The prevalences of and association between nonmedical prescription opioid use and poor sleep among Chinese high school students

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The purpose of this study was to investigate the prevalences of and association between nonmedical prescription opioid use (NMPOU) and sleep quality among Chinese high school students. A cross-sectional study was conducted in Chongqing high school students in 2012, and questionnaires from 18,686 students were completed and eligible for this study. Demographic and NMPOU information was collected using a self-administered questionnaire. The Chinese Pittsburgh Sleep Quality index (CPSQI) was used to assess the occurrence of poor sleep. Among the total sample, 18.0% were classified as poor sleepers (27.4% of the subjects with past-month NMPOU), and the prevalences of lifetime, past-year and past-month NMPOU were 14.6, 4.6 and 2.8% across the entire sample, respectively. The most commonly used medicine was licorice tablets with morphine (9.1, 2.5 and 1.5% for lifetime, past-year and past-month, respectively), followed by cough syrup with codeine, Percocet, diphenoxylate and tramadol. After adjustment for potential confounders, the association between past-month NMPOU and poor sleep remained significant (AOR = 1.47, 95% CI 1.17 to 1.85). Programs aimed at decreasing NMPOU should also pay attention to sleep quality among adolescents.

The nonmedical use of prescription drugs (including pain medications/opioids, sedatives, tranquilizers and stimulants) has increased dramatically in recent years. In the United States, it has reached epidemic levels1. According to the report of the National Youth Risk Behavior Survey (YBRS), 17.8% of students (grades 9–12) surveyed had taken prescription drugs for nonmedical reasons during their lifetime2. In China, a province-based survey conducted in 2007–2009 revealed that 6.0% of the students (grades 7–12) had engaged in nonmedical use of four specific prescription drugs during their lifetime3. Notably, earlier studies had reported that nonmedical prescription opioid use (NMPOU) is prevalent among adolescents and represents a growing public problem4,5. The misuse of prescription opioids can lead to numerous problems, such as sexual violence, heroin use, and drug injection6, and it causes more deaths than overdoses from heroin and cocaine combined7. However, most of these studies were conducted in Western countries, and limited information is available on NMPOU among high school students in developing countries such as China.

Sleep plays a very important role in the physical and mental health of adolescents8. One study reported that 39.6% of high school students in southern China suffered sleep disturbances9. A number of factors, including demographic characteristics, personal habits and psychosocial characteristics, have been related to sleep quality among adolescents. For example, girls are more likely to report sleep disturbances than boys10,11, and the prevalence of sleep disturbance varies with age among school-aged children12. Among personal habits, smoking has been identified as a risk factor for short sleep duration13, and the prevalence of sleep disturbance or insomnia is particularly high among adolescents who drink alcohol14,15. In addition, several studies have indicated that physical activity influences sleep duration among adolescents13,16. A study conducted in China identified a moderate association of psychosocial factors, such as depressive symptoms, loneliness and suicide ideation, with poor sleep9.

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Prior studies have found a bidirectional relationship between sleep and substance abuse, mainly for alcohol, tobacco and illicit drugs\textsuperscript{24–26}. More importantly, sleep has further been identified as an effective therapeutic target in adolescents with substance abuse problems, which indicates that improving sleep quality may lead to a reduction in substance abuse during follow-up\textsuperscript{27,28}. Although an association between opioid dependence and sleep quality has been identified in several studies,\textsuperscript{22,23} it remains unclear whether NMPOU can influence sleep quality or vice versa and whether sleep improvement could be a potential intervention for NMPOU reduction among adolescents. To begin to address these questions, new studies exploring the relationship between NMPOU and sleep quality are needed. To this end, we conducted a large-scale cross-sectional study in Chongqing, China. The two main purposes of our research were as follows:

1. To examine the prevalence of lifetime, past-year and past-month NMPOU and poor sleep in the sample.
2. To explore the relationship between past-month NMPOU and past-month sleep quality after controlling for potential confounders.

