	
Classmate relations												
Good	9909 (14.1)		4127 (12.2)		5808 (15.8)		1800 (2.6)		725 (2.1)		1082 (3.0)	

(continued)

Table 3. (Continued)

Variable	Suicidal ideation				Suicide attempts ^a			
	Total		Boys		Girls		Total	
	N (%)	OR [95% CI]	N (%)	OR [95% CI]	N (%)	OR [95% CI]	N (%)	OR [95% CI]
Average	4734 (20.8)	1.62 [1.53, 1.72]	1851 (18.4)	1.56 [1.49, 1.65]	2896 (22.7)	1.69 [1.49, 1.93]	934 (4.1)	1.56 [1.41, 1.73]
Poor	597 (40.2)	4.37 [3.81, 5.02]	347 (37.8)	4.27 [3.61, 5.05]	253 (44.5)	8.40 [6.92, 10.19]	236 (15.9)	6.54 [5.20, 8.23]
Teacher–classmate relationships								
Good	6616 (12.4)	1.00 [reference]	2743 (10.7)	1.00 [reference]	3887 (14.1)	1.00 [reference]	1146 (2.2)	1.00 [reference]
Average	7545 (19.6)	1.70 [1.61, 1.80]	2887 (16.9)	1.69 [1.61, 1.77]	4680 (21.7)	1.64 [1.45, 1.87]	1434 (3.7)	1.79 [1.62, 1.98]
Poor	1078 (36.4)	4.30 [3.89, 4.75]	697 (33.9)	4.42 [3.86, 5.06]	387 (42.1)	8.00 [6.82, 9.38]	389 (13.1)	6.29 [5.14, 7.69]
CES-D score ^b	21.2 (7.6)	1.02 [1.01, 1.02]	21.2 (8.0)	1.02 [1.01, 1.02]	21.1 (7.2)	1.02 [1.01, 1.03]	21.5 (8.9)	1.02 [1.01, 1.03]
Smoking								
No	13,842 (15.5)	1.00 [reference]	5320 (13.2)	1.00 [reference]	8522 (17.4)	1.00 [reference]	2486 (2.8)	1.00 [reference]
Yes	1437 (26.3)	1.87 [1.73, 2.01]	1009 (22.1)	1.87 [1.73, 2.01]	428 (48.1)	3.07 [2.69, 3.51]	491 (9.0)	7.99 [6.74, 9.47]
Drinking								
No	5551 (11.0)	1.00 [reference]	1917 (9.4)	1.00 [reference]	3634 (12.0)	1.00 [reference]	916 (1.8)	1.00 [reference]
Yes	9728 (22.0)	2.10 [1.96, 2.23]	4412 (18.0)	2.70 [2.58, 2.83]	5316 (26.9)	2.02 [1.78, 2.28]	2061 (4.7)	3.46 [3.12, 3.83]

HSS: household socioeconomic status; CES-D: Center for Epidemiology Scale for

^aFirth's penalized likelihood approach was utilized for the low event rates in these models.

^bCES-D score data are presented as the mean (SD).

Depression; OR: odds ratio; 95% CI: 95% confidence interval.

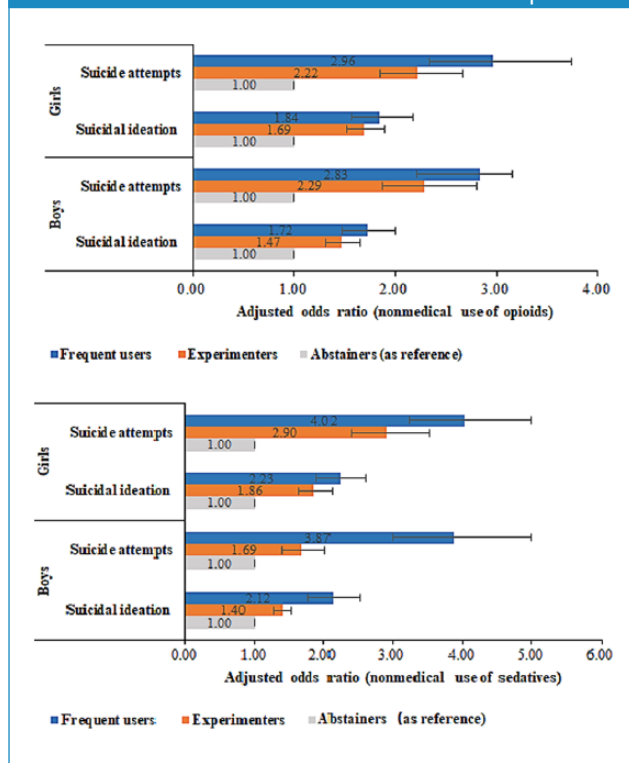
Table 4. Association between nonmedical use of opioids or sedatives and suicidal behavior.

