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EDITORIAL

Adolescent Health: Is it Time to Direct our Attention to Youth in Ohio?

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Welcome to the third issue of the *Ohio Journal of Public Health (OJPH)*, with which we celebrate our one-year anniversary. In this issue, you will find 5 research articles, 1 research brief, and 1 public health practice article. Four of the manuscripts present findings from studies on adolescents, a group that is seldom the focus of conversations about priority populations and issues in Ohio. Yet adolescents represent nearly 14% of the population (over 1.5 million) and while they are a generally healthy group, there are risks unique to them. Moreover, adolescence is critically important from a developmental perspective, because at this time puberty occurs and individuals learn how to be independent.[1] One current concern regarding adolescents is electronic cigarette (e-cigarette) use, as past 30-day use has surged to 27.5% among high school students in the United States.[2] This rate is alarming because we still do not know the long-term health effects of e-cigarettes. A related concern is that most longitudinal studies show that adolescents who use e-cigarettes are at high risk of transitioning to cigarettes, which indubitably cause harm to human health.[3] Another public health issue facing adolescents is poor mental health, as adolescence is a time when several serious mental illnesses manifest. In Ohio, approximately 14% of adolescents aged 12 to 17 years have been diagnosed as having a major depressive episode, and this prevalence is slightly higher than the national average of 13%.[4]

Ohio is taking several steps that have the potential to improve the health of adolescents. One of Governor Mike DeWine's early decisions was to create the Office of Children's Initiatives. While focus is not entirely on adolescents, some of the Office's programs are relevant, specifically those designed to improve the foster care system, create drug abuse prevention programs, and increase the number of mental health professionals in schools.[5] The DeWine administration also advanced Tobacco 21 legislation, which is now the law in Ohio.[6] By raising the legal age to purchase tobacco to 21, these laws are designed to reduce tobacco initiation rates during adolescence, which is the time when most users begin. These initiatives, along with other ongoing programs administered by the Ohio Department of Health, have the potential to improve the health of adolescents in the state.

In this issue, Gray et al report on the prevalence of *Trichomonas vaginalis* (TV) in a sample of incarcerated adolescents in Central Ohio. They detected TV in 10% of females. They conclude that TV should be part of routine screening in juvenile detention facilities. The second article, by Bader et al, is focused on dental health among adolescent males from an urban county and 9 Appalachian counties who were enrolled in a longitudinal cohort study. They report that disparities in dental health are largely driven by behaviors such as tobacco use and diet, which differed between participants in the 2 regions. Using the same cohort of adolescent males, Teferra et al found that less than half of the participants had received a vaccine to prevent human papillomavirus (HPV) at the baseline interview, and among those not vaccinated only about one-third received the HPV vaccine series during the 2-year follow-up period. They conclude with a call for developing strategies to promote HPV vaccination. The fourth piece on adolescents in Ohio is the research brief by Kauffman and Durkin in which they report on the relationship between emotional distress and opioid misuse among adolescents who were involved with the juvenile drug court system in Northwest Ohio. They found that these factors are positively related, despite the fact that, over the reporting period, opioid misuse decreased and emotional distress increased. The paper concludes with a call to address emotional problems among adolescents, as they may lead to substance use.

The other highlights of this issue include an article that reports on the association between American Human Development Index (AHDI) scores and substance prescribing at the county level in Ohio. Factor et al report negative

associations between AHDI scores and opioid and benzodiazepine prescribing but a positive association with stimulant prescribing. They call for more work to understand the mechanisms underlying these relationships. The other research paper in this issue reports on perfluoroalkyl substances, which are found in consumer products and are linked to a number of chronic conditions. Heinle et al examined whether these compounds were related to lung function in a national sample and found no association. Nonetheless, given their relationship with other diseases it is important for cleanup efforts to continue. The last paper, a public health practice article by Ulrich et al, describes a multidisciplinary effort to engage human and animal health groups to address harmful algal blooms in freshwater sources in Ohio. The Centers for Disease Control and Prevention and multiple academic partners rolled out 3 different initiatives to inform Lake Erie area communities of this public health problem. The paper describes the initiatives and the outcomes.

I am very grateful to the scholars who contributed to this latest issue for their dedication to public health in Ohio. The *Ohio Journal of Public Health* continues to be a resource for researchers, practitioners, and educators in Ohio, and it is indeed allowing the Ohio Public Health Association to be the "voice" of public health in Ohio.

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Routine Screening of Adolescents for *Trichomonas vaginalis* in a Juvenile Detention Center

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ABSTRACT

Background: Detained and incarcerated adolescents are at increased risk of sexually transmitted infections (STI), but limited information is currently available regarding the prevalence of *Trichomonas vaginalis* (TV) in detained youth.

Methods: A total of 144 detainees (75 males and 69 females) in the Franklin County Juvenile Detention Facility (FCJDF) in Columbus, Ohio, consented to STI screening between May 2016 and June 2017. Participants were screened for TV in addition to *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT) using urine nucleic acid amplification tests (NAAT).

Results: Among detained youth who consented to testing, TV was identified in 7 of 69 (10.1%) females and 0 of 75 (0%) males ($P <0.01$). *Neisseria gonorrhoeae* was identified in 12 of 69 (17.4%) females and 3 of 75 (4.0%) males ($P = 0.01$), and CT was identified in 16 of 69 (23.2%) female and 7 of 75 (9.3%) male detainees ($P = 0.04$). Among females, positive TV screen was associated with prior history of STI.

Conclusion: Our data support routine screening of female detainees at FCJDF, based on our finding of 10% positivity among females who underwent testing.

Keywords: Detained and incarcerated youth, *Trichomonas vaginalis,* STI screening, Nucleic acid amplification test

INTRODUCTION

Trichomonas vaginalis (TV) is a parasitic sexually transmitted infection (STI) with an estimated 276.4 million new cases per year worldwide, making it the most common nonviral STI.[1] The Centers for Disease Control and Prevention (CDC) estimates that 3.7 million people in the United States are currently infected with TV, compared to 1.6 million with *Chlamydia trachomatis* (CT) and 270000 with *Neisseria gonorrhoeae* (NG).[2] In females, untreated *Trichomonas vaginalis* is associated with increased risk of low birth weight and preterm delivery,[3] increased susceptibility to human immunodeficiency virus (HIV),[4] and pelvic inflammatory disease in HIV-positive women.[5] In males, TV has been associated with nongonoccocal urethritis.[6] Despite its high prevalence and associated morbidity, TV receives limited public health attention. *Trichomonas vaginalis* is not a reportable infection in the state of Ohio; information on rates of infection therefore are lacking.

Incarcerated and detained adolescents are at high risk for STIs.[7] Among arrested or detained adolescent females, prevalence estimates as high as 33% for CT and 13% for NG have been reported.[8]

Among males, prevalence estimates as high as 14% for CT and 7% for NG have been observed.[9] Given the high prevalence of CT and NG, many juvenile correctional facilities routinely screen youth for these infections.

Limited information is available regarding the prevalence of TV in incarcerated and detained youth. Prior studies, using older testing methodologies with lower sensitivity, found that TV prevalence was similar to or higher than that of CT among females.[10] A high-sensitivity nucleic acid amplification test (NAAT) is now approved by the Food and Drug Administration (FDA) for the diagnosis of TV infection in females, using urine or vaginal specimens. The NAATs have shown good performance when testing urine from males as well, and may be used by labs that have performed internal validation studies on these specimens.[11-14] The higher sensitivity of NAAT tests may lead to more accurate estimates of TV prevalence in a given population. A study in adolescent females found a 3-fold higher prevalence of TV when NAAT testing was used as compared to unstained microscopic evaluation of vaginal secretions.[15] Aalsma et al used NAAT testing to screen juvenile detainees for NG, CT, and TV, and found that 1% of males and 11% of females

were positive for TV infection.[16] Rates of infection in detained youth in Ohio have not previously been reported.

In 2015, the CDC stated that screening for TV may be considered for women in high prevalence settings, including correctional facilities. The CDC further advised that screening decisions should be based on the local epidemiology of TV.[11] Given the limited information currently available regarding TV prevalence among detained and incarcerated youth in Ohio, it is unclear whether routine screening for this infection is indicated in this setting. The purpose of the current study was to determine the prevalence of TV infection in youth detained at the Franklin County Juvenile Detention Facility (FCJDF) using NAAT and to compare this to the prevalence of CT and NG. A secondary objective was to explore characteristics associated with testing positive for TV.

METHODS

Setting and Design

The FCJDF in Columbus, Ohio, is a 132-bed maximum security facility, housing detained males and females between the ages of 10-22 years. It is the main booking center for juveniles in Franklin County. The average length of stay is 12.5 days. The population averages 90% males and 10% females with a median age of 16 years. The center averages 79% African American and 21% white juveniles.

This was a cross-sectional survey of incoming detainees. The study protocol was approved by the FCJDF Lead Juvenile Judge. In addition, the protocol was reviewed by Nationwide Children's Hospital's Institutional Review Board (IRB) and deemed a quality improvement project and IRB exempt.

Participants

Adolescents and young adults detained at the FCJDF between April 2016 and June 2017 who consented to STI testing were included in the analysis. Due to the much higher census of males versus females, specimens from males were obtained at a faster rate. In order to attempt to get an equal sample of male and female participants, males were enrolled until June 2016, whereas female participants were enrolled through June 2017.

Procedures

As standard of care, a health assessment is completed by a nurse within 48 hours of an adolescent being admitted to the facility. A standardized medical history collection form is used to record demographic data and medical history, including sexual history. Detainees are offered testing for NG, CT, and HIV. For youth who give verbal consent, a urine sample is collected and tested for NG and CT. During the study period, urine samples were additionally tested for TV.

Testing for TV was performed at the Center of Disease Detection (CDD) or the Nationwide Children's Hospital (NCH) clinical laboratory. Specimens were delivered on the day of collection to NCH via courier. Specimens were delivered to CDD by next day air mail

delivery. Both labs utilized the APTIMA *Trichomonas vaginalis* Assay NAAT (GenProbe, San Diego, CA). All NG and CT testing was completed at CDD utilizing the Cobas 4800 CT/GC NAAT (Roche, Pleasanton, CA).

Measures

The primary study outcome was prevalence of positive TV tests among male and female detainees who consented to STI testing. Secondary outcomes were prevalence of positive NG and CT tests, and patient characteristics associated with a positive TV test.

For detainees who consented to STI screening, medical history forms were reviewed for the following: demographic characteristics; substance use history (reported tobacco, alcohol, and drug use and history of prior drug treatment), mental health history (current mental health conditions, history of suicidal ideation/self-injury, and family history of suicide), and sexual history (reported sexually activity, condom use, history of anal/oral/vaginal sex, age at sexual debut, number of sexual partners in a year, prior pregnancy, and prior STI).

Statistical Analysis

Descriptive statistics included count (percentage) for categorical variables and mean (standard deviation) for continuous variables. Male and female detainees were compared on demographic, substance use, mental health, and sexual activity characteristics utilizing chi-square, Fisher exact, and t tests, as appropriate. Fisher exact tests were used to compare the proportion of males and females positive for TV, NG, and CT.

Since no positive TV results were found in male detainees, exploration of characteristics associated with positive TV screening result was limited to females. Chi-square and t tests were used to examine associations between demographic, substance use, mental health, and sexual characteristics with positive TV screening results. Variables associated with positive TV screen at $P < 0.1$ in bivariate analyses were eligible for multivariable modeling. Stepwise logistic regression was utilized to determine characteristics independently associated with positive TV result. Data analyses were performed using SAS Enterprise Guide 7.1.

RESULTS

Testing was completed on 75 male urine specimens and 69 female urine specimens of detainees who consented to STI testing during the study period. Mean age of the study sample was 16.5 years, and the majority was African American (**Table 1**). Female detainees were significantly more likely than males to report tobacco use (56.5% vs 39.0%, $P = 0.01$) and alcohol use (18.8% vs 5.3%, $P = 0.02$). Marijuana use was similar in both sexes. Female detainees had significantly ($P < 0.01$) higher rates of reported suicidal ideation (18.8% vs 4.0% in males), self-injury (17.4% vs 1.3% in males), and family history of suicide (27.5% vs 2.7% in males). Approximately one-third of participants reported 2-3 sexual partners in the past year (37.1% in females vs 30.1% in males). Although reported rates of sexual activity (85.5% in fe-

Table 1. Demographic, Substance Use, Mental Health, and Sexual Activity Characteristics of Juvenile Detainees, by Sex

Characteristic	Male (N=75)	Female (N=69)	P value
Age (years), mean±SD	16.5±1.14	16.5±1.34	0.88
BMI (kg/m^2), mean±SD	23.0±4.95	26.0±6.72	<0.01
Race, n (%)			
African American	66 (88.0)	50 (72.5)	
White	5 (6.7)	17 (24.6)	<0.01
Other	4 (5.3)	2 (2.9)	
Grade, n (%)			
≤ 9th grade	22 (29.3)	27 (39.1)	
10th grade	19 (25.3)	13 (18.8)	0.34
≥11th grade	28 (37.3)	27 (39.1)	
Unknown	6 (8.0)	2 (2.9)	
Substance Use Characteristics			
Reported Tobacco Use, n (%)	27 (36.0)	39 (56.5)	0.01
Reported Alcohol Use, n (%)	4 (5.3)	13 (18.8)	0.02
Reported Marijuana Use, n (%)	35 (46.7)	31 (44.9)	0.83
Prior Drug Treatment, n (%)	10 (13.3)	11 (15.9)	0.66
Mental Health Characteristics			
Current Mental Health Condition, n (%)	14 (18.7)	23 (33.3)	0.04
History of Suicidal Ideation, n (%)	3 (4.0)	13 (18.8)	<0.01
History of Self Injury, n (%)	1 (1.3)	12 (17.4)	<0.01
Family History of Suicide, n (%)	2 (2.7)	19 (27.5)	<0.01
Sexual Activity Characteristics			
Reported Sexual Activity, n (%)	64 (85.3)	59 (85.5)	0.98
Reported Condom Use, n (%)	51 (68.0)	42 (60.1)	0.37
History of Anal Sex, n (%)	4 (5.3)	0 (0.0)	0.12
History of Oral Sex, n (%)	26 (34.7)	32 (46.3)	0.17
History of Vaginal Sex, n (%)	66 (88.0)	60 (86.1)	0.14
Age (years) at Sexual Debut, n (%)			
≤ 11	10 (13.3)	3 (4.4)	
12	12 (16.0)	6 (8.7)	
13	25 (33.3)	17 (24.6)	
14	10 (13.3)	12 (17.4)	0.01
≥15	6 (8.0)	21 (30.4)	
unknown	3 (4.0)	2 (2.9)	
n/a	9 (12.0)	8 (11.6)	
Sexual Partners in Past Year, n (%)			
0-1	11 (14.1)	19 (27.5)	
2-3	23 (30.1)	26 (37.1)	
4-6	11 (14.1)	9 (13.1)	
≥ 7	11 (14.7)	3 (4.4)	0.13
unknown	9 (12.0)	5 (7.3)	
n/a	10 (13.3)	7 (10.1)	
Current or Prior STI, n (%)	9 (12.0)	23 (33.3)	<0.01
Prior Pregnancy, n (%)	n/a	26 (37.7)	--

males vs 85.3% in males) and condom use (60.1% in females vs 68% in males) were similar, the rate of current or past STI was significantly higher in the female detainees (33.3% in females vs 12.0% in males, *P* <0.01). A prior pregnancy was reported by 37.7% of the female detainees.

Prevalence of each STI among tested detainees are reported in **Table 2**. Females had higher rates of all infections than males. *Trichomonas vaginalis* was identified in 7 of 69 (10.1%) female and 0 of 75 (0.0%) male detainees. *Neisseria gonorrhoeae* was identified in 12 of 69 (17.4%) female and 3 of 75 (4.0%) male detainees,

Table 2. Sexually Transmitted Infection (STI) Screening Results in Juvenile Detainees, by Sex

Sexually Transmitted Infection n (%, 95% CI)	Male (N=75)	Female (N=69)	P value
Neisseria gonorrhoeae	3 (4.0, 95% CI: 0.0-8.4)	12 (17.4, 95% CI: 8.5-26.3)	0.01
Chlamydia trachomatis	7 (9.3, 95% CI: 2.8-15.9)	16 (23.2, 95% CI: 13.2-33.2)	0.04
Trichomonas vaginalis	0 (0.0, 95% CI: 0.0-4.8)	7 (10.1, 95% CI: 4.2-19.8)	<0.01

and CT was identified in 16 of 69 (23.2%) female and 7 of 75 (9.3%) of male detainees.

As TV was identified only in female detainees, associative analyses were limited to this sex group. In unadjusted bivariate analyses, two variables were associated with positive TV screen result in females at significance level adequate for inclusion in multivariable modeling: prior history of STI (P = 0.03) and number of sexual partners (P = 0.01). In stepwise logistic regression, only prior history of STI was independently associated with presence of positive TV screen in female detainees (odds ratio 6.1, 95% CI 1.1 – 34.4).

DISCUSSION

This study assessed the prevalence of TV in detained youth in the FCJDF to determine whether routine screening may be indicated. We found a TV prevalence of approximately 10% among females. *Trichomonas vaginalis* was not identified in any male detainees. Our findings are similar to previously published data utilizing NAAT to screen for TV in detained adolescents.[16] In that study of 1181 detained adolescents, the prevalence of TV was 11% in females and 1% in males.