**Results**

In total, 20,714 students were invited to participate, and questionnaires from 18,686 (90.6%) students were completed and eligible for our study. Table 1 provides the basic demographic information for the total sample and subgroups with poor sleep or past-month NMPOU. Among the final sample, 18,686 high school students were included, and the proportion of girls was 52.5%. The students ranged in age from 11 to 20 years old, and the mean age was 15.43 (±1.76) years; 41.6% were junior high school students, and 58.4% were senior high school or vocational high school students. Approximately 54.9% of the students lived with both biological parents, and 10.5% reported their family economic status as above average. As for school-related factors, 13.6% of the participants thought their academic pressures were above average, whereas 32.2% of the students reported their academic achievement as below average. Regarding personal habits, 8.7% of the students smoked, and 23.3% drank alcohol. Among the students, 15.5% exercised 5–7 days in the past week. Regarding psychosocial characteristics, 9.1% of the students could be classified as having depressive symptoms, 11.0% felt lonely more than 4 days per week, and 2.2% often thought about suicide.

The prevalences of lifetime, past-year and past-month NMPOU were 14.6, 4.6 and 2.8% in the entire sample, respectively. These prevalences and the past-month NMPOU values among subgroups with or without poor sleep are shown in Table 2. Among the total sample, the most commonly used medicine was licorice tablets with morphine (9.1, 2.5 and 1.5% for lifetime, past-year and past-month, respectively), followed by cough syrup with codeine, Percocet, diphenoxylate and tramadol. Generally, the prevalences of any and specific past-month NMPOU was higher among subgroup with poor sleep based on the Chi-square tests.

Of the total sample, 18.0% were classified as poor sleepers (27.4% of the subjects with past-month NMPOU). The mean CPSQI global score in the total sample was 5.24 (±2.62) points. The participants who indicated past-month NMPOU had a mean global score of 5.97 (±3.24) points.

Based on Chi-square tests, past-month NMPOU was significantly correlated with gender, age, grade, academic achievement, smoking habits, drinking habits, having depressive symptoms, feeling lonely and suicide ideation. These results are shown in Table 1.

Without adjustment for other variables, having poor sleep was significantly correlated with past-month NMPOU (OR = 2.09, 95% CI 1.71 to 2.56), gender, age, grade, living arrangement, family economic status, academic pressure, academic achievement, smoking habits, drinking habits, exercise, having depressive symptoms, feeling lonely and suicide ideation. These results are shown in Table 3.

The final multilevel logistic regression that explore the association between past-month NMPOU and poor sleep is presented in Table 3. After adjusting for potential confounders (gender, age, grade, academic achievement, smoking habits, drinking habits, having depressive symptoms, feeling lonely and suicide ideation), the association between past-month NMPOU and poor sleep remained significant (AOR = 1.47, 95% CI 1.17 to 1.85).

Repeated analyses were conducted to investigate the association between lifetime and past-year NMPOU and poor sleep. After adjusting for potential confounders, the association between lifetime and past-year NMPOU and poor sleep remained significant (AOR = 1.43, 95% CI 1.28 to 1.60; and AOR = 1.68, 95% CI 1.41 to 2.00, respectively) (data not shown in Table).

