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Leslie Nicole Lee Date

EVALUATION OF BIOMARKERS OF THIRDHAND SMOKE TO INFORM RISK AND POLICY

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EVALUATION OF BIOMARKERS OF THIRDHAND SMOKE TO INFORM RISK AND POLICY

By
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B.S., University of Georgia, 2003

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An abstract of
A Thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
In partial fulfillment of the requirements of the degree of
Master of Public Health in the Career MPH program
2012

Abstract

Introduction
Thirdhand smoke (THS) is residual tobacco smoke contamination remaining on surfaces and in dust after a cigarette: is extinguished, is re-emitted into the gas phase, or reacts with oxidants and other environmental compounds to produce secondary pollutants. THS leads to involuntary exposure to tobacco smoke pollutants. The health effects and exposure pathways of THS are not fully known, resulting in a lack of sufficient evidence to create laws or regulations in response to potential health risks of exposure. The purpose of this study was, among the current population classified as secondhand smoke (SHS) exposed, to examine and describe the proportion with THS exposure and conduct a needs assessment for THS research.

Methods
Study objectives: 1) determine if cotinine concentrations of nonsmokers (with serum cotinine level $\leq$ 10 ng/mL) display two distinct exposure levels, indicating exposure to SHS and THS; 2) characterize cotinine concentrations and demographics of THS exposed people in the general U.S. population by parsing the nonsmoker population into smaller subsets; and 3) conduct a needs assessment to recommend further areas of research needed to more fully understand the risks related to THS exposure. Drawing from the NHANES 2009-2010 dataset (N=8,251), the nonsmoker subset was selected for analysis to determine whether some subjects were incorrectly classified as having been exposed to SHS when actually exposed to THS.

Results
Serum cotinine concentrations showed a bimodal distribution distinguishing smokers from nonsmokers. Distribution of the nonsmoker population appeared multimodal, suggesting multiple sources of exposure. For this study, THS exposure was defined as nonsmokers with zero smokers in the home and no indication of cigarettes smoked in the home. THS exposed people had serum cotinine levels $\leq$ 0.737 ng/mL with greatest exposure likely among Hispanics and children.

Conclusion
This study suggests approximately 88% of nonsmokers are likely exposed to THS. Findings are similar with previous studies that suggest young children as a vulnerable population for THS exposure. Results confirm the need to further examine low-level toxicity of tobacco smoke constituents and redefine environmental tobacco smoke to include THS exposure. This is the first attempt at defining and describing the THS exposed population.

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Acknowledgements

I would like to express my sincere gratitude for the wisdom, guidance, and availability of both Dana Boyd Barr, my thesis advisor, and Parinya Panuwet, my committee chair. Their encouragement and dedication throughout this thesis effort have been fundamental in the successful completion of this project.

I would also like to acknowledge the love and support of my family, friends and colleagues who have continuously provided only care and motivation to help me balance work, school, and life. A special thanks to my husband, Eunjin, for being ever-patient and always encouraging me to pursue big dreams, for being there from the start and providing me with the space and courage to finish strong. And for the faithfulness of my Father, who has provided me with strength and shown me that possibilities with Him are endless.

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CHAPTER 1 – INTRODUCTION

Introduction and Rationale

The 2006 Surgeon General Report on smoking and tobacco use pointed to smoking as the single greatest and avoidable cause of disease and death (DHHS, 2006). Further, the 2010 report validated the existing evidence that there is no safe level of exposure to tobacco smoke (DHHS, 2010). Nonsmokers (also termed non-active smokers) are susceptible to the same effects from exposure to second hand smoke (SHS)—also referred to as environmental tobacco smoke (ETS)—as smokers (also termed active smokers) are to directly inhaled smoke (CDC, 2011a).

Nonsmokers exposed to SHS have serum cotinine levels measuring 1 ng/mL up to10 ng/mL. Serum cotinine levels >10 ng/mL are associated with active smoking (CDC, 2010). The U.S. Environmental Protection Agency (EPA), National Toxicology Program and the International Agency for Research on Cancer (IARC) have all designated SHS as a known human carcinogen (DHHS, 2006). Despite the existing data on the effects of smoking and tobacco smoke exposure, tobacco use continues to be responsible for over 443,000 deaths annually (CDC, 2011a). Additionally, several million Americans, including children, continue to be exposed to SHS regardless of the considerable progress that has been made in tobacco control in the United States (DHHS, 2006). For example, smoke-free laws protecting nonsmokers from involuntary exposure to SHS in worksites, restaurants and bars expanded from zero in 2000 to 26 states (including D.C.) in 2010, which has resulted in an approximate 70% reduction in measureable biomarkers of SHS exposure. However, nearly 60% (22 million) of children between 3-11 years remain exposed to SHS (CDC, 2011c; CDC, 2012b; DHHS, 2006).

Although the effects of smoking and SHS exposure are inarguable, a less known type of smoke-related exposure is a recent concept in the field of tobacco control, termed thirdhand smoke (THS). THS is the chemical aging of tobacco smoke, consisting of residual tobacco smoke pollutants found in cigarette smoke that 1) remains on surfaces and in dust after a cigarette is extinguished, 2) are remitted back into gas form, or 3) reacts with oxidants and other compounds found in the environment, yielding secondary pollutants (Burton, 2011; Kuschner, Reddy, Mehrotra, & Paintal, 2011; Rehan, Sakurai, & Torday, 2011). The purpose of this paper is to describe the current proportion of people who are exposed to THS that are currently classified as having exposures to SHS. As a part of this analysis, a needs-assessment will be performed to derive recommendations to help guide researchers as they seek to fill the research gaps related to THS exposure.

Problem Statement

In the United States, cigarette smoking is responsible for one out of five deaths each year, including deaths from SHS (American Cancer Society, 2012). The composition of SHS consists of an intricate mixture of over 7,000 chemicals, of which at least 250 are known to be harmful and over 70 that are known to be carcinogenic (DHHS, 2010). As such, the National Institute for Occupational Safety and Health (NIOSH) has implicated SHS to be an occupational carcinogen (DHHS, 2006). Directly following its emission, tobacco smoke changes both physically and chemically, and reacts with the environment (Sleiman et al., 2010). Some SHS pollutants remain principally in the gas phase and can be removed by ventilation, but a significant portion associates with indoor surfaces and resuspendable particles such as dust, resulting in extended residence times (Matt, Quintana, Zakarian, et al., 2011).

As an emerging health concern, potential health effects of THS have been little studied to date and are not fully known (Schick, 2011). Agreement exists regarding the health impacts of tobacco use and SHS exposure, but the nature and consequences of THS remain ambiguous (Matt, Quintana, Destaillats, et al., 2011). As such, it is too early to create laws or regulations in response to the potential health risks of THS exposure.

The presence of THS in indoor environments allows for exposure pathways relevant for children who live in homes where smoking occurs (Matt, Quintana, Destaillats, et al., 2011). The effects of tobacco smoke exposure have already had an enormous impact and burden on the public's health and the health care system in the United States. Cigarette smoking costs over $193 billion annually, and SHS exposure costs is estimated at $10 billion a year (DHHS, 2010). Additionally, nearly 50,000 annual deaths (11%) from smoking and SHS exposure are attributed to SHS exposure alone (CDC, 2012c).

Residual or THS consists of a mixture of tobacco smoke pollutants that remain in an indoor environment (Sleiman et al., 2010). Despite differences in the chemistry, toxicology, and behavior of THS and SHS, they are closely related and coexist during early formation of THS as well as in environments where smoking occurs intermittently (Matt, Quintana, Zakarian, et al., 2011). Indoor environments with regular tobacco use become reservoirs of tobacco smoke pollutants, causing involuntary THS exposure among nonsmokers long after smoking has taken place (Matt, Quintana, Zakarian, et al., 2011). This finding is of significance because the home is the principal location for child and adult exposure to tobacco smoke, according to the Surgeon General (DHHS, 2004).

Termed a "stealth toxin," increased ventilation will not reduce or eliminate THS once contaminants adsorb to surfaces and dust (Kuschner et al., 2011; Schick, 2011). In these

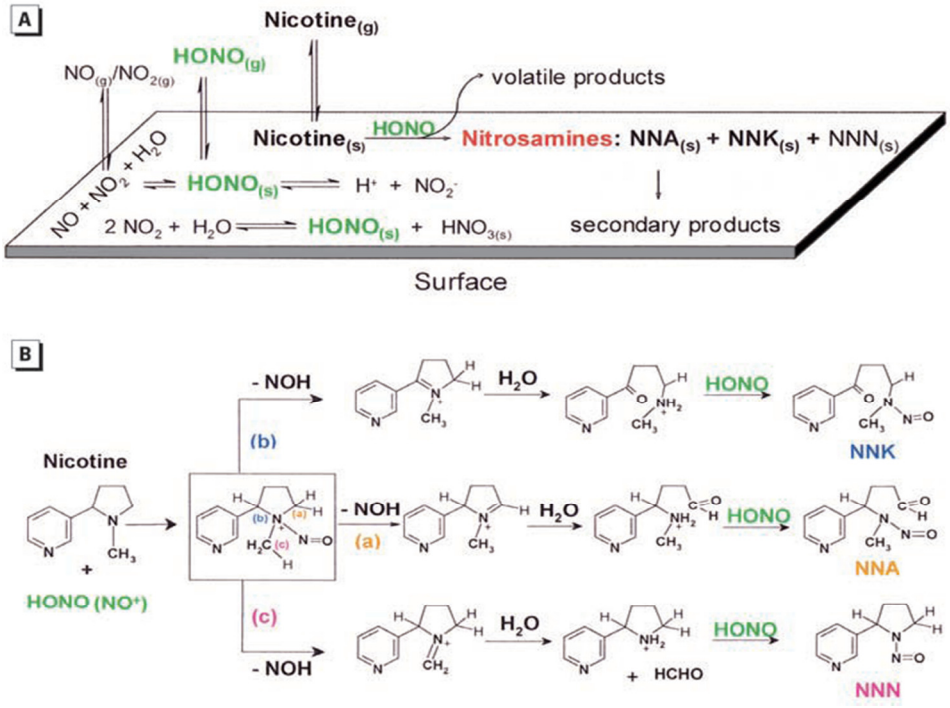
contaminated smoking indoor environments, research on the tobacco combustion process suggests that some gas- and particle-phase compounds found in THS can remain indoors for extended periods of time, even months after the last cigarette was smoked (Matt, Quintana, Zakarian, et al., 2011). In effect, this would prolong the time period for potential exposure to the chemical compounds of THS.

Main exposure pathways for THS include dermal contact with tobacco-specific nitrosamine (TSNA)-contaminated surfaces (skin, clothing, furnishings) and inhalation/ingestion of TSNA-contaminated dust (Sleiman et al., 2010). As such, vulnerable populations include infants and children due to increased exposure and sensitivity, persons with limited mobility, low-income populations living in public housing, and housing environments frequently changing ownership or occupancy (Matt, Quintana, Destaillats, et al., 2011; Sleiman et al., 2010; Winickoff et al., 2009).

THS is comprised of both primary and secondary pollutants. Primary pollutants are directly emitted from tobacco smoke. Secondary pollutants result from either from chemical reactions between 1) primary pollutants with one another, or 2) primary pollutants and oxidants existing in the indoor environment (Rehan et al., 2011). Nicotine is the key chemical compound that causes addiction in humans due to the similarity of a part of the nicotine molecule with brain neurotransmitter, acetylcholine (DHHS, 2010). Ninety-five percent of nicotine emitted in the air is adsorbed by indoor surfaces within two hours of emission and accumulates to greater concentrations with repeated smoking (Rehan et al., 2011). Of particular concern is the reaction of residual nicotine from tobacco constituents adsorbed to indoor and vehicle surfaces with ambient nitrous acid (HONO) to form TSNAs.

TSNAs are carcinogenic, having the potential to induce mutations and breaks in DNA strands (Sleiman et al., 2010). The three main TSNA constituents of THS formed in this reaction with HONO are 1-(N-methyl-N-nitrosamino)-1-(3-pyridinyl)-4-butanal (NNA), 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), and N-nitroso nornicotine (NNN) (Figure 1). NNK is a known constituent of tobacco smoke particles; however, NNA is a TSNA that is absent in freshly produced tobacco smoke (Sleiman et al., 2010). NNK and NNN are known human carcinogens (Burton, 2011). NNK is shown to induce mutations, breakage of DNA strands, and oxidative damage in sunlight (Sleiman et al., 2010). Previous studies conducted examining exposure to NNA and NNK found that that exposure to the developing lung resulted in disrupted homeostatic signaling (Rehan et al., 2011). Sorbed nicotine also reacts with atmospheric ozone indoors to yield secondary oxidation products, including formaldehyde and N-methylformamide, both of which are concerns to human health (Rehan et al., 2011). The low volatility of TSNAs combined with high nicotine levels typical of tobacco smoke-contaminated environments allow TSNAs to persist indoors and on skin (Matt, Quintana, Zakarian, et al., 2011; Sleiman et al., 2010).

Figure 1. TSNA constituents of THS



Adapted from Sleiman et al., 2010.Physical-chemical processes of nicotine reactions with nitrous acid on indoor surfaces. (*A*) Illustration of surface-mediated nitrosation of nicotine. (*B*) Proposed mechanism for the formation of TSNAs. Adapted from Sleiman et al. (2010). Abbreviations: (a), proposed mechanism for formation of NNA; (b), proposed mechanism for formation of NNK; (c), proposed mechanism for the formation of NNN; (g), gas phase; HCHO, formaldehyde; (s), on surface; secondary products are those created by indoor chemical reactions from primary tobacco smoke products (e.g., NNK from nicotine).

Public awareness of THS and potential risks could help modify smoking beliefs and behaviors, thereby encouraging smoking bans among individuals, and promoting smoking cessation (Matt, Quintana, Destaillats, et al., 2011). This raises the need for further research and conclusive evidence that will support public health to draw conclusions regarding THS health hazards. In the long term, much research is needed to better understand the chemistry, exposure, and prevalence of THS pollutants and their health implications. However, as no risk-free level of tobacco smoke exposure exists, identifying and describing the THS exposed population will help to provide further insight to supporting this statement and informing public health risk and policy.

Purpose

The purpose of this research is to describe the current proportion of people who are exposed to THS that are currently classified as having exposures to SHS and conduct a needs assessment for THS research. This information may be used to advise policy and inform risk for involuntary THS exposure, as it is very likely that further studies will continue to be conducted in this area. In particular, this information may be useful to inform policy and risk for vulnerable populations that may unknowingly have continuous exposure to an environment contaminated with THS pollutants.

Theoretical Framework

We will conduct an analysis on an existing National Health and Nutrition Examination Survey (NHANES 2009-2010) dataset that contains demographic information and serum cotinine biomarker levels. Our analysis will focus on 1) defining the nonsmoker population (consisting of SHS and THS exposed subjects), and 2) analyzing the cotinine data that are ≤ 10 ng/mL, to determine if some of the subjects that were classified as having SHS exposure actually were exposed to THS. This dataset is the most comprehensive dataset involving cotinine biomarkers.

