

ORIGINAL RESEARCH

Childhood/Adolescent Smoking and Adult Smoking and Cessation: The International Childhood Cardiovascular Cohort (i3C) Consortium

Tian Hu, MD, PhD; Seana L. Gall, PhD; Rachel Widome, PhD; Lydia A. Bazzano, MD, PhD; Trudy L. Burns, PhD; Stephen R. Daniels, MD, PhD; Terence Dwyer, MD; Johanna Ikonen, MS; Markus Juonala, MD, PhD; Mika Kähönen, MD, PhD; Ronald J. Prineas, MD, PhD; Olli Raitakari, MD, PhD; Alan R. Sinaiko, MD; Julia Steinberger, MD, MS; Elaine M. Urbina, MD, MS; Alison Venn, PhD; Jorma Viikari, MD, PhD; Jessica G. Woo, PhD; David R. Jacobs Jr , PhD

BACKGROUND: Despite declining US adolescent smoking prevalence from 40% among 12th graders in 1995 to around 10% in 2018, adolescent smoking is still a significant problem. Using the International Childhood Cardiovascular Cohort (i3C) Consortium, which includes 7 international cohorts recruited in childhood and followed into adulthood, the present study was designed to confirm the important relation between adolescent smoking and daily adult smoking and present new data on adult smoking into the forties and comparison of smoking in the United States, Finland, and Australia.

METHODS AND RESULTS: Childhood smoking experience during ages 6 to 19 in the 1970s and 1980s was classifiable in 6687 i3C participants who also provided smoking status in their twenties and forties through 2011–2018. Prevalence of daily smoking in their twenties was directly related to degree of smoking during adolescence and inversely related to the age at which that smoking experience occurred (P trend, <0.001). Similar patterns were observed for prediction of smoking during age forties. Among the 2465 smokers in their twenties, cessation by their forties was generally inverse to degree of smoking in ages 6 to 19 (P trend, <0.001). Prevalence of smoking during adolescence and adulthood was similar among US, Finnish, and Australian participants.

CONCLUSIONS: These long-term follow-up data show that smoking intensity increased throughout adolescence. Prevalence of adult smoking and cessation by the forties were both correlated with levels of childhood smoking intensity. These data lend support to preventive strategies designed to reduce, delay, or eliminate any youth access to cigarettes.

Key Words: adult smoking ■ childhood smoking intensity ■ public policy ■ smoking ■ smoking cessation

Despite substantial and successful efforts to reduce cigarette smoking on a population level, the number of daily smokers remained 250 to 270 million in developed countries over the past 3 decades.¹ Smoking is a cardiovascular disease risk factor and a leading world-wide preventable cause of death, accounting for approximately 6 million deaths per year

(12%) among adults aged ≥ 30 years.^{2,3} Smoking is also related to minor illnesses, leading to absenteeism from work, loss of productivity,⁴ and increased financial burden to smokers.⁵ Despite the known benefits of smoking cessation, substantial rates of smoking relapse occur during adulthood because of addiction, withdrawal symptoms, weight gain postcessation, and

Correspondence to: David R. Jacobs Jr, PhD, Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, 1300 S 2nd St, Suite 300, Minneapolis, MN 55454. E-mail: jacob004@umn.edu

Supplementary material for this article is available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.014381>

For Sources of Funding and Disclosures, see page 10.

© 2020 The Authors. Published on behalf of the American Heart Association, Inc., by Wiley. This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- This cohort study independently replicates earlier knowledge that adolescent smoking predisposes to adult smoking and newly extends that knowledge to increased risk among adolescent smokers of adult smoking and reduced cessation in their forties, even those adolescents who only smoked a few cigarettes.

What Are the Clinical Implications?

- The medical community should actively support measures to prevent access to tobacco products before age 21.
- Pediatricians particularly should be alert to smoking among their patients and should explain the lifetime risks to child patients and their parents.

Nonstandard Abbreviations and Acronyms

BHS	Bogalusa Heart Study
CDAH	Childhood Determinants of Adult Health Study
i3C	International Childhood Cardiovascular Cohort Consortium
Insulin	Minnesota Studies: The Insulin Study
Musc	Muscatine
NaKS	Minnesota Studies: Sodium Potassium Study
NGHS	National Growth and Health Study
PHBPC	Minnesota Studies: Prevention of High Blood Pressure in Children
PLRS	Princeton Lipid Research Clinics Study
YFS	Cardiovascular Risk in Young Finns Study

stress.^{6–8} Given the high prevalence of smoking in childhood, its health consequences, and the difficulty of smoking cessation, studies of childhood smoking are highly relevant to development of strategies for prevention of adult cigarette smoking and related health issues.

In the United States, ~87% of adult daily smokers started smoking before age 18 and 95% started before age 21.⁹ Despite a 2015 Institute of Medicine report finding that much adult smoking could be prevented by postponing smoking exposure until age 21,^{10,11} childhood smoking continues to be a major public health problem. Most children/adolescents are not

daily smokers,^{12–14} and previous longitudinal studies have related the lower-intensity cigarette smoking in adolescence to future regular smoking.^{15–18} However, these studies have been short term (2–8 years), and studies with longer-term follow-up have linked smoking during adolescence only to smoking in the early thirties.^{19,20}

Despite declining US adolescent smoking prevalence from nearly 40% among 12th graders in 1995 to around 10% in 2018, adolescent smoking continues to affect a significant proportion of the adolescent population.²¹ Thus, there is an urgency to reinforce the efforts of policies such as Tobacco 21²² to decrease initiation of smoking in adolescence and also effectively develop and distribute new data on the adverse effects of adolescent smoking.

We report epidemiological findings from the International Childhood Cardiovascular Cohort (i3C) Consortium, a collaborative study among 7 international cohorts recruited in childhood and followed longitudinally into adulthood. The report supports the earlier Institute of Medicine findings that greater involvement with cigarettes in childhood and adolescence leads to greater probability of adult smoking, and that the probability of being an adult smoker is higher the earlier that the child or adolescent smokes.^{10,11} But, in addition, we add to the Institute of Medicine conclusions by extending the relation of adolescent smoking to adult smoking into the forties and by comparing data from 3 international settings: the United States, Australia, and Finland.

METHODS

The data that support the findings of this study are available upon reasonable request through the i3C Steering Committee, Chair Terence Dwyer (terence.dwyer@georgeinstitute.ox.ac.uk).

Study Sample

The 7 i3C cohorts are described in detail in an earlier publication²³ and are listed in Table 1. Each cohort recorded smoking behavior in childhood during the 1970s–1990s with follow-up through mid-adulthood. Smoking information was obtained from 6687 i3C participants in childhood/adolescence (age 6–19 years) and again during their twenties and during their forties. Of the 6687 persons, 2465 (36.9%) were smokers in their twenties and constituted the sample for cessation analyses. To assess potential for selection bias, we also identified the 10 352 excluded i3C participants who were asked about smoking during childhood/adolescence and were at least 40 years old in 2016, but were not successfully followed.

Table 1. Studies Participating in the i3C Consortium and General Characteristics of Their Smoking-Related Questions

Study Name	Asked About Childhood Smoking	Information Sufficient to Separate Trier vs Nondaily (excludes Trier) Among Nondaily Smokers in Most Participants
Bogalusa Heart Study	Yes, repeatedly	Yes, not all visits
Australian Childhood Determinants of Adult Health Study	Yes, once	Yes
National Growth and Health Study	Yes, repeatedly	Yes
Minnesota Studies: Prevention of High Blood Pressure in Children	Yes, once	Yes
Minnesota Studies: Sodium Potassium Study	Yes, once	Yes
Minnesota Studies: The Insulin Study	No	No
Princeton Lipid Research Clinics Study	Yes, once	Yes
Muscatine	Yes, but daily smoking only, so not included	No
Cardiovascular Risk in Young Finns Study	Yes, repeatedly	Yes, not all visits

Cohort sample sizes are provided in Table 3. i3C indicates International Childhood Cardiovascular Cohort.

