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## Trajectories of Cannabis Use and Risk for Opioid Misuse in a Young Adult Urban Cohort

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## Abstract

**Background**—Although much of the attention surrounding the opioid epidemic has focused on rural and suburban Whites and prescription opioids, heroin overdoses among urban Blacks are on the rise. While some argue that legalization of cannabis will combat the epidemic, there are concerns it ignores the shift in the epidemic and could increase vulnerability to opioid misuse. The goal of this study is to examine the association between cannabis use from adolescence to young adulthood with opioid misuse in a primarily urban Black cohort.

**Methods**—Data are from a study of 580 youth (85% Black, 67% low SES) residing in Baltimore City followed from ages 626. Cannabis trajectories were identified between ages 14–26 using group-based trajectory modeling. Logistic regressions were conducted to examine the impact of trajectories on opioid misuse in young adulthood adjusting for individual, neighborhood and peer factors. Opioid misuse was defined as using heroin or narcotics or painkillers without a prescription between ages 1926.

**Results**—Four cannabis trajectories were identified: *Low/Non-Users* (59.7%) *Adolescent Onset Limited* (19.5%), *Young Adult Onset* (10.8%), and *Adolescent Onset Chronic* (10.0%). *Adolescent Onset Chronic* cannabis users had the highest rate of opioid misuse (44.8%) followed by *Adolescent Onset Limited* (18.8%), *Young Adult Onset* (14.8%) and *Low/Non-Users* (8.3%). Prevalences were significantly higher for *Adolescent Onset* group relative to *Low/Non-Users* even after adjustment for neighborhood factors.

Corresponding Author: Beth A. Reboussin, Department of Biostatistics and Data Science, Wake Forest School of Medicine, Medical Center Boulevard, Winston-Salem, NC, 27157, USA. brebouss@wakehealth.edu; Telephone: 336-713-5213. **Contributors:** BAR designed the research question, conducted the study analyses and wrote the first draft of the manuscript. NSI originated the study idea. All authors provided critical feedback and approved final submission.

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**Conclusions**—Adolescent onset cannabis use is associated with opioid misuse in young adulthood among urban Blacks even after adjustment for neighborhood factors associated with opioid misuse.

#### Keywords

Blacks; cannabis; longitudinal patterns; opioids; urban

#### 1. Introduction

The opioid epidemic remains a public health emergency with an estimated 130 Americans dying each day from an opioid overdose (Hedegaard et al., 2018). Much of the national attention surrounding the epidemic has focused on White suburban and rural users and the over-prescription of painkillers. However, recent data suggest a shift in the epidemic with heroin more often reported as the first opioid of use rather than prescription opioids (Cicero et al., 2017, 2018). This shift may be due to the success of prescription opioid supply chain reduction efforts (Dart et al., 2015) as well as the increased availability of heroin; a cheaper alternative with a comparable high (Cicero et al., 2014; Compton et al., 2016).

With the majority of opioid overdoses occurring among Whites, less attention has been given to the impact of the epidemic on the Black community. However, there have been substantial increases in opioid overdoses among Blacks from 3.5 per 100,000 in 2000 to 14.0 per 100,000 in 2018 (CDC, 2020). In fact, opioid mortality rates have been increasing more rapidly over the past five years for Blacks compared to Whites (James & Jordan, 2018) with the sharpest increase in opioid overdoses occurring among Blacks living in urban areas (Lippold et al., 2019). Blacks may be at an increased risk for opioid overdoses as heroin and injection drug use has been on the rise in many urban centers in the US where Blacks disproportionately reside (Brighthaupt et al., 2019). In fact, heroin overdoses more than quadrupled for Blacks from 0.9 per 100,000 in 2000 to 4.9 per 100,000 in 2018 (CDC, 2020; SAMHSA, 2020). It is suspected that some of the increase in opioid overdoses in the Black community may be attributable to the more potent fentanyl-laced heroin entering the illict drug supply in urban areas (Katz & Goodnough, 2017; Spencer et al., 2019; SAMHSA, 2020).

