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## Exposure to medicines in the family medicine cabinet: is it a harbinger of later opioid dependence?

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### Abstract

**BACKGROUND:** Despite research on prescription opioids and dependence being a national priority, little is known about the association between several potential adolescent risk factors and later opioid dependence among those who use opioids non-medically.

**OBJECTIVES:** To investigate the association between lifetime opioid dependence and adolescent self-perceived health, health beliefs (thinking there was a pill for everything), health behaviors (onset of alcohol use before 15, onset of prescription opioid use before 15) and parental health practices (having opioids in the family medicine cabinet at age 14, parental suggestions to take pills when sick).

**METHODS:** A sample of 343 community members who non-medically used prescription opioids in the past 12 months were recruited for the *Prescription Drug Misuse, Abuse, and Dependence Study* and retrospectively assessed for adolescent risk factors of lifetime opioid dependence (DSM-IV).

**RESULTS:** Logistic regression revealed the strongest predictor of lifetime opioid dependence was having a prescription opioid in the family medicine cabinet at age 14. Those who grew up believing there was a pill for everything and those who initiated alcohol use before 15 were 1.83 and 1.78 times as likely, respectively, to meet dependence criteria than their counterparts. Demographics and other adolescent predictors were not associated with opioid dependence.

**CONCLUSIONS:** Findings suggest several adolescent exposures can be targeted to reduce opioid dependence. Through their behavior, parents can reduce their teens' risk for opioid dependence.

### Keywords

prescription opioids; opioid dependence; adolescence; opioid use disorder; prescription pain pills

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## 1. Introduction

Approximately 10.3 million people (or 3.6% of persons 12 years or older) in the United States (US) reported using a prescription opioid non-medically in the past 12 months (Substance Abuse and Mental Health Services [SAMHSA], 2019). About 13% of these persons meet criteria for opioid abuse or dependence (Becker et al., 2008). Non-medical use includes use in any way not directed by a doctor, including use of greater amounts, more often, or longer duration than directed by a doctor or use without a prescription (Han et al., 2015; Nattala et al., 2012). Although rates of non-medical use are slowly declining over time, prescription opioid dependence is still a serious public health concern associated with increased health costs, overdose-related mortality, comorbid psychopathology, and transition to illicit drug use (e.g., heroin) (Degenhardt et al., 2014; Seth, 2018). The literature suggests that lack of insurance, mental ill health, low income, self-perceived ill health, and younger age of onset of both alcohol and prescription opioid use may significantly predict dependence among those who non-medically use prescription opioids (Becker et al, 2008). Although understudied, adolescent experiences may also impact escalation from non-medical use to dependence. Thus, it is important to examine adolescent risk factors of dependence among those who non-medically use prescription opioids in order to inform interventions during adolescence.

Opioid prescriptions dispensed by retail pharmacies in the US equate to a rate of about 58.7 prescriptions per 100 persons (Center for Disease Control and Prevention [CDC], 2018). Adolescents often have easy and unsupervised access to these opioid medications in the home (Friese et al., 2013; McCabe et al., 2013; Pham, et al., 2017; Ross-Durow et al., 2013) which may result in adolescents consuming these medications non-medically, subsequently putting them at risk of developing opioid dependence. However, to our knowledge, no studies have examined the relationship between exposure to opioid medications during adolescent years in their own home and subsequent development of opioid dependence.

The average age of initiation of non-medical prescription opioid use is 25.8 years old, with most people initiating use in their mid to late 20s ( Substance Abuse and Mental Health Services [SAMHSA], 2016). Earlier age of initiation of non-medical use of prescription opioids has been associated with an increased likelihood of meeting criteria of DSM-IV opioid abuse and dependence (McCabe et al., 2007) and transitioning to heroin use (Compton, et al., 2016; Cerdá et al., 2013). To our knowledge, no one has examined the relationship between early initiation of prescription opioid use (defined here as before the age of 15), whether medical or non-medical, and the subsequent development of opioid dependence.