Several studies in adults have shown that TV infection disproportionately affects incarcerated populations.[17] A study in San Francisco County Jail inmates using urine NAAT found TV infections in 2.1% of men and 32.0% of women under the age of 25 years, which was a higher prevalence than we found in the current study.[18,19] It is known that TV infections are more prevalent with increasing age which may explain this discrepancy. Ginocchio et al evaluated 1215 women across the United States from multiple clinic sites, STD clinics, juvenile detention centers, and adult detention centers, and found that TV infections were more prevalent among women aged 40 years and older.[20]

In our study of adolescent detainees in Central Ohio, the presence of a current TV infection was associated with having history of a previous STI. *Trichomonas vaginalis* infection was not associated with age, grade, prior pregnancy, substance use, or having a current mental health condition. Of note, TV infections were only found in African American female detainees. Prior studies have demonstrated an increased prevalence of TV in African American female adolescents and young adults.[15,21]

This study does have limitations. STI testing at FCJDF is not mandatory; detainees may decline testing if they desire. Therefore, we are not able to determine a true prevalence of infection in the larger FCJDF population. It is possible that detainees with symptoms or concerns about prior sexual contacts would be more likely to consent to testing. In either case, several adolescents were identified and treated for TV who may have been missed if routine testing was not offered. An additional limitation of our study is the relatively small sample size, particularly for female detainees. Although we oversampled females, collecting data on them for approximately a year longer than males, we still were not able to achieve an equal sample size. The small sample size for females

likely further limited our ability to identify other characteristics associated with TV infection. Our findings are consistent with studies that show an increased prevalence of TV in African American females. In addition, the study population was limited in the number of Hispanic or Asian adolescents. Our findings are not necessarily generalizable to detained adolescents in other parts of the country.

PUBLIC HEALTH IMPLICATIONS

The CDC now suggests that providers consider screening women for TV in high-prevalence settings such as correctional facilities, and that decisions regarding screening be based on the local epidemiology of TV.[11] Our data support routine screening of female detainees at FCJDF, based on our finding of 10% positivity among females who underwent testing. *Trichomonas vaginalis* infections in females are associated with an increased risk of HIV acquisition and adverse pregnancy outcomes.[3,4] To date, no studies have demonstrated that increased case identification and treatment would lead to a reduction in these outcomes, and further investigation in these areas is certainly needed. Nonetheless, adolescents in the juvenile justice system report high rates of unprotected sex, and may be less likely to obtain regular reproductive health care and STI screening because many do not identify a primary care provider.[22, 23] The medical contact during detention provides an opportunity for such care, and STI testing should include the pathogens, including NG, CT, and TV, for which female detainees are at increased risk. Targeted education regarding STI risk reduction is also appropriate during these encounters. However, although such interventions may increase knowledge, they have not been shown to lead to significantly lower rates of STI or unprotected sex.[24] Therefore, such efforts do not diminish the need for STI testing.

Looking more broadly at this cohort of females detained at FCJDF, a number of health risks are apparent. Beyond their higher STI prevalence at the time of detention, they reported higher rates of tobacco and alcohol use, self-injurious thoughts and behaviors, and history of prior STI relative to males. A sizable minority (38%) reported a prior pregnancy. It may be that females detained at FCJDF represent a particularly high-risk group for a number of risky health behaviors, and risk-reduction interventions designed specifically for female detainees may be appropriate.

Our data does not support the routine screening of male detainees for TV at this time, as no TV infections were identified in males. It is not clear whether we would have identified more infections in males if our sample size was larger. Several previous studies have demonstrated higher prevalence of TV in females than males in various settings,[12,16,18] consistent with our findings. Furthermore, TV in males has not been demonstrated to be associated with increased HIV acquisition, or adverse pregnancy outcomes in female partners. The CDC does not recommend routine screening of males for TV in any setting at this time.

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Editorial note regarding this article:

The title of this article was changed on May 18, 2020, to avoid confusion with a 2017 poster presentation given by the author. The original article title was: *Trichomonas vaginalis* **in Detained Adolescents. Is Routine Screening Indicated? This pdf has been altered solely to reflect the new title and to add this editorial note.**

RESEARCH ARTICLE

An Examination of Dental Health Among Metropolitan and Appalachian Adolescents in Ohio

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ABSTRACT

Background: Poor dental health is a common chronic condition among youth. Appalachian versus metropolitan residence, socioeconomic status, and health behaviors contribute to poor dental health. Limited research has directly compared dental health and risk factors for poor dental health among Appalachian and metropolitan youth. We examined the association between dental health and residence among adolescent boys and explored socioeconomic and behavioral factors that may contribute to differences in dental health.

Methods: Adolescent males from metropolitan and rural Appalachian Ohio (n = 1220, age 11-16 years) reported their diet and tobacco use. Parents or guardians reported when boys had last visited the dentist and rated their dental health (excellent/very good/good versus fair/poor). Unadjusted logistic regression modeled the association between fair/poor dental health and residence (metropolitan versus Appalachian). Adjusted analyses controlled for race, household income, dental visits, diet, and tobacco use.

Results: Appalachian (versus metropolitan) boys were more likely to have used tobacco in the past 30 days and consumed fewer fruit and vegetables, more added sugar, and more sugary beverages. The relation between dental health and Appalachian versus metropolitan residence did not reach statistical significance, and adjusting for behavioral factors did little to change the observed association.

Conclusion: Our findings suggest that some of the urban/rural disparities in dental health observed in other studies may be related to behavioral factors like tobacco use and diet, but much remains unexplained. We provide support for behavioral interventions to address these issues in the Appalachian community.

Keywords: Appalachia, Dental health, Diet, Tobacco

INTRODUCTION

Good dental health, or the absence of dental decay and excessive tooth loss, is essential to good general health.[1] Although good dental health should be considered a priority in order to promote good general health, many children and adolescents are not meeting this goal. From 2011 through 2014, for example, 18.6% of youth had untreated dental caries,[1] which is one of the most common childhood chronic conditions.[2] A few years earlier, from 2005 through 2008, approximately 1 in 5 children and 1 in 7 adolescents had at least 1 untreated decayed tooth.[2]

A variety of factors affect overall dental health, including socioeconomic status, health behaviors, and geography. Regarding socioeconomic status, children aged 5 to 9 years from low-income backgrounds are more than twice as likely to have dental caries than children from higher income backgrounds.[3] Dental insurance quality and type may affect dental health. In Ohio, Medicaid covers 40% of all children,[4] and historically many dental professionals did not accept Medicaid.[5] However, expansions of Medicaid coverage have more recently been associated with better dental health and improved access to care among low-income and racial and ethnic minority populations.[6-8] Additionally, observed differences in dental care utilization between children with private versus public insurance are attenuated when confounding factors like overall health status and poverty level are controlled.[9] However, parents' satisfaction with their child's dental care is low when

their child is enrolled in Medicaid, and low satisfaction is associated with not having a regular source of dental care.[10] Travel distance and lack of public transportation may also contribute to poor dental health within low-income rural and urban communities.[11,12] Low health literacy might contribute to differences in dental health outcomes according to socioeconomic status, although results are contradictory and associations are generally weak.[13]

Health behaviors, like diet, tobacco use, and oral hygiene are also related to dental health among children and adolescents. Diet plays a major role in dental health, especially for tooth decay.[14] Moreover, the World Health Organization reported a positive association between increased consumption of free sugars, monosaccharides, and disaccharides that are added to food and sugars naturally present in honey, syrups, and juices and the increased prevalence of dental caries across all ages.[15] Tobacco use also leads to dental health issues including periodontal disease[16] and dental caries among adolescents.[17] Inadequate oral hygiene is another risk factor for poor dental health, especially among adolescents.[18]

Geography is related to dental health, as Appalachian residents are less likely to utilize dental care and have worse dental health than their metropolitan counterparts on average.[19] One cause of reduced dental care utilization in Appalachian areas may be related to fear of visiting the dentist. A study conducted in West Virginia, an entirely Appalachian state with known dental health disparities, reported a high prevalence (47.1%) of dental fear. Importantly, dental fear was associated with having delayed dental care appointments.[20] Dental health might also be less emphasized in Appalachian compared to metropolitan communities; in West Virginia, the need for good dental health was ranked as the lowest priority out of other health issues such as obesity, cancer, and alcohol and drug use.[21] Overall, poor diet, which includes sugary beverages, "low" fruit and vegetable intake, and added sugar, is more prevalent in Appalachian communities compared to metropolitan communities.[22] Also, the prevalence of tobacco use is greater in Appalachian adolescent populations compared to metropolitan adolescent populations.[23]

Although research has examined the overall health differences between Appalachian and metropolitan youth, few studies have directly compared these populations with respect to dental health status. Moreover, in spite of the interplay between geography, socioeconomic status, and health behaviors, examination of these factors in the same study has not been conducted to our knowledge. Understanding how these factors contribute to dental health among male youth has implications for public health in Ohio, which contains both Appalachian and metropolitan populations. The current study had the following objectives: (1) estimate the association between male adolescent dental health and Appalachian versus metropolitan residence and (2) examine how other demographic, socioeconomic, and behavioral risk factors affect the association between geography and adolescent dental health.

METHODS

Participants

Data came from the Buckeye Teen Health Study (BTHS), a sample of 1220 adolescent boys aged 11 to 16 years who resided in Franklin County, Ohio (N = 708), or 1 of 9 Appalachian Ohio counties (N = 512). Franklin County, which includes the city of Columbus, is designated metropolitan by the Office of Management and Budget. Appalachian Ohio counties were designated Appalachian by the Appalachian Regional Commission and included Brown, Clermont, Guernsey, Lawrence, Morgan, Muskingum, Noble, Scioto, and Washington. Only males were included in the study because an aim of the parent study was to measure predictors of smokeless tobacco use. Participants were recruited through probability address-based sampling (N = 991) and nonprobability convenience sampling (N = 229), including advertising at community events, snowball sampling, and advertising in various media outlets. Additional information about sampling and recruitment procedures are provided elsewhere.[24]

Setting and Design

The BTHS is a longitudinal cohort study; only baseline data are reported here. Thus, the current study is cross-sectional. At baseline, trained interviewers, residing in the same region as the participant, obtained informed permission and assent from parents/guardians and adolescent participants, respectively. Nonsensitive items, including age, race, and diet, were interviewer-administered. Sensitive items, including tobacco use, were administered using audio computer-assisted self-interviewing (ACASI). When permitted, participants were separated from their parents/guardians when completing the ACASI portion of the survey. Parents/guardians completed a self-administered questionnaire to provide information about participants' dental health, visits to the dentist, and household income. The Institutional Review Board at The Ohio State University approved all study procedures.

Measures

Outcome Variable

The primary outcome variable of this study was parent/guardian-reported dental health of the male youth participants, which was assessed with the question,[25] "How would you describe the condition of your son's teeth: excellent, very good, good, fair, or poor?" Responses were dichotomized as excellent/very good/good versus fair/poor.

Predictor Variable

The primary predictor variable was the social environment variable of living in metropolitan versus Appalachian Ohio. This variable was assessed upon sampling.

Risk Factors

Additional risk factors included dental visits, diet, tobacco use, and demographic variables. Parents/guardians reported dental visits with the item, "About how long has it been since your son visited a dentist? Include all types of dentists, such as orthodontists, oral surgeons, and all other dental specialists, as well as dental hygienists." Responses were dichotomized as less than a year and more than a year since last visiting the dentist. Participants' diets were assessed using the Block Kids 2004 Food Frequency Questionnaire (FFQ) from NutritionQuest.[26] Briefly, the FFQ asked participants to report how many days they consumed different foods and beverages in the past week and the typical serving size of each food or beverage. From the FFQ results, total cups of fruits and vegetables, teaspoons of added sugars, and average grams of sugary beverages were used. Participants' tobacco use was assessed separately for cigarettes, smokeless tobacco, electronic cigarettes, pipes, cigars, hookah, bidis, and kreteks, and participants who were tobacco users reported the last time they used each product. Product-specific results were combined to use of any tobacco product in the past 30 days (yes versus no). Demographic variables included age, race/ethnicity (white non-Hispanic, black non-Hispanic, and other), and household income (<$50000 versus $50000 or more).

Statistical Analysis

All analyses were survey-weighted to reflect the sampling design; details about weighting procedures are provided elsewhere.[24] Missing values of tobacco use or race/ethnicity were imputed using hot deck single imputation (<9% missing). Stratification variables for the hot deck imputation included age at enrollment (11-12, 13-14, and 15-16 years), residence, and household adult tobacco use. Participants who were missing parent-reported dental data were excluded from the analysis (N = 22). Most of the missing data were due to parents not enrolling in the study, and one parent responded "Don't Know" for both perceived dental health and dental visits.

Our analyses first described the distributions of age, race/ethnicity, dental visits, tobacco use, and diet overall and by metropolitan versus Appalachian residence. Second, we used Rao-Scott chi-square tests and linear regression models to estimate the associations between the predictor variable (ie, residence) and risk factors (ie, dental visits, diet, tobacco use, age, race/ethnicity, and income). Third, we used logistic regression to model the unadjusted association between parent/guardian-rated dental health and metropolitan versus Appalachian residence. Finally, we sequentially added risk factors to the model to estimate adjusted effects. The first model controlled for demographics and tobacco use. The next 3 models added 1 dietary variable at a time to avoid multicollinearity (ie, cups of fruits and vegetables, teaspoons of added sugars, and grams of sugary beverages were added separately to the first adjusted model). Finally, we fit the fifth model which included all risk factors except for sugary beverage intake due to its collinearity with added sugar intake. Only risk factors that were substantively or statistically associated with residence in the bivariable analyses were included in the adjusted models.

An alpha level of 0.05 was used for statistical significance. SAS version 9.4 (SAS Institute Inc., Cary, NC) was used to analyze the data.

RESULTS

Participant Characteristics

Overall, after applying survey weights, male youth were aged 14 years on average, 71.2% were white non-Hispanic, 33.8% had a total household income less than $50000, and 73.6% were from metropolitan Franklin County, Ohio. An estimated 92.8% of boys overall had dental health that was rated by parents as excellent/very good/good, 90.7% had visited the dentist in the past year, and 4.9% had used a tobacco product in the past 30 days. On average, boys consumed 15.6 ± 0.38 teaspoons of added sugar, 2.98 ± 0.08 cups of fruits and vegetables, and 310.8 ± 11.4 grams of sugary beverages per day.

Risk Factors

Compared to metropolitan boys, Appalachian boys were more likely to be white non-Hispanic (**Table 1**; P <0.001), have used tobacco in the past 30 days (P = 0.006), and have a household income less than $50000 ($P$ <0.001). Boys living in Appalachia also consumed fewer fruits and vegetables (P = 0.001), more added sugar (P <0.001), and more sugary beverages than their metropolitan counterparts (P <0.001).

Metropolitan Versus Appalachian Residence and Dental Health

The association between parent/guardian-rated dental health and residence was not statistically significant, although the trend was for boys residing in metropolitan areas to be more likely to have excellent/very good/good dental health than those in Appalachia (**Table 1**; P = 0.07). Results of unadjusted and adjusted logistic regression models that estimated the odds of fair/poor dental health are presented in **Table 2**. In the unadjusted logistic regression model, boys in Appalachian Ohio had somewhat higher odds of fair/poor dental health than boys in metropolitan Ohio, but the odds ratio did not reach statistical significance (OR = 1.61; 95% CI: 0.97, 2.67); they also did not reach statistical significance after accounting for race/ethnicity, household income, tobacco use, and dental visits, or when further controlling for diet variables individually. Age was not controlled for in any models because it was not substantively or statistically associated with parent-reported dental health or metropolitan versus Appalachian residence.

DISCUSSION

This study found an association between rural residence and several risk factors for poor oral health. Regarding diet, Appalachian adolescents consumed fewer total fruit and vegetables, but more

Table 1. Distribution of Parent-Reported Dental Health and Risk Factors by Metropolitan and Appalachian Residence, Ohio, 2015-2016[a]

	Metropolitan (n=708)	Appalachian (n=512)
Parent-reported dental health (%)		
Excellent, very good, or good	93.7	90.3
Fair or poor	6.3	9.7
Dental visits (%)		
Over 1 year ago	8.7	11.0
Within past year	91.3	89.0
Dietary variables (mean ± SEM)		
Total fruit and vegetables*	3.1 ± 0.1	2.6 ± 0.1
Added sugar*	14.6 ± 0.5	18.3 ± 0.6
Sugary beverage*	276.8 ± 13.6	404.6 ± 19.8
Past 30-day tobacco use (%)*		
Not used in 30 days	96.2	92.0
Used in 30 days	3.8	8.0
Age (%)		
11-13 years	51.3	50.0
14-16 years	48.7	50.0
Race/Ethnicity (%)*		
Non-Hispanic White	64.0	91.4
Non-Hispanic Black	22.0	1.6
Other	14.0	7.0
Household Income (%)*		
At or above $50000	70.0	55.3
Below $50000	30.0	44.7

Abbreviations: SEM = standard error of the mean
*$P < 0.01$
[a] Means and proportions are survey-weighted; unweighted subject counts are reported.

