

Symptoms of Tobacco Dependence After Brief Intermittent Use

The Development and Assessment of Nicotine Dependence in Youth–2 Study

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Objective: To extend the findings of the first Development and Assessment of Nicotine Dependence in Youth study by using diagnostic criteria for tobacco dependence and a biochemical measure of nicotine intake. The first study found that symptoms of dependence commonly appeared soon after the onset of intermittent smoking.

Design: A 4-year prospective study.

Setting: Public schools in 6 Massachusetts communities.

Participants: A cohort of 1246 sixth-grade students.

Interventions: Eleven interviews.

Main Outcome Measures: Loss of autonomy over tobacco as measured by the Hooked on Nicotine Checklist, and tobacco dependence as defined in *International Classification of Diseases, 10th Revision (ICD-10)*.

Results: Among the 217 inhalers, 127 lost autonomy over their tobacco use, 10% having done so within 2 days and 25% having done so within 30 days of first inhaling from a cigarette; half had lost autonomy by the time they were smoking 7 cigarettes per month. Among the 83 inhalers who developed ICD-10–defined dependence, half had done so by the time they were smoking 46 cigarettes per month. At the interview following the onset of ICD-10–defined dependence, the median salivary cotinine concentration of current smokers was 5.35 ng/mL, a level that falls well below the cutoff used to distinguish active from passive smokers.

Conclusions: The most susceptible youths lose autonomy over tobacco within a day or 2 of first inhaling from a cigarette. The appearance of tobacco withdrawal symptoms and failed attempts at cessation can precede daily smoking; ICD-10–defined dependence can precede daily smoking and typically appears before consumption reaches 2 cigarettes per day.

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AMONG HIS MANY IMPORTANT contributions, Russell¹⁻⁴ outlined a “model of smoking behavior” in a series of influential essays published more than 30 years ago. In this model, initial experimentation with smoking is motivated by psychosocial factors and curiosity, but quickly the “pharmacological rewards” of nicotine in the form of “indulgent,” “sedative,” or “stimulation” smoking provide the motivation for use prior to dependence. According to Russell, “After 3 or 4 years of intermittent smoking, regular adult-type dependent smoking sets in.”³ When intake exceeds 20 cigarettes per day, “addictive smoking” ensues and the “smoker experiences withdrawal symptoms whenever he has gone 20 to 30 minutes without smoking.”³ This classic description of the natural history of nicotine

dependence was only rarely challenged⁵ through the end of the 20th century.

Russell was a pioneer in recognizing the impact of the first cigarette smoked during adolescence: “It takes no more than three or four casual cigarettes in this sensitive period virtually to ensure evolution to regular dependent smoking within a few years.”^{3,6} In an era when smoking was the social norm, Russell stated that “only about 15 per cent of those who have more than one cigarette avoid becoming regular smokers.”³ Given his assertion that occasional and intermittent adult smokers were truly nondependent,⁷ it was never clear why smoking a few cigarettes had such a profound influence, which he equated to “a 40-year sentence.”⁷

The model describing dependence as a late sequela of regular heavy smoking was challenged in 2000 with the publication

of the first prospective study of the natural history of nicotine dependence.⁸ The Development and Assessment of Nicotine Dependence in Youth (DANDY) study reported that symptoms of dependence develop soon after the first cigarette, with no minimum requirement of the number of cigarettes smoked or the frequency or duration of use.^{8,9} Each of the 11 dependence symptoms examined was reported by at least 1 youth within 2 weeks of initiating monthly smoking. The median frequency of use at symptom onset was 4 days per month, and the median quantity was 8 cigarettes per month. The data made a Poisson curve with symptoms typically presenting immediately after the initiation of intermittent smoking.

