

Nicotine Intake in Cigarette Smokers in England: Distribution and Demographic Correlates

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Abstract

Documenting smoke intake by objective biochemical markers is important for quantification of exposure to toxins. The aim of this report is to show the most definitive distribution of the nicotine metabolite, cotinine, yet available from English smokers in the period before implementation of the legislation banning smoking in indoor public areas. A total of 6,423 cigarette smokers, ages 16 years and above, taking part in the Health Survey for England between 1998 and 2003 provided a saliva cotinine value. Data on cigarette consumption, age, gender, social class, deprivation (as indicated by manual or nonmanual occupation, car ownership, and housing tenure), marital status, and region were collected. Cotinine concentrations showed no overall trend over the study period. The mean value was 289.15 ng/mL (SD 174.43); excluding

those who had not smoked in the past 24 hours, the mean value was 302.08 ng/mL (SD 168.78). A higher cotinine concentration was associated with being middle-aged (peaking at 40 years), being male, being single, greater economic deprivation, and not living in London. After adjusting for cigarette consumption, higher values were associated with middle age, being male, and greater deprivation. This study provides the most complete picture yet of the smoke intake of cigarette smokers in England. The fact that cotinine peaks at around the age of 40 years raises the possibility that nicotine intake continues to increase decades after a person starts to smoke. Greater nicotine intake in more deprived smokers could explain why they find it harder to stop smoking. (Cancer Epidemiol Biomarkers Prev 2008;17(12):3331–6)

Introduction

The levels of nicotine intake among current smokers provide a surrogate index of the extent of smokers' exposure to toxic substances in cigarette smoke and offer the potential to monitor any changes in intake stemming from policy initiatives, such as the recent smoke-free legislation in England. Self-reported cigarette consumption is only an approximate indicator at best of smoke intake, partly due to inaccurate reporting but also due to individual differences (in the way that cigarettes are smoked), depth and speed of inhalation, and number of puffs taken (1). Objective measures of the constituents inhaled by smokers therefore provide the most accurate representation of exposure. The most commonly used objective identifier of smoke intake is the nicotine metabolite cotinine. Between 70% and 80% of nicotine inhaled is converted to cotinine and its half-life of 16 to 20 hours makes cotinine a sensitive and specific marker of nicotine intake over the past few days (2, 3).

Several articles have documented cotinine concentrations in current smokers and examined the distribution of these scores and their association with self-reported

measures of intake (2, 4–6). However, samples are often small and drawn from hospital or university populations, or specific districts, and therefore nonrepresentative of the population of interest. This report uses combined Health Survey for England data from 1999 to 2003 to document the distribution of cotinine in the biggest nationally representative general population sample of its kind.

Smoke intake is associated with sociodemographic characteristics such as age, gender, and socioeconomic status; however, findings are inconsistent. It is not clear how far these differences go beyond what can be captured by self-reported cigarettes per day (1, 4, 7–12). The large sample size of the present study provides an opportunity to address the association between cotinine concentration and sociodemographic factors to understand further how far these characteristics are associated with objective smoke intake beyond daily cigarette consumption.

Materials and Methods

The Health Survey for England. The Health Survey for England provides annual data from a representative sample of households across the country. More details of the survey methodology can be found elsewhere (13); in brief, private households are randomly selected each year according to a multistage stratified probability sampling design. Participants complete an interview on health behaviors, personal characteristics, and health states. A nurse visits each household a few days after the interview to take a number of measurements and

Received 4/3/08; revised 8/18/08; accepted 9/11/08.

Grant support: Cancer Research UK. The Health Surveys were funded by the Department of Health. Cancer Research UK and the Department of Health had no involvement in the design of the study, the analysis or interpretation of the data, the writing of the report, or the decision to submit the report for publication.

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doi:10.1158/1055-9965.EPI-08-0296

associated questions, including obtaining a saliva sample for cotinine assay.

