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Cigarette smoking is associated with acrylamide exposure among the U.S. population: NHANES 2011–2016

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Abstract

2-carbamoylethyl mercapturic acid (2CaEMA, *N*-Acetyl-*S*-carbamoylethyl-L-cysteine) is a urinary metabolite and exposure biomarker of acrylamide, which is a harmful volatile organic compound found in cigarette smoke and in some foods. The goal of this study was to determine the association between cigarette smoking and urinary 2CaEMA concentrations among the U.S. population while considering potential dietary sources of acrylamide intake and demographics. We measured 2CaEMA concentrations in urine specimens collected during the National Health and Nutrition Examination Survey 2011–2012, 2013–2014, and 2015–2016 cycles from eligible participants 18 years and older (n = 5443) using liquid chromatography/tandem mass spectrometry. We developed multiple regression models with urinary 2CaEMA concentrations as the dependent variable and sex, age, race/Hispanic origin, reported primary sources of dietary acrylamide intake, and cigarette smoke exposure as independent variables. This study demonstrates that cigarette smoking is strongly associated with urinary 2CaEMA, suggests that cigarette smoking is likely a primary source of acrylamide exposure, and provides a baseline measure for 2CaEMA in the U.S. population.

Keywords

2-Carbamoylethyl mercapturic acid (2CaEMA); AAMA; GAMA; Acrylamide; Tobacco smoke; The national health and nutrition examination survey (NHANES)

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2022.112774.

1. Introduction

Acrylamide is a volatile organic compound (VOC) and probable human carcinogen (Virk-Baker et al., 2014). It is a product of tobacco combustion, and the smoke of one cigarette contains approximately 0.5–4.3 μg of acrylamide (Moldoveanu and Gerardi, 2011; Smith et al., 2001). Acrylamide is also found in baked or fried food products (Stadler et al., 2002) such as fried potatoes (French fries and potato chips, ca. < 0.01–8 μg/g), breakfast cereals (ca. < 0.01–1.4 μg/g), and ground coffee (ca. 0.07–1.1 μg/g) (Doerge et al., 2008; U.S. Food and Drug Administration, 2019), which are the primary sources of dietary acrylamide exposure in the U.S. population and account for approximately 57% of dietary acrylamide intake (Wilson et al., 2009).

2-carbamoylethyl mercapturic acid (2CaEMA, *N*-Acetyl-*S*-2-carbamoylethyl-L-cysteine) and 2-carbamoyl-2-hydroxyethyl mercapturic acid (2CaHEMA, *N*-Acetyl-*S*-2-carbamoyl-2-hydroxyethyl-L-cysteine) (Tevis et al., 2021) are urinary metabolites of acrylamide (Sumner et al., 1992). Evidence from a relatively small study (n = 29) demonstrated that urinary 2CaEMA and 2CaHEMA concentrations are correlated (Boettcher et al., 2005), however, 2CaHEMA represents only 5% of total acrylamide uptake. In contrast, 2CaEMA represents ~50% of the total acrylamide uptake (Boettcher et al., 2006; Fennell et al., 2006; Fuhr et al., 2006; Kopp and Dekant, 2009). Urinary 2CaEMA concentrations are higher among people exposed to airborne acrylamide (Huang et al., 2011; Sams et al., 2015) and among people who smoke compared to people who do not smoke (Bjellaas et al., 2007; Boettcher et al., 2005; Choi et al., 2019; Huang et al., 2007; Mojska et al., 2016). 2CaEMA concentrations are also positively associated with cigarettes smoked per day (CPD) (Huang et al., 2007). However, these studies either focused on a relatively small number of participants (n = 29–93) (Bjellaas et al., 2007; Boettcher et al., 2005; Huang et al., 2007; Mojska et al., 2016) or were confined to participants under the age of 18 (Choi et al., 2019).