Objectives

The objectives of this research are to:

- Determine if cotinine concentrations of nonsmokers (with serum cotinine level ≤ 10 ng/mL) display two distinct exposure levels, indicating exposure to SHS and THS.
- Characterize the cotinine concentrations and demographics of THS exposed people in the general U.S. population by parsing the nonsmoker population into smaller subsets.
- Conduct a needs assessment to recommend further areas of research needed to more fully

understand the risks related to THS exposure.

Significance Statement

Although much research is yet to be done on THS and its health implications, identifying biomarker concentrations and providing descriptive statistics for THS exposed people will inform policy at federal and state levels and also inform health risk. Currently policies exist in protecting the workplace, bars, and restaurants from SHS exposure; however, the Surgeon General indicates that the home remains the most important source of ETS exposure for children (DHHS, 2006). In addition to the damaging effects of SHS exposure on the developing lungs of young children in a home environment where smoking occurs, exposure may potentially be expanded to include THS. Because children's bodies are continually developing physically, have higher breathing rates than adults, are in close proximity to dust, more frequently insert nonfood items into their mouths, and additionally have little control over their indoor environments, they are a vulnerable population to the exposure of THS (Sleiman et al., 2010). This supports the need for further research in the nature and consequences of THS exposures.

Definition of Terms

Mainstream smoke (MSS): Smoke exhaled by a smoker (DHHS, 2006).

Nonsmoker: Also referred to as "non-active smoker", a nonsmoker is defined as having a serum cotinine value $\leq$ 10 ng/mL. For the purposes of this study, a nonsmoker includes both SHS and THS exposed subjects.

Passive smoking: Also referred to as "involuntary smoking", passive smoking is the inhalation of SHS by nonsmokers and smokers (DHHS, 2006).

Secondhand smoke (SHS): Also referred to as "environmental tobacco smoke", SHS is smoke that contaminates indoor and outdoor environments consisting of a mixture of sidestream smoke (released by a burning cigarette) and mainstream smoke (exhaled by a smoker) (DHHS, 2006).

Sidestream smoke (SSS): Smoke released by a burning cigarette; has higher concentrations of many of the same toxins found in cigarette smoke (DHHS, 2006).

Smoker: Also referred to as "active smoker", a smoker is defined as having a serum cotinine level > 10 ng/mL.

Thirdhand smoke (THS): Also referred to as "aged" or "legacy" tobacco smoke or "residual secondhand smoke", THS is residual tobacco smoke contamination that remains on surfaces and in dust after a cigarette is extinguished, is re-emitted into the gas phase, or reacts with oxidants and other environmental compounds to produce secondary pollutants (Matt, Quintana, Destaillats, et al., 2011; Winickoff et al., 2009). Evolving from SHS, THS leads to involuntary exposure of tobacco smoke pollutants (Matt, Quintana, Destaillats, et al., 2011).

Total tobacco smoke exposure: Collective involuntary exposure to tobacco smoke pollutants during and after the time that cigarettes are smoked (Matt, Quintana, Destaillats, et al., 2011).

CHAPTER 2 – REVIEW OF LITERATURE

Introduction

This chapter provides a review of the literature on tobacco smoke, examining the nature and effects of smoking and exposure to secondhand and thirdhand tobacco smoke. Specifically, the literature review provides information on the current findings on the burden of THS, constituents, and policy.

Burden of Disease

Morbidity and Mortality

The morbidity and mortality resulting from smoking and SHS exposure is incontestable. Smoking has been identified as a leading preventable cause of disease and death (DHHS, 2006). Globally, tobacco use is attributed to causing over 5 million deaths annually; this toll is expected to exceed 8 million deaths per year by 2030 (WHO, 2009). In the United States, smoking and SHS combined causes an estimated 443,000 deaths annually, with 49,400 of these deaths per year caused by exposure to SHS alone (DHHS, 2004, 2010). Although the number of deaths from ETS is only a fraction of deaths from smoking, it is noteworthy as exposure to SHS is involuntary. Since the first published report from the Surgeon General in 1964, over 12 million premature deaths have been attributed to smoking (DHHS, 2004). Specifically, the lifespan of smokers is reduced an average of 14 years when compared with nonsmokers (CDC, 2012c). According to the 2004 Surgeon General report, smoking is the primary cause of 30% of deaths from cancer, 80% deaths from chronic obstructive pulmonary disease, and early death from cardiovascular disease (DHHS, 2004). The chronic diseases attributed to smoking and SHS

exposure are the leading causes of death and disability, which in effect burdens the U.S. healthcare system.

Economic burden of smoking and SHS

In 2010, current tobacco use accounted for 19% of the U.S. adult population, which is approximately 45.3 million people (CDC, 2011d). The burden of disease attributable to smoking and SHS is extensive, encompassing both economic burden in addition to death and disease. According to the 2010 Surgeon General report, cigarette use amounts for over $193 billion each year in both health care costs and productivity losses (DHHS, 2010).

Because the percentage of the population exposed to SHS is so large, the associated costs of the effects of exposure are substantial. Behan, Eriksen and Lin (2005) carried out a review of literature on the morbidity and mortality effects from SHS exposure to calculate resulting economic costs in the United States. One of the major conclusions from this study was the finding that exposure to SHS is estimated to cost a total of more than $10 billion each year in the United States, with over $5 billion attributed to direct medical costs and over $5 billion due to indirect economic costs (Behan et al., 2005). According to another study conducted by the American Legacy Foundation (2002), of the estimated $12 billion spent on smoking-attributable diseases in 2001, $1.1 billion could be saved each year if adult smoking prevalence was reduced to 50%.

Vulnerable populations

Children, in particular, are vulnerable to the damaging health effects of exposure to tobacco smoke because their bodies and lungs are still developing. More than half the population of children in the United States is exposed to SHS (CDC, 2011a). The World Health Organization estimates the economic burden due to SHS for children to be between a range of

$703 - $897 million in the United States, which is three times that of Britain and over three times that of Canada (Rosen et al., 2011). According to current smoking patterns, CDC estimates 5 million children younger than 18 years alive today will be victims to premature death from smoking-related illness (CDC, 2012c).

Summary

In summary, studies measuring the economic burden and the burden of death and disease attributed to smoking and SHS exposure are important to informing the development of policy. Tobacco control and prevention interventions as a whole, including education, clinical, regulatory and economic actions at the state and federal level, have been effective in reducing smoking rates (DHHS, 2004). As such programs are effective in reducing the burden of disease from tobacco smoke, then incorporating the potential harms and reach of THS may further aid in the effectiveness of these programs, particularly among prevention efforts in the home environment and the impact of total smoke exposure.

According to CDC, current state spending on tobacco control and prevention does not meet the current recommended levels: of the $25.3 billion allotted to states from tobacco excise taxes and tobacco industry legal settlements, states are currently only spending 2% on tobacco control programs (DHHS, 2004). Understanding the costs to the already existing economic burden on health care for both the government and for private individuals may encourage the reallocation of additional funding towards the expansion of these programs. A table comparing the exposure, deaths, and economic costs from smoking, SHS, and THS is included in the appendix (Appendix A).

Constituents

Tobacco smoke has been identified by both the International Agency for Research on Cancer (IARC), the U.S. Environmental Protection Agency, and the National Toxicology Program (NTP) as a known human carcinogen (DHHS, 2006). Cigarette smoke contains more than 7,000 chemicals, hundreds are known to be harmful, and at least 69 are known carcinogens (DHHS, 2010).

Therapeutic constituent: Nicotine

Nicotine is the key component in tobacco products that causes and sustains addiction (DHHS, 2010). Nicotine works to stimulate multiple types of nicotinic receptors in the brain (DHHS, 2010). In particular, nicotine indirectly causes dopamine to be released in regions controlling pleasure and motivation (CDC, 2012b).

Mainstream smoke constituents

Mainstream smoke is the main source of exposure to tobacco smoke for smokers, and is produced when the smoker draws air through the cigarette. Although mainstream smoke is a component of SHS, mainstream smoke exposure to smokers is different than the exposure to nonsmokers in that most of the particulate components of mainstream smoke remains in the smoker's lungs (Behan et al., 2005). However, despite different comparative concentrations, many of the chemical components of mainstream and sidestream smoke are the same (National Research Council, 1986).

SHS constituents

SHS is comprised of both mainstream and sidestream smoke. Sidestream smoke is directly emitted into the air from cigarette combustion. Due to the nature in which sidestream

smoke is generated, it also contains higher concentrations of many toxicants found in cigarette smoke (DHHS, 2010).

THS constituents

Thirdhand or aged residual SHS pollutants include semivolatile compounds and particulate matter originating from SHS pollutants and secondary pollutants that adhere to indoor surfaces over time and are later re-emitted (Rehan et al., 2011; Sleiman et al., 2010). These compounds undergo physical and chemical reactions over time. Within a few hours immediately following smoking, THS coexists with SHS until the SHS is removed by ventilation (Matt, Quintana, Destaillats, et al., 2011).

Singer et al. (2003) investigated the effects of sorption interactions and the composition of environmental tobacco smoke over time, and also examined sorption interactions with exposure time-patterns indoors in environments where regular smoking occurs. This study found that nonsmoker exposure to volatile hazardous air pollutants (HAP) and toxic air contaminants (TAC) could be reduced to very low levels through combined ventilation during smoking and prohibition of smoking when a nonsmoker is home. However, these measures did not reduce exposure to lower volatile HAPs/TACs, nicotine, and 3-ethenylpyridine (3-EP), indicating that nonsmokers can still be subjected to exposure to moderate levels of these pollutants in a home where regular smoking occurs even with efforts to avoid direct SHS exposure.

In 2006, Destaillats et al. tested the hypothesis that atmospheric ozone can react with sorbed nicotine to cotton and Teflon at significant rates under representative indoor conditions which also impact nicotine desorption. This study found that desorption occurred throughout the entire experimental period, with a higher rate of desorption in cotton into the gas phase. Additionally, the study observed the formation of formaldehyde and N-methylformamide during

ozone interaction with nicotine for both surfaces. The study concluded that materials and surfaces loaded with environmental tobacco smoke particles can act as long-term sources of secondary pollutants (Destaillats, Singer, Lee, & Gundel, 2006).

A study conducted by Becquemin et al. in 2010 was the first to examine the hypothesis of a resuspension of cigarette smoke contaminants in the air over time from surface contamination, i.e., THS (Becquemin et al., 2010). Concentrations and sizes of smoke particles were measured directly after their deposition and resuspension in a closed room. Findings indicated that these airborne particles were ultrafine in size, and concentration was reduced 100 fold following the initial 4 hours after smoking, and reduced another 100 fold after 24 hours. However, after resuspension, the concentration increased 100 fold back to that observed 4 hours after smoking, which was still a fraction of the concentration of SHS (Becquemin et al., 2010). However, the researchers also suggested that the remainder of the concentration of contaminants originally produced by cigarettes may have attached to surfaces, leading to possible exposure through ingestion, dermal transfer or inhalation (Becquemin et al., 2010).

Sleiman et al. (2011) examined the reaction of residual nicotine from tobacco smoke sorbed to indoor surfaces (within a smoker's vehicle) with ambient nitrous acid (HONO) to form carcinogenic tobacco-specific nitrosamines (TSNAs). This study was the first to identify 1-(N-methyl-N-nitrosamino)-1-(3-pyridinyl)-4-butanal (NNA) as the major product, a TSNA that is missing in freshly emitted tobacco smoke. NNA can induce mutations, DNA strand breaks, and oxidative damage under sunlight (Sleiman et al., 2010). Also detected were the TSNAs 4-(methylnitrosamino)-1-(3-pyridinyl)-1-butanone (NNK) and N-nitroso nornicotine (NNN) (Sleiman et al., 2010). This study concluded that dermal contact with TSNA contaminated

surfaces, including skin and clothing, and inhalation and ingestion of dust contaminated by TSNAs are likely the main pathways for exposure (Sleiman et al., 2010).

Summary

Even early on in research and findings, it is evident that people exposed to THS come in contact with a mixture of chemical pollutants in both gas and particulate phase similar to what is found in mainstream smoke and SHS. Further, THS also exposes individuals to additional chemicals not necessarily found in mainstream smoke or SHS from reactions involving tobacco smoke constituents (Matt, Quintana, Zakarian, et al., 2011). With current research documenting an association between smoking in the home with extended exposure to levels of tobacco toxins for up to months after the period of active smoking, there is a need to further investigate the impact of exposure to THS (Winickoff et al., 2009). The pollutants currently known to be included in THS are products already known to concern human health and irritancy (e.g. formaldehyde, N-methylformamide) (Destaillats et al., 2006). An improved understanding of the components included in THS will help to inform impact of exposure to human health. A table describing sidestream, secondhand and thirdhand smoke constituents is included in the appendix (Appendix B).

Exposure

Smokers' exposure

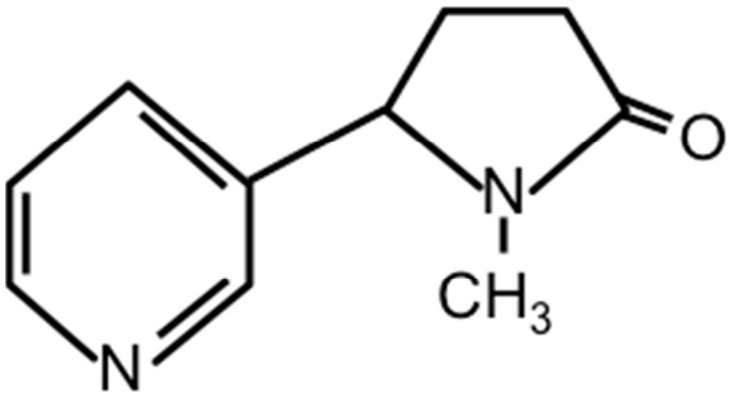
Mainstream smoke is the primary source of smoke exposure for smokers. Additionally, the makeup of mainstream smoke inhaled by smokers is different than that contained in SHS. This is because much of the particulate components of mainstream smoke remain in the smoker's lungs (Behan et al., 2005).

SHS exposure

SHS consists of two separate components: mainstream smoke and sidestream smoke. For the nonsmoker exposed to SHS, mainstream smoke is smoke exhaled by a smoker, and sidestream smoke consists of the smoke resulting from the combustion of a cigarette (Behan et al., 2005). According to the National Research Council (1986), both of these components are chemically similar but differ in relative concentrations.

CDC examined trends in exposure to SHS among nonsmokers through analysis of serum cotinine levels between 1999-2008 using data from NHANES. Cotinine (Figure 2) is a metabolite of nicotine reflecting recent exposure to tobacco smoke (CDC, 2010). The study found that 88 million nonsmokers three years and older are still exposed to SHS. Additional findings indicated that progress has declined in terms of reducing SHS exposure and that difference in exposure remain, one of which is that children are among those with greatest exposure, particularly in the home (CDC, 2010).

Figure 2. Structure of cotinine compound



The only way to fully protect nonsmokers from exposure to SHS is by elimination of smoking indoors (DHHS, 2006). Ventilation will not eliminate exposure to SHS, but may

actually work to counteract elimination through distributing SHS throughout a building and expose additional people to the health risks from SHS (DHHS, 2006).

