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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

Adriana Pérez[1,2]*, Meagan Bluestein[2], Baojiang Chen[1,2], Cheryl L. Perry[3] and Melissa B. Harrell[2,4]

[1]Department of Biostatistics and Data Science, the University of Texas Health Science Center at Houston (UTHealth), School of Public Health, Austin Campus, Austin, TX 78701, USA

[2]Michael & Susan Dell Center for Healthy Living, the University of Texas Health Science Center at Houston (UTHealth), School of Public Health, Austin Campus, Austin, TX 78701, USA

[3]Department of Health Promotion and Behavioral Sciences at the University of Texas Health Science Center at Houston (UTHealth), School of Public Health, Austin Campus, Austin, TX 78701, USA

[4]Department of Epidemiology, Human Genetics and Environmental Sciences, The University of Texas Health Science Center at Houston (UTHealth) School of Public Health in Austin, Austin, TX 78701, USA

Abstract

Context: There is a lack of research that prospectively estimates the age of initiation of electronic cigarette use in U.S. youth. Younger ages of initiation of tobacco product use are associated with greater exposure to nicotine, and recently e-cigarette use has been associated with subsequent cigarette initiation. This study sought to estimate the distribution of the age of first reporting of e-cigarette use outcomes among youth never e-cigarette users overall, by sex and by race/ethnicity, prospectively.

Methods: Secondary analysis of the Population Assessment of Tobacco and Health (PATH) youth dataset (ages 12-17) across waves 1 (2013-2014), 2 (2014-2015), 3 (2015-2016), and 4 (2016-2017) were conducted. Four outcomes are presented, age of first report of: (i) susceptibility to use, (ii) ever, (iii) past 30-day use, and (iv) "fairly regular" e-cigarette use. Each outcome was prospectively estimated using participant age when they entered the study and the number of weeks between the last report of never use and the first report of each outcome across waves. Weighted survival analyses for interval censoring accounting for the complex survey design were implemented.

Results: Among youth non-susceptible to e-cigarettes, 50.2% became susceptible to e-cigarette use by age 18. There were no statistically significant differences in the age of first report of susceptibility to e-cigarette use by sex or by race/ethnicity in this nationally representative sample of U.S. youth. Among never users, 41.7%, 23.5% and 10.3% initiated ever, past 30-day and "fairly regular" e-cigarette use by the age of 18, respectively. Less than 10% initiated ever e-cigarette use between the ages of 18 and 21. Boys had a higher risk of first reporting ever, past 30-day and "fairly regular" e-cigarette use at earlier ages than girls. Non-Hispanic Blacks and Other racial/ethnic groups were less likely than Non-Hispanic Whites to initiate ever e-cigarette use at earlier ages, and there was no difference between Non-Hispanic Whites and Hispanics. Hispanic, Non-Hispanic Black and Other racial/ethnic youth were less likely to first report past 30-day use and "fairly regular" e-cigarette use at earlier ages than Non-Hispanic White youth.

Conclusion: This paper provides information on specific ages of the first report of e-cigarette use behaviors by sex and by race/ethnicity that can be used to tailor culturally e-cigarette interventions on specific windows of opportunity before youth begin using e-cigarettes or escalating their use.

Keywords: Cohort • Interval censoring • Survival analysis • Hazard function • Nationally representative

Introduction

Accurately identifying the age of initiation of tobacco products has been central to achieving reductions in tobacco use nationwide. In the early 1990's, the first Surgeon General's Report on tobacco use specific to young people provided evidence that 88% of adult smokers began smoking cigarettes before the age of 18 [1]. Among adult cigarette smokers at the time, the average age when smokers first recalled trying a cigarette was 14.5 years, and the average age when they recalled becoming daily smokers was 17.7 years [1]. These findings were some of the most important and widely cited from this report. Notably, they were also well-utilized, inspiring advocates, policy makers, and program developers to focus intervention efforts on adolescents, given this new evidence about important patterns of cigarette smoking behaviors that could continue into adulthood. A wide variety of successful approaches to prevention ensued: effective school-based programs [2]; large-scale mass media campaigns (e.g., The "Truth" campaign [3]); and strong enforcement of laws restricting youth access to tobacco, such as the Synar Amendment [4]. Subsequently, the prevalence of cigarette smoking among adolescents peaked in the late 1990's and has fallen steadily ever since [5,6].

Unfortunately, almost thirty years later, the nature of the tobacco epidemic has changed in ways that are compromising these important strides in tobacco control. In 2014, e-cigarette use began to eclipse cigarette smoking, becoming the most widely utilized tobacco product among adolescents nationwide, even through 2019 [7-11]. Promoted by the industry as a potentially successful tool to support cessation of

***Address for Correspondence:** Adriana Pérez, Department of Biostatistics and Data Science, the University of Texas Health Science Center at Houston (UTHealth), School of Public Health, Austin Campus, Austin, TX 78701, USA, Tel: 512-391-2524; E-mail: adriana.perez@uth.tmc.edu*

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cigarette smoking among adults, e-cigarettes have now reversed declines in youth tobacco use overall from previous decades [9]. Past 30-day use of e-cigarettes continued to rise from 20.8% in 2018 to 27.5% in 2019 among high school students and from 4.9% in 2018 to 10.5% in 2019 among middle school students [8,9]. This exponential rise in e-cigarette use reinforce the need for immediate intervention. The development of effective e-cigarette prevention strategies for youth could benefit from more nuanced evidence regarding the age at which specific e-cigarette behaviors become relevant to youth. Behaviors such as susceptibility to e-cigarette use, ever use, and past 30-day use, and "fairly regular" use have all been linked to the onset and progression of cigarette smoking among young people [12,13]. Curbing progression in e-cigarette use behaviors may be important to curtailing not only e-cigarette use among youth, but also tobacco use overall.

Survival analysis is a unique tool that can be used to describe not only the age of initiation, but also the cumulative risk of initiation by age. In doing so, peaks in the onset and progression of these behaviors at certain ages are identified. To date, there has only been one study estimating the hazard function of the risk of ever e-cigarette initiation by age, in 2014 [14].

Although this study addressed both ever and past 30-day e-cigarette use, it estimated the age of initiation of these behaviors by asking participants how old they were when they first used an e-cigarette, which is prone to recall bias [15,16]. Here, we provide a prospective, secondary analysis of the Population Assessment of Tobacco and Health (PATH) study [17] instead. In this study, a nationally-representative sample of youth (aged 12-17 in 2013-2014) were surveyed and followed-up across time (though 2016-2017). Because it is important to understand the full spectrum of e-cigarette use behaviors, the current study examined age of initiation (i.e., first report) of susceptibility to e-cigarette use, ever use, past 30-day use, and "fairly regular" e-cigarette use among never users of e-cigarettes at their first wave of participation in PATH. Although the measure of "fairly regular" use has been examined among adults [18], to the best of our knowledge, this is the first study to examine it among youth. This measure should help identify consistent, committed e-cigarette use [19]. In addition to estimating hazard functions, estimating the cumulative risk of the initiation of these behaviors by age among youth overall, these distributions are also reported by sex and by race/ethnicity.

