



Adolescent Opioid Misuse Attributable to Adverse Childhood Experiences

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Objectives To estimate the proportion of opioid misuse attributable to adverse childhood experiences (ACEs) among adolescents.

Study design A cross-sectional survey was administered to 10 546 seventh-to twelfth-grade students in north-eastern Ohio in Spring 2018. Study measures included self-reported lifetime exposure to 10 ACEs and past 30-day use of nonmedical prescription opioid or heroin. Using generalized estimating equations, we evaluated associations between recent opioid misuse, individual ACEs, and cumulative number of ACEs. We calculated population attributable fractions to determine the proportion of adolescents' recent opioid misuse attributable to ACEs.

Results Nearly 1 in 50 adolescents reported opioid misuse within 30 days (1.9%); approximately 60% of youth experienced ≥ 1 ACE; 10.2% experienced ≥ 5 ACEs. Cumulative ACE exposure demonstrated a significant graded relationship with opioid misuse. Compared with youth with zero ACEs, youth with 1 ACE (aOR 1.9, 95% CI, 0.9-3.9), 2 ACEs (aOR, 3.8; 95% CI, 1.9-7.9), 3 ACEs (aOR, 3.7; 95% CI, 2.2-6.5), 4 ACEs (aOR, 5.8; 95% CI, 3.1-11.2), and ≥ 5 ACEs (aOR, 15.3; 95% CI, 8.8-26.6) had higher odds of recent opioid misuse. The population attributable fraction of recent opioid misuse associated with experiencing ≥ 1 ACE was 71.6% (95% CI, 59.8-83.5).

Conclusions There was a significant graded relationship between number of ACEs and recent opioid misuse among adolescents. More than 70% of recent adolescent opioid misuse in our study population was attributable to ACEs. Efforts to decrease opioid misuse could include programmatic, policy, and clinical practice interventions to prevent and mitigate the negative effects of ACEs. (*J Pediatr* 2020;224:102-9).

Over the past 2 decades, the rates of pediatric deaths related to prescription or illicit opioids have increased threefold in the US, from 0.23 in 1999 to 0.72 per 100 000 in 2017.¹ Although adolescent misuse of heroin and prescription opioids is decreasing,² deaths from opioid overdose among adolescents aged 15-19 years are at an all-time high, largely owing to the recent proliferation of synthetic opioids such as illicitly manufactured fentanyl and fentanyl analogs.^{3,4} The opioid crisis is likely to worsen unless communities, providers, public health officials, and policymakers integrate protective measures for younger generations into the public health response.⁵ Preventing youth initiation of opioid misuse is an important step in reversing the opioid overdose epidemic, particularly because substance use initiation most often occurs during adolescence and early adulthood.^{6,7} Prevention efforts must begin early, with interventions to decrease the risk and strengthen protective factors among children and adolescents.^{8,9}

In the last 2 decades, the availability, pharmacology, and accessibility of prescription pain medications have made it easier for adolescents to misuse opioids and develop opioid use disorder.⁷ Existing research underscores the important role of family in adolescents' nonmedical prescription opioid use; parental nonmedical prescription opioid use is strongly associated with adolescent nonmedical prescription opioid use and one-third of youth report that a family member was the source of their prescription opioids.^{10,11}

One element that has emerged as an important risk factor for adult opioid misuse is adverse childhood experiences (ACEs)—all types of abuse, neglect, and other traumatic experiences occurring to individuals before the age of 18 years.¹² A landmark study from the Centers for Disease Control and Prevention (CDC) and the Kaiser Family Foundation found a strong, graded relationships between adverse experiences in childhood and chronic health conditions, low life potential, risky health behaviors, and early death.¹³⁻²⁰

Retrospective studies of adults' self-reported data have identified ACEs as a critical risk factor for illicit substance use in adulthood, with ACEs accounting for 56%-67% of illicit drug use problems among adults.^{15,17} Persons

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ACE	Adverse childhood experience
CDC	Centers for Disease Control and Prevention
PAF	Population attributable fraction

experiencing ACEs in childhood are at higher risk of opioid dependence, injection drug use, earlier opioid initiation, and lifetime overdose as an adult.²¹⁻²³

Although hypothesized to be a risk factor for opioid misuse during adolescence, few studies examine ACEs' relationship to opioid misuse in the adolescent population.²⁴⁻²⁹ A better understanding of ACEs' contributions to opioid misuse among younger populations may help to guide interventions to prevent initiation of substance use, a critical component of stemming the opioid overdose epidemic.³⁰

To address this gap, we evaluated associations between cumulative and individual ACEs and opioid misuse in the past 30 days in an adolescent population. We also estimated the proportion of adolescents' recent opioid misuse attributable to ACEs.

