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Time to first cigarette and serum cholesterol levels

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Abstract

Rationale—Cigarette smoking is a primary cause of cardiovascular disease (CVD); however, prior research has rarely distinguished smoking *behavior* from nicotine dependence.

Objective—The current study presents a novel investigation into whether time to first cigarette (TTFC), a reliable proxy for nicotine dependence, is associated with lipid cholesterol, a biomarker for CVD, after controlling for smoking behavior and other risk factors.

Methods—In total, 3903 current adult smokers were drawn from four consecutive cross-sectional waves (2005–06, 2007–08, 2009–10, and 2011–12) of the National Health and Nutrition Survey (NHANES). Weighted regressions were used to examine whether earlier TTFC is associated with differences in a) numeric values; b) guideline-based binary outcomes of total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and the LDL/HDL ratio; and c) 10-year risk scores for CVD.

Results—Earlier TTFC (within 5, 30, or 60 min *vs.* >60 min) was significantly ($p < 0.05$) associated with lower HDL (2–3 mg/dL) and a lower odds ratio ($OR = 0.70$) of having optimal HDL levels, and a lower LDL/HDL ratio (0.14–0.32); these results were consistent across three models (unadjusted, adjusted for smoking behavior, and also adjusted for demographics and other CVD risk factors). Earlier TTFC was also associated ($p < 0.05$) with higher odds of having sub-optimal total cholesterol levels ($OR = 1.55$) and higher LDL values (8 mg/dL), but only in the models adjusting for smoking behavior. However, the association of TTFC with 10-year CVD risk scores did not reach significance ($p > 0.05$).

Conclusion—More “addicted” smokers, as indicated by earlier TTFC, have less favorable lipid profiles, even after accounting for current and lifetime smoking history and other CVD risk factors. Future research should further explore whether TTFC could be a useful tool for refining clinically significant CVD risk among smokers.

Keywords

Cholesterol; Cardiovascular disease; Nicotine dependence; Smoking

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1. Introduction

Cigarette smoking remains the leading cause of preventable death and disease (Mokdad et al., 2004), and is a primary causal factor for cardiovascular disease (CVD) (U.S. Department of Health and Human Services, 2014). While the health effects of smoking *behavior* have been well-researched, there is considerably less research on the role that addiction plays in these relationships. Emerging research on the etiology and epidemiology of smoking draws a clear distinction between smoking *behavior* and nicotine dependence (ND). For example, the two constructs have distinct profiles across different subpopulations of smokers, with some novice and light smokers being highly susceptible to ND (DiFranza et al., 2002a; Kandel and Chen, 2000) and others experiencing relatively low ND despite heavy smoking behavior (Kandel and Chen, 2000). Additionally, ND independently predicts future smoking behavior (DiFranza et al., 2002b; Piper et al., 2011), even over and above prior smoking behavior (Dierker et al., 2015; Dierker and Mermelstein, 2010; Ip et al., 2011). Together, these developments indicate that ND may have significant and meaningful effects that occur independently of smoking behavior.

Importantly, a small but growing body of research has documented differences in health outcomes independently associated with ND: “addicted” smoking conveys health risks over and above the risks attributed to the smoking *behavior* itself. That is, more nicotine-dependent smokers are at higher risk for chronic obstructive pulmonary disease (Goodwin et al., 2012; Selya et al., 2016), lung cancer (Gu et al., 2014; Ito et al., 2013; Kunze et al., 2007; Muscat et al., 2011a), and head, neck, and larynx cancers (Muscat et al., 2011b; Muscat et al., 2012). Importantly, these risks associated with higher ND remain even after accounting for previous smoking behavior; this underscores the necessity of examining the contribution of ND when evaluating the risk of smoking-related death and disease.