Sample. All self-reported adult cigarette smokers, ages 16 years and above, who provided a valid saliva cotinine value between 1998 and 2003 were included in the current sample. This is the period for which saliva cotinine is available for the "core" (population representative) sample of adults. In some survey years, ethnic and older adults were oversampled and these "boosted" samples were excluded from analyses. Pipe and cigar smokers were also excluded from analyses, as were participants using nicotine replacement therapy products. Finally, participants were asked on two occasions—during the initial interview and the nurse visit (see below)—whether they were smoking cigarettes, pipes, or cigars. When these responses were inconsistent with each other, participants were excluded to ensure that a change in smoking status, misclassification, or misreporting did not affect the interpretation of cotinine value. After these exclusions ($n = 2,340$), the total sample consisted of 6,423 current cigarette smokers. Cotinine values among non-current smokers in the Health Survey for England have been reported in previous articles (14, 15).

Measures

Saliva Cotinine. A saliva specimen was sought from all participants during the nurse's visit. Consenting individuals (98% of those who took part during the nurse's visit) placed a dental roll in the mouth until it was saturated with saliva. This was then sent for analysis using an established rapid gas chromatographic technique with a detection limit of 0.1 ng/mL (16). Internal quality control checks were run to ensure the stability of results over time (17-22). Valid cotinine values were obtained from saliva samples with sufficient volume to undertake the assay and with no evidence of contamination (82% of samples collected).

Smoking. The question "Do you smoke cigarettes at all nowadays" was used to identify current cigarette smokers at the initial interview. During the nurse's visit, participants were asked the screening question "Can I ask, do you smoke cigarettes, cigars or a pipe at all these days," with the response options "Yes, cigarettes"; "Yes, cigars"; "Yes, pipe"; and "No." During the nurse's visit, participants were also asked when they last smoked a cigarette. This question was used to identify smokers who had smoked within the last 24 h before the cotinine assay. Data on cigarette consumption were collected at the initial interview only. Interviewers also asked current smokers "About how many cigarettes a day do you usually smoke on weekdays?" and "About how many cigarettes do you usually smoke at weekends?" These responses were then multiplied by 5 and 2, respectively, before combining and dividing by 7 to give the average number of cigarettes smoked per day in a week.

Sociodemographic Variables. Sociodemographic factors assessed were gender, age, region (government office region), marital status (single, married, separated, divorced, and widowed), and social class [I, professional occupations; II, managerial and technical occupations; III(N), skilled occupations nonmanual; III(M), skilled occupations manual; IV, partly skilled occupations; and V, unskilled occupations]. In addition, a composite index

of household deprivation was computed by summing data on head of household's occupation (nonmanual = 0/manual = 1), access to a car (car = 0/no car = 1), and housing tenure (owner-occupied housing = 0/rented = 1). Scores therefore ranged from 0 in the most affluent households to 3 in the most deprived. Self-assigned ethnicity was requested in the Health Survey for England; however, the number of ethnic minority participants in the core sample was low and therefore ethnicity has not been included as a focus in this report.

Statistical Analysis. The linear planned comparison in an ANOVA was used to assess change in mean cotinine values between 1998 and 2003 and to establish whether data from these years could reasonably be combined. Histograms are used to present the distribution of cotinine. Means, SD, and percentiles of the cotinine distribution were also calculated. Sociodemographic determinants of cotinine concentrations were examined using a series of ANOVAs with a separate ANOVA for each determinant. When appropriate, linear and polynomial contrasts were used to test for the shape of functions relating quantitative variables with cotinine. Then, to examine the independent association of these factors with cotinine, they were all combined in a single multifactorial ANOVA. Finally, the multifactorial ANOVA was repeated, including daily cigarette consumption (split into seven consumption categories; see Table 2) as a factor. Because body mass index (derived from height and weight data obtained during the nurse's visit) has been found to be associated with cotinine concentrations, a further analysis was undertaken with this variable included (23). As the sample was large and multiple comparisons were done, the α level was set to $P < 0.01$.

Results

Table 2 shows the mean cotinine values of self-reported smokers at each Health Survey for England survey between 1998 and 2003. Although there was some fluctuation, there was no evidence of a significant linear trend.

Figure 1 displays the distribution of cotinine values in all current cigarette smokers. The mean overall cotinine value (289.15 ng/mL) and deciles of the distribution are displayed in Table 1. A smoker with a cotinine value of less than 59 ng/mL is therefore in the bottom 10% of smokers on this cotinine distribution, whereas a smoker with a cotinine value of more than 517 ng/mL is in the top 10%. The distribution was approximately in the reference range but with a slightly higher proportion of lower cotinine values. Cotinine values are likely to be low among occasional smokers who may not have smoked recently (339 of the 6,423 current smokers in the sample reported smoking less than one cigarette per day). The sample was therefore limited to only those who had smoked in the last 24 hours (Fig. 2), which largely eliminated the negative skew in the distribution. The mean cotinine value of these recent smokers was 302.08 ng/mL, and again deciles are presented in Table 1. Very few smokers (1.6 %) had cotinine values that would be indicative of not drawing the smoke into their lungs (<15 ng/mL).