Table 2. Odds of Fair/Poor Dental Health Among Adolescent Boys in Metropolitan and Appalachian Ohio, 2015-2016[a]

	Model 1[b] OR (95% CI)	Model 2[b] OR (95% CI)	Model 3[b] OR (95% CI)	Model 4[b] OR (95% CI)	Model 5[b] OR (95% CI)	Model 6[b] OR (95% CI)
Residence						
Metropolitan	1.00	1.00	1.00	1.00	1.00	1.00
Appalachian	1.61 (0.97-2.67)	1.79 (0.96-3.33)	1.73 (0.93-3.21)	1.74 (0.95-3.19)	1.70 (0.92-3.13)	1.58 (0.86-2.90)
Race/Ethnicity						
White		1.00	1.00	1.00	1.00	1.00
Black		2.02 (0.89-4.56)	2.14 (0.95-4.78)	2.09 (0.93-4.70)	2.08 (0.93-4.67)	2.12 (0.95-4.74)
Other		0.79 (0.26-2.41)	0.83 (0.27-2.50)	0.79 (0.26-2.41)	0.79 (0.26-2.39)	0.85 (0.28-2.61)
Household income						
<$50000		1.00	1.00	1.00	1.00	1.00
≥$50000		0.66 (0.35-1.23)	0.65 (0.35-1.22)	0.66 (0.35-1.23)	0.67 (0.36-1.25)	0.69 (0.37-1.28)
Past 30-day tobacco use						
No		1.00	1.00	1.00	1.00	1.00
Yes		1.13 (0.40-3.23)	1.05 (0.37-3.01)	1.08 (0.37-3.10)	1.07 (0.37-3.09)	1.00 (0.35-2.88)
Dental visits						
Within year		1.00	1.00	1.00	1.00	1.00
>1 year ago		1.95 (0.85-4.44)	1.92 (0.83-4.45)	1.90 (0.83-4.35)	1.89 (0.82-4.34)	1.93 (0.83-4.49)
Fruit/Vegetable intake (per cup)			0.91 (0.82-1.02)			0.89 (0.79-1.00)
Sugary beverage intake (per gram)				1.00 (1.00-1.01)		
Added sugar intake (per teaspoon)					1.01 (0.99-1.03)	1.02 (1.00-1.04)

Abbreviations: OR=odds ratio; CI=confidence interval
[a] Logistic regression models were survey-weighted to represent the sampling design.
[b] Model 1 is the unadjusted model that includes residence only. Model 2 includes residence and controls for race/ethnicity, household income, dental visits in the last year, and any tobacco use. Model 3 includes the variables in Model 2 plus fruit and vegetable intake. Model 4 includes the variables in Model 2 plus total sugary beverage intake. Model 5 includes the variables in Model 2 plus added sugar intake. Model 6 includes the variables in Model 2 plus fruit and vegetable intake and added sugar intake.

added sugar and sugary beverages. We did not find support for an association between having visited the dentist in the past year and residence in the current study, with the prevalence of having visited the dentist in the past year being around 90% in both areas. Yet the prevalence of past 30-day tobacco use was higher among adolescents in Appalachia. These findings suggest that some behavioral and dental health risk factors might contribute to the dental health differences between urban and rural populations that have been found in other studies. However, when directly comparing the dental health of Appalachian and metropolitan adolescents in Ohio, we only found that Appalachian adolescents had a marginally higher proportion of fair or poor dental health than metropolitan adolescents. It is possible that significant dental health differences will emerge between these populations as they age, but that is a question for future research.

Our findings that multiple risk factors for marginally higher odds of fair or poor dental health were associated with residence agree with existing literature on rural disparities. In our study, household income was lower among the Appalachian compared to metropolitan boys. Other work in Appalachia has reported that more than one-fourth of households had an income of less than $10000, and more than half earned $30000 or less.[27] Regarding tobacco use, Appalachian males in our study were more likely to use any tobacco product in the past 30 days. In 2017, past 30-day tobacco use among adolescents aged 12 to 17 years in nonmetropolitan areas was 7.8%, while it was 3.8% in large metropolitan areas and 5.6% in small metropolitan areas.[23] Moreover, rural adolescents were more likely to become daily smokers than urban and suburban adolescents.[28] Additionally, Appalachian populations in Ohio are more likely to consume a poor diet compared to African American and white urban populations in Ohio.[22]

Because access to dental care is a major barrier to proper dental health, we examined whether having visited a dentist in the past year was associated with metropolitan versus Appalachian residence. Our findings showed that there was no difference in frequency of dental visits by residence. Interestingly, previous research has found that rural residents were less likely to visit the dentist in the past year.[29] An explanation for this difference could be due to all participants living in Ohio and not fully being representative of all rural areas in the country. Because Appalachian residents in Ohio could nonetheless live fairly close to more populous Ohio cities with pediatric dentists, distance might not be a major barrier to receiving care for our study participants. Another reason could be that most of our Appalachian counties included midsized cities that had at least a few practicing pediatric dentists. An additional possible explanation could be Ohio's Medicaid expansion in 2013. From preexpansion in 2012 to postexpansion in 2015, the prevalence of uninsured Ohio children decreased by half (4.6% to 2.2%).[30] While coverage for children is normally high, the expansion could have made visiting the dentist more feasible for some of our participants.

Strengths and Limitations

A key strength of the study was the large sample that was representative of metropolitan and Appalachian adolescent boys in our study counties, which allowed us to directly compare dental health between groups. The sample was survey-weighted and adjusted during the analysis to represent the target population. Another strength was that we were able to examine many variables that appear to explain some of the association between dental health and metropolitan versus Appalachian residence.

A major limitation of this study was that the participants' dental health status was obtained from the parent/guardian-reported survey; a more valid diagnosis of dental health would come from dental professionals or use of a comprehensive, validated self-administered scale (eg, the short-form oral health impact profile[31]). In fact, it is possible that using parent/guardian-reported dental health contributed to our marginally significant findings. For example, given the perceived low susceptibility to poor dental health among Appalachian adults,[11] it is possible that Appalachian parents might have been less likely to rate their child's dental health as poor than metropolitan parents in cases where the youth had the same dental health. As dental health was not the focus of the parent study, we also lacked additional oral health variables.

Another limitation was that we used cross-sectional data and were therefore unable to determine the temporality of our outcome and predictor variables. The FFQ, for example, inquired about foods and beverages consumed in the past week. Therefore, we had to assume that the adolescent's diet over the past week was representative of his diet when his level of dental heath was being established. Finally, data were obtained from a parent study which focused on smokeless tobacco use and thus was restricted to boys. Therefore, we were not able to identify possible differences in dental health and behavioral factors between genders. Further, there were only a few dental health questions asked and we could not gather a more comprehensive analysis of dental health and dental risk factors in relation to metropolitan versus Appalachian residence, such as number of times participants brush and floss per day.

PUBLIC HEALTH IMPLICATIONS

Disparities in risk factors for poor dental health between metropolitan and Appalachian Ohio adolescents are a public health problem. The Ohio Department of Health determined that 7 of the 11 counties with the poorest dental health in the state were Appalachian.[32] Furthermore, the prevalence of untreated cavities among Appalachian adolescents (27%) is greater than in the rest of Ohio (16%) and 69% higher than in urban or suburban areas.[32] Our results identify some risk factors that could potentially be addressed to improve dental health among Appalachian adolescents, including tobacco prevention and nutrition interventions.

Regarding tobacco prevention programs, many localities in Ohio, including Columbus in Franklin County, have adopted a Tobacco

21 law over the past few years, which prohibits all sales of tobacco products and paraphernalia to those under 21 years of age.[33] Recently, the state of Ohio also adopted Tobacco 21 policy. Tobacco 21 laws have been shown, in some cases, to reduce the prevalence of tobacco purchases among adolescents.[34] However, the effect of Tobacco 21 in Ohio has not yet been evaluated.

In order to target Appalachian adolescent populations, community and policy interventions in school meals could help improve the nutritional intake among students. The National School Lunch Program and the Ohio School Breakfast Program allow students to have free or reduced-price school meals based on multiple factors surrounding the household income.[35] Therefore, improving the nutritional standards of school lunches could help improve the dietary choices made by students, especially those who qualify for the program.[36] Considering Appalachian households have lower incomes, these families might benefit most from these programs. Dental practices also provide a natural setting to counsel both metropolitan and Appalachian Ohio adolescents about the dangers of tobacco use and poor nutrition to dental health.

The Ohio Department of Health has dental health care programs to help residents who struggle to access the proper care. Safety net dental programs include public dental clinics, dental programs in schools, and mobile programs which provide dental care to Medicaid patients and those who cannot afford a private dentist. Though this improves dental health care accessibility, some Appalachian counties do not have these clinics, and some require the patient to be a resident of the county to receive care.[37] Increased funding directed toward opening more safety net dental clinics in counties that do not have them would decrease travel obstacles as well as provide an opportunity for dental health professionals to counsel patients of all ages on good dental health practices.

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HPV Vaccine Coverage Among Adolescent Males in Ohio: Results of a Longitudinal Study

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ABSTRACT

Background: Human papillomavirus (HPV) vaccine has been recommended for males in the United States since 2011, yet little is known about vaccine coverage among adolescent males in Ohio. Our longitudinal study examined HPV vaccine coverage among adolescent males in Ohio and identified predictors of vaccination.

Methods: The Buckeye Teen Health Study recruited adolescent males aged 11 to 16 years and their parents from 1 urban county and 9 rural counties in Ohio. We report longitudinal vaccination data on 1126 adolescent males, with baseline data from 2015-2016 and follow-up data from 2017-2018. We used multivariable Poisson regression to identify predictors of HPV vaccine initiation that occurred between baseline and follow-up.

Results: At baseline, 42.4% of parents reported their sons had initiated the HPV vaccine series. Among parents whose sons were unvaccinated at baseline, 36.3% indicated initiation at follow-up. Initiation at follow-up was more common among sons who had received influenza vaccine (RR = 1.54, 95% CI = 1.08-2.18) or whose parents indicated lack of a recent visit to a doctor as the main reason for not yet vaccinating at baseline (RR = 1.41, 95% CI = 1.02-1.95). Initiation was less common among sons whose parents had an associate degree or some college education (RR = 0.28, 95% CI = 0.46-0.99). Main reasons for not vaccinating changed from baseline to follow-up among parents of unvaccinated sons.

Conclusion: Although HPV vaccine initiation increased over time, many adolescent males in Ohio remain unvaccinated. Findings can help guide future strategies for increasing HPV vaccine coverage among this population.

Keywords: Adolescent males, HPV vaccine, Parents, Longitudinal

INTRODUCTION

Human papillomavirus (HPV) is the most common sexually transmitted infection in the United States (US).[1] Data from 2013-2014 National Health and Nutrition Examination Survey (NHANES) show that about 45% of adult men in the US have a genital infection with at least one type of HPV, and about 25% have a genital infection with at least one oncogenic type of HPV.[2] In males, infection with nononcogenic HPV types can cause genital warts, while infection with oncogenic types can cause penile, anal, and oropharyngeal cancers.[3,4] From 1999 to 2015, HPV-associated cancer incidence rates among males increased, particularly for oropharyngeal and anal cancers.[5] In fact, the incidence rate of oropharyngeal cancer among males is expected to be higher than the incidence rate of cervical cancer among females by 2020.[6]

Human papillomavirus vaccine is approved by the Food and Drug Administration (FDA) to prevent HPV-associated cancers and geni-

tal warts in both males and females. The Advisory Committee on Immunization Practices (ACIP) recommends routine HPV vaccination for adolescents aged 11 to 12 years, and recently voted unanimously to support catch-up vaccination for persons through age 26.[7] Prior to this recent update, catch-up vaccination was recommended only for males aged 13 to 21 years, though males aged 22 to 26 years could still be vaccinated.[8] The HPV vaccine series consists of 2 doses if the series is initiated prior to age 15 years and 3 doses if the series is initiated after turning 15.[8] Despite recommendations, recent national data show that only about 63% of adolescent males in the US have received any doses of the HPV vaccine series (ie, vaccine initiation) and only about 44% are up to date with the vaccine series.[9] The HPV vaccine coverage remains much lower than coverage with other vaccines recommended for adolescents (eg, meningococcal and tetanus booster vaccines).[9]

Various parental, adolescent, and health characteristics are associated with HPV vaccination among adolescent males. There are

racial/ethnic differences in parents' intentions to vaccinate,[10] HPV vaccine initiation,[11–15] and completion of the HPV vaccine series[16] among adolescent males. Maternal education level also impacts vaccine initiation among adolescent males.[12,16] Health care providers' recommendation for HPV vaccination increases parents' intention to vaccinate their sons,[10,17] reduces parents' vaccine hesitancy and safety concerns about the vaccine,[18] and increases vaccine initiation.[15] Additional factors associated with HPV vaccination include receipt of other vaccines[13,14,16] as well as the ages of the parents[12,13] and the adolescent.[12] However, much of this evidence is derived from cross-sectional surveys, with only a few longitudinal studies[19,20] examining predictors of HPV vaccine coverage among adolescent males.

Little research has explored HPV vaccine coverage in Ohio. Recent data suggest that HPV vaccine coverage among adolescents in Ohio is slightly lower than the US as a whole.[9] However, there is potentially important variation within the state of Ohio, as vaccine coverage tends to be higher among adolescent males residing in urban and suburban areas compared to those residing in rural areas.[12] One predominantly rural area in Ohio is Appalachian Ohio, a 32-county region in the southern and eastern part of the state. Appalachia has several existing HPV-associated health disparities, including higher incidence rates of multiple HPV-related cancers.[21] Past studies have shown that knowledge about HPV vaccine is low among parents of adolescent males in Appalachian Ohio, though many are willing to vaccinate their sons.[22,23]

In this article, we report longitudinal data on HPV vaccine coverage among adolescent males in Ohio. In doing so, we identify predictors of HPV vaccination, including how vaccination may differ between an urban area of Ohio and a rural area (ie, Appalachian Ohio). We also examine parents' reasons for not vaccinating their sons and their willingness to vaccinate in the future. Findings will be useful for better understanding HPV vaccination among adolescents in Ohio and developing future strategies for increasing vaccine coverage.

METHODS

Setting and Design

The Buckeye Teen Health Study was a prospective cohort study that examined the impact of tobacco advertising on adolescent tobacco use in Ohio. As part of this study, data were collected on a range of health behaviors among adolescents, including HPV vaccination. We analyzed the resulting data for the current report.

The methodologies of the Buckeye Teen Health Study have been described elsewhere[24] and briefly here. Both probability and nonprobability sampling methods were used to recruit participants for this study. All recruiting efforts occurred in 1 urban county (Franklin) and 9 Appalachian counties (Brown, Guernsey, Lawrence, Muskingum, Scioto, Clermont, Noble, Morgan, and Washington) in Ohio. For probability sampling, we used address-based sampling of US Postal Service addresses to select house-

holds to contact. A packet with study information and a brief screener was sent to each selected household to determine if there were any eligible adolescents in the household. For nonprobability sampling, we used strategies such as snowball sampling, attending community events, and advertisements in local newspapers and radio to identify potentially eligible households.

Participants

To be eligible, adolescents had to be male, aged 11 to 16 years, living in a county included in the study, and able to complete study surveys. Data were also collected from parents of the adolescents. Parents included legal guardians and other adults who were involved in the care of the adolescent and living in the same household as the adolescent (hereafter referred to as "parents"). Adolescents who had hearing and vision impairments and parents or adolescents who were unable to speak English were excluded from the study.

Procedures

The Institutional Review Board at The Ohio State University approved the study protocol. Parents at potentially eligible households were contacted via telephone to confirm eligibility and arrange a baseline interview. Prior to the start of baseline interviews, parents provided consent to participate and adolescents provided assent. Trained interviewers administered the baseline survey to the adolescents, which included both interviewer-administered and audio-administered portions. Parents completed self-administered baseline surveys. Adolescents completed follow-up surveys at months 6, 12, 18 (telephone survey), and 24 (in-person or telephone survey) after baseline. Parents completed follow-up telephone surveys at months 12 and 24 after baseline. We report data from only the baseline and 24-month follow-up surveys of parents since these are the only surveys that assessed HPV vaccination among the adolescents. The HPV vaccination items were asked to the parent in the household that was identified as knowing the most about the adolescent's health. For the remainder of this article, we refer to the 24-month parent survey as the "follow-up survey." Baseline data collection occurred from January 2015 to June 2016, and data collection for the 24-month follow-up survey occurred from January 2017 to August 2018. Parents received a $10 gift card for the baseline survey and a $5 gift card for the follow-up survey.

The current study includes HPV vaccination data on a total of 1126 adolescents, as reported by parents. Of the 1126 parents who completed a baseline survey, 817 also completed a follow-up survey.

Measures

All HPV vaccination items were included on parent surveys at both baseline and follow-up. We assessed parents' reports of whether or not their sons had received at least 1 dose of HPV vaccine (ie, HPV vaccine initiation) at each time point. If parents indicated HPV vaccine initiation, we then assessed the number of HPV vaccine doses the sons had received. Our primary outcome was HPV

vaccine initiation at follow-up among sons who were not vaccinated at baseline, though we report HPV vaccine coverage estimates at both baseline and follow-up.

Among parents of unvaccinated sons (ie, those who had not received any doses of HPV vaccine), the survey assessed their willingness to vaccinate their son if the vaccine was free. This survey item included a 5-point scale with responses of "definitely not willing," "probably not willing," "not sure," "probably willing," and "definitely willing." We classified responses into 1 of 3 categories (definitely/probably not willing, not sure, or definitely/probably

willing). The survey also asked parents of unvaccinated sons the main reason why their son had not yet received HPV vaccine. Parents indicated only 1 reason from a predefined list of potential reasons, though parents were provided the option to specify a reason not included in the list.

We collected information on various demographic and health-related characteristics of parents and sons from parent surveys at baseline to examine as potential predictors of HPV vaccine initiation (**Tables 1 and 2**). For county type, "urban" was defined as Franklin County and "rural" was defined as the 9 Appalachian Ohio

Table 1. Characteristics of Parents and Their Adolescent Sons

	Baseline Only n=309	Both Baseline and Follow-up n=817	*P* value
Parent Characteristics			
Gender			
Female	266 (86.6)	710 (87.1)	0.83
Male	41 (13.4)	105 (12.9)	
Age (years)			
Less than 40	135 (43.7)	198 (24.3)	<0.0001
Between 40 and 50	130 (42.7)	430 (52.6)	
Greater than 50	44 (14.2)	189 (23.1)	
Race/ethnicity			
Non-Hispanic white	235 (77.3)	665 (81.8)	0.21
Non-Hispanic black	45 (14.8)	91 (11.2)	
Other	24 (7.9)	57 (7.0)	
Education status			
High school or below	70 (22.7)	111 (13.6)	<0.0001
Associate degree or some college	142 (46.1)	256 (31.4)	
College degree	67 (21.8)	249 (30.5)	
More than a college degree	29 (9.4)	200 (24.5)	
Income			
Less than $25000	69 (23.5)	100 (12.5)	<0.0001
$25000 - $50000	77 (26.3)	135 (16.9)	
More than $50000	147 (50.2)	563 (70.6)	
Marital status			
Married	193 (63.7)	600 (74.3)	<0.01
Not married	110 (36.3)	208 (25.7)	
County type			
Urban	150 (48.5)	501 (61.3)	<0.0001
Rural	159 (51.5)	316 (38.7)	
Adolescent Male Characteristics			
Age (years)			
11-12	82 (26.5)	264 (32.3)	0.09
13-14	111 (35.9)	294 (36.0)	
15-16	116 (37.6)	259 (31.7)	
Race/ethnicity			
Non-Hispanic white	214 (69.7)	630 (77.4)	0.03
Non-Hispanic black	49 (16.0)	91 (11.2)	
Other	44 (14.3)	93 (11.4)	

Totals may not sum to stated sample size due to missing data. Percentages may not sum to 100% due to rounding. "Baseline Only" includes parents who only completed the baseline survey, and "Both Baseline and Follow-up" includes parents who completed both a baseline and 24-month follow-up survey.

counties. Parents indicated whether their sons had received other vaccines recommended for adolescents (tetanus booster vaccine, influenza vaccine, and meningococcal vaccine).[25]

Statistical Analysis

We first calculated descriptive statistics (eg, frequencies and percentages for categorical variables) and used chi-square tests to examine potential differences between participants who completed only the baseline survey and those who completed both the baseline and follow-up surveys. We used Poisson regression to identify baseline characteristics associated with HPV vaccine initiation at follow-up among sons who were unvaccinated at baseline. We first identified variables associated with HPV vaccine initiation in bivariate analyses ($P <0.10$). We then entered these variables into a multivariable model. Poisson regression models produced relative risks (RRs) and 95% confidence intervals (CIs).

