Associations Between Perceptions of e-Cigarette Harmfulness and Addictiveness and the Age of E-Cigarette Initiation Among the Population Assessment of Tobacco and Health (PATH) Youth

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ABSTRACT

INTRODUCTION: Youth perceptions of harmfulness and addictiveness of e-cigarettes may impact the age that they initiate e-cigarette use, but this has not been investigated previously.

METHODS: Youth (12-17 years old) never e-cigarette users at their first wave of PATH participation (waves 1-3, 2013-2016) were included. PATH questions on absolute perceptions of e-cigarette harmfulness and addictiveness were used as exposures. Interval-censored Cox proportional hazards models were used to estimate the impact of perceptions of harmfulness, and perceptions of addictiveness on (i) the age of initiation of ecigarette use and (ii) age of first reporting past 30-day e-cigarette use, while controlling for covariates.

RESULTS: Youth who perceive e-cigarettes as having no/little harm had increased risk of initiating both ever e-cigarette use (AHR = 2.04; 95%CI = 1.74-2.40) and past 30-day e-cigarette use (AHR = 2.64; 95% CI = 2.07-3.37) at earlier ages compared to youth who perceive e-cigarettes as having a lot of harm. Youth who perceive the likelihood of becoming addicted to e-cigarettes to be very/somewhat unlikely had increased risk of an earlier age of both ever (AHR = 1.28; 95% CI = 1.07-1.52) and past 30-day (AHR = 1.36; 95% CI = 1.04-1.79) e-cigarette initiation compared to youth who perceived the likelihood of becoming addicted to e-cigarettes to be somewhat/very likely.

CONCLUSION: These results highlight the importance of communicating to youth the potential for health harms and addiction from e-cigarette use in prevention and intervention campaigns, as those with the lowest perceptions of harmfulness and addictiveness had the earliest ages of ecigarette initiation.

KEYWORDS: electronic cigarettes, risk perceptions, interval censoring, survival analysis

TYPE: Original Research Article

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Introduction

There are a variety of factors that contribute to the decision-making process of adopting certain behaviors. The Health Belief (HB) model posits that a person's belief in the threat of an illness or disease in addition to a person's belief in the effectiveness of the recommended health behavior will result in the behavior the person adopts.¹ In terms of e-cigarette use, according to the HB model, the greater the perceived likelihood of e-cigarette-related diseases and the greater the perceived benefits of quitting, the less likely it is that

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a person will initiate e-cigarette use.¹ Thus, a person's beliefs about the potential for health harms and addiction from e-cigarettes contributes to their decision to adopt e-cigarette use behaviors. In addition, there are other factors that contribute to the appeal and use of e-cigarettes, such as peer or family use,² flavors and design characteristics,³ e-cigarette marketing,⁴ and other external factors.

Some of the toxic and carcinogenic compounds, first identified in cigarettes, are also found in e-cigarettes emissions, although at lower levels compared to cigarettes.⁵ Younger ages



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (https://creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage). of e-cigarette use initiation increase young people's risk for nicotine addiction and harm to health.⁶ By 2014, e-cigarettes were the most widely used tobacco product on the market among middle and high school students,⁷ a finding that remains true to this day.^{8,9} Prior research with the nationally representative Population Assessment of Tobacco and Health (PATH) study prospectively estimating the age of e-cigarette initiation found that among youth never e-cigarette users at their first wave of participation in waves 1-3 (2013-2016), 18.6%, 7.4%, and 3.8% initiated ever, past 30-day, and fairly regular e-cigarette use, respectively by age 15 (waves 2-4: 2014-2017).¹⁰ In addition, the 2014 National Youth Tobacco Survey among 11-19-year-olds found that the average age of ever ecigarette initiation was 17.5 (95%CI = 17.47-17.52) years old.¹¹ These findings are concerning because early adoption of ecigarette use behaviors may be associated with nicotine addiction¹² as users of e-cigarettes can also use e-liquids with higher concentrations of nicotine than cigarettes.^{13,14}

Previous studies on perceptions of harmfulness and addictiveness of e-cigarettes have shown that a substantial proportion of youth do not consider e-cigarettes to be harmful or addictive. A previous 2013-2015 PATH study found that the proportion of youth (12-17 years old) never e-cigarette users who thought that e-cigarettes posed "no/little harm" was 29.6% and 43.8% for "some harm".¹⁵ In this study, only 26.6% of youth considered e-cigarettes to cause "a lot of harm", which was the lowest of all tobacco products studied.¹⁵ In addition, among ecigarette never users at PATH wave 1, youth who believed ecigarettes caused no/little harm had increased risk of initiating e-cigarette use one year later.¹⁵ Similar findings have been reported for perceptions of e-cigarette addictiveness, with 38.1% of susceptible youth and 24.8% of non-susceptible youth reporting that they perceived the likeliness of someone becoming addicted to e-cigarettes to be very unlikely, somewhat unlikely, or neither likely nor unlikely among PATH youth (12-17 years old) in 2013-2014.¹⁶ Interestingly, older youth (aged 14-15 or 16-17) perceived e-cigarettes to be less harmful (absolute instead of relative to cigarettes), as well as less addictive (absolute instead of relative to cigarettes), compared to younger youth (aged 12-13) (p's < .01).¹⁷ Recent national data from 2021 middle and high school students, reported that 42% of these students thought that e-cigarettes when used intermittently (some days but not every day) posed "some harm", 16% as "no/little harm" and 42% as "a lot of harm".9 Furthermore, people typically adopt beliefs that correspond to their behaviors,¹ so among e-cigarette users, it may be easier for them to believe or rationalize that e-cigarettes are not harmful or addictive.

While previous studies have shown that lower perceptions of harmfulness and addictiveness predict subsequent e-cigarette initiation, no studies have examined the impact of these perceptions on the age of e-cigarette initiation. In addition, earlier ages of e-cigarette initiation are associated with increased nicotine dependence, and those who start earlier are less likely to quit.^{6,18-20} Identifying windows of opportunity to direct prevention and education campaigns to age-appropriate youth would be helpful to deter youth from initiating e-cigarette use. Therefore, this study conducted secondary analyses of the PATH study waves 1-4 (2013-2017), estimating the impact of (i) perceptions of e-cigarettes harmfulness and (ii) perceptions of e-cigarette addictiveness among US youth never e-cigarette users on the age of initiation of e-cigarette use outcomes prospectively.