Table 2 displays mean cotinine values as a function of a range of sociodemographic variables. All sociodemographic variables showed significant associations with

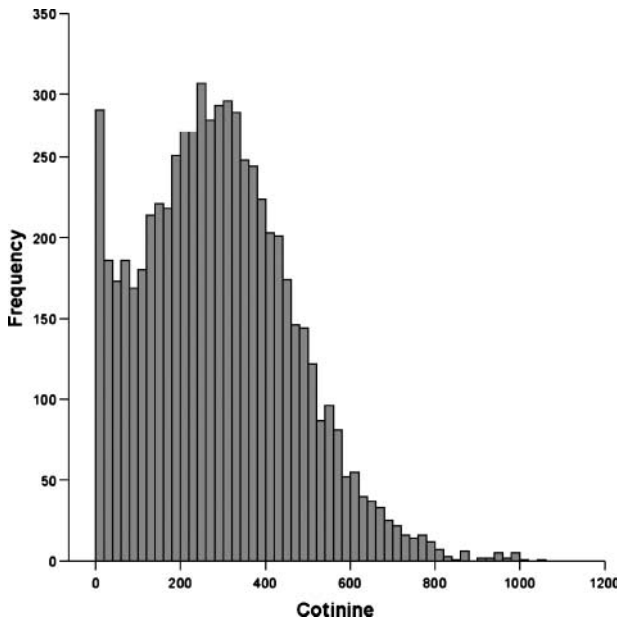


Figure 1. Distribution of cotinine among current smokers.

cotinine. Post hoc tests showed that significantly lower cotinine values were observed among women compared with men; single individuals compared with those who were married, divorced, or widowed; Londoners compared with individuals from the North West, Yorkshire, the East Midlands, and the West Midlands; and individuals with a higher social class and a lower level of deprivation than those with lower social class and higher deprivation. There was also a significant relationship between age and cotinine, although this was nonlinear, with cotinine increasing with age until around age 40 years, then decreasing from age 70 years, even when adjusted for cigarette consumption (Fig. 3).

When all sociodemographic variables were included in a single ANOVA, social class became nonsignificant and the deprivation score remained (model 1, Table 3).

When reported usual cigarette consumption was added to the model (see Fig. 4 for an illustration of cotinine by cigarettes per day), age, sex, and deprivation

Table 1. Mean cotinine values and percentile groupings by smoking status

	Current smokers	Current smokers who smoked in the last 24 h
<i>n</i>	6,423	6,085
Mean (SD)	289.15 (174.43)	302.08 (168.78)
Percentiles		
10th	59.02	85.36
20th	129.50	151.30
30th	187.42	203.90
40th	236.36	248.50
50th	279.50	289.70
60th	323.44	331.36
70th	371.58	380.42
80th	431.52	438.18
90th	516.80	522.14

remained significantly associated with cotinine value (model 2, Table 3). The curvilinear relationship between age and cotinine was maintained (linear contrast, $P = 0.36$, quadratic contrast, $P < 0.001$). There were no interactions among sociodemographic variables, or between sociodemographic variables and cigarette consumption, except for a significant age \times cigarettes per day interaction [$F_{(48, 6,119)} = 2.00$, $P < 0.0001$] with the curvilinear relationship described above observed among smokers of 10 or more cigarettes per day whereas lighter smokers showed a monotonic increase in cotinine over the age range. Including body mass index as a covariate did not change the results.