The DANDY study reported another unexpected finding: withdrawal symptoms among nondaily smokers. Conventional wisdom held that withdrawal symptoms appeared only with moderate levels of daily smoking,³ and their presence required that an individual maintain a constant presence of nicotine in the body, which takes at least 5 cigarettes per day.¹⁰⁻¹²

The Nicotine Dependence in Teens (NDIT) study in Quebec, Canada, replicated and extended the DANDY study by demonstrating that withdrawal symptoms can appear before the onset of daily smoking¹³ and that *International Statistical Classification of Diseases, 10th Revision (ICD-10)*, diagnostic criteria for tobacco dependence appear during intermittent tobacco use.^{13,14} Using survival analysis and measuring from the first puff, the NDIT study reported that 25% of all puffers had advanced to inhalation by 1.5 months, to craving by 4.5 months, to monthly smoking by 8.8 months, to other withdrawal symptoms by 11 months, to weekly smoking by 19.4 months, and to *ICD-10*-defined dependence (the presence of 3 criteria) by 40.6 months.¹⁵ These estimates overstate the true latencies, as they are based on the date of the survey following each event. During the 3 months between the first inhalation (latency of 1.5 months) and the first craving (4.5 months), youths who were not yet monthly smokers smoked fewer than 3 cigarettes (the latency to monthly smoking was 8.8 months). The NDIT data suggest that, for adolescents, inhaling smoke from only 1 or 2 cigarettes is sufficient to induce craving, the most common symptom of *ICD-10*-defined dependence.

The empirical data from the DANDY and NDIT studies necessitated a reexamination of Russell's model. Derived from these data, the sensitization-homeostasis theory asserts that the neurophysiological processes that underlie nicotine dependence are set in motion by the first cigarette.¹⁶ Relieving physiologically driven craving and withdrawal becomes the primary motivator for those who smoke only a few cigarettes each month. Initially, craving and withdrawal symptoms can be kept at bay by smoking 1 cigarette every week or so, but as tolerance builds, the duration of relief provided by each cigarette shortens progressively. If the smoker does not restrain consumption, he or she may experience "withdrawal symptoms whenever he [or she] has gone 20 to 30 minutes without smoking," as Russell observed.³

Thus, the literature entertains 2 models of the development of dependence. The purpose of the Development and Assessment of Nicotine Dependence in Youth-2 (DANDY-2) study was to test the sensitization-homeo-

stasis theory by determining if craving, withdrawal, and other symptoms of nicotine dependence appear during the period of intermittent smoking that typically precedes daily smoking. The DANDY-2 study improved on its predecessor by employing a biochemical measure of nicotine intake, assessing *ICD-10*-defined tobacco dependence, using survival analyses, measuring latency from the first self-reported inhalation of nicotine, and considering the impact of 45 potential smoking risk factors.

METHODS

This was a 4-year longitudinal study of a cohort of sixth-grade students. All procedures were approved by the University of Massachusetts Medical School institutional review board and local school administrators.

STUDY POPULATION

Subjects were recruited from schools in 6 urban and suburban Massachusetts communities selected to provide a racially and ethnically diverse sample. The study was publicized through the schools. Informed consent was obtained from the subject and one of his or her parents. The only exclusionary criterion was an inability on the part of the student to communicate in English. (Smoking status did not determine eligibility.) Subjects who changed schools were retained if the new school was within a 1-hour drive and the new school consented.

PROCEDURES

Each year from January 2002 to January 2006, 3 private, confidential, face-to-face, scripted interviews were conducted with each subject in the schools for a total of 11 waves of data collection. Interviewers were trained to facilitate the accurate recall of dates and events.^{17,18} A calendar of personal events was created for each tobacco user to establish the timing and sequence of symptom and tobacco use milestones. Milestones included the first puff; first inhalation; the onset of monthly, weekly, and daily smoking; the endorsement of items on the Hooked on Nicotine Checklist (HONC); and fulfillment of the *ICD-10* criteria for tobacco dependence. Specific dates for milestones were recorded when available. Otherwise, if a milestone occurred at the beginning of the month, it was recorded as having occurred on the 7th; in the middle, as the 15th; and at the end of the month, as the 25th. The shortest reported latency times were least subject to recall bias. If events were widely spaced, the subject had to independently recall 2 dates. However, if events occurred on the same day or on sequential days, the date of the second event was computed by adding the appropriate number of days to that of the first event.