Methods

Study design and participants

PATH used a four-stage stratified area probability sampling design to obtain a nationally representative sample of U.S. youth and adults in 2013-2014 (wave 1) with measurements conducted annually thereafter (wave 2: 2014-2015, wave 3: 2015-2016, wave 4: 2016-2017). Additional details about sampling methodology are described elsewhere [17]. The target population consisted of the civilian household population of individuals aged 12 and older in all 50 U.S. states; 13,651 youth (aged 12-17) completed wave 1 with a 78.4% response rate [20]. In addition, "shadow youth" (i.e., family members of PATH participants who were 9-11 years old at wave 1) were eligible to participate when they reached 12 years of age at waves 2-3; 2,091 and 2,045 12 year old youth were added as new participants to PATH in waves 2 and 3, respectively [21]. When youth turned 18, they were invited to participate in the adult measurements, instead; 1,915, 1,907, and 1,900 of youth did so from waves 2-4, respectively [21]. The response rates in PATH youth in waves 2-4 were: 87.3%, 83.3% and 79.5%, respectively [21].

This study is a secondary analysis of the youth and adult restricted-use datasets completed on the Inter-university Consortium for Political and Social Research (ICPSR) server where the data are located. Analyses of first report of susceptibility to e-cigarette use were limited to never users who were not susceptible when they entered the study in waves 1-3 (n=9,354; N= 17,637,679). Analyses of first report of ever use, past 30-day use, and "fairly regular" use includes youth never e-cigarette users who entered the PATH study at waves 1-3 (n=16,143; N=30,194,853). Outcomes were tracked longitudinally from waves 2-4. 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.

Measures

Four e-cigarette outcomes are presented, age of first report of: (i) susceptibility to use, (ii) ever use, (iii) past 30-day use, and (iv) "fairly regular" use of e-cigarettes.

Susceptibility to use

In PATH wave 1, the following questions were used to measure susceptibility to e-cigarette use among participants who reported never having used an e-cigarette: (i), "Have you ever been curious about using e-cigarettes?", (ii), "Do you think that you will try an e-cigarette soon?", and (iii) "If one of your best friends were to offer you an e-cigarette, would you use it?". Response options for the first question were "very curious", "somewhat curious", "a little curious", and "not at all curious". Response options for the next two questions were "definitely yes", "probably yes", "probably not" and "definitely not". In PATH waves 2-4, the susceptibility questions asked about an "electronic nicotine product" (Electronic nicotine products include e-cigarettes, vape pens, personal vaporizers and mods, e-cigars, e-pipes, e- hookahs and hookah pens.)" instead. These questions are assumed to measure the same construct. Participants who answered "not at all curious" to the first question and "definitely not" to the next two questions were considered non-susceptible. Participants who had any other combination of answers were considered susceptible to e-cigarette use.

Ever use

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?". Response options were "yes", "no", and "I don't know". Participants who answered "no" to this question at wave 1 were included in the analytic sample. In waves 2-4, PATH, in both the youth and adult data, 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", and "don't know".

Past 30-day use

In waves 2-4, in both the youth and adult surveys, past 30-day 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.

Fairly regular use

In wave 2, in both the youth and adult surveys, "fairly regular" use was measured with the question: "Have you ever used e-cigarettes fairly regularly?". In waves 3 and 4, participants were instead asked: "Have you ever used electronic nicotine products fairly regularly?" These questions were assumed to measure the same construct across waves. Response options for both questions included "yes", "no", and "don't know".

Age of initiation

Age of first reporting of each e-cigarette use outcome was estimated by adding participants' age at their first PATH wave of participation (waves 1-3) to the number of weeks between relevant subsequent waves (waves 2-4) based on when the outcome was first reported for those who become users or the last report of never/non-use among those who did not report the behavior. PATH uses a derived variable for participant age at each wave, in years; age of birth is not included in the restricted-use data. In addition, PATH uses another derived variable to represent the number of weeks between waves that youth participate in. Participant age was converted from years to weeks, then added to this second variable to give us a more

precise estimate of participant age, rather than using age in years at the wave that the participant reported the outcome. Then, age was converted from age in weeks back to age in years on a continuous scale, to provide a more precise measure of age.

Sex and race/ethnicity

Answers to a question about participant sex classified participants as either boys or girls. PATH imputed sex, race and Hispanic ethnicity at wave 1 but was not imputed at waves 2 and 3 [20]. PATH used the following categories to measure participant race: White race alone, Black race alone, Asian race alone, and Other race (including multi-racial). In addition, ethnicity categorized participants as either Hispanic or Non-Hispanic. Answers to race and ethnicity questions were combined to create race/ethnicity categories that are comparable to those in prior Surgeon General's reports [5,22] and include: Non-Hispanic White, Hispanic, Non-Hispanic Black, Non-Hispanic Other (Non-Hispanic Asian, multi-race, and other races).

Statistical analysis and data management

All statistical analyses incorporated the use of sampling weights and 100 balance repeated replicate (BRR) weights to account for PATH's complex survey design with Fay's adjustment set to 0.3 to increase estimate stability. Sampling weights were used according to each participants' first wave of entry into PATH. Statistical analyses were completed in SAS version 9.4-TSlevel1M6. Weighted frequencies and percentages are reported for categorical variables and weighted means and standard errors are reported for continuous variables. The distributions of the age of initiation with respect to the four e-cigarette use outcomes were estimated using time-to-event (survival) analyses. Weighted nonparametric survival analyses for interval-censored data were implemented because the exact dates for each of these outcomes [23-27] were not measured in PATH. In waves 2-4, a lower and upper age bound for each outcome was calculated. For all participants, the lower age bound contained the age at the last wave where they reported non-use (or non-susceptibility) of e-cigarettes. For participants who become users, the upper age bound reflects the age between the last wave that they reported non-use and the first wave that they report use (or susceptibility).

The upper age bound for never users (or non-susceptible) was considered censored. We developed macros to estimate the overall distribution of the age of initiation for each outcome incorporating the use of the 100 replicate weights. The hazard function for each outcome was estimated overall and stratified by sex and by race/ethnicity, resulting in seven interval-censored hazard functions per outcome using the Turnbull non-parametric estimator [28]: (i) overall, (ii) boys, (iii) girls, (iv) Non-Hispanic White, (v) Hispanic, (vi) Non-Hispanic Black, and (vii) Non-Hispanic Other. These hazard functions showing the full distribution of ages calculated within a week's precision are displayed in figures. Differences by sex and by race/ethnicity were explored by fitting weighted Cox proportional hazards regression models to interval-censored data with a piecewise constant function as the baseline hazard function. Hazard ratios (HR) and 95% confidence intervals (CI) are reported. A type I error level of 0.05 was used to determine statistical significance for all two-sided statistical tests. If there was not enough sample size for certain ages to produce stable estimates for the age of first reporting of e-cigarette outcomes the results are not shown for that age. For susceptibility to e-cigarette use, these analyses required approximately 30 hours to complete using the ICPSR server, with an additional 30 hours each for sex and 30 hours each for the race/ethnicity analyses. The number of hours was similar for the other outcomes (ever use, past 30-day use, and "fairly regular" use) resulting in a total run time of approximately 360 hours for all analyses to complete.