Variable	Boys, aOR [95% CI] ^a		Girls, aOR [95% CI] ^a	
	Suicidal ideation	Suicide attempts ^b	Suicidal ideation	Suicide attempts ^b
Opioids use				
Abstainers	1.00 [reference]	1.00 [reference]	1.00 [reference]	1.00 [reference]
Experimenters	1.47 [1.31, 1.65]	2.29 [1.87, 2.80]	1.69 [1.52, 1.89]	2.22 [1.85, 2.66]
Frequent users	1.72 [1.47, 2.00]	2.83 [2.21, 3.62]	1.84 [1.57, 2.17]	2.96 [2.34, 3.74]
Sedative use				
Abstainers	1.00 [reference]	1.00 [reference]	1.00 [reference]	1.00 [reference]
Experimenters	1.40 [1.27, 1.54]	1.69 [1.40, 2.03]	1.86 [1.64, 2.11]	2.90 [2.39, 3.52]
Frequent users	2.12 [1.78, 2.52]	3.87 [3.00, 5.00]	2.23 [1.91, 2.60]	4.02 [3.25, 4.99]

aOR: adjusted odds ratio; 95% CI: 95% confidence interval.

^aThe multivariable logistic regression models for nonmedical use of opioids or sedatives used the Firth penalized likelihood approach for the low event rates and were adjusted for age, weight status, living arrangement, HSS, academic pressure, classmate relations, relationships with teachers, smoking, drinking and depressive symptoms.

^bFirth's penalized likelihood approach was utilized for the low event rates in these models.

Figure 1. Adjusted associations of nonmedical use of opioids or sedatives with suicidal ideation and suicide attempts.

addition, we found that adolescents who were overweight or obese were at a higher risk of suicidal behavior. Similarly, Pan et al. (2017) reported that adolescents who were obese were at a threefold increased risk of having suicidal ideation. Overweight or obese adolescents are more likely to experience peer victimization, which is a known factor for suicidal ideation and suicide attempts (Pearce et al., 2002). Unsurprisingly, compared to their corresponding groups, adolescents who admitted smoking or drinking had higher

odds of reporting suicidal ideation and suicide attempts. Higher CES-D score and poor relationships with classmates or teachers were positively associated with higher risk for suicidal behaviors. The univariable analysis findings will be useful to identify adolescents who may be at risk of suicidal behavior, and we should focus on high-risk groups who present with the adverse characteristics mentioned above.

After adjusting for demographics, smoking, drinking and depressive symptoms, our stratified multivariable logistic regression results showed that both boys and girls were at an elevated risk of suicidal behavior. Similarly, Ford et al., using the data from the 2012 NSDUH, illustrated that respondents who admitted NMUPD were more likely to report that they had seriously thought about killing themselves (Ford and Perna, 2015). Ashrafioun et al. (2017) also using the data from the 2014 NSDUH reported that non-medical use of opioids was positively associated with suicidal ideation and suicide attempts. Our previous study using data from 3273 students showed that the relationship between baseline prescription opioid or sedative misuse and subsequent suicidal attempts was statistically significant (Guo et al., 2016). One possible explanation for these results is that prescription opioid or sedative misuse may lead to suicidal behavior through impaired judgment, loss of inhibition or impulsiveness (Crews and Boettiger, 2009). Another explanation is that possessing prescription opioids or sedatives equates to access to means of suicide and increases the risk of suicidal behavior to some extent (Ilgen et al., 2016). Notably, a novel finding of this study was the results of the separate analyses by sex, which showed that the adjusted associations between frequent use of opioids or sedatives, suicidal ideation and suicide attempts appeared slightly stronger in girls than boys. These results might be related to the fact that females are more likely than males to experience psychological and emotional distress and to non-medically use opioids or sedatives for longer periods and in