THS exposure

The study conducted by Sleiman et al. (2011) concluded that dermal contact with TSNA contaminated surfaces, including skin and clothing, and inhalation and ingestion of dust contaminated by TSNAs are likely the main pathways for exposure. Supporting the findings from Becquemin et al. (2010) and Singer et al. (2003), these studies further highlight the need to focus attention on indirect exposures to tobacco smoke through THS exposure.

Following the study by Destaillats et al. (2006), Rehan et al. (2011) hypothesized that components of THS in addition to nicotine could adversely affect lung development. Lung explants of fetal rats were exposed to nicotine, 1-(N-methyl-N-nitrosamino)-1-(3-pyridinyl)-4-butanal (NNA), or 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), the two main tobacco-specific N-nitrosamine constituents of THS, for 24 hours to determine the effects on the developing lung. Findings indicated that NNK or NNA exposure to the developing lung, like nicotine, resulted in disrupted homeostatic signaling. This study is significant to further THS exposure because although both NNK and NNA are identified lung carcinogens, their effects on lung development and differentiation were unknown (Rehan et al., 2011). These pollutants combined with additional THS constituents could potentially present a significant hazard to young infants and children who inhale re-emitted THS pollutants or come in contact with THS pollutants adhered to indoor surfaces and dust through dermal contact or ingestion.

Matt, Quintana, Zakarian, et al. (2011) examined the accumulation and persistence of THS in former smokers' homes and the exposure of nonsmoking residents that move into these homes to THS. Before the former residents moved out, nicotine and cotinine levels were

measured. These measures were also gathered for nonsmokers that moved into these homes (Matt, Quintana, Zakarian, et al., 2011). Additionally, dust, surfaces and air were measured for nicotine. Findings indicated that although nicotine levels found in dust, surfaces and air decreased following change of occupancy, there were higher contamination levels in dust and surfaces of former smoker homes than former nonsmoker homes (Matt, Quintana, Zakarian, et al., 2011). Additionally, finger nicotine levels in nonsmokers living in former smoker homes were significantly higher ($p<0.05$) compared to levels in former nonsmoker homes, which suggest that THS accumulates in former smoker homes and remains in dust and on surfaces even after vacancy for two months, cleaning, and preparation for new residents, thereby exposing them to THS. This study also suggests that multiunit and other housing spaces that experience frequent changes in occupancy may present high risk of involuntary exposure to THS pollutants (Matt, Quintana, Destaillats, et al., 2011).

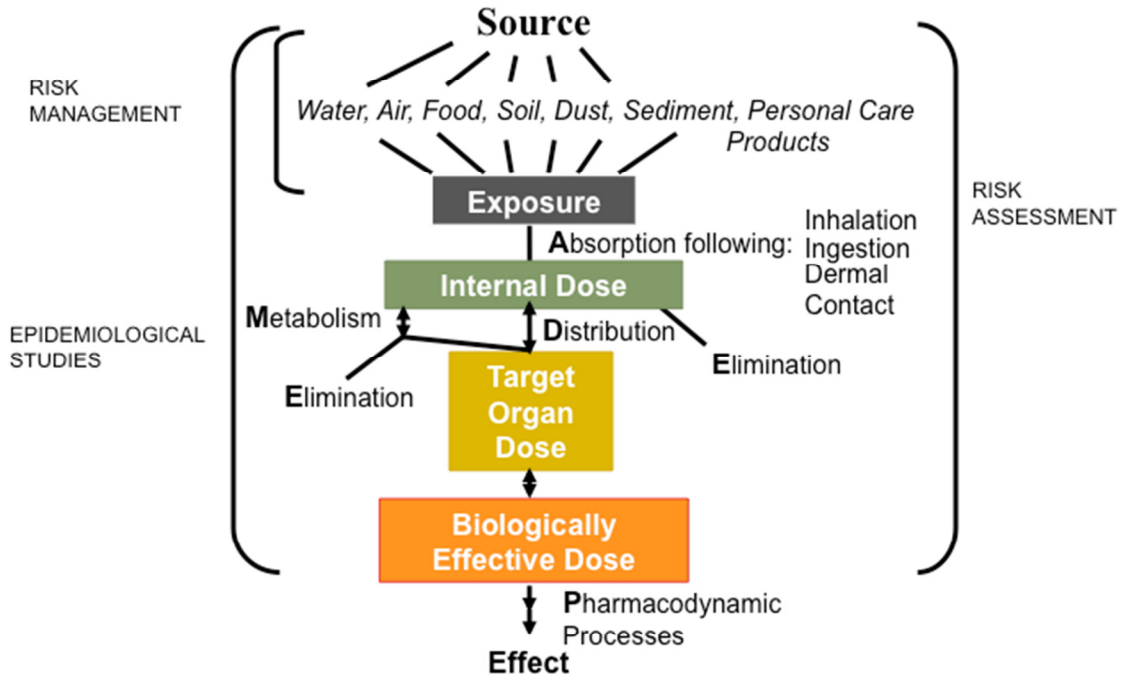
A study completed by Dreyfuss (2010) further supports the potency of THS. The removal of residual nicotine requires acidic cleansers, such as vinegar; alkaline soaps would not prove effective (Kuschner et al., 2011). Therefore, efforts to eliminate any potential health risks that may be linked with THS would need to include removal of furniture, carpets, curtains and wallboards of spaces contaminated with THS pollutants (Kuschner et al., 2011).

Indicators of tobacco smoke exposure

Biomarkers assess recent exposure to tobacco smoke. Cotinine**,** a metabolite of nicotine, is currently the most widely used biomarker to assess exposure in active smokers and nonsmokers to tobacco smoke, which may be attributed to its specificity, ease of measurement, and half-life (DHHS, 2006). Nicotine is the most tobacco-specific component in cigarettes at approximately 1-2 mg/cigarette and is measurable in active and passive smokers (Benowitz &

Jacob, 1993; Robinson, Balter, & Schwartz, 1992). With a half-life of 18-20 hours, cotinine remains much longer in the body than nicotine, which has a half-life of only 1-2 hours; thus cotinine it is preferred over measuring for nicotine as an appropriate marker for chronic exposure (Benowitz & Jacob, 1993). Nonsmokers exposed to SHS have serum cotinine levels measuring 1 ng/mL up to10 ng/mL. Serum cotinine levels >10 ng/mL are associated with active smoking (CDC, 2010). As confirmed by the study conducted by Sleiman et al. (2010), cotinine is also able to detect THS exposure, as was done for nonsmoking residents living in homes previously owned by smokers. Monitoring cotinine in blood, saliva and urine are all regarded as acceptable methods for measuring nicotine exposure (Jarvis, Russell, Benowitz, & Feyerabend, 1988; Watts, Langone, Knight, & Lewtas, 1990).

Figure 3. Exposure-effect continuum for environmental chemicals



Angerer et al. Tox Sci, doi: 10.1093/toxsci/kfl042, online 19 June 2006

According to research conducted by Bernert et al. (1997), serum cotinine distinguishes smokers from nonsmokers through HPLC coupled with an atmospheric pressure chemical

ionization tandem mass spectrometer. This methodology has exhibited analytical accuracy by NIST cotinine standards and has additionally been applied to the examination of serum samples from the National Health and Nutrition Examination Survey (NHANES 2009-2010) (Bernert et al., 1997).

Summary

Although there is still much to be learned about the exposure to THS and health implications thereof, it is evident that THS persists indoors on surfaces, in the air, and in dust. Studies have found that nonsmokers who move into former smoker homes are exposed to THS, indicated by elevated nicotine and cotinine levels (Matt, Quintana, Zakarian, et al., 2011). However, in examining the known components of THS and how people may affected from exposure, it is known that components such as TSNAs, PAHs, heavy metals and nicotine can be categorized as irritants, carcinogens and mutagens (Matt, Quintana, Destaillats, et al., 2011). Additionally, when compared with SHS and active smoking, THS exposure consists of differing exposure intervals, concentrations of pollutants in different media, and routes of exposure (Matt, Quintana, Destaillats, et al., 2011). These factors may lead to similarities as well as differences in the health risks that are potentially involved with THS, which warrants further investigation.

Adverse effects

The effects of smoking are detrimental, harming virtually all body organs and causing several cancers in addition to cardiovascular and respiratory disease and disability (DHHS, 2004) (Appendix C). The Surgeon General confirms that no level of exposure to tobacco smoke is safe: the only proven ways to reduce risk for disease are preventing initiation of smoking, smoking cessation, and removing SHS exposure (DHHS, 2010). Low levels of tobacco smoke have

similar effects in nonsmokers with reduced risk; however, because exposure to SHS is so prevalent, it is a considerable public health concern (Strulovici-Barel et al., 2010).

THS

There is substantial evidence to identify the potential health effects resulting from THS exposure; yet current evidence supports the toxic effects of nicotine and carcinogenic TSNAs. Recent studies also found that residual nicotine reacts with ozone and nitrous acid to produce secondary pollutants that are recognized as potential pulmonary toxins (Rehan et al., 2011). Additionally, studies indicate that increasing ventilation indoors will not remove or reduce THS exposure (Singer, 2003). This identifies the need to consider sources of long-term exposure to low levels of tobacco smoke, which has the potential to have a widespread impact on the U.S. population.

Vulnerable populations

Infants and Children. Though involuntary exposure to SHS has reduced significantly over the last ten years, progress has lagged in the home, which is the most important tobacco smoke exposure setting for infants and children (DHHS, 2006). This population is particularly at risk because young children may crawl or occupy spaces with contaminated surfaces, increasing their susceptibility to THS exposure. The ingestion rate of infants, estimated at about 0.05-0.25 g per day, exceeds that of adults by two fold. Additionally, because infants have a higher respiration rate and lower body weight in comparison with adults, these low doses of carcinogenic TSNAs found contaminated surfaces could, over time, present a public health hazard (EPA, 2008).

Previous studies have provided evidence that low levels of tobacco smoke leads to biological changes in the small airway epithelium, thereby affecting their risk to lung health

(Strulovici-Barel et al., 2010). A study conducted by Rehan et al. (2011) examined the effects of the exposure of THS components on lung development in fetal rat lung explants. Exposure to nicotine, NNK and NNA resulted in a disruption of homeostatic signaling mechanisms necessary for lung development, indicating exposure-induced pulmonary damage (Rehan et al., 2011). This speaks to the importance of understanding the possible risks of THS and impact of long-term exposure.

People living in multiunit, low-income, or public housing. Between 2008-2009, 41% of households in public housing included children (HUD, 2010). A study conducted by Wilson et al. (2011) examined the impact of multiunit housing on children's exposure to SHS by comparing cotinine levels in children living in nonsmoking households in multiunit versus detached housing through analysis of data from the 2001–2006 National Health and Nutrition Examination Survey (NHANES). Study findings indicated that cotinine levels of children living in apartments were 45% higher than that of children living in detached housing, signifying that children are still exposed to SHS inside the home (Wilson et al., 2011). This is particularly relevant to THS exposure as well, as indoor walls, furnishings, carpet and other surfaces are repositories for THS (Rehan et al., 2011). Because occupancy in multiunit housing changes frequently, they present a high risk of involuntary exposure to THS, particularly if smoking bans are not implemented or properly monitored.

Others. In addition to infants and children who have closer proximity and sensitivity to THS pollutants, additional vulnerable populations include persons with limited mobility that may live in a household with someone who smokes. Risks to THS pollutants also exist for casino workers, bars, and hotels where smoking is permitted (Rehan et al., 2011).

Policy

Federal initiatives

Federal initiatives to enact and support policies and regulations to protect people from the hazards of tobacco smoke are ongoing. The U.S. Food and Drug Administration (FDA) was granted regulatory authority over tobacco products on behalf of the nation's health through the enactment of the 2009 Family Smoking Prevention and Tobacco Control Act (DHHS, 2010). The Centers for Disease Control and Prevention (CDC) has incorporated the World Health Organization's (WHO) MPOWER approach at federal, state and local levels, which focuses on key interventions that have been proven to reduce tobacco use and support prevention efforts (DHHS, 2010).

State smoke-free laws

An objective of Healthy People 2010 called for states and D.C. to enact laws for smoke-free indoor air to eliminate smoking in public places and worksites. This was extended to be included as an objective for Healthy People 2020 (CDC, 2011c). Upon review of state laws prohibiting smoking in private-sector worksites, restaurants and bars using CDC's State Tobacco Activities Tracking and Evaluation (STATE) System database, researchers found that states that enacted statewide complete smoke-free policies in indoor areas increased from zero states in 2000 to 26 states (including D.C.) in 2010, estimating nearly 50% of U.S. residents who are covered by state or local smoke-free laws (CDC, 2011c).

Smoke-free laws have demonstrated reductions in SHS exposure among nonsmokers and have also aided to help smokers quit (CDC, 2011a). In an effort to further protect people from the exposures of THS, Indiana University Health medical center went from being a smoke-free campus to prohibiting smoking during the workday, on or off campus in 2011 (Peeples, 2011).

As policies also influence local social consequences, local policies such as this one may help to create a new culture that disassociates smoking completely and further improve health and smoking related costs. Based on a study examining prevalence, trends, and determinants of smoke-free home policies in smokers' homes with their effect on smoking cessation, smoke-free public areas tended to stimulate the adoption of smoke-free homes in four different countries surveyed by the International Tobacco Control (ITC) (Borland et al., 2006).

Attitudes, beliefs, and smoking bans

Winickoff et al. (2009) examined the health beliefs of adults with regards to THS exposure of children, among smokers and nonsmokers, and associated these with household smoking bans. Findings showed that 65.2% of nonsmokers believed that THS is harmful to children, versus 43.3% of smokers (Winickoff et al., 2009). Additionally, smoke-free policies in the home were more prevalent among nonsmokers (88%) versus smokers (27%). After performing a multivariate logistic regression, the belief that THS harms children continued to have an independent association with smoke-free rules in the home (Winickoff et al., 2009). This is a significant finding because of the susceptibility of children and their proximity to surfaces contaminated with THS pollutants. Rehan et al. (2011) indicated that urine cotinine levels of children living in homes where strict nonsmoking policies are enforced are six times lower than in homes without nonsmoking policies in place. Additionally, the concept of THS can be incorporated into current and future initiatives, programs and policy without much difficulty in order to raise awareness of THS, which may lead to increased strict home smoking bans to protect children from exposure to both SHS and THS.

Summary

With the increase in smoke-free workplaces and public places, private settings (e.g. homes, vehicles) are becoming larger sources of exposure to SHS (CDC, 2010). The only way to ensure protection of nonsmokers from exposure to tobacco smoke is to eliminate smoking in indoor spaces, both public and private (CDC, 2010). Because there are difficulties in implementing legislative bans in private settings, there has been little action to prevent SHS exposure to children in the home. Several identified challenges in the reduction and prevention of children's exposure to SHS involve parental beliefs and practices with regards to the impact of their smoking on their children. Such challenges include denial of the harmful effects of SHS from their own smoking, or reliance on ineffective harm-reduction strategies (e.g., opening a window) (Rosen et al., 2011). These challenges are not only relevant to SHS exposure, but also to the exposure to THS in the home. As it remains early to enact public policies in response to THS, strict home smoking bans have been associated with significantly lower levels of biochemical markers of tobacco exposure in addition to lower health risks in nonsmokers (Winickoff et al., 2009).