**Discussion**

NMPOU is a growing public concern, and many studies focused on this problem have been conducted\textsuperscript{24–26}. In this study, the prevalences of lifetime, past-year and past-month NMPOU were 14.6, 4.6 and 2.8% among the participants, respectively. The most commonly used medicine was licorice tablets with morphine (9.1, 2.5 and 1.5% for lifetime, past-year and past-month nonmedical use, respectively), followed by cough syrup with codeine, Percocet, diphenoxylate and tramadol. The prevalence of past-year NMPOU was lower than that described in a Canadian survey, which reported that 6.6% of the participants (aged 15–17) had engaged in past-year NMPOU\textsuperscript{27}. A possible explanation for the discrepancy in the prevalence could be the differences in the classes of medicines considered in these two studies. The Canadian survey included all pain relievers, whereas our study included only five specific categories of medicine. The prevalence of past-month NMPOU was slightly higher than that described in the latest report from the 2014 National Survey on Drug Use and Health (NSDUH), which found that 1.9% of adolescents (aged 12–17) had used pain relievers nonmedically during the past month\textsuperscript{28}. Differences in the study samples may contribute to part of the variance in the prevalence. The NSDUH is a national representative survey of the civilian, noninstitutionalized population (aged 12 years or older) of the United States; therefore, it reveals the average prevalence of NMPOU among the entire country. However, our study was conducted.
| Variable                        | Total (N = 18686) | With poor sleep (n = 3361) | With past-month NMPOU (n = 519) | p value<sup>1</sup> |
|--------------------------------|-------------------|-----------------------------|---------------------------------|---------------------|
| Gender                         |                   |                             |                                 | 0.03                |
| Girls                          | 9803              | 52.5                        | 1943                            | 57.8                |
| Boys                           | 8883              | 47.5                        | 1418                            | 42.2                |
| Age (years)                    |                   |                             |                                 | <0.001              |
| 11–13                          | 3371              | 18.0                        | 339                             | 10.1                |
| 14–16                          | 9196              | 49.2                        | 1676                            | 49.9                |
| 17–20                          | 6119              | 32.8                        | 1346                            | 40.0                |
| Grade                          |                   |                             |                                 | <0.001              |
| 7th-9th                        | 7771              | 41.6                        | 992                             | 29.5                |
| 10th-12th                      | 10915             | 58.4                        | 2369                            | 70.5                |
| Living arrangement             |                   |                             |                                 | 0.22                |
| Two biological parents         | 10256             | 54.9                        | 1743                            | 51.9                |
| Only father or mother          | 3101              | 16.6                        | 574                             | 17.1                |
| Others                         | 5329              | 28.5                        | 1044                            | 31.0                |
| Family economic status         |                   |                             |                                 | 0.05                |
| Above average                  | 1970              | 10.5                        | 268                             | 8.0                 |
| Average                        | 10760             | 57.6                        | 1786                            | 53.1                |
| Below average                  | 5956              | 31.9                        | 1307                            | 38.9                |
| Brothers and sisters           |                   |                             |                                 | 0.81                |
| None                           | 6790              | 36.3                        | 1173                            | 34.9                |
| ≥1                             | 11896             | 63.7                        | 2188                            | 65.1                |
| Academic pressure              |                   |                             |                                 | 0.98                |
| Above average                  | 2536              | 13.6                        | 323                             | 9.6                 |
| Average                        | 8209              | 43.9                        | 1014                            | 30.2                |
| Below average                  | 7941              | 42.5                        | 2024                            | 60.2                |
| Academic achievement           |                   |                             |                                 | <0.001              |
| Above average                  | 5805              | 31.1                        | 852                             | 25.4                |
| Average                        | 6863              | 36.7                        | 1218                            | 36.2                |
| Below average                  | 6018              | 32.2                        | 1291                            | 38.4                |
| Smoking habits                 |                   |                             |                                 | <0.001              |
| No                             | 17053             | 91.3                        | 2901                            | 86.3                |
| Yes                            | 1633              | 8.7                         | 460                             | 13.7                |
| Drinking habits                |                   |                             |                                 | <0.001              |
| No                             | 14341             | 76.7                        | 2236                            | 66.5                |
| Yes                            | 4345              | 23.3                        | 1125                            | 33.5                |
| Exercise                       |                   |                             |                                 | 0.22                |
| 0 days                         | 4283              | 22.9                        | 1129                            | 33.6                |
| 1–2 days                       | 8029              | 43.0                        | 1303                            | 38.8                |
| 3–4 days                       | 3475              | 18.6                        | 485                             | 14.4                |
| 5–7 days                       | 2899              | 15.5                        | 444                             | 13.2                |
| Depressive symptoms            |                   |                             |                                 | <0.001              |
| No                             | 16994             | 90.9                        | 2404                            | 71.5                |
| Yes                            | 1692              | 9.1                         | 957                             | 28.5                |
| Loneliness                     |                   |                             |                                 | <0.001              |
| Less than 1 day/week           | 9716              | 52.0                        | 1025                            | 30.5                |
| 1 to 4 days/week               | 6917              | 37.0                        | 1564                            | 46.5                |
| More than 4 days/week          | 2053              | 11.0                        | 772                             | 23.0                |
| Suicide ideation               |                   |                             |                                 | <0.001              |
| Never                          | 14669             | 78.5                        | 2026                            | 60.3                |
| Occasionally (1–2 times/year)  | 3062              | 16.4                        | 895                             | 26.6                |
| Sometimes (3–6 times/year)     | 539               | 2.9                         | 215                             | 6.4                 |
| Often (>6 times/year)          | 416               | 2.2                         | 225                             | 6.7                 |