Results

Table 1 presents demographic characteristics of PATH youth (aged 12-17) who were non-susceptible or never users of e-cigarette use at their first wave of study participation (waves 1-3, 2013-2016). There were 9,354 (N= 17,637,679) youth who were non-susceptible never e-cigarette users when they first entered the study and were included in the analysis of susceptibility to e-cigarette use. Among these participants, their mean age at wave of entry was 13.7 (SE= 0.02); 49.2% were girls, 56.5% were Non-Hispanic White, 20.4% Hispanic, 13.5% Non-Hispanic Black, and 9.6% Non-Hispanic Other. Most of these participants entered the study at wave 1 (72.3%). Overall, 16,143 (N= 30,194,853) youth never e-cigarette users were included in the analysis of the first report of ever use, past 30-day use, and "fairly regular" e-cigarette use. Among these participants, their mean age at wave of entry was 13.8 (SE= 0.01); 49.5% were girls, 52.8% were Non-Hispanic White, 23.3% Hispanic, 14.0% Non-Hispanic Black, and 9.9% Non-Hispanic Other. Most of these youth entered the study at wave 1 (73.3%).

Table 2 shows the distribution of the estimated age of initiation for each of the four outcomes overall, reported as cumulative probability written as percentages (i.e., cumulative incidence) and the full distribution of ages within a week's precision are displayed in Figure 1. By the age of 21 years, these models estimated that 65.6% as susceptible to e-cigarette use and

Table 1. Demographic characteristics of non-susceptible or never e-cigarette users in PATH USA youth (aged 12-17).

Variables		Non-susceptible to e-cigarette use	Never e-cigarette users
		n=9,354; N=17,637,679	n=16,143; N=30,194,853
		N (Weighted%)	N (Weighted%)
Wave of entry into study	Wave 1 (2013-2014)	12,760,024 (72.3)	22132919 (73.3)
	Wave 2 (2014-2015)	2,500,640 (14.2)	3964885 (13.1)
	Wave 3 (2015-2016)	2,377,015 (13.5)	4097049 (13.6)
Age at entry into study	Weighted mean (SE)	13.7 (0.02)	13.8 (0.01)
Sex	Male	8,952,585 (50.8)	15242424 (50.5)
	Female	8,678,900 (49.2)	14939879 (49.5)
	Missing	6,194	12,550
Race/Ethnicity	Non-Hispanic White	9,835,725 (56.5)	15737490 (52.8)
	Hispanic	3,551,427 (20.4)	6941729 (23.4)
	Non-Hispanic Black	2,354,983 (13.5)	4,162,698 (14.0)
	Non-Hispanic Other*	180,473 (9.6)	2,949,890 (9.9)
	Missing	215,071	403,046

Non-Hispanic Other includes asian, multi-race, etc.

¥ PATH restricted file received disclosure to publish: January 28, 2020 and March 25, 2020.United States Department of Health and HumanServices. 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 [UnitedStates] Restricted-UseFiles. ICPSR36231-v13.AnnArbor,MI: Inter-university Consortium for Political and Social Research [distributor], November 5, 2019. https://doi.org/10.3886/ICPSR36231.v23

Table 2. Estimated hazard function* (95% confidence intervals)a of the age of initiation of e-cigarette outcomes for non-susceptible or never e-cigarette users in PATH USA youth (aged 12-17).

Age	Susceptibility to use	Ever use	Past 30-day use	Fairly regular use
13	11.8% (11.0-12.6)	3.0 (1.7-4.3)	0.8 (0.0-2.0)	0.45% (0.13-0.77)
14	18.9% (18.0-19.6)	6.6 (6.1-7.1)	2.3 (1.2-3.5)	1.0% (0.54-1.5)
15	25.8% (24.7-26.9)	11.7 (11.0-12.4)	4.4 (3.9-4.9)	2.2% (1.5-2.9)
16	33.7% (32.5-35.0)	18.6 (17.4-19.9)	7.4 (6.6-8.2)	3.8% (3.3-4.2)
17	43.8% (40.6-47.0)	30.4 (27.6-31.2)	13.1 (10.2-15.9)	6.6% (5.9-7.4)
18	50.2% (48.4-52.0)	41.7 (37.4-45.9)	23.5 (22.0-25.1)	10.3% (9.2-11.4)
19	53.9% (48.7-59.0)	43.9 (41.1-46.6)	23.5 (21.8-25.3)	10.8% (9.6-12.0)
20	57.1% (54.9-59.3)	47.5 (44.7-50.4)	28.4 (26.0-30.7)	12.4% (10.9-13.9)
21	65.6% (50.6-80.5)	51 (42.8-59.1)	N/A	N/A

*Hazard function is reported as weighted cumulative percentages (i.e., cumulative incidence) a: 95%CI: Turnbull 95% confidence interval

¥ PATH restricted file received disclosure to publish: January 28, 2020 and April 08, 2020.United States Department of Health and HumanServices. 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 [UnitedStates] Restricted-UseFiles. ICPSR36231-v13.AnnArbor,MI: Inter-university Consortium for Political and Social Research [distributor], November 5, 2019. https://doi.org/10.3886/ICPSR36231.v23