We compared baseline and follow-up data on parents' reasons why their sons had not been vaccinated and their willingness to vaccinate their sons. These comparisons were made using McNemar chi-square test for paired data. All analyses were carried out using SAS version 9.4 (SAS Institute Inc., Cary, NC) with an alpha level of 0.05.

RESULTS

Participant Characteristics

Parents who completed both the baseline and follow-up surveys were mostly female (87.1%), 40 years of age or older (75.8%), non-Hispanic white (81.8%), married (74.3%), and reported an income of more than $50000 (70.6%) (**Table 1**). Most sons were also non-Hispanic white (77.4%). Compared to parents who completed both surveys, parents who completed only the baseline survey tended to be younger, have less education, report lower incomes, not be married, live in a rural county, and have sons who were not non-Hispanic white (all $P <0.05$).

HPV Vaccination

At baseline, parents indicated that 477 of 1126 (42.4%) adolescents had initiated the HPV vaccine series. Among these, 188 of 477 (39.4%) had received 1 dose, 75 of 477 (15.7%) had received 2 doses, 201 of 477 (42.1%) had received 3 doses, and 13 of 477 (2.7%) were not sure about the number of doses received. There was no difference in vaccine initiation at baseline among sons whose parents completed both surveys and sons whose parents completed only the baseline survey (41.1% vs 45.6%, P = 0.17). Among sons who were unvaccinated at baseline and whose parents completed a follow-up survey, 166 of 457 (36.3%) had initiated the HPV vaccine series at follow-up. Among these, 69 of 166 (41.6%) had received 1 dose, 42 of 166 (25.3%) had received 2 doses, 54 of 166 (32.5%) had received 3 doses, and 1 of 166 (0.6%) was not sure about the number of doses received.

Predictors of HPV Vaccine Initiation

Multivariable analyses identified several predictors of HPV vaccine initiation at follow-up among sons who were unvaccinated at baseline. Initiation was lower among sons of parents with an associate degree or some college education compared to parents with a high school degree or less (RR = 0.28, 95% CI = 0.46-0.99) (**Table 2**; see Supplemental Material for bivariate results). Receipt of other recommended adolescent vaccines also predicted HPV vaccine initiation, albeit in different directions. Sons whose parents indicated they had received influenza vaccine were more likely to initiate the HPV vaccine series (RR = 1.54, 95% CI = 1.08-2.18), while sons whose parents indicated they had received tetanus booster vaccine were less likely to initiate the HPV vaccine series (RR = 0.68, 95% CI = 0.50-0.94). Parents who indicated their sons had not visited a doctor recently as the main reason for not yet vaccinating at baseline were more likely to indicate initiation at follow-up than parents who did not provide this reason at baseline (RR = 1.41, 95% CI = 1.02-1.95). Compared to parents who were definitely or probably willing to vaccinate their sons against HPV at baseline, parents who were not sure (RR = 0.58, 95% CI = 0.43-0.78) or who were definitely or probably not willing to vaccinate (RR = 0.22, 95% CI = 0.11-0.46) were less likely to report initiation at follow-up. No additional variables predicted HPV vaccine initiation, including whether participants resided in an urban or rural county.

Reasons for Not Vaccinating and Willingness to Vaccinate

The 3 most common reasons given at baseline for why parents had not yet vaccinated their son against HPV were "His doctor did not recommend it" (16.3%, 97 of 595), "I do not know enough about it yet" (12.6%, 75 of 595) and "My son is too young" (10.6%, 63 of 595) (**Table 3**). At follow-up, the most common reasons were "It might be unsafe" (18.2%, 49 of 270), "His doctor did not recommend it" (15.6%, 42 of 270), and "It is too new" (11.9%, 32 of 270). Reasons more commonly reported at follow-up compared to baseline were "It is too new" and "My son is not having sex yet" (both $P <0.05$). Conversely, reasons more commonly reported at baseline than follow-up were "I never heard of the vaccine" and "My son is too young" (both $P <0.05$).

Among parents of unvaccinated sons, willingness to vaccinate their sons against HPV decreased from baseline to follow-up ($P <0.01$). The percentage of parents who were definitely or probably willing to vaccinate decreased from baseline to follow-up (41.8% vs 30.6%), while the percentage of parents who were definitely or probably not willing to vaccinate increased from baseline to follow-up (21.8% vs 43.0%).

DISCUSSION

Our longitudinal study provides important insight into HPV vaccine coverage among adolescent males in Ohio. At baseline, just over 40% of adolescent males had initiated the HPV vaccine series. In a similar time period as our study's baseline data

Table 2. Longitudinal Predictors of HPV Vaccine Initiation Among Adolescent Males

	Number of Parents Reporting HPV Vaccine Initiation Among Sons at Follow-up/ Total Number of Parents in the Category (%)	Multivariable RR (95% CI)
Parent Characteristics		
Race/ethnicity		
Non-Hispanic white	129/377 (34.2)	Ref
Non-Hispanic black	25/46 (54.4)	0.68 (0.28-1.69)
Other	11/31 (35.5)	0.55 (0.23-1.29)
Education status		
High school or below	31/70 (44.3)	Ref
Associate degree or some college	48/157 (30.6)	0.28 (0.46-0.99)*
College degree	52/141 (36.9)	0.88 (0.60-1.29)
More than a college degree	35/88 (39.8)	0.84 (0.57-1.25)
Reasons for Not Vaccinating		
I do not know enough about it yet		
Yes	10/52 (19.2)	0.63 (0.35-1.14)
No	134/365 (36.7)	Ref
It might be unsafe		
Yes	4/38 (10.5)	0.72 (0.25-2.04)
No	140/379 (36.9)	Ref
My son is too young		
Yes	25/48 (52.1)	1.09 (0.80-1.50)
No	119/369 (32.3)	Ref
My son has not been to the doctor recently		
Yes	11/16 (68.8)	1.41 (1.02-1.95)*
No	133/401 (33.2)	Ref
Willingness to Vaccinate		
Definitely/Probably willing	101/185 (54.6)	Ref
Not sure	52/164 (31.7)	0.58 (0.43-0.78)**
Definitely/Probably not willing	9/99 (9.1)	0.22 (0.11-0.46)**
Adolescent Male Characteristics		
Age (years)		
11-12	75/176 (42.6)	Ref
13-14	57/163 (35.0)	0.91 (0.69-1.21)
15-16	34/118 (28.8)	0.79 (0.57-1.10)
Son's race/Ethnicity		
Non-Hispanic white	125/363 (34.4)	Ref
Non-Hispanic black	25/45 (55.6)	2.39 (0.99-5.74)
Other	16/48 (33.3)	1.01 (0.51-2.00)
Received influenza vaccine		
Yes	130/306 (42.5)	1.54 (1.08-2.18)*
No	35/150 (23.3)	Ref
Received tetanus booster vaccine		
Yes	131/385 (34.0)	0.68 (0.50-0.94)*
No	35/72 (48.6)	Ref

Note. Predictors were assessed during the baseline survey, and the outcome of HPV vaccine initiation was assessed during the 24-month follow-up survey. Analyses included parents (n = 466) who reported at baseline their sons had not received any doses of HPV vaccine and completed a follow-up survey. Totals may not sum to stated sample size due to missing data.
HPV=human papillomavirus; RR= relative risk; CI=confidence interval; Ref=referent group.
* P <0.05
** P <0.001

Table 3. Reasons Given by Parents for Their Sons Not Receiving HPV Vaccine

	Baseline % (n=595)	Follow-up % (n=270)
I never heard of the vaccine	7.2	2.6*
I do not know enough about it yet	12.6	10.7
I did not know boys are allowed to get it	9.4	4.1
It is too new	4.7	11.9*
It might be unsafe	9.1	18.2
My son is too young	10.6	4.1*
My son is not having sex yet	5.9	8.5*
My son has not been to the doctor recently	4.5	5.6
His doctor did not recommend it	16.3	15.6

* *P* <0.05

collection, national data showed that 56% of adolescent males in the US had initiated the vaccine series.[26] The estimate from our study is likely lower than this national estimate since our study included a younger age range (11 to 16 years) than the national data (13 to 17 years), and HPV vaccination tends to be lower among younger adolescents.[26] Among participants who were unvaccinated at baseline, over one-third initiated the vaccine series by follow-up. The increase between baseline and follow-up is much larger than the 6% increase observed in a past longitudinal study of HPV vaccination among adolescent males in the US from 2010-2011.[19] This may be largely attributable to the follow-up period of this past study being shorter (ie, about a 1 year follow-up period) and that it began before the recommendation for routine HPV vaccination for males in the US was issued in 2011.[27] Despite the increase in HPV vaccination found in our study, it is important to continue to monitor changes in vaccination over time since many adolescent males in Ohio remain unvaccinated.

We found that several variables predicted HPV vaccine initiation between baseline and follow-up. Initiation was higher among participants whose parents had a high school education or less compared to those whose parents had more education, though the only comparison that reached statistical significance involved parents with an associate degree or some college education. This overall pattern is similar to past research where parents with higher educational attainment had sons who tended to be less likely to have initiated the HPV vaccine series.[12,28] Although parents with higher educational attainment know more about the HPV vaccine,[29] they also have expressed more concerns about the effectiveness and safety of HPV vaccine,[30] and this may help explain why vaccination was lower among parents with greater education in our study.

Parents who indicated their sons had not been to the doctor recently as a main reason for not yet vaccinating at baseline were more likely to report initiation among their sons at follow-up. Many of these sons likely had visits to a health care provider between baseline and follow-up, providing opportunities for vaccination to occur. The results reiterate the importance of adolescents attending health care visits in order to improve HPV vaccine coverage.[31,32] At visits, it is critical that health care providers offer recommendations for HPV vaccine, as it is a key factor influencing vaccination decisions.[33] Indeed, one of the most common reasons that parents reported for not yet vaccinating was lack of a health care provider recommendation. It is possible that some of these parents forgot receiving a recommendation or misunderstood information about HPV vaccine from a health care provider.[12] Thus, it is important that health care providers are explicit in their messages about adolescent vaccinations.[12] Explicit health care provider recommendations for HPV vaccination may be especially important in Ohio, as Ohio has one of the lowest vaccination rates among adolescent males whose parents have not received a provider recommendation to vaccinate.[12] Further, in addition to health care providers in traditional medical settings, it is important to continue to explore the potential impact that nontraditional settings (eg, pharmacies) can have on increasing HPV vaccine coverage. [34]

We found an association between parents' willingness to vaccinate at baseline and HPV vaccine initiation at follow-up. Interestingly, willingness to vaccinate decreased from baseline to follow-up. This is contrary to a previous study reporting no change in willingness of parents to vaccinate their sons for HPV over a 3-year period, though this was a serial cross-sectional study that included different parents in each data year.[35] In our longitudinal study, parents' willingness was only assessed among those whose sons were unvaccinated at each survey time point. Many parents who indicated a willingness to vaccinate at baseline vaccinated their sons by follow-up (and were therefore not asked about willingness at follow-up), leaving a higher proportion of parents at follow-up who likely had less interest in vaccinating but were still asked about their willingness. This may also help explain the observed changes in parents' reasons for not vaccinating between baseline and follow-up.

Parents were more likely to report HPV vaccine initiation at follow-up if they indicated their son had received influenza vaccine at baseline. These findings are similar to past studies showing that receipt of other recommended adolescent vaccines was correlated with HPV vaccination.[13,16,36,37] This is likely reflective of these parents having greater acceptability of vaccines in general, but it also underscores the potential to increase HPV vaccine coverage by administering the vaccine concomitantly with other recommended vaccines. Indeed, one of the recommendations of the President's Cancer Panel Report is to reduce missed clinical opportunities and provide HPV vaccine during the same health care visit as other adolescent vaccinations.[38] Given that Ohio has mandates currently in place that require tetanus booster and meningococcal vaccination for school entry for adolescents,[39] administering HPV vaccine during the same visits as these other vaccines may be a promising approach for increasing HPV vaccine coverage in the state.

We did not find differences in HPV vaccination initiation across racial/ethnic groups (which is contrary to past studies[12-14,16]) or between the urban (ie, Franklin County) and rural (ie, Appalachian Ohio) counties in our study. The lack of differences between the urban and rural counties is actually encouraging since HPV vaccine coverage has tended to be lower among adolescent males who reside in rural areas.[9,12,40] Moreover, past research has shown that HPV vaccine coverage among adolescent females may be lower in some parts of Appalachia compared to the rest of the US,[41] but our findings suggest this pattern may not be occurring among males in Appalachian Ohio. Further research is needed to better understand how rurality affects vaccine coverage across the entire state of Ohio.

Study strengths include the longitudinal design, large sample size, and assessment of a range of potential predictors. The study also has some limitations. For our primary outcome, we relied on parents' reports of their sons' HPV vaccination status, though most parents are able to accurately remember if their children have received this vaccine.[42] It is also possible that some adolescents went on to receive HPV vaccine after the follow-up data collection period ended. In addition, we did not collect data on the age of the sons when they received the HPV vaccine, which prevented us from examining how many were vaccinated during the ideal age range of 11 to 12 years. We also did not collect data on HPV infection or HPV-associated disease among parents or other family members, which could impact parents' decisions on vaccinating their sons. Participants in our study were from 10 counties in Ohio, though both probability and nonprobability sampling methods were used to increase the generalizability of the sample. Lastly, there were differences between participants who completed both the baseline and follow-up survey and those who completed only the baseline survey, which could have resulted in selective attrition.

PUBLIC HEALTH IMPLICATIONS

To our knowledge, this is the first longitudinal study of HPV vaccine coverage among adolescent males in Ohio. Despite the observed increases in HPV vaccine coverage during our study's duration, many adolescent males in Ohio remain unvaccinated. Study findings also highlight several key predictors of HPV vaccine initiation and the most common reasons why parents are not vaccinating their sons. We believe this information can be used to guide the development of future strategies and programs to increase HPV vaccine coverage in Ohio.

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Human Development and Controlled Substance Prescribing in Ohio Counties

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ABSTRACT

Background: Human development is a holistic measure of well-being. The American Human Development Index (AHDI) operationalizes the concept for the American context, using a composite measure of income, education, and health. This work presents the first county-level examination of AHDI for the state of Ohio and examines the relationship between human development and controlled substance prescribing.

Methods: Publicly available data from the census and prior publications were compiled to calculate county-level AHDI for all 88 Ohio counties. Correlations were examined between AHDI and 4 classes of controlled substances, opioids, benzodiazepines, stimulants, and sedatives, using Pearson product moment correlation coefficient.

Results: County AHDI scores ranged from 3.3 to 7.6, with mean and median values of 4.8. At the county level, human development is negatively correlated with opioid (r = -0.46, r^2 = 0.22, P <0.0001) and benzodiazepine (r = -0.43, r^2 = 0.18, P <0.0001) prescribing and positively associated with stimulant prescribing (r = 0.49, r^2 = 0.24, P <0.0001). Neither sedative prescribing practices (r = 0.09, P = 0.40) nor median age (r = -0.09, P = 0.41) were significantly correlated with AHDI.

Conclusion: There is a strong correlation between AHDI and prescribing of several classes of controlled substances. Work remains to ascertain mechanisms and directionality of these relationships. Whether higher prescribing in areas with lower human development is an attempt to medicate health inequity or low human development is an additional manifestation of the opioid epidemic, this study underscores the necessity of pursuing equity in all policies.

Keywords: Opioids, Controlled substances, Prescribing, Human development, Human development index

INTRODUCTION

Improving the well-being of populations is the central work of public health. Human development is a capabilitarian construction of well-being, that is, one which posits one's ability to act and exist in a manner consistent with one's values as the ultimate measure of utility.[1,2] Introduced in 1990, the Human Development Index (HDI) was an attempt by the United Nations to operationalize this idea by combining health, education, and economics into a single, holistic measure of human well-being in populations.[3]

The American HDI (AHDI), an adaptation for use within the United States, employs the same dimensions, but utilizes context-appropriate measures. Specifically, AHDI measures economic well-being using median personal earnings, health using life expectancy

at birth, and education using a composite measure of educational attainment and school enrollment.[4] Measure of America, a project of the Social Science Research Council, has applied the AHDI at national, state, and, in some areas, county and local levels, examining geographic, demographic, and temporal trends.

The Ohio Automated Rx Reporting System (OARRS), a prescription drug monitoring program, was established by the State of Ohio Board of Pharmacy using powers granted by Ohio Rev Code §4729.75, a 2005 law.[5,6] The Ohio Automated Rx Reporting System seeks to reduce the misuse and diversion of controlled substances by identifying potentially criminal behavior by health care providers, identifying individuals who may need help with addiction, and driving policy decisions such as prescribing guidelines.