Methods

In April and May 2018, the Ohio Department of Health conducted the Northeast Ohio Youth Health Survey in response to a cluster of youth suicides in Stark County, Ohio. The Northeast Ohio Youth Health Survey is an anonymous, online, school-based, cross-sectional survey of self-reported risk and protective factors among seventh- to twelfth-grade students created by staff at the Ohio Department of Health, the Stark County Health Department, and the CDC.³¹

The Northeast Ohio Youth Health Survey was administered to students attending 27 public middle and high schools in Stark County under the direction of school administrators and teachers using school-specific web links. Estimated 2017-2018 enrollment at participating schools was 17 255 students. Study data were collected using Ohio Department of Health's REDCap electronic data capture tools.³² Students' parents/guardians were notified of the survey in advance via phone and mail and could refuse their child's participation. Students could opt out of survey participation at any time and skip questions by selecting "Prefer not to say" as a response. A standardized script was read before administration, introducing the survey as a confidential, anonymous, voluntary public health activity to prevent youth suicide. Immediately after administration, all participating students were given a list of locally available mental health resources. Students absent from the school/classroom at the time of survey administration were unable to participate. Students were included in analyses if they completed and submitted the survey. Primary data were collected anonymously as a part of a larger public health response to a suicide cluster and did not qualify as human subject research, as determined by a CDC Institutional Review Board/Office of Management and Budget official; secondary data analyses were also determined to be exempt from human subjects' regulations by CDC Institutional Review Board/Office of Management and Budget.

Exclusions from Study Cohort

The total number of respondents was 12 448. We excluded respondents with incomplete data on any measures of

interest. After the exclusion of 1902 respondents with missing information on variables in main model (race, grade, sex, gender/sexual minority, ACEs, recent opioid misuse), the final sample included 84.7% of respondents (n = 10 546).

ACEs

ACE variables are defined in [Table I](#). All questions about ACEs referred to the respondent's lifetime. Questions were adapted from the Behavioral Risk Factor Surveillance System ACE module and Violence Against Children Surveys.^{33,34} Students were asked to choose the response that best reflected their lifetime experiences; response options were yes, no, not sure, or prefer not to say.

Substance Use

Substance use questions were adapted from relevant questions on the Youth Risk Behavior Survey.³⁵ To assess misuse of substances, respondents were provided a list of substances: alcohol, marijuana, synthetic marijuana, cocaine, ecstasy, glue/huffing, heroin, prescription pain medicines without a doctor's prescription, and prescription muscle relaxers or anxiety medicine without a doctor's prescription. For recent substance misuse, students were asked, "During the past 30 days, have you used any of the following substances at least once? Please select all that apply." Respondents who reported using heroin or prescription pain medicines without a doctor's prescription in the past 30 days were considered to have recent opioid misuse. For lifetime substance misuse, students were asked if they had used the substance at least once in their lifetime.

Statistical Analyses

All analyses were conducted using SAS v9.4 (SAS Institute, Cary, North Carolina) and R v3.4.0 (The R Foundation, Vienna, Austria). Two-sided tests of significance were performed. A *P* value of <.05 was considered significant. Counts and percentages were computed to describe the distribution of ACEs, opioid misuse, lifetime misuse of other substances, and sociodemographic factors in the survey population.

Using generalized estimating equations based on the logistic distribution and an exchangeable correlation structure to account for clustering of students within schools, we examined associations between ACE exposure and recent opioid misuse. We estimated unadjusted and aORs and 95% CIs for associations between each ACE and recent opioid misuse. To assess cumulative ACE exposure, the number of ACEs was summed for each respondent (range, 0-10). Owing to small sample size, ACE scores of 5, 6, 7, 8, 9, or 10 were combined into one category (≥ 5). Cumulative ACE exposure analyses were calculated using five dichotomous variables for 1 to ≥ 5 ACEs (yes/no) and 0 ACEs as the referent. Covariates in all adjusted models were included on a priori reasoning and included sex (male/female), race/ethnicity (white, non-Hispanic; black or African American, non-Hispanic; other, non-Hispanic; Hispanic), grade (range, 7-12), and gender/sexual minority status. Gender/sexual minority status was defined as self-reporting as gay, lesbian, bisexual,

Table I. Definition of ACE variables used in Northeast Ohio Youth Health Survey, Spring 2018

ACEs	Definition
Emotional abuse	Emotional abuse was defined as a “yes” response to either statement: “A parent or adult in my home swore at me, insulted me, humiliated me, put me down, or acted in a way that made me afraid I might be physically hurt” “I often felt that no one in my family loved me or thought I was important or special.”
Physical abuse	Physical abuse was defined as a “yes” response to either statement: “A parent or adult in my home pushed, grabbed, slapped, hit, beat, kicked, or physically hurt me (not including spanking)” “A person I was dating pushed, grabbed, slapped, hit, beat, kicked, or physically hurt me (not including spanking).”
Sexual abuse	Sexual abuse was defined as a “yes” response to either statement: “A parent or person at least 5 years older than me sexually touched me, made me sexually touch them, attempted sex, or actually had sex with me” “A person I was dating sexually touched me, made me sexually touch them, attempted sex, or actually had sex with me when I didn’t want to.”
Witnessed intimate partner violence	Witnessed intimate partner violence was defined as a “yes” response to the statement: “My parents or adults in my home slapped, hit, kicked, punched, or beat each other up.”
Household substance abuse	Household substance abuse was defined as a “yes” response to the statement: “I lived with someone who was a problem drinker, alcoholic, used illegal street drugs or abused prescription medications.”
Mental illness in household	Mental illness in household was defined as a “yes” response to the statement: “I lived with someone who was depressed, mentally ill, or suicidal.”
Parental separation or divorce	Parental separation was defined as a “yes” response to the statement: “My parents separated or divorced.”
Incarcerated household member	Having an incarcerated household member was defined as a “yes” response to the statement: “I lived with someone who went to jail or prison.”
Physical neglect	Physical neglect was defined as a “yes” response to the statement: I often felt that I didn’t have enough to eat, I had to wear dirty clothes, I had no one to protect me, or my parents were too drunk or high to take care of me.
Emotional neglect	Emotional neglect was defined as a “yes” response to the statement: I often felt that no one in my family loved me or thought I was important or special.

transgender, other, or unsure of one’s sexual orientation. We considered lifetime misuse of alcohol, marijuana, and other substances as a mediator of the relationship between ACEs and recent opioid misuse and, as such, did not include lifetime misuse of nonopioid substances in the main model.