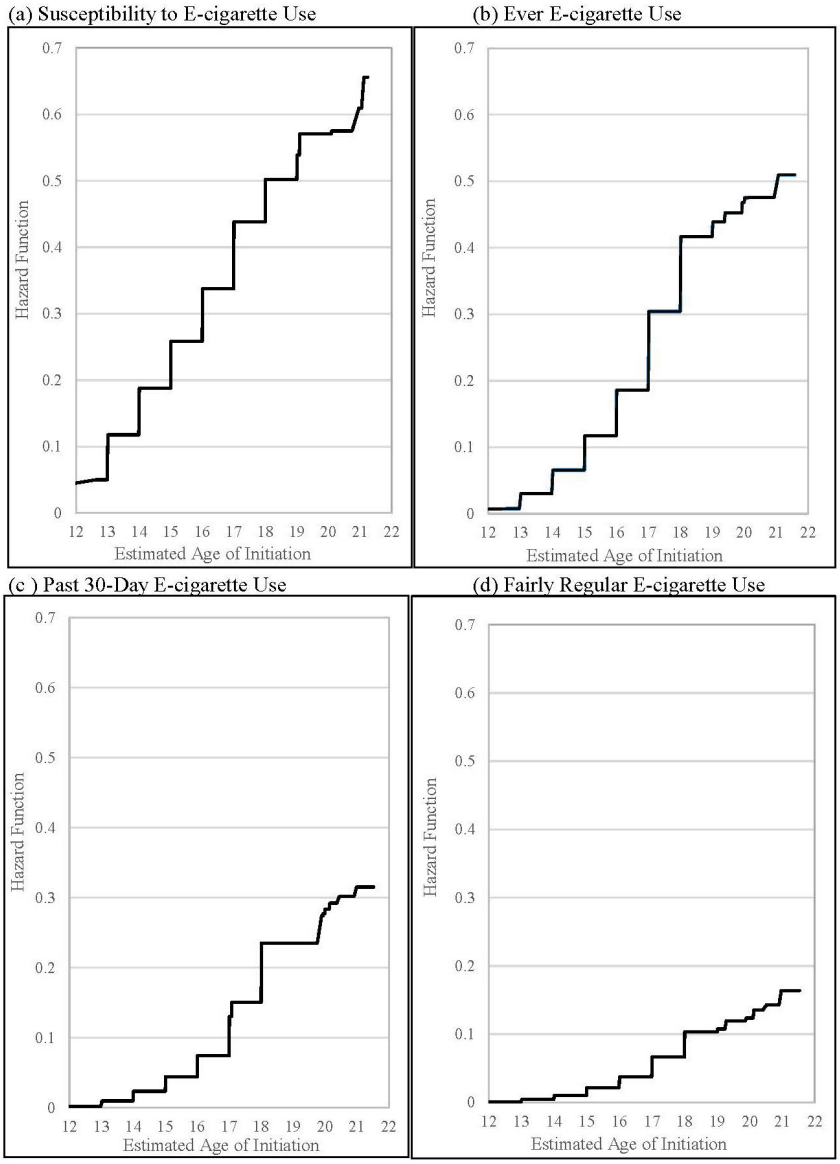

Figure 1. Estimated hazard function for age of intiation by e-cigarette use type.

51% as ever e-cigarette use. There was not enough initiation at age 21 to provide stable estimates for 21 years of age for past 30-day use and fairly regular e-cigarette use, but by age 20, 28.4%, and 12.4% reported these outcomes, respectively. The most notable increases in first report of susceptibility to e-cigarette use occurred at earlier ages, between 13 and 14 years and between 16 and 17 years. The most notable increases in first report of ever e-cigarette use occurred between ages 16 and 17, and 17 and 18. The most notable increase in first report of past 30-day e-cigarette use

occurs between ages 17 and 18. The most notable increase in first reports of "fairly regular" e-cigarette use occurred between 17 and 18 years.

Table 3 presents results from the interval-censored Cox proportional hazards models comparing the age of initiation of each e-cigarette outcome by sex. The interval-censored Cox proportional hazards models for first report of susceptibility to e-cigarette use revealed that there were no significant differences in the age of initiation by sex. Our analysis revealed that the risk of initiating ever e-cigarette use at earlier ages was 10% higher in boys compared to girls (HR: 1.10; 95%CI: 1.01-1.19). The risk of first reporting past 30-day e-cigarette use at earlier ages was 20% higher for boys compared to girls (HR: 1.20; 95%CI: 1.08-1.33). The risk of first reporting "fairly regular" e-cigarette use at earlier ages was 58% higher for boys compared to girls (HR: 1.58; 95%CI: 1.34-1.87). Figure 2 displays the full distribution of the hazard function of ever e-cigarette use, past 30-day e-cigarette use, and fairly regular e-cigarette use stratified by sex. Table 4 shows the distribution of the estimated age of initiation for each of the outcomes that were found to exhibit significant differences by sex and are reported as cumulative percentages (i.e., cumulative incidence). Findings show that the largest increase in initiation occurred between 16 and 17 years of age for both boys (12%= 31.0-18.9%) and girls (11.2%= 29.5-18.3%), respectively). Similarly, the biggest increase in first reporting past 30-day e-cigarette use occurred between 17 and 18 years for both boys (12.3%= 25.6-13.3%) and girls (8.5%= 21.3-12.8%), respectively. The biggest increase in first reporting of "fairly regular" e-cigarette use occurred between 20 and 21 years of age for boys (6.5%), but there was not enough sample size at that age for girls so no estimates are provided, but from 13-20 years girls only exhibited minor increases in first reporting fairly regular e-cigarette use. Table 4 shows the hazard function stratified by sex and the full distribution of ages within a week's precision are displayed in Figure 2.

We also found differences in the distribution of the age of first reporting across ever, past 30-day and "fairly regular" e-cigarette use by race/ethnicity (Table 3). Our analysis revealed that the difference in the age of initiation of ever e-cigarette use between Hispanic and Non-Hispanic White youth was not statistically different. The risk of initiating ever e-cigarette use at earlier ages was 34% (HR: 0.66; 95%CI: 0.57-0.75) lower for non-Hispanic Black compared to non-Hispanic White youth, and 20% (HR: 0.80; 95%CI: 0.68-0.94) lower in Non-Hispanic other compared to Non-Hispanic White. The risk of first reporting past 30-day e-cigarette use at earlier ages was 53% (HR: 0.47; 95%CI: 0.38-0.59) lower for non-Hispanic Black, 19% (HR= 0.81; 95%CI: 0.68-0.96) lower in Non-Hispanic other, and 28% (HR: 0.72; 95%CI= 0.62-0.84) lower in Hispanic compared to Non-Hispanic White youth. Overall, the risk of first reporting "fairly regular" e-cigarette use at earlier ages was 62% (HR= 0.38; 95%CI= 0.27-0.54) lower in Non-Hispanic Black, 28% (HR= 0.72; 95%CI= 0.56-0.93) lower in Non-Hispanic other, and 40% (HR= 0.60; 95%CI= 0.49-0.75) lower in Hispanic youth compared to Non-Hispanic White. Table 4 shows the distribution of the estimated age of initiation for each of the outcomes that were found to exhibit significant differences by race/ethnicity and Figure 3 displays their corresponding full distribution of the hazard function of ever e-cigarette use, past 30-day e-cigarette use, and fairly regular e-cigarette use by race/ethnicity. We found that 13.4% (34%-20.6%) of Non-Hispanic White and 17.8% (30%-12.1%) of Hispanic youth had the highest increase in initiation of ever