Table 1. Basic demographic information for the sample (N = 18686). NMPOU, nonmedical prescription opioid use. *Chi-square tests were used to test the association between the above-mentioned categories and NMPOU status.
programs to decrease NMPOU or poor sleep among adolescents should consider the influence of the other factor. The correlations between these two variables suggest that preventive and intervention studies on these issues. We also found a significant association between past-month NMPOU and poor sleep, school students; thus, this topic warrants more attention from policymakers, schools and families, as well as further studies. Regarding sleep quality, 18.0% of the students in this study could be classified as poor sleepers (27.4% among the subgroup with past-month NMPOU). The prevalence of poor sleep was slightly lower than that reported in a study conducted in northern China, which found that 16.9% of the adolescents suffered sleep problems. This result indicates that although sleep disturbance was not rare among the study sample, it was particularly high among the subgroup with past-month NMPOU, meriting further consideration.

To the best of our knowledge, the current investigation is the first study to examine the relationship between past-month NMPOU and sleep quality among Chinese high school students. In this study, we found that the prevalences of any and specific past-month NMPOU were generally higher among subgroups with poor sleep than those without poor sleep. The association between past-month NMPOU and poor sleep was significant after adjusting for gender, age, grade, academic achievement, smoking habits, drinking habits, the presence of depressive symptoms, loneliness and suicide ideation. Previous studies have shown that health risk behaviors (e.g., smoking, alcohol drinking, substance use, etc.) tend to cluster together. Our research further supported that theory: among participants with past-month NMPOU, the prevalences of smoking and drinking were significantly higher than those in non-users. Although we did not assess the participants' knowledge and attitudes towards sleep hygiene, given the clustering of the risk behaviors mentioned above and the fact that the most common motivations for nonmedical opioid users are to "experiment or relax or get high," it is possible that participants with NMPOU also had bad sleep habits and thus suffered poor sleep.

Recent evidence also suggests a biological plausibility of the relationship between NMPOU and poor sleep. There are two speculations of the mechanism of this association. First, opioid use can induce the reduction of adenosine in sleep-regulating brain regions (the pontine reticular formation and substantia innominata region of the basal forebrain), and adenosine has long been known as a promoter of sleep. Furthermore, prior studies have also shown that by activating μ-opioid receptors, opioids can decrease GABAergic transmission in the oral part of the pontine reticular nucleus, which regulates sleep and wakefulness, thereby disrupting sleep. Based on data from the National Survey on Drug Use and Health, Mark and colleagues found that a major depressive episode is an important risk factor for NMPOU among adolescents. Sleep problems have also been strongly associated with depression in prior studies, potentially explaining the association between past-month NMPOU and poor sleep from a different perspective. Overall, it is clear that NMPOU and poor sleep are correlated with each other, and programs to decrease NMPOU should also pay attention to sleep hygiene and vice versa. Longitudinal studies are also needed to further examine the causal relationship between these two variables.