Population attributable fractions (PAF) were calculated for each individual ACE (eg, physical abuse, household substance abuse, etc) and for an ACE score of ≥ 1 , under an assumption that the observed association between ACEs and opioid misuse is causal.¹⁵ PAF is the proportional reduction in a health problem (eg, adolescent opioid misuse) that would occur if exposure to a risk factor (eg, ≥ 1 ACEs) were eliminated from the population (eg, no ACEs).³⁶ For diseases with multiple risk factors, PAFs can sum to $<100\%$, because calculations assume mutual exclusivity of risk factors.³⁷ Adjusted PAFs were estimated using the R package AF to identify the proportion of adolescent opioid misuse attributable to ACEs.³⁸

Sensitivity analyses examining differences between included and excluded students were conducted using χ^2 tests. To assess the association between ACEs and opioid misuse, independent of participants’ misuse of other substances, we conducted sensitivity analyses including lifetime misuse of alcohol, marijuana, and other substances as covariates in the model.

Results

The study included 5287 (50.1%) females and 5259 (49.9%) males (Table II). The majority of students were white, non-Hispanic (83.6%). One in 10 students (11.4%) self-reported as a gender/sexual minority. Prevalence of ACEs varied from 3.1% of students experiencing physical neglect to 37.5% of students reporting parental separation or divorce. Emotional abuse was the most commonly reported form of abuse (21.3%). More than 1 in 6 students (17.4%) reported substance abuse by a household member in the past year. Among students, 39.8% experienced zero ACEs, 60.2% experienced ≥ 1 ACE, and 1 in 10 (10.2%) experienced ≥ 5 ACEs. Nearly 2% of youth (1.9%) reported misusing an opioid in the past 30 days. Among students reporting opioid misuse in the past 30 days, 12.8% used heroin and 96.4% misused prescription opioids.

Lifetime Misuse of Other Substances among Adolescents with Recent Opioid Misuse

Lifetime misuse of alcohol, marijuana, and other substances was common among adolescents with recent opioid misuse. Among students endorsing opioid misuse within the past 30 days, 83.0% used alcohol, 62.2% used marijuana, 53.2%

Table II. Characteristics of the survey population (n = 10 546), Northeast Ohio Youth Health Survey, 2018

Characteristics	No. (%)
Race/ethnicity	
White, non-Hispanic	8816 (83.6)
Other, non-Hispanic	668 (6.3)
Black or African American, non-Hispanic	612 (5.8)
Hispanic	450 (4.3)
School grade	
7	1889 (17.9)
8	1983 (18.8)
9	1824 (17.3)
10	1826 (17.3)
11	1679 (15.9)
12	1345 (12.8)
Sex	
Male	5259 (49.9)
Female	5287 (50.1)
Gender/sexual minority	
Yes	1204 (11.4)
No	9342 (88.6)
ACEs	
Emotional abuse	2250 (21.3)
Physical abuse	1274 (12.1)
Sexual abuse	756 (7.2)
Witnessed intimate partner violence	633 (6.0)
Household substance abuse	1835 (17.4)
Mental illness in household	2285 (21.7)
Parental separation or divorce	3959 (37.5)
Incarcerated household member	1848 (17.5)
Physical neglect	329 (3.1)
Emotional neglect	1904 (18.1)
ACE score	
0	4201 (39.8)
1	2414 (22.9)
≥1	6345 (60.2)
2	1340 (12.7)
3	898 (8.5)
4	615 (5.8)
≥5	1078 (10.2)
Opioid misuse in the past 30 d	
Yes	195 (1.9)
No	10 351 (98.2)
Lifetime misuse of other substances*	
Alcohol (n = 10 338)	4457 (43.1)
Marijuana (n = 10 494)	1724 (16.4)
Cocaine (n = 10 529)	116 (1.1)
Ecstasy (n = 10 532)	135 (1.3)
Glue/huffing (n = 10 531)	159 (1.5)
Synthetic marijuana (n = 10 531)	230 (2.2)
Methamphetamine (n = 10 538)	66 (0.6)
Prescription muscle relaxant without a doctor's prescription (n = 10 529)	460 (4.4)

*Because lifetime misuse of other substances was not included in primary model, participants with missing data on additional substance use variables were not excluded. The n for each substance use variable is noted.

used a nonmedical prescription muscle relaxant or anxiety medication, 28.2% used synthetic marijuana, 24.5% used ecstasy, 21.8% used cocaine, 20.7% used glue or huffed, and 13.8% used methamphetamines.

Associations between ACEs and Recent Opioid Misuse

All ACEs were significantly associated with increased adjusted odds of recent opioid misuse (aOR, 1.7-6.8) (Table III). Sexual abuse was associated with the highest

odds of recent opioid misuse (aOR, 6.8; 95% CI, 5.1-9.0). Students reporting emotional abuse or neglect were 4.3 (95% CI, 3.3-5.7) and 5.0 (95% CI, 3.7-6.8) times more likely than unexposed students to report misuse of opioids in the past 30 days.