Childhood Data

Table 1 presents an overview of the smoking-related questions by cohort. The specific algorithms used to generate childhood/adolescent smoking information are provided in Table 2, and detailed questionnaires used in childhood/adolescence are provided in Data S1. Smoking questions differed among the cohorts and were harmonized for this study into childhood/adolescent smoking intensity categories: (1) never; (2) trier (self-reported any of the following to survey questions: “tried”; “a few puffs”; “<10 cigarettes lifetime”; “only once”; “once or twice”; “a few times”; and “at least tried” coupled with either

“not habitual” or “never smoked”); (3) nondaily (excludes triers and includes adolescents who smoked more than a few times, but not daily); and (4) daily smoking. Children/adolescents who said they had smoked other than daily, but had insufficient information to classify into the trier versus nondaily categories ($n=424$) were included in the denominator to achieve unbiased prevalence estimates, but they were not included in any other analysis. In the Bogalusa Heart Study, the National Heart, Lung, and Blood Institute Growth and Health Study, and the Young Finns Study, repeated measures during childhood and/or adolescence were often available. In that case, the participant was assigned his or her highest mentioned intensity category. An additional category, adolescent quitter, was used when the participant categorized him- or herself during childhood/adolescence as a quitter or in repeated measures when a report of daily smoking was followed only by reports of quitting or not smoking during adolescence.

Table 2. Childhood/Adolescent Smoking Categories and Algorithms*

Category	Algorithms
Never smoked	Never smoked
Adolescent quitter	Reported quitting or was a nonsmoker after reporting daily smoking
Trier	Smoking intensity was minimal: Bogalusa: “Tried” Australia: Smoked “a few puffs”, “<10 cigarettes lifetime” Minnesota Prevention of High Blood Pressure in Children: Smoked “only once” National Growth and Health Study: Smoked “once or twice”, “a few times” Finnish: “At least tried” with (“not habitual” or “never smoked”)
Nondaily (excludes triers)	Smoked more than a trier, but never daily or adolescent quitter
Indeterminate	Nondaily smokers who were not asked questions which would separate out triers from other nondaily smokers
Daily smoker	Smoked daily

*For people with repeated measures of smoking, the most intense category (except for the quitters) among the repeats was selected in the order Never <Trier<Non-daily<Daily <Quitter.

Adult Data

Adult data were obtained in sporadic visits, the timing of which varied by cohort. In addition, between 2015 and 2018, an attempt was made to recontact all US and Australian i3C participants to complete a Heart Health Survey, which was designed to assess health status in middle age, including smoking. The Cardiovascular Risk in Young Finns Study did not complete the i3C Heart Health Survey, but participated in a clinic examination in 2011–2012, which served as a middle-age assessment. All examinations were approved by the institutional review board of each cohort. Informed consent was obtained from all adult participants, and participants aged <18 years all assented with parental signed consent.

Adulthood Smoking Outcomes

Primary adult smoking outcomes were defined by the i3C Heart Health Survey questions asking about daily smoking status (answered as either yes or no) during ages twenties and forties (these questions were modeled after questions asked in both the 12- and 15-year surveys of The Million Women Study²⁴). In the i3C Heart Health Survey, smokers were categorized by their answer to the question, “Have you ever smoked?” Daily smokers in their twenties then answered the question, “In your 20’s, ___typical number of cigarettes a day.” Daily smokers in their forties also answered the question, “In your 40s, ___typical number of cigarettes a day.” An adult quitter was defined as a daily smoker in their twenties who said they were nonsmokers in their forties. In the Young Finns Study and in the sporadic adult visits preceding the i3C Heart Health Survey, smoking in the twenties was determined from smoking status at the last visit during ages 20 to 29, and smoking in the forties was determined from the last visit during ages 40 to 49 (adult smoking asked in the sporadic adult visits used a variety of questions).

Of the 6687 participants in the analysis, 2802 had repeated measures during ages 20 to 29 years and 2029 had repeated measures during ages 40 to 49 years. For most persons, the last measure within the age decade was unambiguous, showing consistency of either smoking or cessation through the decade. However, 53 participants whose last age twenties measure was “nonsmoker” had been smokers at a previous examination earlier in their twenties. Correspondingly, 24 participants whose last age forties measure was “nonsmoker” had been smokers at a previous examination earlier in their forties. These persons were interpreted as being nonsmokers in the early adulthood and mid-adulthood decades, respectively. A sensitivity analysis was performed in which they were classified as smokers.

Statistical Analysis

Each participant was categorized in 1 childhood/adolescent smoking category and in 1 category of age at which smoking information was last queried. Selection bias was studied by comparing characteristics in the analyzed sample (N=6687) with those in the excluded sample (N=10 352). Our first focus was on the association of adult smoking and cessation with extent of childhood/adolescent smoking. We examined the association of childhood smoking with daily smoking status (yes/no) during the twenties and forties and with smoking cessation by the forties using unadjusted counts. To account for confounding, we back-transformed smoking and smoking cessation probabilities computed in logistic regression after adjustment for sex, race/ethnicity (white,

black, or other), and cohort. Socioeconomic status, a critical correlate of smoking behavior,²⁵ was assessed as a covariate, as represented by parental educational level. Parental education was restricted to 3 categories to harmonize across countries, given international differences in educational systems. The person’s own education as reported in adulthood was assessed in 5 categories. Despite significant differences in smoking in adolescence and in adulthood based on education, such adjustment for either parental or own education did not alter findings substantially, and socioeconomic status is not included as a covariate in the tables.

In the several i3C cohorts, the last age at which childhood/adolescent smoking information was queried was often before adolescence ended (ie, 18–19 years old). Because those who attained a given smoking status at an earlier age had the opportunity to become more

Table 3. Characteristics Among Participants Who Were Followed for Smoking in Their Forties and Those Who Were Age Eligible* but Not Followed†

Characteristics	Followed, Smoking Asked in Childhood/Adolescence (Ages 6–19) (N=6687)	Not Followed, Smoking Asked in Childhood/Adolescence (N=10 352)
Sex		
Female	57.0% (3814)	45.9% (4746)
Male	43.0% (2873)	54.1% (5606)
Race-country		
US white	30.6% (2032)	29.8% (3069)
US black	15.0% (999)	15.5% (1593)
Australian	34.9% (2319)	39.3% (4049)
Finnish	19.4% (1290)	15.5% (1595)
US cohorts		
Bogalusa	25.5% (1706)	30.1% (3116)
Muscantine	0% (0)	0% (0)
Minnesota	9.8% (652)	4.2% (430)
National Growth and Health Study	1.2% (83)	0.6% (62)
Princeton	9.5% (637)	10.6% (1098)
Parental education		
≤High school	50.3% (2641)	57.3% (2945)
>High school and <college	23.8% (1252)	24.0% (1231)
≥College	25.9% (1363)	18.7% (961)
Own education, as reported in adulthood		
<High school	5.1% (341)	17.4% (560)
=High school	20.3% (1356)	25.0% (805)
>High school and <college	37.1% (2479)	32.2% (1040)
=College	23.0% (1538)	19.3% (623)
>College	14.4% (959)	6.0% (194)

Cohort abbreviations are defined in Table 1.

*Age eligible: aged at least 40 in 2016.

†P for difference, <0.001 among groups for all (chi-square testing).

involved with cigarettes before adolescence ended, people who attain a given childhood/adolescent smoking category at an early age are expected to have a higher adult smoking prevalence than the corresponding subgroup of people who attained that childhood/adolescent smoking category at a later age. However, the reverse should be true for quitters: The expectation is that those who stated that they quit later in adolescence should be less likely to smoke as adults than those who said they quit at a more-vulnerable, younger age. We categorized participants according to the age at which smoking status was last queried (6–12, 13–14, 15–17, and 18–19 years old) and stratified the analyses of adult smoking by childhood/adolescent smoking age.

$P < 0.05$ was regarded as statistically significant. All analyses were conducted in SAS software (version 9.4; SAS Institute Inc., Cary, NC).

RESULTS

Of the 6687 persons included in this study, 45.6% (N=3078) were from the United States, 34.9% (N=2319) were Australian, and 19.4% (N=1290) were Finnish (Table 3). There was a wide spread of parental and participant's own education. The 6687 analyzed persons included 57.0% female (N=3814), 37.4% who completed at least college (N=2497), and 25.9% whose parents completed at least college (N=1363). These percentages were higher than in the 10 352 who were asked about smoking during childhood/adolescence and were at least 40 years old in 2016, but were not successfully followed (4746 or 45.9%, 817 or 25.3%, and 961 or 18.7%, respectively; $P < 0.001$ for all comparisons).