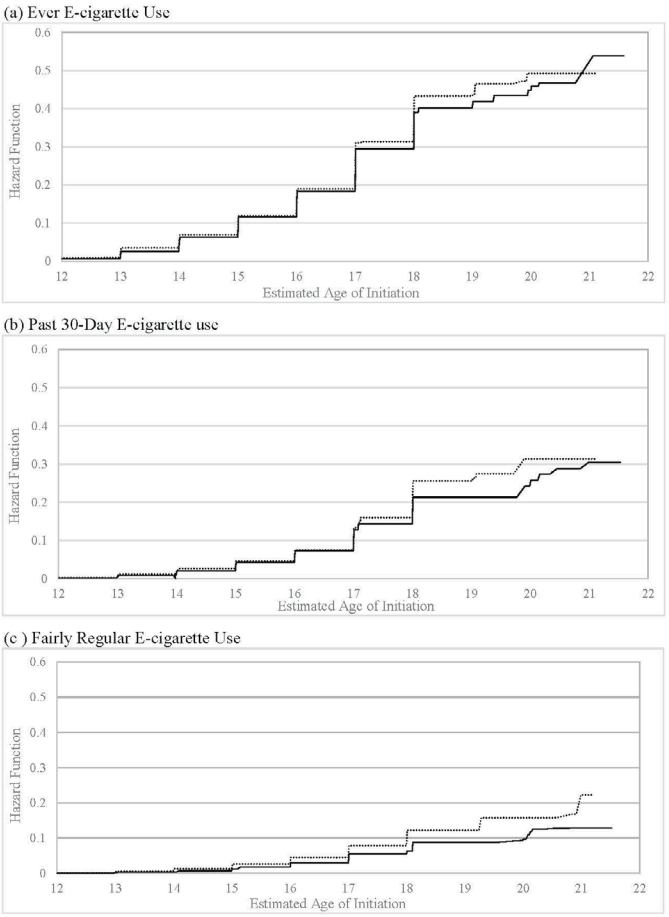

Figure 2. Estimated hazard function for age of intiation by e-cigarette use, stratified by sex: boys are the dotted line and girls are the black line.

Table 3. Hazard function (95% confidence interval) for each e-cigarette initiation outcome by sex and by race/ethnicity for non-susceptible or never e-cigarette users in PATH USA youth (aged 12-17).

Variables	Susceptibility to use	Ever use	Past 30-day use	Fairly regular use
Sex				
Female	1.00	1.00	1.00	1.00
Male	0.98 (0.90-1.06)	**1.10 (1.01, 1.19)**	**1.20 (1.08, 1.33)**	**1.58 (1.34, 1.87)**
Race/Ethnicity				
Non-Hispanic White	1.00	1.00	1.00	1.00
Hispanic	1.09 (1.00-1.19)	0.86 (0.68-1.09)	0.72 (0.62-0.84)	0.60 (0.49-0.75)
Non-Hispanic Black	0.98 (0.87-1.11)	0.66 (0.57-0.75)	0.47 (0.38-0.59)	0.38 (0.27-0.54)
Non-Hispanic Other*	1.07 (0.92 (1.23)	0.80 (0.68-0.94)	0.81 (0.68-0.96)	0.72 (0.56-0.93)

*Non-Hispanic Other includes asian, multi-race, etc.

¥PATH restricted file received disclosure to publish: January 28, 2020. United States Department of Health and HumanServices. 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 [UnitedStates] Restricted-UseFiles. ICPSR36231-v13.AnnArbor,MI: Inter-university Consortium for Political and Social Research [distributor], November 5, 2019. https://doi.org/10.3886/ICPSR36231.v23

Table 4. Estimated hazard function* (95% confidence interval) of age of initiation of e-cigarette outcomes for never e-cigarette user PATH USA youth (aged 12-17) by sex and by race/ethnicity.

Age	Sex		Race/Ethnicity			
	Male	Female	Non-Hispanic White	Hispanic	Non-Hispanic Black	Non-Hispanic Other**
Initiation of ever e-cigarette use						
13	3.5% (2.2-4.8)	2.6% (0.0-5.4)	2.4% (0.0-5.0)	3.1% (2.2-4.5)	2% (0.60-3.3)	2.9% (0.0-5.9)
14	6.9% (4.0-9.7)	6.3% (5.4-7.1)	7% (5.3-8.7)	7.1% (4.6-9.5)	4.2% (0.0-8.4)	5.8% (4.6-7.0)
15	11.8% (11.0-12.7)	11.6% (10.5-12.7)	12.8% (11.8-13.8)	12.1% (10.6-13.6)	7.2% (1.0-13.5)	9.8% (4.8-14.8)
16	18.9% (15.7-22.2)	18.3% (16.7-19.9)	20.6% (18.5-22.7)	12.1% (7.6-17.0)	12.6% (8.6-16.7)	17.5% (11.9-23.3)
17	31.0% (25.8-36.2)	29.5% (25.3-33.6)	34% (29.2-38.8)	30% (23.3-36.8)	20.2% (13.6-26.8)	17.8% (12.5-23.1)
18	43.3% (35.8-50.8)	39.0% (33.6-44.4)	43.5% (39.8-47.3)	36.5% (26.5-46.6)	27.1% (14.0-40.2)	30.2% (19.8-40.7)
19	43.8% (39.7-47.9)	41.9% (38.6-45.1)	47.6% (42.0-53.1)	43.1% (40.0-46.6)	35.8% (32.0-40.0)	39% (33.5-44.5)
20	49.3% (46.1-52.4)	46.0% (42.3-49.7)	48.4% (45.0-51.8)	48% (43.4-52.7)	45.8% (37.0-54.5)	46.9% (39.0-54.9)
21	N/A	53.8% (39.2-68.4)	N/A	58.7% (41.2-76.1)	N/A	N/A
Initiation of past 30-day e-cigarette use						
13	1.1% (0.0-2.4)	0.8% (0.37-1.3)	1.1% (0.76-1.4)	1.1% (0.5-1.6)	0.5% (0.1-0.8)	0.9% (0.0-1.7)
14	2% (0.0-4.2)	2.1% (0.77-3.4)	1.9% (0.0-4.2)	2% (0.6-3.4)	0.8% (0.1-1.6)	2.2% (0.7-3.6)
15	4.6% (3.8-5.4)	4.2% (3.6-4.9)	5.6% (4.7-6.4)	3.6% (2.6-4.6)	1.3% (0.2-2.4)	4.6% (2.2-7.0)
16	7.5% (6.4-8.7)	7.3% (5.6-9.0)	9.4% (8.1-10.7)	5.6% (4.5-6.6)	2.7% (0.2-5.2)	7.8% (5.2-10.3)
17	13.3% (9.4-17.2)	12.8% (8.7-17.0)	16.1% (12.0-20.2)	6.9% (3.9-9.9)	5.3% (1.5-9.0)	12.6% (5.2-20.0)
18	25.6% (22.8-28.4)	21.3% (19.5-23.0)	26.4% (24.1-28.6)	22% (18.0-25.7)	12.7% (5.4-19.9)	21.5% (13.3-30.0)
19	26.3% (22.6-29.9)	21.3% (19.5-23.0)	26.4% (24.2-28.6)	22% (19.2-24.7)	15.6% (12.5-18.7)	22.2% (16.8-27.6)
20	31.4% (28.5-34.2)	25.8% (22.2-29.3)	30.4% (26.7-34.1)	27.3% (22.7-31.9)	22% (16.1-27.8)	31.3% (24.7-37.9)
Initiation of fairly regular e-cigarette use						
13	0.6% (0.2-0.9)	0.3% (0.0-0.8)	0.5% (0.0-0.9)	0.4% (0.0-0.9)	0.1% (0.0-0.2)	0.6% (0.2-1.0)
14	1.4% (0.7-2.1)	0.4% (0.0-0.8)	1.1% (0.6-1.6)	0.8% (0.0-1.6)	0.5% (0.1-0.8)	1.5% (0.0-3.0)
15	2.6% (1.5-3.8)	1.2% (0.4-2.1)	2.6% (1.7-3.4)	1.9% (1.1-2.8)	1.2% (0.0-2.5)	2.2% (0.9-3.4)
16	4.5% (3.8-5.2)	3.0% (2.5-3.5)	4.6% (3.9-5.4)	3.2% (1.0-5.4)	1.4% (0.7-2.1)	4.2% (2.6-5.8)
17	7.9% (6.4-9.4)	5.5% (2.9-8.1)	8.4% (5.6-11.1)	5.1% (3.9-6.2)	3.5% (1.7-5.2)	5.4% (3.5-7.4)
18	12.2% (10.6-13.9)	6.3% (4.1-8.5)	13.1% (11.5-14.7)	7.7% (4.3-11.1)	5.2% (1.4-9.0)	10.6% (7.1-14.0)
19	12.2% (10.6-13.9)	8.9% (7.4-10.2)	13.1% (11.4-15.0)	8.0% (5.8-10.2)	6.8% (4.4-9.1)	10.6% (7.2-14.0)
20	15.8% (13.6-18.0)	9.7% (7.8-11.6)	16.2% (13.7-18.7)	9.6% (7.1-12.1)	8.5% (2.6-14.4)	13.9% (6.3-21.6)
21	22.3% (9.4-35.2)	N/A	N/A	17.5% (1.9-33.0)	N/A	N/A