A strong and independent trend was observed for associations between ACE score and recent opioid misuse by adolescents (Table IV). The prevalence of opioid misuse increased from 0.5% to 1.0%, 2.0%, 2.0%, 3.3%, and 8.1%, respectively, for those with exposure to 0, 1, 2, 3, 4, or ≥5 ACEs. Among those adolescents with 0 ACEs who reported recent opioid misuse, 35% used heroin and 90% misused prescription opioids. Among adolescents with ≥1 ACE and recent opioid misuse, 10.3% used heroin and 97.1% misused prescription opioids. We observed a significant, graded relationship between ACE score (Table IV) and recent opioid misuse, with the odds of opioid misuse significantly increasing as the number of ACEs increased (with the exception of experiencing one ACE, which was not statistically significant). Students experiencing ≥5 ACEs were >15 times more likely to report recent opioid misuse than those experiencing zero ACEs (aOR, 15.3; 95% CI, 8.8-26.6).

PAF

The PAF of recent opioid misuse attributable to experiencing one or more ACEs was 71.6% (95% CI, 59.8%-83.5%). PAFs for individual ACEs ranged from 14.1% (95% CI, 9.0%-19.2%) for physical neglect to 44.1% (95% CI, 35.8%-52.5%) for emotional abuse, indicating the relative contributions of individual ACEs to recent opioid misuse (Table III).

Sensitivity Analyses

In sensitivity analyses, participants with complete data differed from excluded participants for 22 of 24 variables examined (Table V; available at www.jpeds.com). Participants with missing data were more likely to report recent opioid misuse, lifetime misuse of other substances, and all ACEs (except alcohol and sexual abuse). Bivariate and unadjusted generalized estimating equations models did not significantly differ when missing data were included (Table VI and Table VII; available at www.jpeds.com). In participants with nonmissing data on variables of interest, when lifetime misuse of alcohol, marijuana, and other substances were included as covariates in the model, independent associations between ACE exposure and recent opioid misuse were attenuated, but remained statistically significant (with the exception of parental separation/divorce; Table VIII [available at www.jpeds.com])). Adjusting for sociodemographic factors and lifetime misuse of alcohol, marijuana, and other substances, the PAF of recent opioid misuse attributable to experiencing one or more ACEs was 45.5% (95% CI, 22.2%-68.9%).

Table III. Prevalence, unadjusted, adjusted odds, and PAF of recent opioid misuse by category of ACEs (n = 10 546), Northeast Ohio Youth Health Survey, 2018

ACEs	Opioid misuse in the past 30 d			
	Prevalence, %	Unadjusted OR (95% CI)	aOR* (95% CI)	PAF (95% CI)
Emotional abuse (n = 2250)				
No	1.0	1.0	1.0	
Yes	5.0	5.0 (3.9-6.5)	4.3 (3.3-5.7)	44.1 (35.8-52.5)
Physical abuse (n = 1274)				
No	1.2	1.0	1.0	
Yes	6.7	5.8 (4.4-7.8)	4.9 (3.7-6.5)	34.3 (25.7-43.0)
Sexual abuse (n = 756)				
No	1.3	1.0	1.0	
Yes	9.1	7.5 (5.6-10.1)	6.8 (5.1-9.0)	29.8 (24.5-35.0)
Witnessed intimate partner violence (n = 633)				
No	1.5	1.0	1.0	
Yes	7.9	5.7 (4.1-7.8)	4.5 (3.3-6.3)	19.7 (12.3-27.0)
Household substance abuse (n = 1835)				
No	1.2	1.0	1.0	
Yes	4.9	4.0 (3.2-5.0)	3.5 (2.8-4.5)	32.7 (26.2-39.2)
Mental illness in household (n = 2285)				
No	1.1	1.0	1.0	
Yes	4.6	4.2 (3.2-5.6)	3.7 (2.7-5.0)	39.3 (30.1-48.5)
Parental separation or divorce (n = 3959)				
No	1.4	1.0	1.0	
Yes	2.6	1.9 (1.4-2.5)	1.7 (1.2-2.2)	21.2 (8.8-33.6)
Incarcerated household member (n = 1848)				
No	1.2	1.0	1.0	
Yes	4.7	3.9 (3.0-5.0)	3.2 (2.5-4.2)	30.7 (23.3-38.1)
Physical neglect (n = 329)				
No	1.6	1.0	1.0	
Yes	10.3	7.0 (5.0-9.9)	5.7 (3.9-8.3)	14.1 (9.0-19.2)
Emotional neglect (n = 1904)				
No	1.0	1.0	1.0	
Yes	5.6	5.7 (4.3-7.6)	5.0 (3.7-6.8)	43.5 (34.8-52.3)

*ORs adjusted for sex, race/ethnicity, grade, gender/sexual minority status.

Discussion

Examining the cumulative effect of ACEs, we found a strong graded relationship between number of ACEs and adolescents' recent opioid misuse, with adolescents experiencing ≥5 ACEs being >15 times more likely to report recent opioid misuse. Moreover, we found the estimated attributable fraction for recent opioid misuse related to having experienced any childhood adversity was large (71.6%).