Childhood Smoking

As shown in Table 4, data on childhood/adolescent smoking intensity were available for analysis from ages 6 to 12 (N=2136 or 31.9% of participants) to

ages 18 to 19 (N=1628 or 24.3% of participants). Overall, prevalence of never smoking was 46.9% (3138 of 6687), but 53.1% (3549 of 6687) smoked at some point during childhood/adolescence. Daily smoking occurred in 12.9% (865 of 6687), with only 14 persons aged 6 to 12 and 90 persons aged 13 to 14 years categorized as daily smokers. Over half of the smokers who did not smoke daily were classified as triers. Evolution of smoking intensity was reflected in the decreasing prevalence of the never and trier subgroups with increasing age, whereas prevalence of nondaily (excluding triers) and daily smoking increased with age.

Prediction of Smoking During Age Twenties

Overall, prevalence of daily smoking in age twenties was 36.9% (unadjusted $n/N=2465$ of 6687), varying across race-country from 29.6% (382 of 1290, Finns) and 33.8% (338 of 999, US blacks) to 39.8% (922 of 2319, Australians) and 39.5% (803 of 2032, US whites; $P < 0.001$). Data on parental education were available on 5256 of the children/adolescents. Prevalence of smoking in age twenties decreased with increasing levels of parental education: 36.7% (969 of 2641) high school and below, 33.5% (419 of 1252) beyond high school but no college degree, and 32.2% (439 of 1363) college degree and above (P trend, < 0.001). Prevalence also decreased with increasing levels of the individual's (N=6673) own education: 58.1% (198 of 341) less than high school, 47.3% (641 of 1356) with high school degree, 39.5% (978 of 2479) with education beyond high school but no college degree, 26.5% (407 of 1538) with college degree, and 24.3% (233 of 959) with a degree higher than college (P trend, < 0.001).

Prevalence of daily smoking in the twenties was graded by intensity of smoking across never, trier, nondaily (excluding triers), adolescent quitter, and

Table 4. Childhood/Adolescent Smoking Intensity According to Age*

Age (y)	All†	Never	Trier	Nondaily (Excludes Triers)	Adolescent Quitter	Daily
	Column % (N)	Row % (n)	Row % (n)	Row % (n)	Row % (n)	Row % (n)
18 to 19	24.3% (1628)	24.6% (400)	12.5% (204)	26.7% (434)	6.8% (111)	28.0% (456)
15 to 17	23.7% (1583)	32.2% (509)	24.6% (390)	10.9% (173)	1.4% (22)	19.3% (305)
13 to 14	20.0% (1340)	48.1% (645)	30.5% (409)	4.9% (66)	0.2% (3)	6.7% (90)
6 to 12	31.9% (2136)	74.2% (1584)	19.6% (418)	1.4% (29)	0.1% (1)	0.7% (14)
All	100 (6687)	46.9% (3138)	21.3% (1421)	10.5% (702)	2.0% (137)	12.9% (865)

*Each participant entered this table once at the oldest age through which childhood/adolescent smoking intensity was known.

†Also included 424 who had tried smoking during adolescence (not daily smokers), but who could not be classified as trier or nondaily based on available information. These persons were included in the denominator in this table to achieve unbiased prevalence estimates, but not included in any other analysis. These were 6.3% of the sample: 1.4% (n=23) for query at ages 18 to 19; 11.6% (n=184) for query at ages 15 to 17; 9.5% (n=127) for query at ages 13 to 14; and 4.2% (n=90) for query at ages 6 to 12. All but 90 of the 2136 persons in the 6 to 12 category were aged 9 to 12.

Table 5. Adult Smoking Adjusted Prevalence and Cessation* According to Childhood/Adolescent Smoking Intensity, i3C Consortium, N=6687

Age (y)	Never	Trier	Nondaily (Excludes Triers)	Adolescent Quitter	Daily	P Trend
Prevalence of daily smoking in the twenties						
18 to 19	2.6%	7.8% [†]	20.7% ^{†‡}	31.5% ^{†‡§}	76.3% ^{†‡§}	<0.001
15 to 17	13.3%	33.2% [†]	58.3% ^{†‡}	59.1% ^{†‡}	87.1% ^{†‡§}	<0.001
13 to 14	21.7%	48.3% [†]	79.5% ^{†‡}	N/A	88.0% ^{†‡}	<0.001
6 to 12	31.5%	50.4% [†]	78.1% ^{†‡}	N/A	72.6% [†]	<0.001
Prevalence of daily smoking in the forties						
18 to 19	3.2%	5.7%	11.2% ^{†‡}	19.1% ^{†‡§}	47.0% ^{†‡§}	<0.001
15 to 17	8.9%	21.1% [†]	32.6% ^{†‡}	42.9% ^{†‡}	59.4% ^{†‡§}	<0.001
13 to 14	10.5%	20.6% [†]	44.6% ^{†‡}	N/A	59.5% ^{†‡}	<0.001
6 to 12	13.2%	21.5% [†]	45.1% ^{†‡}	N/A	35.2% [†]	<0.001
Smoking cessation by the forties among 2465 smokers in the twenties						
18 to 19	76.0%	44.0%	57.7%	63.7%	42.5% ^{†§}	0.004
15 to 17	42.2%	40.2%	38.2%	N/A	32.9%	0.086
13 to 14	52.0%	56.0%	47.6%	N/A	31.8% ^{†‡}	0.005
6 to 12	59.2%	56.4%	45.6%	N/A	53.0%	0.270

i3C indicates International Childhood Cardiovascular Cohort; N/A, not applicable.

*Multivariable logistic regression models were adjusted for sex, race/ethnicity, and cohort. In crude analyses, numerators and denominators for smoking prevalence during the twenties and the forties are given in Table 6.

[†]Pairwise $P < 0.05$, compared with never.

[‡]Pairwise $P < 0.05$, compared with trier.

[§]Pairwise $P < 0.05$, compared with nondaily (excludes triers).

^{||}Pairwise $P < 0.05$, compared with quitter.

daily subgroups within each childhood/adolescent age group and inversely related to age when each childhood/adolescent smoking intensity was reached (except among childhood/adolescent daily smokers), after adjustment for sex, race, and cohort (P for trend, <0.001 for each age; Tables 5 and 6). For instance, the gradient for smoking prevalence in

the twenties across childhood/adolescent smoking intensity categories within the age group 18 to 19 years was 2.6% in the childhood/adolescent never smokers, 7.8% in the trier subgroup, 20.7% in nondaily (excluding triers) smokers, and 76.3% in daily smokers ($P < 0.05$ for all pairwise comparisons). At the same time, among those who were classified as a

Table 6. Adult Smoking Prevalence and Cessation (Crude Number and Rate) According to Childhood/Adolescent Smoking Intensity, i3C Consortium, N=6687

Age (y)	Never	Trier	Nondaily (Excludes Triers)	Adolescent Quitter	Daily
Prevalence of daily smoking in the twenties					
18 to 19	3.5% (14/400)	9.3% (19/204)	19.8% (86/434)	26.1% (29/111)	75.2% (343/456)
15 to 17	16.9% (86/509)	33.1% (129/390)	48.6% (84/173)	54.5% (12/22)	85.6% (261/305)
13 to 14	24.8% (160/645)	45.2% (185/409)	77.3% (51/66)	66.7% (2/3)	86.7% (78/90)
6 to 12	31.6% (500/1584)	51.0% (213/418)	75.9% (22/29)	0% (0/1)	71.4% (10/14)
Prevalence of daily smoking in the forties					
18 to 19	3.5% (14/400)	6.4% (13/204)	11.3% (49/434)	18.0% (20/111)	46.9% (214/456)
15 to 17	11.2% (57/509)	20.3% (79/390)	28.9% (50/173)	40.9% (9/22)	58.7% (179/305)
13 to 14	14.1% (91/645)	17.6% (72/409)	40.9% (27/66)	66.7% (2/3)	58.9% (53/90)
6 to 12	14.6% (231/1584)	19.9% (83/418)	44.8% (13/29)	0% (0/1)	42.9% (6/14)
Smoking cessation by the forties among 2465 smokers in the twenties					
18 to 19	71.4% (10/14)	42.1% (8/19)	58.1% (50/86)	65.5% (19/29)	42.9% (147/343)
15 to 17	40.7% (35/86)	44.2% (57/129)	40.5% (34/84)	25.0% (3/12)	33.7% (88/261)
13 to 14	45.6% (73/160)	62.2% (115/185)	49.0% (25/51)	0% (0/2)	32.1% (25/78)
6 to 12	56.4% (282/500)	62.4% (133/213)	45.5% (10/22)	N/A (0/0)	40.0% (4/10)

i3C indicates International Childhood Cardiovascular Cohort; N/A, not applicable.