higher doses (also termed as frequent use) (Back et al., 2011), so females might be at an increased risk for adverse outcomes (e.g. drug dependence or suicidal behavior) from prescription drug misuse. Moreover, a previous study demonstrated that girls aged 12–17 years were more likely to become dependent, and drug dependence has been widely related to suicide risk (Office On Women's Health (OWH), 2017). In addition, evidence suggests a biological plausibility of the sex difference in the association between NMUPD and suicidal behavior. Girls may exhibit a pattern of neuroendocrine hyperactivity compared to boys who experience similar levels of stress due to the sex differences in stress-related hypothalamus–pituitary–adrenal (HPA) axis reactivity and psychological responses to stress (Guo et al., 2017a; Kudielka and Kirschbaum, 2005). Therefore, girls tend to report higher levels of negative emotions (e.g. suicidal ideation), which appear to result in a reliance on NMUPD to cope with negative emotions (Doom et al., 2013; Guo et al., 2017a). Moreover, these findings suggest providing earlier detection and treatment services to promote resilience among adolescents who are current non-medical users of prescription drugs to prevent suicidal behavior. In addition, these results may provide preliminary evidence about the importance of focusing on different prevalent drugs and inconsistent reasons for NMUPD between adolescent boys and girls. Given the effect of intervention programs might vary between various population subgroups, sex-specific prevention and intervention strategies are recommended to pay attention to girls who experience psychological distress and boys who have higher probability of risk health behavior.

Our study also showed that the association between NMUPD and suicidal behavior in experimental users of opioids or sedatives was weaker than that in frequent users. Ashrafioun et al. also reported that frequency of nonmedical use of opioids was significantly associated with suicidal ideation, and individuals who admitted 'weekly or more frequency use' presented a greater likelihood of reporting suicidal ideation than those who reported 'monthly to weekly use' and 'less than monthly use' (Ashrafioun et al., 2017). Based on the interpersonal theory of suicide, these results might be related to the fact that compared to experimental users of opioids or sedatives, more frequent users are at a higher risk of becoming dependent users who experience more interpersonal conflict, adverse events and negative physical consequences, leading to suicidal behavior (Van Orden et al., 2010).

Limitations

There are limitations associated with this study. First, the study is based on a cross-sectional design, which indicates that causal relations cannot be determined. It can be only stated that there are significant associations between NMUPD and suicidal behavior. Second, the use of the adolescent self-report questionnaires to collect data may subject our findings to

retrospective bias, and some sensitive data (e.g. NMUPD and suicidal behavior) in this study may be underreported due to social desirability. However, the anonymity of the questionnaires is assured, and this method may have helped to collect accurate information from adolescents. Third, the opioids and sedatives covered in this study were only the most widely used drugs among Chinese adolescents, and more prescription drugs need to be included in future studies. Fourth, considering that suicidal ideation and suicide attempts are more common in adolescence, this study only focuses on suicidal ideation and suicide attempts among adolescents, and the completed suicide cases are not included. The strength of our study is that it uses a large-scale sample of Chinese adolescents, which gave us sufficient statistical power to detect the possible associations between nonmedical use of prescription opioids or sedatives, suicidal ideation and suicide attempts even after adjusting for many control variables (including demographics, family and school factors, weight status, smoking, drinking and depressive symptoms). In addition, to our knowledge, no study has specifically considered the influence of the child's sex on the association of NMUPD with suicidal ideation and suicide attempts. We conducted this study among Chinese adolescents and found a sex-differential association.

Implications

NMUPD and suicidal behavior are major public health concerns in China. The results of this study clearly show that girls have greater prevalence of suicidal ideation and suicide attempts than boys, boys have higher prevalence of experimental and frequent use of opioids compared to girls, and there exist significant sex differences in the sources and reasons for NMUPD. Our study also shows that although both boys and girls who reported nonmedical use of opioids or sedatives are at an increased risk of suicidal behavior, the association between frequent misuse of opioids or sedatives, suicidal ideation and suicide attempts is slightly stronger in girls than boys in China. This finding is an important addition to the existing literature. The significant sex differences found above may provide a basis for early identification of adolescents at high risk of suicidal behavior, such as girls who may have psychological distress or other mental health problems and boys who are more likely to participate in risk- or sensation-seeking behavior. Based on the findings of this study, specific prevention and intervention programs are recommended: (1) to improve adolescents' awareness of the adverse effects of NMUPD and suicidal behavior through educational campaigns; (2) to promote resilience among adolescents who have engaged in NMUPD by providing suitable health services; (3) to strengthen regulations to limit the sales of prescription drugs to adolescents; and (4) to establish a nation-wide active monitoring system (such as the NSDUH in the United States) to surveil NMUPD, suicidal behavior and other risky health behaviors among adolescents in China.

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