Our results are consistent with previous PAF estimates for illicit drug use in adults: 56%-64% of drug use outcomes

were associated with childhood adversity.¹⁷ The high PAFs for individual ACEs highlight emotional abuse and neglect's considerable contributions to adolescent opioid misuse at a population level. These forms of childhood maltreatment are often underappreciated as important risk factors for negative health outcomes.³⁹

Our results are consistent with previous studies demonstrating strong associations between ACEs and substance use in adolescence.^{17,21,24-29} The relationship between adult opioid misuse and individual ACEs—such as sexual abuse and household substance abuse—is well-documented in the literature.^{26,40,41} However, few reports address the cumulative impact of exposure to ACEs on opioid misuse, particularly among adolescents.^{24,25} In the context of the current opioid overdose epidemic, our findings of strong associations between ACEs and misuse of opioids by adolescents— independent of other substance misuse—highlight the urgent need to address upstream factors in the response to this public health crisis.⁴²

The robust relationships observed in this study raise an important question: why do adolescents exposed to ACEs misuse opioids? A number of biological and environmental factors likely contribute to the associations between ACEs and adolescent opioid misuse. Adolescence—typified by risk taking, experimentation, and modeling of peer behavior—is a critical at-risk period for opioid misuse.^{7,43,44}

Table IV. Prevalence, unadjusted, and adjusted odds of recent opioid misuse by number of ACEs (n = 10 546), Northeast Ohio Youth Health Survey, 2018

No. of ACEs	Opioid misuse in the past 30 d		
	Prevalence, %	Unadjusted OR (95% CI)	aOR* (95% CI)
0 (n = 4201)	0.5	1.0	1.0
1 (n = 2414)	1	2.0 (0.95-4.1)	1.9 (0.9-3.9)
2 (n = 1340)	2.0	4.2 (2.0-9.1)	3.8 (1.9-7.9)
3 (n = 898)	2.0	4.2 (2.4-7.1)	3.7 (2.2-6.5)
4 (n = 615)	3.3	6.8 (3.4-13.5)	5.8 (3.1-11.2)
≥5 (n = 1078)	8.1	17.8 (10.5-30.1)	15.3 (8.8-26.6)

*ORs adjusted for sex, race/ethnicity, grade, and gender/sexual minority status.

During this period, adolescents exposed to ACEs are particularly vulnerable.⁴⁵ ACEs are associated with impaired emotional, social, and cognitive development, including a decreased ability to cope with stressful emotional stimuli and increased risk of substance initiation.^{45,46} Youth experiencing violence, neglect, and household challenges may feel powerless, anxious, dysregulated, or other negative emotions.⁴⁷⁻⁴⁹ Opioid misuse may provide an outlet for these negative feelings—a maladaptive way to escape the emotional turmoil that accompanies ACEs.

How do we prevent ACEs or mitigate their harms when they do occur? First, we prevent ACEs by developing and expanding programs and policies proven to prevent ACEs or impact key risk and protective factors for ACEs. Examples of strategies to prevent ACEs include strengthening economic supports for families (eg, tax credits, paid family leave, access to affordable childcare); promoting social norms that protect against violence and adversity (eg, norms to support parents and positive parenting); and ensuring a strong start for children (eg, early childhood home visitation, preschool enrichment programs with family engagement).⁵⁰ ACEs can also be prevented by teaching skills to handle stress, manage emotions, and tackle everyday challenges; and connecting youth to caring adults and activities (eg, mentoring, after-school programs).⁵⁰ For example, skills-based programs such as *Life Skills Training* and *Strengthening Families 10-14* can prevent ACE exposure (eg, peer violence, bullying) and reduce consequences (eg, prescription opioid misuse among adolescents and young adults).⁵⁰⁻⁵⁴ Efforts to expand implementation of these preventive interventions are urgently needed.

Second, effective interventions and policies need to be implemented to lessen harms and prevent future risk among children already exposed to ACEs.^{50,55} Primary care settings offer a unique opportunity to identify and address ACEs through enhanced screening and referral to intervention support.⁵⁰ For children, this includes assessments with parents or caregivers to identify risks in the family environment, such as parental substance misuse, depression, stress, the use of harsh punishment, and intimate partner violence. For adults, this includes assessments to identify a history of ACE exposures to mitigate risk and improve treatment outcomes.⁵⁰ Trauma-informed therapeutic treatment of children and families with ACEs can lessen the negative social, emotional, behavioral, and health consequences of these exposures and decrease the risk for violence victimization, perpetration, and substance misuse.^{50,55} Treatment, through modalities like trauma-focused cognitive behavioral therapy and cognitive behavioral intervention for trauma in schools, effectively decreases trauma-related symptoms in children and improves parenting-related behaviors, emotional distress, and depressive symptoms in parents.^{56,57} Such interventions safeguard the next generation from misusing opioids when they become adults, despite negative experiences in childhood.

Last, incorporating trauma-informed and trauma-specific approaches into medical treatment of youth with opioid use

disorder can help them to return to productive, healthy lives and achieve sustained recovery.⁵⁸ Trauma-informed care translates the neuroscience of how trauma is processed in the brain into all aspects of healthcare delivery to mitigate the symptoms of trauma and prevent retraumatization.^{59,60} Trauma-specific services directly address the impact of trauma on people's lives and facilitate recovery and healing.⁶¹ Recovery from opioid use disorder is unlikely to be stable and long term without addressing underlying trauma.⁶²⁻⁶⁴ As providers and public health officials work to improve the infrastructure required to identify and treat youth with opioid use disorder, trauma-informed environments and trauma-specific services can be integrated to address factors related to ACEs.