According to the 2009 WHO report on the global tobacco epidemic, recommendations indicated voluntary policies to be unacceptable in implementing 100% smoke-free environments (Borland et al., 2006). Rather, laws that are implemented and properly enforced were noted as effective measures toward this effort. With the understanding that low and brief exposures to SHS affect the health of nonsmokers, a policy preventive effort to protect vulnerable populations from THS would be a noteworthy effort.

CHAPTER 3 - METHODOLOGY

Introduction

This study examined an existing dataset collected via the ongoing National Health and Nutrition Examination Survey (NHANES). This population was selected because it reflected a comprehensive, representative dataset that included serum cotinine biomarker measures as a part of its data collection.

This research effort focused on examining the nonsmoker population, specifically the subset of people exposed to THS that are currently classified as having exposures to SHS, and to conduct a needs assessment for THS research. Descriptive and quantitative analyses were performed and supplemented with a review of existing literature on THS. This chapter describes the methodology utilized to conduct the study.

Population and Sample

The study population was drawn from the NHANES conducted by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention (CDC). NHANES is an extensive national survey that collects a widespread amount of health data from interviews and medial exams (CDC, 2012a). These data include demographics, health behaviors, physical exams, and both medical and nutritional lab tests.

The NHANES population consists of a stratified, multistage, national probability sample of the general, non-institutionalized, U.S. population. Data are collected in two-year cycles and data are released as available for each cycle. Participants are sampled in numerous counties via mobile examination centers (MEC) which are trailers equipped for clinical sampling and testing. For logistic purposes, the northern states are sampled in the spring and summer and the southern

states are sampled in the winter and fall. Certain population segments were oversampled in order to enable appropriate representation of typically underrepresented groups such as minorities, children and the elderly. About 5,000 persons were examined annually, located in various counties across the country, 15 of which were visited each year.

Specifically, data from the NHANES 2009-2010 cycle were examined for this study. The study population consisted of 10,537 persons who were MEC- or home-examined and the data are representative of the years 2009-2010. The NHANES dataset expanded the collection of environmental chemical data to include serum cotinine measurements. This sample was selected because it was the most recent and most comprehensive dataset involving cotinine biomarkers. Of the 10,537 subjects enrolled, 8,251 subjects had valid serum cotinine measurements. Of these, 6,678 subjects had serum cotinine measures ≤ 10 ng/mL, indicative of non-active smoking (with exposure to SHS and/or THS). These 6,678 subjects were used to evaluate serum cotinine levels attributable to SHS and/or THS.

Because the methodology and data analysis for this study was conducted using an extant dataset collected by NCHS via NHANES, this study was considered exempt from Internal Review Board (IRB) approval. Prior IRB approval was obtained by NCHS/CDC for human subject participation.

Research Design and Data Collection Instruments

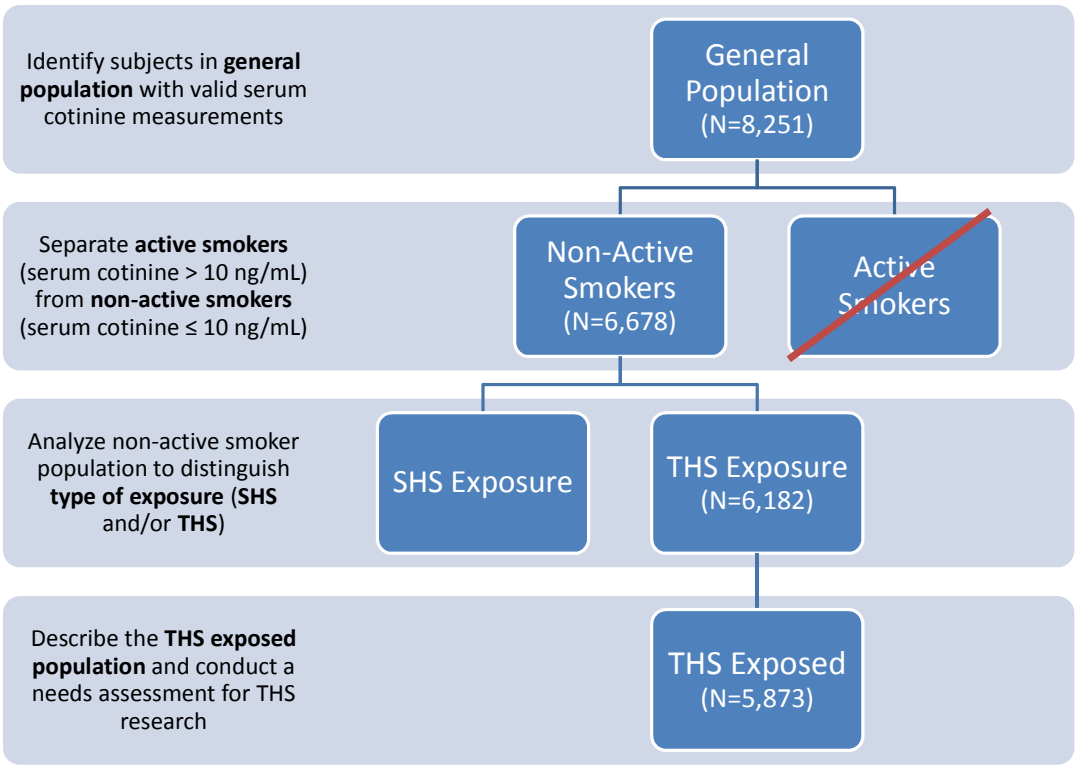
As mentioned in previous studies, serum cotinine has been demonstrated as an effective and accurate method to assess exposure to mainstream smoke and ETS. These measurements were made at CDC's Environmental Health Laboratory using a sophisticated, accurate and precise high performance liquid chromatography-tandem mass spectrometry method with a limit of detection (LOD) of 0.015 ng/mL and relative standard deviations less than 10%. Isotope

dilution quantification ensured the most accurate and reliable data were generated. Each sample run contained both positive and negative controls to further ensure data quality (Bernert et al., 1997).

The data files were downloaded from the CDC NHANES website and imported into Microsoft Excel (CDC, 2011b). All data processing and analyses were conducted off-line with the use of Excel procedures. Although weighting of the data are typically performed to ensure that the estimates are population-based, sophisticated, expensive license and training for SUDAAN software (RTP, NC) was required for this analysis. Because we were more interested in the relative contribution of THS values to those previously believed to be SHS values, the non-weighted analysis was sufficient.

Figure 4 describes the framework of this study; a more detailed description of the procedures and analysis are described in the following section.

Figure 4. Study framework



Procedures and Data Analysis

Analysis focused on the nonsmoker subset of data, examining cotinine data that were measured at or below 10 ng/mL. The following definitions for nonsmokers (non-active smokers) and smokers (active smokers) were utilized for this study:

- **Nonsmoker**: Also referred to as "non-active smoker", a nonsmoker is defined as having a serum cotinine value ≤ 10 ng/mL. For the purposes of this study, a nonsmoker includes both SHS and THS exposed subjects.
- **Smoker**: Also referred to as "active smoker", a smoker is defined as having a serum cotinine level > 10 ng/mL.

Subjects exposed to THS were defined as: 1) those with a serum cotinine concentration below 10 ng/mL), 2) those who did not reside in a household with other people who smoked, and

3) those who did not provide a number of cigarettes that were smoked in their personal space each day. Only 6,182 of the 8,251 subjects met this criterion for THS exposure with valid cotinine measurements. Descriptive analysis of this nonsmoker subset of data was performed. Further analyses were performed on this dataset, including student t-tests and descriptive analysis of the demographics of people likely to be exposed to THS in the general U.S. population. Graphics and tables depicting the data were created for comparability and summarization of data.

Based on this final dataset, cotinine concentrations of this population were examined and characterized to determine the logical cutoff for THS exposure. Prior to conducting this study, it was determined that should a logical cutoff not be distinguishable, the serum cotinine level for the sample not exposed at home or work from the dataset were to be utilized.

The analysis and evaluation of the data were then compared with the supplemental review of the literature to assess recommendations for further research necessary to expand current understanding of the risks related to THS exposure.

Limitations

Use of sampling weights and sample design variables is recommended for NHANES datasets because the sampling design is a complex clustered design, incorporating differential probabilities of selection (CDC, 2011b). This leads to one potential limitation inherent in this study design, as weighted samples were not utilized, which may lead to biased estimates and exaggerated significance levels.

Summary

This study focused on taking existing comprehensive data that were likely representative of the U.S. population and furthering analysis to identify the THS exposed population and inform

public health risk for THS exposure. The information collected through the NHANES contained both qualitative and quantitative measures; quantitative measures were examined pertaining to the demographics of the nonsmoking subset of the data and in the analysis of cotinine levels among this group of responders. This study was designed in collaboration with faculty from the Department of Environmental Health at the Rollins School of Public Health at Emory University.

CHAPTER 4 - RESULTS

Introduction

Serum cotinine data collected from the NHANES 2009-2010 cycle (N=8,251) were examined to describe the non-active smoker population with serum cotinine levels ≤ 10 ng/mL (N=6,678). Brief descriptive analysis of the entire cotinine dataset was performed in order to describe the general population exposed to tobacco smoke both actively and passively. Serum cotinine concentrations display a bimodal distribution distinguishing smokers from nonsmokers. The remainder of analyses focused on the nonsmoker population, which was further analyzed to identify a cutoff for THS exposure (serum cotinine level ≤ 0.737 ng/mL) and describe the THS exposed population subset (N=5,873). Exposure is found to be significantly greater among the Hispanic population (student t-test, $p<0.01$) and children (student t-test, $p<0.01$). This chapter describes the results and summary of findings from the study.

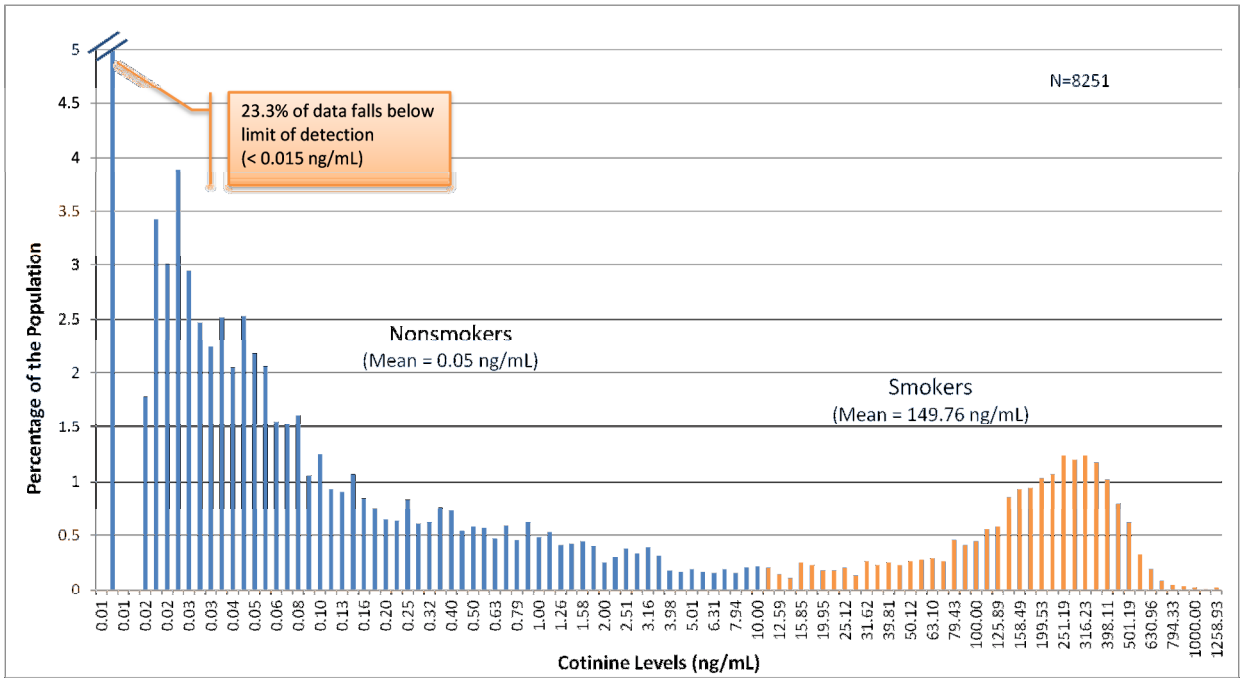
Findings

Overall sample (N=8,251)

Serum cotinine levels were examined across the entire sample of 8,251 subjects, which displayed a bimodal distribution of data, indicating a distinct separation between smokers (also referred to as active smokers) and nonsmokers (also referred to as non-active smokers) (Figure 5). Nonsmokers were defined earlier as individuals with serum cotinine levels ≤ 10 ng/mL. Geometric means are indicated for both smokers and nonsmokers in the histogram below.

During analysis of the data, several histograms were constructed, using various bin sizes, in order to display the data in a way that showed the multiple modes with the most optimal resolution. Previous histogram attempts are included in the appendix (Appendix D).

Figure 5. Exposure of the U.S. Population to Tobacco Smoke: Serum Cotinine Levels (NHANES 2009-2010)



The results of descriptive analysis of the entire dataset is depicted in Table 1, which examines the serum cotinine levels of the sample with respect to the demographics of the population, including sex, and race/ethnicity.