Literature shows that parenting practices during adolescence can have a long-lasting impact on the later development of substance use disorders (SUD) (McCabe et al., 2016; Thatcher et al, 2008). Although past literature has focused mainly on parental supervision, the health beliefs and practices of parents may also affect SUD development. The expansion in use of medicine in recent decades has led to a concern that western societies, the U.S. in particular, want a pill for every ailment (even those considered a normal part of the human condition) and are susceptible to “disease-mongering” (or the creation or extension of

disease terminology to identify new ailments that require drug remediation). Despite several reports on the danger of markets inundated with direct pharmaceutical advertisements and the push to develop a pill for every problem and a problem for every pill (Triggle, 2007; Busfield, 2010), there is no literature discussing the outcomes of growing up with the health belief that there is a pill for everything or having a parent always give you pharmaceutical medication when you are sick as a teen. The belief that there is a “pill for every ill” seems to be particularly prevalent in the US, where less than 5% of the world’s population lives, but over 80% of the world’s opioid supply is consumed (Manchikanti et al., 2010; Busfield, 2010). Some scientists have suggested that pharmaceutical media messaging, patients’ insistence of immediate symptom relief, and the increasing tendency to recommend or prescribe drugs during doctor or hospital outpatient visits (Busfield, 2010; Triggle, 2007) may be contributing to large public health problems, like the opioid epidemic (Donnelly, 2017). Nevertheless, the potential link between adolescent health beliefs, parental health practices and opioid dependence is under-investigated.

Self-perceived general health in adulthood is a strong predictor of morbidity and mortality for a range of diseases, even after controlling for demographic factors and objective health status (Vie et al., 2018; DeSalvo et al., 2006). Few studies have examined the relationship between self-perceived health in adolescence and health as an adult, but a recent prospective cohort study in Norway (Vie et al., 2017) revealed that level of self-perceived health in adolescence predicted use of prescription opioid medications in adulthood. Although the link between adolescent self-perceived health and the use of prescription opioids in adulthood has been established, there is little research examining adolescent self-perceived health and the development of SUDs.

Despite research on prescription opioids and dependence being a national priority, there is a gap in the literature on the association between several potential adolescent risk factors and later opioid dependence among those who used opioids non-medically. To address this gap, we tested the association between adolescent self-perceived health, health beliefs (thinking there was a pill for everything), health behaviors (onset of alcohol use before 15, onset of prescription opioid use before 15) and parental health practices (having opioids in the family medicine cabinet at age 14, having a parent always give a medicine when sick) with lifetime opioid dependence among a community sample of people who recently (past 12 months) used prescription opioids non-medically. We hypothesized that the following experiences during adolescence - having a prescription opioid in the home medicine cabinet, believing that there was a pill for everything, having a parent who always gave medicine for sickness, and having an early onset of alcohol use and prescription opioid use - were all independent risk factors for development of lifetime opioid dependence.

## 2. Material and methods

### 2.1. Study Sample

Participant interview data from the *Prescription Drug Misuse, Abuse, and Dependence Study* (also known as the Rx Study) was used for this analysis. The primary purpose of this NIDA-funded study was to examine the test-retest reliability of DSM-IV criteria for drug use disorders among past 12 month non-medical users of prescription drugs (including

prescription opioids, stimulants, and sedatives). Targeted sampling procedures (Watters & Biernacki, 1989; Nattala et al., 2012; Nattala et al., 2011; Acheampong et al., 2016), were used to recruit community-dwelling participants from a large Midwestern city who had non-medically used a prescription opioid, stimulant, and/or sedative in the last 12 months. Treatment status was not considered in study eligibility. Recruitment flyers were displayed in community centers, grocery stores, colleges, medical centers, doctor offices and pain management clinics. Between 2008 and 2010, 427 individuals were recruited to participate in the study. Eligibility for inclusion in the present analysis included persons over 18 years of age who met criteria for using prescription opioids non-medically in the past 12 months. Non-medical use was operationalized by answering one or more days to either of the following questions: 1) “How many days in the last 365 days did you use opioids that were prescribed for you but used them in a way other than prescribed—like by using them more than prescribed or after your prescription ended or for a different reason?” or 2) “How many days in the last 365 days did you use opioids that were not prescribed for you?” (Nattala et al., 2012). The study received university IRB approval and followed the principles of the Declaration of Helsinki.