The intergenerational “transmission” of ACEs also needs to be addressed. Studies indicate that higher parental ACEs predict higher child ACEs.⁶⁵ Parent ACE exposures are also associated with worse child health, health behaviors, and health care access and use.⁶⁶ Strategies to mitigate the negative impact of ACEs on 1 generation may act as primary prevention for the next generation. One study of white, rural, lower SES communities found that high perceived community social cohesion was associated with a decrease in ACEs across generations.⁶⁷ Community-based solutions are one way to mitigate the negative effects of parental ACEs; additional intergenerational strategies include broad dissemination of ACEs-related research, trauma-informed care for parents, science-based prevention, and treatment interventions such as evidence-based home visiting.^{68,69}

There are limitations to our study. First, our cross-sectional study can only present associations, not causality. To strengthen the likelihood that ACE exposures predated our outcome, we limited our outcome to the past 30 days. Although some studies have suggested a causal relationship between ACEs and opioid misuse among adults, more research into the pathways between ACEs and substance abuse is needed before conclusive statements on causality and risk can be made.^{15,17} Our results should be interpreted with the cross-sectional study design in mind. PAF estimates may be biased if observed associations are underestimates or overestimates of aORs. Second, the study only included complete data from students attending participating public middle and high schools in Stark County. ACEs and recent opioid misuse were more prevalent among excluded participants; results may underrepresent the true prevalence of these experiences and associations. Data are not available for students attending nonparticipating schools; absent from school; or who opted out of participating. The prevalence of ACEs and opioid misuse may differ for these populations. Third, given the sensitive subject matter, it is possible that students underreported ACE exposure and opioid misuse, biasing our findings towards the null. Fourth, our study population's racial/ethnic profile was largely white, non-Hispanic heterosexual youth; as such, the results of this study may not be generalizable beyond northeast Ohio. Although other studies have demonstrated an increased prevalence of ACEs among participants identifying as black, Hispanic, multiracial, gay,

lesbian or bisexual, we find that ACEs are prevalent among white, heterosexual adolescents, as well.⁷⁰ Repeated analysis in diverse settings is merited.

Understanding the contributions of ACEs to opioid misuse can help public health officials and clinicians determine how best to deploy policies, programs, and clinical practices to stop the opioid crisis. The strong associations between ACEs and opioid misuse, already apparent by adolescence, underscore the importance of upstream interventions. To prevent opioid overdose deaths in the future, we must effectively prevent and mitigate the negative consequences of ACEs in the present. ■

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Table V. Comparison of characteristics of subjects included in analyses vs excluded owing to missing data, Northeast Ohio Youth Health Survey, 2018

Characteristics	Included (n = 10 546)	Excluded (n = 1902)	P value*
Race/ethnicity			
White, non-Hispanic	8816 (83.6)	1326 (79.3)	<.001
Other, non-Hispanic	668 (6.3)	120 (7.2)	
Black or African American, non-Hispanic	612 (5.8)	125 (7.5)	
Hispanic	450 (4.3)	101 (6.0)	
Missing		230	
School grade			
7	1889 (17.9)	406 (22.4)	<.001
8	1983 (18.8)	336 (18.6)	
9	1824 (17.3)	340 (18.8)	
10	1826 (17.3)	288 (15.9)	
11	1679 (15.9)	248 (13.7)	
12	1345 (12.8)	192 (10.6)	
Missing		92	
Sex			
Male	5259 (49.9)	749 (46.2)	.006
Female	5287 (50.1)	873 (53.8)	
Missing	–	280	
Sexual minority			
Yes	1204 (11.4)	354 (24.3)	<.001
No	9342 (88.6)	1102 (75.7)	
Missing		446	
ACEs			
Emotional abuse			
Yes	2250 (21.3)	398 (28.0)	<.001
No	8296 (78.7)	1022 (72.0)	
Missing		482	
Physical abuse			
Yes	1274 (12.1)	265 (16.5)	<.001
No	9272 (87.9)	1344 (83.5)	
Missing		293	
Sexual abuse			
Yes	756 (7.2)	136 (8.5)	.06
No	9790 (92.8)	1469 (91.5)	
Missing		297	
Witnessed intimate partner violence			
Yes	633 (6.0)	119 (8.1)	.003
No	9913 (94.0)	1357 (91.9)	
Missing		426	
Household substance abuse			
Yes	1835 (17.4)	383 (25.4)	<.001
No	8711 (82.6)	1125 (74.6)	
Missing		394	
Mental illness in household			
Yes	2285 (21.7)	484 (32.0)	<.001
No	8261 (78.3)	1029 (68.0)	
Missing		389	
Parental separation or divorce			
Yes	3959 (37.5)	779 (50.5)	<.001
No	6587 (62.5)	763 (49.5)	
Missing		360	
Incarcerated household member			
Yes	1848 (17.5)	401 (26.4)	<.001
No	8698 (82.5)	1116 (73.6)	
Missing		385	
Physical neglect			
Yes	329 (3.1)	85 (5.5)	<.001
No	10 217 (96.9)	1461 (94.5)	
Missing		356	

(continued)