Notably, however, very little is known about CVD indicators associated with more severe ND, over and above smoking behavior. This is a substantial gap in the literature, considering that CVD is the leading cause of death in the US many other industrialized nations. The current study focuses on outcomes of blood cholesterol as an indicator of CVD. High total cholesterol levels (≥ 240 mg/dL is considered high, and ≥ 200 mg/dL is borderline high) are in general a risk factor for CVD, but it is also important to consider separately certain components of this score, especially high-density lipoprotein (HDL) which is protective against CVD (optimally ≥ 40 mg/dL for men and ≥ 50 mg/dL for women), and low-density lipoprotein (LDL) which is a risk factor for CVD (≥ 160 mg/dL is considered high, and ≥ 130 mg/dL is borderline high) (NIH Medline Plus, 2012). Since total cholesterol score does not account for the competing directions of risk for LDL vs. HDL, the LDL-to-HDL ratio (optimally below 3.5) is another useful measure for assessing CVD risk (American Heart Association, 2016; Kannel, 1983). The current study is a novel examination of whether time to first cigarette (TTFC) after waking in the morning, which is considered the best single-item validated measure of ND (Fagerstrom, 2003; Transdisciplinary Tobacco Use Research Center Tobacco et al., 2007), is associated with each of these four blood cholesterol measures, after controlling for current and lifetime smoking behavior, demographic characteristics, and other CVD risk factors. Data are drawn from four consecutive, cross-sectional waves of the National Health and Nutrition Examination Survey (NHANES).

2. Methods

2.1. Sample and study design

The current study analyzes four cross-sectional waves (2005–06, 2007–08, 2009–10, and 2011–12) of NHANES, a nationally-representative sample of the civilian, non-institutionalized US population, and has been described in detail elsewhere (Johnson et al., 2013). Three exclusion criteria were applied to the full sample of pooled waves from NHANES ($N = 40,790$) from these years. First, those who did not participate in the examination component of NHANES were excluded ($N = 1487$) because cholesterol levels were not measured in these participants. Second, those younger than 20-years old were excluded ($N = 17,445$) because NHANES did not ask these participants about smoking behavior. Finally, those who did not self-report being a current smoker were excluded ($N = 17,955$) because NHANES did not ask TTFC of these participants. The final analytic sample contains 3903 current adult smokers.

The questionnaire component of NHANES assessed demographic characteristics, smoking behavior, physical activity, environmental conditions, and self-reported medical conditions. Physical examinations and laboratory testing for a subsample of NHANES was carried out in mobile examination centers, which yielded measurements of body mass index (BMI), apolipoprotein B (ApoB), blood pressure (BP), and blood lipids.

This research on publicly available data from NHANES was approved by the University of North Dakota IRB on 8/2014 under project number IRB-201407-036. All analysis took place at the University of North Dakota, Grand Forks, ND, between February, 2015 and November, 2016.

2.2. Measures

2.2.1. Outcomes—Fasting blood cholesterol was measured in NHANES' laboratory component, and includes total cholesterol, HDL and LDL. The LDL/HDL ratio was derived from LDL and HDL values. All four cholesterol outcomes were used both 1) numerically in linear regressions and 2) as binary outcomes in logistic regressions based on clinical guidelines. The variables were dichotomized as follows: total cholesterol was coded as <200 mg/dL (desirable) vs. 200 mg/dL (borderline high and high) (NIH Medline Plus, 2012); HDL was coded using cutoffs of 40 mg/dL for men and 50 mg/dL for women (below the cutoff represents high risk; above is desirable and even protective) (NIH Medline Plus, 2012); LDL was coded as <130 mg/dL (optimal or near optimal) vs. 130 mg/dL (borderline high, high, and very high) (NIH Medline Plus, 2012); and the LDL/HDL ratio was coded as <3.5 (optimal) vs. 3.5 (sub-optimal) (American Heart Association, 2016; Kannel, 1983). Total cholesterol and HDL variables had 265 missing observations; LDL and LDL/HDL variables had 2202.

Finally, 10-year atherosclerotic CVD risk was calculated based on the American College of Cardiology (ACC)/American Heart Association (AHA) 2013 risk calculation equations (Goff et al., 2014). Risk scores for individuals older than 79 and with total cholesterol scores over 320 were removed from analyses due to uncertainty in risk prediction (Goff et al., 2014).

2.2.2. TTFC—TTFC after waking in the morning was self-reported with four possible responses (5, 5 to 30, 30 to 60, and >60 min; 95 missing observations).

2.2.3. Current and lifetime smoking behavior—Pack-years (lifetime smoking behavior) was calculated by multiplying the number of years of regular smoking (self-reported current age minus self-reported age of first regular smoking) by self-reported number of cigarettes smoked per day, divided by 20 cigarettes/pack (45 missing observations).

Past-month smoking frequency (current smoking behavior) was self-reported as the number of days smoked in the past 30 days (3 missing observations).

2.2.4. Demographics—Poverty ratio was measured as the ratio of self-reported family income to poverty guidelines for each year (289 missing observations). Race/ethnicity was self-reported and was grouped into “Non-Hispanic White,” “Non-Hispanic Black,” “Hispanic” (combining “Mexican-American” with “Other Hispanic” due to small sample size). Those reporting “Other” race/ethnicity ($N = 212$) were excluded from current analyses, due to small sample size. Age and biological sex were self-reported.