Discussion

We report on the largest sample of cotinine values among smokers in a representative population currently available. The histograms presented in this report therefore show the most accurate picture of the smoke intake of the English population of smokers. The data provide a stable benchmark of the level of smoke intake among smokers before the smoke-free legislation came into force in England and can be used for positioning individual cotinine scores along this average distribution, providing an important reference for charting relative smoke exposure. For example, a current smoker with a cotinine value of more than 500 ng/mL will likely be in the highest 10% of nicotine intake, and hence risk exposure, although differences in individual metabolism preclude definitive placement along the population distribution. When only presenting data from those smokers who report smoking in the last 24 hours, the disproportionate number of smokers with low cotinine values disappears. This confirms that there are few regular smokers

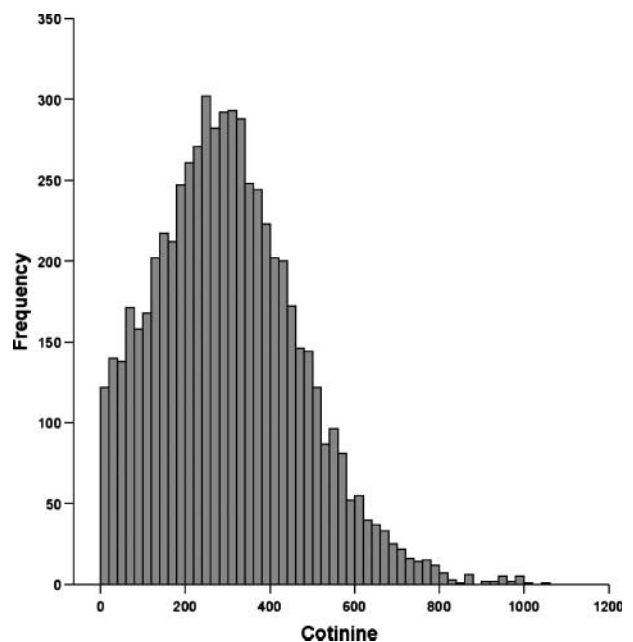


Figure 2. Distribution of cotinine among current smokers who have smoked in the last 24 h.

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Table 2. Mean cotinine values of current smokers by year, gender, age, deprivation, social class, region, and marital status (univariate analyses)

	<i>n</i>	Mean (SD)	Significance test
Year			
1998	2,377	287.00 (171.67)	$F(5, 6,417) = 2.952, P = 0.012, \text{partial } \eta^2 = 0.002$
1999	120	313.91 (164.02)	
2000	576	298.31 (168.78)	
2001	1,946	284.26 (171.05)	
2002	1,052	286.13 (184.79)	
2003	352	316.29 (189.00)	
Cigarettes per day			
0-4	733	103.83 (120.83)	$F(7, 6,388) = 333.90, P < 0.001, \text{partial } \eta^2 = 0.268$
5-9	993	198.29 (144.80)	
10-14	1,526	288.33 (152.99)	
15-19	1,127	334.31 (148.49)	
20-24	1,362	368.03 (157.69)	
25-29	261	375.03 (145.96)	
30-34	244	418.73 (166.50)	
35+	150	402.30 (168.63)	
Gender			
Men	2,687	314.96 (181.22)	$F(1, 6,421) = 102.7, P < 0.001, \text{partial } \eta^2 = 0.016$
Women	3,736	270.58 (166.94)	
Age (y)			
16-20	513	202.88 (137.53)	$F(7, 6,415) = 64.22, P < 0.001, \text{partial } \eta^2 = 0.065$
21-30	1,252	237.01 (162.00)	
31-40	1,586	299.59 (177.98)	
41-50	1,237	331.20 (175.14)	
51-60	971	328.09 (175.88)	
61-70	529	324.29 (168.63)	
71-80	274	258.82 (151.34)	
81+	61	172.03 (106.14)	
Deprivation*			
Least deprived	1,740	262.08 (171.61)	$F(3, 6,419) = 25.66, P < 0.001, \text{partial } \eta^2 = 0.012$
2	2,364	289.21 (177.35)	
3	1,488	304.76 (166.78)	
Most deprived	831	317.70 (177.56)	
Social class[†]			
I	207	251.19 (157.82)	$F(5, 6,236) = 18.97, P < 0.001, \text{partial } \eta^2 = 0.015$
II	1,507	262.30 (175.33)	
IIIN	902	273.77 (171.13)	
IIIM	1,916	305.56 (174.09)	
IV	1,260	306.97 (171.66)	
V	450	316.13 (174.76)	
Region			
North East	454	300.34 (158.93)	$F(8, 6,339) = 4.26, P < 0.001, \text{partial } \eta^2 = 0.005$
North West	1,009	300.17 (169.67)	
Yorkshire	545	300.11 (166.68)	
West Midlands	635	299.75 (172.92)	
East Midlands	655	300.57 (174.58)	
Eastern	712	286.62 (187.88)	
London	697	263.47 (174.30)	
South East	961	279.29 (175.83)	
South West	740	279.27 (177.51)	
Marital status			
Single	2,168	248.10 (169.00)	$F(4, 6,416) = 49.76, P < 0.001, \text{partial } \eta^2 = 0.030$
Married	2,895	307.51 (173.07)	
Separated	242	325.74 (184.37)	
Divorced	792	323.31 (173.06)	
Widowed	324	289.64 (167.06)	