Table 7. Adult Smoking Prevalence in the Forties Conditional on Smoking Status in the Twenties (Crude Rate and Number) According to Childhood/Adolescent Smoking Intensity, i3C Consortium, N=3979)

Age (y)	Never	Trier	Nondaily (Excludes Triers)	Adolescent Quitter	Daily
Smoking in the forties among those who smoked in the twenties					
18 to 19	28.6% (4/14)	57.9% (11/19)	41.9% (36/86)	34.5% (10/29)	57.1% (196/343)
15 to 17	59.3% (51/86)	55.8% (72/129)	59.5% (50/84)	75.0% (9/12)	66.3% (173/261)
13 to 14	54.4% (87/160)	37.8% (70/185)	51.0% (26/51)	100% (2/2)	67.9% (53/78)
6 to 12	43.6% (218/500)	37.6% (80/213)	54.5% (12/22)	N/A (0/0)	60.0% (6/10)
Smoking in the forties among those who did not smoke in the twenties					
18 to 19	2.6% (10/386)	1.1% (2/185)	3.7% (13/348)	12.2% (10/82)	15.9% (18/113)
15 to 17	1.4% (6/423)	2.7% (7/261)	0% (0/89)	0% (0/10)	13.6% (6/44)
13 to 14	0.8% (4/485)	0.9% (2/224)	6.7% (1/15)	0% (0/1)	0% (0/12)
6 to 12	1.2% (13/1084)	1.5% (3/205)	14.3% (1/7)	0% (0/1)	0% (0/4)

i3C indicates International Childhood Cardiovascular Cohort; N/A, not applicable.

never smoker, prevalence of smoking in the twenties was 2.6%, 13.3%, 21.7%, and 31.5% for smoking last asked at ages 18 to 19, 15 to 17, 13 to 14, and 6 to 12, respectively.

Among the 2.0% (n=137 of 6687) who had been daily smokers in adolescence, but who quit before adulthood, most (n=111) reported quitting during ages 18 to 19. Of these 111, 31.5% relapsed (were smokers in their twenties). The few adolescent smokers who quit by ages 15 to 17 (n=26) had relapse rates in the twenties of 50% to 60%, which was significantly higher than those who quit in later adolescence ($P<0.001$).

Prediction of Smoking During Age Forties and Smoking Cessation by the Forties

Smoking prevalence during the forties followed a pattern across childhood/adolescent smoking intensity categories similar to smoking prevalence during the twenties, but generally at a lower smoking prevalence (20.8%; 1394 of 6687; Tables 5 and 6). Only 2.6% (10 of 386) of participants were smokers in their forties among those who said they never smoked when last asked about smoking at ages 18 to 19 and were nonsmokers in their twenties (Table 7).

Cessation by their forties was generally inversely graded across the 5 childhood/adolescent smoking intensity subgroups. Among the 2465 persons who were smokers in their twenties, adjusted cessation rate in the forties was 56.4% (unadjusted n/N=400 of 760) in the childhood/adolescent never smoked subgroup, 52.3% (313 of 546) in the childhood/adolescent triers, 47.5% (119 of 243) in the childhood/adolescent nondaily (excluding triers) subgroup, and 37.3% (264 of 692) in the childhood adolescent daily smokers (P trend, <0.001), after adjustment for sex, race, cohort, and age. Childhood/adolescent age-stratified analyses

of cessation (Tables 5 and 6) were generally consistent with age-adjusted values.

Smoking Prevalence by Country

The association between childhood/adolescent smoking intensity and adult smoking (during age twenties or forties) was not modified by sex, parental education, or own education. The pattern of a positive association of smoking prevalence in the twenties across childhood/adolescent smoking categories and an inverse association with age at which smoking was asked were observed in each country (Table 8). The few country-specific exceptions to this pattern are either slight deviations from the pattern (ie, in Australia age 15 years, 91.3% [21 of 23] of nondaily smokers versus 88.2% [60 of 68] of daily smokers) or based on small sample size (ie, in the US participants smoking in the twenties was less frequent in those aged ≤ 12 years than in those aged 13–14 years, but among those aged ≤ 12 years, the 62.5% [5 of 8] smoking in the twenties among nondaily smokers and the 70.0% [7 of 10] smoking in the twenties among daily smokers were based on small sample sizes). Nevertheless, smoking prevalences in the twenties were lowest in Finland and highest in Australia. In each country, smoking cessation in the forties was lower for childhood/adolescent daily smokers than for other childhood/adolescent subgroups (Table 9), but cessation was unrelated to age at which childhood/adolescent smoking was asked.

DISCUSSION

This international study of smoking in children, and its longitudinal effects on adult smoking, confirms the important points made in the 2015 Institute of Medicine report^{10,11} that: (1) smoking in children very often leads to regular smoking in adulthood; (2) smoking

Table 8. Adult Smoking Prevalence in the Twenties (Crude Rate and Number) According to Childhood/Adolescent Smoking Intensity Stratified by the United States, Australia, and Finland, i3C Consortium, N=6687*

	Never	Trier	Nondaily (Excludes Triers)	Daily
United States				
18 to 19 y	5.7% (10/174)	10.5% (9/86)	28.8% (34/118)	84.4% (119/141)
15 to 17 y	18.4% (74/402)	35.5% (57/163)	50.0% (44/88)	87.4% (167/191)
13 to 14 y	30.1% (111/369)	38.7% (29/75)	84.0% (21/25)	80.0% (36/45)
≤12 y	31.0% (196/633)	49.3% (33/67)	62.5% (5/8)	70.0% (7/10)
Australia				
18 to 19 y	N/A	N/A	N/A	N/A
15 y	11.8% (9/76)	36.8% (63/171)	91.3% (21/23)	88.2% (60/68)
13 to 14 y	17.6% (48/272)	46.7% (156/334)	73.2% (30/41)	93.3% (42/45)
≤12 y	32.2% (299/929)	52.4% (178/340)	82.4% (14/17)	66.7% (2/3)
Finland				
18 y	1.8% (4/221)	7.8% (9/115)	16.3% (50/306)	71.2% (218/306)
15 y	9.7% (3/31)	16.7% (9/54)	28.8% (17/59)	69.2% (27/39)
13 to 14 y [†]	N/A	N/A	N/A	N/A
≤12 y	N/A	N/A	N/A	N/A

i3C indicates International Childhood Cardiovascular Cohort; N/A, not applicable.

*Adolescent quitters are omitted because of small numbers.

[†]Not applicable because of limited sample size (N=34).

experimentation continues to occur throughout adolescence and is more likely to be associated with adult smoking the earlier it occurs; and (3) even trying a cigarette during childhood/adolescence is associated with substantial excess risk of adult smoking.

In addition, the findings from the present study expand on the Institute of Medicine report.^{10,11} First, older adolescent smokers seem less susceptible than the younger adolescent and childhood smokers to

becoming adult smokers: Smoking cessation during ages 18 to 19 was much less likely to be followed by relapse than was cessation earlier in adolescence; we speculate that this finding may be attributed to maturation, which would be greater at the older adolescent age. Also, prevalence of smoking in the twenties was much lower for persons who were nondaily smokers (excluding triers) in ages 18 to 19 than it was for the same groups earlier in childhood/adolescence, although it continued

Table 9. Adult Smoking Cessation in the Forties (Crude Rate and Number), According to Childhood/Adolescent Smoking Intensity Stratified by the United States, Australia, and Finland, i3C Consortium, N=2465 Smokers in the Twenties*

	Never	Trier	Nondaily (Excludes Triers)	Daily
United States				
18 to 19 y	70% (7/10)	44.4% (4/9)	64.7% (22/34)	37.8% (45/119)
15 to 17 y	35.1% (26/74)	28.1% (16/57)	27.3% (12/44)	27.5% (46/167)
13 to 14 y	38.7% (43/111)	44.8% (13/29)	28.6% (6/21)	5.6% (2/36)
≤12 y	33.2% (65/196)	45.5% (15/33)	40% (2/5)	28.6% (2/7)
Australian				
18 to 19 y				
15 y	66.7% (6/9)	57.1% (36/63)	71.4% (15/21)	50% (30/60)
13 to 14 y	62.5% (30/48)	65.4% (102/156)	63.3% (19/30)	54.8% (23/42)
≤12 y	71.9% (215/299)	65.7% (117/178)	50% (7/14)	100% (2/2)
Finnish				
18 y	75% (3/4)	44.4% (4/9)	52% (26/50)	46.8% (102/218)
15 y	100% (3/3)	55.6% (5/9)	41.2% (7/17)	40.7% (11/27)
13 to 14 y [†]	N/A	N/A	N/A	N/A
≤12 y	N/A	N/A	N/A	N/A

i3C indicates International Childhood Cardiovascular Cohort; N/A, not applicable.