Larger U.S. population-based assessments using the Population Assessment of Tobacco and Health (PATH) and the National Health and Nutrition Examination Survey (NHANES) have also shown that people who smoke have higher 2CaEMA compared to people who do not smoke (De Jesús et al., 2020; Jain, 2015; Wei et al., 2016). However, these analyses did not determine the association between 2CaEMA and cigarette smoking intensity or consider primary dietary sources of acrylamide, which may confound the association between 2CaEMA and tobacco smoking. For example, consuming fried potatoes causes urinary 2CaEMA concentrations to increase (Fuhr et al., 2006; Wang et al., 2016; Watzek et al., 2012), and higher urinary 2CaEMA concentrations are associated with consumption of fried potatoes and coffee in studies which determined dietary consumption of acrylamide-containing foods with questionnaires (Bjellaas et al., 2007; Brantsæter et al., 2008; Choi et al., 2019; Heudorf et al., 2009).

In this report, we used multiple regression models to characterize the association between cigarette smoke exposure and 2CaEMA from the 2011–2016 NHANES cycles. Our analyses controlled for other variables such as prominent known sources of dietary acrylamide (fried potatoes, coffee, and cereal) determined from NHANES questionnaire data, age, sex, and demographics as part of one multivariate regression model. This report provides

a comprehensive determination of the association between urinary 2CaEMA concentrations and cigarette smoking while also controlling for the primary dietary sources of acrylamide exposure. Additionally, this study provides a baseline analysis of 2CaEMA in the U. S. population that may be utilized for future biomonitoring studies.

2. Materials and methods

2.1. Study design and variable definitions

Spot urine samples were collected through NHANES, which is a cross-sectional study that combines physical examination and interviews to assess the health and nutrition of the U.S. population (The National Center for Health Statistics, 2017). NHANES uses a complex sample design to select a nationally representative sample of the civilian, noninstitutionalized US population. The National Center for Health Statistics (NCHS), U.S. Centers for Disease Control and Prevention (CDC) conducts NHANES. The Research Ethics Review Board of NCHS, CDC reviewed and approved the NHANES study ("NCHS Research Ethics Review Board (ERB) Approval," 2017).

We measured urinary 2CaEMA (URXAAM) and 2CaHEMA (URXGAM) concentrations from 7207 participants from NHANES cycles 2011–2012, 2013–2014, and 2015–2016 from special subsets UVOCS_G, UVOCS_H, and UVOCS_I, which oversamples tobacco smokers and does not include children. We excluded participants with missing urinary creatinine concentrations, 2CaEMA, concentrations, or dietary information values, leaving 5443 participants. We stratified participants into tobacco smoke exposure categories using a combination of NHANES questionnaire data and serum cotinine concentrations as previously described (Kenwood et al., 2021a). Briefly, we categorized participants who answered 'no' to NHANES question 'Used any tobacco/nicotine product within the last five days?' (NHANES dataset SMQRTU) and had serum cotinine concentrations (LBXCOT) ≤3.08 ng/mL as participants who did not smoke (Benowitz et al., 2009). We categorized participants who did not smoke and had serum cotinine concentrations from >0.015 to ≤3.08 ng/mL as participants exposed to secondhand smoke (SHS), and we categorized participants who did not smoke and had serum cotinine concentrations of ≤0.015 ng/mL as nonexposed participants. We also categorized participants who smoked cigarettes and did not use other tobacco or nicotine products at the time of specimen collection (referred to as participants who exclusively smoked cigarettes) as having smoked 1–9 CPD, 10–19 CPD, and >19 CPD as previously described (Kenwood et al., 2021b) using a serum cotinine concentration cutoff of 3.08 ng/mL (Benowitz et al., 2009). We categorized age (RIDAGEYR) into the following ranges: 18–39, 40–59, and ≥60 years, and we categorized race/Hispanic origin group (RIDRETH1) into Non-Hispanic White, Non-Hispanic Black, Hispanic, and Multi-race/other. We created binary indicators for consumption of acrylamide-containing food into three categories from dietary data from the 24-h recall period in the NHANES Individual Foods – First Day file (NHANES dataset: DR1IFF) based on the eight-digit USDA food code, which consisted of fried potatoes (fried potatoes and potato chips, 71,400,990–71, 411,170 and 71,200,010–71,203,030, respectively), coffee (92,100, 000–92,171,010), and cereal (57,100,100–57,418,000) (US Department of Agriculture, 2019).

