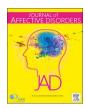
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## Research paper

# The mediating effects of depressive symptoms on the association of childhood maltreatment with non-medical use of prescription drugs



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#### ABSTRACT

Background: Childhood maltreatment might increase the risk of subsequent drug use behavior, and depressive symptoms have been reported to be associated both childhood maltreatment and non-medical use of prescription drugs (NMUPD). This large-scale study aimed to test the mediating effects of depressive symptoms on the association of childhood maltreatment with NMUPD among Chinese adolescents.

Methods: A secondary analysis of the cross-sectional data collected from 7th to 12th graders who were sampled using a multistage, stratified cluster, random sampling method in the 2015 School-based Chinese Adolescents Health Survey. There were 24,457 students who were invited to participate and 23,039 students' questionnaires were completed and qualified for our survey (response rate: 94.2%).

Results: In the adjusted models without mediation, the results showed that students who reported that they had experienced emotional abuse were at a higher risk of past year use and past month use of opioids (past year: Adjusted OR [AOR] = 1.07, 95% CI = 1.05-1.10; past month: AOR = 1.08, 95% CI = 1.06-1.10) and sedatives (past year: AOR = 1.06, 95% CI = 1.03-1.08; past month: AOR = 1.15, 95% CI = 1.13-1.16). The results of mediation analyses demonstrated that there were significant standardized indirect effects of emotional abuse on opioids use and sedatives use through depressive symptoms, respectively (P < 0.001).

Limitations: Our study sample only included school students, and causal inference could not be examined due to the cross-sectional design.

Conclusions: Depressive symptoms play a significant mediator role on the association of childhood maltreatment with NMUPD. Interventions targeted at adolescents who are involved in NMUPD should pay attention to their histories of childhood maltreatment.

# 1. Introduction

The growing non-medical use of prescription drugs (NMUPD) has been a global health concern (Novak et al., 2011). NMUPD is defined as taking medications without a doctor's prescription or solely for the feeling or experience caused by the drug (United Nations Office on Drugs and Crime, 2011). Adolescence is the period of transition between puberty and adulthood, and is often characterized as a stage of increased imitation and exploration along with a range of health-risky behaviors (e.g., drug use) (Crockett and Beal, 2012). During this period, individuals may be responsible for their own medication management and especially vulnerable to the damaging effects of drug use for their sill developing brains (Casey et al., 2008). According to the 2014

National Survey on Drug Use and Health (NSDUH), prescription drugs were the second most popular drug among adolescents in the United States, and 655,000 adolescents aged 12-17 years admitted NMUPD (Hedden et al., 2015). Our previous study also indicated that NMUPD was prevalent among Chinese adolescents, and the total lifetime prevalence of non-medical use of prescription pain relievers was 11.3% (Guo et al., 2015).

Childhood maltreatment is the abuse and neglect that occurs to children under 18 years of age, including all types of physical and emotional neglect/abuse and sexual abuse. Previous studies demonstrated that childhood maltreatment can not only have long-lasting effects on psychological and social functioning, development or dignity into adulthood, but also place heavy financial burden (e.g., lower

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incomes, higher health care costs, and disability-adjusted life years [DALYs] lost) on individuals and society resulting directly or indirectly from the aforementioned loss of psychological and social functioning (e.g., impaired capacity of adults to generate income, lower level of academic achievement, and reduced health-related quality of life) (Fang et al., 2015; World Health Organization, 1999, 2006). A history of childhood maltreatment is reported to be related to elevated risks of serious behavior problems, including internalizing (e.g., mental health) and externalizing (e.g., drug use) behaviors (Afifi et al., 2012; Al et al., 2013; Child Welfare Information Gateway, 2013). A diathesis-stress model using the psychological theory has been promoted to illustrate that early stressful events may result in a lot of health-risky behaviors among individuals with vulnerability diathesis, and exposure to stressors early in life and accumulation of stress (chronicity) could have long-lasting and adverse effects on the development of brain systems involved in learning, motivation, and stress-related adaptive behaviors (such as NMUPD) (Reinelt et al., 2013). Moreover, our previous study also found that maltreatment while a child is related to an increased risk of NMUPD among Chinese adolescents (Guo et al., 2017). Although some evidence suggests an association between NMUPD and a history of adverse life events, there is a dearth of study addressing the potential associations between each specific type of childhood maltreatment and NMUPD among general adolescents.

