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Cardiovascular Outcomes in Nonsmokers Exposed to Secondhand Smoke: Results From The National Health and Nutrition Examination Survey (NHANES) 2015-2016

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CARDIOVASCULAR OUTCOMES IN NONSMOKERS EXPOSED TO SECONDHAND SMOKE: RESULTS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES) 2015-2016

by

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ABSTRACT

While the adverse health risks associated with smoking have been well-documented, few studies have examined the cardiovascular outcomes associated with secondhand smoking. The purpose of the study was to assess the distributions and association of cardiovascular diseases (CVDs) in nonsmokers exposed to secondhand smoke (SHS). Data were extracted from the National Health and Nutrition Examination Survey (NHANES) 2015-2016 cycle. Self-reported smoking status and cotinine levels were used to identify exposure groups (smokers, nonsmokers, and secondhand smokers), and medical history of several cardiovascular diseases such as coronary heart diseases and stroke were also collected via self-report survey. The association between exposure to SHS and seven cardiovascular outcomes were analyzed using chi-square analysis and odd ratios (OR) with 95% confidence intervals (CIs) were calculated using two logistic regression models. The data included 5,709 subjects including 18.5% smokers, 23.6% secondhand smokers, and 57.9% nonsmokers. There was statistically significant association between exposure to SHS and only two out of seven cardiovascular outcomes, hypertension (OR 1.554, 95% CI [1.066, 2.265]) and cholesterol levels (OR 1.213, 95% CI [1.017, 1.446]). This study is one of the first to determine an association between SHS and seven cardiovascular outcomes, thus highlighting the importance of reducing SHS exposure and can be used for further research on SHS and cardiovascular health.

Key words: Cardiovascular disease, cardiovascular health, secondhand smoke, passive smoking, environmental tobacco smoke, hypertension, cholesterol levels.

DEDICATION

To my parents, Yaser and Widad Chaar, thank you for always being there for me; supporting me through the ups and downs and believing me in times that I did not even believe in myself. Without your support throughout the years, I would not have made it that far. My successes and achievements are dedicated for both of you. Thank you for all of your sacrifices to make sure I had the best life. Thank you for working hard to support me and encourage me to go after my dreams. I hope I made you proud. Love you both!

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INTRODUCTION

Statement of the Problem

According to the World Health Organization (WHO), over one-third of all people are regularly exposed to secondhand smoke (SHS) across the world, including 40% of children, 33% of male nonsmokers, and 35% of female nonsmokers (World Health Organization, n.d.). Additionally, the Centers for Disease Control and Prevention (CDC) estimated that, even with tobacco bans in public places, 58 million people—roughly one in four nonsmokers—were exposed to SHS during 2013-2014 (Tsai et al., 2018). Previous work has shown that more than 20 million Americans have died due to causes related to SHS, including nearly 2.5 million who died due to lung cancer or cardiovascular diseases (CVDs) (Tsai et al., 2018; U.S. Department of Health and Human Services, 2014). Exposure to SHS also increase the risk of stroke by 20% to 30%. Additionally, SHS may even lead to reproductive concerns, such as low birth weight (U.S. Department of Health and Human Services, 2014). As nonsmokers exposed to SHS are more likely to develop these outcomes, it is critical to understand the relation between SHS exposure and CVDs.

Also known as passive smoking or environmental tobacco smoke, SHS, is the inhalation of burning tobacco products—such as cigarettes, pipes, hookah, or e-cigarettes by people other than the active smoker (Centers for Disease Control and Prevention, 2018c; U.S. Department of Health and Human Services, 2014). Secondhand smoke is a known cause of many diseases in adults and children, including stroke, nasal irritation, lung cancer, and CVDs. Exposure to SHS was highest among people who have respiratory diseases, CVDs, and cancer (Asfar et al., 2019). Additionally, children aged 3 to 11 years have the highest exposure to SHS, including 67.9% of non-Hispanic blacks, 37.2% of non-Hispanic whites, and 29.9% of Mexican Americans (Homa