2.2. Laboratory measurements

We stored and prepared urine specimens collected during NHANES 2011–2016 (National Center for Health Statistics, 2021) as previously described (Kenwood et al., 2021a), and measured 2CaEMA and 2CaHEMA using ultra-high-performance liquid chromatography with tandem mass spectrometry (LC-MS/MS) (Alwis et al., 2012). The analytical limits of detection for 2CaEMA and 2CaHEMA were 2.2 ng/mL and 9.4 ng/mL, respectively, and we imputed measurements below the limit-of-detection (LOD) by dividing the LOD by the square root of two (Hornung and Reed, 1990). Urinary creatinine (URXCUR) was measured using an enzymatic assay (Eckfeldt, 2014).

2.3. Quality control (QC)

We met the accuracy and precision specifications of the quality control/quality assurance program of the CDC National Center for Environmental Health, Division of Laboratory Sciences, and we accepted and rejected analytical results using modified Westgard rules (Caudill et al., 2008) by measuring 2CaEMA and 2CaHEMA in two preparations of two separate QC pools (high and low) in each run. We characterized the QC material by measuring 2CaEMA and 2CaHEMA in each pool with twenty separate runs, and we determined the standard deviation associated with mean QC results (S_m), the standard deviation associated with individual QC results (S_i), and the within-run standard deviation (S_w). We accepted QC results if the mean measured 2CaEMA and 2CaHEMA concentrations from each pool were within $2S_m$ and individual measurements were within $2S_i$. If mean analyte concentrations were outside $2S_m$, we rejected the run if the mean analyte concentrations were either outside $3S_m$, if both QC pool run means were outside of $2S_m$ in the same direction, or if the current and previous nine run means were on the same side of the characterization mean. If one individual measurement was outside of $2S_i$, we rejected the run if an individual result was outside $4S_i$ or if the pooled within-run ranges for both QC pools were greater than $4S_w$. We also measured 2CaEMA and 2CaHEMA among five blinded proficiency testing specimens twice per year. We considered an analyte to be passing if four out of five specimens were ±25% of the target value.

2.4. Statistical analysis

We conducted all statistical analyses using SAS 9.4 (SAS Institutes, Cary, NC). We evaluated statistical reliability to ensure all proportions follow the NCHS Data Presentation Standards (Parker et al., 2018), and our analysis considered the complex sampling design of NHANES by incorporating complex survey design variables SDMVPSU and SDMVSTRA, and special smoking subsample weights (WTFSM) (Chen et al., 2020). We expressed 2CaEMA concentrations in ng/mL, as well as in μg/g creatinine to normalize for participant hydration (Cone et al., 2009). Dietary variables were categorized either as “yes” to indicate consumption or “no” to indicate no consumption, rather than continuous, due to the wide range of acrylamide concentration in food products such as fried potatoes (Martinez et al., 2019; Michalak et al., 2011; Palazoglu et al., 2010; U.S. Food and Drug Administration, 2019; Williams, 2005).

We also determined the association between urinary 2CaEMA and each independent variable using a multiple linear regression model as previously described (Kenwood et al.,

2021a, 2021b). We fit the model with 2CaEMA (ng/mL) as the dependent variable and CPD, age, sex, race/Hispanic origin, urinary creatinine, and dietary consumption as independent variables. We log-transformed 2CaEMA concentrations in the model to normalize the distribution of values. We included urinary creatinine an independent variable and expressed 2CaEMA in ng/mL rather than expressing 2CaEMA as μg/g creatinine because urinary creatinine concentrations vary across demographic groups (Barr et al., 2005). The reference category for each dietary consumption variable were participants who did not consume the dietary product. We also investigated interactions between CPD and other independent variables in our regression model. The interactions were not included in our final model because they were either not statistically significant or did not significantly affect the associations between 2CaEMA concentrations and independent variables. We derived least squares geometric means of 2CaEMA by tobacco smoke exposure from the regression results, and we compared means to each other using Bonferroni correction (two-tailed) to adjust for multiple comparisons. Finally, we calculated the percent change in 2CaEMA associated with an independent variable from regression model coefficients using Equation (1):

$$\%\,(\Delta\, dependent\ variable) = (exponentiated\ coefficient - 1) \times 100. \quad (1)$$