2.2.5. Other CVD risk factors—Secondhand smoke (SHS) exposure was self-reported and dichotomized into any vs. no SHS in the home (16 missing observations). Moderate physical activity was defined by NHANES as at least 10 min of any physical activity that causes small increases in breathing and heart rate. There were substantial differences in questions across different waves of NHANES. In 2005, participants were asked “Over the past 30 days, did you do moderate activities for at least 10 min that cause only light sweating or a slight to moderate increase in breathing or heart rate? Some examples are brisk walking, bicycling for pleasure, golf, and dancing.” In 2007, 2009, and 2011, participants were asked about moderate physical activity in a “typical week,” and separate questions were asked for work activity (“Does your work involve moderate-intensity activity that causes small increases in breathing or heart rate such as brisk walking or carrying light loads for at least 10 min continuously?”) and recreational activity (“Do you do any moderate-intensity sports, fitness or recreational activities that cause a small increase in breathing or heart rate such as brisk walking, bicycling, swimming, or golf for at least 10 min continuously?”). To best harmonize across the different NHANES waves, responses were dichotomized into any vs. no self-reported moderate physical activity in the past 30 days (1 missing observation).

BMI was obtained during NHANES’ examination component based on height and weight (54 missing observations). Diabetes status was self-reported using the question “ever been told by a doctor or health professional that you have diabetes?”, and the response options were dichotomized into diabetes vs. borderline diabetes or no diabetes (3 missing observations). ApoB was also measured in NHANES’ laboratory component (2149 missing observations).

Resting BP was also measured in NHANES’ laboratory component following procedures developed by the American Heart Association. Briefly, the physician used the participant’s right arm (unless specific conditions prohibited the use of the right arm, or participants self-

reported any reason why their right arm should not be used) and took measurements using a mercury sphygmomanometer, after the participant was seated and resting for five minutes. Three measurements were taken, each 5 min apart; only the first measurement was used in the current analyses due to having the least missing data. BP was categorized based on guidelines from the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) into normal (systolic BP < 120 and diastolic BP < 80) vs. pre-hypertensive (systolic BP 120 to 139 or diastolic BP 80 to 89) vs. hypertensive (systolic BP = 140 or diastolic BP = 90) (195 missing observations). Dietary intake of saturated fat was estimated from self-reported total food intakes over a 24-h period. If two days of dietary intake were reported, total saturated fat intake was averaged across the two days (236 missing observations).

Cholesterol-lowering or blood-pressure-lowering medication usage were each self-reported using a separate sequence of questions (“To lower your blood cholesterol/blood pressure, have you ever been told by a doctor or health professional to take prescribed medication?” and “Are you now following this advice to take prescribed medicine?”). Responses were coded as currently taking medication vs. not currently taking medication (combining those who were prescribed medication but do not take it, and those who were not told to take medication), and was further dichotomized as taking either medication vs. taking neither medication (any vs. none; 2852 missing observations).

2.4. Analyses

Missing data were imputed using the statistical software R and its “mice” package for multiple imputation. Gibbs sampling was used to generate imputed data based on all other variables described above. Predictive mean matching was used for numeric variables, logistic regression with bootstrap was used for binary variables, and polytomous logistic regression was used for multilevel categorical variables. Ten imputed datasets were created and fit to each regression model (described below), and the results were pooled.

Weighted linear regressions were performed in accordance with NHANES Analytic Guidelines (Johnson et al., 2013) using R’s “survey” package for survey weighting. Regressions examined the relationship between TTFC and each cholesterol outcome (total cholesterol, HDL, LDL, and HDL/LDL ratio) separately. Weighted linear regressions were performed on numeric cholesterol outcomes, and weighted logistic regressions were performed on guideline-based binary cholesterol outcomes. Three models of varying complexity were run for each outcome: 1) an unadjusted model; 2) a model adjusted for current and lifetime smoking behavior; and 3) a model adjusted for current and lifetime smoking behavior, demographics, and other CVD risk factors. An interaction term between TTFC and pack-years was tentatively included based on previous literature (Selya et al., 2016) for preliminary analysis of models 2) and 3), and was included in the final analyses only if at least trending ($p < 0.10$).

Finally, follow-up analyses were performed examining the relationship between TTFC and the ACC/AHA 10-year risk score 1) at the unadjusted level, and 2) after adjusting for current and lifetime smoking behavior.