Table 1. Serum cotinine levels stratified by age, sex, race/ethnicity and smoking status

		Mexican Americans (n=1800)		Other Hispanic (n=887)		Non-Hispanic White (n=3589)		Non-Hispanic Black (n=1483)		Other Race - Including Multiracial (n=492)	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Overall	**Subjects**	901	899	417	470	1800	1789	733	750	245	247
	Mean age (y)	30.79	32.6	33.2	35.98	42.82	42.77	35.87	35.04	33.47	33.21
	Geomean age (y)	27.78	24.16	25.01	27.58	33.57	34.11	27.15	26.93	24.47	25.63
	Mean cotinine (ng/mL)	13.93	8.8	26.16	12.79	65.75	46.2	63.65	46	39.02	21.55
	Geomean cotinine (ng/mL)	0.11	0.05	0.16	0.07	0.41	0.24	0.77	0.44	0.25	0.09
	50th percentile cotinine (ng/mL)	0.03	0.02	0.04	0.02	0.06	0.04	0.21	0.15	0.06	0.03
	95th percentile cotinine (ng/mL)	140	39.17	194.4	89.61	368.35	320	367.2	344.1	270.8	189.6
Smokers (> 10 ng/mL)	**Subjects**	124	61	72	40	474	372	199	155	46	30
	Mean age (y)	40.46	46.18	41.56	39.75	43.09	40.22	43.45	41.78	40.24	34.17
	Geomean age (y)	36.36	43.63	37.58	36.71	39.04	37.31	39.63	38.3	37.1	31.25
	Mean cotinine (ng/mL)	121.2	127.62	150.1	147.6	248.78	221.09	233.12	220.62	206.15	176.49
	Geomean cotinine (ng/mL)	83.76	84.52	95.41	90.63	184.97	171.6	164.35	147.24	143.41	126.13
	50th percentile cotinine (ng/mL)	101	104	98.2	125.5	227.5	202.5	233	179	190.5	189
	95th percentile cotinine (ng/mL)	296.8	298	391.3	341.9	526.45	455	487	536.9	468.75	382.2
Nonsmokers (≤ 10 ng/mL)	**Nonsmokers**	777	838	345	430	1326	1417	534	595	199	217
	Mean age (y)	29.24	31.61	31.45	35.63	42.72	43.44	33.04	33.74	31.91	33.07
	Geomean age (y)	21.14	23.18	22.97	26.86	31.81	33.32	23.58	24.57	22.22	24.94
	Mean cotinine (ng/mL)	0.29	0.15	0.29	0.25	0.31	0.28	0.5	0.51	0.38	0.13
	Geomean cotinine (ng/mL)	0.04	0.03	0.04	0.03	0.05	0.04	0.1	0.1	0.06	0.04
	50th percentile cotinine (ng/mL)	0.02	0.02	0.03	0.02	0.03	0.02	0.07	0.07	0.04	0.03
	95th percentile cotinine (ng/mL)	1.5	0.52	1.21	0.64	1.59	1.46	2.55	2.78	2.49	0.59

Nonsmoker data

Brief analysis of the entire dataset was followed by a closer analysis of nonsmokers, as defined by having serum cotinine levels ≤ 10 ng/mL (N= 6,678). Nonsmoker data were differentiated from smoker data and examined based on both 1) the number of cigarettes smoked in the home, and 2) the number of smokers in the home with corresponding mean cotinine levels. The table below displays the findings from descriptive analysis of the nonsmoker data based on age and race/ethnicity, in addition to serum cotinine levels based on the number of smokers in the home and number of cigarettes smoked in the home (Table 2). Several n-values were too few in order to calculate an accurate value; as such, categories containing an n-value < 5 were noted as not calculated (NC). The bottom of the table describes the subset of nonsmokers who had no smokers in the home and no cigarettes smoked in the home (highlighted with a red box). This subset was targeted for further analysis for exposure to THS.

Table 2. Nonsmoker data (serum cotinine levels ≤ 10 ng/mL) by race/ethnicity

Group		Descriptive	Overall	Mexican Americans	Other Hispanic	Non-Hispanic White	Non-Hispanic Black	Other Race - Including Multiracial
Overall (≤ 10 ng/mL)		**Subjects**	**6678**	**1615**	**775**	**2743**	**1129**	**416**
		Arithmetic mean, age (y)	36.66	30.47	33.77	43.09	33.41	35.52
		Geometric mean, age (y)	26.83	22.18	25.05	32.58	24.10	23.60
		Arithmetic mean, cotinine (ng/mL)	0.31	0.22	0.27	0.30	0.51	0.25
		Geometric mean, cotinine (ng/mL)	0.05	0.08	0.04	0.04	0.10	0.05
		Median, cotinine (ng/mL)	0.03	0.02	0.02	0.03	0.07	0.03
		95th percentile, cotinine (ng/mL)	1.57	0.85	1.05	1.53	2.76	1.32
With X smokers in the home	1 Smoker	Subjects	313	40	21	131	117	4
		Arithmetic mean, cotinine (ng/mL)	1.36	0.86	0.66	1.39	1.61	NC
		Geometric mean, cotinine (ng/mL)	0.75	0.31	0.01	0.88	1.01	NC
		Median, cotinine (ng/mL)	0.85	0.32	0.26	0.93	1.07	NC
		95th percentile, cotinine (ng/mL)	4.45	3.30	1.87	3.96	5.13	NC
	2 Smokers	Subjects	126	14	3	71	33	5
		Arithmetic mean, cotinine (ng/mL)	2.36	1.60	NC	2.62	2.03	2.48
		Geometric mean, cotinine (ng/mL)	1.59	1.17	NC	1.66	1.54	2.37
		Median, cotinine (ng/mL)	1.82	1.32	NC	2.15	1.92	2.56
		95th percentile, cotinine (ng/mL)	6.20	3.90	NC	7.22	4.73	3.44
	3 Smokers	Subjects	12	0	0	6	5	1
		Arithmetic mean, cotinine (ng/mL)	2.50	--	--	2.54	2.88	NC
		Geometric mean, cotinine (ng/mL)	1.31	--	--	1.19	1.95	NC
		Median, cotinine (ng/mL)	1.83	--	--	1.24	2.30	NC
		95th percentile, cotinine (ng/mL)	8.23	--	--	7.91	6.09	NC

NC: Not calculated; indicates n-values were insufficient to accurately calculate a value (n<5)

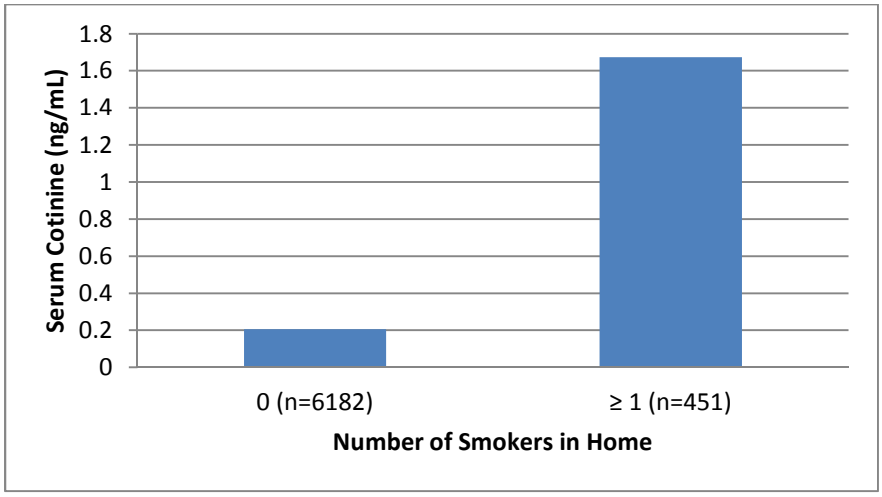
Table 3 (Continued). Nonsmoker data (serum cotinine levels ≤ 10 ng/mL) by race/ethnicity

Group		Descriptive	Overall	Mexican Americans	Other Hispanic	Non-Hispanic White	Non-Hispanic Black	Other Race - Including Multiracial
With X cigarettes smoked in the home	1-5 Cigarettes	Subjects	163	30	16	52	64	1
		Arithmetic mean, cotinine (ng/mL)	1.31	1.03	0.66	1.43	1.53	NC
		Geometric mean, cotinine (ng/mL)	0.62	0.37	0.29	0.67	0.92	NC
		Median, cotinine (ng/mL)	0.58	0.36	0.26	0.56	0.99	NC
		95th percentile, cotinine (ng/mL)	5.74	5.04	2.50	6.20	5.23	NC
	6-10 Cigarettes	Subjects	122	16	8	45	49	4
		Arithmetic mean, cotinine (ng/mL)	1.45	0.76	1.67	1.28	1.76	NC
		Geometric mean, cotinine (ng/mL)	0.85	0.32	0.64	0.91	1.14	NC
		Median, cotinine (ng/mL)	0.86	0.44	0.67	0.86	1.07	NC
		95th percentile, cotinine (ng/mL)	4.93	2.53	6.05	3.29	5.37	NC
	11-20 Cigarettes	Subjects	105	6	0	66	29	4
		Arithmetic mean, cotinine (ng/mL)	1.85	1.39	--	1.83	1.86	NC
		Geometric mean, cotinine (ng/mL)	1.29	1.15	--	1.23	1.33	NC
		Median, cotinine (ng/mL)	1.47	1.29	--	1.42	1.92	NC
		95th percentile, cotinine (ng/mL)	4.57	2.63	--	4.81	4.00	NC
	21-30 Cigarettes	Subjects	29	1	0	16	11	1
		Arithmetic mean, cotinine (ng/mL)	2.82	NC	--	3.50	2.08	NC
		Geometric mean, cotinine (ng/mL)	2.06	NC	--	2.37	1.78	NC
		Median, cotinine (ng/mL)	1.51	NC	--	2.43	1.46	NC
		95th percentile, cotinine (ng/mL)	7.94	NC	--	8.02	4.19	NC
	31-40 Cigarettes	Subjects	32	1	0	29	2	0
		Arithmetic mean, cotinine (ng/mL)	2.75	NC	--	2.59	NC	--
		Geometric mean, cotinine (ng/mL)	2.01	NC	--	1.88	NC	--
		Median, cotinine (ng/mL)	2.33	NC	--	2.17	NC	--
		95th percentile, cotinine (ng/mL)	6.36	NC	--	5.84	NC	--
No smokers or cigarettes smoked in the home		Subjects	6182	1545	749	2519	964	405
		Arithmetic mean, cotinine (ng/mL)	0.21	0.19	0.25	0.17	0.30	0.21
		Geometric mean, cotinine (ng/mL)	0.04	0.03	0.03	0.03	0.07	0.04
		Median, cotinine (ng/mL)	0.03	0.02	0.02	0.02	0.05	0.03
		95th percentile, cotinine (ng/mL)	0.74	0.62	0.85	0.51	1.29	0.66

NC: Not calculated; indicates n-values were insufficient to accurately calculate a value (n<5)

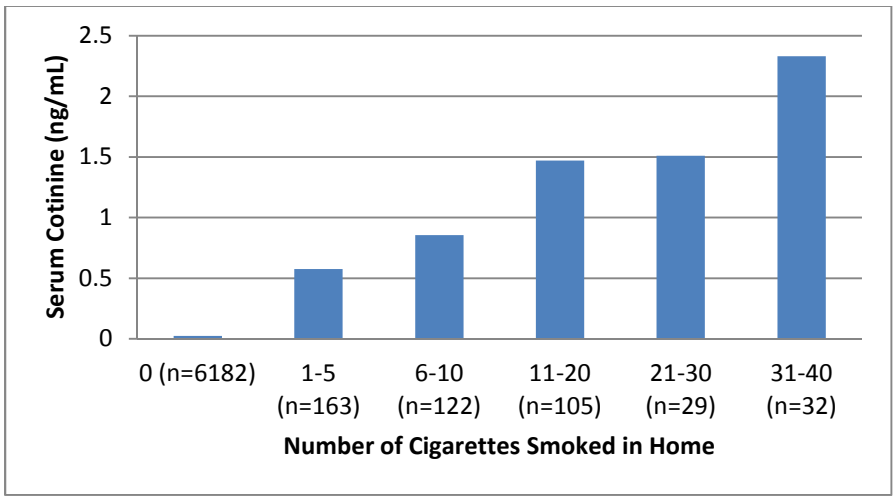
A student t-test analysis was performed using Excel on the nonsmoker data examining average cotinine levels for nonsmokers based on the number of smokers in the home (Figure 6). Results suggest that among nonsmokers, subjects residing with one or more smokers in the home have significantly greater exposure to serum cotinine than subjects living with zero smokers in the home (student t-test, $p<0.01$).

Figure 6. Mean cotinine levels for nonsmokers (≤ 10 ng/mL) based on number of smokers living at home



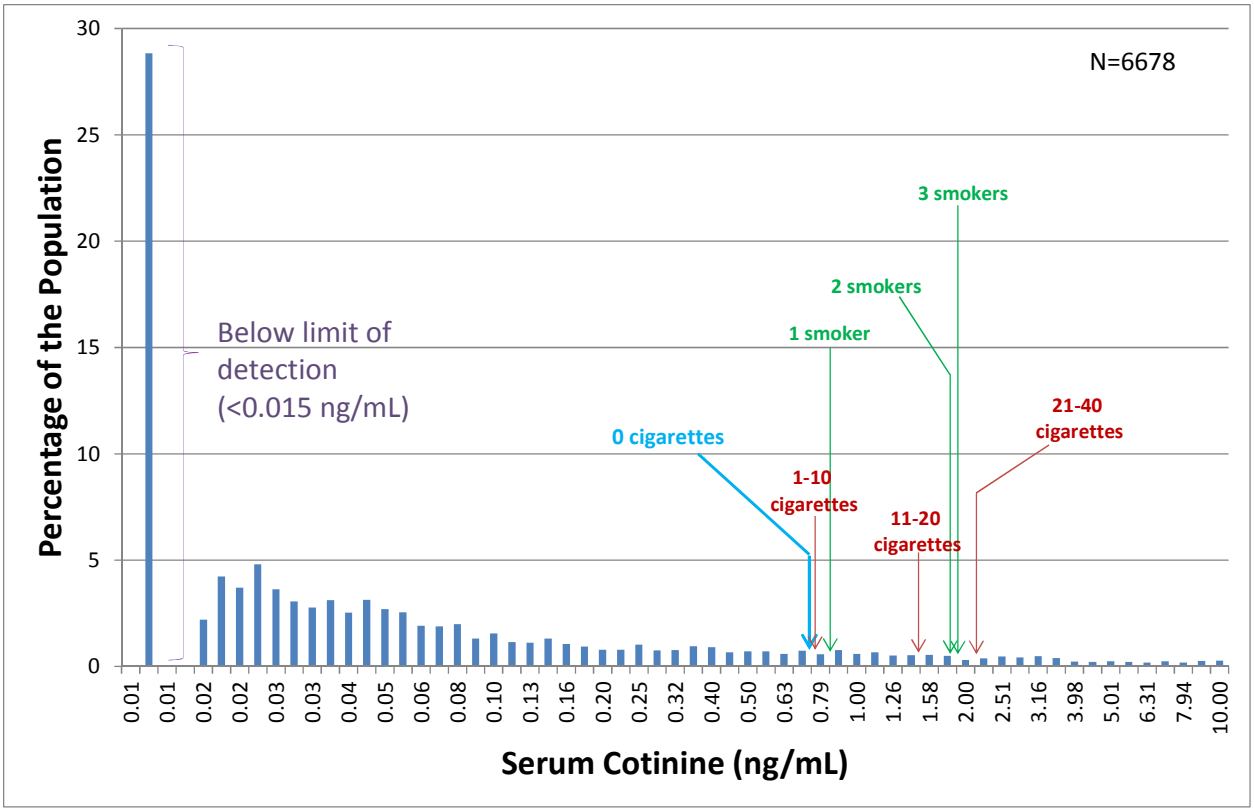
Upon comparison of serum cotinine values of nonsmokers based on the number of cigarettes smoked in the home, there appears to be a dose-response relationship (Figure 7). However, statistical analyses were not performed to prove this assumption.

Figure 7. Median cotinine levels for nonsmokers (≤ 10 ng/mL) with X number of cigarettes smoked at home



The following histogram depicts the distribution of serum cotinine levels among the nonsmoking population (Figure 8). This figure appears to show several modalities among this nonsmoking group, which may indicate additional sources of SHS and THS exposure. The figure also indicates cotinine levels based on number of smokers/cigarettes smoked in the home. The mean serum cotinine level for nonsmokers with zero smokers/cigarettes smoked in the home was identified as 0.737 ng/mL, which is also depicted in the histogram.