The Ohio Automated Rx Reporting System gathers data on Drug Enforcement Agency Schedule II, III, IV, and V drugs, and publicly releases quarterly county-level data on 4 classes of drugs: (1) opioids commonly used to treat acute or chronic pain (excluding buprenorphine, which is used to treat opioid dependence), (2) benzodiazepines used in the treatment of panic and anxiety disorders, (3) stimulants used to treat attention and hyperactivity disorders, obesity, or sleep-related disorders, and (4) nonopioid sedatives used for treatment of insomnia.

As an example of how ecological studies are conducted, one of the authors (RMK) assembled a set of state-level data for students to conduct their own studies in an introductory epidemiology class. One of the stronger relationships observed was between AHDI[7] and opioid prescription,[8] which had a strong, negative correlation coefficient.[9] To explore this relationship further, the current study calculates the AHDI for all 88 counties in Ohio, and examines the correlation between human development and physician prescribing practices at the county level. The AHDI and constituent index scores for each Ohio county are also presented for use in future research.

METHODS

Setting and Design

We used county-level data for all 88 Ohio counties. The data were collected during or around 2016. An ecological study was performed using publicly available data.

Procedures

Publicly available data were gathered from multiple sources to calculate the AHDI for each of Ohio's 88 counties. Ohio Northern University's Institutional Review Board reviewed and determined the project to be exempt from review due to the use of aggregate data.

Measures

Dependent Variables

Prescribing Practices. County-level data on controlled substance prescribing practices were downloaded from OARRS through the quarterly county data.[10] Total number of doses prescribed per capita in 2016 were compiled for opioids, benzodiazepines, stimulants, and sedatives.

Independent Variables

American HDI. The AHDI is calculated as the mean of the Income, Health, and Education Indices, constructed in accordance with published methodologies for the report Measuring America: Ten Years and Counting.[11]

Income Index. Median personal earnings were evaluated using 5-year estimates from the 2016 American Community Survey drawn from table S2001, Earnings in the Past 12 Months (In 2016 Inflation-adjusted Dollars).[12] To calculate the Income Index, the log of the median earnings (HC01_EST_VC02) was rescaled so that values of log ($16009) -log ($67730) remapped to a 0 to 10 scale.

Health Index. Life expectancy at birth in 2014, the most recent year for which data were available, was accessed via the Global Health Data Exchange to calculate the Health Index.[13,14] Life expectancy was linearly rescaled so that life expectancies from 66 to 90 years remapped to a 0 to 10 scale.

Education Index. Educational attainment drew data from 9-year estimates from the 2016 American Community Survey drawn from table DP02, Selected Social Characteristics in the United States.[15] An Educational Attainment Score was determined by summing the percentage of residents aged 25 years and older with at least a high school degree (HC03_VC95), at least a bachelor's degree (HC03_VC96), and a professional degree (HC03_VC92) and dividing the result by 100. An Educational Attainment Index was calculated by linearly rescaling scores so that Educational Attainment Scores of 0.5 to 2.0 remapped to a 0 to 10 scale.

Educational enrollment data were 5-year estimates from the 2016 American Community Survey drawn from table S1401, School Enrollment.[16] The net gross enrollment ratio was calculated by dividing the population aged 3 years and over enrolled in school (HC01_EST_VC01) by the population aged 3 to 24 years (sum of HC01_EST_VC16, HC01_EST_VC18, HC01_EST_VC21, HC01_EST_VC24, and HC01_EST_VC39). For the Enrollment index, the enrollment ratio was linearly rescaled so that values of 60% to 95% remapped to a 0 to 10 scale.

The Education Index was calculated as a weighted average of the Educational Attainment and Enrollment Indices, with Educational Attainment receiving twice the weight of Enrollment.

Age. County-level data on median age (HD01_VD02), a potential confounder, was evaluated using 5-year estimates from the 2016 American Community Survey drawn from table B01002, Median Age by Sex.[17]

Statistical Analysis

Tests for association between paired samples were obtained using Pearson product moment correlation coefficients in R (64-bit, version 3.4.3 for Windows) using the cor.test function.[18,19] Full R code for the analyses is included in the Supplemental Material. Maps showing the geographic distributions of key variables were constructed using the free and open-source geographic information system QGIS (version 2.18.3 for Windows).[20] A shapefile containing county boundaries was obtained from the Ohio Department of Transportation's Transportation Information Mapping System (TIMS).[21] Detailed methodology for constructing choropleth maps are found in Supplemental Material Appendix B. Figure designs were implemented using the Solarized color palette.[22]

RESULTS

The AHDI scores for Ohio counties ranged from a minimum of 3.3 to a maximum of 7.6, with a median and mean value of 4.8. Full study data are presented in tabular form in the Supplemental Material. The minimum score of 3.3 was observed in Holmes County, where a low Income Index and state-minimum Education Index

offset a top 10 ranking on the Health Index. Delaware County had not only the highest AHDI score of 7.6, but also the first- or second-highest score in each of the subindices. A map showing the geographic distribution of human development scores is presented in **Figure 1**.
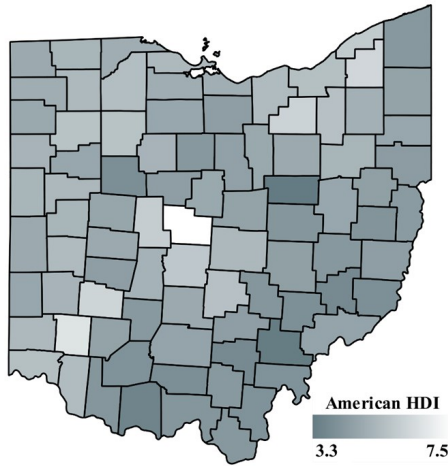
The geographic distribution of prescribing practices for controlled substances, as reported in OARRS, are illustrated in **Figure 2**. Opioids (r = -0.46, P <0.0001), benzodiazepines (r = -0.43, P <0.0001), and stimulants (r = 0.49, P <0.0001) were all significantly associated with AHDI score at the county level (**Figure 3**). Prescribing practices for sedatives were not significantly associated with human development at the county level (r = 0.09, P = 0.40). Median age was also not significantly associated with human development in the sample (r = -0.09, P = 0.41).

DISCUSSION

In the current study, the AHDI was significantly correlated with 3 of the 4 classes of controlled substances: opioids, benzodiazepines, and stimulants. Interestingly, human development was negatively correlated with the former 2 classes of drugs, meaning better-off populations are less likely to have high rates of opioid and benzodiazepine prescribing, but positively correlated with stimulant prescriptions.

The ecological design of the current study necessitates caution when interpreting results, especially with regard to the ecological

Figure 1. Geographic Distribution of the American HDI in Ohio Counties, 2016
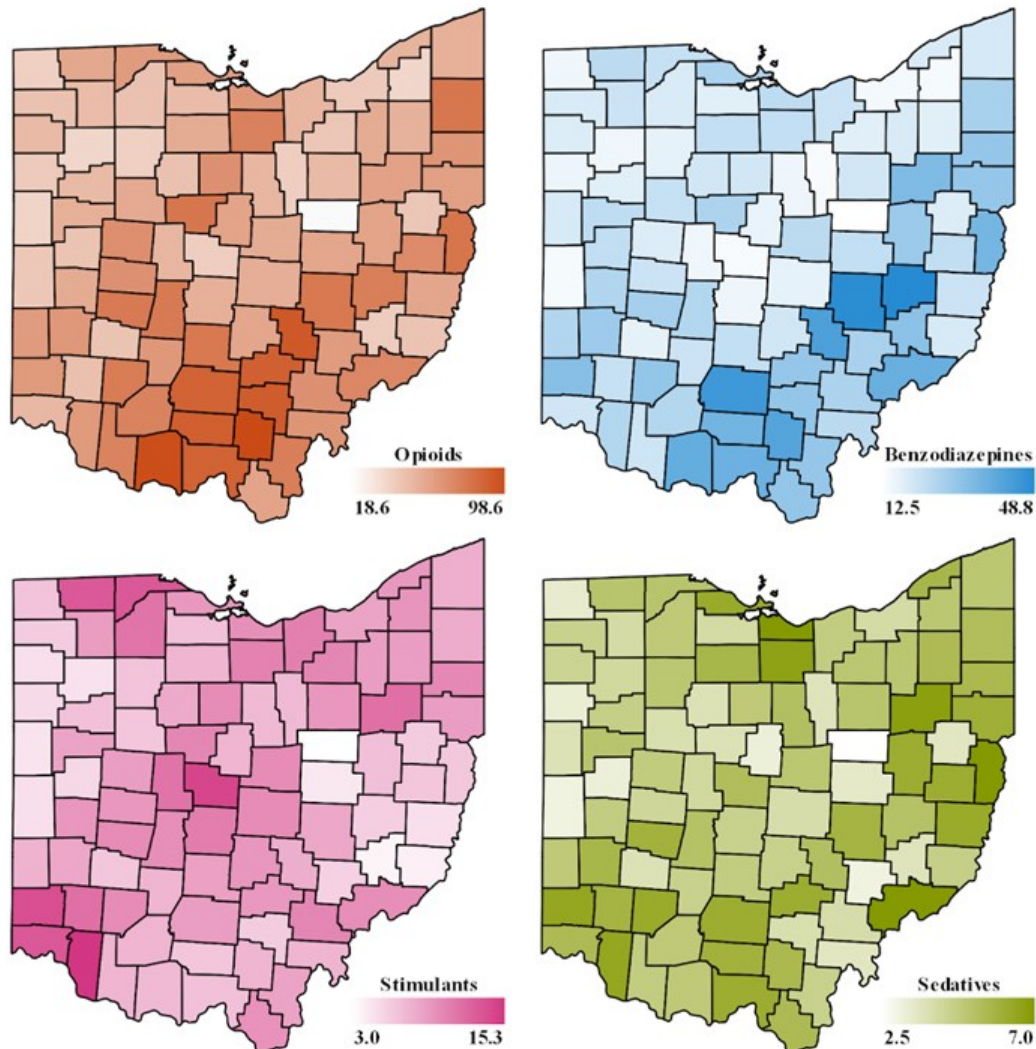

Figure 2. Geographic Distribution of Prescribing Practices in Ohio Counties, 2016. Annual Per Capita Prescribed Doses for 4 Classes of Controlled Substances as Reported in the Ohio Automated Rx Reporting System (OARRS)
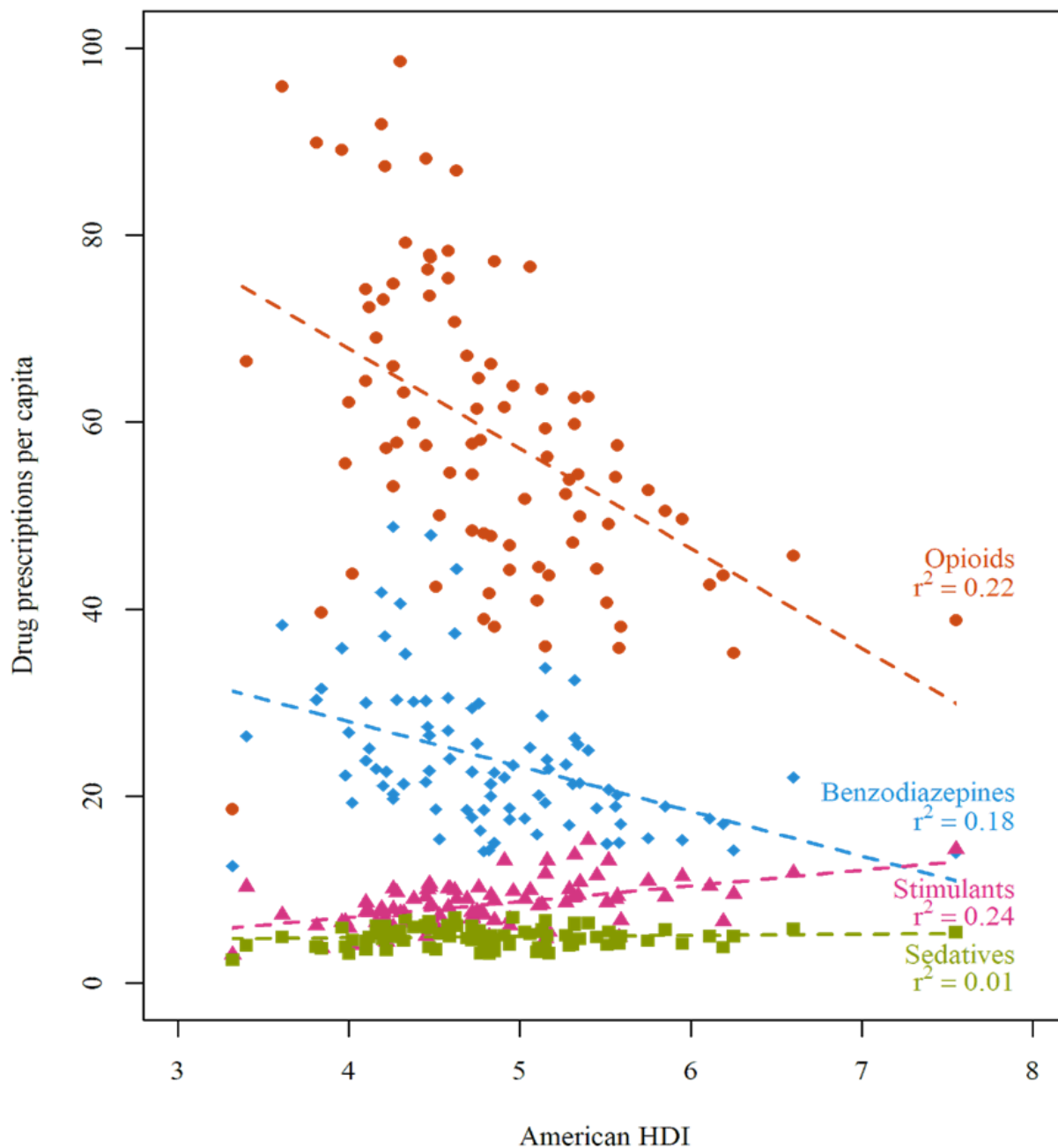
Figure 3. Scatterplot of Per Capita Prescriptions of 4 Classes of Controlled Substances Versus American HDI in 88 Ohio Counties in 2016

fallacy.[23] An association at the group level does not necessarily imply that such a relationship holds at the individual level. Further, individual-level studies would be needed to determine if one or more of the components comprising the American HDI are individually linked to prescribing practices.

Confounding is another key consideration in determining validity. Age is a frequent source of confounding in observational research,[24] and so received special attention in the current study. While prescribing practices are known to vary with age,[25] the degree of relationship between human development and age distribution is less clear. A population's age distribution might potentially impact multiple components of HDI. For example, edu-

cational attainment can only be achieved over time and earnings typically increase with age. However, age distribution, as measured by median age, was not significantly associated with American HDI score in this study. As confounders must be associated with both the cause and effect, age does not appear to be a confounder here.

Work remains to fully map the complex pathways through which social determinants influence health, but the central importance of such factors is well established.[26] As a composite measure of social determinants, causal relationships involving human development are likely similarly complex and bidirectional. The strength of the observed relationships and consistency across multiple classes of

drugs support the utility of human development as a measure of well-being at the county level despite this ambiguity.

Several possible mechanisms could explain the observed relationships, in both causal directions. The components underlying the American HDI are all core social determinants of health, and in this way may shape outcomes like prescribing practices.[27] Education shapes occupation. Manual jobs may predominate in areas with less education, which may increase the prevalence of injuries requiring opioid prescriptions.[28] Low-income areas might have inferior housing options, with higher rates of crime and less access to stress-relieving green space, increasing the prevalence of anxiety disorders and subsequent benzodiazepine prescriptions.[29,30] While children from lower-socioeconomic status (SES) have been found to have higher diagnosed rates of attention deficit/hyperactivity disorder (ADHD), children from high-SES households have had higher rates of treatment, potentially explaining greater stimulant prescriptions.[31]

It is also possible that the higher prescribing of opioids and benzodiazepines in low AHDI areas are, in a literal sense, an attempt by our health care system to medicate the sequelae of social inequity. Compelling recent work has demonstrated higher rates of reported physical pain among those who experience emotional trauma.[32] Prescribing differences may highlight physical manifestations of differing levels of human development.

There are also valid hypotheses with the opposite causal direction. For example, overprescribing of opioids and benzodiazepines, drugs with a strong potential for abuse, may undermine the social fabric in ways that reduce human development.

In all likelihood, there is a complex, bidirectional relationship between AHDI and prescribing practices. Elucidating the relative strength of these components could be valuable direction for future work.

A major limitation of the AHDI derives from its goal of adapting the concept of human development for a typical "American" context. Holmes County, the primary outlier in our sample, illustrates the limitations of the selected measures. Holmes County lies at the heart of one of the largest Amish settlements in the world.[33] Amish culture does not strongly value formal education, as evidenced by Holmes County's state-minimum Educational Index score. Despite the low score, Holmes County also had the lowest rate of opioid prescriptions, likely due to Amish patterns of medical utilization.[34]

Future studies should examine the contributions of the component indices as independent and concurrent predictors of health outcomes. More focused measures (eg, life expectancy at birth) may prove more useful for predicting specific outcomes than the composite AHDI measure. Full data are appended to facilitate such research.

The concept of human development is consistent with a vision of health as "complete physical, mental, and social well-being."[35] This is the first publication of county-level AHDI in Ohio. The strength of relationships observed in the current study suggest that AHDI may be useful for future researchers as a proxy for social determinants or wellness-related outcome.

PUBLIC HEALTH IMPLICATIONS

This work presents the first county-level examination of the AHDI for the state of Ohio and provides a potentially valuable measure for use by future researchers and public health professionals. Human development is predictive of prescribing practices, though the directionality of the relationship is not clear. Future work should explore potential causal pathways linking human development and prescribing practices. The opioid epidemic is a significant public health crisis. Whether higher prescribing in areas with lower human development is an attempt to medicate health inequity or low human development is an additional manifestation of the opioid epidemic, this study underscores the necessity of pursuing equity in all policies.