Reactions to the first time inhaling were recorded at the interview immediately following that event. Demographic data were collected at the first interview. At each interview, the subject's record was updated concerning the types of tobacco used; the duration, frequency, and amount of use; and periods of abstinence.

Saliva samples were collected at each interview from subjects who reported any tobacco use during the preceding 30 days, and the number of cigarettes smoked during the previous 3 days was recorded. Cotinine, a metabolite of nicotine, has a half-life of 17 hours and can be detected in saliva for several days after the last cigarette.^{19,20} Subjects who refused to provide a saliva sample remained in the study. Saliva samples were centrifuged, frozen at -20°C, and shipped on dry ice to an independent laboratory for blind cotinine quantification using gas-liquid chromatography.²¹

Table 1. Interview Questions Used to Assess Loss of Autonomy and Diagnosis of Tobacco Dependence

Question
A strong desire or sense of compulsion to take tobacco (any 1 symptom) ^a
Have you ever had strong cravings to smoke? ^b
Have you ever felt like you were addicted to tobacco? ^b
Have you ever felt like you really needed a cigarette? ^b
Is it hard to keep from smoking/chewing in places where you are not supposed to, like school? ^b
Difficulties in controlling tobacco-taking behavior in terms of its onset, termination, or levels of use (any 1 symptom) ^a
Have you ever tried to quit smoking but couldn't do it? ^b
Do you smoke now because it is really hard to quit? ^b
Are you smoking more now than you planned to when you started?
A physiological withdrawal state (any 2 symptoms) ^a
When you have tried to stop smoking or when you haven't been able to smoke. . .
Did you find it hard to concentrate because you couldn't smoke? ^b
Did you feel more irritable because you couldn't smoke/chew? ^b
Did you feel a strong need or urge to smoke/chew? ^b
Did you feel nervous, restless or anxious because you couldn't smoke/chew? ^b
Do you smoke to avoid withdrawal symptoms?
Evidence of tolerance (any 1 symptom) ^a
Do you still get the same effect from smoking a cigarette as you did when you started?
Do you have to smoke more now to feel relaxed than you used to?
Compared to when you started smoking, do you need to smoke more now to be satisfied?
Neglect of alternative pleasures (any 1 symptom) ^a
Do you find that you are spending more of your free time trying to get cigarettes?
Have you cut down on your physical activities or sports because you smoke?
Do you ever give up going places or doing things because smoking isn't allowed?
Have you stopped hanging out with certain friends because you smoke?
Use despite harm (any 1 symptom) ^a
Has a doctor or nurse told you that you should quit smoking because it was damaging your health?

^a International Statistical Classification of Diseases, 10th Revision, criterion for tobacco dependence; 3 or more are required during the previous year for a diagnosis.¹⁴

^b From the Hooked on Nicotine Checklist.²³ A loss of autonomy is indicated by endorsement of any of these items.

MEASURES

Outcome measures included diminished autonomy over nicotine and an ICD-10–defined diagnosis of nicotine dependence. Full autonomy is lost when the sequelae of tobacco use, either physical or psychological, present a barrier to quitting.²² Eleven items were used to assess autonomy in the first DANDY study; 10 of these compose the HONC (Table 1).²² The HONC has demonstrated concurrent and predictive validity, good test-retest reliability, a stable single-factor structure, and excellent internal reliability, with a Cronbach α of 0.90 to 0.94 in 4 studies of adolescents.²²⁻²⁹ Now used in 12 languages, the HONC has been more thoroughly evaluated with adolescents than any other measure of nicotine dependence.²³

With the appearance of the first HONC symptom, the smoker has lost full autonomy. The date of onset of each HONC symptom, and the frequency (days per 28-day month) and amount