*Adolescent quitters are omitted because of small numbers.

[†]Not applicable because of limited numbers of persons (N=4, 2, 3, 0, and 1 across groups of childhood/adolescent smoking intensity, respectively).

to be important at a rate of around 30%. Second, the present study extends longitudinal evaluation of childhood/adolescent smoking into the forties. Among 386 persons who never smoked throughout childhood, adolescence, and their twenties, only 10 persons (2.6%) smoked in their forties. Third, this study includes both a European and an Australian cohort, showing that the relationship of childhood/adolescence smoking to adult smoking in those countries follows the same pattern as documented in the United States.

It is not clear why smokers with an earlier and more-intense smoking history tend to establish daily smoking and have trouble quitting in adulthood. A strong possibility is the early exposure to nicotine. In line with findings of the 2012 Surgeon General's Report,⁹ it has been suggested that nicotine addiction is stronger when smoking initiation occurs earlier in childhood (although no age cut point has been identified),^{26–29} and the developing neurological system of younger children is particularly vulnerable to nicotine.³⁰ Although we showed that smoking in the twenties was more likely in those whose parents had lower education, we did not have other relevant information, such as the extent of exposure to secondhand smoke in the childhood/adolescent home or the smoking behavior of childhood/adolescent peers. The present study had no specific measure related to nicotine addiction, nor did it have any measure of other possible explanators, including deviance proneness, behavioral and emotional dysregulation, and both adult and peer smoking modeling.^{31,32}

The data reported in Table 5 could be the basis for antismoking counseling. Although few individuals who never smoked at ages 18 to 19 became daily smokers, even triers at that age had an excess risk of taking up smoking by their twenties compared with those who never smoked during childhood/adolescence. In particular, 33% of triers at ages 15 to 17 as opposed to 9% at ages 18 to 19, were smokers in their twenties. Triers during ages 6 to 14 had a 50% chance of smoking in their twenties, and 18% were still smokers in their forties. These data emphasize the health benefits likely to occur by preventing any childhood smoking exposure, particularly beginning in early adolescence.

Like our results predicting smoking in the twenties from childhood/adolescent smoking, previous studies reported that adolescent puffers (analogous to our trier category) and more-intensive nondaily smokers (analogous to our nondaily [excluding triers] category) are at 1.9 to 3.5 times and 3.1 to 10.8 times the risk, respectively, of daily smoking 2 to 8 years later than those who never smoked in adolescence,^{15,16,18} and more-intensive experimenters compared with puffers had 1.9 to 2.7 times the likelihood of smoking in 4 years.¹⁷ The Australian Childhood Determinants of Adult Health

study, a member of i3C, followed 3559 children aged 9 to 15 years and reported that children who smoked only a few puffs or <10 cigarettes lifetime were at 1.3 to 3.0 times higher risk of becoming daily smokers in early adulthood compared with those who had never smoked by ages 9 to 15 years.¹⁹ A study conducted in the United States reported that smokers aged 12 to 21 years who smoked over 3 packs per month, but did not smoke daily, were as likely as daily smokers to be smoking 14 years later (odds ratio, 0.97; 95% CI, 0.53, 1.80), whereas nondaily smokers of 1 to 5 cigarettes per month and 6 to 60 cigarettes per month were less likely than daily smokers to be smoking 14 years later (odds ratio, 0.21; 95% CI, 0.15–0.29 and odds ratio, 0.22; 95% CI, 0.14–0.34, respectively).²⁰ Similar to previous studies, our study showed a graded prevalence of smoking during young adulthood across levels of childhood smoking intensity. However, our results extend those findings to show the adverse effect of childhood/adolescent smoking into the forties in relation to the finding that daily smoking in the twenties was followed by difficulty with smoking cessation by the forties.

Our i3C findings contribute to the ongoing debate for the Tobacco 21 policy, showing the adverse effect of initiating smoking in childhood/adolescence, thus strengthening the Tobacco 21 aims to prevent or delay access to cigarettes by making sale of cigarettes illegal through age 21. Laws prohibiting the sale of tobacco products to anyone under the age of 21 have been implemented in 19 US states and at least 500 localities, but cover only approximately half the US population, according to the Campaign for Tobacco-Free Kids.³³ A US measure starting in 2020 was signed into law on December 20, 2019.³⁴ Tobacco 21 laws have not been passed in Europe,³⁵ and limited evidence of the benefits of offsetting preadult smoking has limited progression in Australia.³⁶

The present study has some strengths. The available i3C Consortium data had a large sample size in 3 countries, a variety of measurements of smoking variables in childhood and adulthood, and extended duration of follow-up relative to the earlier CDAH report.¹⁹ In addition, the study collected childhood smoking data individually in clinics or through research staff independent of schools, which would minimize desirability bias that might otherwise occur in the school classroom environment.

Limitations include that misclassification of childhood smoking status is possible. First, i3C included heterogeneous questionnaires on childhood smoking across i3C cohorts, so not all studies contributed equally to the findings. Second, children may have difficulty in understanding and responding to some smoking questions, and this difficulty is greatest for young children. Third, the natural history of smoking is inevitably affected by policy change, such as the Master

Settlement Agreement in 1998 in the United States, and can change over time; US adolescent smoking prevalence has declined since i3C data were collected.²¹ Nevertheless, the results of this study remain relevant in terms of the greater the adolescent smoking intensity, the higher the likelihood of becoming an adult smoker. Fourth, our findings may underestimate the prevalence of smoking in both childhood and adulthood, given that those excluded (Table 3) had lower parental and own education than those included. Fifth, we did not consider smoking products other than cigarettes, particularly electronic cigarettes, which have become increasingly popular since 2010.³⁷ Conflicting data have been reported regarding the association between electronic cigarettes and cigarette smoking cessation.^{37,38} Finally, our results may not be generalizable to populations from low- and middle-income countries, where there is currently higher prevalence of established smoking and where societal conditions unique to those countries may influence the probability that an adolescent will smoke as an adult.¹

In summary, these international, long-term follow-up data showed that smoking in children and adolescents, even only a few times, was associated with substantially higher probability of being a daily smoker not only in young adulthood, but also into mid-adulthood. There was also a lower probability of cessation through the forties, graded by childhood/adolescent smoking intensity, among individuals who smoked in the twenties. Smoking experimentation continued to evolve throughout adolescence. These data reinforce that children who might otherwise be inclined to try smoking should instead completely avoid smoking. Our findings were consistent with concepts reported by the Institute of Medicine that postponing smoking exposure until age 21 remarkably reduced smoking prevalence^{10,11} and may be interpreted as supporting policy strategies in the United States, Europe, and Australia, which effectively make nicotine products harder for children to access, such as Tobacco 21 in the United States. Quitting cigarette smoking is well known to be difficult, and the surest approach not to be a smoker in adulthood is never to start smoking at any point in time. However, extra efforts should be made to prevent smoking experimentation and/or initiation earlier in the life course given that it appears to be critically related to more-unbreakable lifelong smoking patterns.

ARTICLE INFORMATION

Received August 26, 2019; accepted February 3, 2020.