Figure 8. Nonsmoker exposure to tobacco smoke among the U.S. population



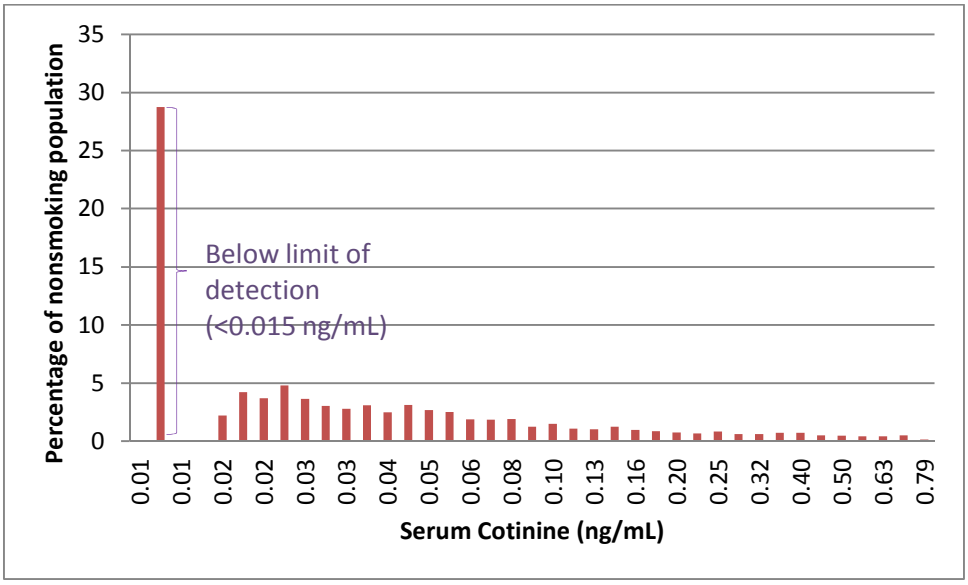
Thirdhand smoke data

People exposed to THS were defined as those who did not live in a home with other people who smoked or who did not provide a number of cigarettes that were smoked in their personal space each day. Based on this definition, the nonsmoker dataset was further analyzed to a subset with serum cotinine levels below the limit of detection to the 95th percentile cotinine

level of nonsmokers with no smokers/cigarettes smoked in the home (0.737 ng/mL). This value was determined to be the serum cotinine cutoff value for THS exposure. This subset of nonsmokers with THS exposure (serum cotinine ≤ 0.737 ng/mL) contained 5,873 subjects with a median serum cotinine level of 0.023 ng/mL.

The histogram below displays the serum cotinine levels among the nonsmoking population exposed to THS (Figure 9).

Figure 9. Serum cotinine, THS exposed individuals among nonsmoking population



Further descriptive analysis was performed in an effort to demographically define this subset of THS exposed individuals among the U.S. population. Table 3 displays the results of descriptive analysis based on age, race/ethnicity, and sex.

Table 3. Descriptive analysis of THS exposed population, N=5873 (nonsmokers with zero smokers at home, serum cotinine ≤ 0.737 ng/mL)

Group	Descriptive	Number of THS exposed individuals	Number of subjects (overall)	Median, serum cotinine (ng/mL)	% of overall subjects	% of nonsmokers (serum cotinine ≤10ng/mL, n=6678)
Age	3-5 y	296	388	0.04	76.29	4.43
	6-11 y	806	971	0.02	83.01	12.07
	12-19 y	875	1180	0.03	74.15	13.10
	20+ y	3896	5712	0.02	68.21	58.34
Race/Ethnicity	Mexican Americans	1478	1800	0.02	82.11	22.13
	Other Hispanic	709	887	0.02	79.93	10.62
	Non-Hispanic White	2415	3589	0.02	67.29	36.16
	Non-Hispanic Black	885	1483	0.04	59.68	13.25
	Other Race - Including Multiracial	386	492	0.03	78.46	5.78
Sex	Male	2771	4096	0.03	67.65	41.49
	Female	3102	4155	0.02	74.66	46.45

Race/Ethnicity

Mexican Americans and other Hispanics display the greatest percentage of exposure among their respective race/ethnicity; however, non-Hispanic blacks are exposed to a significantly greater level of cotinine with regards to THS (student t-test, $p<0.01$).

Age

Age of the THS exposed population was also examined, with ages broken down into the following categories: 3-5 y; 6-11 y; 12-19 y; 20+ y. An in depth examination of the 3-5 y age group exposed to THS yield the following figure (Figure 10); the greatest THS exposure of significance is found among non-Hispanic whites (student t-test, $p<0.01$).

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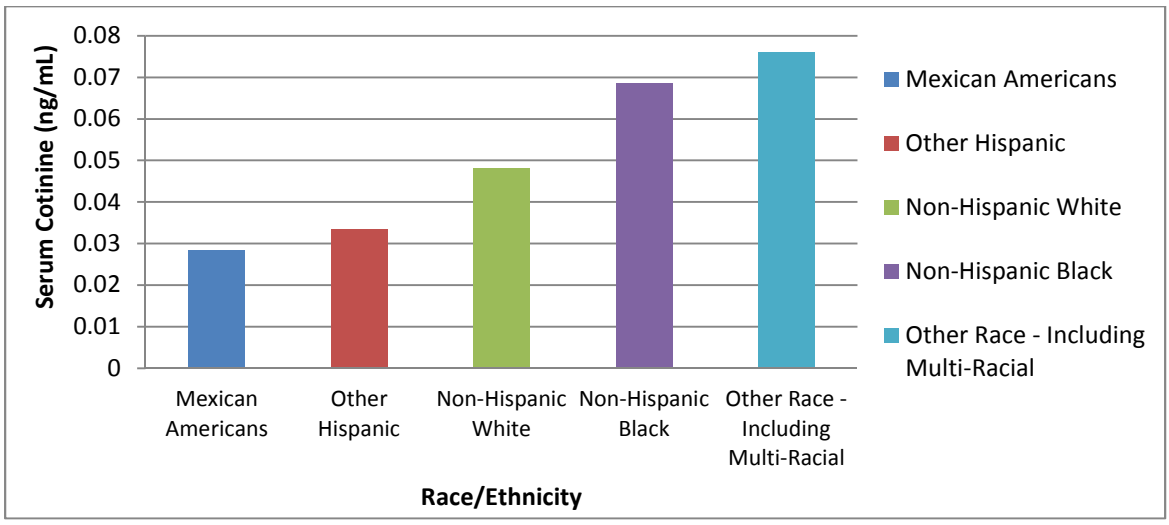
Figure 10. THS exposure among the 3-5 y age group by race/ethnicity (median, serum cotinine)



Among the nonsmoker population, findings suggest the greatest percentage of exposure to THS among the 20+ y age group.

Sex

Overall, THS exposure appeared to be slightly higher among the female population than the male population. Among nonsmoking population, THS exposure for each sex is between 41-46%.

Descriptive analysis was also performed on THS exposure by sex with respect to race and ethnicity, which is displayed in the table below (Table 4). Overall, serum cotinine levels are similar across males and females according to their respective race/ethnicity except among non-Hispanic whites, where males appear to have a slightly higher serum cotinine level than females. Non-Hispanic blacks have the highest mean serum cotinine among males and females (student t-test, $p<0.01$).

Table 4. THS exposure by sex and race/ethnicity

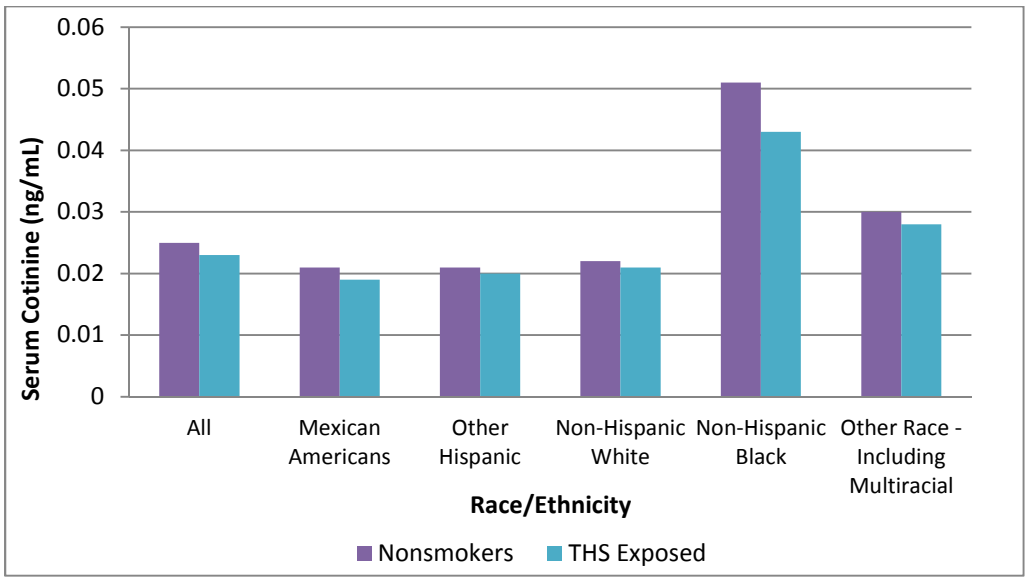
n=5873	Number of individuals		Median, serum cotinine (ng/mL)		% of nonsmokers, respective of gender (serum cotinine ≤10ng/mL, n=6678)	
	Male	Female	Male	Female	Male	Female
Mexican Americans	693	785	0.02	0.02	89.19	93.68
Other Hispanic	313	396	0.02	0.02	90.72	92.09
Non-Hispanic White	1162	1253	0.02	0.02	87.63	88.43
Non-Hispanic Black	422	463	0.05	0.04	79.03	77.82
Other Race - Including Multiracial	181	205	0.03	0.21	90.95	94.47

Among the nonsmoking population, THS exposure for each sex appear to impact greater than 75% of both sexes when examining the race/ethnicity of the exposed population. Additional histograms illustrating results of analysis of THS data are included in Appendix E.

Other findings

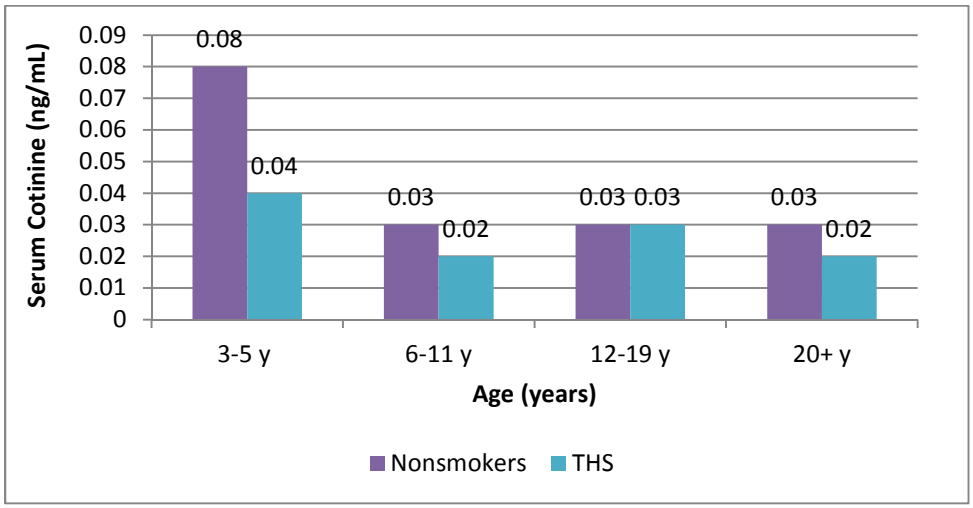
Comparisons of descriptive analysis between the nonsmoker population (exposed to both SHS and THS) and the THS exposed subset within the nonsmoker population appear to display some similarities across both groups. For example, exposure to greater levels of serum cotinine among non-Hispanic blacks is observed among both THS exposed subjects (student t-test, $p<0.01$) and the entire nonsmoker population (student t-test, $p<0.01$). A comparison of cotinine levels by race/ethnicity among SHS and the THS exposed subset is illustrated in Figure 11.

Figure 11. Mean serum cotinine levels for THS and nonsmoker exposure to tobacco smoke by race/ethnicity



Data indicate that the age range between 3-5 y has a significantly greater level of serum cotinine exposure than other age groups among the THS exposed subset of nonsmokers (student t-test, $p<0.01$). Similarly, the 3-5 y age range among the overall nonsmoking population also has a significantly higher concentration of serum cotinine exposure than other age groups in the same population (student t-test, $p<0.01$) (Figure 12).

Figure 12. Median, serum cotinine concentration comparison of tobacco smoke exposure among nonsmokers and THS exposed



Summary

For this study, THS exposed individuals were defined as those who did not reside in a home with other people who smoked or those who did not provide a number of cigarettes smoked in their home each day. The results from the analysis of the data indicate that this subset of nonsmokers may be defined as having a serum cotinine level between that under the limit of detection (<0.015 ng/mL) and 0.737 ng/mL, which is the 95th percentile cotinine value of nonsmokers (defined as individuals with serum cotinine levels ≤ 10 ng/mL) with no smokers/cigarettes smoked in the home. Descriptive analysis was performed on this subset of nonsmokers with THS exposure as an initial attempt at describing this population, its demographics and cotinine levels. A histogram of this data subset shows several modalities within this nonsmoking subgroup which could indicate THS exposure or other non-home sources of tobacco smoke exposure. The latter is one limitation of this dataset as these individuals may have been exposed to tobacco smoke elsewhere outside the home. However, it is likely that if there are no smokers or cigarettes smoked in the home, these individuals would attempt to avoid tobacco smoke exposure elsewhere. Thus, exposure of this population to tobacco smoke from residual contamination may be a more plausible source.

A summary of results for the description of THS exposed individuals based on the study findings are as follows.

Definition

THS exposed individuals: People who did not live in a home with other people who smoked or who did not provide a number of cigarettes that were smoked in their personal space each day.

