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## Pills to Powder: A 17-Year Transition from Prescription Opioids to Heroin Among U.S. Adolescents Followed into Adulthood

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### Abstract

**Objectives:** To examine the longitudinal relationships between U.S. adolescents' prescription opioid use and misuse and any subsequent heroin use in adulthood.

**Methods:** Nationally representative samples of adolescents from 25 independent cohorts were surveyed via self-administered questionnaires and followed from ages 18–35 (n=11,012). Adolescents were divided into five subgroups based on survey responses at age 18: no lifetime exposure to prescription opioids (population controls), medical prescription opioid use without a history of nonmedical misuse (medical use only), medical use followed by nonmedical misuse, nonmedical misuse followed by medical use, and nonmedical misuse only. These five subgroups were compared on their risk for any heroin use through age 35 (1993–2017). Adolescents who reported lifetime heroin use at age 18 were excluded.

**Results:** Adolescents who reported nonmedical prescription opioid misuse followed by medical use or nonmedical misuse only had greater odds of any heroin use in adulthood than population controls. More recent cohorts of adolescents who reported nonmedical misuse or medical use only (compared to older cohorts) had greater odds of any heroin use in adulthood relative to population controls. Nearly one in three adolescents in recent cohorts who reported nonmedical prescription opioid misuse transitioned to any heroin use.

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**Conclusions:** There is increased risk for heroin use among adolescents who initiated nonmedical misuse or adolescents prescribed opioids in more recent cohorts. These findings indicate historical variation and reinforce the critical role of vigilant monitoring and drug screening to detect high-risk individuals who would benefit from an intervention to reduce later heroin use.

#### Keywords

Substance use; Adolescence; Epidemiology; Opioids; Heroin

#### INTRODUCTION

While prescription opioid use and misuse in the United States have declined in recent years,  $^{1-4}$  an estimated 10 million people have misused prescription opioids at least once in the past-year. Despite the efficacy of prescription opioids for pain management, there are public health concerns based on the high abuse potential of these medications, risk of transitioning to heroin use, and increases in opioid overdoses.<sup>5–8</sup>

The percentage of people in the United States using heroin has increased from 373,000 people in 2007 to 808,000 people in 2018.<sup>3,9</sup> Although the vast majority of prescription opioid exposure does not lead to heroin use, heroin incidence and prevalence rates were significantly greater among those who reported nonmedical prescription opioid misuse.<sup>6,9,10</sup> Based on retrospective data, only 1% of individuals who reported past-year nonmedical prescription opioid misuse had used heroin before prescription opioids, whereas approximately 80% of those who reported past-year heroin use had misused prescription opioids before starting heroin.<sup>9</sup>

Most adolescents who are prescribed opioids use them appropriately without an increased risk for substance misuse.<sup>7,11</sup> Prior evidence demonstrates a robust association between nonmedical prescription opioid misuse and heroin use, however, this has not been examined prospectively over multiple years while accounting for medical prescription opioid use.<sup>5,6,9</sup> The primary objective of this study is to examine the transition from medical and nonmedical prescription opioid misuse during adolescence to any heroin use over a 17-year period into adulthood.

#### **METHODS**

#### **Study Design**

The Monitoring the Future (MTF) study, beginning in 1976, annually surveys a nationally representative sample of high school seniors using self-administered paper-and-pencil questionnaires in classrooms. From each 12<sup>th</sup> grade cohort, a random sample (oversampled for drug use) was longitudinally followed biennially through age 30 and then again at age 35. For this study, we focused on 25 independent cohorts of 12<sup>th</sup> graders (1976–2000) who were followed through age 35 (1993–2017). All panel respondents who provided at least one wave of follow up data were included (reflecting an 83.6% retention rate). We incorporated attrition weights in all analyses to account for potential attrition bias by age 35.<sup>4</sup> Details

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about the MTF design and methods are available elsewhere.<sup>4</sup> IRB approval was granted by the UM Institutional Review Board Health Sciences.

#### Sample

As illustrated in Table 1, the weighted longitudinal sample who completed Form 1 of the MTF survey included 11,012 individuals (51.8% female). The sample was 74.1% White, 11.5% Black, 6.5% Hispanic, and 8.0% other racial/ethnic categories.

#### Measures

*Age 18 lifetime medical prescription opioid use* was assessed by asking respondents at baseline whether they had ever taken prescription opioids (e.g., morphine, opium, codeine) because a doctor told them to use the medication. Respondents were informed that prescription opioids are prescribed by doctors and drugstores are not supposed to sell them without a prescription. The response options included: 1) No; 2) Yes, but I had already tried them on my own; 3) Yes, and it was the first time I took any.

*Age 18 lifetime nonmedical prescription opioid misuse* was assessed by asking respondents at baseline how many occasions (if any) they used prescription opioids on their own—that is, without a doctor telling them to take them. The response scale ranged: 1) no occasions to 7) 40 or more occasions.