3. Results

Summary statistics are shown in Table 1 for the full analytic sample ($N = 3903$) and within each level of TTFC. Cholesterol levels were similar across the full sample and each subgroup, with total cholesterol levels just under 200 mg/dL, HDL levels just under 50 mg/dL, LDL levels just over 110 mg/dL, and an LDL/HDL ratio of about 2.2. In terms of clinical cholesterol guidelines, this corresponded to approximately 45% having unfavorable (i.e., at least borderline-high) cholesterol levels, 60% having desirable or protective HDL levels, 30% having unfavorable (i.e., at least borderline-high) LDL levels, and 16% having an unfavorable LDL-to-HDL ratio. Those reporting TTFC within 5 min were more likely to report suboptimal levels of HDL relative to those reporting longer TTFC (all $p < 0.01$). Those reporting earlier TTFC in the morning had heavier smoking histories, reported more prevalent SHS exposure at home, reported a lower prevalence of past-month moderate physical activity, had a lower poverty ratio, were older on average, were more likely to be White (all $p < 0.05$), and trended towards having higher BP ($p < 0.10$). All other comparisons did not reach significance.

At the unadjusted level, earlier TTFC was associated with lower numeric HDL values (by 2.34 mg/dL for TTFC 5 vs. >60 min, $p = 0.02$) and with a higher numeric LDL-to-HDL ratio (by 0.21 and 0.18 for TTFC 5 and TTFC 30 to 60, both vs. >60 min and $p = 0.01$) (Table 2, row 1). The effect on HDL was also significant when examining guideline-based binary outcomes, in that those smoking within 5 min of waking were only 71% as likely to have desirable HDL levels based on NIH guidelines relative to those smoking more than one hour after waking ($p = 0.01$). TTFC was not associated with total cholesterol or LDL at the unadjusted level, either for numeric values or for binary outcomes.

After adjusting for current (past-month smoking frequency) and lifetime smoking behavior (pack-years) (Table 2, row 2) and the interaction between TTFC and pack-years (if $p < 0.10$), earlier TTFC remained associated with lower numeric HDL values (by 2.92 mg/dL for TTFC 5 vs. >60 min, $p = 0.01$) and higher numeric LDL-to-HDL ratios (by 0.32 and 0.27 for TTFC 5 and TTFC 30 to 60 vs. TTFC >60 min, $p < .01$ and $p = 0.03$, respectively), and became associated with higher numeric LDL values (by 8.27 mg/dL for TTFC 5 vs. >60 min, $p = 0.01$). Additionally, more pack-years of smoking was associated with higher numeric values of LDL and the LDL-to-HDL ratio: For each additional pack-year smoked, LDL values increased by 0.42 mg/dL ($p < .01$) and the LDL-to-HDL ratio increased by 0.01 ($p = 0.01$). The significant interaction terms for these models (TTFC 5 vs. >60 min, $p = .01$) indicates that the effect of TTFC was less positive with increasing pack-years.

For the guideline-based binary cholesterol outcomes, adjusting for current and lifetime smoking behavior revealed significant associations between earlier TTFC with increased odds of having high total cholesterol (odds ratio (OR) = 1.55 for TTFC 30 to 60 vs. TTFC >60 min, $p = 0.01$) and decreased odds of having desirable HDL levels ($OR = 0.69$ for TTFC 5 vs. >60 min, $p = 0.01$). Pack-years was also a significant predictor of the odds of having high total cholesterol ($OR = 1.04$, $p < 0.01$), and again interacted with TTFC (TTFC 5 vs.

>60 min, $p = 0.01$) such that the effect of TTFC was less positive with increasing pack-years.

After adjusting for current and lifetime smoking behavior, demographic characteristics, and other CVD risk factors (Table 2, row 3), earlier TTFC was significantly associated with lower numeric HDL values (by 2.10 mg/dL for TTFC 5 vs. >60 min, $p = 0.02$) and a higher LDL/HDL ratio (by 0.14 for TTFC 5 vs. >60 min, $p = 0.01$). In terms of risk based on clinical guidelines, earlier TTFC was associated with decreased odds of having desirable HDL levels ($OR = 0.72$, $p = 0.04$). The association between TTFC and the guideline-based binary outcomes of total cholesterol, LDL, and the LDL-HDL ratio did not reach significance.