THS exposure cutoff: Serum cotinine level ≤ 0.737 ng/mL

Overall

- Median serum cotinine = 0.023 ng/mL
- 5,873 individuals
- 71% of the U.S. population is likely to be exposed to THS
- 88% of nonsmokers previously categorized with SHS exposure are likely exposed to THS

Race/ethnicity

- Respective to race, greatest percentage of exposure is likely among Mexican Americans (82% of all Mexican Americans are exposed) and other Hispanics (80% of all other Hispanics are exposed), followed by other races (79% of other races are exposed)
- Greatest concentration of exposure is significant among non-Hispanic blacks at 0.04 ng/mL (student t-test, $p<0.01$), regardless of sex
- Among nonsmokers, greatest exposure is suggested to be among non-Hispanic whites (36% of all nonsmokers exposed to THS are likely non-Hispanic whites)

Age

- 3-5 year olds are exposed to the greatest concentration of serum cotinine at a significant level of 0.04 ng/mL (student t-test, $p<0.01$); suggests 76% of all 3-5 year olds are exposed to THS
    - Within this age range, cotinine concentrations are greatest among non-Hispanic blacks at a significant level of 0.069 ng/mL (student t-test, $p<0.01$)
- Greatest percentage of THS exposure is likely among 6-11 year olds (suggests 83% of all 6-11 year olds are exposed)

- Among nonsmokers, greatest exposure among individuals aged 20+ y (suggests 58% of all nonsmokers exposed to THS are aged 20+ y)

Sex

- 68% of all males and 75% of all females are likely exposed to THS
- Among nonsmoking population, THS exposure for each sex was between 41-46%

THS and SHS comparison of exposure

- Non-Hispanic blacks were exposed to greater levels of serum cotinine among both THS exposed subjects and the overall nonsmoker population (student t-test, $p<0.01$)
- Children aged 3-5 y were exposed to the greatest level of serum cotinine among both THS exposed subjects and the overall nonsmoker population (student t-test, $p<0.01$)

CHAPTER 5 – CONCLUSIONS, IMPLICATIONS, AND RECOMMENDATIONS

Introduction

Responsible for one out of five deaths each year, including deaths from SHS (American Cancer Society, 2012), cigarette smoking is the primary avoidable cause of disease and death in the United States (DHHS, 2006). According to the Surgeon General, there is no safe level of exposure to tobacco smoke (DHHS, 2010). With growing interest in THS within the sphere of tobacco smoke exposure research, an increasing number of studies are exploring the nature, effects, and exposure pathways of THS, the chemical aging of tobacco smoke, and its secondary pollutants.

The purpose of this study was, among the current population of people classified as having exposures to SHS, to examine and describe the proportion of this population actually exposed to THS and conduct a needs assessment for THS research accordingly. As a rising concern in public health, the effects of THS on human health are not fully known, resulting in a lack of sufficient evidence to create laws or regulations in response to potential health risks of THS exposure (Schick, 2011).

Despite the lack of substantial research on THS to date, studies have shown that THS contaminates indoor environments where smoking has occurred, creating reservoirs of tobacco smoke pollutants and exposing nonsmokers to THS long after smoking has taken place through both primary and secondary pollutants, including carcinogenic TSNAs (Matt, Quintana, Zakarian, et al., 2011). Because the home is the principal location for child and adult exposure to tobacco smoke, THS may subject vulnerable populations to continual exposure to an environment contaminated with THS pollutants (DHHS, 2006).

Drawing from the NHANES 2009-2010 dataset, the nonsmoker subset of the population was selected for analysis. In particular, this study specifically focused on those with serum cotinine levels ≤ 10 ng/mL, which is the nominal cutoff for a smoker, to examine whether some subjects were incorrectly classified as having been exposed to SHS when they were actually exposed to THS.

Results and Conclusions Summary

General Population

Cotinine levels and related demographic data were examined for the entire NHANES 2009-2010 cycle dataset. The distribution of cotinine data is bimodal, clearly marking two major sources of cotinine exposure and separating smokers from nonsmokers.

Nonsmokers

Further analysis was completed on the left-hand mode of nonsmokers defined with a serum cotinine level of ≤ 10 ng/mL. Noticeably, there are several modes displayed in this nonsmoking distribution, suggesting another source of cotinine exposure among nonsmokers in addition to SHS. Based on the findings, subjects with one or more smokers living in the home have significantly greater concentrations of serum cotinine than subjects who do not reside at home with smokers (student t-test, $p<0.01$). Similarly, the appearance of a dose-response relationship between serum cotinine levels and the number of cigarettes smoked in the home is also observed among the nonsmoking population.

THS exposed

The dataset of nonsmokers was further parsed to examine nonsmokers who did not reside with smokers and who did not indicate a number for cigarettes smoked in the home. The cutoff

for this subset is determined to be at a serum cotinine level ≤ 0.737 ng/mL. This subset of nonsmokers (N=5,873) have a median serum cotinine level of 0.023 ng/mL. Because nonsmokers with zero smokers at home and zero cigarettes smoked in the home should not have detectable cotinine levels, this finding indicates that this subset of individuals are being exposed to nicotine or cotinine through another source. With the many initiatives to eliminate smoking in public places and worksites, exposure to tobacco smoke pollutants in the workplace is less likely. Based on the known characteristics of THS, exposure to residual nicotine from THS pollutants is a plausible source.

This subset of smokers with cotinine levels ≤ 0.737 ng/mL is defined as the population of THS exposed individuals. In an attempt to further describe this THS exposed population, demographic information, including race/ethnicity, age, and sex were examined for this subset. The findings from this study suggest that 88% of nonsmokers in the United States previously categorized with SHS exposure is likely to be actually exposed to THS.

According to the literature, children are identified as being a vulnerable population for THS exposure. In addition, the 2006 Surgeon General Report indicates the continued exposure of children to SHS, stating that 22 million children (nearly 60%) between 3-11 years are exposed to SHS (DHHS, 2006). Findings from this study indicate that an estimated 76% of 3-5 year olds and 83% of 6-11 year olds are exposed to THS, which suggests a substantial amount of potential exposure among children aged 3-11 years exposed to THS in the United States. Infants and young children are more susceptible to increased exposure and sensitivity to THS. Findings from this study suggest that among all age groups examined, children 3-5 years of age are exposed to the greatest concentration of serum cotinine from THS exposure (0.04 ng/mL) at a significant amount (student t-test, $p<0.01$). Although children were oversampled for NHANES, resulting in

a possible overestimation, it is important to note that these results support current research which suggests the likelihood of THS exposure pathways through dermal contact with contaminated surfaces and inhalation/ingestion of TSNA-contaminated dust (Sleiman et al., 2010).

With respect to race and ethnicity, the study findings suggest that among the nonsmoking population, the greatest THS exposure is likely to be among non-Hispanic whites (36% of nonsmokers) and individuals aged 20 years and older (58% of nonsmokers).

The aforementioned 1) correlation between serum cotinine levels and the number of smokers in the home, and 2) suggested dose-response relationship between serum cotinine levels and the number of cigarettes smoked in the home may have significance with THS exposure in multiunit housing and other similar home environments where owners and occupancy change frequently. This frequency in turnover within housing environments where cigarettes are smoked could increase the levels of THS pollutants that settle on surfaces in these environments, thereby increasing exposure of future occupants to these long-term sources of secondary pollutants. A future study of THS exposure comparing demographics with multiunit or public housing and cotinine levels may aid to more clearly define the THS exposed population.

Strengths and Limitations

A strength of this study was the use of a large dataset. The NHANES dataset is population representative and also utilized developed and standardized measures for cotinine. One limitation inherent in this study was the absence of data on occupational or other sources of exposure to tobacco smoke. A second limitation of the data was that it lacked any description or categorization of the type of home environment (e.g., housing type, home previously occupied by smokers, etc.). Having these data would have contributed to enhancing the description of the THS exposed population, particularly as previous studies have indicated a greater exposure to

residual tobacco pollutants through homes previously occupied or owned by smokers. A third limitation previously mentioned in the methodology was that weighted samples were not utilized. As such, although the data provide an idea of the magnitude of exposure to THS, it cannot be generalizable to the U.S. population. Lastly, this is the first attempt at defining and describing the THS exposed population. It is understood that as more research and information become available, this population will be more clearly and accurately defined.

Recommendations

With consideration of the strengths and limitations of this study, the study findings lead to several recommendations that would help to further the efforts on future THS research.

First, there is a need to clarify the definition of environmental tobacco smoke. Currently, ETS is synonymous to exposure to SHS. Findings from this study suggests the existence of a subset of the current nonsmoking population categorized with SHS exposure that may in actuality be exposed to another source of tobacco smoke in addition to SHS. Current research strongly points to THS pollutants as a second source of exposure; as such, the definition of ETS needs be expanded to include the population of subjects exposed to THS. Involuntary exposure to THS pollutants can be substantial because these chemicals remain in the indoor environment for up to extended periods of time following the last smoked cigarette. Additional stratification of exposure to ETS by either degree or source of exposure would be one solution to enhancing the definition of this term.

Similarly, because persons exposed to SHS and THS are currently categorized together, there is a need for standardized criteria to differentiate between SHS and THS exposed individuals. This raises the question of what is required to define or understand low-level toxicity of tobacco smoke constituents. Currently, the Surgeon General indicates that there is no safe

level of exposure to tobacco smoke (DHHS, 2010). If there is such a risk associated with any level of exposure to tobacco smoke, including THS, this level needs to be clearly defined and confirmed.

Third, in support of the first two recommendations, further research is necessary to measure THS exposure and its components. Studies to determine all harmful constituents of THS components and defining their air level measurements will be beneficial to further research and confirm the potential harms associated with THS exposure. Additionally, a biomarker study evaluation of THS will be beneficial to targeting individuals involuntarily exposed to THS pollutants.

This information may be used to advise policy and inform risk for involuntary THS exposure as it is very likely that further studies will continue to be conducted in this area. In particular, this information may be useful to inform policy and risk for vulnerable populations that may unknowingly have continuous exposure to an environment contaminated with THS smoke pollutants.

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APPENDIX

Appendix A: Comparison of exposure, deaths, and economic cost from smoking, SHS, and THS

Measure	Smoker	Secondhand Smoke	Thirdhand Smoke
Method of exposure	Voluntary inhalation of MSS by the smoker and SHS in surrounding air	Involuntary inhalation of MSS and SSS in the air	Involuntary inhalation, ingestion, or dermal uptake of THS pollutants in the air, dust, and on surfaces
Annual deaths	443,000 deaths (includes SHS)	49,400 deaths	TBD
Annual Economic Cost	> $193 billion	> $10 billion	TBD

(Matt, Quintana, Zakarian, et al., 2011; Sleiman et al., 2010)

Appendix B: Levels of carcinogens in sidestream, secondhand, and thirdhand smoke

Carcinogen	Representative amounts			Study
	Sidestream (per cigarette)	Secondhand (per cubic meter [m^3])	Thirdhand[†]	
Polycyclic aromatic hydrocarbons				
Benz[*a*]anthracene	201 ng	0.32–1.7 ng	NR	Grimmer et al. 1987; Chuang et al. 1991
Benzo[*a*]pyrene	45–103 ng	0.37–1.7 ng	NR	Adams et al. 1987; Grimmer et al. 1987; Chuang et al. 1991
Benzo[*b*] uoranthene Benzo[*j*] uoranthene Benzo[*k*] uoranthene	196 ng	0.79–2.0 ng	NR	Grimmer et al. 1987; Chuang et al. 1991
Dibenz[*a, h*]anthracene	NR*	1 ng	NR	Vu-Duc and Huynh 1989
Indeno[1,2,3-*cd*]pyrene	51 ng	0.35–1.1 ng	NR	Grimmer et al. 1987; Chuang et al. 1991
5-Methylchrysene	NR	35.5 ng	NR	Vu-Duc and Huynh 1989
N -Nitrosamines				
N-Nitrosodiethanolamine	43 ng	NR	NR	Brunnemann and Hoffmann 1981
N-Nitrosodiethylamine	8.2–73 ng	0–20 ng	NR	Brunnemann et al. 1977; Hoffmann et al. 1987
N-Nitrosodimethylamine	143–1,040 ng	4–240 ng	NR	Brunnemann et al. 1977; Hoffmann et al. 1987; Klus et al. 1992
N-Nitrosoethylmethylamine	3–35 ng	NR	NR	Brunnemann et al. 1977; Hoffmann et al. 1987
N'-Nitroso nornicotine (NNN)	110–857 ng	0.7–23 ng	Present; detected at levels too low for accurate quantification	Brunnemann et al. 1983, 1992; Adams et al. 1987; Klus et al. 1992, Sleiman et al., 2010
N-Nitrosopiperidine	4.8–19.8 ng	NR	NR	Adams et al. 1987
N-Nitrosopyrrolidine	7–700 ng	3.5–27.0 ng	<0.05%*	Brunnemann et al. 1977; Hoffmann et al. 1987; Klus et al. 1992; Mahanama and Daisey 1996, Sleiman et al., 2010
4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	201–1,440 ng	0.2–29.3 ng	<0.05%* Household furniture: 5.3-36.5 ng m^{-2} Household dust: 0.44-2.2 ng m^{-2} Vehicle dashboard: 2.5-4.3 ng m^{-2} Vehicle dust: 6.1-9.7 ng m^{-2} Skin: >40 ng m^{-2}; 0.31-31 ng m^{-2} Cotton: 500 ng m^{-2}	Brunnemann et al. 1983, 1992; Adams et al. 1987; Klus et al. 1992, Sleiman et al., 2010
1-(N-methyl-N-nitrosamino)-1-(3-pyridinyl)-4-butanal (NNA)	NR	NR	0.35%* Household furniture: 37-256 ng m^{-2} Household dust: 3-15 ng m^{-2}	Sleiman et al., 2010

Carcinogen	Representative amounts			Study
	Sidestream (per cigarette)	Secondhand (per cubic meter [m^3])	Thirdhand[†]	
			Vehicle dashboard: 17-30 ng m^{-2} Vehicle dust: 41-68 ng m^{-2} Skin: >280 ng m^{-2}; 2.2-220 ng m^{-2} Cotton: 3500 ng m^{-2}	
Aromatic amines				
2-Naphthylamine	63.1–128 ng	NR	NR	Government of British Columbia Ministry of Health Services 2001
2-Toluidine	3,030 ng	NR	NR	Patrianakos and Hoffmann 1979
4-Aminobiphenyl	11.4–18.8 ng	NR	NR	Government of British Columbia Ministry of Health Services 2001
Aldehydes				
Acetaldehyde	961–1,820 μg	268 μg	✓	Martin et al. 1997; Government of British Columbia Ministry of Health Services 2001
Formaldehyde	233–485 μg	143 μg	<0.05%*	Martin et al. 1997; Government of British Columbia Ministry of Health Services 2001; Sleiman et al., 2010
Miscellaneous organics				
Acrylonitrile	42–109 μg	NR	NR	Government of British Columbia Ministry of Health Services 2001
Benzene	163–353 μg	4.2–63.7 μg	NR	Scherer et al. 1995; Heavner et al. 1996; Martin et al. 1997; Government of British Columbia Ministry of Health Services 2001; Kim et al. 2001
Catechol	98–292 μg	1.24 μg	NR	Sakuma et al. 1983; Martin et al. 1997; Government of British Columbia Ministry of Health Services 2001
Isoprene	668–1,260 μg	657 μg	NR	Martin et al. 1997; Government of British Columbia Ministry of Health Services 2001
1,3-Butadiene	98–205 μg	0.3–40 μg	NR	Heavner et al. 1996; Martin et al. 1997; Government of British Columbia Ministry of Health Services 2001; Kim et al. 2001
Inorganic compounds				
Cadmium	330–689 ng	4–38 ng	NR	Wu et al. 1995; Government of British Columbia Ministry of Health Services 2001

Carcinogen	Representative amounts			Study
	Sidestream (per cigarette)	Secondhand (per cubic meter [m^3])	Thirdhand[†]	
Chromium	57–79 ng	NR	NR	Government of British Columbia Ministry of Health Services 2001
Hydrazine	94 ng	NR	NR	Liu et al. 1974
Lead	28.9–46.6 ng	NR	NR	Government of British Columbia Ministry of Health Services 2001
Nickel	51 ng	NR	NR	Government of British Columbia Ministry of Health Services 2001
Polonium-210	0.091–0.139 picocurie	NR	NR	Ferri and Baratta 1966