Methods

Study Design and Participants

The PATH study is a nationally representative sample of U.S. youth and adults that began in 2013-2014 with annual or biannual data collection, and its methodology is described elsewhere.²¹ The current study is a secondary analysis of waves 1-4 (2013-2017) youth and adult restricted-use datasets. Wave 1 data was collected from September 2013 to December 2014, with 13,651 youth (aged 12-17) completing the study.²¹ Wave 2 data was collected from October 2014- October 2015, wave 3 from October 2015- October 2016 and wave 4 from December 2016- January 2018. At wave 1, a total of 13,651 youth participated in PATH. In addition, family members of PATH participants who were 9-11 years old at wave 1 were eligible to participate when they turned 12 years old at waves 2-3, with 2091 and 2045 youth entering the PATH study at waves 2 and 3^{22} . When youth turned 18, they were invited to participate in the adult measurements, with 1,915, 1,907, and 1900 aged-up youth participating in waves 2-4, respectively.²² Following up our youth participants into adulthood across four waves of participation results in a final age range of 12-21 years old. Youth were eligible for the current study if they were never users of e-cigarettes at their first wave of PATH participation in waves 1-3 (2013-2016). E-cigarette initiation outcomes were followed-up in waves 2-4 (2014-2017) as youth or as adults. The sample size was a total of n = 16,143 youth never e-cigarette use at the first wave of PATH participation, representing a total of N = 30,194,853 youth in the USA. Parents of youth provided informed written consent and youth provided verbal assent. IRB approval for this study was obtained from the Committee for the Protection of Human Subjects at the University of Texas Health Science Center at Houston with number HSC-SPH-17-0368.

E-Cigarette Use Measures

In wave 1, PATH measured ever e-cigarette use with the question: "Have you ever used an e-cigarette, such as NJOY, Blu, or Smoking Everywhere, even one or two times?". In waves 2-4, in both the youth and adult surveys, this question was modified: "Have you ever used an electronic nicotine product, even one or two times? (Electronic nicotine products include e-cigarettes, e-cigars, e-pipes, e-hookahs, personal vaporizers, vape pens and hookah pens.)". These questions were

assumed to measure the same construct across waves. Response options included "yes", "no", "don't know", and "refused". Ever e-cigarette use has been characterized as experimentation.^{20,23,24}

In waves 2-4, in both the youth and adult surveys, past 30day e-cigarette use was measured with the question: "In the past 30 days, on how many days did you use an e-cigarette?". Numeric response options included 0-30 days and participants were considered past 30-day users if they reported e-cigarette use on 1 or more days. Past 30-day use of e-cigarettes serves as a proxy for e-cigarette use frequency.^{20,23,24}

Outcomes: Age of initiation of ever e-cigarette use and age of first reporting past 30-day e-cigarette use

PATH uses a variable for participant age in years at each wave, as date of birth is not included in the restricted-use data. PATH also uses a variable to represent the number of weeks between waves that youth participate in. Age of initiation of ever e-cigarette use was estimated by adding participants' age at their first wave of PATH participation (waves 1-3) to the number of weeks between relevant subsequent waves (waves 2-4) based on the first report of ever use for those who became users or the last report of never use among those who did not report initiation across waves. A lower and upper age bound for initiating ever use was determined. For all youth, the lower age bound was the age at the last wave where they did not report initiation of ever use. For those who reported initiation of ecigarettes, the upper age bound reflects the age at the last wave that they did not report ever use plus the number of weeks between survey waves when they first reported initiation to give a more precise estimate of age of initiation. The upper age bound for never users was considered censored. The age of first reporting past 30-day use was estimated in the same way.

Exposures

At each participant's first wave of PATH participation, they were asked "Have you ever heard of e-cigarettes?". Perceptions of harmfulness and addictiveness were only asked among participants who had heard of e-cigarettes. Perceptions of harmfulness and addictiveness of e-cigarettes were measured with survey questions, which were examined at the youth's first wave of PATH participation. Perceptions of e-cigarette harmfulness were measured with the question: "How much do you think people harm themselves when they use e-cigarettes?". Response options included: "no harm", "little harm", "some harm", "a lot of harm", "don't know", and "refused". This variable was collapsed based on previous research²⁵ into: no harm/little harm, some harm, a lot of harm, don't know, and never heard of e-cigarettes. Perceptions of addictiveness of ecigarettes were measured with the question: "How likely is someone to become addicted to e-cigarettes?". Response options included: "very unlikely", "somewhat unlikely", "neither likely nor unlikely", "somewhat likely", "very likely", "don't know", and "refused". This variable was collapsed based on previous research²⁵ into: very unlikely/somewhat unlikely, neither likely nor unlikely, somewhat likely/very likely, don't know, and never heard of e-cigarettes. Those who refused to answer either question were coded as missing and excluded from analysis.

Covariates

Sex and race/ethnicity. Answers to a question about participant sex classified youth as either males or females. Answers to race and ethnicity questions were combined to create race/ethnicity categories that are comparable to previous publications,^{10,26-28} which include: Non-Hispanic White, Hispanic, Non-Hispanic Black, and Non-Hispanic Other (Non-Hispanic Asian, multirace, and other races).

Previous use of other tobacco products. PATH asked all participants about ever use (Have you ever used [tobacco product], even once or twice/one or two puffs?) for the following [tobacco products]: cigarettes, traditional cigars, cigarillos, filtered cigars, hookah, and smokeless tobacco. The three variables for cigar product subtypes were collapsed to represent "any cigar use" for a total of four variables representing previous use of other tobacco products. Previous use of other tobacco products was examined at the wave prior to initiation of each e-cigarette outcome for youth who become users and at the latest wave of PATH participation for youth who remain non-users.

Statistical Analysis

Sampling weights at the first wave of youth's participation with their corresponding balanced repeated replicate (BRR) weights and Fay's adjustment set to .3 were used.²¹ Weighted means, standard errors, and proportions are provided. Weighted interval-censoring multivariable Cox proportional hazards models with a piecewise constant baseline hazard function²⁹ were used to assess differences in the age of initiation of each e-cigarette outcome by each exposure variable, while adjusting for sex, race/ethnicity, and previous use of other tobacco products. Two models are reported for estimating the association between perceptions of e-cigarette harmfulness on the age of initiation of e-cigarette use (model 1) and the age of first reporting past 30-day e-cigarette use (model 2). Two additional models are reported for estimating the association between perceptions of e-cigarette addictiveness on the age of initiation of e-cigarette use (model 3) and the age of first reporting past 30-day e-cigarette use (model 4). Adjusted hazard ratios (AHRs) and 95% confidence intervals (CI) are reported. A type I error level of .05 was used to determine statistical significance for all two-sided statistical tests. In addition, weighted interval-censored survival analyses and 95% CIs²⁹⁻³² were used to estimate the hazard function for the age of initiation of ever use and age of first reporting past 30-day use stratified by perceptions of e-cigarette

harmfulness and e-cigarette addictiveness. Hazard functions and 95% CIs are reported as cumulative incidence by age. All statistical analyses were completed in SAS version 9.4-TSlevel1M6. Missing values were little and shown in tables.

Results

Table 1 displays demographic characteristics of PATH youth (aged 12-17) who were never e-cigarette users at their first wave of PATH participation (2013-2016). Among these youth, (n = 16,143; N = 30,194,853), the majority entered the PATH study at wave 1 (73.3%), 49.5% were female, and 53.0% were Non-Hispanic White. Previous tobacco product use ranged from 2.8% for smokeless tobacco to 9.1% for cigarettes. The proportion of youth (12-17 years old) never e-cigarette users who perceived that e-cigarettes posed "no/little harm" was 4.3%, 51.9% for "some harm", 27.1% for "a lot of harm", 2.2% did not know the harm and 14.5% "never heard of e-cigarettes". The proportion of youth (12-17 years old) never e-cigarette users who perceived that e-cigarettes are "Very/Somewhat unlikely" to be addictive was 3.5%, 57.4% for "Somewhat/Very likely" to be addictive, 19.3% for "neither likely/unlikely", and 5.3% did not know if e-cigarettes were addictive.