Table 2. Self-reported Tobacco Use

Tobacco Use	Subjects at the First Interview, % (n = 1246)	Subjects at Any Time During Follow-up, %
Puffed on a cigarette	15.4	29.7
Inhaled	6.1	17.4
Tried > 1 cigarette	3.9	13.7
Tried a cigar	2.3	10.5
Tried chewing tobacco	0.6	3.3
Used tobacco monthly	1.8	11.5
Used tobacco weekly	1.3	10.4
Used tobacco daily	0.7	7.5

of tobacco use (cigarettes per month) at the time of the first HONC symptom were recorded. The severity of diminished autonomy was computed by summing the cumulative number of endorsed HONC items (0-10). To determine if the loss of autonomy is associated with smoking progression, we used the χ^2 test to compare daily smoking among subjects who had no HONC symptoms and those who had 1 or more symptoms. The populations for these analyses were all subjects who had puffed on a cigarette and, separately, those who had inhaled.

We used a 22-item interview to establish an ICD-10–defined diagnosis of tobacco dependence; 3 or more symptoms are required for a diagnosis (Table 1).¹⁴ We recorded the date when the ICD-10 criteria were first attained and the level of tobacco use at that time.

DATA ANALYSIS

Fewer than half of youths inhale from their first cigarette.³⁰ As dependence symptoms would not be expected in the absence of drug exposure, we limited our analyses to subjects who reported inhaling and calculated latencies (the number of days between 2 events) by subtracting the date of inhalation from the date of subsequent milestones.

For the 6 subjects who reported monthly use prior to inhaling, the calculation of the latency to monthly smoking produced a negative number. For these 6 subjects, the date of the first inhalation was used as the date of the onset of monthly smoking. Two subjects reported HONC symptoms after puffing but before the reported date of inhalation; this also produced latency values with negative time units. On the assumption that nicotine exposure occurred earlier than reported, the date for inhaling was recorded as missing, thereby excluding these 2 subjects from the analyses of latency. The only subject who had used chewing tobacco regularly before inhaling was dropped from the analyses of latency, as nicotine exposure preceded the first inhalation.

Due to differences in age, race, sex, metabolism, and the way the cigarette is smoked (eg, number of puffs and puff volume), it is not possible to translate a cotinine level into cigarettes smoked at the individual level.³¹ In adults, cotinine levels show a nonlinear association with cigarette consumption across the range from light to heavy smoking ($r=0.44$) but show a linear association when consumption equals fewer than 10 cigarettes in the previous 17 hours ($r=0.53$).³¹ McNeill et al³² reported a mean salivary cotinine level of 201 ng/mL among adolescents who smoked an average of 210 cigarettes per month. Based on this rough correspondence, we found it convenient to use the same x-axis intervals to display self-reported consumption (cigarettes per month) and cotinine levels in the figures so that the curves' shapes could be compared, but this should not be misinterpreted as indicating that cotinine levels are equivalent to cigarettes smoked per month.