NR = Data were not reported.
*Nicotine conversions (secondary products)
[†]Primary and secondary pollutants. Other compounds identified as THS constituents include phenol, cresols, naphthalene, N-methylformamide, myosmine, and ethyl pyridyl ketone (Rehan et al., 2011).
✓Representative amounts not yet determined
Source: Adapted from DHHS, 2006

Appendix C: Diseases and other adverse effects caused from smoking (DHHS, 2004)

Table 1.1 Diseases and other adverse health effects for which smoking is identified as a cause in the current Surgeon General's report

Disease	Highest level conclusion from previous Surgeon General's reports (year)	Conclusion from the 2004 Surgeon General's report
Cancer		
Bladder cancer	"Smoking is a cause of bladder cancer; cessation reduces risk by about 50 percent after only a few years, in comparison with continued smoking." (1990, p. 10)	"The evidence is sufficient to infer a causal relationship between smoking and. . .bladder cancer."
Cervical cancer	"Smoking has been consistently associated with an increased risk for cervical cancer." (2001, p. 224)	"The evidence is sufficient to infer a causal relationship between smoking and cervical cancer."
Esophageal cancer	"Cigarette smoking is a major cause of esophageal cancer in the United States." (1982, p. 7)	"The evidence is sufficient to infer a causal relationship between smoking and cancers of the esophagus."
Kidney cancer	"Cigarette smoking is a contributory factor in the development of kidney cancer in the United States. The term 'contributory factor' by no means excludes the possibility of a causal role for smoking in cancers of this site." (1982, p. 7)	"The evidence is sufficient to infer a causal relationship between smoking and renal cell, [and] renal pelvis. . . cancers."
Laryngeal cancer	"Cigarette smoking is causally associated with cancer of the lung, larynx, oral cavity, and esophagus in women as well as in men. . . ." (1980, p. 126)	"The evidence is sufficient to infer a causal relationship between smoking and cancer of the larynx."
Leukemia	"Leukemia has recently been implicated as a smoking-related disease. . .but this observation has not been consistent." (1990, p. 176)	"The evidence is sufficient to infer a causal relationship between smoking and acute myeloid leukemia."
Lung cancer	"Additional epidemiological, pathological, and experimental data not only confirm the conclusion of the Surgeon General's 1964 Report regarding lung cancer in men but strengthen the causal relationship of smoking to lung cancer in women." (1967, p. 36)	"The evidence is sufficient to infer a causal relationship between smoking and lung cancer."
Oral cancer	"Cigarette smoking is a major cause of cancers of the oral cavity in the United States." (1982, p. 6)	"The evidence is sufficient to infer a causal relationship between smoking and cancers of the oral cavity and pharynx."

Table 1.1 Continued

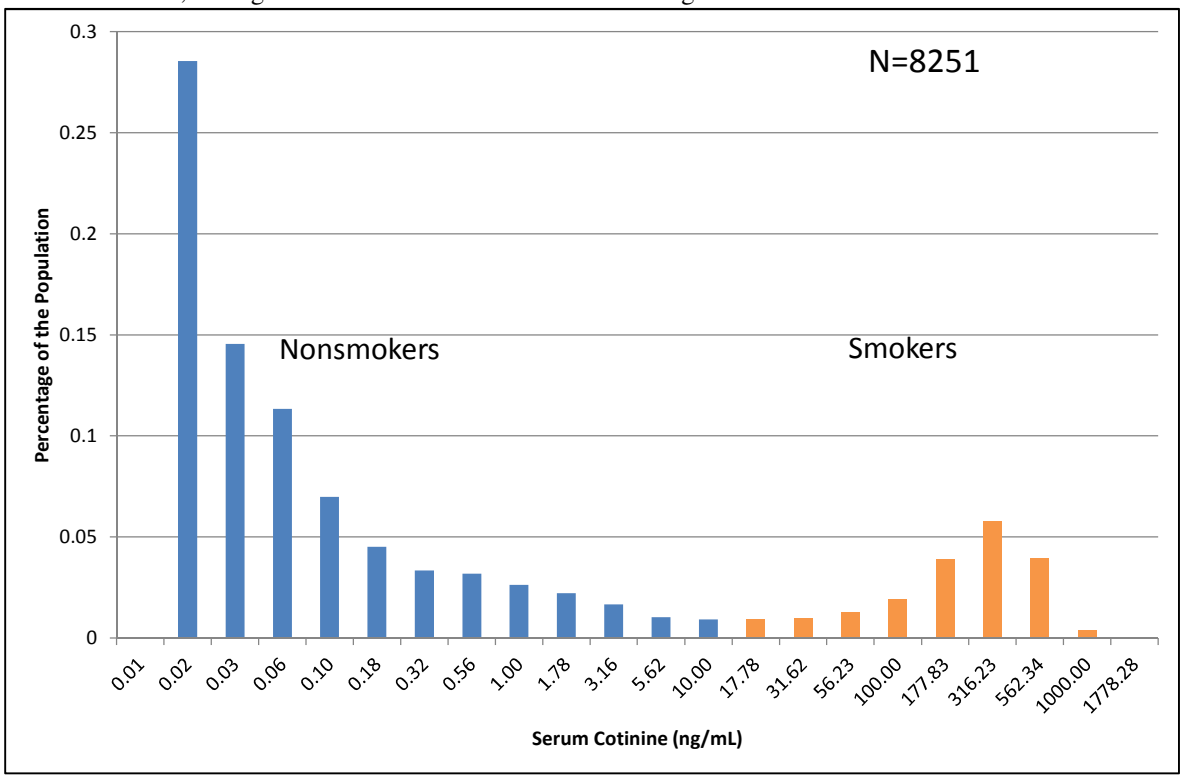
Disease	Highest level conclusion from previous Surgeon General's reports (year)	Conclusion from the 2004 Surgeon General's report
Pancreatic cancer	"Smoking cessation reduces the risk of pancreatic cancer, compared with continued smoking, although this reduction in risk may only be measurable after 10 years of abstinence." (1990, p. 10)	"The evidence is sufficient to infer a causal relationship between smoking and pancreatic cancer."
Stomach cancer	"Data on smoking and cancer of the stomach. . .are unclear." (2001, p. 231)	"The evidence is sufficient to infer a causal relationship between smoking and gastric cancers."
Cardiovascular diseases		
Abdominal aortic aneurysm	"Death from rupture of an atherosclerotic abdominal aneurysm is more common in cigarette smokers than in nonsmokers." (1983, p. 195)	"The evidence is sufficient to infer a causal relationship between smoking and abdominal aortic aneurysm."
Atherosclerosis	"Cigarette smoking is the most powerful risk factor predisposing to atherosclerotic peripheral vascular disease." (1983, p. 8)	"The evidence is sufficient to infer a causal relationship between smoking and subclinical atherosclerosis."
Cerebrovascular disease	"Cigarette smoking is a major cause of cerebrovascular disease (stroke), the third leading cause of death in the United States." (1989, p. 12)	"The evidence is sufficient to infer a causal relationship between smoking and stroke."
Coronary heart disease	"In summary, for the purposes of preventive medicine, it can be concluded that smoking is causally related to coronary heart disease for both men and women in the United States." (1979, p. 1-15)	"The evidence is sufficient to infer a causal relationship between smoking and coronary heart disease."
Respiratory diseases		
Chronic obstructive pulmonary disease	"Cigarette smoking is the most important of the causes of chronic bronchitis in the United States, and increases the risk of dying from chronic bronchitis." (1964, p. 302)	"The evidence is sufficient to infer a causal relationship between active smoking and chronic obstructive pulmonary disease morbidity and mortality."
Pneumonia	"Smoking cessation reduces rates of respiratory symptoms such as cough, sputum production, and wheezing, and respiratory infections such as bronchitis and pneumonia, compared with continued smoking." (1990, p. 11)	"The evidence is sufficient to infer a causal relationship between smoking and acute respiratory illnesses, including pneumonia, in persons without underlying smoking-related chronic obstructive lung disease."

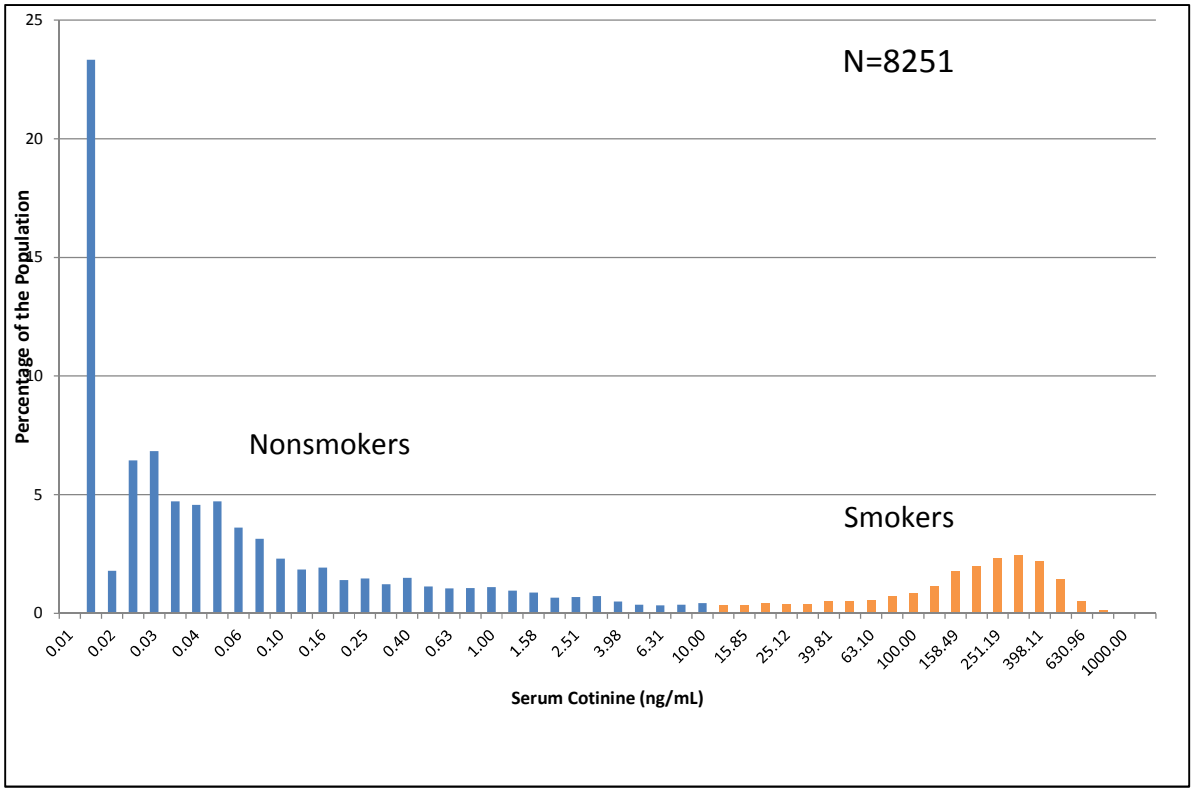
Table 1.1 Continued

Disease	Highest level conclusion from previous Surgeon General's reports (year)	Conclusion from the 2004 Surgeon General's report
Respiratory effects in utero	"In utero exposure to maternal smoking is associated with reduced lung function among infants. . . ." (2001, p. 14)	"The evidence is sufficient to infer a causal relationship between maternal smoking during pregnancy and a reduction of lung function in infants."
Respiratory effects in childhood and adolescence	"Cigarette smoking during childhood and adolescence produces significant health problems among young people, including cough and phlegm production, an increased number and severity of respiratory illnesses, decreased physical fitness, an unfavorable lipid profile, and potential retardation in the rate of lung growth and the level of maximum lung function." (1994, p. 41)	"The evidence is sufficient to infer a causal relationship between active smoking and impaired lung growth during childhood and adolescence." "The evidence is sufficient to infer a causal relationship between active smoking and the early onset of lung function decline during late adolescence and early adulthood. " "The evidence is sufficient to infer a causal relationship between active smoking and respiratory symptoms in children and adolescents, including coughing, phlegm, wheezing, and dyspnea." "The evidence is sufficient to infer a causal relationship between active smoking and asthma-related symptoms (i.e., wheezing) in childhood and adolescence."
Respiratory effects in adulthood	"Cigarette smoking accelerates the age-related decline in lung function that occurs among never smokers. With sustained abstinence from smoking, the rate of decline in pulmonary function among former smokers returns to that of never smokers." (1990, p. 11)	"The evidence is sufficient to infer a causal relationship between active smoking in adulthood and a premature onset of and an accelerated age-related decline in lung function." "The evidence is sufficient to infer a causal relationship between sustained cessation from smoking and a return of the rate of decline in pulmonary function to that of persons who had never smoked."

Appendix D: Histograms, combined smoker/nonsmoker data

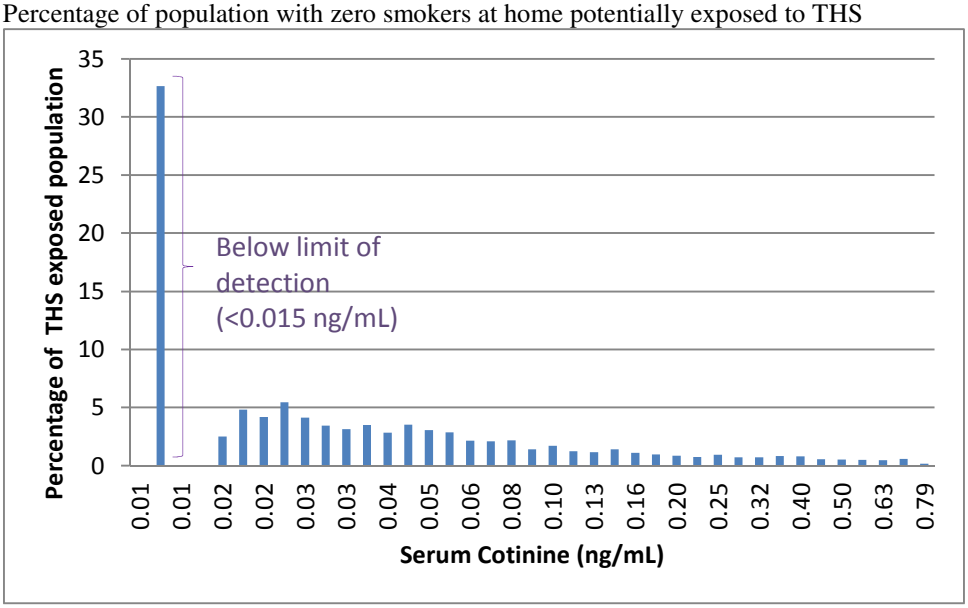
All cotinine data; average cotinine levels based on number of cigarettes smoked in the home





Appendix E: Additional THS histograms

Percentage of population with zero smokers at home potentially exposed to THS



Percentage of population with potential THS exposure