*Hazards are reported as weighted cumulative percentages (i.e., cumulative incidence).
95%CI: Turnbull 95% confidence interval.
**Non-Hispanic Other includes asian, multi-race, etc.
N/A: there was not enough sample size to produce a stable probability estimate at this age.
¥PATH restricted file received disclosure to publish: January 28, 2020 and April 08, 2020.United States Department of Health and HumanServices. 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 [UnitedStates] Restricted-UseFiles. ICPSR36231-v13.AnnArbor,MI: Inter-university Consortium for Political and Social Research [distributor], November 5, 2019. https://doi.org/10.3886/ICPSR36231.v23

e-cigarette use between ages 16 and 17 years old. Non-Hispanic other had 12.8% (30.2-17.8%) as the highest increase in initiation between ages 17 and 18 years old. Non-Hispanic Black had 10% (45.8-35.8%) as the highest increase in initiation between ages 19 and 20. For past 30-day e-cigarette use, 10.3%(26.4%-16.1%) of Non-Hispanic White, 15.1%(22%-6.9%) of Hispanics, and 7.4%(12.7%-5.3%) of Non-Hispanic Black youth exhibit the highest increase in first reporting between ages 17 and 18 years old, while 9.1%(13.%-22.2%) of Non-Hispanic other youth exhibit the biggest increase between ages 19 and 20. For fairly regular e-cigarette use, 4.7% (13.1-8.4%) of Non-Hispanic White and 5.2% (10.6%-5.4%) of Non-Hispanic other had the highest increase in first reporting between ages 17 and 18, 7.9% of Hispanic youth had the highest increase in first reporting between ages 20 and 21, and Non-Hispanic Black youth had steady increases in initiation (ages 13-20 years old). Table 4 shows the hazard function stratified by race/ethnicity and the full distribution of ages within a week's precision are displayed in Figure 3.

Discussion

This study is the first to provide prospective estimates for the distribution of the ages of initiation (i.e. first report) for susceptibility to e-cigarettes, ever use of e-cigarettes, past 30-day use of e-cigarettes, and "fairly regular" use of e-cigarettes among youth (12-17 years old) in the USA from 2013-2017 who were non-susceptible to e-cigarettes and/or had never used e-cigarettes at their first wave of PATH participation. Age of first reporting of the different e-cigarette use behaviors is an important factor to explore, and we have identified the ages at which youth are most vulnerable to first report these e-cigarette use behaviors. Historically, the first time that individuals use a tobacco product is typically before they turn 18 [29-36]. The information provided about the age of first reporting of four e-cigarette use outcomes is important to tobacco regulatory science, as age defines the legal ability to buy tobacco products. As of December 20, 2019 [37]

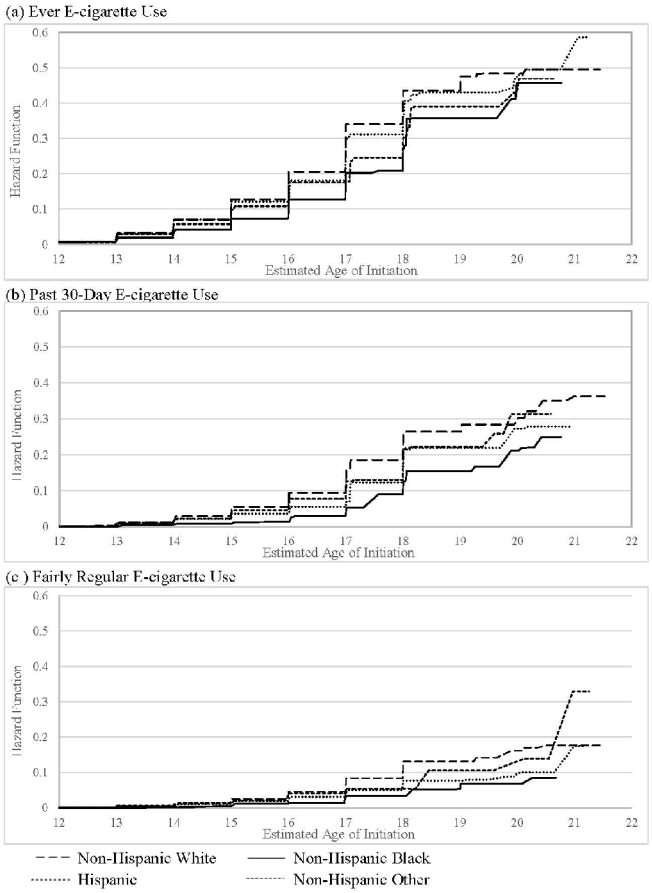

Figure 3. Estimated hazard function for age of intiation by e-cigarette use.

the legal age to purchase tobacco is now 21. Prior to this time, during the period under study here (2013-2017), the legal age to purchase tobacco products was 18. Our estimates of age of initiation presented here serve as a reference point that might be compared in the future with any evaluation of the Tobacco21 law [37], nationwide.