3. Results

The relationship between urinary 2CaEMA and 2CaHEMA concentrations (ng/mL) among NHANES participants with reported 2CaEMA and 2CaHEMA concentrations (n = 6961) is shown in Supplementary Fig. 1, but we focused our analyses on 2CaEMA concentrations because the sample-weighted detection rate of 2CaHEMA was relatively low (41%) compared to 2CaEMA (99%). Table 1 lists the distributions of the 5443 participants in our analyses by age, sex, and race/Hispanic origin. The sample-weighted geometric means of urinary 2CaEMA concentrations among cigarette smoke exposure categories, dietary categories, and demographic groups expressed in μg/g creatinine and ng/mL are shown in Table 2 and Supplementary Table 1, respectively. We observed that mean 2CaEMA concentrations among unexposed participants (n = 1523) and participants exposed to SHS (n = 2030) were 44.3 μg/g creatinine and 45.3 μg/g creatinine, respectively. Participants who exclusively smoked 1–9 CPD (n = 721), 10–19 CPD (n = 678), and >19 CPD (n = 491) had mean urinary 2CaEMA concentrations of 104 μg/g creatinine, 136 μg/g creatinine, and 159 μg/g creatinine, respectively. We also observed that among participants who did not smoke (unexposed participants and participants exposed to SHS), the mean 2CaEMA concentrations among participants who consumed fried potatoes (n = 674) and did not consume fried potatoes (n = 2879) were 60.9 μg/g creatinine and 41.6 μg/g creatinine, respectively. Among participants who exclusively smoked cigarettes, participants that consumed and did not consume fried potatoes had a mean 2CaEMA concentrations of 145 μg/g creatinine and 124 μg/g creatinine, respectively. Mean 2CaEMA concentrations among participants who did not smoke and consumed or did not consume coffee or cereal ranged from 42.8 to 46.7 μg/g creatinine and ranged from 123 to 139 μg/g creatinine among participants who exclusively smoked cigarettes.

We further characterized the association between cigarette smoking and urinary 2CaEMA concentrations among NHANES participants using a multiple log-linear regression model (Table 3). The dependent variable was log-transformed 2CaEMA concentrations (ng/mL), and independent variables included tobacco smoke exposure, dietary sources of acrylamide, urinary creatinine, age, sex, and race/Hispanic origin. Compared to nonexposed participants, participants who smoked 1–9 CPD had 141% higher 2CaEMA ($p < 0.0001$), participants who smoked 10–19 CPD had 204% higher 2CaEMA ($p < 0.0001$), and participants who smoked >19 CPD had 260% higher 2CaEMA ($p < 0.0001$). We then calculated the geometric least squares mean concentrations from the multiple regression model among each tobacco smoke exposure category (Fig. 1 and Supplementary Table 2). The geometric least-squared mean concentration of 2CaEMA (ng/mL) among participants who exclusively smoked cigarettes and smoked 1–9 CPD was 106 ng/mL, which was higher compared to unexposed participants (43.9 ng/mL, $p < 0.0001$, Supplementary Table 3) and participants exposed to SHS (46.7 ng/mL, $p < 0.0001$), and lower compared participants who smoked 10–19 CPD (133 ng/mL, $p < 0.0001$) and >19 CPD (158 ng/mL, $p < 0.0001$). Additionally, participants who smoked >19 CPD had a higher mean 2CaEMA concentration compared to participants who smoked 10–19 CPD ($p = 0.0038$). Dietary exposure sources of acrylamide associated with higher 2CaEMA concentrations included fried potatoes (49.7% higher, $p < 0.0001$) and coffee (6.76% higher, $p = 0.0279$). Race/Hispanic origin was also significantly associated with 2CaEMA concentrations; Non-Hispanic Black and Other Race/Multi-Racial participants had lower 2CaEMA compared to Non-Hispanic White participants (10% lower, $p = 0.0135$ and $p = 0.00920$, respectively).