*A composite index comprising of head of household's occupation, access to a car, and housing tenure.

[†]I, professional occupations; II, managerial and technical occupations; III(N), skilled occupations nonmanual; III(M), skilled occupations manual; IV, partly skilled occupations; and V, unskilled occupations.

who do not draw smoke into their lungs. It should be noted that the smokers excluded as not having smoked in the last 24 hours were significantly more likely to be younger, single, from London, of a higher social class, and less deprived than those who smoked recently (all $P < 0.01$).

The findings also extend our knowledge of the extent to which smoke intake is associated with a number of

sociodemographic factors. Although interesting relationships among cotinine concentration and marital status and region were observed, these findings seem to be a function of cigarettes per day. However, when adjusting for usual daily cigarette consumption and body mass index, cotinine concentrations remained higher among men than women. This is in line with some past studies (9, 12), although it is also in contrast with other studies

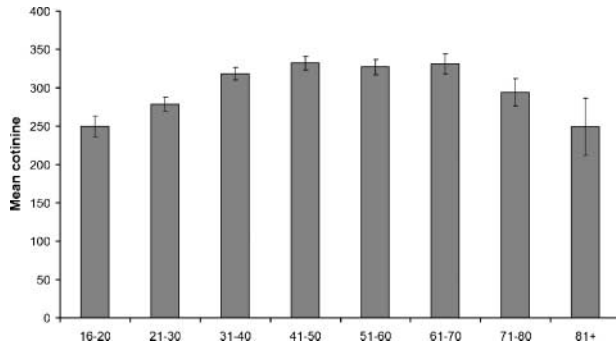


Figure 3. Mean cotinine value and 95% confidence interval of current smokers by age; adjusted for cigarettes per day.

(8). There are a number of possible explanations for this finding: One is that cotinine is metabolized faster among women than men (11), resulting in a lower cotinine value among women despite equivalent intake; another is that men may be seeking a higher level of nicotine concentration than women. This would be comparable with other drugs of dependence, including alcohol, in which men use at a higher rate than women (24).

There has been limited research on the association between cotinine and deprivation, although the association between smoking behavior and social class is well known (25). Two previous studies, in a sample of Czech men (26) and a subset of the Health Survey for England data reported here (25), support our finding that objective measures of smoke intake increase in parallel with deprivation. Bobak et al. found in the Czech sample that once cigarettes per day were controlled for, the linear trend disappeared. Our findings clearly show in English smokers that the trend remains once cigarettes per day are taken into account. The higher nicotine intake of more deprived smokers could explain, at least in part, why they are less likely to stop smoking (24).

We also found a strong association between age and cotinine, independent of cigarettes per day. The shape of this distribution among the majority of smokers is notable, with cotinine levels increasing at each age group to peak among those ages 41 to 50 years and then declining again among those more than the age of 70 years. The weak association observed between age and cotinine in other studies (1, 4, 7, 10, 11), which frequently disappeared once cigarettes consumed were controlled for,

may have been attenuated by this curvilinear relationship. There are a number of explanations for this relationship. The cross-sectional nature of the data means a birth cohort effect is possible, with the pattern observed reflecting differences in the preferred nicotine intake of smokers who began smoking at certain periods in time. However, any evidence of a change in nicotine intake over time is small at best (27). It may be that lighter smokers are more likely to quit at a younger age, which could contribute to the increasing cotinine values observed with increasing age. However, the increase in cotinine concentrations observed is higher than could be accounted for by the selective removal of lighter smokers from the smoking population as quit rates at this age range are typically around 2% per year (28). It is also possible that individual smokers escalate their intake over time, long after smoking habits are established. This suggests that there may be a long-term process of habituation to the effects of nicotine lasting more than a decade. The decline in cotinine in older smokers is likely to be due in part to the death of smokers with higher intake. It is also possible, however, that older smokers begin to smoke less, or inhale less deeply, perhaps because of a reduced need for nicotine. Further prospective research is required to investigate these hypotheses.