Finally, brief follow-up analyses of the ACC/AHA 10-year CVD risk score did not show a significant main association with TTFC, either at the unadjusted level or after adjusting for current and lifetime smoking behavior (all $ps > 0.05$). However, there was a significant interaction between TTFC and pack-years, such that smoking within 5 min of waking weakened (by 0.2%, $p = 0.02$) the effect of pack-years (by 0.3%, $p < 0.01$), relative to smoking more than 60 min after waking.

4. Discussion

The current study presents a novel and preliminary examination of the relationship between TTFC, an indicator of ND, and cholesterol outcomes, a biomarker for CVD. Smoking sooner in the morning after waking was found to be significantly associated with less favorable cholesterol profiles, including higher odds of exceeding the total cholesterol cutoff, lower numeric HDL values and lower odds of having optimal HDL, higher numeric LDL values, and lower numeric LDL/HDL ratios, after adjusting for current and lifetime smoking behavior. Notably, earlier TTFC remained significantly associated with lower numeric HDL values, lower odds of attaining the desirable HDL cutoff, and a higher numeric LDL-to-HDL ratio, after also adjusting for demographic characteristics, and other CVD risk factors. However, TTFC was not significantly associated with ACC/AHA 10-year CVD risk scores, though it did significantly moderate the effect of pack-years.

To extrapolate the clinical significance of these findings, the impact on 10-year CVD risk as defined by ACC/AHA (Goff et al., 2014) was calculated for hypothetical individuals using the estimated 2.1 mg/dL reduction in HDL for those smoking within 5 min of waking, relative to those smoking more than one hour after waking, in the fully-adjusted model. For an individual 55 years old with total cholesterol of 213 mg/dL and BP of 120 mm Hg, who does not take BP medication, does not have diabetes, and is a smoker, a reduction in HDL from 50 to 47.9 mg/dL corresponds to an increase of 0.1–0.3% in 10-year CVD risk depending on sex and race. For example, the 10-year CVD risk for an African-American woman with these characteristics increases from 2.28% to 2.37% with this 2.1 mg/dL reduction in HDL levels, and the 10-year risk for a white male increases from 10.0% to 10.3%.

The current study supports a small but growing body of literature documenting the independent effects of aspects of ND over and above smoking behavior, and extends it in important ways. Previous research has documented that earlier TTFC is associated with a higher risk for chronic obstructive pulmonary disease (Goodwin et al., 2012; Selya et al., 2016) and smoking-related cancers (Gu et al., 2014; Ito et al., 2013; Kunze et al., 2007; Muscat et al., 2011a, 2012a, 2011b), independently of smoking behavior. The current study, to the authors' knowledge, is the first to show that TTFC, a validated measure of ND (Fagerstrom, 2003), is associated with less favorable cholesterol profiles (especially low HDL). Although there was no significant main effect of TTFC on outcomes of ACC/AHA 10-year CVD risk, its significant interaction with pack-years may indicate a trend with CVD risk that calls for future research using other clinically-relevant measures of global CVD risk.

The mechanism underlying this relationship is currently unknown. One potential explanation is that ND behaviors such as TTFC and cholesterol profiles are common phenotypes of a common genetic risk. While no genetic risks common to ND and cholesterol appear to have been identified, similar findings have been reported in other smoking outcomes. For example, genetic variations on the nicotinic receptor *CHRNA3/5* have been simultaneously linked to ND, lung cancer, and pulmonary impairment, independently of smoking *behavior* (Hancock et al., 2015; Improgo et al., 2010; Kaur-Knudsen et al., 2012; Pillai et al., 2009).

Alternatively, it is possible that ND plays a causal role in less favorable cholesterol profiles. Research on smoking topography (e.g. number of puffs per cigarette, duration of inhalation) shows that smokers often smoke in a way that titrates their nicotine intake to a desired level (Hammond et al., 2005; Kassel et al., 2007), and more nicotine-dependent smokers may alter their smoking topographies in a way that allows them to extract more nicotine from each cigarette. This explanation has been proposed as a mechanism explaining the link between ND and obstructive pulmonary disease (Jiménez-Ruiz et al., 2004; Kim et al., 2011) and is feasible here in explaining the current findings. Given that nicotine is a causal agent in CVD, increasing one's nicotine intake from cigarettes as a result of more severe ND may increase associated biomarkers for CVD, notably lower HDL and a higher LDL-to-HDL ratio.