Despite alarming increases in overdoses in the Black community and the national framing of the epidemic as a public health problem, Blacks are more likely to be arrested as a result of their opioid use, while Whites are more often refered to treatment (Human Rights Watch, 2009). Hence, the public health focus remains on prescription opioids and physician prescribing practices. In fact, some states are attempting to modify existing medical cannabis laws to allow patients to substitute their prescription opioids with medical cannabis to treat chronic pain as a means to attenuate the epidemic, despite conflicting evidence of the impact of these laws (Bachhuber et al., 2014; Bradford et al., 2018; Chihuri & Li 2019; Flexon et al., 2019; Nugent et al., 2017; Shover et al., 2019; Wen et al., 2015; Wen & Hockenberry, 2018). Not only does this approach ignore the role heroin is playing in the epidemic, it ignores the fact that Blacks are less likely to be prescribed opioids than Whites (Green et al., 2003; Meghani et al., 2012).

Efforts to legalize medical cannabis also ignore preliminary data suggesting cannabis use may increase vulnerability to opioid misuse. This could place individuals no necessarily prescribed opioids, like Blacks, at increased risk for opioid misuse. Pharmacologic evidence suggests that exposure to cannabis increases opioid intake and impacts the rewarding properties of opiates (Chen et al., 1990; Corchero et al., 1997; Ellgren et al., 2007; Hurd et al., 2014; Ledent et al., 1999; Manzanares et al., 1998, 1999; Tanda et al., 1997). Animal studies have demonstrated a cross-sensitization for a wide range of delta-9tetrahydrocannabinol (THC) doses and opioids (Cadoni et al., 2001; 2008; Gorriti et al., 1999; Lamarque et al., 2001). Finally, clinical studies suggest cannabis use may lead to behavioral disinhibition, which can increase the risk of using opioids (Fergusson et al., 2003; Lopez-Quintero et al., 2011; Lynskey et al, 1998). Longitudinal epidemiologic data examining the cannabis-opioid causal pathway, however, are limited. In a twin study, use of cannabis before the age of 17 was significantly associated with opioid misuse and dependence in adulthood (Lynskey et al., 2003). A study using data from the National Epidemiologic Survey of Alcohol and Related Conditions (NESARC) found that cannabis use before the age of 18 was associated with prescription opioid misuse between ages 18–25 (Fiellin et al., 2013) while another study, also using NESARC data, found that cannabis use at baseline was associated with prescription opioid misuse and disorder at follow-up (Olfson et al., 2018). These few studies examining the association between cannabis and opioids were limited to examining cannabis use at one point in time and were conducted in primarily White samples.

In the present study, we seek to identify trajectories of cannabis use from ages 14–26 in a sample of primarily low-income, urban-dwelling Blacks and examine their impact on opioid misuse in young adulthood (ages 19-26). We focus on trajectories because there is likely a great deal of heterogeneity in longitudinal patterns of cannabis use that may reflect different etiologic pathways and different susceptibilities to opioid misuse (Ellickson et al., 2004; Kelly & Vuolo, 2018; Lee et al., 2018; Scalco & Colder, 2017). Because individuals are embedded within social contexts, an examination of socioecological factors is necessary to understand etiological pathways associated with cannabis use over time. Therefore, we examine whether neighborhood violence, neighborhood disorder, deviant peer affiliation, and early use of other drugs are predictive of cannabis trajectories in addition to individual level socio-demographics. These factors are particularly salient in impoverished urban neighborhoods where residents may be unable to monitor activities in their neighborhoods and, as a result, drug use (both licit and illicit) may flourish promoting ease of availability as well as reinforcement of positive drug-using norms (Sampson et al., 1997). These neighborhoods also often lack the social capital to provide positive experiences for youth which can result in the formation of deviant peer groups where values conducive to drug use can arise and spread (Dishion et al., 1999; Patterson et al., 1992). In addition, early use of alcohol and tobacco may provide a surrogate both for availability of drugs and exposure to positive drug -taking norms, as well as a possible 'common liability' to use other drugs and may, thus, be important to consider in relation to cannabis use trajectories, as well as opioid misuse (Degenhardt et al., 2009; Palmer et al., 2009). The purpose of this study is to provide longitudinal evidence as to whether cannabis use increases vulnerability to opioid misuse after adjusting for socioecological risk factors particularly salient in

low-income, Black communities to better understand potential unintended consequences of cannabis legalization in these vulnerable communities.