The strengths of the current study include the large epidemiological sample, the number of control variables and the use of well-validated measures to examine sleep quality. More importantly, this study is the first to investigate the association between past-month NMPOU and sleep quality among high school students. However, this study is subject to several limitations that are common to survey studies. First, because of the cross-sectional design, the cause-effect relationships between past-month NMPOU and sleep could not be determined. We cannot draw conclusions about causality, and longitudinal studies are necessary in the future. Second, because the data were based on high school students, the findings may not be generalizable to younger populations, out-of-school adolescents or older populations. Moreover, NMPOU was narrowly defined in this study because we included only the most frequently used drugs; therefore, the association between past-month NMPOU and sleep may not be generalizable to other opioid drugs. Finally, our research was based on self-report surveys in a school setting, and we thus cannot completely eliminate the possibility of recall bias and reporting bias.

In conclusion, the current study indicates that NMPOU and poor sleep are not rare among Chinese high school students; thus, this topic warrants more attention from policymakers, schools and families, as well as further studies on these issues. We also found a significant association between past-month NMPOU and poor sleep, wherein past-month NMPOU was more prevalent among participants with poor sleep than those without poor sleep. Additionally, students who engaged in NMPOU during the past month reported a higher prevalence of poor sleep than non-users. The correlations between these two variables suggest that preventive and intervention programs to decrease NMPOU or poor sleep among adolescents should consider the influence of the other factor.

| NMPOU                  | Lifetime NMPOU (N = 18686) | Past-year NMPOU (N = 18686) | Past-month NMPOU (N = 18686) |
|------------------------|-----------------------------|-----------------------------|-----------------------------|
|                        | n %                         | n %                         | n %                         |
| Any NMPOU*             | 2719 14.6                   | 854 4.6                     | 519 2.8                     |
| Cough syrup with        | 1705 9.1                    | 467 2.5                     | 283 1.5                     |
| codeine*               | 1324 7.1                    | 412 2.2                     | 244 1.3                     |
| Percocet*              | 1010 5.4                    | 329 1.8                     | 205 1.1                     |
| Dihydrocodeine*        | 198 1.1                     | 69 0.4                      | 59 0.3                      |
| Tramadol*              | 134 0.7                     | 75 0.4                      | 46 0.2                      |

Table 2. Prevalence of adolescent use of any and specific opioid drugs (N = 18686). Note: Chi-square tests were used to compare the prevalence of past-month NMPOU between subjects with and without poor sleep. *p<0.001 NMPOU, nonmedical prescription opioid use.

*only in Chongqing, a single city in central China. Moreover, Shield's research has indicated that inconsistent questions assessing the presence of NMPOU in different studies could result in large variation. Regarding sleep quality, 18.0% of the students in this study could be classified as poor sleepers (27.4% among the subgroup with past-month NMPOU). The prevalence of poor sleep was slightly lower than that reported in a study conducted in northern China, which found that 16.9% of the adolescents suffered sleep problems. This result indicates that although sleep disturbance was not rare among the study sample, it was particularly high among the subgroup with past-month NMPOU, meriting further consideration.

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Recent evidence also suggests a biological plausibility of the relationship between NMPOU and poor sleep. There are two speculations of the mechanism of this association. First, opioid use can induce the reduction of adenosine in sleep-regulating brain regions (the pontine reticular formation and substantia innominata region of the basal forebrain), and adenosine has long been known as a promoter of sleep. Furthermore, prior studies have also shown that by activating μ-opioid receptors, opioids can decrease GABAergic transmission in the oral part of the pontine reticular nucleus, which regulates sleep and wakefulness, thereby disrupting sleep. Based on data from the National Survey on Drug Use and Health, Mark and colleagues found that a major depressive episode is an important risk factor for NMPOU among adolescents. Sleep problems have also been strongly associated with depression in prior studies, potentially explaining the association between past-month NMPOU and poor sleep from a different perspective. Overall, it is clear that NMPOU and poor sleep are correlated with each other, and programs to decrease NMPOU should also pay attention to sleep hygiene and vice versa. Longitudinal studies are also needed to further examine the causal relationship between these two variables.