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RESEARCH ARTICLE

Association of Perfluoroalkyl Substance with Lung Function in the US Population

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ABSTRACT

Background/Aim: Perfluoroalkyl substances (PFASs) are chemical compounds used in consumer products and are linked with increases in cholesterol, thyroid disease, and pregnancy-induced hypertension. However, their association with lung function is not completely understood.

Methods: Cross-sectional 2011-2012 US population data from the National Health and Nutrition Examination Survey (NHANES) were analyzed (n = 1450, aged 12 to 79 years, 50.5% females). Serum concentrations of 4 PFASs, perfluorononanoic acid (PFNA), perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS), and perfluorohexane sulfonic acid (PFHxS), were assessed using mass spectrometry and categorized into quartiles. Lung function was measured by spirometry as forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and the ratio of FEV1/FVC (%). Survey weighted sex stratified adjusted linear regression analysis was used to predict lung function with PFASs quartiles.

Results: In males, compared to females, all 4 PFASs serum concentrations and lung function indices were higher, except FEV1/FVC (%) which was lower than females. No association of any PFAS with decrease in lung function was seen in multivariable-adjusted models in both males and females.

Conclusion: In this exploratory analysis, PFAS exposure was not associated with lung function. PFAS contamination has been ongoing for many years across the US and Ohio, and cleanup efforts are now underway. The association between PFAS exposure and lung function needs further exploration in longitudinal studies.

Keywords: Perfluoroalkyl substances, PFAS, NHANES, Lung function

INTRODUCTION

There are many environmental risk factors that can affect lung function. Common lung conditions such as chronic obstructive pulmonary disease (COPD) and asthma have become more prominent in the United States (US) and Ohio.[1] The prevalence of COPD within the adult population of the US is 6.3% whereas adults in Ohio have a higher COPD prevalence (7.2%).[2] Characterized by a limitation of airflow in the lungs,[3] COPD is more prevalent in males than females, mainly due to the higher smoking rate among males.[4] However, females develop COPD earlier than males due to the smaller lung capacity, leading to faster decline in lung function.[4] Conversely, asthma is more prevalent among females than males in the general population,[3,4] although the prevalence and severity changes with age.[3,4] Prevalence of asthma among adults in the US is 7.9%[5] and among Ohio adults is 9.9%.[6]

Chemical exposures are a relevant public health concern due to the vast amount of chemicals in the environment. Perfluoroalkyl and polyfluoroalkyl substances (PFASs) are a group of chemicals that can be found in carpets, clothing, food packaging, firefighting foam, and nonstick cookware coatings.[7,8] Perfluoroalkyl substances have a high chemical and thermal stability[9] which makes them less likely to break down over time. This stability allows industries to use PFASs in many consumer products. Once absorbed through inhalation, oral, or dermal routes, PFASs can accumulate in multiple tissues in humans, including the lungs.[10] Perfluoroalkyl substances have been associated with increased serum cholesterol levels, increased risk of thyroid disease, decreased fertility, and pregnancy-induced hypertension in humans.[9,11]

The lungs are one of the main tissues that accumulate PFASs after exposure.[10] In a study conducted by Timmermann[12] on PFASs exposure and asthma in children, it was noted that children with higher serum PFASs had lower vaccine antibody response to measles, mumps, and rubella (MMR) vaccination. Another recent study in children noted significant association between PFASs exposure and impaired lung function.[13]

There has been scant research on the association between exposures to PFASs and lung function among adults; most of the research has been on animal models or among asthmatic children.[13-15] Given

the limited amount of evidence found in the animal models and conflicting evidence in children in human population, it is important to explore the potential impact of PFASs on lung function among adults.

Perfluoroalkyl substances are endocrine disruptors (ED), and ED can impact males and females differently.[16] Several published studies report sex dependent PFASs impacts such as thyroid function[17] and serum cholesterol.[18] The objective of this exploratory research was to determine the association between PFASs exposure and lung function among the US population. Using the National Health and Nutrition Examination Survey (NHANES) 2011-2012, we tested the hypothesis that increasing serum levels of PFASs, specifically perfluorononanoic acid (PFNA), perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS), and perfluorohexane sulfonic acid (PFHxS), in the US population will be associated with decreased lung function, and will differ by sex.

METHODS

Setting and Design

This was a cross-sectional study to evaluate the association between PFASs and lung function measured by spirometry (FEV1, FVC, and FEV1/FVC). We used NHANES 2011-2012 data, a population-based survey conducted on individuals within the US.

Participants

The total number of individuals who were interviewed in the 2011-2012 NHANES was 9756, and 9338 of those individuals completed the medical exam. Participants were excluded if they did not have serum PFAS or lung function data. The final sample was comprised of 1450 individuals aged 12 to 79 years.

Procedures

In addition to a household survey that collects data on a variety of risk factors, NHANES conducts clinical assessments in a mobile examination center (MEC).[19] The MEC is used to ensure a standardized examination environment for laboratory measurements, physical assessments, and examinations. All survey materials, consent documents and examination information for the NHANES 2011-2012 data set are publicly available on the NHANES website as part of the Centers for Disease Control and Prevention (CDC).[20]

Measures

Perfluoroalkyl substances biomonitoring was completed on blood samples collected in the MEC. At least 0.5 mL of serum from the blood samples was collected and refrigerated. To test the serum, online solid phase extraction-high performance liquid chromatography-turbo ion spray-tandem mass spectrometry was used to quantitatively detect PFOA, PFOS, PFNA and PFHxS.[20] The lower limit of detection (LLOD) of each PFAS substance is stated as: PFOA (0.10 ng/mL), PFOS (0.20 ng/mL), PFNA (0.08 ng/mL), and PFHxS (0.10 ng/mL).[21] If a sample had results below the LLOD, the NHANES study designers placed an imputed value in the data. This value is calculated by taking the LLOD divided by $\sqrt{2}$ which can be

calculated for each PFAS substance: PFOA (0.07 ng/mL), PFOS (0.14 ng/mL), PFNA (0.06 ng/mL), and PFHxS (0.07 ng/mL).

The spirometry measurements were performed in the MEC. The MEC used the Ohio 822/827 dry-rolling seal volume spirometer. Before each spirometry test, a calibration syringe was used to calibrate the spirometer. Individuals were asked a series of safety questions and if the questions were answered with an answer of "Yes," "Refused," or "Don't Know," then the individual did not perform a spirometry test.[20] Spirometry was performed while a participant was standing up, with extended neck and elevated chin. The NHANES examiner had the individual take the deepest breath possible so that the lungs would fill with the maximum amount of air and then blow the air out as fast and forcibly as possible. Forced vital capacity (FVC), the maximum volume of air exhaled forcefully after a maximal inspiration, was calculated. Among individuals aged 11 to 79 years, the forced exhalation has a minimum of 6 seconds of exhalation.[21] Forced expiratory volume in 1 second (FEV1), the volume of air exhaled during the first second, was calculated.[21]

Statistical Analysis

Analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). All tests were exploratory, 2-sided, and conducted at $\alpha = .05$ level of significance. Data were analyzed using survey weights overall and separately by sex. The survey design variables were also included in the analyses to adjust for standard errors due to the complex survey design and to present nationally representative estimates. Descriptive statistics computed for continuous variables (age, PFNA, PFOA, PFOS, PFHxS, FEV1, FVC and FEV1/FVC) included measures of centrality (mean, median) and dispersion (standard error, interquartile range). Frequency distributions were examined for categorical variables (race/ethnicity and annual household income). Race/ethnicity was recoded into 3 values: non-Hispanic white (reference), non-Hispanic black, and all others. Annual household income was recoded into 3 values: <$25000 (reference), $25000 to <$55000, and ≥$55000.

Rao-Scott chi-square tests were used to determine the statistical significance between the categorical variables across sex. The statistical significance of associations between the continuous variables across sex was tested using Proc Surveyreg for normally distributed variables (age, FEV1, FVC, and FEV1/FVC) or by the Mood's Median test (svyranktest procedure in R) for nonnormally distributed continuous variables (PFNA, PFOA, PFOS, and PFHxS).

As PFASs were not normally distributed, each individual PFAS was categorized into quartiles. Four individual PFASs (exposures/predictor) were tested in each of the lung function test (outcome/dependent) analyses (FVC, FEV1, and FEV1/FVC).

Survey weighted linear regression analysis was performed to assess association between each PFAS categorical variable separately as a predictor (PFNA, PFOA, PFOS, and PFHxS) and the outcome variable (FEV1, FVC, or FEV1/FVC). First, unadjusted linear mod-

els were analyzed, followed by age-adjusted linear regression, and then multivariable regression for other covariates including age, annual household income, race/ethnicity. A total of 12 unadjusted linear regressions, 12 age-adjusted linear regressions, and 12 multivariable linear regressions were analyzed. Categorical variables with more than 2 levels were dummy coded including PFAS quartiles, annual household income, and race/ethnicity. The assumptions for each of the regression models were checked. Although the study was exploratory in nature, a Bonferroni correction was applied due to the number of tests to protect from type 1 error. The new P value was the alpha value (α original = 0.05) divided by the number of comparisons (36): (α altered = 0.05/36) = .001. To determine if any of the 36 models was statistically significant, the P value must be less than 0.001.

RESULTS

Table 1 summarizes information for study participants overall and by sex. Among the overall weighted sample of 1450 NHANES participants, 50.5% were female. The mean age of individuals was 40.9 ± 0.8 years. A higher proportion of this group had annual household income ≥$55000. Compared to non-Hispanic black and other races, non-Hispanic white constituted the preva-

lent group at 67% overall and when comparing males versus females. No significant differences between sexes were noted for age, annual household income and race/ethnicity.

Male participants had a higher median serum concentration for all 4 PFASs (0.9, 2.4, 8.5, 1.8 vs 0.8, 1.8, 5.2, 0.9, $P = 0.001$, $P = 0.004$, $P <0.0001$ and $P <0.0001$) respectively, compared to females. Males also had higher lung function, FEV1 (3758.6 vs 2737.5; $P <0.0001$) and FVC (4815.7 vs 3425.1; $P <0.001$) compared to females. However, the reverse was seen in the ratio of FEV1/FVC in which female had the highest spirometry measure (79.9 vs 78.0; $P = 0.002$) compared to males, respectively.

In survey weighted and multivariable linear regression analysis presented in **Tables 2, 3, and 4** none of the 4 PFASs exposures were associated with any of the 3 lung function tests in males or females at Bonferroni corrected alpha level (0.05/36) = $P <0.001$.

Tables S1, S2, and S3 (see Supplemental Materials) provide unadjusted, age-adjusted, and multivariable-adjusted regression results; no significant association between PFASs exposure and lung function was seen at Bonferroni corrected alpha level (0.05/36) = $P <0.001$.

Table 1. Weighted Characteristics of 2011-2012 NHANES Participants, Overall and by Sex				
Characteristic	**Overall** (N = 61244861)	**Male** (49.5%)	**Female** (50.5%)	***P* value***
Age (years), *mean (se)*	40.9 (0.8)	40.5 (1.0)	41.3 (1.0)	0.55
Household income, % *(se)*				0.55
<$25000	19.6 (2.5)	18.6 (2.8)	20.6 (2.9)	
$25000-$54999	29.8 (2.4)	29.1 (2.7)	30.6 (3.1)	
≥$55000	50.6 (3.4)	52.3 (3.5)	48.8 (3.7)	
Race/Ethnicity, % *(se)*				0.32
Non-Hispanic white	67.0 (3.8)	65.9 (3.6)	68.1 (4.4)	
Non-Hispanic black	11.1 (2.4)	10.9 (2.2)	11.3 (2.7)	
All Other	21.9 (2.6)	23.3 (3.6)	20.6 (2.7)	
PFAS (ug/L), *median (IQR)*				
PFNA	0.9 (0.6, 1.3)	1.0 (0.7, 1.4)	0.8 (0.6, 1.2)	0.001†
PFOA	2.1 (1.5, 3.1)	2.5 (1.8, 3.4)	1.8 (1.3, 2.7)	<.001†
PFOS	6.6 (4.2, 10.4)	8.5 (5.5, 12.8)	5.2 (3.2, 7.9)	<.0001†
PFHxS	1.3 (0.8, 2.3)	1.8 (1.1, 2.9)	1.0 (0.6, 1.7)	<.0001†
Lung function tests, *mean (se)*				
FEV1 (mL)	3243.3 (25.6)	3758.6 (43.7)	2737.5 (25.9)	<.0001
FVC (mL)	4113.9 (34.9)	4815.7 (62.4)	3425.1 (34.7)	<.0001
FEV1/FVC (%)	79.0 (0.3)	78.0 (0.5)	79.9 (0.4)	0.002

*P values reported from Rao-Scott chi-square test for categorical variables and Proc Surveyreg for continuous variables comparing males to females
†P values reported from the Mood's Median test for nonnormally distributed continuous variables

Table 2. Association of PFASs Serum Concentration with FEV1 in NHANES 2011-2012 Participants in Multivariable Survey Weight Adjusted Linear Regression

	Male			Female		
	B (95% CI)	**f-value**	**P**	**B (95% CI)**	**f-value**	**P**
PFOA	Referent	2.43	0.10	Referent	1.14	0.36
2nd	89.62 (-177.18, 356.42)			-66.16 (-232.69, 100.37)		
3rd	14.90 (-221.68, 251.47)			18.37 (-128.28, 165.02)		
4th	170.13 (-60.48, 400.73)			12.59 (-142.57, 167.75)		
PFOS	Referent	4.14	0.02	Referent	1.04	0.40
2nd	356.25 (120.62, 591.88)			26.87 (-126.13, 179.88)		
3rd	355.75 (99.69, 611.80)			32.63 (-133.7, 198.99)		
4th	303.90 (89.92, 517.89)			132.49 (-27.29, 292.28)		
PFNA	Referent	0.25	0.86	Referent	1.15	0.36
2nd	-69.01 (-240.62, 102.60)			-25.62 (-204.14, 152.90)		
3rd	-26.81 (-227.21, 173.59)			74.73 (-97.75, 247.22)		
4th	12.07 (-193.83, 219.97)			47.91 (-131.26, 227.07)		
PFHxS	Referent	1.68	0.21	Referent	1.91	0.17
2nd	29.11 (-258.25, 316.49)			118.54 (-19.45, 256.52)		
3rd	167.37 (-104.11, 438.85)			29.4 (-114.20, 173.06)		
4th	215.99 (-50.01, 482.01)			31.02 (-146.78, 208.82)		

*In all models, the reference category was the respective first PFAS quartile.
Variables that were adjusted for: age, annual household income and race/ethnicity
Note: Degrees of freedom for each f-value is 3
Bonferroni corrected adjusted alpha was .001 (.05/36).

Table 3. Association of PFASs Serum Concentration with FVC in NHANES 2011-2012 Participants in Multivariable Survey Weight Adjusted Linear Regression

	Male			Female		
	B (95% CI)	**f-value**	**P**	**B (95% CI)**	**f-value**	**P**
PFOA	Referent	1.62	0.22	Referent	0.15	0.93
2nd	116.06 (-170.20, 402.32)			-41.72 (-230.72, 147.27)		
3rd	-4.39 (-270.07, 261.28)			-51.87 (-233.32, 129.58)		
4th	164.60 (-128.41, 457.61)			-8.36 (-214.27, 197.54)		
PFOS	Referent	3.13	0.05	Referent	0.06	0.98
2nd	412.95 (103.30, 722.60)			15.17 (-185.23, 215.57)		
3rd	381.33 (85.26, 677.40)			16.29 (-175.35, 207.94)		
4th	311.99 (15.47, 608.53)			43.93 (-177.57, 265.42)		
PFNA	Referent	0.19	0.90	Referent	0.54	0.66
2nd	-62.61 (-247.17, 121.96)			-46.40 (-284.68, 191.89)		
3rd	-27.76 (-289.88, 234.36)			73.08 (-197.81, 343.97)		
4th	-7.57 (-219.71, 204.57)			-21.50 (-263.17, 220.13)		
PFHxS	Referent	1.15	0.36	Referent	3.01	0.06
2nd	45.02 (-306.17, 396.21)			188.51 (7.60, 369.42)		
3rd	170.75 (-138.62, 480.12)			87.18 (-128.04, 302.40		
4th	231.36 (-68.31, 531.02)			20.40 (-226.05, 266.85)		

*In all models, the reference category was the respective first PFAS quartile.
Variables that were adjusted for: age, annual household income and race/ethnicity
Note: Degrees of freedom for each f-value is 3
Bonferroni corrected adjusted alpha was .001 (.05/36).

Table 4. Association of PFASs Serum Concentration with FEV1/FVC in NHANES 2011-2012 Participants in Multivariable Survey Weight Adjusted Linear Regression

		Male			Female		
		B (95% CI)	**f-value**	**P**	**B (95% CI)**	**f-value**	**P**
PFOA		Referent	0.43	0.74	Referent	3.24	0.05
	2nd	-0.09 (-2.63, 2.46)			-0.99 (-2.76, 0.77)		
	3rd	0.70 (-1.92, 3.33)			1.65 (0.20, 3.10)		
	4th	0.98 (-1.16, 3.11)			0.43 (-1.65, 2.52)		
PFOS		Referent	2.23	0.12	Referent	6.51	0.004
	2nd	0.59 (-1.25, 2.44)			0.57 (-0.91, 2.05)		
	3rd	1.22 (-0.12, 2.56)			0.41 (-1.61, 2.43)		
	4th	1.06 (-1.01, 3.13)			3.01 (1.50, 4.51)		
PFNA		Referent	0.26	0.85	Referent	3.33	0.04
	2nd	-0.33 (-2.17, 1.52)			0.41 (-0.82, 1.63)		
	3rd	0.08 (-2.06, 2.23)			0.21 (-1.39, 1.82)		
	4th	0.71 (-1.24, 2.67)			2.05 (0.46, 3.64)		
PFHxS		Referent	0.28	0.84	Referent	1.36	0.29
	2nd	-0.24 (-2.03, 1.55)			-0.66 (-1.99, 0.68)		
	3rd	0.59 (-1.33, 2.50)			-1.44 (-3.25, 0.38)		
	4th	0.57 (-2.08, 3.22)			0.41 (-1.18, 1.99)		

*In all models, the reference category was the respective first PFAS quartile.
Variables that were adjusted for: age, annual household income and race/ethnicity.
Note: Degrees of freedom for each f-value is 3
Bonferroni corrected adjusted alpha was .001 (.05/36).