## 2. Method

#### 2.1 Sample

Data were derived from a randomized prevention trial conducted by the Baltimore Prevention Research Center at the JHU Bloomberg School of Public Health. A total of 798 children and families entering 1<sup>st</sup> grade in nine Baltimore City public elementary schools in 1993 were recruited to participate in two school-based, preventive interventions targeting early learning and aggressive and disruptive behavior. Students were randomly assigned to one of two intervention or control classrooms (9 schools, 3 classrooms per school). Interventions were provided during the 1<sup>st</sup> grade year. The sample of 798 children was predominantly Black (85%) and 46% were male. The mean age at entrance into first grade was 6.2 years (SD=0.37). About 2/3 of children were receiving free or reduced price meals; a proxy for low socioeconomic status. Annual structured interviews were conducted through age 26 in 2013 using an audio-computer assisted interview to increase accurate reporting of sensitive behavior. The sample for this analysis included 580 youth with an assessment in 8<sup>th</sup> grade and at least one young adult (ages 19–26) assessment. This sample in 1<sup>st</sup> grade was 87% Black, 54% male, and 71% were receiving free or reduced-price meals.

### 2.2 Measures

**Frequency of Substance Use**—Frequency of cannabis, opioid, alcohol and tobacco use in the past year was assessed annually with questions adapted from the Monitoring the Future (MTF) study (Johnston et al., 2000). Participants reported on the frequency of use in the past year on a 0–7 Likert scale: (0=none, 1=once, 2=twice, 3=3–4 times, 4=5–9 times, 5=10–19 times, 6=20–39 times, 7=40 or more times). Data on opioid misuse were collected beginning at age 19. Opioid misuse included heroin and the misuse of prescription narcotics (e.g., morphine, oxycodone, hydrocodone, hydromorphone, etc.). Participants who reported misusing any of these substances in the past year at any of the assessments between ages 19 and 26 were coded as positive for opioid misuse. Data on cannabis, alcohol and tobacco use were collected annually beginning at age 14. Past year frequency of use of cannabis from ages 14–26 was used for trajectory modeling. Early use of alcohol and tobacco was included as a covariate and defined as using the substance before age 15.

**Neighborhood Disorder**—Perceptions of neighborhood disorder were assessed in 8<sup>th</sup> grade using 10 items from the Neighborhood Environment Scale (Elliott et al., 1985). This scale contains true- false items that assess neighborhood safety, violent crime, and drug use and sales. Items are rated on a 4-point Likert scale (1=not at all true to 4=very true) and summed to create a total score.

**Neighborhood Violence**—Exposure to violence in the community was measured in 8<sup>th</sup> grade using the Children's Report of Exposure to Violence (Cooley-Quille et al., 1995). This is a self-report measure of exposure to violence that is directly witnessed, as well as victimization. The events include being beaten up, robbed or mugged, stabbed or shot,

witnessing someone else experience one of these events or witnessing a murder in the community. Youth who experienced any exposure to violence were compared to all others using a binary indicator.

**Deviant Peer Affiliation**—We used a subset of items from Capaldi and Patterson's youth self-report scale to measure deviant peer affiliation in sixth, seventh and eighth grades (Capaldi & Patterson, 1989). Youth were asked in multiple choice format to indicate how many of their friends (1 = none to 5 = all of them) have engaged in antisocial behavior, such as hitting or threatening someone, stealing, and damaging others' property and how many of their friends have used marijuana. This scale was the sum of seven items with higher scores indicating more deviant peer affiliation.

**Sociodemograyhics**—The school district provided information on students' sex and ethnicity. School records and parent reports indicating each student's free and reduced-price meal status were collapsed into a dichotomous variable of free or reduced price meals versus self-paid meals at any time during high school as an individual indicator of student socioeconomic status. Intervention status was coded 1 for youth in a 1<sup>st</sup> grade intervention classroom and 0 otherwise.