Susceptibility to any tobacco product has been validated to be an indicator of later tobacco product use [38], and measuring susceptibility helps to identify youth who are vulnerable to tobacco products use in a timely manner before they initiate the behavior [38]. A previous longitudinal study of e-cigarette use in middle and high school students found that among never e-cigarette users in 2013, susceptibility to e-cigarette use was an independent predictor of actual e-cigarette initiation 6 months later [39], indicating that susceptibility is an accurate predictor of subsequent e-cigarette use. However, it should be noted that Bold et al. [39] used two similar questions to measure susceptibility instead of the three questions used in PATH [38]. Susceptibility to e-cigarette use is an important factor to explore because among youth (12-17 years old) who have never used e-cigarettes, 38.1% reported susceptibility to e-cigarette use in 2013-2014 [40], while a different research study of middle and high school students from 2018 found that 45.0% reported that they are susceptible to e-cigarette use in 2019 [8]. In our study, we extend these findings by reporting the risk of first reporting susceptibility among participants who were previously non-susceptible by age. Importantly, we found that the risk of first reporting susceptibility to e-cigarette use among participants who were previously non-susceptible and never users of e-cigarettes was 33.7% by age 16, 43.8% by age 17, and 50.2% by age 18. For tobacco regulatory science, the specific risk of becoming susceptible identifies the appropriate window to implement intervention programs to prevent youth from using e-cigarettes. This indicates that waiting an additional year for a prevention campaign that communicates the health risks associated with e-cigarette use, from 16 to 17 years old represents a 10.1% increase in the risk of becoming susceptible to e-cigarette use, and is likely too late to have an impact on those susceptible youth. PATH has previously reported that 27.4% of their 2013-2014 wave 1 youth sample were susceptible to e-cigarette use, and while they found that older adolescents (15-17 years) had increased odds of any tobacco product use compared to younger adolescents (12-14 years) [40], until our study, the age at which non-susceptible youth first reported susceptibility to e-cigarettes remained unclear. Prevention interventions specific to e-cigarette use should clearly begin prior to age 16.

Since e-cigarettes entered the U.S. market in 2007, their popularity has increased exponentially among youth from 2011 to 2019 [7-9]. We reported in a previous analysis of PATH that among youth never users of e-cigarettes (ages 12-17 years old in 2013-2014), 8.6% reported e-cigarette initiation (ever use), and 2.4% reported past 30-day e-cigarette initiation one year later (2014-2015) [41]. Recently in PATH, among 12-17 year old never users of e-cigarettes in 2013-2014, 6.4% reported past 30-day e-cigarette initiation in either 2014-2015 or 2015-2016. Our findings extend this previous work by prospectively obtaining the distribution of the age of initiation for up to 4 years of follow-up rather than incidence after only 1 year. We estimated the risk initiating ever e-cigarette use by age 17 was 30.4% and the risk for youth to first report past 30-day e-cigarette use by age 17 was 13.1%. This indicates that the risk of initiating e-cigarette use at younger ages has increased across time, in just a few years as they have gained popularity.

While some studies have reported the average age of e-cigarette initiation [14,42,43] among youth, these studies all relied on self-reports, which are subject to recall bias [15,16]. In addition, these studies examined age of initiation cross-sectionally among e-cigarette users via the recalled age of initiation [8,9,14,42,43]. Recently, PATH reported cross-sectional analysis of the prevalence of initiation of e-cigarettes per year from 2013-2016 [44]. Our study is the first to circumvent these methodological shortcomings by prospectively estimating age of initiation among never users of e-cigarettes and following their e-cigarette use outcomes longitudinally from 2013 through 2017. A national study of middle and high school students (NYTS) from 2014-2016 [43] found that 22.8% of these students (9-18 years old) reported ever e-cigarette use with a weighted median recalled age of e-cigarette initiation of 14.1 years (weighted Interquartile range (IQR)= 12.6-15.4 years) among those who had ever used e-cigarettes (n= 12,904) [43]. This is a marked difference from our study, which estimated between 2014-2017 that only 6.6% (95%CI= 6.1-7.1) of youth initiated ever e-cigarette use by 14 years. However, a different research study which used data from the 2014 NYTS (11-19 year olds), did a survival analysis for the recalled age of e-cigarette initiation and found that 45.29% initiated ever e-cigarette use by age 18 [14]. This is similar to our finding of 41.7% (95%CI: 37.4- 45.9) of e-cigarette initiation by 18 years of age. This difference in findings could be explained by the fact that survival analysis takes into account the age of the non-users, and we believe that survival analysis is a more accurate way to measure age of initiation as age is part of the outcome in combination with initiation.

It is important to note that cross-sectional analyses of NYTS data from 2014-2018 which analyzed 16 and 17 year olds at each year of data collection only, found that the recalled age of e-cigarette initiation has changed, with 8.8% reporting e-cigarette initiation at 14 years or younger in 2014 and 28.6% reporting e-cigarette initiation at 14 years or younger in 2018 [42]. Thus, the reporting of different ages of initiation may reflect differences in e-cigarette availability and popularity as the years progress. Future research with subsequent waves of PATH data is needed in order to compare these results.

Using "past 30-day" e-cigarette use as a measure for "current" e-cigarette use has been criticized because it may not accurately capture habitual e-cigarette users [45-47], however, this measure was included in the current study for comparison purposes to previous Surgeon General's Reports [5,48,49]. Given that we prospectively examined the age of initiation of the first report of past 30-day use, as well as first report of "fairly regular" use among youth who had never used e-cigarettes, the nature of our study has made it impossible to find other studies to compare to, as no one has previously studied the age of first reporting of these outcomes prospectively

among youth to determine when these behaviors emerge. Importantly, Sharapova et al. [43] found that recalling initiating ever e-cigarette use at age 13 or younger was significantly associated with daily use of e-cigarettes in the past 30-days after one year of follow-up. This indicates that age is an important factor to consider, and delaying e-cigarette use to later ages could delay the onset of nicotine dependence and more harmful e-cigarette use behaviors [43]. While some studies have been moving towards e-cigarette use frequency as a stricter timeframe for initiation [44,47], we included a subjective measure of "fairly regular" e-cigarette use in the hope to capture youth who consider themselves habitual users.

We found that boys have a higher risk of first reporting ever, past 30-day and "fairly regular" e-cigarette use at earlier ages than girls, but there was no difference in the age of first reporting of susceptibility to e-cigarette use. A different study on susceptibility using the 2019 NYTS found that there was no statistically significant difference in susceptibility to e-cigarette use between girls and boys [8], which is similar to the findings in our study. However, it should be noted that this study used four similar questions to measure susceptibility instead of the three questions used in PATH. Similar to our study, the findings from PATH wave 1 indicated that there was not a statistically significant difference between boys and girls in susceptibility to any tobacco product use, including e-cigarettes [40]. Future research should resolve these discrepancies in measures of susceptibility, so that more accurate comparisons can be made between studies, informing appropriate intervention development.