4. Discussion

Our findings suggests that cigarette smoking is a major source of acrylamide exposure in the U.S. population. We found that smoking 1–9 CPD, 10–19 CPD, and >19 CPD was associated with 141%, 204%, and 260% higher urinary 2CaEMA, respectively (Table 3). This is consistent with a previous finding which demonstrated that 2CaEMA was associated with cigarettes smoked per day (Huang et al., 2007), and that acrylamide hemoglobin adducts are associated with serum cotinine, a nicotine exposure biomarker, among NHANES participants (Tran et al., 2010). Our analysis also demonstrates that participants who exclusively smoked cigarettes have approximately 3-fold higher mean 2CaEMA concentrations compared to unexposed participants. Smoking was associated with a similar effect (3.4-fold higher) among participants in the Population Assessment for Tobacco and Health (PATH) (De Jesús et al., 2020), and we found that the geometric mean urinary 2CaEMA concentrations among unexposed nonsmokers (44.3 μg/g creatinine) was similar to previous population-based reports by our laboratory (45.0 μg/g creatinine, PATH, Wave 1, 2013–2014) (De Jesús et al., 2020). However, the mean concentration of 2CaEMA among PATH participants who smoked was 152 μg/g creatinine, but the mean 2CaEMA concentration among participants in NHANES who exclusively smoked cigarettes was only 128 μg/g creatinine (Table 2). This may be due to differences in study design between the two studies; specifically, PATH is designed around tobacco use and thus smoking intensity may be higher in PATH compared with NHANES. Furthermore, PATH urine samples

are collected in the study participant's home with no required smoking abstinence, while NHANES urines are collected at a mobile exam center that has a no smoking policy.

We also found that consumption of fried potatoes and coffee were associated with 49.7% higher 2CaEMA and 6.9% higher 2CaEMA, respectively (Table 3). However, this study was limited by our analysis of dietary intake. We included dietary intake in our statistical models, but only included predominant sources of dietary acrylamide. Other food sources, such as cookies and popcorn, also contain acrylamide, but their relative dietary contributions are thought to be lower compared to fried potatoes, cereals, and coffee (Wilson et al., 2009). We also relied on reported consumption from dietary questionnaires, which rely on participant accuracy and truthfulness and underestimate dietary consumption of fat and carbohydrates (Archer et al., 2013, 2015). In support of this, we did not find any observable association between the mass of fried potatoes reported to be consumed and 2CaEMA concentrations among participants who reported eating fried potatoes (not shown). However, the association between reported consumption and 2CaEMA is likely further complicated by the large disparities of acrylamide content in fried potato products. Thus, we constructed categorical dietary variables, but did not report an association between the mass of a food product consumed and 2CaEMA in our statistical models. Finally, we did not compare the association between 2CaEMA and dietary variables to other studies because our analysis was focused on cigarette smoke exposure, and comparisons across questionnaire-based dietary studies are difficult due to differences in methods used to record dietary intakes and food categorization (Dybing et al., 2005).

Characterizing the associations between acrylamide exposure and cigarette smoking is critical for determining the potential public health impact of acrylamide exposure. This report provides public health researchers a recent and comprehensive population-based assessment of 2CaEMA concentrations in the U.S. population, and is the most thorough characterization of acrylamide exposure using 2CaEMA to date. In sum, this analysis demonstrates that cigarette smoking is strongly associated with higher urinary 2CaEMA concentrations and is likely a primary source of acrylamide exposure in the U.S. population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbrevations:

2CaEMA	2-carbamoylethyl mercapturic acid
2CaHEMA	2-carbamoyl-2-hydroxyethyl mercapturic acid
PATH	Population Assessment for Tobacco and Health
NHANES	National Health and Nutrition Examination Survey