#### 2.3 Analysis

Group-based trajectory modeling was used to identify patterns of past-year cannabis use frequency from age 14 to 26 (Nagin & Tremblay, 1999). Models used zero-inflated Poisson distribution to account for the large number of youth that did not use cannabis. Linear and quadratic terms for each trajectory group were included and compared. One to five group models were considered. The best model was selected based on a combination of the Bayesian information criteria (BIC), entropy, group interpretability, and having reasonably large groups (at least 10% of the sample). Trajectory models were constructed using PROC TRAJ in SAS version 9.4. Maximum likelihood estimation was used to estimate model parameters. Participants were assigned to the cannabis trajectory group with the highest probability of membership. Bivariate associations between trajectory group membership and measures of individual, peer and neighborhood characteristics were tested using chi-squared tests for categorical outcomes and F- tests for continuous measures. Bivariate associations between cannabis trajectory membership and opioid misuse in young adulthood were tested using chi-squared tests. We examined the relationship between cannabis trajectories and opioid misuse overall, as well as prescription opioid misuse and heroin separately. A logistic regression model was then fitted to estimate the strength of the association in specific cannabis use trajectory groups before and after adjustment for socioecological factors and other substance use behaviors.

## 3. Results

For modeling cannabis trajectories from age 14 to 26, the BIC increased with the addition of each trajectory group, but the rate of improvement declined and reached an elbow at four groups (Table 1). Entropy measures indicated the classification accuracy was adequate for all models. The four-group cannabis trajectory model is presented in Figure 1. The most

common trajectory was a group with little to no cannabis use between the ages of 14 and 26 (*Low/Non-Users*; 59.7%). The largest cannabis user group was a group that was using cannabis by age 14 with increasing frequency until age 18 followed by declines in use (*Adolescent Onset Limited*; 19.5%). A second group was also using cannabis by age 14, but their frequency of use increased into adulthood (*Adolescent Onset Chronic*; 10.0%). The third group of cannabis users did not begin using cannabis until after the age of 18 (*Young Adult Onset*; 10.8%).

As shown in Table 2, after assigning youth to their most likely cannabis trajectory group, youth in the *Young Adult Onset, Adolescent Onset Limited*, and *Adolescent Onset Chronic* trajectory groups were more likely to be male, exposed to violence in their neighborhood and to be early drinkers compared to those in the *Low/Non-User* group. Both *Adolescent Onset Limited* and *Adolescent Onset Chronic* trajectory groups were more likely to affiliate with deviant peers, live in disordered neighborhoods and initiate tobacco use early compared to *Low/Non-User* and *Young Adult Onset* groups.

As shown in Figure 2, *Adolescent Onset Chronic* cannabis users had the highest rates of opioid misuse (44.8%), prescription opioid misuse (39.7%) and heroin use (13.8%) followed by *Adolescent Onset Limited* (18.8%, 13.4%, 8.9%), *Young Adult Onset* (14.8%, 13.1%, 3.3%) and *Low/Non-Users* (8.3%, 6.9%, 2.0%). Overall, 14.7% of our sample misused opioids in young adulthood. Specifically, 12.1% misused prescription opioids and 4.7% used heroin. Only 20% of opioid users reported using opioids more than five times in the past year between ages 19 and 21, increasing to 33–47% between ages 22 and 26.

In unadjusted logistic regression models presented in Table 3, Adolescent Onset Limited and Adolescent Onset Chronic cannabis use trajectories were significantly associated with opioid misuse overall and prescription opioid misuse and heroin use specifically in young adulthood. The effect sizes were highest for the Adolescent Onset Chronic cannabis use trajectory group compared to Low/Non-Users (OR=9.0, 95% CI=4.7, 17.0; OR=8.9, 95%CI=4.6, 17.4; OR=7.8, 9'%CI=2.7, 22.5, respectively) with effect sizes for the Adolescent Onset Limited (OR = 2.5, 95% CI=1.4, 4.7; OR=2.1, 95% CI=1.1, 4.1; OR=4.8, 95% CI=1.8, 12.9) trajectory group much smaller. The Young Adult Onset trajectory was not associated with opioid misuse in unadjusted models. Blacks had a significantly reduced risk of opioid misuse (OR=0.4, 95%CI=0.2, 0.8), prescription opioid misuse (OR=0.4, 95%CI=0.2, 0.8) and heroin use (OR=0.4, 95%CI=0.2, 1.0). Males (OR=1.8; 95%CI=1.1, 2.9), early drinkers (OR=1.9; 95%CI=1.1, 3.3) and early tobacco users (OR=1.8; 95%CI=1.2, 2.9) were significantly more likely to report opioid misuse and, in particular, heroin use (OR=5.2, 95% CI=1.8, 15.2 for males OR=3.0, 95% CI=1.0, 8.9 for early drinkers and OR=2.6, 95% CI=1.2, 5.6 for early tobacco users). Affiliating with deviant peers was significantly associated with an increased risk of heroin use (OR=1.7; 95%CI=1.0, 2.7).