Table 2 shows the results for the multivariable models for the associations between perceptions of e-cigarette harmfulness (models 1 and 2) and perceptions of e-cigarette addictiveness (models 3 and 4) separately, while adjusting for sex, race/ethnicity, and previous use of other tobacco products among all PATH youth never e-cigarette users. We found that youth who perceived e-cigarettes as having "some harm" (AHR = 1.55; 95%CI = 1.37-1.76) and "no/little harm" (AHR = 2.04; 95%CI = 1.74-2.40) had 1.55 and 2.04 (respectively) hazard ratio of initiating ever e-cigarette use at earlier ages compared to youth who perceive e-cigarettes as having "a lot of harm". Similarly, youth who reported their perception of ecigarettes as having "some harm" (AHR = 1.67; 95%CI = 1.39-2.02) and "no/little harm" (AHR = 2.64; 95%CI = 2.07-3.37) had 1.67 and 2.64 (respectively) hazard ratios of an earlier age of first reporting past 30-day e-cigarette use compared to youth who reported their perception of ecigarettes as having "a lot of harm". Never having heard of e-cigarettes was protective against initiating ever e-cigarette use at earlier ages (AHR = .65; 95%CI = .53- .79), but did not reach statistical significance in its relationship with past 30day e-cigarette use (AHR = .78; 95%CI = .55-1.10). For those who answered don't know to the question about e-cigarette harmfulness perceptions, there was no statistically significant association with either the age of ever e-cigarette initiation or the age of first reporting past 30-day use. The categories of response for harm perceptions suggest a dose-response relationship with the age of both ever e-cigarette initiation and first reporting past 30-day e-cigarette use, as the hazard ratios for an earlier age of e-cigarette initiation increase among those with lower harm perceptions.

In addition, youth who perceived the likelihood of ecigarette addictiveness as "very/somewhat unlikely" (AHR = 1.28; 95%CI = 1.07-1.52) had 1.28 hazard ratio of an earlier age of ever e-cigarette initiation compared to youth who perceived the likelihood of e-cigarette addictiveness as "somewhat/very likely". Similarly, youth who perceived the likelihood of ecigarette addictiveness as "very/somewhat unlikely" (AHR = 1.36; 95%CI = 1.04-1.79) had 1.36 hazard ratio of an earlier age of first reporting past 30-day e-cigarette use compared to youth who perceived e-cigarette addictiveness as "somewhat/very likely". Never having heard of e-cigarettes was protective against initiating ever e-cigarette use (AHR = .49; 95%CI = .41-.59) and first reporting past 30-day e-cigarette use (AHR = .56; 95%CI = .41- .76) at earlier ages compared to youth who perceived the likelihood of e-cigarette addictiveness as "somewhat/very likely".

Table 3 shows the results of the weighted interval-censored survival analysis estimating the age of ever e-cigarette initiation stratified by perceptions of e-cigarette harmfulness and addictiveness. By age 14, among those who perceived e-cigarettes as having "no/little harm" 11% initiated ever e-cigarette use, while 7.7%, 5.3%, 4.1% and 3.2% of those who perceived ecigarettes as having "some harm", "a lot of harm", "don't know", and had "never heard of e-cigarettes" initiated ever e-cigarette use, respectively. Furthermore, while 19.2% of youth who perceived e-cigarettes as having "no/little harm" initiated by age 15, 20.8% of youth who perceived e-cigarettes as having "a lot of harm" did not initiate e-cigarette use until age 17, indicating that youth with lower harm perceptions initiate e-cigarette use at earlier ages. In addition, by age 20, among youth who perceived the likelihood of e-cigarette addictiveness to be "very/ somewhat unlikely", 67.2% initiated ever e-cigarette use, while 60.5%, 45.1%, 44.2% and 31.1% of youth who perceived the likelihood of e-cigarette addictiveness to be "neither likely nor unlikely", "somewhat/very likely", "don't know", and had "never heard of e-cigarettes" initiated ever e-cigarette use respectively. Again, indicating that youth with "unlikely" perceptions of ecigarette addictiveness initiate e-cigarette use at earlier ages.

Table 4 shows the results of the weighted interval-censored survival analysis estimating the age of first reporting past 30-day e-cigarette use stratified by perceptions of e-cigarette harmfulness and addictiveness. By age 16, among youth who perceived e-cigarettes as having "no/little harm", 9.1% first reported past 30-day e-cigarette use, while 8.7%, 5.3%, 3.9% and 2.5% of youth who perceived e-cigarettes as having "some harm", "a lot of harm", "don't know", and had "never heard of e-cigarettes" first reported past 30-day e-cigarette use, respectively. In addition, by age 16, 10% of youth who perceived the likelihood of e-cigarette addictiveness to be "very/somewhat unlikely" first reported past 30-day e-cigarette use, while 9.8%, 7.3%, 6%, and 2.5% of youth who perceived the likelihood of e-cigarette addictiveness to be "neither likely nor unlikely", "very/ somewhat likely", "don't know", and "never heard of e-cigarettes" first reported past 30-day e-cigarette use, respectively.

VARIABLES NEVER E-CIGARETTE USERS AT THEIR FIRST WAVE OF PATH PARTICIPATION N (N) WEIGHTED % 16,143 (30,294,853) 100 First wave of PATH participation Wave 1 (2013-2014) 12,156 (22,132,919) 73.3 Wave 2 (2014-2015) 2010 (3,964,885) 13.1 Wave 3 (2015-2016) 1977 (4,097,049) 13.8 Age at entry into study weighted mean (SE) 13.8 (.01) 8186 (15,242,424) 50.5 Sex Male Female 7950 (14,939,879) 49.5 7 Missing Race/ethnicity Non-Hispanic White 7679 (15,977,089) 53.0 Non-Hispanic Black 2245 (4,206,126) 14.0 1505 (2,995,420) 9.9 Non-Hispanic Other Hispanic 4670 (6,941,729) 23.0 44 Missing Previous use of other tobacco products Cigarettes Yes 1529 (2,744,882) 9.1 14,594 (27,411,705) 90.9 no Missing 20 Any cigar product Yes 917 (1,663,170) 5.6 14,885 (27,898,837) 94.4 No Missing 341 Hookah Yes 958 (1,765,696) 5.9 No 15,159 (28,384,465) 94.1 Missing 26 Yes 454 (832,455) 2.8 Smokeless tobacco No 15,609 (29,209,845) 97.2 Missing 80 Perceptions of e-cigarette harmfulness^c No/little harm 742 (1,298,422) 4.3 Some harm 8420 (15,673,511) 51.9 A lot of harm 4265 (8,185,085) 27.1 Don't know 356 (666,715) 2.2 2354 (4,362,907) 14.5 Never heard of e-cigarettes Missing 6 Perceptions of e-cigarette addictiveness Very/Somewhat unlikely 589 (1,058,167) 3.5 Neither likely/unlikely 3176 (5,837,752) 19.3 Somewhat/very likely 9166 (17,307,755) 57.4 Don't know 845 (1,608,226) 5.3 Never heard of e-cigarettes 2354 (4,362,907) 14.5 Missing 13

Table 1. Demographic characteristics of PATH USA youth (aged 12-17) never e-cigarette users at their first wave of PATH participation (2013-2016).