While, the 2014 NYTS study indicated that boys have higher risk of initiating ever e-cigarette use earlier than girls, neither the NYTS 2019 study [8] nor the NYTS data from 2014-2016 [43] observed statistically significant differences in the initiation or the recalled age of e-cigarette initiation between boys and girls, respectively. Moreover, PATH youth (12-17 years old) never users of e-cigarettes in 2013-2014 did not observe statistically significance differences between boys and girls in initiating past-30 day e-cigarette use after one year of follow-up [50]. We found that boys have higher risk of initiating ever, past 30-day use and "fairly regular" e-cigarette use at earlier ages than girls. Moreover, both groups followed the same pattern of initiation with initiation peaks occurring between 16 and 17 years and 17 and 18 years for ever e-cigarette use and between 17 and 18 years for past 30-day e-cigarette use. Boys exhibited the highest increase in "fairly regular" e-cigarette use at 21 years, with girls exhibiting only modest increases in "fairly regular" e-cigarette use from 13 to 20 years of age. The earlier age of e-cigarette initiation among boys in our study and the 2014 NYTS study [14] may reflect the greater sensitivity of survival analysis in estimating the full distribution of the age of initiation because age is part of the outcome in combination with e-cigarette initiation, rather than examining e-cigarette initiation alone.

In terms of race/ethnicity, while previous research has established clear patterns of differences in initiation of cigarettes, cigars, and/or hookah use between racial/ethnic groups, it remains unclear how these patterns extend to use e-cigarette use. We found that Non-Hispanic other and Non-Hispanic Black youth have lower risk of initiating ever and past 30-day e-cigarette use at earlier ages compared to Non-Hispanic White youth, but there was no difference between Hispanic and Non-Hispanic White. Our results are consistent with what PATH found in 2013-2014 [50] as well as the NYTS 2019 study [8], although they used slightly different race/ethnicity categories, indicating that the patterns of e-cigarette initiation across these groups has not changed much in the last few years. This is different from the NYTS 2014 study [14] which found that there were statistically significant differences in the age of e-cigarette initiation between Non-Hispanic White, Hispanic, and multi-racial youth versus Non-Hispanic Black and Asian. In addition, our pattern of results is different from the NYTS 2014-2016 study [43], which found that there were statistically significant differences in the recalled age of initiation between Hispanic and Non-Hispanic Black versus Non-Hispanic White youth, with all of them initiating e-cigarettes around 14 years of age. The advantage of our study is that we report the proportion of first reporting of past 30-day e-cigarette use by race/ethnicity across different ages and within one week of precision.

Taken together, the current study adds to the body of tobacco literature by providing prospective estimates for the age of first reporting initiation of multiple e-cigarette behaviors among youth across 4 years of follow-up, providing these estimates stratified by sex and by race/ethnicity. Estimating the age of initiation of first reporting of each one of these e-cigarette use behaviors, or stages in use, is important as researchers can use this information to develop intervention strategies and communication campaigns tailored to each behavior. These proportions of initiation by age and race/ethnicity can be used by policy makers to tailor interventions that target specific subpopulations at the appropriate age before the initiation of susceptibility, ever use, past 30-day use or fairly regular use of e-cigarettes are exhibited. It is important to understand the full distribution of the age of initiation as it provides the window of opportunity for intervention based on the age at which patterns of e-cigarette use change over time and are culturally specific [51].

Previous research has identified many strategies for reducing e-cigarette initiation, which include increasing the price of e-cigarettes, protecting youth from exposure to secondhand e-cigarette aerosol, sustaining media campaigns warning about the health risks of using e-cigarettes that contain nicotine, restricting youth access to e-cigarettes, reducing the amount of nicotine available in e-cigarettes [42,52], prohibiting the sales of flavored e-cigarettes [42,52], educating parents and teachers about the different types of e-cigarette devices used by youth, training them on how to positively influence youth with tobacco/e-cigarette free environments, communicating to youth about nicotine harm and addiction from e-cigarettes, adopting specific e-cigarette-free school campus policies, requesting pediatric healthcare providers to screen youth for e-cigarette use and help those who want to quit [8]. What has previously been missing from intervention strategies is the age at which these campaigns would be the most effective to implement to prevent youth from becoming susceptible to e-cigarette and engaging in harmful e-cigarette use behaviors, such as past 30-day and fairly regular e-cigarette use.

Preventing youth from initiating e-cigarettes at earlier ages will be essential to protecting public health. There is considerable evidence that earlier ages of e-cigarette initiation are associated with greater nicotine dependence and greater exposure to nicotine [53-55], which can result in adverse health outcomes, including altering brain development [5] among youth and novel respiratory illnesses [42]. Importantly, previous research has established that nicotine-dependent youth are less likely to want to quit using e-cigarettes [56], and youth are uniquely vulnerable to developing nicotine addiction, even at low levels of nicotine use [52]. Finally, a 2017 meta-analysis found that e-cigarette use was associated with greater risk for subsequent cigarette initiation and past 30-day cigarette use [57-59], and cigarettes are well known to result in adverse health outcomes, especially the earlier a person starts using them.

Strengths: Conducting secondary data analyses with the PATH Study that has already collected data for a nationally representative longitudinal cohort provides strong evidence that aligns with the purposes and interests of tobacco regulatory science concerning e-cigarettes. Estimating the age of initiation of four e-cigarette use outcomes using time-to-event analyses which accounts for the age of the non-users is more efficient than simply reporting prevalence or incidence [60], including estimates by sex and race/ethnicity groups which have never been reported before. The contribution of a more precise calculation of the age of initiation for the four outcomes using prospective not recalled self-report data, and identifying which subgroups are most at risk is unique to the tobacco literature.

Limitations: We had to estimate the age of initiation with interval censoring using BRR and non-parametric Turnbull estimators, as participants were not asked to report the exact date of initiation of each e-cigarette use outcome. Still, we depend on self-reported data for e-cigarette use outcomes from these youth. However, these limitations were overcome by the way age of initiation was derived, and upheld the privacy protections for participants. The survival analyses implemented in this report each took 30 hours to run due to the 100 replicate weights, which is a time-consuming process and affects the rapidity of the publication process.

Conclusion

Our study suggests e-cigarette preventive interventions should begin before the age of 18 and are especially relevant for youth between the ages of 16 and 17. Specific interventions focused on boys, non-Hispanic White, and Hispanic youth are needed. As a previous study noted that the age of e-cigarette initiation has been decreasing as they become more popular to use among youth [42], we feel that the targeted information about age of first reporting across different e-cigarette use outcomes will be important for researchers, intervention strategists, and policy makers to use in the future. Additionally, the information in this report can serve as a reference point for age of e-cigarette initiation in the years before the federal legal age to purchase tobacco products changed to 21 in the US. It is believed that raising the minimum of age of tobacco sales will prevent an earlier age of initiation for e-cigarette use. Future analyses building upon the ones presented here, could help researchers determine the impact of this new law on youth e-cigarette use in the future.

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