In fully adjusted models, the associations between *Adolescent Onset Limited* and *Adolescent Onset Chronic* trajectories and opioid misuse including prescription opioids and heroin remained significant. However, the magnitude of the association between the *Adolescent Onset Limited* (aOR=3.4, 95%CI=1.2, 10.0) and *Adolescent Onset Chronic* 

(aOR=4.7 95%CI=1.5, 14.8) trajectories and heroin use were diminished, while the magnitude of the association for prescription opioid misuse changed very little (aOR=2.1; 95%CI=1.1, 4.4 and aOR=8.1, 95%CI=3.9, 16.8). Blacks retained a significantly reduced risk for opioid misuse, specifically prescription opioid misuse (aOR=0.5, 95%CI=0.2, 0.9) and male gender remained significant for heroin use (aOR=4.6, 95%CI=1.5, 13.9). Affiliation with deviant peers, and early use of other substances did not retain statistical significance in fully adjusted models.

## 4. Discussion

In this sample of primarily low-income, urban Blacks, we identified four trajectories of cannabis use reflecting variation in timing of onset and patterns of use, consistent with other studies in urban samples (Brook, 2011; Finlay et al., 2012; Juon et al., 2011; Reboussin et al., 2018). Male gender, early onset drinking and exposure to neighborhood violence were predictive of cannabis using trajectories regardless of timing of onset relative to the non-using trajectory. In contrast, affiliation with deviant peers and living in more disordered neighborhoods distinguished Adolescent Onset (both Chronic and Limited) from Young Adult Onset cannabis trajectories. Involvement with deviant peers and living in disordered neighborhoods during adolescence may result in increased availability and exposure to positive drug-taking norms placing individuals at risk for early cannabis use (Dishion et al., 1999; Patterson et al., 1992; Sampson et al., 1997). Black youth are particularly vulnerable to these neighborhood level risk factors for early cannabis use as they disproportionately reside in socially-disadvantaged neighborhoods characterized by poverty, crime, violence. and physical disorder (Garbarino, 1995; Wallace and Muroff, 2002). We also found an association between early tobacco use and Adolescent Onset cannabis trajectories. This is consistent with studies showing that co-use of cannabis and tobacco is common (Agrawal et al., 2012; Lemyre et al., 2019; Schauer et al., 2015). Further, most users of cigarillos also report past month blunt use, i.e. smoking cannabis in a cigarillo wrapper (Antognoli et al., 2018). Therefore, early tobacco use, possibly in the form of cigarillos, which are disproportionately used by Blacks (Cohn et al., 2016), may result in an earlier transition to cannabis use due to the use of a common vehicle for administering tobacco and cannabis.

Prevalence of opioid misuse overall in this sample was almost three times current rates in the general population aged 18–25 (14.7% vs 5.6%) (SAMSHA, 2019). Opioid misuse was primarily misuse of prescription opioids not heroin, although the prevalence of heroin use was almost ten times that in the general population aged 18–25 (4.7% vs 0.5%). Prevalence of prescription opioid misuse and heroin use were also higher in our sample than for Blacks in the general population aged 18–25 (4.6% and 0.1%, respectively). Higher rates of heroin use in this sample is not surprising given that heroin has been endemic in Baltimore City since the 1960s (Agar & Reisinger, 2002; Schwartz et al., 2015). The higher prevalence of prescription opioid misuse is somewhat surprising given evidence of physicians' underprescribing of opioids to Blacks (Burgess et al., 2008). However, recent data find that almost two-thirds of Black prescription opioid misusers get opioids from sources other than a physician (SAMHSA, 2020). Baltimore City in particular has seen increases in morbidity and mortality due to prescription drug misuse since 2000 consistent with national trends (Wejnert, 2016). Male gender, affiliation with deviant peers, early drinking and early tobacco

use were associated with increased risk of heroin but not prescription opioid misuse and may be reflective of increased access to heroin, alcohol, and tobacco in deviant peer groups during adolescence in low-income, urban neighborhoods.