^aNon-Hispanic Other includes Asian, multi-race, etc.

^bPATH restricted file received disclosure to publish: August 4, 2021. United States Department of Health and Human Services. National Institutes of Health. National Institute on Drug Abuse, and United States Department of Health and Human Services. Food and Drug Administration. Center for Tobacco Products. Population Assessment of Tobacco and Health (PATH) Study [United States] Restricted-Use Files. ICPSR36231-v29.Ann Arbor, MI: Inter-university Consortium for Political and Social Research [distributor], December 16, 2021. https://doi.org/10.3886/ICPSR36231.v29

^cPerceptions of harmfulness and addictiveness were measured at participants' first wave of PATH participation (waves 1-3).

		EVER E-CIGARETTE USE	PAST 30-DAY E-CIGARETTE USE
		MODEL 1	MODEL 2
Perceptions of E-cigarette Harmfulness ¹	A lot of harm	1.00	1.00
	Some harm	1.55 (1.37- 1.76)	1.67 (1.39- 2.02)
	No/little harm	2.04 (1.74- 2.40)	2.64 (2.07- 3.37)
	Don't know	1.18 (.88- 1.59)	1.33 (.86- 2.05)
	Never heard of e-cigarettes	.65 (.5379)	.78 (.55- 1.10)
Sex	Female	1.00	1.00
	Male	1.10 (1.01- 1.20)	1.21 (1.09- 1.34)
Race/Ethnicity	Non-Hispanic White	1.00	1.00
	Hispanic	.94 (.84- 1.05)	.74 (.6386)
	Non-Hispanic Black	.68 (.5977)	.50 (.4162)
	Non-Hispanic Other ²	.79 (.6891)	.81 (.6896)
Previous Other Tobacco Product Use			
Cigarettes	No	1.00	1.00
	Yes	1.46 (1.32- 1.62)	1.56 (1.36- 1.80)
Any Cigar Product	No	1.00	1.00
	Yes	.89 (.78- 1.01)	.88 (.75- 1.02)
Hookah	No	1.00	1.00
	Yes	1.33 (1.20- 1.48)	1.18 (1.03- 1.35)
Smokeless Tobacco	No	1.00	1.00
	Yes	1.20 (1.06- 1.35)	1.27 (1.06- 1.52)
		Model 3	Model 4
Perceptions of E-cigarette Addictiveness ¹	Somewhat/very likely	1.00	1.00
	Very/somewhat unlikely	1.28 (1.07- 1.52)	1.36 (1.04- 1.79)
	Neither likely nor unlikely	1.31 (1.21- 1.41)	1.38 (1.21- 1.56)
	Don't know	.81 (.6798)	.91 (.68- 1.23)
	Never heard of e-cigarettes	.49 (.4159)	.56 (.4176)
Sex	Female	1.00	1.00
	Male	1.10 (1.01- 1.20)	1.21 (1.09- 1.34)

Table 2. Multivariable³ hazard ratios (95% confidence intervals) for the associations between perceptions¹ of harmfulness and perceptions of addictiveness with the age of e-cigarette use initiation outcomes PATH USA youth (aged 12-17) between 2013-2017.

(Continued)

Table 2. Continued.

		EVER E-CIGARETTE USE	PAST 30-DAY E-CIGARETTE USE
		MODEL 1	MODEL 2
Race/Ethnicity	Non-Hispanic White	1.00	1.00
	Hispanic	.92 (.83- 1.02)	.73 (.6285)
	Non-Hispanic Black	.67 (.5976)	.51 (.4163)
	Non-Hispanic Other ²	.77 (.6788)	.79 (.6694)
Previous Tobacco Product Use			
Cigarettes	No	1.00	1.00
	Yes	1.27 (1.15- 1.40)	1.60 (1.39- 1.85)
Any Cigar Product	No	1.00	1.00
	Yes	.82 (.7392)	.89 (.76- 1.04)
Hookah	No	1.00	1.00
	Yes	1.41 (1.24- 1.62)	1.18 (1.03- 1.35)
Smokeless Tobacco	No	1.00	1.00
	Yes	.54 (.4368)	1.28 (1.07- 1.52)

¹Perceptions of harmfulness and addictiveness were measured at participants' first wave of PATH participation (waves 1-3).

²Non-Hispanic Other includes Asian, multi-race, etc.

³PATH restricted file received disclosure to publish: August 4, 2021. United States Department of Health and Human Services. National Institutes of Health. National Institute on Drug Abuse, and United States Department of Health and Human Services. Food and Drug Administration. Center for Tobacco Products. Population Assessment of Tobacco and Health (PATH) Study [United States] Restricted-Use Files. ICPSR36231-v29.Ann Arbor, MI: Inter-university Consortium for Political and Social Research [distributor], December 16, 2021. https://doi.org/10.3886/ICPSR36231.v29

Discussion

Taken together, these findings are the first to show that youth who perceive e-cigarettes to be of "no" harm and "unlikely" for addictiveness had increased hazard ratios of initiating ever e-cigarette use, as well as first reporting past 30-day e-cigarette use, at earlier ages compared to youth who understand the potential for ecigarette harmfulness and addictiveness. There are clear differences in both ever e-cigarette initiation and first report of past 30day e-cigarette initiation across youth ages, in which those with lower risk perceptions of e-cigarette harmfulness and addictiveness have higher incidence of initiation compared to those with high risk perceptions. The cumulative incidence of initiation was also higher among youth with lower perceptions of harmfulness and addictiveness compared to youth overall. For example, among youth who perceived e-cigarettes to be of no/little harm, 19.2% initiated ever e-cigarette use, compared to 11.7% of youth overall who initiated ever e-cigarette use by age 15.¹⁰

The findings presented here can be used to compare with future studies that have been conducted after federal law changed the minimum age of tobacco sale from 18 to 21 years³³ to determine the impact this law has had on the age of e-cigarette initiation. Furthermore, the e-cigarette market has diversified in recent years with JUUL entering the market in 2017, and nicotine concentration in e-cigarettes sold increased between 2013-2018,¹³ yet it is unknown how these factors will influence the age of e-cigarette initiation. While there are other risk factors that contribute to e-cigarette use that should be explored, such as

exposure to e-cigarette advertisements, other drugs or alcohol use, state/region of the USA, peer³⁴ and family influences,²⁰ e-cigarette flavors,³⁵ and perceived costs and benefits to e-cigarette use,³⁶ future research should explore these factors to determine their impact on the age of e-cigarette initiation.