4.1. Limitations

Limitations of this study should be taken into account. First, since this study uses cross-sectional data, temporality and causation cannot be examined, and the possibility of residual confounding cannot be ruled out. Second, the results may be limited due to the accuracy of self-report for some variables. Third, the assessment of ND is limited in NHANES to only one item, TTFC; therefore, it is not possible to examine other aspects of ND (e.g. drive, tolerance, withdrawal). Fourth, the results cannot be generalized to those reporting "Other" race, those under 20-years old, or former smokers. Finally, findings are preliminary, and future research should examine whether the associations between TTFC and cholesterol translate into clinically significant outcomes, such as more rigorous measures of global CVD risk, diagnoses, heart attacks, or long-term mortality outcomes. Further research is necessary to explore the timing, correlation vs. causality, and mechanisms underlying these findings.

4.2. Strengths

This study has several notable strengths. First and foremost, the current finding that earlier TTFC is associated with less favorable cholesterol profiles is novel and important. Second, this study draws data from NHANES, a large, nationally-representative sample, thus the results are likely to be generalizable to the US population of adult smokers. Finally, this study utilizes laboratory-based measures of blood cholesterol available from NHANES, thus reducing reliance on self-report.

4.3. Implications

This study has novel implications for assessing cardiovascular risk in healthcare settings. The current findings that earlier TTFC is strongly associated with less favorable cholesterol outcomes, above and beyond smoking behavior alone, may prove valuable in providing a graded risk assessment for CVD. Specifically, screening smokers based on TTFC may be effective in providing degrees of risk that are more informative than smoking status alone in assessing CVD risk. Ultimately, TTFC may prove a valuable screening tool that can identify those who need timely and preventive treatment in order to reduce the burden of CVD.

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Table 1

Study sample characteristics by each category of TTFC.

Measure	Full sample (N = 3903)	TTFC 5 min (N = 1218)	TTFC 5–30 min (N = 1172)	TTFC 30–60 min (N = 693)	TTFC > 60 min (N = 725)
Total cholesterol (mg/dL)	193 (165, 223)	192 (165, 220)	194 (165, 225)	196 (166, 226)	195 (192, 222)
High cholesterol (> 200)	1602 (44%)	480 (42%)	488 (45%)	299 (47%)	299 (44%)
HDL (mg/dL)	47 (39, 59)	46 (37, 58)	48 (40, 60)	47 (39, 57)	49 (40, 60)
High HDL (Male: 40; Female 50)	2245 (62%)	648 (57%)	692 (63%)	406 (63%)	437 (64%)
LDL (mg/dL)	112 (89, 137)	111 (90, 134)	113 (87, 139)	115 (93, 140)	112 (91, 138)
High LDL (> 130)	545 (32%)	156 (30%)	174 (33%)	106 (34%)	100 (33%)
LDL/HDL ratio	2.23 (1.68, 3.08)	2.34 (1.67, 3.13)	2.17 (1.68, 3.01)	2.38 (1.76, 3.10)	2.19 (1.65, 3.17)
High ratio (> 3.5)	274 (16%)	85 (16%)	81 (15%)	48 (16%)	55 (18%)
Pack-years	15 (5.4, 30.0)	24 (10.5, 42.0)	18 (8.1, 33.0)	11.4 (4.8, 23.4)	5.5 (2.5, 12.5)
Past-month smoking frequency (# days)	30 (30, 30)	30 (30, 30)	30 (30, 30)	30 (30, 30)	30 (30, 30)
Secondhand smoke exposure					
None	1422 (37%)	246 (20.2%)	400 (34.2%)	317 (46.0%)	407 (56.7%)
Any	2465 (63%)	970 (79.8%)	769 (65.8%)	372 (54.0%)	311 (43.3%)
Past-month moderate physical activity					
None	1868 (48%)	649 (53.3%)	535 (45.7%)	291 (42.0%)	350 (48.3%)
Any	2034 (52%)	569 (47.7%)	636 (54.3%)	402 (58.0%)	375 (51.7%)
Body mass index (kg/m ²)					
Normal weight (<25)	1490 (39%)	473 (39%)	479 (41%)	249 (36%)	254 (36%)
Overweight (25–30)	1190 (31%)	355 (30%)	343 (30%)	223 (33%)	237 (33%)
Obese (> 30)	1169 (30%)	371 (31%)	334 (29%)	213 (31%)	223 (31%)
Self-reported diabetes status					
No diabetes	3467 (89%)	1070 (87.9%)	1042 (88.9%)	618 (89.2%)	653 (90.4%)
Prediabetes or diabetes	433 (11%)	148 (12.2%)	130 (11.1%)	75 (10.8%)	69 (9.6%)
ApoB (mg/dL)	92.5 (77.0, 113.0)	90.0 (78.0, 111.0)	93.0 (76.0, 113.0)	94.0 (77.0, 114.0)	94.0 (78.0, 114.0)
Blood pressure					
Normal	1773 (48%)	517 (45%)	542 (48%)	334 (51%)	350 (51%)
Pre-hypertensive	1297 (35%)	409 (36%)	401 (35%)	218 (33%)	236 (34%)
Hypertensive	638 (17%)	223 (19%)	189 (17%)	100 (15%)	103 (15%)