The strengths of the current study include the large epidemiological sample, the number of control variables and the use of well-validated measures to examine sleep quality. More importantly, this study is the first to investigate the association between past-month NMPOU and sleep quality among high school students. However, this study is subject to several limitations that are common to survey studies. First, because of the cross-sectional design, the cause-effect relationships between past-month NMPOU and sleep could not be determined. We cannot draw conclusions about causality, and longitudinal studies are necessary in the future. Second, because the data were based on high school students, the findings may not be generalizable to younger populations, out-of-school adolescents or older populations. Moreover, NMPOU was narrowly defined in this study because we included only the most frequently used drugs; therefore, the association between past-month NMPOU and sleep may not be generalizable to other opioid drugs. Finally, our research was based on self-report surveys in a school setting, and we thus cannot completely eliminate the possibility of recall bias and reporting bias.

In conclusion, the current study indicates that NMPOU and poor sleep are not rare among Chinese high school students; thus, this topic warrants more attention from policymakers, schools and families, as well as further studies on these issues. We also found a significant association between past-month NMPOU and poor sleep, wherein past-month NMPOU was more prevalent among participants with poor sleep than those without poor sleep. Additionally, students who engaged in NMPOU during the past month reported a higher prevalence of poor sleep than non-users. The correlations between these two variables suggest that preventive and intervention programs to decrease NMPOU or poor sleep among adolescents should consider the influence of the other factor.
| Variables                             | OR  | 95% CI     | AOR  | 95% CI     |
|--------------------------------------|-----|------------|------|------------|
| Past-month NMPOU                     |     |            |      |            |
| No                                   | 1.00| 1.00       |      |            |
| Yes                                  | 2.09| 1.71–2.56  | 1.47 | 1.17–1.85  |
| Gender                               |     |            |      |            |
| Girls                                | 1.00|            |      |            |
| Boys                                 | 0.83| 0.77–0.90  |      |            |
| Age (years)                          |     |            |      |            |
| 11–13                                | 1.00|            |      |            |
| 14–16                                | 1.55| 1.35–1.79  |      |            |
| 17–20                                | 1.66| 1.40–1.96  |      |            |
| Grade                                |     |            |      |            |
| 7th–9th                              | 1.00|            |      |            |
| 10th-12th                            | 1.87| 1.42–2.46  |      |            |
| Living arrangement                   |     |            |      |            |
| Two biological parents              | 1.00|            |      |            |
| Only father or mother                | 1.14| 1.02–1.27  |      |            |
| Others                               | 1.16| 1.06–1.27  |      |            |
| Family economic status              |     |            |      |            |
| Above average                        | 1.00|            |      |            |
| Average                              | 1.17| 1.01–1.35  |      |            |
| Below average                        | 1.61| 1.38–1.87  |      |            |
| Brothers and sisters                 |     |            |      |            |
| None                                 | 1.00|            |      |            |
| ≥1                                   | 1.04| 0.95–1.14  |      |            |
| Academic pressure                    |     |            |      |            |
| Above average                        | 1.00|            |      |            |
| Average                              | 0.93| 0.81–1.06  |      |            |
| Below average                        | 2.08| 1.82–2.37  |      |            |
| Academic achievement                 |     |            |      |            |
| Above average                        | 1.00|            |      |            |
| Average                              | 1.18| 1.07–1.30  |      |            |
| Below average                        | 1.52| 1.38–1.67  |      |            |
| Smoking habits                       |     |            |      |            |
| No                                   | 1.00|            |      |            |
| Yes                                  | 2.03| 1.80–2.29  |      |            |
| Drinking habits                      |     |            |      |            |
| No                                   | 1.00|            |      |            |
| Yes                                  | 1.89| 1.74–2.06  |      |            |
| Exercise                             |     |            |      |            |
| 0 days                               | 1.00|            |      |            |
| 1–2 days                             | 0.57| 0.52–0.62  |      |            |
| 3–4 days                             | 0.49| 0.44–0.56  |      |            |
| 5–7 days                             | 0.56| 0.50–0.64  |      |            |
| Depressive symptoms                  |     |            |      |            |
| No                                   | 1.00|            |      |            |
| Yes                                  | 8.03| 7.21–8.95  |      |            |
| Loneliness                           |     |            |      |            |
| Less than 1 day/week                 | 1.00|            |      |            |
| 1 to 4 days/week                     | 2.45| 2.25–2.67  |      |            |
| More than 4 days/week                | 5.15| 4.60–5.76  |      |            |
| Suicide ideation                     |     |            |      |            |
| Never                                | 1.00|            |      |            |
| Occasionally (1–2 times/year)        | 2.71| 2.47–2.98  |      |            |
| Sometimes (3–6 times/year)           | 4.54| 3.78–5.46  |      |            |
| Often (>6 times/year)                | 8.27| 6.73–10.15 |      |            |