Our findings are similar to previous research, which has found that lower perceptions of e-cigarette harmfulness and addictiveness are associated with e-cigarette initiation. For example, among PATH youth (12-17 years old) who were never users of e-cigarettes in 2013-2014, compared to those who perceived e-cigarettes to be "high" in harm (i.e., a lot of harm), those who perceived e-cigarettes to be of "low" (i.e., no/little harm) or "medium" (i.e., some harm) harmfulness had an increased probability of ever e-cigarette initiation at follow-up in 2014-2015.²⁵ Specifically, among youth who found e-cigarettes to be "low" in harmfulness, the probability of ever e-cigarette initiation at follow-up was 14% (95%CI = 12-15%) compared to 8% (95%CI = 7-10%) and 6% (95%CI = 5-7%) among youth who perceived e-cigarettes to be "medium" and "high" harmfulness.²⁵ Our findings extend this previous work by finding that perceptions of e-cigarette harmfulness are associated with earlier ages of ever e-cigarette initiation and first reporting past 30-day e-cigarette use among never e-cigarette users.

In terms of perceived addictiveness, ever e-cigarette initiation at follow-up was also highest among youth (12-17 years old) who perceived e-cigarettes to be of "low" addictiveness (i.e., very or somewhat unlikely) compared to youth who perceived e-cigarettes to

AGE	AGE OF INITIATION OF EVER E-CIGARETTE USE						
	PERCEPTIONS OF E-CIGARETTE HARMFULNESS						
	NO/LITTLE HARM	SOME HARM	A LOT OF HARM	DON'T KNOW	NEVER HEARD OF E-CIGARETTES		
12	0.0	0.0	0.0	0.0	0.0		
13	4.9 (3.1- 6.6)	3.7 (3.2- 4.2)	1.3 (.0- 3.0)	1.9 (.2- 3.6)	1.6 (.0- 3.1)		
14	11.0 (3.8- 18.2)	7.7 (7.0- 8.4)	5.3 (2.9- 7.8)	4.1 (.8- 7.4)	3.2 (.0- 6.3)		
15	19.2 (6.2- 32.1)	13.7 (12.8- 14.6)	9.3 (7.8- 10.8)	7.1 (.2- 14.1)	4.8 (3.2- 6.4)		
16	26.8 (17.8- 35.8)	22.2 (19.7- 24.7)	13.3 (9.6- 17.1)	14.1 (5.7- 22.6)	7.4 (3.0- 11.8)		
17	41.0 (30.0- 52.0)	35.9 (32.8- 38.9)	20.8 (15.0- 26.6)	24.1 (6.9- 41.3)	8.6 (3.8- 13.4)		
18	46.1 (34.7- 57.5)	46.5 (41.3- 51.6)	32.4 (24.9- 40.0)	31.2 (21.4- 41.0)	14.6 (9.8- 19.5)		
19	59.6 (45.2- 73.9)	48.4 (45.5- 51.4)	34.3 (30.2- 38.4)	36.7 (27.6- 45.8)	23.9 (17.2- 30.7)		
20	65.0 (54.2- 75.9)	52.3 (49.3- 55.2)	37.9 (32.8- 43.0)	56.2 (32.6- 79.9)	31.1 (22.6- 39.5)		
21	N/A	58.6 (47.2-70.0)	N/A	N/A	N/A		

Table 3. Estimated hazard functions^a (95% confidence intervals^b) of the age of initiation of ever e-cigarette use for PATH^d US youth (12-17 years old at their first wave of PATH participation) stratified by perceptions^c of e-cigarette harmfulness and addictiveness.

AGE	AGE OF INITIATION OF EVER E-CIGARETTE USE					
	PERCEPTIONS OF E-CIGARETTE ADDICTIVENESS					
	VERY/SOMEWHAT UNLIKELY	NEITHER LIKELY NOR UNLIKELY	VERY/SOMEWHAT LIKELY	DON'T KNOW	NEVER HEARD OF E-CIGARETTES	
12	0.0	0.0	0.0	0.0	0.0	
13	3.3 (.0- 6.7)	4.0 (3.1- 4.9)	3.1 (1.6- 4.6)	2.8 (1.6- 3.9)	1.6 (.0- 3.1)	
14	5.9 (.0- 12.3)	8.7 (7.5- 9.8)	6.6 (5.8- 7.3)	5.7 (1.6- 9.9)	3.2 (.0- 6.3)	
15	12.7 (4.9- 20.5)	14.9 (8.3- 21.6)	12.0 (11.0- 13.1)	9.9 (5.8- 14.0)	4.8 (3.2- 6.4)	
16	19.3 (7.0- 31.5)	23.9 (19.8- 28.0)	18.7 (17.4- 20.0)	15.5 (7.4- 23.6)	7.4 (3.0- 11.8)	
17	23.5 (17.5- 29.5)	39.0 (30.9- 47.1)	29.9 (27.1- 32.7)	24.1 (12.2- 36.0)	8.6 (3.8- 13.4)	
18	45.7 (31.5- 59.9)	51.7 (42.5- 60.9)	40.7 (34.9- 46.5)	25.9 (20.7- 31.0)	14.6 (9.8- 19.5)	
19	56.9 (49.3- 64.5)	51.7 (48.5- 55.0)	42.6 (39.3- 45.9)	38.4 (31.4- 45.5)	23.9 (17.2- 30.7)	
20	67.2 (46.9- 87.5)	60.5 (54.7- 66.3)	45.1 (42.3- 47.9)	44.2 (32.8- 55.6)	31.1 (22.6- 39.5)	
21	N/A	N/A	50.6 (39.5- 61.7)	N/A	N/A	

^aHazards are reported as cumulative percentages (i.e., cumulative incidence).

^bTurnbull 95% confidence interval.

^cPerceptions of harmfulness and addictiveness were measured at participants' first wave of PATH participation (waves 1-3).

^dPATH restricted file received disclosure to publish: March 15, 2022.United States Department of Health and Human Services. National Institutes of Health. National Institute on Drug Abuse, and United States Department of Health and Human Services. Food and Drug Administration. Center for Tobacco Products. Population Assessment of Tobacco and Health (PATH) Study [United States] Restricted-Use Files. ICPSR36231-v13.Ann Arbor, MI: Inter-university Consortium for Political and Social Research [distributor], November 5, 2019. https://doi.org/10.3886/ICPSR36231.v29

be of "high" (i.e., somewhat or very likely) addictiveness (P < .001).²⁵ A different PATH study that used multiple logistic regression to estimate the odds of ever e-cigarette initiation in 2014-2015 among never e-cigarette users in 2013-2014 found that youth (12-17 years) who perceived that e-cigarettes are of "no/little harm" had increased risk of ever e-cigarette initiation compared to youth who believed

these products posed "a lot of harm".¹⁵ Our results are consistent with and extend these previous studies by finding that youth who perceived the likelihood of someone becoming addicted to e-cigarettes to be "very/somewhat unlikely" or "neither likely nor unlikely" had increased risk of initiating ever e-cigarette use and first reporting past 30-day e-cigarette use at earlier ages compared to

Table 4. Estimated hazard functions^a (95% confidence intervals^b) of the age of first reporting past 30-day e-cigarette use for PATH^c US youth stratified by perceptions of e-cigarette harmfulness and addictiveness^d.

