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.

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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

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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