Table 3. Crude and adjusted odds ratios and 95% confidence intervals of poor sleep among adolescents. Bold type indicates that the CI does not include the null according to logistic regression analyses. OR, odds ratio by univariate logistic regression; AOR, adjusted odds ratio by multilevel multivariate logistic regression; NMPOU, nonmedicinal prescription opioid use.
Methods
Participants. A cross-sectional study was conducted to investigate the prevalence of past month NMPOU and to examine its relationship with sleep quality. The participants were high school students from Chongqing, China. Multistage stratified cluster sampling was used to randomly sample high school students from schools in Chongqing. In stage 1, based on GDP level (i.e., more developed district, moderately developed district and less developed district), we randomly selected two counties from each of the three district types. In stage 2, schools in each county were selected. The schools were divided into the following three categories: junior high schools (grades 7–9), senior high schools (grades 10–12) and vocational high schools (grades 10–12). Six junior high schools, four senior high schools and two vocational high schools were randomly selected from each county. In stage 3, two classes were randomly selected from each grade at the selected schools, and all available students in the classes were surveyed. To avoid any potential information bias, students were asked to complete the anonymous questionnaires with the supervision of research assistants while their teachers were absent. In total, 20,714 students were invited to participate, and questionnaires from 18,686 (90.6%) students were completed and qualified for our study. The students’ ages ranged from 11 to 20 in the final sample, and girls comprised 52.5% of the sample. All data were collected between March 2012 and May 2012. This study was approved by the Institutional Review Board of the Sun Yat-sen University School of Public Health. All participants were fully informed of the purpose of the study and were invited to voluntarily participate. Written informed consent letters were obtained from the schools, each participant and one parent of each participant. The methods were carried out in accordance with the approved guidelines.

Measures. Sociodemographic characteristics. Demographic variables: Data were collected on the participants’ gender, age, and grade.

Family-related and school-related factors: Living arrangements were assessed by asking who lived in their primary home. Family economic status was measured by asking about the student’s perception of his or her family’s current economic status (responses were coded as “above average”, “average” and “below average”). Brothers and sisters were assessed by asking the number of blood brothers and sisters (responses were coded as ‘none’ and ‘≥1’). Academic pressure and academic achievement were measured by asking about the student’s personal appraisal of academic stress or achievement relative to that of his or her classmates (responses were coded as ‘above average’, ‘average’ and ‘below average’).

Personal habits: Smoking habits were assessed by asking the following question: “Have you smoked one or more cigarettes at least one day during the past month?” The response options were either (1) “Yes” or (2) “No”. Drinking habits were assessed by asking the following question: “Have you drunk at least one glass of alcohol (a glass of alcohol is equivalent to a half bottle or can of beer, a small cup of white spirits, or a glass of wine or rice wine) at least one day during the past month?” The response options were either (1) “Yes” or (2) “No”. Physical habits were assessed by asking the following question: “In the past week, how many days have you exercised longer than 30 minutes (sports such as running, swimming, and basketball, or similar activities)?” The response options were (1) “0 days”, (2) “1–2 days”, (3) “3–4 days”, or (4) “5–7 days”.