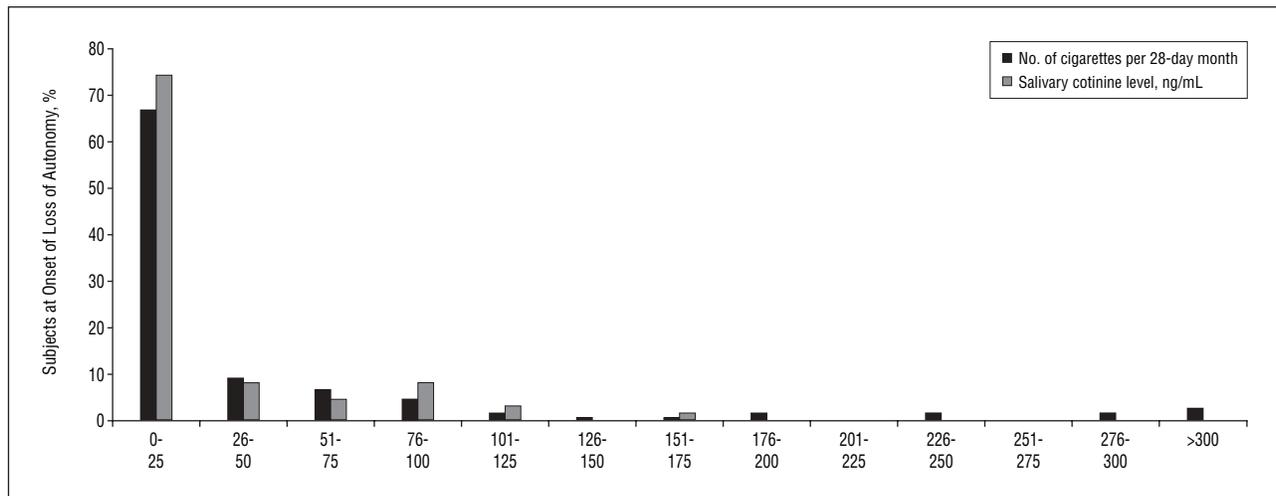


Figure 1. Percentage distribution of cotinine values and self-reported tobacco consumption at the loss of autonomy. At the interview following the onset of symptoms, subjects provided a saliva sample for cotinine determination and reported what their cigarette consumption had been when they first experienced a symptom. For the salivary cotinine level, the x-axis represents cotinine concentration in nanograms per milliliter ($n=62$); for tobacco consumption, it represents cigarettes per 28-day month ($n=106$). The sample size for cotinine determination is smaller than tobacco consumption because saliva was not collected if the subject had quit smoking or declined our request for a sample.

A Kaplan-Meier analysis was used to determine the cumulative probability of reaching each milestone, taking into account individual differences in length of exposure (tobacco use).¹⁵ Subjects were assumed to be at risk for the onset of dependence from the first inhalation. Subjects who continued to smoke until their last interview were considered to be censored at that interview date if they had not yet achieved the outcome of interest. Subjects who discontinued smoking and did not restart before their last interview were considered to be censored 30 days after their last cigarette (allowing time for the emergence of withdrawal symptoms).

RESULTS

A total of 1246 of 1808 students (68.9%) enrolled in sixth grade volunteered for the study. Of these, 77.8% (970) were retained through 11 waves of data collection; 208 subjects moved away. The sample was 51.9% female, with a mean age of 12.2 years (range, 11-14 years) at the first interview. The population was 70.2% white, 18.4% Hispanic, 5.0% black, 3.7% Asian, and 2.7% American Indian. Lifetime tobacco use is given in **Table 2**; only 1.1% of subjects had used tobacco in the previous 30 days at baseline. The 370 subjects who puffed on a cigarette had an average age of 11.7 years at first puff (range, 2.5-16.7; SD, 3.0 years), and 217 inhalers had an average age at first inhalation of 12.8 years (range, 2.5-17.1; SD, 2.6 years). Of the 217 inhalers who are the focus of this analysis, 127 (58.5%) lost autonomy and 83 (38.2%) developed *ICD-10*-defined dependence.

Percentiles and medians are reported when the data had a Poisson distribution. The 25th percentile for the frequency of smoking when autonomy was lost was 1 day per month ($n=106$; median, 5.5 days per month; range, 0-28 days); for the quantity of tobacco consumed, it was 1 cigarette per month (median, 7 cigarettes; range, 0-560 cigarettes). The 25th percentile salivary cotinine level at the interview following the first HONC symptom was 0.4 ng/mL ($n=61$; median, 1.9 ng/mL; range, 0-168.5 ng/mL).

Figure 1 compares self-reported tobacco use and cotinine levels at the time when autonomy was lost. Saliva was not collected from subjects who refused or had not smoked in the previous 30 days. Thus, the cotinine data are based on a subset of subjects for whom tobacco use data were recorded. Both curves indicate that the loss of autonomy occurred primarily at the lowest level of nicotine intake.