AGE	AGE OF INITIATION OF PAST 30-DAY E-CIGARETTE USE					
	PERCEPTIONS OF E-CIGARETTE HARMFULNESS					
	NO/LITTLE HARM	SOME HARM	A LOT OF HARM	DON'T KNOW	NEVER HEARD OF E-CIGARETTES	
12	0.0	0.0	0.0	0.0	0.0	
13	2.4 (1.4- 3.5)	1.2 (.2- 2.2)	.5 (.0- 1.3)	1.0 (.0- 2.1)	.3 (.07)	
14	5.0 (.0- 10.2)	2.8 (1.5- 4.1)	1.3 (.0- 2.8)	1.0 (.0- 2.1)	.8 (.2- 1.4)	
15	8.5 (5.7- 11.4)	5.2 (4.5- 5.8)	3.3 (2.4- 4.2)	2.7 (.6- 4.8)	2.0 (.3- 3.7)	
16	9.1 (4.5- 13.7)	8.7 (7.8- 9.6)	5.3 (1.6- 8.9)	3.9 (1.0- 6.9)	2.5 (1.3- 3.8)	
17	24.7 (10.2- 39.1)	14.6 (10.7- 18.5)	8.9 (4.8- 13.1)	17.2 (.0- 36.6)	5.4 (2.3- 8.5)	
18	29.2 (19.4- 38.9)	27.6 (25.5- 29.6)	16.4 (13.3- 19.6)	17.2 (7.4- 27.1)	12.3 (3.7- 20.8)	
19	36.5 (29.3- 43.7)	27.6 (25.5- 29.6)	16.4 (13.5- 19.4)	26.6 (13.6- 39.5)	12.3 (7.8- 16.7)	
20	48.1 (30.9- 65.2)	32.7 (29.8- 35.6)	18.5 (14.6- 22.3)	27.3 (7.6- 47.0)	19.2 (10.6- 27.8)	
21	N/A	N/A	31.2 (7.8- 54.6)	N/A	N/A	

AGE		AGE OF INITIATION OF EVER E-CIGARETTE USE					
		PERCEPTIONS OF E-CIGARETTE ADDICTIVENESS					
	VERY/SOMEWHAT UNLIKELY	NEITHER LIKELY NOR UNLIKELY	VERY/SOMEWHAT LIKELY	DON'T KNOW	NEVER HEARD OF E-CIGARETTES		
12	0.0	0.0	0.0	0.0	0.0		
13	N/A	1.6 (1.0- 2.2)	.9 (.0- 2.2)	.2 (.05) ^d	.3 (.07)		
14	1.1 (.0- 2.4) ^a	2.7 (.0- 5.4)	2.3 (1.2- 3.3)	2.3 (.9- 3.6)	.8 (.2- 1.4)		
15	6.2 (3.5- 9.0) ^b	5.6 (1.1- 10.4)	4.4 (3.9- 5.0)	3.2 (.7- 5.7)	2.0 (.3- 3.7)		
16	10.0 (1.1- 18.8)	9.8 (7.6- 11.9)	7.3 (6.2- 8.4)	6.0 (1.9- 10.0)	2.5 (1.3- 3.8)		
17	11.9 (6.8- 17.0)	13.1 (6.9- 19.3)	13.2 (9.9- 16.6)	12.1 (3.3- 20.9)	5.4 (2.3- 8.5)		
18	31.9 (24.0- 39.8)	31.0 (24.9- 37.2)	22.6 (20.5- 24.6)	13.9 (4.8- 23.1)	12.3 (3.7- 20.8)		
19	31.9 (24.8- 39.1)	31.0 (28.4- 33.6)	22.7 (20.8- 24.6)	24.8 (14.7- 34.9)	12.3 (7.8- 16.7)		
20	44.0 (26.3- 61.7)	40.0 (35.0- 45.0)	25.2 (22.7- 27.8)	28.3 (16.6- 40.1)	19.2 (10.6- 27.8)		
21	N/A	N/A	31.8 (23.2- 40.4) ^c	31.6 (18.7- 44.5)	N/A		

^aHazards are reported as cumulative percentages (i.e., cumulative incidence)

^bTurnbull 95% confidence interval

^oPATH restricted file received disclosure to publish: March 29, 2022.United States Department of Health and Human Services. National Institutes of Health. National Institute on Drug Abuse, and United States Department of Health and Human Services. Food and Drug Administration. Center for Tobacco Products. Population Assessment of Tobacco and Health (PATH) Study [United States] Restricted-Use Files. ICPSR36231-v13.Ann Arbor, MI: Inter-university Consortium for Political and Social Research [distributor], November 5, 2019. https://doi.org/10.3886/ICPSR36231.v29 a: midpoint of interval represents 14 and 23 weeks; b: midpoint of interval represents 15 and 30 weeks; c: midpoint of interval represents 21 and 18 weeks; d: midpoint of interval represents 13 and 20 weeks

^dPerceptions of harmfulness and addictiveness were measured at participants' first wave of PATH participation (waves 1-3)

youth who perceived the likelihood of someone becoming addicted to e-cigarettes to be "very/somewhat likely". It should be noted that e-cigarette use is associated with nicotine dependence, ^{23,24,37} with a previous study of youth (13-18 years old) e-cigarette users finding that e-cigarette dependence significantly increased after one year among past 30-day e-cigarette users (P = .004).²⁴

Previous research has shown that many youth think that ecigarettes don't contain nicotine. Specifically, one study found that 63% of JUUL users (15-24 years old) did not know that JUUL products always contain nicotine.³⁸ Other troubling findings include a previous study by the CDC, which found that 99% of e-cigarettes tested and on the market in the U.S. in 2013-2014 contain nicotine of varying levels, even in ecigarettes with labels claiming they contain 0% nicotine.^{5,39} In fact, a different study of young people ages 12-21 in 2017-2018 found that 27% of e-cigarette users who said their e-cigarette contained no nicotine had cotinine levels above the cutoff that indicates nicotine exposure.⁴⁰ These findings suggest that e-cigarette companies are not forthcoming about the addiction potential posed by their products. The U.S. needs stronger policies around regulating nicotine content level claims made by e-cigarette companies and e-cigarette labels⁴¹ since several studies have shown that they are not accurate.^{5,39,40} Future research should examine if perceptions of e-cigarette harmfulness and addictiveness have changed as nicotine concentration in e-cigarettes increased with JUUL entering the market and the number of flavors grew.