## 2.2. Measures

Assessments included the Substance Abuse Module (SAM) and the Washington University Risk Behavior Assessment (WU-RBA). The SAM is a fully-structured assessment for evaluating lifetime and past 12 month DSM substance use disorders (Horton et al., 2000); the DSM-IV version was used in this study. The WU-RBA covered demographics, drug use, sexual activity, health conditions and utilization of health care, family environment and social support, and perceptions of harm (Shacham & Cottler, 2010).

The outcome variable, lifetime opioid dependence, was determined based on SAM DSM-IV opioid dependence criteria questions. To meet criteria for opioid dependence, a participant had to endorse three or more of the following seven dependence criteria in any one year time period: tolerance, withdrawal, recurrent use in larger quantities or for longer than intended, persistent desire/attempts to stop or cut down on use, excessive time spent obtaining, using or recovering from use, continued use despite knowledge of substance-related physical/psychological problems, and important activities given up in favor of use.

Six independent variables of exposure were captured via the SAM and WU-RBA (see Table 1). In addition, demographic variables (age, gender, race, and highest level of education), used in multivariate regression modelling as covariates, were taken from the SAM.

## 2.3. Statistical analyses

Chi-square or t-tests evaluated differences between those who met criteria for lifetime DSM-IV opioid dependence and those who did not. Multivariate logistic regression was then conducted; adjusted odds ratios (AORs) and 95% confidence intervals (95% CIs) are reported. A regression model was fit with demographics and adolescent exposures. The model showed good model fit with a p-value for Pearson chi-square and Hosmer-Lemeshow goodness of fit tests above 0.05. All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC).

### 3. Results

#### 3.1. Sample demographics

A total of 343 participants recruited for the Rx Study reported past 12 month non-medical use of opioids. Of them, 141 (41.1%) met DSM-IV criteria for opioid dependence in their lifetime. Table 1 shows demographic characteristics and adolescent risk factors of the overall sample and by opioid dependence status. The average age of the sample was 39.1 years old, with an age range of 18 to 65. A little over half of the sample was male (56.3%) or Black/African American (56.0%). A significant proportion of the sample (84.6%) had at least a high school or equivalent degree and reported good/excellent health as a teen (89.2%). About half (46.1%) agreed that their parents always gave them medicine when they were sick as a teen and a little over one-fourth (28.3%) believed there was a pill for everything when they were a teen. A small proportion started using prescription opioids before the age of 15 (8.2%) or recalled having a prescription opioid in their cabinet as a teen (7.0%). A considerable proportion of the sample started using alcohol before the age of 15 (44.0%).

#### 3.2. Adolescent predictors of lifetime opioid dependence

As shown in Table 2, there were no differences in mean age, gender, race, education or perceived general health as a teen between those who did or did not meet criteria for lifetime opioid dependence. Non-medical opioid users with lifetime opioid dependence versus those without were more likely to report growing up believing there was a pill for everything (36.2% vs 22.7%), having a prescription opioid in their medicine cabinet at age 14 (11.4% vs 4.0%), and initiating alcohol use before the age of 15 (52.5% vs 38.1%).

As shown in Table 3, results from multivariate regression analysis showed that the strongest predictor of lifetime opioid dependence was having a prescription opioid in their medicine cabinet at age 14, with an odds ratio of 2.65 – meaning those with an opioid in their medicine cabinet at age 14 were 2.65 times as likely to meet criteria for lifetime opioid dependence as those who did not have a prescription opioid in their medicine cabinet at age 14 (95% CI: 1.05, 6.69). The next most strongly associated covariate with opioid disorder was growing up believing there was a pill for everything, followed by initiating alcohol use before the age of 15. People who grew up believing there was a pill for everything were 1.83 times as likely to meet criteria for lifetime opioid dependence as those who did not share this belief (95% CI: 1.09, 3.07). Those initiating alcohol use before the age of 15 were 1.78 times as likely to meet criteria for lifetime opioid dependence than those who started using alcohol at age 15 or older (95% CI: 1.12, 2.82). Three out of six adolescent variables modelled (self-perceived health as a teen, having a parent always give a medicine when you were sick as a teen, and onset of prescription opioid use before the age of 15) were not associated with lifetime opioid dependence. General demographics such as age, gender, race, and highest level of education were not associated with lifetime opioid dependence among this sample of people who had non-medically used opioids in the past 12 months.