Our study has some limitations. A simple spot cotinine documents intake over the past few days only and may not reflect longer-term nicotine intake. Concentrations are also subject to between-individual genetic variation in nicotine metabolism, which was not measured in this study. However, such individual variation should not influence mean differences in population samples unless the groups being compared differ genetically. A second limitation is the lack of data on ethnicity. The number of participants with ethnicity data in the core representative sample of the Health Survey for England is very small and therefore ethnicity data were not analyzed. However, cotinine has previously been shown to differ by ethnic group even after adjusting for cigarettes per day (29, 30). Ethnicity may therefore play a role in the socioeconomic differences in cotinine observed here. There are also other factors that may influence cotinine aside from actual smoke intake; for example, certain medical conditions and medications have been shown to alter the rate of nicotine metabolism (31). However, the overall effect of this in a population sample is likely to be small.

In conclusion, the findings presented provide the clearest picture yet of smoke intake in English smokers and supply robust estimates of cotinine values. They

Table 3. Independent associations between sociodemographic factors and cotinine

	Model 1* [F (∂η ²)]	Model 2 [†] [F (∂η ²)]
Age	F _(7, 6,197) = 39.54 [‡] (0.043)	F _(7, 6,167) = 18.26 [‡] (0.020)
Sex	F _(1, 6,197) = 126.20 [‡] (0.020)	F _(1, 6,167) = 83.29 [‡] (0.013)
Social class	F _(5, 6,197) = 2.17 (0.002)	F _(5, 6,167) = 0.90 (0.001)
Deprivation	F _(3, 6,197) = 11.34 [‡] (0.005)	F _(3, 6,167) = 6.55 [‡] (0.003)
Marital status	F _(4, 6,197) = 4.28 [§] (0.003)	F _(4, 6,167) = 2.14 (0.001)
Region	F _(8, 6,197) = 3.50 [‡] (0.004)	F _(8, 6,167) = 1.45 (0.002)
Cigarettes per day	—	F _(7, 6,167) = 253.45 [‡] (0.223)
Adjusted R ²	0.105	0.303

*Model 1: all sociodemographic factors included as independent variables.

[†]Model 2: all sociodemographic factors and cigarettes per day included as independent variables.

[‡]P < 0.001.

[§]P < 0.01.

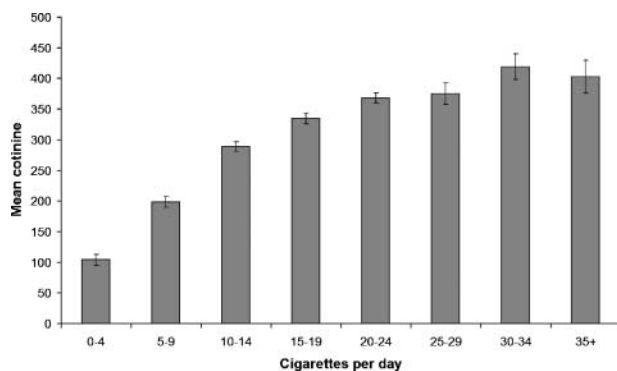


Figure 4. Mean cotinine value and 95% confidence interval by cigarettes per day.

offer a benchmark for future comparisons and allow the positioning of individual cotinine scores along the distributions presented. It seems that smokers from lower social grades need more nicotine than those from higher grades and that nicotine intake increases over a period of decades into middle age. This latter finding may present a challenge to conceptualizations about the development of nicotine dependence, which merits further investigation.

Disclosure of Potential Conflicts of Interest

R. West undertakes research and consultancy for developers and manufacturers of smoking cessation treatments such as nicotine replacement products; commercial research with Pfizer, Inc., GlaxoSmithKline, Johnson & Johnson, and Sanofi-Aventis; speakers bureau/honoraria for Pfizer, Inc., Novartis, GlaxoSmithKline, and Johnson & Johnson; ownership interest with a nicotine device.

Acknowledgments

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We thank those who conducted and participated in the Health Surveys for England, and Colin Feyerabend and his team at the Medical Toxicology Unit, New Cross Hospital, London.

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