Based on the lifetime medical use and nonmedical misuse questions at age 18 the following mutually exclusive subgroups were created: 1) no exposure to prescription opioids (population controls), 2) medical use only, 3) medical use followed by nonmedical misuse, 4) nonmedical misuse followed by medical use, and 5) nonmedical misuse only.

*Heroin use* was assessed by asking respondents at baseline (age 18) and all subsequent follow-up waves (ages 19 to 35) on how many occasions (if any) they used heroin during their lifetime.

#### **Statistical Analysis**

All analyses incorporated weights to account for attrition and the complex sample design of MTF. For the analysis, we excluded individuals who reported any lifetime heroin use at age 18 (n=179). Multivariable logistic regression analyses were conducted to determine whether medical use and nonmedical misuse history of prescription opioids at baseline was significantly associated with subsequent heroin use between ages 19 and 35, controlling for potential confounders (see Table 1). All statistical analyses were performed using STATA svy commands (Stata Corp, College Station, Texas).

#### RESULTS

Table 2 shows the incidence of heroin use from ages 19 to 35 as a function of baseline (age 18) prescription opioid exposure. Among adolescents who reported medical use and nonmedical misuse of prescription opioids, individuals who reported nonmedical misuse before medical use had a higher incidence of subsequent heroin use (15.1%) than adolescents who reported nonmedical misuse after medical use of prescription opioids

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As illustrated in Table 2, adolescents who reported medical prescription opioid use without a history of nonmedical misuse had higher odds of heroin use after the age of 18 compared to population controls (AOR=1.7, 95% CI=1.1, 2.6). Adolescents who reported exclusively nonmedical prescription opioid misuse had greater odds of heroin use after the age of 18 relative to non-opioid exposed population controls (AOR=5.5, 95% CI=3.6–8.2). Moreover, adolescents who reported medical use after initiating nonmedical misuse had greater odds of subsequent heroin use relative to non-opioid exposed population controls (AOR=4.3, 95% CI=2.4–7.6). The odds of any heroin use were similar between adolescents who were prescribed opioids after nonmedical misuse and adolescents who reported only nonmedical use (see Supplemental Table A).

As shown in Table 2, among adolescents in the 1997–2000 cohort who reported nonmedical misuse before medical use had a higher incidence of any subsequent heroin use (21.6%) than adolescents who reported nonmedical misuse after medical use of prescription opioids (9.2%). Adolescents who reported nonmedical prescription opioid misuse without a history of medical prescription opioid use had the highest incidence of heroin use between ages 19 and 35 (31.8%). Interaction analysis revealed the associations of (1) medical only use with later heroin use and (2) nonmedical only misuse (compared to population controls) with later heroin use were significantly stronger in the 1997–2000 cohort compared to earlier cohorts.

The frequency of heroin use from ages 19 to 35 and the initiation of any heroin use in young adulthood between ages of 19 and 22 and found similar results (see Supplemental Tables B and C). Finally, adolescents excluded from this study who had a history of using heroin at age 18 or earlier at baseline (n=179) had initiation sequences as follows: (a) 25.4% used heroin only, (b) 13.5% used heroin followed by nonmedical misuse of prescription opioids, (c) used heroin and nonmedical misuse of prescription opioids the same year (38.9%), and misused prescription opioids followed by heroin (22.2%) (see Supplemental Table D).

#### DISCUSSION

This is the first national prospective study to examine the relationships between adolescents' prescription opioid use and misuse and subsequent heroin use over a 17-year period. There was an increased risk for any subsequent heroin use among adolescents who had already initiated nonmedical prescription opioid misuse and adolescents prescribed opioids in more recent cohorts. The stronger association between medical use of prescription opioid and transitioning to heroin use in more recent cohorts could be due to the changes in opioid prescribing.

While self-report drug use data in the MTF study are reliable and valid,<sup>2,4</sup> studies on youth suggest that misclassification and under-reporting of drug use occurs.<sup>2,12</sup> Furthermore,

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students absent from class at the time of data collection and students who dropped out of school were missing from our data, suggesting that our findings are conservative estimates of heroin use.<sup>4</sup> Finally, medical and nonmedical use of prescription opioids during adulthood was not examined and more research is needed to examine such use. Trajectories of heroin use as well as the length of time from use of medical and nonmedical prescription opioids to use of heroin are important areas of future research.

#### CONCLUSIONS

Nearly one in three adolescents who reported nonmedical prescription opioid misuse went on to report any heroin use in adulthood between ages 19 and 35 in recent cohorts. These findings reinforce the critical role of drug screening for prior nonmedical misuse and providing brief interventions when misuse is indicated.<sup>13,14</sup> Recovery goals and treatment preferences should be discussed with patients indicating misuse to maximize treatment initiation.<sup>15</sup> This strategy could help clinicians reduce subsequent heroin use in patients prescribed opioids.

#### **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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#### Table 1.