Measure	Full sample (N = 3903)	TTFC 5 min (N = 1218)	TTFC 5–30 min (N = 1172)	TTFC 30–60 min (N = 693)	TTFC > 60 min (N = 725)
Dietary intake of saturated fat (g)	24.7 (16.8, 35.12)	25.0 (16.9, 35.6)	25.0 (16.8, 34.8)	24.1 (17.0, 35.2),	24.3 (16.4, 34.1)
Current medication usage ^a					
Does not take any medication	115 (11%)	40 (11%)	33 (10%)	21 (12%)	19 (11%)
Takes at least one medication	936 (89%)	317 (89%)	286 (90%)	157 (88%)	156 (89%)
Poverty ratio	1.4 (0.8, 2.9)	1.2 (0.7, 2.2)	1.4 (0.9, 2.9)	1.6 (0.9, 3.0)	1.6 (0.9, 3.3)
Race/ethnicity					
Non-Hispanic White	2093 (57%)	732 (63.0%)	699 (62.6%)	359 (55.2%)	278 (41.2%)
Non-Hispanic Black	962 (26%)	322 (27.7%)	263 (23.6%)	175 (26.9%)	166 (22.9%)
Hispanic	636 (17%)	107 (9.2%)	154 (13.8%)	116 (17.9%)	231 (31.9%)
Sex					
Female	1693 (43%)	544 (44.7%)	502 (42.8%)	306 (44.2%)	311 (42.9%)
Male	2210 (57%)	674 (55.3%)	670 (57.2%)	387 (55.8%)	414 (57.1%)
Age (years)	44.0 (32.0, 45.0)	45.0 (34.0, 55.0)	46.0 (34.0, 58.0)	42.0 (30.0, 56.0)	42.0 (29.0, 54.0)

Note. TTFC = Time to first cigarette. HDL = High-density lipoprotein. LDL = Low-density lipoprotein. ApoB = Apolipoprotein B. Categorical variables are presented as *N* (valid percentage). Continuous variables are presented as median (inter-quartile range).

^aRefers to medication for lowering cholesterol and/or medication for lowering BP.

Table 2

Weighted linear regression results examining the relationship between TTFC and blood cholesterol outcomes.