Table V. Continued

Characteristics	Included (n = 10 546)	Excluded (n = 1902)	P value*
Emotional neglect			
Yes	1904 (18.1)	380 (27.6)	<.001
No	8642 (82.0)	999 (72.4)	
Missing		523	
ACE score			
0	4201 (39.8)	498 (29.8)	<.001
1	2414 (22.9)	390 (23.3)	
2	1340 (12.7)	241 (14.4)	
3	898 (8.5)	175 (10.5)	
4	615 (5.8)	139 (8.3)	
≥5	1078 (10.2)	230 (13.7)	
Missing		229	
Recent opioid misuse			
Yes	195 (1.9)	51 (3.7)	<.001
No	10 351 (98.2)	1335 (96.3)	
Missing		516	
Lifetime misuse of nonopioid substances[†]			
Alcohol			
Yes	4457 (43.1)	639 (44.0)	.53
No	5881 (56.9)	814 (56.0)	
Missing	208	449	
Marijuana			
Yes	1724 (16.4)	300 (19.6)	.002
No	8770 (83.6)	1230 (80.4)	
Missing	52	372	
Cocaine			
Yes	116 (1.1)	38 (2.3)	<.001
No	10 413 (98.9)	1583 (97.7)	
Missing	17	281	
Ecstasy			
Yes	135 (1.3)	39 (2.4)	.001
No	10 397 (98.7)	1586 (97.6)	
Missing	14	277	
Glue/huffing			
Yes	159 (1.5)	55 (3.4)	<.001
No	10 372 (98.5)	1562 (96.6)	
Missing	15	285	
Synthetic marijuana			
Yes	230 (2.2)	52 (3.2)	.01
No	10 301 (97.8)	1559 (96.8)	
Missing	15	291	
Methamphetamines			
Yes	66 (0.6)	35 (2.1)	<.001
No	10 472 (99.4)	1593 (97.9)	
Missing	8	274	
Nonmedical prescription muscle relaxers or anxiety medicine			
Yes	460 (4.4)	109 (6.8)	<.001
No	10 069 (95.6)	1497 (93.2)	
Missing	17	296	

*P values calculated from χ^2 test.

†Because lifetime misuse of other substances was not included in primary model, participants with missing data on additional substance use variables were not excluded. N_{missing} for substance use variables are noted in both included and excluded groups.

Table VI. Outcome prevalence by cohort characteristics in excluded participants, Northeast Ohio Youth Health Survey, 2018

Characteristics	Opioid misuse in the past 30 d			
	n	Total	%*	P value†
Race/ethnicity				
White, non-Hispanic	20	943	2.1	<.001
Other, non-Hispanic	5	90	5.6	
Black or African American, non-Hispanic	5	96	5.2	
Hispanic	10	74	13.5	
Missing	699			
School grade				
7	12	350	3.4	.94
8	10	27	3.7	
9	7	248	2.8	
10	7	193	3.6	
11	6	158	3.8	
12	2	110	1.8	
Missing	573			
Sex				
Male	15	519	2.9	.58
Female	16	673	2.4	
Missing	710			
Sexual minority				
Yes	27	289	9.3	<.001
No	18	754	2.4	
Missing	859			
ACEs				
Emotional abuse				
Yes	22	282	7.8	<.001
No	12	771	1.6	
Missing	849			
Physical abuse				
Yes	23	190	12.1	<.001
No	12	1041	1.2	
Missing	671			
Sexual abuse				
Yes	15	105	14.3	<.001
No	18	1124	1.6	
Missing	673			
Witnessed intimate partner violence				
Yes	12	89	13.5	<.001
No	17	1021	1.7	
Missing	792			
Household substance abuse				
Yes	20	277	7.2	<.001
No	12	863	1.4	
Missing	762			
Mental illness in household				
Yes	23	349	6.6	<.001
No	10	792	1.3	
Missing	761			
Parental separation or divorce				
Yes	25	589	4.2	.007
No	9	568	1.6	
Missing	745			
Incarcerated household member				
Yes	25	304	8.2	<.001
No	7	842	0.8	
Missing	756			
Physical neglect				
Yes	15	60	25.0	<.001
No	16	1114	1.4	
Missing	728			
Emotional neglect				
Yes	20	274	7.3	<.001
No	10	748	1.3	
Missing	880			

(continued)

Table VI. Continued

Characteristics	Opioid misuse in the past 30 d			
	n	Total	%*	P value†
ACE score				
0	2	397	0.5	<.001
1	1	301	0.3	
2	2	183	1.1	
3	6	134	4.5	
4	4	98	4.1	
≥5	20	164	12.2	
Missing	625			
Lifetime misuse of non-opioid substances				
Alcohol				
Yes	29	440	6.6	<.001
No	5	728	0.7	
Missing	734			
Marijuana				
Yes	21	183	11.5	<.001
No	15	1058	1.4	
Missing	661			
Cocaine				
Yes	14	30	46.7	<.001
No	22	1237	1.8	
Missing	635			
Ecstasy				
Yes	14	32	43.8	<.001
No	23	1235	1.9	
Missing	635			
Glue/huffing				
Yes	15	43	34.9	<.001
No	21	1220	1.7	
Missing	639			
Synthetic marijuana				
Yes	15	42	35.7	<.001
No	20	1223	1.6	
Missing	637			
Methamphetamines				
Yes	15	29	51.7	<.001
No	21	1240	1.7	
Missing	633			
Nonmedical prescription muscle relaxers or anxiety medicine				
Yes	23	72	31.9	<.001
No	14	1187	1.2	
Missing	643			

*Row percent.

†The P values are calculated from the χ^2 test.