Ever after adjustment for other risk factors, *Adolescent Onset Chronic* cannabis use conferred an eight-fold increased risk of prescription opioid misuse and an almost five-fold increased risk of heroin use compared to *Low/Non-Use*. Cannabis use that begins early but declines in young adulthood (*Adolescent Onset Limited*) was still associated with an increased risk of prescription opioid misuse and heroin use although the effect was much smaller (two to three times the risk, respectively). Findings for *Young Adult Onset* cannabis users were not statistically significant. These results are consistent with other prospective epidemiologic studies in primarily White samples demonstrating that early cannabis use is a risk factor for opioid misuse (Lynskey et al., 2003; Fiellen et al. 2013). These findings demonstrate that even after adjustment for other risk factors that are particularly salient among Blacks living in urban neighborhoods, adolescent cannabis use, whether it continues into young adulthood or declines, further increases their vulnerability for opioid misuse.

It is possible that some of the association between cannabis use initiated in adolescence with opioid misuse in young adulthood may be driven by shared morphology and neurobiological systems (Wiese & Wilson-Poe, 2018). For example, there is evidence that receptors within the endocannabinoid and opioidergic systems are found in many of the same neurobiological regions underlying reward and reinforcement, suggesting overlapping expression (Wiese & Wilson-Poe, 2018). These two systems are integrally connected such that in the nucleus accumbens, increased cannabinoid administration increases endogenous opioid levels (Caillé & Parsons, 2006; Valverde et al., 2001).

At the behavioral level, cannabis use in adolescence may increase exposure to drug-using peers or access to illicit mg markets, particularly for Blacks living in urban areas, that may confer an increased risk for using other substances such as opioids (Fergusson et al., 2003; Lopez-Quintero et al., 2011; Lynskey et al., 2003; Reboussin et al., 2016; Wilcox et al., 2002). While the associations between adolescent onset cannabis use and opioid misuse remained significant after adjustment for factors associated with both cannabis use and opioid misuse, including early use of other substances and affiliation with deviant peers, there was a notable attenuation in the magnitude of the effects for heroin use suggesting that some of the impact of early cannabis use in urban Black samples may be mediated by affiliation with deviant peers and early use of other substances, while the impact on prescription opioid misuse may be more independent of these environmental factors and potentially driven by brain cross-sensitization. These findings are consistent with family studies demonstrating the shared environment plays little role in the nonmedical use of analgesics with heritability playing a moderate role (Gillespie et al., 2019; Kendler et al., 2003).

Limitations of the study should be noted. First, we relied on self-report to measure drug use, which is subject to bias. Biological assays of drug use would have strengthened this study. Second, this study did not assess opioid use until age 19, so that we are unable to account for prior opioid use or draw conclusions about its' incidence. We also did

not collect data on the source of prescription opioids (e.g. street markets, overprescribing or illegal prescribing), which would have been helpful in understanding mechanisms. These data were also collected prior to the introduction of fentanyl into the illicit drug market, which may explain the higher rates of prescription opioid misuse relative to heroin misuse in this sample. Third, this study was limited to Baltimore City. Although national probability studies have provided critical information on drug use in the U.S. population as a whole, they are less informative in understanding prevalence in subgroups; particularly socioeconomically disadvantaged, ethnic minority populations living in large urban areas Our ability to accurately reflect minority drug use in the context of the urban neighborhoods and illuminate within group differences makes this a unique contribution to the literature. Lastly, our study followed up participants through young adulthood and future research is needed to investigate whether cannabis use during adolescence similarly confer risk for opioid misuse later into adulthood.

#### Implications

Our findings highlight that the magnitude of the risk of opioid misuse in young adulthood seems dependent upon the course of cannabis use, with the greatest risk conferred by cannabis use that begins in adolescence and escalates into young adulthood. Early, schoolbased prevention programs that address cannabis use among primarily low-income, urban Blacks are warranted to help prevent opioid misuse in young adulthood in this vulnerable population. Mechanistically, our results are in line with pharmacologic findings suggesting a cross-sensitization between cannabis and opioids. However, some of the association between cannabis and heroin use was explained by neighborhood factors suggesting the environment plays a larger role in the risk for heroin use than it does for prescription opioid misuse in this sample. Therefore, prevention programs that also target the neighborhood context are especially important for preventing heroin use among Blacks. As shown in Reboussin et al (2019), prosocial neighborhood activities (e.g. youth playing outside, adults interacting in a positive manner) have the potential to modify the negative effects of living in physically disordered, urban environments and should also be considered when developing interventions. While cannabis legalization may provide alternative pain treatment for primarily White adult patients who would normally be prescribed opioids, it ignores the impact of legalization on low-income, urban Blacks who are less often prescribed opioids. Legalization instead has the potential to increase adolescent cannabis use through greater availability and exposure to cannabis placing youth at increased risk for later opioid misuse, both prescription opioids and heroin Therefore, it is important that policymakers and clinicians consider and closely monitor the potential unintended consequences of cannabis legalization on these vulnerable populations.