## 4. Discussion

This study is the first to examine adolescent self-perceived health, health beliefs, health behaviors, and parental health practices as risk factors of lifetime opioid dependence among a community sample of people who non-medically used opioids in the past 12 months. We identified three adolescent risk factors that were associated with the subsequent development of opioid dependence: having a prescription opioid in the family medicine cabinet at age 14, growing up believing there is a pill for everything, and initiating alcohol use before the age of 15. Although recollection of having an opioid in the medicine cabinet as a teen was uncommon (7.0%), we found a significant relationship between having access to prescription opioids in the home during adolescence and subsequent development of opioid dependence. Those who had a prescription opioid in their cabinet during adolescence were over two and a half times as likely to later develop opioid dependence. This suggests a need to continue to implement prevention strategies that address adolescent exposure to prescription opioids in the home. These strategies should include safe and secure storage of prescription opioids so that they are not accessible to adolescents residing in the household. Additionally, education related to the safe disposal of unused or expired prescription opioids is necessary; parents need to remove these medications from their home when they are no longer needed (Egan et al, 2019). There are several disposal programs that have been implemented to ensure safe and secure disposal opportunities, including take-back events, permanent disposal boxes (also known as “drop-boxes”) and drug deactivation pouches (e.g., Deterra® Drug Deactivation System and DisposeRx™).

This analysis was also the first to examine the potential consequences of the health belief that there is a “pill for every ill” during adolescence. Importantly, we found that those who grew up believing there was a pill for everything were 1.83 times as likely to develop opioid dependence later in life. This finding suggests a potential link between the belief that there is a pill for everything and opioid dependence in the United States, where less than 5% of the world’s population lives but over 80% of the world’s opioid supply is consumed (Manchikanti et al., 2010; Busfield, 2010). It lends support to the theory proposed by Donnelly (2017) that the belief of a “pill for every ill” is contributing to the current opioid epidemic in the United States and that we may be able to change this health belief by intervening during adolescence. Although having a “pill for every ill” was associated with development of opioid dependence, there was not a significant association between having a parent always give a medicine when sick as a teen and opioid dependence in our sample. This finding may suggest that the development of the health belief that there is a “pill for every ill” may not be dependent on parental treatment of sickness during adolescence. As this adolescent health belief may be a risk factor for many other preventable adult diseases, future research should examine what modifiable factors drive this belief to develop early interventions aimed at changing it.

Among our sample of past 12 month non-medical opioid users, we also found that compared to someone who had their first alcoholic drink at age 15, a person who initiated alcohol use before the age of 15 had 1.78 times the odds of developing lifetime opioid dependence. This finding expands upon results from studies that found prior alcohol consumption (Fiellin et al., 2013) and earlier age of onset (Arterberry et al., 2016) are associated with subsequent



opioid use. Several explanations have been proposed for this relationship including the “gateway” phenomenon (Kandel & Logan, 1984) or that individuals who report multiple substances of use may have an underlying behavior problem, such as conduct disorder, that makes them susceptible to polysubstance use (Jessor, 1987).

Previous research has found that an earlier age of initiation of non-medical use of prescription opioids is associated with an increased likelihood of meeting criteria for DSM-IV opioid abuse and dependence (McCabe et al., 2007) and that medical use of a prescription opioid in 12<sup>th</sup> grade is associated with an increased likelihood of non-medical use of opioids after graduation (Miech et al., 2015). To our knowledge, the current analysis is the first to examine the relationship between early initiation of prescription opioid use (before the age of 15), whether medical or non-medical, and the subsequent development of opioid dependence. Interestingly, we found no association between onset of prescription opioid use before the age of 15 and the subsequent development of lifetime opioid dependence. Together these findings may suggest that late adolescence is the opportune time for interventions against future non-medical opioid use and opioid dependence.