The 25th percentile for the frequency of use at the onset of *ICD-10*-defined dependence was 8 days per 28-day month ($n=81$; median, 28 days; range, 0-28 days); for the quantity of cigarettes smoked, it was 8 cigarettes per month (median, 46 cigarettes; range, 0-560 cigarettes). The 25th percentile salivary cotinine level at the interview following *ICD-10*-defined dependence was 0.4 ng/mL ($n=54$; median, 5.35 ng/mL; range, 0.0-211.4 ng/mL). **Figure 2** displays both self-reported consumption and cotinine levels at the onset of *ICD-10*-defined dependence. The cotinine data show a higher concentration of subjects at the lowest intensity of consumption at the onset of *ICD-10*-defined dependence.

Table 3 compares the incidence of each of the 10 HONC symptoms and how frequently each appeared prior to the onset of daily smoking. As indicated by the second column of data, every milestone occurred in some subjects before they had advanced to daily smoking. Loss of autonomy preceded daily smoking in 70.1% of subjects who lost autonomy; *ICD-10*-defined dependence preceded daily smoking 38.6% of the time. The 10th and 25th percentiles for the latency from inhalation to the loss of autonomy were 2 and 30 days, respectively ($n=111$; range, 0-3898 days), and from inhalation to the onset of *ICD-10*-defined dependence, they were 61 and 139 days ($n=81$; range, 13-3712 days), respectively. There were no significant sex differences in latency to dependence, the loss of autonomy, or any of the 10 individual HONC symptoms.

Among subjects who had puffed on a cigarette, the loss of autonomy was associated with daily smoking with an odds ratio of 195.8 (95% confidence interval, 62-614; posi-

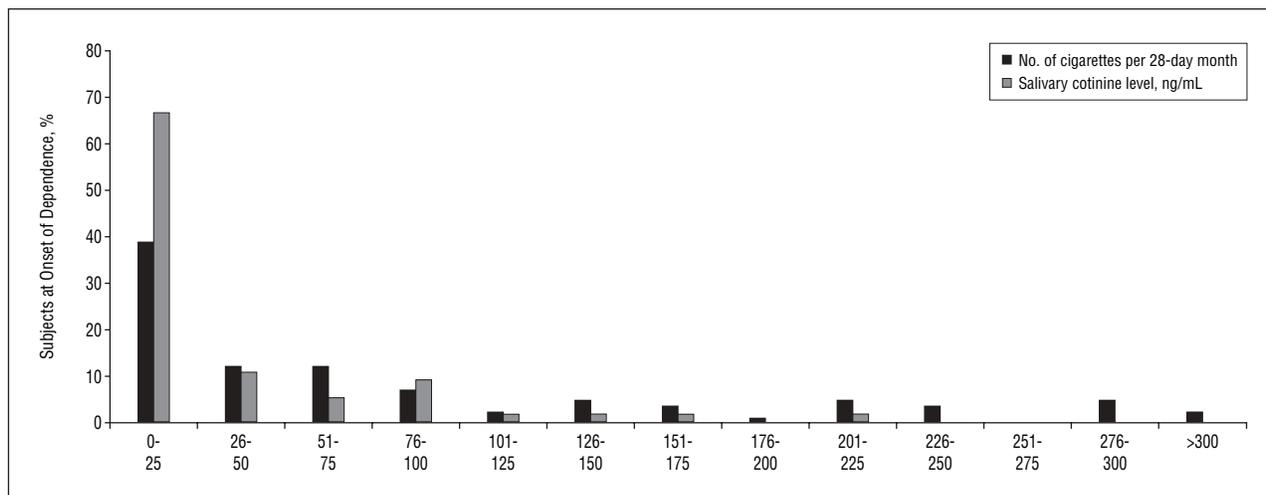


Figure 2. Percentage distribution of cotinine values and self-reported cigarette consumption at the onset of *International Statistical Classification of Diseases, 10th Revision (ICD-10)*–defined dependence. At the interview following the onset of symptoms, subjects provided a saliva sample for cotinine determination and reported what their cigarette consumption had been when they first met the criteria for *ICD-10*–defined dependence. For the salivary cotinine level, the x-axis represents the cotinine concentration in nanograms per milliliter (n=54); for cigarette consumption, it represents cigarettes per 28-day month (n=82). The sample size for cotinine determination is smaller than tobacco consumption because saliva was not collected if the subject had quit smoking or declined our request for a sample.