et al., 2015). Few studies have examined the exposure to SHS and different biomarkers of CVDs, but results suggest a direct relation (Saxena, Liang, Muhammad-Kah, & Sarkar, 2017; Venn & Britton, 2007). None of these studies, however, examined the different types of CVDs in nonsmokers exposed to SHS, which would be critical, given the fact that heart diseases are the leading cause of death in the United States (CDC). Therefore, the purpose of this study is to assess the distribution of CVDs in nonsmokers exposed to SHS. It is hypothesized that individuals who are nonsmokers, but exposed to secondhand smoke, will have similar likelihood of having CVDs compared to firsthand smokers. The following question will guide the study's analysis:

Do nonsmokers who have an exposure to SHS have similar likelihood of developing CVDs compared to firsthand smokers?

Literature Review

Secondhand Smoke: Overview

Although smoking among U.S. adults has declined from 20.9% in 2005 to 15.5% in 2016, it is still an ongoing epidemic in the United States (Centers for Disease Control and Prevention, 2018d). According to the Surgeon General, if smoking rates remain unchanged, 5.6 million Americans younger than 18 years of age are projected to die due to smoking-related illness (U.S. Department of Health and Human Services, 2014).

Exposure to SHS is harmful to health and has been linked to several fatal illnesses among infants and adults. Although exposure to SHS has declined by over 50% (25.3% in 2011-2012 from 52.5% in 1999-2000), 58 million people—roughly one in four nonsmokers—were still exposed to SHS during 2013-2014 (Homa et al., 2015; Tsai et al., 2018; U.S. Department of Health and Human Services, 2014). In 2006, more than 42,000 Americans died from illnesses

related to SHS exposure, including more than 41,000 adults and nearly 900 infants (Max, Sung, & Shi, 2012). Additionally, exposure to SHS causes significantly more death due to CVDs than due to lung cancer (U.S. Department of Health and Human Services, 2014). In 2005-2009, 32% of all deaths from CHD were attributed to smoking and exposure to SHS (U.S. Department of Health and Human Services, 2014). Since there is still a large number of people exposed to SHS and are more likely to develop CVDs compared to unexposed individuals, more research assessing CVDs in nonsmokers who are exposed to SHS is warranted.

Secondhand Smoke: Related Conditions

While SHS does not have the same elevated risk levels as firsthand smoking, SHS exposure is still not risk free. According to report of the Surgeon General, in adults, exposure to SHS can increase the risk of stroke, nasal irritation, lung cancer, coronary heart disease (CHD), and reproductive effect in women such as lower low birthweight (U.S. Department of Health and Human Services, 2014). The CDC also states that nonsmokers who are exposed to SHS increase their risk for developing lung cancer by 20% to 30% and SHS causes more than 7,300 lung cancer–related deaths each year in the United States (Centers for Disease Control and Prevention, 2018a).

Moreover, nonsmokers who are exposed to SHS increase their risk of developing CVDs by 25% to 30%, leading to approximately 34,000 premature deaths from heart diseases every year in the United States (Centers for Disease Control and Prevention, 2018a). Also, inhaling SHS can have immediate effects on blood platelets and the lining of blood vessels since individuals exposed to SHS are still inhaling many types of toxins, which increase the risk of having heart attack (Centers for Disease Control and Prevention, 2018a). People exposed to SHS share similar risks with smokers in developing CVDs, which can be expensive and fatal if not

diagnosed and treated early (U.S. Department of Health and Human Services, 2014). Unfortunately, many people exposed to SHS are not aware of their increased risk of developing CVDs and, thus, more research assessing the relation between CVDs and exposure to SHS in nonsmokers is warranted.