While previous research has found that poorer self-rated adolescent health is associated with the use of more prescription opioids in young adulthood (Vie et al., 2018), we found no association between self-perceived health as a teen and subsequent opioid dependence. In fact, none of the sociodemographic variables modelled in this analysis were associated with opioid dependence. This finding is consistent with earlier research (Becker et al., 2008) among individuals who non-medically used prescription opioids in the past 12 months, which found only 1 of 12 sociodemographic variables (Medicaid coverage) predictive of opioid abuse or dependence in the past 12 months. This may suggest that among non-medical users of opioids, risk of opioid dependence is high regardless of sociodemographic variables.

#### 4.1. Limitations

Findings should be interpreted in the light of a few limitations. First, causality cannot be assumed due to the cross-sectional nature of the study, but variables were selected with temporality (i.e., predictors preceded opioid dependence) which strengthens the likelihood of a causal relationship. Second, models predicting lifetime opioid dependence generally include measures of both physical and mental health as covariates, but self-perceived mental health as a teen was unavailable for the current analyses. The  $R^2$  for Model 2 is 0.06, indicating that there are likely other factors contributing to the risk of opioid dependence in addition to demographics and adolescent exposures. Future studies should consider assessing adolescent mental health and patterns of opioid non-medical use as predictors of later opioid dependence. Third, although prescription opioids (e.g., Percocet, hydrocodone/paracetamol) were used for pain treatment for several decades before the 1990s, the expansion of the prescription opioid market did not occur until the mid-1990s (Van Zee, 2009); thus the older participants within our sample (our sample ranged from 18-65 years of age) may have been less likely to have a prescription opioid in their cabinet during adolescence. To examine these potential age differences, a sensitivity analysis (not shown here) was conducted where people born after 1972 (or 17 years old or younger in

1990) were compared to those born in or before 1972 (18 years old or older in 1990) and no differences in the report of an opioid in the family medicine cabinet were found ( $p=0.56$ ). Finally, the low frequency of reporting an opioid in the family medicine cabinet at age 14 led to a finding with a large confidence interval. We hypothesize that the percent of our sample who recalled having a prescription opioid in their home medicine cabinet at the age of 14 is a conservative estimate of reality for two reasons. First, participants were not prompted in any way to list specific medications or categories of medications. Perhaps asking about the type of pain medications in the family medicine cabinet would have elicited different responses. Second, non-specific answers such as “pain medication” were not coded as prescription opioids because it was impossible to ascertain if a participant meant a prescription opioid or an over-the-counter pain reliever.

#### 4.2. Conclusion

Despite these limitations, the findings provide conservative but strong evidence from a community sample that adolescent risk factors can be used to predict later opioid dependence among past 12-month non-medical opioid users. Adolescent parental health practices (having opioids in the family medicine cabinet at age 14), adolescent health beliefs (thinking there was a pill for everything), and adolescent health behaviors (onset of alcohol use before 15) were all significant predictors of opioid dependence. Restricting exposure to prescription opioids in the home is a critical first step to the prevention of prescription opioid addiction even as young as adolescence. Findings can be used to inform and support the need for interventions designed to moderate adolescent risk factors of future opioid addiction, including secure storage and safe disposal of prescription opioids. As years of past research has shown, drug use trajectories can be changed and risk reduced through childhood interventions, and family and school prevention efforts (Volkow, 2019). We add to this important literature giving direction to efforts to intervene with the family before non-medical use and abuse starts.

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**Table 1.**

## Variable Description

Variable Category	Variable	Coded	SAM or WU-RBA Question
Adolescent self-perceived health	Self-perceived health as teen	Excellent/good vs fair/poor	When you were growing up, from 11 to 14 years old, was your health excellent, good, fair, or poor?
Adolescent health beliefs	Believed there was a pill for everything	Yes vs no	Did you grow up thinking there was a pill for everything?
Adolescent health behaviors	Onset of prescription opioid use before 15	<15 years old = yes 15 years old = no	How old were you the first time you used (Rx Opioids)?
Adolescent health behaviors	Onset of alcohol use before 15	<15 years old = yes 15 years old = no	How old were you the first time you had a drink, not just sips from someone else's drink?
Parental health practices	Opioid in family medicine cabinet at 14	Prescription opioid mentioned = yes No prescription opioid mentioned = no	If we looked in your family's medicine cabinet when you were 14, what medicines would we have found?
Parental health practices	Parent always gave meds	Always = yes Sometimes/rarely = no	In general, when you were 11 to 14 and you got sick, did your parents always, sometimes, or rarely give you medicine to feel better?