Affiliations

From the Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis, MN (T.H., R.W., D.R.J.); Division of Biostatistics and Epidemiology (J.G.W.) and The Heart Institute (E.M.U.),

Cincinnati Children's Hospital Medical Center, Cincinnati, OH; Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH (E.M.U., J.G.W.); Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia (S.L.G., A.V.); Department of Epidemiology, School of Public Health and Tropical Medicine, Tulane University, New Orleans, LA (L.A.B.); Department of Epidemiology, College of Public Health, University of Iowa, Iowa City, IA (T.L.B.); Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO (S.R.D.); Oxford Martin School, Oxford University, Oxford, United Kingdom (T.D.); Department of Internal Medicine (M.J., J.V.) and Research Centre of Applied and Preventive Cardiovascular Medicine (J.I., O.R.), University of Turku, Turku, Finland; Division of Medicine, Turku University Hospital, Turku, Finland (M.J., J.V.); Murdoch Children's Research Institute, Parkville, Victoria, Australia (M.J.); Department of Clinical Physiology, Tampere University Hospital, Tampere, Finland (M.K.); Faculty of Medicine and Health Technology, University of Tampere, Tampere, Finland (M.K.); Division of Public Health Science, Wake Forest University, Winston-Salem, NC (R.J.P.); Department of Pediatrics, University of Minnesota School of Medicine, Minneapolis, MN (A.R.S., J.S.).

Sources of Funding

This work was supported by the National Institutes of Health (NIH; Grant No.: R01 HL121230). Harmonization and other data work before obtaining NIH funding were supported by the Australian National Health and Medical Research Council Project (Grant Nos.: APP1098369, APP211316), the Academy of Finland (Grant No.: 126925, 121584, 124282, 129378, 117787, and 41071), the Social Insurance Institution of Finland; Kuopio, Tampere, and Turku University Hospital Medical Funds, Juho Vainio Foundation, Paavo Nurmi Foundation, Finnish Foundation of Cardiovascular Research, Finnish Cultural Foundation, Sigrid Juselius Foundation, and Yrjö Jahnsson Foundation. Seana Gall is funded by the National Heart Foundation of Australia (FLF 100446 and 102061).

Disclosures

None.

Supplementary Materials

Data S1

REFERENCES

1. Ng M, Freeman MK, Fleming TD, Robinson M, Dwyer-Lindgren L, Thomson B, Wollum A, Sanman E, Wulf S, Lopez AD, et al. Smoking prevalence and cigarette consumption in 187 countries, 1980–2012. *JAMA*. 2014;311:183–192.
2. Bilano V, Gilmour S, Moffiet T, d'Espaignet ET, Stevens GA, Commar A, Tuyl F, Hudson I, Shibuya K. Global trends and projections for tobacco use, 1990–2025: an analysis of smoking indicators from the WHO Comprehensive Information Systems for Tobacco Control. *Lancet*. 2015;385:966–976.
3. World Health Organization (WHO). WHO global report: mortality attributable to tobacco. Geneva, Switzerland: World Health Organization; 2012:1–392.
4. Hozawa A, Houston T, Steffes MW, Widome R, Williams OD, Iribarren C, Pletcher MJ, Daviglius ML, Carr JJ, Jacobs DR Jr. The association of cigarette smoking with self-reported disease before middle age: the Coronary Artery Risk Development in Young Adults (CARDIA) study. *Prev Med*. 2006;42:193–199.
5. Alberg AJ, Diette GB, Ford JG. Invited commentary: attendance and absence as markers of health status—the example of active and passive cigarette smoking. *Am J Epidemiol*. 2003;157:870–873.
6. Husten CG. Smoking cessation in young adults. *Am J Public Health*. 2007;97:1354–1356.
7. US Department of Health and Human Services. How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2010.
8. Caraballo RS, Kruger J, Asman K, Pederson L, Widome R, Kiefe CI, Hitsman B, Jacobs DR Jr. Relapse among cigarette smokers: the CARDIA longitudinal study—1985–2011. *Addict Behav*. 2014;39:101–106.

9. US Department of Health and Human Services. Preventing Tobacco Use Among Youth and Young Adults: A Report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2012.
10. Institute of Medicine. Public Health Implications of Raising the Minimum Age of Legal Access to Tobacco Products. 2015. Available at: <http://iom.nationalacademies.org/Reports/2015/TobaccoMinimumAgeReport.aspx>. Accessed January 6, 2020.
11. Committee on the Public Health Implications of Raising the Minimum Age for Purchasing Tobacco Products. Board on Population Health and Public Health Practice. Institute of Medicine; Washington (DC): National Academies Press (US), 2015.
12. Guerin N, White V. ASSAD 2017 Statistics & Trends: Australian Secondary Students' Use of Tobacco, Alcohol, Over-the-counter Drugs, and Illicit Substances. Cancer Council Victoria. 2018.
13. National Health Service. Smoking, Drinking and Drug Use Among Young People in England—2016. London: National Health Service; 2017.
14. Kann L, McManus T, Harris WA, Shanklin SL, Flint KH, Hawkins J, Queen B, Lowry R, Olsen EO, Chyen D, et al. Youth risk behavior surveillance—United States, 2015. *MMWR Surveill Summ*. 2016;65:1–174.
15. Chassin L, Presson CC, Sherman SJ, Edwards DA. The natural history of cigarette smoking: predicting young-adult smoking outcomes from adolescent smoking patterns. *Health Psychol*. 1990;9:701–716.
16. Wakefield M, Kloska DD, O'Malley PM, Johnston LD, Chaloupka F, Pierce J, Giovino G, Ruel E, Flay BR. The role of smoking intentions in predicting future smoking among youth: findings from Monitoring the Future data. *Addiction*. 2004;99:914–922.
17. Choi WS, Pierce JP, Gilpin EA, Farkas AJ, Berry CC. Which adolescent experimenters progress to established smoking in the United States. *Am J Prev Med*. 1997;13:385–391.
18. Sargent JD, Gabrielli J, Budney A, Soneji S, Wills TA. Adolescent smoking experimentation as a predictor of daily cigarette smoking. *Drug Alcohol Depend*. 2017;175:55–59.
19. Paul SL, Blizzard L, Patton GC, Dwyer T, Venn A. Parental smoking and smoking experimentation in childhood increase the risk of being a smoker 20 years later: the Childhood Determinants of Adult Health Study. *Addiction*. 2008;103:846–853.
20. Saddleson ML, Kozlowski LT, Giovino GA, Homish GG, Mahoney MC, Goniewicz ML. Assessing 30-day quantity-frequency of US adolescent cigarette smoking as a predictor of adult smoking 14 years later. *Drug Alcohol Depend*. 2016;162:92–98.
21. Johnston LD, Miech RA, O'Malley PM, Bachman JG, Schulenberg JE, Patrick ME. Monitoring the Future National Survey Results on Drug Use 1975–2018: Overview, Key Findings on Adolescent Drug Use. Ann Arbor, MI: Institute for Social Research, University of Michigan; 2019.
22. ClearWay Minnesota. Tobacco 21. Available at: <http://clearwaymn.org/tobacco-21/>. Accessed January 6, 2020.
23. Sinaiko AR, Jacobs DR Jr, Woo JG, Bazzano L, Burns T, Hu T, Juonala M, Prineas R, Raitakari O, Steinberger J, et al. The International Childhood Cardiovascular Cohort (i3C) Consortium outcomes study of childhood cardiovascular risk factors and adult cardiovascular morbidity and mortality: design and recruitment. *Contemp Clin Trials*. 2018;69:55–64.
24. The Million Women Study. Available at: <http://www.millionwomenstudy.org/introduction>. Accessed February 21, 2020.
25. Kiefe CI, Williams OD, Lewis CE, Allison JJ, Sekar P, Wagenknecht LE. Ten-year changes in smoking among young adults: are racial differences explained by socioeconomic factors in the CARDIA study? *Am J Public Health*. 2001;91:213–218.
26. Doubeni CA, Reed G, DiFranza JR. Early course of nicotine dependence in adolescent smokers. *Pediatrics*. 2010;125:1127–1133.
27. DiFranza JR, Savageau JA, Fletcher K, O'Loughlin J, Pbert L, Ockene JK, McNeill AD, Hazelton J, Friedman K, Dussault G, et al. Symptoms of tobacco dependence after brief intermittent use: the Development and Assessment of Nicotine Dependence in Youth-2 study. *Arch Pediatr Adolesc Med*. 2007;161:704–710.
28. Gervais A, O'Loughlin J, Meshefedian G, Bancej C, Tremblay M. Milestones in the natural course of onset of cigarette use among adolescents. *CMAJ*. 2006;175:255–261.
29. DiFranza JR. A 2015 update on the natural history and diagnosis of nicotine addiction. *Curr Pediatr Rev*. 2015;11:43–55.
30. Dwyer JB, McQuown SC, Leslie FM. The dynamic effects of nicotine on the developing brain. *Pharmacol Ther*. 2009;122:125–139.
31. Novak SP, Clayton RR. The influence of school environment and self-regulation on transitions between stages of cigarette smoking: a multi-level analysis. *Health Psychol*. 2001;20:196–207.
32. Chassin L, Presson C, Morgan-Lopez A, Sherman SJ. "Deviance proneness" and adolescent smoking 1980 versus 2001: has there been a "hardening" of adolescent smoking? *J Appl Develop Psychol*. 2007;28:264–276.
33. Campaign for Tobacco-Free Kids. States and Localities that Have Raised the Minimum Legal Sale Age for Tobacco Products to 21. Available at: https://www.tobaccofreekids.org/assets/content/what_we_do/state_local_issues/sales_21/states_localities_MLSA_21.pdf. Accessed January 6, 2020.
34. US Food and Drug Administration. Selling Tobacco Products in Retail Stores. Available at: <https://www.fda.gov/tobacco-products/retail-sales-tobacco-products/selling-tobacco-products-retail-stores>. Accessed February 21, 2020.
35. Nuyts PAW, Kuipers MAG, Willemsen MC, Kunst AE. An increase in the tobacco age-of-sale to 21: for debate in Europe. *Nicotine Tob Res*. 2019 Aug 13. pii: ntr135. doi: 10.1093/ntr/ntz135. [Epub ahead of print].
36. Dean I. The Public Health Amendment (Prevention of Sale of Smoking Products to Underage Persons) Bill 2018. Available at: http://www.parliament.tas.gov.au/bills/Bills2018/pdf/notes/45_of_2018-SRS.pdf. Accessed January 6, 2020.
37. Kasza KA, Bansal-Travers M, O'Connor RJ, Compton WM, Kettermann A, Borek N, Fong GT, Cummings KM, Hyland AJ. Cigarette smokers' use of unconventional tobacco products and associations with quitting activity: findings from the ITC-4 US cohort. *Nicotine Tob Res*. 2014;16:672–681.
38. Kalkhoran S, Glantz SA. E-cigarettes and smoking cessation in real-world and clinical settings: a systematic review and meta-analysis. *Lancet Respir Med*. 2016;4:116–128.