CPD	Cigarettes per day
QC	Quality control

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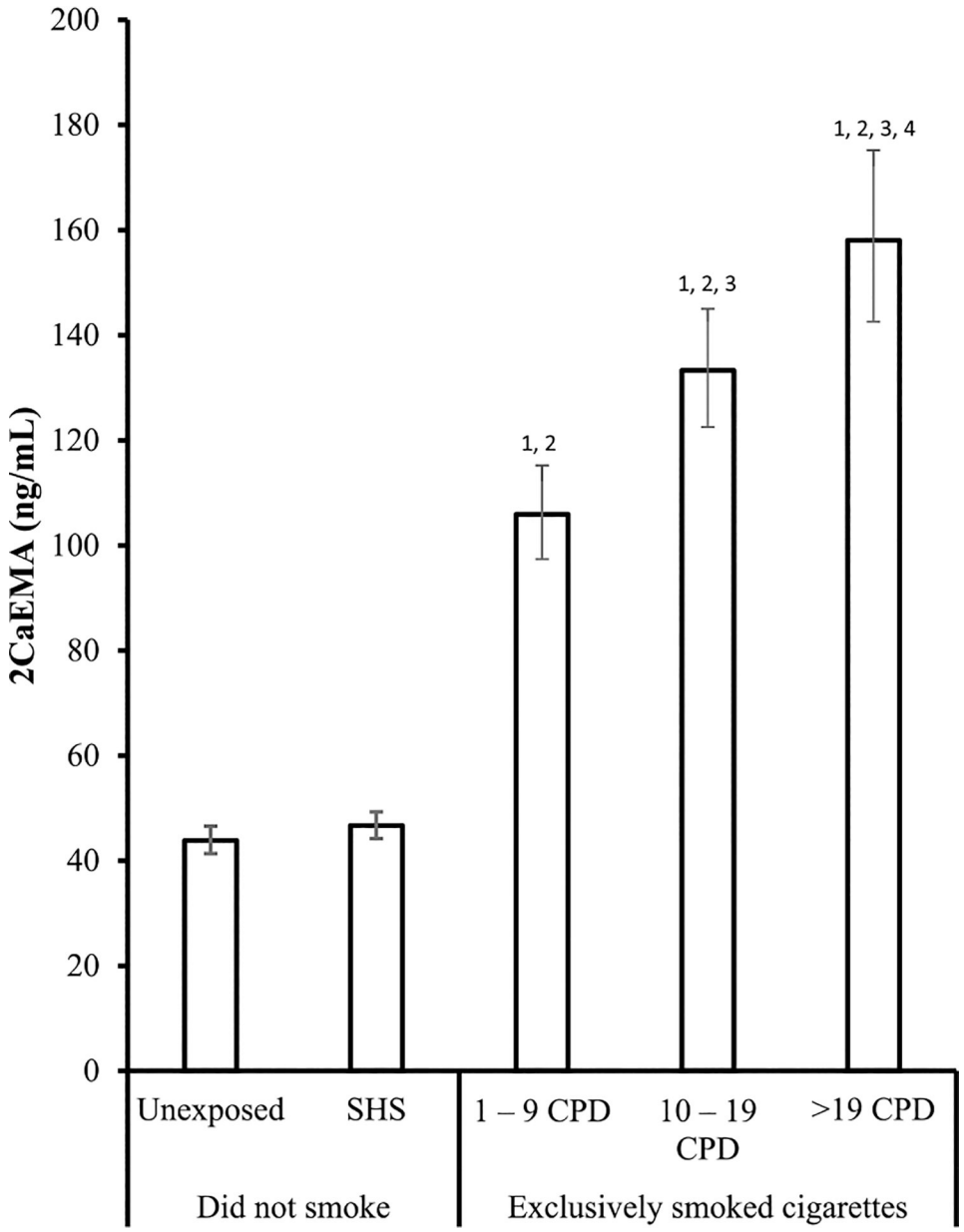

Fig. 1.

Geometric least-squares means of urinary 2CaEMA (ng/mL) among NHANES 2011–2016 participants stratified by tobacco smoke exposure categories (n = 5443).

1. Significantly different compared to unexposed participants.
2. Significantly different compared to participants exposed to SHS.
3. Significantly different compared to participants who smoked 1–9 CPD.
4. Significantly different compared to participants who smoked 10–19 CPD.

CPD, cigarettes per day

SHS, secondhand smoke

Table 1

Distributions of study participants who did not smoke and exclusively smoked cigarettes by age, sex, and race/ethnic group from NHANES 2011–2016 (N = 5443).

Category	Did not smoke			Exclusively smoked cigarettes		
	n[a]	%[b]	SE[b]	n[a]	%[b]	SE[b]
Overall	3553	83.5	0.7114	1890	16.5	0.7114
Sex						
Female	1903	45.6	1.06	820	8.00	0.445
Male	1650	37.9	0.862	1070	8.53	0.428
Age						
18–39	1298	30.0	1.22	716	6.66	0.381
40–59	1084	28.9	1.07	750	6.92	0.442
60 or older	1171	24.5	1.04	424	2.96	0.226
Race/ethnicity						
Hispanic	1003	13.7	1.42	311	1.92	0.271
Non-Hispanic Black	674	7.76	0.903	507	2.39	0.304
Non-Hispanic White	1310	55.3	2.14	884	11.1	0.735
Other Race/Multi-Racial	566	6.74	0.575	188	1.14	0.149

SE, standard error of the percentage.