Table VII. Prevalence and unadjusted odds of recent opioid misuse by category and number of ACEs among all participants (n = 12 448), Northeast Ohio Youth Health Survey, 2018

ACEs	Opioid misuse in the past 30 d	
	Prevalence, %	Unadjusted OR (95% CI)
Emotional abuse		
No	1.1	1.0
Yes	5.3	4.8 (3.6-6.4)
Missing	849	
Physical abuse		
No	1.2	1.0
Yes	7.4	5.7 (4.3-7.6)
Missing	671	
Sexual abuse		
No	1.3	1.0
Yes	9.8	7.3 (5.5-9.8)
Missing	673	
Witnessed intimate partner violence		
No	1.5	1.0
Yes	8.6	5.3 (3.8-7.4)
Missing	792	
Household substance abuse		
No	1.2	1.0
Yes	5.2	3.8 (3.1-4.9)
Missing	762.0	
Mental illness in household		
No	1.1	1.0
Yes	4.9	4.3 (3.3-5.6)
Missing	761	
Parental separation or divorce		
No	1.4	1.0
Yes	2.8	1.8 (1.4-2.4)
Missing	745	
Incarcerated household member		
No	1.2	1.0
Yes	5.2	4.0 (3.2-5.2)
Missing	756	
Physical neglect		
No	1.6	1.0
Yes	12.6	6.9 (4.9-9.7)
Missing	728	
Emotional neglect		
No	1.0	1.0
Yes	5.8	5.5 (4.2-7.2)
Missing	880	
Number of ACEs		
0	0.5	1.0
1	0.9	2.0 (0.99-4.0)
≥1	2.9	5.8 (3.7-9.3)
2	1.9	4.0 (1.9-8.7)
3	2.3	5.3 (3.3-8.4)
4	3.4	7.7 (3.9-15.1)
≥5	8.6	18.1 (10.8-30.3)
Missing	650	

Table VIII. Prevalence, unadjusted, and adjusted odds of recent opioid misuse by category and number of ACEs, adjusting for sociodemographics and lifetime history of nonopioid substance use (n = 10 293), Northeast Ohio Youth Health Survey, 2018

ACEs	Opioid misuse in the past 30 d		
	Prevalence, %	Unadjusted OR (95% CI)	aOR (95% CI)
Lifetime misuse of alcohol*			
No	0.6	1.0	1.0
Yes	3.5	6.4 (4.5-9.2)	1.9 (1.1-3.3)
Lifetime misuse of marijuana*			
No	0.8	1.0	1.0
Yes	6.8	8.5 (6.1-11.8)	1.6 (0.99-2.7)
Lifetime misuse of other substances*†			
No	0.7	1.0	1.0
Yes	16.8	27.2 (19.7-37.6)	13.6 (9.3-19.8)
Emotional abuse‡			
No	1.0	1.0	1.0
Yes	4.9	5.0 (3.9-6.5)	1.9 (1.5-2.5)
Physical abuse‡			
No	1.2	1.0	1.0
Yes	6.6	5.8 (4.3-7.8)	1.9 (1.5-2.4)
Sexual abuse‡			
No	1.3	1.0	1.0
Yes	8.9	7.3 (5.4-9.9)	2.2 (1.7-3.0)
Witnessed intimate partner violence‡			
No	1.5	1.0	1.0
Yes	7.5	5.3 (3.9-7.3)	1.7 (1.2-2.4)
Household substance abuse‡			
No	1.2	1.0	1.0
Yes	4.8	4.0 (3.1-5.1)	1.4 (1.1-1.9)
Mental illness in household‡			
No	1.1	1.0	1.0
Yes	4.5	4.2 (3.2-5.5)	1.8 (1.4-2.3)
Parental separation or divorce‡			
No	1.4	1.0	1.0
Yes	2.5	1.8 (1.3-2.4)	1.0 (0.7-1.4)
Incarcerated household member‡			
No	1.2	1.0	1.0
Yes	4.6	3.8 (2.9-5.0)	1.5 (1.2-1.9)
Physical neglect‡			
No	1.6	1.0	1.0
Yes	9.9	6.7 (4.6-9.9)	1.9 (1.2-2.9)
Emotional neglect‡			
No	1.0	1.0	1.0
Yes	5.5	5.6 (4.1-7.6)	2.2 (1.6-3.1)
Number of ACEs‡			
0	0.5	1.0	1.0
1	0.9	2.0 (0.9-4.3)	1.6 (0.8-3.2)
≥1	2.7	5.7 (3.4-9.4)	2.1 (1.3-3.6)
2	2.0	4.3 (2.0-9.3)	2.1 (1.04-4.3)
3	2.1	4.4 (2.5-7.7)	1.9 (1.1-3.4)
4	3.3	7.0 (3.4-14.5)	2.2 (1.1-4.6)
≥5	7.9	17.7 (10.2-30.7)	3.5 (2.1-5.9)

*ORs adjusted for sex; race; grade; lifetime misuse of alcohol, marijuana, other substance use; sexual minority status; and exposure to ≥1 ACEs.

†Self-reported use of synthetic marijuana, cocaine, ecstasy, glue/huffing, prescription muscle relaxers or anxiety medicine without a doctor's prescription at least once in participant's lifetime.

‡ORs adjusted for sex; race; grade; lifetime misuse of alcohol, marijuana, other substance use; and sexual minority status.