While research on the health harms associated with ecigarette use is in its early stages, there are studies that indicate the potential for harmful respiratory outcomes associated with e-cigarette use.^{42,43} There are also e-cigarette flavorings that when inhaled result in respiratory disease and respiratory flow resistance.^{42,44,45} Other pulmonary toxicants often found in e-cigarettes include propylene glycol, diacetyl, cinnamaldehyde, benzaldehyde, and trace metals, which may contribute to poor respiratory health.⁴³ Ecigarette use has also been shown to contribute to cardiovascular disease in animal models.^{46,47} Thus, it is important to communicate the harms associated with e-cigarette use, as the use of nicotine products is a lifelong behavior among many people. These data were also collected prior to the COVID-19 pandemic, and a recent national survey of youth and young adults (n = 4,351, aged 13-24 years old) has shown that COVID-19 infections were more common among ever e-cigarette users (AOR = 5.05; 95%CI = 1.82-13.96) compared to never users.³⁷ It is possible that youth may be more inclined to protect their respiratory health given the association between e-cigarette use and COVID-19, but more research is needed to determine if these historical events have translated to changes in e-cigarette risk perceptions and changes in e-cigarette use. Our findings can serve as a baseline to compare with future studies conducted after this historical event.

Strengths and Limitations

One limitation of our study is the subjectivity in the perception measures questions, but it is not possible to quantify a person's perceptions. While measures of relative perceived harmfulness and addictiveness (i.e., compared to cigarettes) have been the standard in tobacco research, youth often have misperceptions about how "less harmful/addictive than cigarettes" does not mean that e-cigarettes are not harmful or addictive.¹⁵ However, these relative perceived harmfulness and addictiveness of e-cigarette in comparison to cigarette

could be for example more appropriate to explore among cigarette users who may initiate e-cigarette to reduce cigarette use. In addition, the question used to measure ecigarette use at wave 1 uses the term "e-cigarettes", while in waves 2-4 the term "electronic nicotine products" is used. Another limitation of the study is that we rely on selfreported data for e-cigarette use to estimate the age of initiation because asking participants the exact date they initiated e-cigarettes is unrealistic. However, we overcome this limitation with the use of weighted interval-censoring Cox proportional hazards models. In addition, there are other risk factors that contribute to e-cigarette use that should be explored, such as exposure to e-cigarette marketing, use of other drugs, alcohol use, state/region of the USA, peer/family influences, e-cigarette flavors, etc. We did not include wave as a covariate as the "shadow youth" sample sizes only accounted for youth who became adults in the following wave, and therefore, the wave of entry does not measure changes in e-cigarettes products on the market. These factors were outside the scope of the current study. Perceived addictiveness of e-cigarettes were not measured among adults therefore exploring time varying effects was not possible. Finally, the study data was collected from 2013-2017, and research is needed with more recent data to see how changes in the e-cigarette marketplace and historical events such as COVID-19 have impacted the age of ecigarette initiation. It is unclear how these events have impacted perceptions of e-cigarette harmfulness and addictiveness. However, conducting nationally representative research is time consuming and we were only funded to use data until wave 4. Strengths of the study include the use of a nationally representative dataset and the longitudinal prospective analysis on the age of initiation of e-cigarette use across PATH waves 1-4.

Conclusion

In conclusion, we provide novel evidence that youth with lower risk perceptions of e-cigarette harmfulness and addictiveness had increased hazard risk of initiating ever ecigarette use and first reporting past 30-day e-cigarette use at earlier ages compared to youth with higher risk perceptions. If policies were implemented with the goal of achieving a 10% reduction in e-cigarette use, prevention and intervention campaigns would need to be implemented in youth before age 14 among youth with lower risk perceptions (i.e., those who perceive e-cigarettes to be of "no/little harm" and "very/somewhat unlikely" for addictiveness). Prevention and education campaigns need to create stronger messaging around the potential harms and potential for addictiveness associated with e-cigarette use, not only to researchers but for the general public, including parents, teachers, and pediatricians.

REFERENCES

- Abraham C, Sheeran P. The health belief model. Predicting bealth behaviour: Research and practice with social cognition models. 2015;2:30-55.
- Barrington-Trimis JL, Berhane K, Unger JB, et al. Psychosocial factors associated with adolescent electronic cigarette and cigarette use. *Pediatrics*. 2015;136(2): 308-317.
- Barnes AJ, Bono RS, Lester RC, Eissenberg TE, Cobb CO. Effect of flavors and modified risk messages on e-cigarette abuse liability. *Tobacco Regulatory Science*. 2017;3(4):374-387.
- Marynak K, Gentzke A, Wang TW, Neff L, King BA. Exposure to electronic cigarette advertising among middle and high school students— United States, 2014–2016. *Morbidity and Mortality Weekly Report*. 2018; 67(10):294-299.
- Goniewicz ML, Gupta R, Lee YH, et al. Nicotine levels in electronic cigarette refill solutions: A comparative analysis of products from the U.S., Korea, and Poland. *Int J Drug Policy.* 2015;26(6):583-588.
- Branstetter SA, Mercincavage M, Muscat JE. Predictors of the Nicotine Dependence Behavior Time to the First Cigarette in a Multiracial Cohort. Nicotine & tobacco research : Official Journal of the Society for Research on Nicotine and Tobacco. 2015;17(7):819-824.
- Arrazola RA, Singh T, Corey CG, et al. Tobacco use among middle and high school students - United States, 2011-2014. MMWR Morbidity and mortality weekly report. 2015;64(14):381-385.
- Gentzke AS, Wang TW, Jamal A, et al. Tobacco Product Use Among Middle and High School Students - United States, 2020. MMWR Morbidity and mortality weekly report. 2020;69(50):1881-1888.
- Gentzke AS, Wang TW, Cornelius M, et al. Tobacco Product Use and Associated Factors Among Middle and High School Students - National Youth Tobacco Survey, United States, 2021. MMWR Surveill Summ. 2022;71(5):1-29.
- Pérez A, Bluestein M, Chen B, Perry CL, Harrell MB. Prospectively estimating the age of initiation of e-cigarettes among U.S. youth: Findings from the Population Assessment of Tobacco and Health (PATH) study, 2013-2017. *Journal of biometrics & biostatistics*. 2020;11(4).
- Chen X, Yu B, Wang Y. Initiation of Electronic Cigarette Use by Age Among Youth in the U.S. *Am J Prev Med.* 2017;53(3):396-399.
- 12. US Department of Health Human Services. *The health consequences of smoking—50 years of progress: A report of the Surgeon General.* Atlanta, GA: US Department of Health and Human Services, Centers for disease control and prevention; 2014.
- Romberg AR, Miller Lo EJ, Cuccia AF, et al. Patterns of nicotine concentrations in electronic cigarettes sold in the United States, 2013-2018. Drug and alcohol dependence. 2019;203:1-7.
- Wang L, Wang Y, Chen J, Liu P, Li M. A Review of Toxicity Mechanism Studies of Electronic Cigarettes on Respiratory System. *Int J Mol Sci.* 2022; 23(9):5030.
- Parker MA, Villanti AC, Quisenberry AJ, et al. Tobacco Product Harm Perceptions and New Use. *Pediatrics*. 2018;142(6):e20181505.
- Kwon E, Seo D-C, Lin H-C, Chen Z. Predictors of youth e-cigarette use susceptibility in a U.S. nationally representative sample. *Addictive behaviors*. 2018;82: 79-85.
- Strong DR, Messer K, White M, et al. Youth perception of harm and addictiveness of tobacco products: Findings from the Population Assessment of Tobacco and Health Study (Wave 1). Addictive behaviors. 2019;92:128-135.
- Sharapova S, Reyes-Guzman C, Singh T, Phillips E, Marynak KL, Agaku I. Age of tobacco use initiation and association with current use and nicotine dependence among US middle and high school students. *Tobacco control*. 2020; 29(1):49-54.
- Morean ME, Krishnan-Sarin S, O'Malley SS. Assessing nicotine dependence in adolescent E-cigarette users: The 4-item Patient-Reported Outcomes Measurement Information System (PROMIS) Nicotine Dependence Item Bank for electronic cigarettes. Drug and alcohol dependence. 2018;188:60-63.
- Vogel EA, Ramo DE, Rubinstein ML. Prevalence and correlates of adolescents' ecigarette use frequency and dependence. *Drug and alcohol dependence*. 2018;188: 109-112.
- Hyland A, Ambrose BK, Conway KP, et al. Design and methods of the Population Assessment of Tobacco and Health (PATH) Study. *Tobacco control*. 2017;26(4):371-378.
- 22. United States Department of Health and Human Services, National Institutes of Health, National Institute on Drug Abuse, Food and Drug Administration. Center for Tobacco Products. Population Assessment of Tobacco and Health (PATH) Study [United States] Restricted-Use Files User Guide Westat. Rockville, MD: National Institute on Drug Abuse, Food and Drug Administration; 2021.
- Mantey DS, Case KR, Omega-Njemnobi O, Springer AE, Kelder SH. Use frequency and symptoms of nicotine dependence among adolescent E-cigarette users: Comparison of JUUL and Non-JUUL users. Drug and alcohol dependence. 2021;228:109078.