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## Highlights

- Four cannabis trajectories were identified reflecting differences in timing of onset and progression
- Adolescent onset cannabis trajectory groups were most likely to affiliate with deviant peers, live in disordered neighborhoods and initiate tobacco use early
- The adolescent onset chronic trajectory group had the highest rates of opioid misuse even after adjustment for individual, peer and neighborhood factors

Reboussin et al.

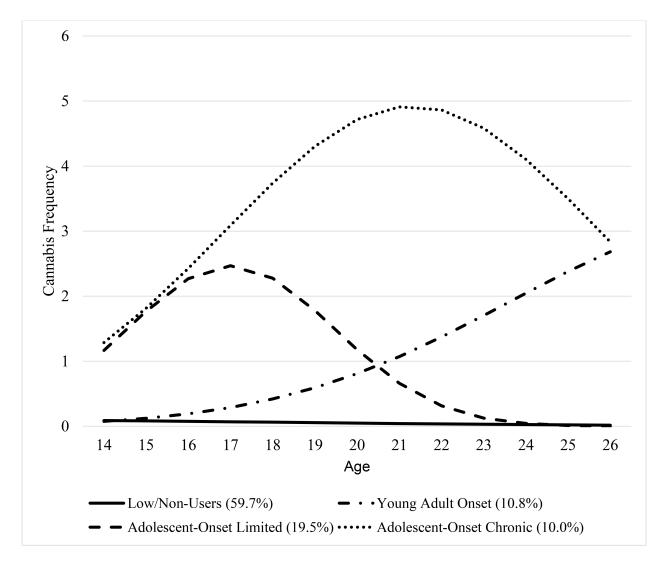
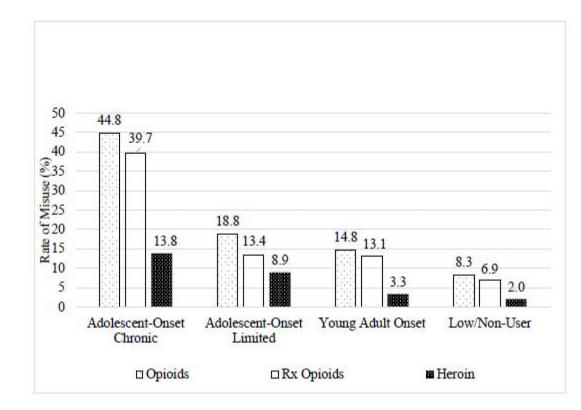


Figure 1.

Cannabis Trajectories Ages 14-26



## Figure 2.

Rates of Opioid Misuse Between Ages 19-26 by Cannabis Trajectory Group

#### Table 1.

Fit indices for cannabis trajectory group solutions.

Number of Trajectory Groups	BIC	Entropy	Minimum Class Size (%)
1	-10780.2	1.00	100.0
2	-7538.1	0.99	29.1
3	-6791.6	0.98	17.2
4	-6359.0	0.98	10.0
5	-6279.9	0.96	9.8
6	-6147.8	0.95	5.4

Drug Alcohol Depend. Author manuscript; available in PMC 2021 October 01.