SUPPLEMENTAL MATERIAL

Data S1. Study-specific questionnaires

Bogalusa Heart Study (BHS, 4 visits)

Study description

Visit	1	2	3	4
Study visit name	B600	C300	C600	Z810
Year of exam	1978-79	1984-85	1987-88	1998-01
Description	School children	School children	School children	Post High School Sibship genetic study
Age mean (range), year	11.3 (3.7, 19.9)	13.0 (6.8, 19.9)	11.1 (3.6, 19.9)	17.1 (12,3, 19.9)

Childhood/adolescent smoking intensity variables

1) V1 B600

Variable Name	Question	Responses
SMOKE	Ever tried or experimented with smoking	1 = no 2 = yes
SMOKENOW	Smoke now	1 = no 2 = yes
NUMSMK1	How many cigarettes did/do smoke	__(continuous)
NUMSMK2	Frequency of (answer to NUMSMK 1), Per _____	1 = day 2 = week 3 = month

		4 = other
--	--	-----------

2) V2 C300

Variable Name	Question	Responses
SMOKH	Current smoking	1 = current smoker (≥ 1 cigarette per week) 2 = used to smoke (≥ 1 cigarette per week) 3 = tried 4 = < 1 per week 5 = never 9 = unknown
NO_WEEK	No. cigarettes do smoke per week	___(Continuous)
NO_WEEK2	No. cigarettes did smoke per week	___(Continuous)
EVERYSM	Smoke every day?	1 = yes 2 = no
EVERYSM2	Used to smoke every day?	1 = yes 2 = no
QUITSMOK	When quit smoking	1 = < 1 week ago 2 = 1-4 weeks ago 3 = 1-3 months ago 4 = 4-12 months ago 5 = > 1 year ago

3) V3 C600

Variable Name	Question	Responses
SMOKH	Current smoking	1 = current smoker (≥ 1 cigarette per week) 2 = used to smoke (≥ 1 cigarette per week)

		3 = tried 4 = <1 per week 5 = never 9 = unknown
NO_WEEK	No. cigarettes do smoke per week	___(continuous)
NO_WEEK2	No. cigarettes did smoke per week	___(continuous)
EVERYSM	Smoke every day?	1 = yes 2 = no
EVERYSM2	Used to smoke every day?	1 = yes 2 = no
QUITSMOK	When quit smoking	1 = <1 week ago 2 = 1-4 weeks ago 3 = 1-3 months ago 4 = 4-12 months ago 5 = >1 year ago

4) V4 Z810

Variable Name	Question	Responses
CIG_HIST	Current smoking	1 = current smoker (≥ 1 cigarette per week) 2 = used to smoke (≥ 1 cigarette per week) 3 = tried 4 = <1 per week 5 = never 9 = unknown
NO_SMOK	No. cigarettes do smoke per week	___(continuous)
NO_SMOK2	No. cigarettes did smoke per week	___(continuous)
SMKDAILY	Smoke every day?	1 = yes 2 = no
SMKD_DAY	Used to smoke every day?	1 = yes 2 = no

QUITSMOK	When quit smoking	1 = <1 week ago 2 = 1-4 weeks ago 3 = 1-3 months ago 4 = 4-12 months ago 5 = >1 year ago
----------	-------------------	--

Childhood Determinants of Adult Health (CDAH) Study (Australia, 1 visit)

Study description

Visit	1
Study visit name	CASHFS
Year of exam	1985
Description	Baseline survey children
Age mean (range), year	11.4 (6.3, 16.2)

Childhood/adolescent smoking intensity variables

Question	Annotation	Responses
A_17	Have you ever smoked even part of a cigarette?	1 = no 2 = yes, a few puffs 3 = yes, <10 lifetime 4 = yes, >10 lifetime
A_18	How many cigarettes have you smoked in the last 7 days?	
A_19	How long have you been smoking regularly?	1 = none 2 = just started 3 = 1-6 mo 4 = 7-12 mo 5 = 1-2 y 6 = 2-4 y 7 = >4 y

Prevention of High Blood Pressure in Children (PHBPC, Minnesota, 1 visit)

Study description

Study visit name	MP19
Year of exam	1988-1990
Description	Post high school
Age mean (range), year	18.3 (16.3, 19.9)

Childhood/adolescent smoking intensity variables

1) MP19, 1988-1990, Post high school survey

Variable Name	Question	Responses
PHB133Q1	Q1 Ever smoke a cigarette?	1 = no 2 = yes, only once 3 = yes, >1 time
PHB133Q7	Q7: How frequently have smoked cigarettes during the past 30 days?	1 = not at all 2 = <1 cigarettes per day 3 = 1-5 cigarettes per day 4 = ~ 0.5 pack per day 5 = 1 pack per day 6 = 1.5 packs per day 7 = ≥2 packs per day 9 = unknown

PRINCETON Lipid Research Clinics Study (Cincinnati, 1 visit)

Study description

Study visit name	Visit 2
Year of exam	1976-1978
Description	lipid study among students
Age mean (range), year	12.6 (6.5, 19.3)

Childhood/adolescent smoking intensity variables

1) Visit 2, 1976-1978, lipid study among students

Variable Name	Question	Responses
CIGARETTES_EVER	Ever smoke	1 = current smoker 2 = never smoker 3 = quit>2 y ago 4 = quit<2 y ago
CIGARETTES_DAY	No. cigarettes per day?	___ (continuous) 99 = unknown

National Growth and Health Study (NGHS, Cincinnati, 5 visits, female only)

Study description

Visit	1	2	3	4	5
Study visit name	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10
Year of exam	1992	1993	1994	1995	1996
Description	14-15 y girls survey	15-16 y girls survey	16-17 y girls survey	17-18 y girls survey	18-19 y girls survey
Age mean (range), year	15.0 (13.9, 16.3)	16.0 (14.9, 17.4)	17.0 (15.8, 18.3)	18.0 (16.9, 19.3)	19.0 (17.6, 19.9)