**Table 2.**

Sample Characteristics by Opioid Dependence among Persons Who Used Opioids Non-medically in the Past Year (n=343)

	<b>Total n=343 N (%)</b>	<b>Opioid Dependence * n=141 (41.1) N (%)</b>	<b>No Opioid Dependence * n= 202 (58.9) N%</b>	<b>p-value</b>
<u>Age</u>	39.1 (12.8)	39.1 (12.2)	39.1 (13.2)	0.9765
Mean (sd) [range]	[18-65]	[18-60]	[18-65]	
<u>Gender</u>				0.9404
Male	193 (56.3)	79 (56.0)	114 (56.4)	
Female	150 (43.7)	62 (44.0)	88 (43.6)	
<u>Race</u>				0.8395
White	131 (38.2)	55 (39.0)	76 (37.6)	
Black/African American	192 (56.0)	79 (56.0)	113 (55.9)	
Other	20 (5.8)	7 (5.0)	13 (6.4)	
<u>Highest Level of Education</u>				0.5882
Less than high school	53 (15.5)	25 (17.7)	28 (13.9)	
High school or equivalent	218 (63.6)	86 (61.0)	132 (65.4)	
College Degree	72 (21.0)	30 (21.3)	42 (20.8)	
<u>Self-Perceived Health as Teen</u>				0.7799
Excellent/Good	306 (89.2)	125 (88.7)	181 (89.6)	
Fair/Poor	37 (10.8)	16 (11.4)	21 (10.4)	
<u>Believed There Was a Pill for Everything</u>				<b>0.0067</b>
Yes	97 (28.3)	51 (36.2)	46 (22.7)	
No	246 (71.7)	90 (63.8)	156 (77.2)	
<u>Onset of Prescription Opioid Use Before 15</u>				0.1619
Yes	28 (8.2)	15 (10.6)	13 (6.4)	
No	315 (91.8)	126 (89.4)	189 (93.6)	
<u>Onset of Alcohol Use Before 15</u>				<b>0.0084</b>
Yes	151 (44.0)	74 (52.5)	77 (38.1)	
No	192 (56.0)	67 (47.5)	125 (61.9)	
<u>Parent Always Gave Meds</u>				0.8173
Yes	158 (46.1)	66 (46.8)	92 (45.5)	
No	185 (53.9)	75 (53.2)	110 (54.5)	
<u>Opioid in Family Medicine Cabinet at 14</u>				<b>0.0083</b>
Yes	24 (7.0)	16 (11.4)	8 (4.0)	
No	319 (93.0)	125 (88.7)	194 (96.0)	

\* Refers to Dependence on Prescription Opioids

**Table 3.**

Multivariate Logistic Regression Predicting Lifetime Opioid Dependence among Persons Who Used Opioids Non-medically in the Past Year (n=343)

	<b>AOR (95% CI)</b> <b>R<sup>2</sup> = 0.0597</b>
Age mean (sd)	1.00 (0.98-1.02)
<u>Gender</u>	
Male	-
Female	1.07 (0.68-1.69)
<u>Race</u>	
White	-
Black/African American	1.04 (0.62-1.75)
Other	0.89 (0.32-2.49)
<u>Highest Level of Education</u>	
Less than high school	-
High school or equivalent	0.73 (0.39-1.38)
College Degree	0.91 (0.42-1.98)
<u>Self-Perceived Health as Teen</u>	
Excellent/Good	1.01 (0.49-2.10)
Fair/Poor	-
<u>Believed There Was a Pill for Everything</u>	
Yes	<b>1.83 (1.09-3.07) *</b>
No	-
<u>Onset of Prescription Opioid Use Before 15</u>	
Yes	1.29 (0.56-3.00)
No	-
<u>Onset of Alcohol Use Before 15</u>	
Yes	<b>1.78 (1.12-2.82) *</b>
No	-
<u>Parent Always Gave Meds</u>	
Yes	0.93 (0.58-1.50)
No	-
<u>Opioid in Family Medicine Cabinet at 14</u>	
Yes	<b>2.65 (1.05-6.69) *</b>
No	-

\* p<0.05