Page 18

## Table 2.

Individual, peer and neighborhood factors by cannabis trajectory group

Characteristic	Overall N=580	Low/Non-Users N=349	Young Adult Onset N=61	Adolescent Onset Limited N=112	Adolescent Onset Chronic N=58	
Binary indictors	N (%)	N (%)	N (%)	N (%)	N (%)	p-value
Male Sex	314 (54.1)	171 (49.0)	38 (62.3)	66 (58.9)	39 (67.2)	0.016
Black Race	505 (87.1)	304 (87.1)	56 (91.8)	100 (89.3)	45 (77.6)	0.096
Free/Reduced Price Lunch	369 (70.0)	214 (66.5)	39 (73.6)	73 (73.7)	43 (81.1)	0.110
Intervention Group	378 (65.2)	234 (67.1)	41 (67.2)	65 (58.0)	38 (65.5)	0.366
Violence Exposure	334 (57.6)	167 (47.8)	43 (70.5)	86 (76.8)	38 (65.5)	<0.001
Early Alcohol Use	385 (66.4)	196 (56.2)	45 (73.8)	95 (84.8)	49 (84.5)	<0.001
Early Tobacco Use	195 (33.6)	77 (22.1)	19 (31.2)	68 (60.7)	31 (53.4)	<0.001
Scales	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	p-value
Deviant Peer Affiliation	1.56 (0.64)	1.58 (0.56)	1.58 (0.72)	1.74 (0.68)	1.72 (0.81)	0.0004
Neighborhood Disorder	1.73 (0.64)	1.66 (0.60)	1.70 (0.70)	1.81 (0.62)	1.97 (0.73)	0.0032

### Table 3

Associations Between Cannabis Trajectory Groups, Socioecological Factors and Opioid Misuse in Young Adulthood (age 19–26)

Cannabis Trajectory	Opioids		Prescription Opioids		Heroin	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Non-Users	1.0	1.0	1.0	1.0	1.0	1.0
Young Adult Onset	1.9 (0.8, 4.3)	1.8 (0.8, 4.1)	2.0 (0.9, 4.8)	2.0 (0.8, 4.9)	1.7 (0.3, 8.2)	1.4 (0.3, 7.2)
Adolescent Onset Limited	2.5 (1.4, 4.7)	2.2 (1.2, 4.4)	2.1 (1.1, 4.1)	2.1 (1.0, 4.4)	4.8 (1.8, 12.9)	3.4 (1.2, 10.0)
Adolescent Onset Chronic	9.0 (4.7, 17.0)	7.2 (3.6, 14.4)	8.9 (4.6, 17.4)	8.1 (3.9, 16.8)	7.8 (2.7, 22.5)	4.7 (1.5, 14.8)
Male Sex	1.8 (1.1, 2.9)	1.5 (0.9, 2.6)	1.3 (0.8, 2.2)	1.1 (0.6, 1.9)	5.2 (1.8, 15.2)	4.6 (1.5, 13.9)
Black Race	0.4 (0.2, 0.8)	0.5 (0.2, 0.9)	0.4 (0.2, 0.8)	0.5 (0.2, 0.9)	0.4 (0.2, 1.0)	0.4 (0.2, 1.2)
Free/Reduced Price Lunch	1.1 (0.7, 1.9)	1.0 (0.6, 1.8)	1.2 (0.7, 2.1)	1.1 (0.6, 2.0)	0.8 (0.4, 1.8)	0.8 (0.3, 1.8)
Intervention Group	1.0 (0.6, 1.6)	1.0 (0.6, 1.7)	1.0 (0.6, 1.6)	1.0 (0.6, 1.7)	0.9 (0.4, 2.0)	0.9 (0.4, 2.1)
Violence Exposure	1.3 (0.8, 2.0)	1.0 (0.6, 1.7)	1.2 (0.7, 2.0)	1.1 (0.6, 1.9)	1.5 (0.7, 3.4)	0.8 (0.3, 2.2)
Early Alcohol Use	1.9 (1.1, 3.3)	1.4 (0.7, 2.6)	1.7 (0.9, 3.0)	1.3 (0.6, 2.5)	3.0 (1.0, 8.9)	2.0 (0.6, 6.8)
Early Tobacco Use	1.8 (1.2, 2.9)	1.1 (0.6, 2.0)	1.5 (0.9, 2.4)	0.9 (0.5, 1.6)	2.6 (1.2, 5.6)	1.2 (0.5, 3.2)
Deviant Peer Affiliation	1.1 (0.8, 1.6)	0.9 (0.6, 1.3)	1.0 (0.7, 1.5)	0.8 (0.5, 1.3)	1.7 (1.0, 2.7)	1.3 (0.8, 2.2)
Neighborhood Disorder	1.3 (0.9, 1.8)	1.1 (0.7, 1.6)	1.3 (0.9, 1.9)	1.1 (0.7, 1.7)	1.4 (0.8, 2.5)	1.1 (0.6, 2.0)