DISCUSSION

In this exploratory analysis using data from US adults, we did not observe an association between serum PFASs concentration with lung function. To our knowledge this analysis is one of the very first population studies conducted to assess impact of PFASs on lung function among US adults.

Previous research[22] on the impact of PFASs on lung function is generally limited to children and show mixed results. Similar to our results, a recent study in adolescents, who as children were exposed to the World Trade Center (WTC) disaster dust (living nearby), showed no significant association between serum PFASs and lung function parameters measured by spirometry, plethysmography, and oscillometry, asthma diagnosis, or eosinophil count. As compared to unexposed age matched controls, these adolescents had higher serum PFASs levels due to exposure to WTC-linked dust exposure containing PFASs and other chemicals when they were children. These results underscore the need for more longitudinal studies to explore impact of PFASs on lung function.

Conversely, in other population studies, children diagnosed with asthma had higher mean serum PFAS levels compared to healthy children.[13] In a study conducted among Taiwanese children, serum PFASs were positively associated with decreased lung function and immunological markers among those diagnosed with asthma.[14] Perfluoroalkyl substances were not significantly associated with pulmonary function among healthy children. A previous study using data from adolescents enrolled in NHANES 1999-2000 and 2003-2008 reported a positive relationship between PFOA and self-report of asthma, and wheezing.[15] However, serum PFOS, PFNA, and PFHxS concentrations were unrelated to asthma. Higher serum PFASs concentrations have been associated with increased inflammatory markers,[23] suggesting that PFASs may induce inflammation and predispose people to impaired lung function. In another NHANES analysis in children, no association between lung function and serum PFASs concentrations was noted, although antibody response to routine vaccine was muted, suggesting that PFASs may impair immunological responses in children.[24]

Relatively more studies have been conducted using animal models to explore PFASs exposure and lung function. In a study by Ye,[7] PFAS exposure was linked with neonatal mortality in mice, which was caused by underdeveloped lungs. In a separate study of mice pups, exposure to PFAS altered airway function, induced airway inflammation, and increased the airway response.[4] Perfluoroalkyl substances negatively impact the development of mammals, resulting in lower birth weight and neonatal mortality.[12] Neonatal

mortality in animals was caused by underdeveloped lungs and the failure of lung function.[12] Other outcomes associated with PFAS and lungs include an increase in airway inflammation and altered airway function in animal models.[9]

Chance could be an explanation of our findings; even though our results show somewhat consistent negative associations between different PFASs and lung function. Other possible explanations for this negative association could include bias and residual confounding. We adjusted for known confounders, except smoking. This was due to the complexity of methods utilized to collect smoking data in NHANES 2011-2012. However there could still be unmeasured confounders that bias the observed negative association. One of those unmeasured confounders could be genetic/biological factors that cannot be measured quantitatively.

As this was a cross-sectional study, based on a national survey, selection bias was minimized by utilizing random sampling. To reduce information bias, the data collection team was provided extensive training to reduce errors in data collection, interviews, and data entry.

PUBLIC HEALTH IMPLICATIONS

Perfluoroalkyl substances contamination has been noted all across the country, including Ohio. Of particular concern is PFAS presence in the Ohio drinking water supply given Ohio's industrial legacy. Perfluoroalkyl substances contamination is a public health concern because having a safe drinking water supply is an essential requirement for protecting public health. Several regions in Ohio have a history of PFAS water contamination including the mid-Ohio Valley communities, which were exposed to PFOA release in the water since 1950s from upstream industry in Parkersburg, West Virginia.[23] Other water systems that have been contaminated in Ohio include Cleveland, Cuyahoga County, Greene County, Gallia, Mahoning, and Montgomery County.[24] In the mid-Ohio Valley population, PFOA exposure was associated with a number of diseases including high cholesterol, ulcerative colitis, testicular cancer, kidney cancer, and pregnancy-induced hypertension.[23] With all of the PFAS exposure within Ohio over the years, there could be more negative health impacts which can only be determined through further studies in areas affected by PFAS contamination. Overall, people are concerned about the health impacts of PFAS, which are not clearly understood, and more scientific evidence and epidemiological studies are needed.

Conclusion

This cross-sectional study provides some evidence that current population exposure to PFASs may not adversely impact lung function. The existing evidence of effect of PFASs on lung function in different age groups and among those diagnosed with asthma is inconsistent, and prospective studies are needed.

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RESEARCH BRIEF

Impact of Emotional Distress on Prescription Opioid Abuse in a Rural Juvenile Drug Court Sample

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ABSTRACT

Background: Ohio is at the epicenter of the opioid epidemic, and the current crisis disproportionately burdens rural areas. The Self-Medication Hypothesis and work examining adverse childhood experiences posit that drug use may be understood as a coping strategy to address emotional distress.

Methods: Juvenile drug court participants in a Northwest Ohio county were administered a standardized biopsychosocial assessment. Intake interviews from January 2010 and November 2018 were used to evaluate the relationship between emotional distress reported using the Emotional Problem Scale (EPS) and lifetime nonmedical use of prescription opioids. Linear regression was used to examine temporal trends in EPS scores. Logistic regression was used to examine the relationship between EPS scores and prescription opioid misuse, controlling for temporal trends.

Results: Linear regression showed a significant increase in emotional distress over the study period for both prescription opioid users and nonusers. Average scores increased 29.5 points (on a 100 point scale) over the duration of the study (P <0.0001). A 10-point increase in EPS score was associated with a nearly 50% increase in the lifetime odds of prescription opioid misuse (OR = 1.46, 95% CI: 1.19-1.82, P = 0.0004). The odds of prescription opioid misuse declined each year (OR = 0.63, 95% CI: 0.48-0.81, P = 0.0006).

Conclusion: Rates of prescription opioid misuse have decreased over time despite a significant association between emotional distress and opioid misuse and trend toward increasing EPS scores. While efforts to reduce prescription opioid misuse appear to have been effective in this population, significant work is needed to reduce underlying risk factors.

Keywords: Opioid abuse, Prescription painkillers, Emotional distress, Juveniles

INTRODUCTION

The opioid epidemic gripping the United States constitutes an unprecedented public health crisis. In 2017, more than 72000 Americans lost their lives to drug overdoses, the vast majority of which involved opioids.[1] Currently, drug overdoses are the most common cause of accidental death in the United States (US), accounting for more fatalities than gun violence, suicide, or motor vehicle accidents.[2,3] The estimated yearly costs of the opioid crisis, including health care, criminal justice, lost lives and productivity, are over $500 billion.[4]

Ohio is an epicenter of this epidemic, with opioid mortality rates increasing an astonishing 918% since the early 2000s.[5] In 2015, Ohio had the highest heroin overdose death rate in the country.[6] In 2017, Ohio had 4854 drug overdose deaths, a 20% increase from 2016.[7] In Ohio, drug overdoses now kill more than 2.5 times as many people as automobile accidents.[8] The deadly synthetic

opioid fentanyl now drives the increase in overdose deaths. An examination of unintentional drug overdose deaths from 24 Ohio counties in January and February of 2017 revealed that approximately 90% involved fentanyl, its analogs, or both.[9]

However, the current drug crisis differs from well-established historical trends, with rural communities suffering a disproportionate burden.[10,11] Compared to urban areas, rural areas have higher rates of opioid-related overdoses and deaths.[12,13] These problems are exacerbated because rural areas are "treatment deserts" for opioid abusers.[10] Compared to urban and suburban areas, rural areas have fewer inpatient detoxification,[4] rehabilitation,[5,12,14] and medication assisted treatment (MAT) programs providing drugs like methadone and buprenorphine.[4,8,12,15] Furthermore, rural areas have a general shortage of behavioral health professionals including clinical psychologists, psychiatrists, psychiatric nurse practitioners, and social workers.[14,16] Whites have

been disproportionally impacted in the current opioid crisis, with racial disparities in opioid prescription rates hypothesized as a contributing factor.[17]

Youth misuse of prescription opioids may act as a stepping-stone to eventual heroin use, which in recent years has led in turn to increased risk of fentanyl exposure and overdose.[18,19] Individuals abusing prescription opioids are several times more likely than their peers to turn to heroin use,[20] and the vast majority of heroin users report first abusing prescription opioids.[21,22] Unfortunately, rural youth are at a greater risk of prescription opioid abuse than their suburban and urban peers.[23–27]

The current opioid epidemic traces to a complex interplay between personal, social, cultural, and economic factors.[15] While understanding higher-level factors is key to addressing the epidemic as a public health crisis, it is also invaluable to understand individual factors leading to the initiation and maintenance of opioid abuse, especially for those in treatment and enforcement settings.

While biological explanations elucidate the physiological and genetic factors leading certain substances to be addictive, dramatic changes in addiction rates over time suggest that environmental factors likely play a key role in shaping addiction. People may turn to opioid abuse to alleviate suffering as opposed to seeking pleasure or a "high" from the drugs.[28] Opioid abusers generally have extensive psychological and emotional distress.[29] Qualitative studies have found that opioid abusers indicate the drugs provide them with an escape from various types of psychological and emotional discomfort.[30–32] These problems include stress,[33,34] emotional trauma,[31,33] symptoms of comorbid psychological conditions,[30] and a general discontentment with life.[35]

Two related theories envision drug taking behavior as a coping mechanism. The Self-Medication Hypothesis of drug addiction posits that specific classes of drugs are used by addicts as a means of modifying specific negative affective states.[36,37] The theory complements physiological and sociological perspectives on addiction with a psychological explanation. Closely related is the body of literature exploring the impact of adverse childhood experiences (ACEs), including neglect, abuse, and other trauma, on drug addiction. In fact, the strong relationship between ACEs and substance abuse has been cited as supporting evidence for the Self-Medication Hypothesis,[28] though some have questioned whether ACEs are truly a causal risk factor or merely a risk marker associated with underlying psychological pathology.[38] Adverse childhood experiences have been found to predict multiple potential mediators leading to more serious opioid use including anxiety, delinquency, depression, impulsivity, risk-taking, and suicidality.[39] Childhood exposure to abuse and neglect has consistently been associated with psychological distress,[40] illicit drug use, generally,[41] injection drug use and opioid dependence, specifically,[42–44] and more severe opioid abuse.[45]

METHODS

Setting and Design

The setting for this study was a juvenile drug court in a predominantly white (>96%), rural county in Northwest Ohio between January 2010 and November 2018. We conducted a secondary analysis of data previously collected by the court and provided to the researchers as part of an ongoing evaluation process.

Participants

All juvenile court participants were interviewed as part of the standard intake procedures. For individuals with more than one contact with the court, only the most recent intake interview was included in the analysis to ensure the independence of observations.

Procedures

The analysis examines pooled data from the Global Appraisal of Individual Needs (GAIN),[46] a standardized biopsychosocial assessment interview that has 8 core sections including mental health and substance use indicators, with these items combined into more than 100 indexes, scales, and subscales.[47] The GAIN is administered by court staff trained by Chestnut Health Systems and the procedures are done in strict accordance with HIPAA (Health Insurance Portability and Accountability Act) rules (45 CFR Parts 160 and 164, Subparts A and E).[48] Use of this data for secondary analysis is allowed by Chestnut Health Systems as it is conducted with general consent under federal guidelines (42 CFR Part 2) that allow record abstraction for program evaluation and development as long as the data is deidentified and kept confidential. The pooled data provided by Chestnut Health Systems for this study included no identifying information for any individual.

The study was determined to be exempt from further review by the Ohio Northern University Institutional Review Board as it involved the analysis of existing data, and information was recorded in such a way that individual subjects cannot be identified.

Measures

The main mental health scales have outstanding internal consistency ($\alpha \geq 0.9$) and subscales have very strong internal consistency ($\alpha \geq 0.7$).[47,49] The scales were developed using Rasch measurement analysis and normed using over 100000 subjects.[50] The specific mental health questions are largely based on various DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) criteria.[51]

The independent variable, emotional distress, was measured using the Emotional Problem Scale (EPS) which measures mental health functioning and functional impairment.[52] The EPS is a 7-item scale that measures: proportional days of the previous 90 the subject was bothered by psychological problems, traumatic memories, and difficulty with self-control; the number of days these mental health issues interfered with the subject's daily responsibilities;

and the recency of the respective mental health issues.[53] Lifetime prescription opioid misuse was measured by asking subjects to indicate whether they had ever used prescription opioids in any manner that was not under the direction of a medical professional.

Statistical Analysis

The impact of emotional distress on prescription opioid misuse was evaluated using a logistic regression model in R (version 3.2.1) using the glm() function using the binomial family type and logit link function.

RESULTS

During the study period 174 assessments were conducted involving 158 unique individuals. Participants ranged from 12 to 17 years of age. Descriptive statistics are presented in **Table 1**. The EPS scores were available for all but 1 individual, who was excluded from the analysis. Information on prescription pill use was available for the full sample. Only the most recent assessment was analyzed for the 17 repeat offenders completing 2 assessments (duration between: range = 45 days-3.8 years, mean = 1.4 years). The EPS scores for the second assessment were higher for 11 repeat offenders and lower for the remaining 6 (mean change = +7.3).

A scatterplot of EPS scores shows an increase in the average score among individuals taken into the program over time (**Figure 1**). A linear regression model was fit to evaluate temporal trends in EPS score while controlling for prescription opioid misuse. Average scores increased 29.5 points (on a 100 point scale) over the duration of the study ($P < 0.0001$), controlling for use of prescription pills. Prescription drug misuse was associated with a 19.8 point higher EPS score compared with nonuse.

In a logistic regression model, both EPS score ($P = 0.0004$) and time ($P = 0.0006$) were significant predictors of opioid misuse. An individual with an EPS score 10 points higher than someone in the same time frame had 1.46 times the odds of lifetime prescription opioid misuse (95% CI: 1.19-1.82). An individual interviewed at one point in the study was predicted to have 0.63 times the odds of opioid misuse compared with someone with the same EPS score interviewed one year earlier (95% CI: 0.48-0.81).

DISCUSSION

Both the Self-Medication Hypothesis and theories of adverse childhood experiences posit that adult drug abuse may be a coping mechanism for negative events early in life and their sequelae. The

Table 1. Descriptive Statistics for Participants in a Juvenile Court in Northwest Ohio, 2010-2018, by Lifetime Prescription Opioid Misuse

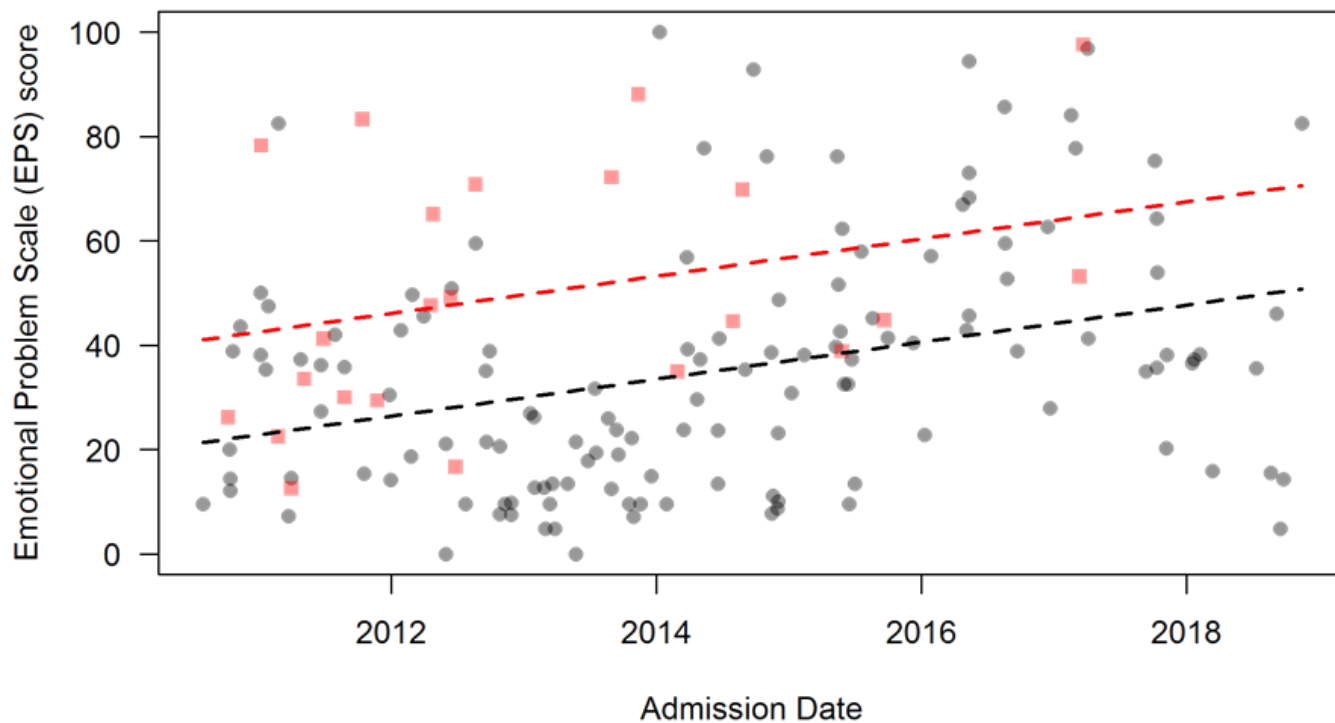|	Full Sample n = 157 Mean±SD/%	Opioid misusers n = 23 Mean±SD/%	Nonmisusers n = 134 Mean±SD/%	Repeat offenders n = 17 Mean±SD/%
Dependent Variable				
Lifetime Opioid Misuse	14.5%	100.0%	0.0%	17.6%
Independent Variable				
Emotional Problem Scale Score	37.3±24.0	50.0±22.0	35.1±25.1	33.9±13.6
Sociodemographic Factors				
Race/Ethnicity				
Non-Hispanic white	86.0%	95.7%	84.3%	82.4%
Non-Hispanic black	0.6%	0.0%	0.7%	0%
Hispanic	1.9%	0.0%	2.2%	5.9%
Two or More Races	7.0%	0.0%	8.2%	11.8%
Other	4.5%	4.3%	4.5%	0%
Age	15.4±1.4	15.4±1.4	15.3±1.4	14.5±1.6
Gender				
Male	59.9%	52.2%	61.2%	70.6%
Female	40.1%	47.8%	38.8%	29.4%

Figure 1. Trend in Emotional Problem Scale (EPS) Score Over Time Among Prescription Opioid Misusers (red squares) and Nonusers (black circles) in a Northwest Ohio County

current work supports such claims by demonstrating an association between emotional distress, as measured by the EPS, and prescription opioid misuse, while simultaneously documenting secular trends in drug selection. The significant drop in the likelihood of opioid misuse over the study period corresponds with current understandings of the opioid epidemic. The first wave of the opioid crisis, marked by the rise of prescription opioid abuse, is generally cited as running from the late 1990s until 2010, the year that the current study began.[15] Starting in 2010, a policy emphasis on reducing prescription opioid overdose reduced supply, increasing the cost of prescription opioids and encouraging many with opioid abuse disorder to transition to cheaper heroin.