Depressive symptoms or depression is one of the mental health problems. A previous longitudinal study demonstrated that adolescents with greater childhood emotional abuse severity experienced higher increases in depressive symptoms (Shapero et al., 2014), a prior crosssectional study indicated sexual abuse were significantly associated with depressive symptoms in adults (Schalinski et al., 2016), and a systematic review also showed a significant association between physical abuse experiences and adulthood depressive symptoms among women (Al-Modallal et al., 2008). Moreover, it has also been reported that the associations between NMUPD and depressive symptoms are statistically significant (Guo et al., 2016a, 2016b, 2016c; Sundbom and Bingefors, 2013; Zullig and Divin, 2012). Therefore, it is reasonable to hypothesize that depressive symptoms may play a mediator role on the associations between childhood maltreatment and NMUPD, but no study has examined these mediating effects before. We thus conducted this large-scale study to test the mediating effects of depressive symptoms on the association of childhood maltreatment with non-medical use of prescription drugs among Chinese adolescents.

## 2. Methods

# 2.1. Sample and procedure

The present study analyzed the cross-sectional data collected in the 2015 School-based Chinese Adolescents Health Survey (SCAHS), (Guo et al., 2016a, 2016b, 2016c), as it was the most recent version at the time of analysis and added additional questions about childhood maltreatment. SCAHS is an ongoing study of the health-related behaviors among Chinese adolescents (7th to 12th grade), and collects large-scale cross-sectional data (conducted every two years since 2007) (Guo et al., 2016a, 2016b, 2016c, 2015; Wang et al., 2014) and longitudinal data (between 2009 and 2012) (Guo et al., 2016c) via questionnaires administered in classrooms. The current study used secondary data from 7th and 12th graders who were sampled using a multistage, stratified cluster, random sampling method in the 2015 SCAHS. The procedures for data collection have been described in detail elsewhere (Guo et al., 2017). Briefly, in stage 1, we divided China into three economic stratifications by gross domestic product (GDP) per capita (high-level, middle-level, and low-level), and then randomly selected two representative cities from each stratification. In stage 2, two junior high schools, two senior high schools, and two vocational high schools 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. There were 24,457 students who were invited to participate and 23,039 students' questionnaires were completed and qualified for our survey (response rate: 94.2%). The study was approved by the Sun Yat-Sen University School of Public Health Institutional Review Board. 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).

#### 2.2. Measures

#### 2.2.1. Non-medical use of prescription drugs

In this study, the two measures of NMUPD included non-medical use of opioids and sedatives. Non-medical use of opioids or sedatives was assessed by the following questions: "Have you ever/how many times in the past 12 months/how many times in the past 30 days have you used the following prescription drugs for a non-medical purpose?" The responses to these questions were used to create the corresponding variable of NMUPD status which was grouped into 4 categories: non-user (0 = never use), lifetime non-medical use (1 = have used prescription drugs non-medically but not in the past 12 months or in the past 30 days), non-medical use in the past 12 months (2 = have been involved in NMUPD in the past 12 months but not in the past 30 days), and non-medical use in the past 30 days (3 = have used prescription drugs non-medically in the past 30 days); the category "non-user" was treated as reference group in multinomial logistic regression analyses.

The list of prescription drugs was developed with a focus on medications that were reported to be used widely by adolescent drug abusers in rehabilitation centers of China. Opioids included compounded cough syrup with codeine (codeine), compounded liquorice tablets (opium), tramadol hydrochloride, and diphenoxylate. Sedatives included compounded aminopyrine phenacetin tablets (barbiturates), diazepam or triazolam (benzodiazepines), and scopolamine hydrobromide tablets (barbiturates).

#### 2.2.2. Childhood maltreatment

A history of childhood maltreatment was assessed using the short form of the Childhood Trauma Questionnaire (the CTQ-SF) in Chinese, (Bernstein et al., 1997; Bernstein et al., 2003); the Chinese version of the CTQ-SF has also been validated by Zhao et al. (2005), and exhibits good test-retest reliability over a 2 month interval (ICC = 0.88) and high internal consistency (the total Cronbach's alpha = 0.77) in Chinese adolescents (Zhao et al., 2005). Five subscales of the CTQ-SF assess different types of childhood maltreatment including physical abuse, emotional abuse, sexual abuse, physical neglect, and emotional neglect. Each subscale was based on five questions about experiences that occurred in childhood, with the answers given on a 5-point scale as follows: 1 = never, 2 = rarely, 3 = sometimes, 4 = often, and 5 = very often. Each of the 5 CTQ subscale scores ranged from 5 to 25, and higher scores indicated more severe maltreatment.

#### 2.2.3. Mediators

Depressive symptoms were measured with the Chinese version of the Center for Epidemiology Scale for Depression (CES-D), which was translated into Mandarin Chinese to better reflect the meaning of the original items in the CES-D; the Chinese version of this scale has been validated and extensively utilized in Chinese studies (Cheng et al., 2012; Lee et al., 2008), and exhibits a satisfactory reliability (the total Cronbach's alpha = 0.88) in Chinese adolescents (Zhi-yan et al., 2009). The respondents were asked to rate the frequency of 20 symptoms of depression by choosing one of 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 (Radloff, 1991).

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