Model	Covariate	Total Cholesterol		HDL		LDL		LDL/HDL ratio	
		Numeric <i>B</i> (<i>CI</i>)	Binary <i>OR</i> (<i>CI</i>)	Numeric <i>B</i> (<i>CI</i>)	Binary <i>OR</i> (<i>CI</i>)	Numeric <i>B</i> (<i>CI</i>)	Binary <i>OR</i> (<i>CI</i>)	Numeric <i>B</i> (<i>CI</i>)	Binary <i>OR</i> (<i>CI</i>)
Unadjusted	TTFC (min)	5	3.10 (−2.80, 9.01)	1.02 (0.77, 1.36)	−2.34 (−4.38, −0.29)	0.71 (0.55, 0.91)	3.71 (−1.53, 8.95)	1.10 (0.94, 1.73)	1.12 (0.69, 1.81),
		5–30	4.87 (−0.83, 10.46)	1.09 (0.85, 1.40)	−0.18 (−1.94, 1.59)	1.00 (0.78, 1.29)	4.04 (−1.27, 9.36)	1.14 (0.86, 1.50)	0.86 (0.54, 1.38),
		30–60	3.91 (−2.12, 9.93)	1.28 (0.94, 1.73)	−1.75 (−3.69, 0.18)	0.96 (0.75, 1.24)	4.64 (−0.97, 10.2)	1.27 (0.80, 1.53)	1.05 (0.59, 1.85),
		>60	–	–	–	–	–	–	–
Adjusted for smoking behavior ^a	TTFC (min)	5	6.38 (−0.78, 13.55)	1.22 (0.88, 1.69)	−2.92 (−5.10, 0.75)	0.69 (0.52, 0.92)	8.27 (2.07, 14.46)	1.37 (0.99, 1.90)	1.16 (0.73, 1.84)
		5–30	0.28 (−5.77, 6.34)	1.08 (0.81, 1.44)	−0.60 (−2.56, 1.36)	0.99 (0.75, 1.31)	1.51 (−4.44, 7.46)	1.16 (0.84, 1.61)	0.99 (0.65, 1.49)
		30–60	5.03 (−3.67, 13.72)	1.55 (1.02, 2.37)	−2.00 (−4.01, 0.02)	0.96 (0.75, 1.24)	6.70 (−1.31, 14.71)	1.49 (0.99, 2.25)	1.17 (0.74, 1.86)
		>60	–	–	–	–	–	–	–
Fully adjusted ^b	TTFC × Pack-Years	Pack-Years	0.49 (0.20, 0.77)	1.04 (1.02, 1.06)	0.02 (−0.01, 0.06)	1.00 (1.00, 1.01)	0.42 (0.19, 0.66)	1.03 (1.01, 1.04)	1.00 (1.00, 1.01)
		5	−0.45 (−0.76, −0.14)	0.97 (0.95, 0.99)	–	–	−0.44 (−0.69, −0.20)	0.97 (0.96, 0.99)	–
		5–30	−0.11 (−0.43, 0.19)	0.98 (0.96, 1.00)	–	–	−0.15 (−0.42, 0.11)	0.98 (0.97, 1.00)	–
		30–60	−0.29 (−0.67, 0.08)	0.97 (0.95, 0.99)	–	–	−0.31 (−0.67, 0.04)	0.98 (0.96, 1.00)	–
Fully adjusted ^b	TTFC (min)	>60	–	–	–	–	–	–	–
		5	1.00 (−2.22, 4.23)	0.86 (0.58, 1.28)	−2.10 (−3.85, −0.36)	0.72 (0.53, 0.99)	2.30 (−0.81, 5.40)	1.17 (0.65, 2.09)	1.14 (0.56, 2.33)
		5–30	1.78 (−1.63, 5.19)	0.87 (0.58, 1.29)	−0.96 (−2.67, 0.74)	0.95 (0.69, 1.31)	2.23 (−1.80, 6.26)	1.13 (0.67, 1.88)	0.93 (0.49, 1.75)
		30–60	0.04 (−3.66, 3.75)	1.16 (0.73, 1.85)	−1.51 (−3.21, 0.18)	0.99 (0.74, 1.33)	1.06 (−2.75, 4.87)	1.07 (0.64, 1.80)	1.01 (0.52, 1.96)
Fully adjusted ^b	Pack-Years	>60	–	–	–	–	–	–	–
		–	−0.32 (−0.09, 0.03)	1.00 (0.98, 1.07)	0.01 (−0.03, 0.05)	1.00 (0.97, 1.02)	−0.04 (−0.09, 0.12)	1.00 (0.99, 1.01)	1.00 (0.99, 1.01)

Note: Each outcome is shown in a separate column. Left sub-columns present weighted linear regressions on numeric outcomes of total cholesterol, HDL, LDL values (all mg/dL), and the LDL/HDL ratio. Right sub-columns present weighted logistic regressions based on cutoff values from NIH and American Heart Association guidelines (total cholesterol: 200 mg/dL; HDL: 40 mg/dL for men and 50 mg/dL for women; LDL: 130 mg/dL; LDL/HDL ratio: 3.5). TTFC = Time to first cigarette. HDL = High-density lipoprotein. LDL = Low-density lipoprotein. ApoB = Apolipoprotein B. BP = Blood pressure. *B* = Unstandardized regression coefficient.

^a Adjusted for current (number of days smoked in the past 30) and lifetime (pack-years) smoking behavior, and the interaction between TTFC and pack-years (only if $p < .10$ in preliminary analyses).

^b Adjusted for current (number of days smoked in the past 30) and lifetime (pack-years) smoking behavior, demographic factors (age, biological sex, race/ethnicity, and poverty ratio), other risk factors for cardiovascular disease (secondhand smoke exposure in the home, body mass index, binary past-month moderate physical activity, current prescription medication usage for cholesterol and/or BP; ApoB value, diabetes status – normal vs. pre-diabetic or diabetic; and BP status – normal vs. pre-hypertensive vs. hypertensive). The interaction between TTFC and pack-years did not reach $p < .10$ in preliminary analyses for any model, and was therefore not included.