Psychosocial factors: Loneliness was assessed by asking the following questions: “During the past 12 months, how often did you feel lonely per week?” The response options ranged from 1 (“never”) to 4 (“more than 4 days”). Suicide ideation was assessed by asking the following question: “During the past 12 months, have you ever thought about suicide?” The response options were (1) “never”, (2) “occasionally (1–2 times)”, (3) “sometimes (3–6 times)”, and (4) “often (more than 6 times)”. Depressive symptoms were assessed using the Center for Epidemiology Scale for Depression (CES-D). The participants were asked to rate the frequency of 20 depressive symptoms over the past week by choosing 1 of 4 response options ranging from “rarely or none of the time” to “most or all of the time”. The scores ranged from 0 to 60. We adopted the 80th percentile as the cut-off (i.e., a score greater than 28 indicated depressive symptoms), and the area under the ROC curve was 0.78.

NMPOU. Lifetime NMPOU was assessed by the following question: “Have you ever used the following medications, even once, when you were not sick or just for the intended purpose to experiment or to get high without a doctor's prescription?” The question was followed by a list of prescription opioid drugs. The response options were “Yes” and “No”. If the answer was yes, we then asked about the participant’s past-year NMPOU, and students who reported NMPOU during the past year were further asked about the past-month NMPOU. In this study, we included only five opioid drugs: licorice tablets with morphine, cough syrup with codeine, Percocet, diphenoxylate and tramadol. Lifetime, past-year and past-month NMPOU prevalences were calculated for any use (i.e., use of at least one category at least once) and then separately for each of the five drug categories (the variables are not mutually exclusive). The list of medications was developed based on a list provided by the Center for ADR Monitoring of Chongqing and medicines reported to be widely used by adolescent drug abusers in local rehabilitation centers.

Sleep quality. The Chinese Pittsburgh Sleep Quality Index (CPSQI) was used to assess sleep quality over a 1-month time interval. The global CPSQI score ranges from 0 to 21, with higher scores indicating worse sleep quality. It contains seven subscales (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleep medications and daytime dysfunction), and the score for each subscale ranges from 0 to 3 points. In China, a PSQI global score greater than 7 points indicates poor sleep, although an original cut-off of 5 points was recommended by the scale developers. The Chinese version of the PSQI has been demonstrated to be valid and reliable in the Chinese population.

Statistical analysis. Two investigators independently entered all data using EpiData 3.1. All statistical analyses were conducted using SPSS V.20.0 and SAS V.9.2. Descriptive analyses were used to describe the sociodemographic characteristics for the entire sample and for subgroups with poor sleep or with past-month NMPOU.
Chi-square tests were used to test differences between the categorical variables. When the participants were grouped by schools, the ICC (intra-class correlation coefficient) was 0.11, indicating the existence of a group effect. Therefore, multilevel analyses (generalized linear mixed effects models adopting the GLMMIX procedure in SAS) were used in which the schools were treated as clusters. The presence of poor sleep was considered the dependent variable, and past-month NMPOU (i.e., use of at least one category at least once during the past month) was the predictor variable. Covariates that were associated (p value less than 0.05) with both past-month NMPOU and poor sleep, according to the univariate analyses or based on significant evidence in the literature, were entered as confounders in the final regression analysis. Repeated analyses were conducted between life-time and past-year NMPOU (i.e., the use of at least one category at least once during lifetime or during the past year) and poor sleep. All statistical tests were two-sided, and a p value less than 0.05 was considered statistically significant.

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**Author Contributions**

Authors C.L. and J.D. designed the study. Authors L.G. and P.L. managed the literature searches and summaries of previous related work. Authors Y.X., X.G., J.H., G.H., H.W. and Y.Y. performed the field research and acquired the data. Author D.T.T. undertook the statistical analysis and wrote the first draft of the manuscript. All authors reviewed the manuscript.

**Additional Information**

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