The reduction in the frequency of opioid misuse in the sample, though unquestionably a good sign, is offset by a troubling trend toward higher reported EPS scores among all study participants. This mirrors broader trends among US adolescents.[54] The available data does not give clear evidence for the cause of this trend, though the impacts of the opioid epidemic on families in rural Northwest Ohio may be an important component.

The national epidemic of opioid overdose deaths appears to be part of a broader pattern termed "deaths of despair."[55] Deaths of despair are associated with a sense of hopelessness, fatalism, perceived helplessness and deprivation. This concept has been used to account for the increasing mortality in the US from opioid overdoses, suicides, and liver disease among noncollege educated middle-aged whites. Such deaths noticeably increased around the time of the economic downturn in the mid-2000s.[15] There has been a recent trend of disengagement in institutional engagement among groups particularly hard hit by opioid abuse (eg, rural residents; working-class white).[55] This involves a decreasing rate of participation in family, work, and religion.[56,57] It also includes declining rates of participating in labor unions, fraternal organizations, and other voluntary associations.[58]

The ideas of sociologist Emile Durkheim are useful in interpreting these trends.[59-61] Durkheim noted that societies need to provide social integration and moral regulation to constrain the individual. He believed that unbridled individual passions could result in a state of normlessness or anomie. In turn, this anomie can translate into self-destructive behavior such as suicide. Case and Deaton have claimed the current decline in institutional participation among working-class whites creates a Durkheimian recipe for individual self-destruction.[55] Due to an increasing absence of stable institutional bonds (eg, work, family, religion), there are insufficient social supports to prevent the individual from falling into despair. Believing that their situation is hopeless, they may turn to opioids as a temporary reprieve from their fatalistic despair. Tragically, this temporary reprieve from this anomic condition all too often turns into a life-threatening addiction.

PUBLIC HEALTH IMPLICATIONS

Data from this sample of juvenile offenders suggest that efforts to reduce access to prescription opioids have successfully decreased lifetime risk of prescription opioid misuse by adolescents in this rural, Northwest Ohio county. This study lends still more support to the well-documented association between emotional problems and prescription drug misuse, and finds that rates of emotional problems among high-risk adolescents are climbing at an alarming rate. Identifying ways to respond to emotional problems and prevent the traumatic events that contribute to them should be a key public health priority.

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PUBLIC HEALTH PRACTICE

One Health Outreach Efforts in Responding to Harmful Algal Blooms Issues in Hotspot Regions

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ABSTRACT

Background: Globally, harmful algal blooms (HABs) in freshwater are both a historical and an ongoing issue for human, animal, and ecosystem health and have dramatic impacts on local communities. Multiple taxa of cyanobacteria, including *Microcystis*, *Planktothrix*, and *Anabaena* species can produce cyanotoxins. Exposure to these toxins may cause mild to severe adverse health effects.

Methods: An orchestrated effort was made by a team from multiple academic disciplines, public health agencies including the Centers for Disease Control and Prevention (CDC), and community stakeholders to engage the human and animal health communities to prepare for and respond to the emerging health threat of cyanotoxins from HABs.

Results: Our public health practice approaches reached multiple targeted stakeholders from public health, human, and animal health sectors. The team also helped promote the newly established nationwide One Health Harmful Algal Bloom (OHHABs) initiative in a HABs hotspot in Ohio.

Conclusion: Harmful algal blooms are a One Health issue demonstrating the interactions between animal, human, and ecological health. Environmental monitoring can provide early detection of environmental events, such as HABs, that pose both public health and ecological health threats. Public health surveillance can identify human and animal health events that may be linked to local environmental events

Keywords: One Health, Harmful algal blooms, Outreach and education, Early detection, Public health surveillance

INTRODUCTION

Exposure to cyanotoxins can cause mild to severe adverse health outcomes. For example, ingestion of microcystins (MCs) or cylindrospermopsin can lead to liver and kidney damage. A microcystin has been identified as a liver tumor promotor in experiments with rats and as a possible human carcinogen according to the International Agency for Research on Cancer.[1] An ecological study showed that nonalcoholic liver disease mortality is significantly associated with the occurrence of cyanobacteria bloom-affected surface waters in counties in the United States (US).[2] In laboratory experiments, exposure to neurotoxins, including anatoxins produced by *Anabaena* species resulted in death due to respiratory system failure as rapidly as within 15 minutes of exposure.[3]

While researchers are trying to better understand this public health threat, state and local public health agencies are at the forefront of addressing environmental public health crises associated with the increasing intensity and frequency of harmful algal blooms (HABs) in freshwater.[4] Harmful algal blooms in marine (eg, red tides) and freshwater (eg, cyanobacterial HABs) are both a historical and an ongoing issue for human, animal, and ecosystem health and have dramatic impacts in all 50 states of the US and communities around the globe. There are multiple types of cyanobacteria, including *Microcystis*, *Planktothrix*, and *Anabaena* species that can produce cyanotoxins and exposure to these toxins may cause mild to severe adverse health effects.[5]

A growing body of evidence suggests that animals, particularly dogs and cattle, can be sentinel species for HAB poisonings.[6] Ani-

mals and humans may experience similar signs when exposed to HABs. Vomiting, diarrhea, rash, difficulty breathing, weakness, liver failure, seizures, and potentially death are all signs of HAB exposure.[7,8,6] However, not all veterinarians are likely to be familiar with or trained to consider cyanotoxin poisoning when their patients present with compatible signs. Thus, even when poisonings occur in these sentinel species, most cases are suspected to go undocumented because of misdiagnosis, failure to confirm the toxin in a biological specimen, or failure to report the case to a surveillance system.[6] A review of reports in the HAB-related Illness Surveillance System (HABISS), case files from a large veterinary teaching hospital in California, and publicly available documents revealed 231 HABs events and 368 toxicity cases in canines across the US from the late 1920s to 2012.[7] The researchers suggested that these cases of canine cyanotoxin poisonings represent a small fraction of overall cases in the US because of misdiagnoses and underreporting. Researchers also provided insights on using an animal diagnosis as an early warning for public health. Animals tend to have multiple routes of exposure (ie, direct contact, inhalation, and ingestion) and potentially higher levels of exposure than people because of their activities (eg, swimming in visibly contaminated water, ingesting scum, or licking algae from their fur).[7,9] Recognizing the need for animal health surveillance, public health agencies and researchers formed the HABISS program, led by the CDC between 2007 and 2011. The HABISS program set the groundwork for the One Health Harmful Algal Bloom System (OHHABS). Their efforts helped improve public health understanding and the importance of a One Health approach.

In August 2014, the Collins Park Water Treatment Plant in Lucas County, Ohio, detected MC levels above the Environmental Protection Agency (EPA) drinking water advisory threshold of 1.0 μg/L in finished drinking water, which had been sourced from western Lake Erie. The county issued a 2-day do not drink advisory. This was an unprecedented event that uncovered gaps in knowledge about how to respond to a HAB-related public health crisis that poses various threats to Toledo and the many adjacent jurisdictions that rely on Toledo's water treatment plant. We reached out to Toledo-Lucas County Health Department (TLCHD), an agency experienced with the 2014 HAB event that resulted in a 2-day do not drink advisory impacting over 500000 people,[10] to learn more about lessons they learned and recommendations for researchers.

We partnered with TLCHD and the Ohio Department of Health (ODH) to learn about the gaps in awareness and education on HABs they had identified after the 2014 event. During this event, it was widely acknowledged that information about animal exposures to MC was an area where education and information needed to be more widely available and disseminated to the community. Over the course of 2 years, we took a comprehensive approach to increase HAB awareness among public health and medical practitioners for both human and animal health.

METHODS

Setting and Design

In autumn 2015, The Ohio State University (OSU), College of Public Health partnered with the TLCHD to develop a plan to address gaps in HAB-related medical needs in humans and animals. Ohio, particularly Toledo, was a HABs hotspot in 2014 when TLCHD responded to a HABs event.[10]

Procedures

We conducted 3 HAB-related initiatives between 2016 and 2018: a workshop held in Toledo, Ohio, for the medical community (summer 2016) on the impacts of HABs on human, animal, and environmental health that included an introduction to the CDC's One Health Harmful Algal Bloom (OHHABs) surveillance system; a survey of veterinarians to assess their HAB knowledge and practices (fall 2016 through early 2017) in Ohio and Michigan, which was completed by veterinarians; and a statewide distribution of CDC's Veterinarian Reference Card to members of the Ohio Veterinary Medical Association (OVMA).

Workshop

A 1-day workshop with 63 participants (including speakers and the organizing team) was conducted in Toledo, Ohio, in May 2016, preceding Ohio's peak HAB season of June through September. The workshop targeted local human and animal health officials and included speakers from academic institutions and public health institutions from local, state, and federal public health agencies to share their studies and practices. The workshop included presenters from ODH, CDC, University of Toledo, Bowling Green State University, and TLCHD. During the workshop, we addressed gaps in HABs education and practice in the animal health sector by providing reference cards and information about CDC's public health surveillance to veterinarians and other practitioners in publications such as this article (see Supplemental Materials).

Survey

We conducted a survey on veterinary practices to assess the knowledge and practices of veterinarians from Michigan and Ohio, 2 states affected by the 2014 bloom in Lake Erie. We asked Ohio and Michigan Veterinary Medical Associations (OVMA and MVMA, respectively) to contact their approximately 3000 members, consisting mainly of veterinarians, with an introductory message and follow up with a link to the survey. The survey included 12 questions that consisted of both open-ended and closed formats. The survey was approved as exempt (ie, not human subjects research) by OSU's Institutional Review Board. A total of 83 members (including veterinary medicine students) responded to the survey. To fulfill our target group of veterinarians, we only reported here on the 23 responses that were completed by currently practicing licensed veterinarians (**Tables 1, 2, and 3**). The survey tool is available upon request.

Table 1. Case Definition Sufficiency

Level of agreement with:	Strongly Agree/ Agree	Neutral	Disagree/ Strongly Disagree	Total
Sufficiency of CDC case definitions for identifying suspect, probable, or confirmed cases	60.9% (n=14)	26.1% (n=6)	13.0% (n=3)	23*
Adequacy of criteria of CDC's case definition for determining whether a case is suspect, probable, or confirmed	47.8% (n=11)	39.1% (n=9)	13.0% (n=3)	23*

*Currently practicing licensed veterinarians only.

Table 2. Information to Detect and Treat Cases of HABs Toxicity

Response	Frequency	Percent
Yes	5	21.7
No	12	52.2
Unsure	6	26.1
Total	23*	100

*Currently practicing licensed veterinarians only.

Table 3. Experience with Water Quality Monitoring Initiatives

	Sufficient	Lacking	Don't Know	Total
For recreation	13.0% (n=3)	56.5% (n=13)	30.4% (n=7)	23*
For consumption	13.0% (n=3)	56.5% (n=13)	30.4% (n=7)	23*

*Currently practicing licensed veterinarians only.

Outreach

In response to our survey completed by veterinarians, the Ohio Veterinary Medical Association helped us deliver 2600 veterinarian reference cards to their members via direct mail. The veterinarian reference card is one of the health promotion materials[11] made available by the CDC through a multi-sector and local-state-federal partnership that was formed to increase awareness on HABs and One Health surveillance and to improve understanding of HABs and HAB-related effects.

Analysis

For our survey completed by veterinarians, descriptive statistics were generated using statistical software (SAS, version 9.4; SAS Institute Inc). For categorical values, the number of responses and percentages were calculated. The survey results in **Table 2** show that more than 52% of respondent veterinarians were unsure if they have enough information to detect and treat HABs toxicity in animals, which indicates a follow-up intervention with educational and outreach material was needed.

RESULTS

The workshop was at full capacity with 63 participants representing local medical and public health practitioners. To assess the effectiveness and outcomes of the workshop, we provided participants with a postworkshop evaluation survey, which was completed by 23 of 51 participants (excluding speakers and organizing team, 45% of participants completed the survey). Between 17 and 23 (74% and 100%) of the participants rated either *agree* or *strongly agree* in the 4 areas across all 6 topics: Microcystin and Environmental Health, Impacts on Human Health and Public Health, Microcystin and Lake Erie, Sandusky Bay and *Planktothrix*, Impacts on Animal Health, and Surveillance and Monitoring. A comments section captured consistently positive feedback related to the presentations, information, and resources provided.

For the survey completed by veterinarians, results showed the need for more education to which we responded by distributing CDC's Veterinarian Reference Card on HABs. All 83 respondents reported that they were unfamiliar with public health surveillance, cyanotoxin exposure pathways, and the importance of mitigating exposures by posting warnings to identify contaminated waters. More than half of the veterinarians (n = 23) felt that the CDC case definition was sufficient to help identify if cases are suspect, probable, or confirmed. After reviewing the case definition, veterinarians were asked to recall any potentially missed canine cases they might have examined since 2014. From the survey responses, 14 suspected canine poisonings were reported for the years 2014

through 2016 from Washtenaw and Gladwin Counties in Michigan and Hamilton County in Ohio. Twelve veterinarians (52%, n = 23) reported asking owners during their animal's health assessment about contact with any bodies of water for recreation or consumption. More than three-quarters of respondents (78%, n = 23) reported not having or being unsure if they had sufficient information on how to diagnose and treat animals that may have been exposed to HAB-related toxins. The majority of veterinarians also believed that they did not know or lacked knowledge regarding public, animal, and wildlife initiatives for monitoring the quality of water for recreation (86.9%, n = 23) and consumption (86.9%, n = 23) (see **Tables 1, 2, and 3**).

DISCUSSION

Through our workshop and follow-up survey, we identified an opportunity for public health professionals to partner with veterinary professionals to provide education and training on the diagnosis, treatment, and reporting of HAB-related poisonings. The aim of the workshop was to inform the public health and medical communities of the emerging public health threat from HABs. Throughout the session, engaging questions were asked of participants and partnerships were formed to strengthen the One Health approach to public health concerns. As the severity and frequency of HAB events in freshwater increase, it is important to bridge the gaps between public health and the human and veterinary medical communities.[7,8]

Data obtained through our survey can guide public health education efforts through a One Health approach. Because of the relatively low response rate, we are not able to generalize our results to the entire veterinary community. However, our survey revealed gaps in knowledge related to diagnosis and treatment of HAB-related animal poisonings. Respondents indicated that educational materials, such as fact sheets for the animal's owner and guidance on clinical practice would help them increase HAB-related knowledge. The aim of this survey was to identify gaps in knowledge among the veterinary community regarding CDC's HAB-related poisoning case definitions and how to diagnose, treat, and report cases of HAB-related animal poisonings.[12]

All too often the animal or One Health approach is missing in public health messaging.[11] On a local level, the uncertainty expressed in the veterinary community on probing about HAB exposures is important and suggests a focus area for veterinary training and for practicing veterinarian outreach and education. Increased communication and partnerships with the veterinary community are integral to public health surveillance and education. Based on the feedback and need for integration of veterinary medicine into public health, the TLCHD has increased engagement with veterinarians, offering education on HABs and other public health issues that cross species lines (eg, mosquito-borne diseases, tick-borne diseases, animal bites, and rabies) and has strengthened relationships with the local veterinary medical community.

There were limitations to our findings. First, we had a low survey response and some surveys were incomplete; thus, we excluded these from our analysis. Second, we were not able to limit our communication to currently practicing veterinarians as there were other categories of membership including students and retirees in the email lists.

PUBLIC HEALTH IMPLICATIONS

Animal, human, and ecosystem health are interrelated; thus, actions to protect one system can serve to protect all. Harmful algal blooms are a One Health issue demonstrating the interactions between animal, human, and ecological health. For example, environmental monitoring can provide early detection of environmental events, such as HABs, that pose both public health and ecological health threats. Public health surveillance can identify human and animal health events that may be linked to local environmental events such as HABs, and rapid detection can help public health officials, decision makers, and regulators protect public health by minimizing exposures.[13] With reporting of animal HAB toxicity cases through OHHABS and collaboration with animal health and environmental health sectors, public health agencies can identify bodies of water with ongoing HABs, conduct responsive water quality monitoring, and post warnings about potential hazards. Thus, collaboration between public and environmental health professionals, researchers, and veterinarians establishes a comprehensive One Health approach for HAB-related health risk management. Harmful algal blooms are ecological issues that require ecological and comprehensive approaches. While research continues, public health institutions and practitioners are at the front line to prevent and address HABs and HAB-associated illnesses.

Our collaborative efforts demonstrated the benefits of public health practice, multi-sectoral, and One Health approaches. We promoted a newly established surveillance program, OHHABS, created by state and federal public health institutes to link ecological health with public health to better understand HABs and HAB-associated illnesses prevention (see Supplemental Material).

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