- Vogel EA, Prochaska JJ, Ramo DE, Andres J, Rubinstein ML. Adolescents' E-Cigarette Use: Increases in Frequency, Dependence, and Nicotine Exposure Over 12 Months. J Adolesc Health. 2019;64(6):770-775.
- Strong DR, Leas E, Elton-Marshall T, et al. Harm perceptions and tobacco use initiation among youth in Wave 1 and 2 of the Population Assessment of Tobacco and Health (PATH) Study. *Prev Med.* 2019;123:185-191.
- Chen B, Sterling KL, Bluestein MA, et al. Age of initiation of cigarillos, filtered cigars and/or traditional cigars among youth: Findings from the Population Assessment of Tobacco and Health (PATH) study. *PloS one*. 2020; 15(12):e0243372.
- Pérez A, N'hpang RS, Callahan E, et al. Age at Initiation of Cigarette Use in a Nationally Representative Sample of US Youth, 2013-2017. *JAMA Network Open*. 2021;4(2):e210218.
- Pérez A, Kuk AE, Bluestein MA, Harrell MB, Perry CL, Chen B. Prospective estimation of the age of initiation of hookah use among youth: Findings from the Population Assessment of Tobacco and Health (PATH) study waves 1. *Addictive behaviors*. 2021;117:106838.
- Finkelstein DM. A proportional hazards model for interval-censored failure time data. *Biometrics*. 1986;42:845-854.
- Ng MP. A modification of Peto's nonparametric estimation of survival curves for interval censored data. *Biometrics*. 2002;58(2):439-442.
- Goodall RL, Dunn DT, Babiker AG. Interval-censored survival time data: confidence intervals for the non-parametric survivor function. *Statistics in medicine*. 2004;23(7):1131-1145.
- 32. Turnbull BW. The empirical distribution function with arbitrarily grouped, censored and truncated data. J Roy Stat Soc B. 1976;38(3):290-295.
- U.S. Food and Drug Administration. *Tobacco 21*; 2022. https://www.fda.gov/ tobacco-products/retail-sales-tobacco-products/tobacco-21. Accessed 02/14/ 2022.
- Rocheleau GC, Vito AG, Intravia J. Peers, Perceptions, and E-Cigarettes: A Social Learning Approach to Explaining E-Cigarette Use Among Youth. *J Drug Issues*. 2020;50(4):472-489.
- Morean ME, Butler ER, Bold KW, et al. Preferring more e-cigarette flavors is associated with e-cigarette use frequency among adolescents but not adults. *PloS one*. 2018;13(1):e0189015.
- Nicksic NE, Snell LM, Barnes AJ. Reasons to use e-cigarettes among adults and youth in the Population Assessment of Tobacco and Health (PATH) study. *Addictive behaviors*. 2019;93:93-99.
- Gaiha SM, Cheng J, Halpern-Felsher B. Association Between Youth Smoking, Electronic Cigarette Use, and COVID-19. J Adolesc Health. 2020; 67(4):519-523.
- Truth Initiative. JUUL e-cigarettes gain popularity Among youth, but Awareness of nicotine presence remains low; 2018. https://truthinitiative.org/press/press-release/ juul-e-cigarettes-gain-popularity-among-youth-awareness-nicotine-presence. Accessed 1216, 2021.
- Centers for Disease Control and Prevention. Quick Facts on the Risks of E-cigarettes for Kids, Teens, and Young Adults; 2021. https://www.cdc.gov/tobacco/basic_ information/e-cigarettes/Quick-Facts-on-the-Risks-of-E-cigarettes-for-Kids-Teens-and-Young-Adults.html. Accessed 12/14/2021.
- Boykan R, Messina CR, Chateau G, Eliscu A, Tolentino J, Goniewicz ML. Self-Reported Use of Tobacco, E-cigarettes, and Marijuana Versus Urinary Biomarkers. *Pediatrics*. 2019;143(5):e20183531.
- Marynak KL, Gammon DG, Rogers T, Coats EM, Singh T, King BA. Sales of Nicotine-Containing Electronic Cigarette Products: United States, 2015. *American Journal of Public Health*. 2017;107(5):702-705.
- Barrington-Trimis JL, Samet JM, McConnell R. Flavorings in electronic cigarettes: an unrecognized respiratory health hazard? *Jama*. 2014;312(23): 2493-2494.
- Bhatta DN, Glantz SA. Association of E-Cigarette Use With Respiratory Disease Among Adults: A Longitudinal Analysis. *Am J Prev Med.* 2020;58(2): 182-190.
- Farsalinos KE, Kistler KA, Gillman G, Voudris V. Evaluation of electronic cigarette liquids and aerosol for the presence of selected inhalation toxins. Nicotine & tobacco research : Official Journal of the Society for Research on Nicotine and Tobacco. 2015; 17(2):168-174.
- Wu Q, Jiang D, Minor M, Chu HW. Electronic cigarette liquid increases inflammation and virus infection in primary human airway epithelial cells. *PloS one*. 2014;9(9):e108342.
- Olfert IM, DeVallance E, Hoskinson H, et al. Chronic exposure to electronic cigarettes results in impaired cardiovascular function in mice. *Journal of applied physiology*. 2018. 124(3):573-582.
- Navas-Acien A, Martinez-Morata I, Hilpert M, Rule A, Shimbo D, LoIacono NJ. Early Cardiovascular Risk in E-cigarette Users: the Potential Role of Metals. *Current environmental health reports*. 2020;7(4):353-361.