[a]Not sample-weighted.

[b]Sample-weighted.

Table 2

Sample-weighted geometric means of urinary 2CaEMA concentrations (μg/g creatinine) among NHANES 2011–2016 participants (n = 5443).

Category	Did not smoke				Exclusively smoked cigarettes			
	n	GM	95% CI		n	GM	95% CI	
All participants	3553	44.8	43.0	46.6	1890	128	120	137
Tobacco smoke exposure								
Nonexposed	1523	44.3	42.6	46.1				
Exposed to SHS	2030	45.3	42.6	48.1				
1–9 CPD					721	104	95.8	112
10–19 CPD					678	136	126	147
>19 CPD					491	159	146	173
Diet								
Consumed fried potatoes	674	60.9	56.8	65.4	396	145	132	160
Did not consume fried potatoes	2879	41.6	39.9	43.3	1494	124	115	134
Consumed coffee	1795	46.7	44.3	49.3	1058	132	123	142
Did not consume coffee	1758	42.8	40.9	44.8	832	123	114	133
Consumed cereal	635	45.6	42.6	48.9	238	139	128	152
Did not consume cereal	2918	44.6	42.8	46.5	1652	127	118	136
Age								
18–39	1298	45.1	42.5	47.9	716	120	110	132
40–59	1084	44.6	42.1	47.3	750	141	131	152
60 or older	1171	44.6	42.0	47.4	424	118.9	108.4	130
Sex								
Male	1650	42.5	40.6	44.6	1070	119	110	128
Female	1903	46.8	44.5	49.2	820	139	128	152
Race/Hispanic origin								
Non-Hispanic White	1310	46.2	43.9	48.7	884	136	124	148
Non-Hispanic Black	674	38.3	36.0	40.8	507	114	106	121
Hispanic	1003	44.5	41.6	47.5	311	113	101	127
Other Race/Multi-Racial	566	42.1	38.8	45.7	188	120	109	133

SHS, Secondhand smoke.

Table 3

Association between % (Δ 2CaEMA) (ng/mL) and CPD using a multiple regression analysis of urinary 2CaEMA (ng/mL) from NHANES 2011–2016 (n = 5443).

Independent Variable	Coefficient[a]	95% CI		P-value	% (Δ 2CaEMA)[b,c,d]
Cigarette smoke exposure					
Nonexposed	Reference				
Exposed to SHS	0.0615	−0.00413	0.127	0.0656	N.S.
1–9 CPD	0.882	0.803	0.960	<0.0001	141% higher
10–19 CPD	1.11	1.02	1.20	<0.0001	204% higher
>19 CPD	1.28	1.18	1.38	<0.0001	260% higher
Diet [e]					
Fried potatoes	0.403	0.330	0.477	<0.0001	49.7% higher
Coffee	0.0654	0.00742	0.123	0.0279	6.76% higher
Cereal	0.0493	−0.00972	0.108	0.0995	N.S.
Age					
18–39	Reference				
40–59	0.00154	−0.0733	0.0763	0.967	N.S.
60 or older	−0.00869	−0.0966	0.0792	0.843	N.S.
Sex					
Male	Reference				
Female	0.0236	−0.0397	0.0869	0.458	N.S.
Race/Hispanic origin					
Non-Hispanic White	Reference				
Non-Hispanic Black	−0.106	−0.188	−0.0229	0.0135	10% lower
Hispanic	0.0199	−0.0729	0.113	0.668	N.S.
Other Race/Multi-Racial	−0.109	−0.190	−0.0283	0.00920	10% lower
Creatinine (mg/mL)	0.808	0.746	0.869	<0.0001	124% higher per mg/mL creatinine
Intercept	2.61	2.51	2.72	<0.0001	N/A

CPD, Cigarettes per day.

SHS, Secondhand smoke.

N.S., Not significant.

N/A, Not applicable.

[a] 2CaEMA concentrations were natural log transformed.

[b] Calculated by multiplying the expected 2CaEMA concentration by the exponentiated coefficient.

[c] % (Δ 2CaEMA) associated with each food group was calculated from median consumption.

[d] Adjusted for all independent variables shown in the Table.

[e] Reference variables were participants who did not consume the indicated food.