Table 3. Incidence of Milestones and Their Association With Daily Smoking

Milestone	Inhalers Ever Reporting Milestone, % (n = 217)	% of Time Milestone Appeared Prior to Daily Smoking
Monthly use	58.1	100
Weekly use	53.0	100
Loss of autonomy	58.5	70.1
Needed a cigarette	48.6	62.5
Craving	48.1	57.3
Daily use ^a	40.6	NA
Strong urges	37.9	46.9
Irritable	32.2	42.0
Felt addicted	36.0	40.3
Impaired concentration	28.0	40.0
<i>ICD-10</i> -defined dependence	38.2	38.6
Hard to refrain	18.2	33.3
Hard to quit	25.7	30.9
Failed quit attempt	26.6	29.8
Restless, anxious	29.0	25.8

Abbreviation: *ICD-10*, *International Statistical Classification of Diseases, 10th Revision*; NA, not applicable.

^aMilestones listed above “Daily use” typically preceded daily use and those listed below typically followed it.

tive predictive value=0.71; negative predictive value=0.99). Among those who had inhaled, the odds ratio was 83.4 (95% confidence interval, 26-265; positive predictive value=0.74; negative predictive value=0.97).

COMMENT

Ten percent of the subjects who lost autonomy over tobacco had done so within 2 days of inhaling from a cigarette for the first time. Half had done so by the time they were smoking 7 cigarettes per month. This is in excellent agreement with the first DANDY study, in which half

of those who lost autonomy had done so by the time they were smoking 8 cigarettes per month. Half of those who met the criteria for *ICD-10*–defined dependence had done so by the time they were smoking 1 to 2 cigarettes per day. The biochemical assay confirmed a very low level of tobacco use at the onset of *ICD-10*–defined dependence; the median salivary cotinine level (5.35 ng/mL) fell within the range achieved by passive smoking³³ and is well below the recommended cutoff point (15 ng/mL) for distinguishing smokers from passive smokers.²⁰ To place the cotinine data in perspective, McNeill et al³² reported that youths who smoked less than 1 cigarette per week had a mean salivary cotinine level of 13.1 ng/mL, and those who smoked 1 to 6 cigarettes per week had a mean level of 26.1 ng/mL. Our data refute the theory that a nicotine intake sufficient to sustain blood levels throughout the day is required to initiate dependence.

Tobacco dependence as defined by the *ICD-10* was diagnosed as early as 13 days after the first inhalation, and several subjects lost autonomy the day after inhaling for the first time. The appearance of symptoms of dependence within days of the initiation of smoking was first reported in DANDY and has now been confirmed by the NDI study (using the *ICD-10* diagnostic criteria), by the current study, and by an ongoing study using *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition) criteria.^{13,15,34}

Russell¹⁻⁴ was correct in recognizing the important role of first cigarettes. We believe the first inhalation is the most important tobacco-use milestone, as our data indicate that some youths experience symptoms of tobacco dependence within a day of first inhaling. Craving and withdrawal symptoms commonly appear with infrequent smoking and, as we have reported previously, can be relieved for many days by smoking a single cigarette.³⁵ Half of those who will lose their autonomy over tobacco have done so by the time they are smoking 7 or 8 cigarettes per month. The data from both the DANDY studies and the NDI study are entirely consis-

tent with the description of the natural history of nicotine dependence, as outlined in the sensitization-homeostasis theory.^{15,16}

Measuring the speed of onset in terms of the time from the first inhalation to the first symptom can give the false impression that dependence develops slowly. Two youths could lose autonomy the day after inhaling from their second cigarette, with one having a latency of 3 days and the other 3 years. The extreme variability in the spacing of the first cigarettes contributes to the large range in observed latencies (0-3898 days for the loss of autonomy). We do not know how quickly dependence could be induced in an unselected youth population under an optimal dosing schedule. When describing the onset of dependence, measures of tobacco consumption are less prone to misinterpretation than is the duration of use.