Childhood/adolescent smoking intensity variables

1) Visit 6

Variable Name	Question	Responses
SMK30AMT	During the past 30d (on the days you smoked), how many cigarettes smoked per day?	1 = none 2 = <1 per day 3 = 1 per day 4 = 2-5 per day 5 = 6-10 per day 6 = 11-20 per day 7 = >20 per day
SMKAMT	How much do you smoke cigarettes?	1 = never smoked 2 = once or twice 3 = a few times 4 = < once/mo

		5 = weekly but not every day 6 = every/nearly every day
SMK30DAY	During the past 30 days, on how many days did you smoke cigarettes?	1 = none 2 = 1 or 2 days 3 = 3 to 5 days 4 = 6 to 9 days 5 = 10 to 19 days 6 = 20 to 29 days 7 = all 30 days

2) Visit 7

Variable Name	Question	Responses
NCIGDAY	During the past 30d (on the days you smoked), how many cigarettes smoked per day?	___ (continuous) 99 (missing) (write "0" if you did not smoke during the last 30 days.)
SMKAMT	How much do you smoke cigarettes?	1 = never smoked 2 = once or twice 3 = a few times 4 = < once/mo 5 = weekly but not every day 6 = every/nearly every day
SMK30DAY	During the past 30 days, on how many days did you smoke cigarettes?	1 = none 2 = 1 or 2 days 3 = 3 to 5 days 4 = 6 to 9 days 5 = 10 to 19 days 6 = 20 to 29 days 7 = all 30 days

3) Visit 8

Variable Name	Question	Responses
NCIGDAY	During the past 30d (on the days you smoked), how many cigarettes smoked per day?	___(continuous) 99 (missing) (write "0" if you did not smoke during the last 30 days.)
SMKAMT	How much do you smoke cigarettes?	1 = never smoked 2 = once or twice 3 = a few times 4 = < once/mo 5 = weekly but not every day 6 = every/nearly every day
SMK30DAY	During the past 30 days, on how many days did you smoke cigarettes?	1 = none 2 = 1 or 2 days 3 = 3 to 5 days 4 = 6 to 9 days 5 = 10 to 19 days 6 = 20 to 29 days 7 = all 30 days

4) Visit 9

Variable Name	Question	Responses
NCIGDAY	During the past 30d (on the days you smoked), how many cigarettes smoked per day?	___(continuous) 99 (missing) (write "0" if you did not smoke during the last 30 days.)
SMKAMT	How much do you smoke cigarettes?	1 = never smoked 2 = once or twice 3 = a few times 4 = < once/mo 5 = weekly but not every day

		6 = every/nearly every day 7 = in the past but not now
SMK30DAY	During the past 30 days, on how many days did you smoke cigarettes?	1 = none 2 = 1 or 2 days 3 = 3 to 5 days 4 = 6 to 9 days 5 = 10 to 19 days 6 = 20 to 29 days 7 = all 30 days

5) Visit 10

Variable Name	Question	Responses
NCIGDAY	During the past 30d (on the days you smoked), how many cigarettes smoked per day?	___ (continuous) 99 (missing) (write "0" if you did not smoke during the last 30 days.)
SMKAMT	How much do you smoke cigarettes?	1 = never smoked 2 = once or twice 3 = a few times 4 = < once/mo 5 = weekly but not every day 6 = every/nearly every day 7 = in the past but not now
SMK30DAY	During the past 30 days, on how many days did you smoke cigarettes?	1 = none 2 = 1 or 2 days 3 = 3 to 5 days 4 = 6 to 9 days 5 = 10 to 19 days 6 = 20 to 29 days 7 = all 30 days

Sodium Potassium Study (NaKS, Minnesota, 1 visit)

Study description

Visit	1
Study visit name	MNN1
Year of exam	1986-88
Description	School survey
Age mean (range), year	13.3 (10.5, 16.0)

CSE variable

1) MNN1, 1986-88, School survey

Question	Annotation	Responses
NAK016Q36	Smoke cigarettes now?	1 = yes 2 = no 9 = unknown
NAK016Q37	How many cigarettes smoked per day during the past 30 days?	1 = <1 per day 2 = 1-5 per day 3 = 6-10 per day 4 = 11-20 per day 5 = >20 per day 9 = unknown

Young Finns Study (YFS, Finland, 5 visits, ages 12 and over, only)

Study description

Visit	1	2	3	4	5
Study visit name	Y1980	Y1983	Y1986	Y1989	Y1992
Year of exam	1980	1983	1986	1989	1992
Description	Baseline	FU1	FU2	FU3	FU4
Age mean (range), year	10.8 (2.7, 18.9)	12.2 (5.7, 18.9)	13.7 (8.8, 18.8)	15.2 (11.8, 18.8)	16.8 (14.9, 18.9)

CSE variable

1) Y1980

Variable Name	Question	Responses
STUPAK80	Habitual smoking (habitual: ≥ 1 cigarette per day)	1 = not habitual 2 = yes 9 = never smoked
TUPKOK80	Has tried smoking	1 = not even tried 2 = at least tried
NYKTUP80	Current smoking	1 = smokes 1+ time per day 2 = smokes 1+ time per week 3 = smokes <1 per week 4 = quit or attempt to quit 9 = never smoked

TLAKKO80	Time from latest instance of smoking if attempting to quit	1 = <1 week 2 = 1 week to 2 mo 3 = 2 to 6 mo 4 = >6 mo 9 = never or not attempting to quit
TUPSAL80	Daily smoking (No. cigarettes)	___ (continuous) currently or before quitting 99 = never smoked or not habitually
TUPISL80	Daily smoking (No. self-rolled cigarettes)	___ (continuous) currently or before quitting 99 = never smoked or not habitually

2) Y1983

Variable Name	Question	Responses
STUPAK83	Habitual smoking (≥ 1 cigarette per day)	1 = not habitual 2 = yes 9 = never smoked
TUPKOK83	Has tried smoking	1 = not even tried 2 = at least tried
NYKTUP83	Current smoking	1 = smokes 1+ time per day 2 = smokes 1+ time per week 3 = smokes <1 per week 4 = quit or attempt to quit 9 = never smoked
TLAKKO83	Time from latest instance of smoking if attempting to quit	1 = <1 week 2 = 1 week to 2 mo 3 = 2 to 6 mo 4 = >6 mo 8 = not attempting to quit 9 = never smoked
TUPSAL83	Daily smoking (No. cigarettes)	___ (continuous) currently or before quitting

		88 = n/a: smokes habitually 98 = not smoked habitually 99 = never smoked
TUPISL83	Daily smoking (No. self-rolled cigarettes)	__ (continuous) currently or before quitting 88 = n/a: smokes habitually 98 = not smoked habitually 99 = never smoked

3) Y1986

Variable Name	Question	Responses
STUPAK86	Habitual smoking (≥ 1 cigarette per day)	1 = not habitual 2 = yes
TUPKOK86	Has tried smoking	1 = has not even tried 2 = at least tried
NYKTUP86	Current smoking	1 = smokes 1+ time per day 2 = smokes 1+ time per week 3 = smokes <1 per week 4 = quit or attempt to quit 5 = never smoked
TUPSAL86	Daily smoking (No. cigarettes)	__ (continuous) currently or before quitting
TUPISL86	Daily smoking (No. self-rolled cigarettes)	__ (continuous) currently or before quitting

4) Y1989

Variable Name	Question	Responses
TUPNYK89	Current smoking	1 = smokes 1+ time per day 2 = smokes 1+ time per week 3 = smokes <1 per week 4 = quit or attempt to quit 5 = never smoked
TUPSAL89	Daily smoking (No. cigarettes)	__ (continuous) 99 = never or not habitually
TUPISL89	Daily smoking (No. self-rolled cigarettes)	__ (continuous) 99 = never or not habitually

5) Y1992

Variable Name	Question	Responses
NYKTUP92	Current smoking	1 = smokes 1+ time per day 2 = smokes 1+ time per week 3 = smokes <1 per week 4 = quit or attempt to quit 5 = never smoked
TUPSAL92	Daily smoking (No. cigarettes)	___ (continuous) 99 = never or not habitually
TUPISL92	Daily smoking (No. self-rolled cigarettes)	___ (continuous) 99 = never or not habitually