Descriptive statistics for the longitudinal sample at baseline (n = 11,012)

Baseline characteristics (modal age 18)	$(\mathbf{n})^a \%^b$	(n) % missing
Sex		
Male	(5415) 48.2%	(2) 0 020/
Female	(5595) 51.8%	(2) 0.02%
Race/Ethnicity		
White	(8310) 74.1%	
Black	(1140) 11.5%	(0) 0.00/
Hispanic	(688) 6.5%	(0) 0.0%
Other race	(874) 8.0%	
Parental Education		
At least one parent has a college degree or higher	(6085) 42.4%	(400) 4 40(
Neither parent has a college degree	(4437) 57.6%	(490) 4.4%
Region		
Northeast	(2430) 21.4%	
Midwest	(3058) 27.9%	(0) 0.0%
South	(3553) 33.2%	(0) 0.0%
West	(1971) 17.5%	
Urbanicity		
Large metropolitan statistical area	(2882) 26.0%	
Other metropolitan statistical area	(5054) 45.7%	(0) 0.0%
Non-metropolitan statistical area	(3076) 28.3%	
12th Grade Cohort Year		
1976–1980	(2347) 19.7%	
1981–1985	(2395) 20.6%	
1986–1990	(2281) 21.4%	(0) 0.0%
1991–1996	(2396) 23.5%	
1997–2000	(1593) 14.8%	
Substance use at baseline		
Did not binge drink during the past two weeks	(6575) 70.1%	(550) 5.00(
Engaged in binge drinking during the past two weeks	(3887) 29.9%	(550) 5.0%
Did not use <i>cigarettes</i> during the past 30 days	(6778) 69.9%	(292) 2 (0)
Used cigarettes during the past 30 days	(3952) 30.1%	(282) 2.6%
Did not use marijuana during the past 30 days	(7002) 76.8%	(122) 2 90/
Used marijuana during the past 30 days	(3587) 23.2%	(423) 3.8%
Medical/nonmedical opioid subgroups at baseline		
Non-use	(7812) 80.2%	
Medical use only	(1098) 11.2%	(721) 6.5%

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Baseline characteristics (modal age 18)	(n) <sup><i>a</i></sup> % <sup><i>b</i></sup>	(n) % missing
Medical use before nonmedical misuse	(498) 3.7%	
Nonmedical misuse before medical use	(280) 1.5%	
Nonmedical misuse only	(603) 3.3%	

Note:

<sup>a</sup>Sample sizes were unweighted.

b Percentages were weighted. Individuals who reported any lifetime heroin use at baseline (modal age 18) were excluded (n = 179).

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# Table 2.

Prevalence and adjusted odds of heroin use over 17 years as a function of medical use and nonmedical misuse history of prescription opioids during adolescence

Baseline opioid exposure (modal age 18)	All baseline Heroin	cohorts (1976–2000) ise ages 19 to 35	Older baselin Heroin u	e cohorts (1976–1996) ise ages 19 to 35	Recent baselin Heroin u	e cohorts (1997–2000) ise ages 19 to 35
	%	AOR (95% CI) <sup>a</sup>	%	AOR (95% CI) <sup>a</sup>	%	AOR (95% CI) <sup>a</sup>
Lifetime medical use/nonmedical misuse						
No medical or nonmedical use	2.1%	Reference	2.0%	Reference	2.4%	Reference
Medical use only	3.7%	$1.65 \ (1.06, 2.57)^{*}$	3.2%	1.51 (.928, 2.48)	7.1%	2.68 (1.01, 7.17)*
Medical use followed by nonmedical use	5.5%	$1.93 \ (1.05, 3.55)^{*}$	4.8%	1.81 (.904, 3.63)	9.2%	2.90 (.911, 9.25)
Nonmedical misuse followed by medical use	15.1%	4.30 (2.41, 7.67) ***	13.8%	4.88 (2.59, 9.20) ***	21.6%	6.84 (2.33, 20.0) <sup>***</sup>
Nonmedical use only	16.4%	5.52 (3.67, 8.29) ***	12.6%	4.44 (2.87, 6.84) <sup>***</sup>	31.8%	$13.4~(5.46, 32.9)^{***}$
	<i>b</i> (n = 8449)	c(n = 8143)	$b_{(n = 7390)}$	$b_{(n = 7117)}$	$b_{(n = 1059)}$	$b_{(n = 939)}$

\* p<.05,

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\*\*\* p<.001 <sup>a</sup>All analyses control for race/ethnicity (i.e., White, Black, Hispanic, Other race), sex (i.e., Male and Female), highest level of parental education, geographic region (i.e., Northeast, Northcentral, South and West), metropolitan statistical area (i.e., large MSA, other MSA, and non-MSA), and baseline cohort year, and baseline measures of past two week binge drinking, past 30 day marijuana use, and past 30 day cigarette use.

(modal age 18) were excluded (n = 179). A random one-sixth of the overall panel sample received the questions regarding medical and nonmedical prescription opioid use. All percentages and adjusted odds b Sample size varies based on cohorts, attrition in the panel sample and missing data on the control variables (sample sizes are unweighted). Individuals who reported any lifetime heroin use at baseline ratios (AOR) use attrition weights at age 35.