Each of the nicotine withdrawal symptoms appeared in some subjects prior to daily smoking. It may seem implausible that smoking 1 cigarette provides intermittent smokers relief from withdrawal and craving for periods that dwarf nicotine's 2-hour half-life by orders of magnitude.^{35,36} However, the nicotine obtained from 1 to 2 puffs on a cigarette will occupy 50% of the brain's nicotinic receptors,³⁷ and a single dose of nicotine increases both nor-adrenaline synthesis in the hippocampus and long-lasting potentiation of neurons (allowing them to discharge an action potential at a lower threshold of stimulation) for at least a month.^{38,39} Including the current study, 4 longitudinal^{8,13,28} and many cross-sectional studies^{5,35,40-43} have reported withdrawal symptoms in nondaily smokers.

Although intermittent and passive smoking can produce the same mean salivary cotinine levels, in theory, active smoking should produce higher spikes in brain nicotine levels. If passive smoke exposure increased the risk of dependence, we might have seen this among those exposed to smoking parents, siblings, or peers, but we did not.⁴⁴

Strengths of this study are its use of 2 outcome measures (loss of autonomy and ICD-10–defined dependence), 2 measures of smoking (smoking frequency and duration), 2 measures of exposure (self-report and biochemical assay), interviews for 11 waves of closely spaced prospective data collection; its 4-year follow-up; its collection of actual dates for tobacco use and outcome measures rather than the date of data collection; its use of survival analyses with censoring after cessation; and its consistency with previous reports.

The study's limitations are that data collection was not entirely prospective; the data are subject to recall bias; all dependence measures are self-reported; and the roles of puberty, alcohol, or other drugs were not considered. The ICD-10 does not provide a validated instrument to assess its criteria. Because the HONC has favorable psychometric properties, we used its items to assess the ICD-10 criteria, as appropriate. Our sample may not be representative of other populations or age groups. However, the nearly identical results in the first and second DANDY studies, in terms of the mean amount (8 vs 7 cigarettes per month, respectively) and frequency of smoking (4.0 vs 5.5 days per month, respectively) at the onset of lost autonomy, suggest that these values may be stable across populations.

Prudence dictates that youths must be warned that it may take only 1 cigarette to initiate a life-long dependence on tobacco. In the Teenage Attitudes and Practices Survey,⁴⁵ some adolescents who had smoked fewer than 20 cigarettes in their lifetime reported difficulty quitting. Even youth who smoke only a few cigarettes per month may need assistance to understand and overcome craving and withdrawal. This population should be the focus of future cessation research.

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Author Contributions: Dr DiFranza had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* DiFranza, Ockene, and McNeill. *Acquisition of data:* DiFranza, Hazelton, Friedman, Dussault, and Wood. *Analysis and interpretation of data:* DiFranza, Savageau, Fletcher, O'Loughlin, Pbert, McNeill, and Wellman. *Drafting of the manuscript:* DiFranza, Savageau, Fletcher, O'Loughlin, Pbert, and Wellman. *Critical revision of the manuscript for important intellectual content:* DiFranza, Savageau, Fletcher, O'Loughlin, Pbert, Ockene, McNeill, Hazelton, Friedman, Dussault, Wood, and Wellman. *Statistical analysis:* Savageau, Fletcher, and O'Loughlin. *Obtained funding:* DiFranza and Ockene. *Administrative, technical, and material support:* DiFranza and Savageau. *Study supervision:* DiFranza and Dussault.

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Youngest Civil War Soldier

Avery Brown joined the Ohio volunteer infantry at the age of 8 years 11 months; he lied about his age, claiming to be 12.

—From University of South Dakota, National Music Museum report