Evaluation Exposure to Secondhand Smoke Using Biological Markers

Tobacco smoke consists of thousands of chemicals, including carbon dioxide, carbon monoxide, nicotine, carbonyls, hydrocarbons, nitrogen oxides, pyridines, and ammonia ("Evaluating Exposure to Secondhand Smoke," 2010). Nonsmokers exposed to SHS are subjected to two components of SHS: side-stream smoke (85%), which is the smoke emerging from the burning tip of the cigarette, and main-stream smoke (15%), which is the smoke inhaled by a smoker when puffing on a cigarette (Kritz, Schmid, & Sinzinger, 1995). Compounds about three to four times more toxic are emitted through side-stream compared to main-stream smoke ("Evaluating Exposure to Secondhand Smoke," 2010; Schick & Glantz, 2005). Additionally, both side- and main-stream smoke are capable of generating oxidative stress–inducing chemicals—such as acrolein, xanthine oxidase, and oxides of nitrogen, which may mediate many of the smoke effects on the cardiovascular system ("Experimental Studies Relevant to the Pathophysiology of Secondhand Smoke," 2010). Thus, the toxicity that nonsmokers are exposed to via SHS can leads to increased risk of different CVDs.

Nicotine is present in all tobacco products, as well as in some foods although at very low concentrations (Benowitz, 1999). Once nicotine enters the body, it will be converted to cotinine, which is then converted to trans-3'-hydroxycotinine by the hepatic enzyme cytochrome P450 2A6 (Hukkanen, Jacob, & Benowitz, 2005). About 70% to 80% of nicotine is converted to cotinine, which makes it the primary metabolite ("Evaluating Exposure to Secondhand Smoke,"

2010; Hukkanen et al., 2005). Cotinine can be measured in blood, saliva, urine, and other biologic fluids. The average half-life of cotinine (16 hours) in plasma is 8 times longer than nicotine (2 hours). Additionally, the concentrations of cotinine in blood and saliva are highly similar. However, urinary cotinine concentrations are four to five times higher than those in blood or saliva, which makes urine a more sensitive matrix for detection of low exposure of cotinine (Benowitz, Bernert, Caraballo, Holiday, & Wang, 2009; Hukkanen et al., 2005). Therefore, cotinine concentrations are more stable than nicotine due to the longer half-life and the ability to measure it in different body fluids, making it the preferred biomarker of smoke exposure to SHS and to differentiate smokers from nonsmokers.

Cardiovascular Diseases Due to Secondhand Smoke Exposure

Effects of Secondhand Smoke at the Cellular Level

Endothelial Dysfunction

The normal function of endothelial cells is to promote vasodilation and inhibit thrombosis and atherosclerosis, which is mediated by the release of nitric oxide (NO) (Glantz & Parmley, 2001). However, a dysfunction in the endothelial cells can lead to the development of atherosclerosis—a build-up of cholesterol plaque in the arterial walls. Otsuka and colleagues (2001) conducted a cross-sectional study to determine the acute effects of SHS on coronary circulation in healthy nonsmokers, Japanese men, found that only 30 minutes of exposure to SHS can cause endothelial dysfunction of the coronary circulation in nonsmokers (Otsuka et al., 2001). Additionally, there was a similar endothelial-dependent vasodilation impairment between active smokers and people who had exposure to SHS.

Similar to the previous study by Otuska et al., (2001), a more recent study investigated endothelial cells and the flow-mediated dilation by sampling endothelial cells in three groups: 1)

active smokers; 2) individuals exposed to SHS; and 3) nonsmokers. The study confirmed that SHS exposure increases vascular inflammation and reduces endothelial NO synthase to the same levels as an active smoker (Adams et al., 2015). Even though these studies were published more than ten years apart, they indicate direct toxic effects of SHS exposure on the endothelial cells, which can lead to more serious types of CVDs.

Inflammation

Tobacco smoke produces systemic inflammation via an increase of oxidative stress mediators and the reduction of NO bioavailability (Ambrose & Barua, 2004). There are many biological markers for inflammation, including C reactive protein (CRP), white blood cell (WBC) count, fibrinogen, and blood viscosity (Ambrose & Barua, 2004; Jefferis et al., 2010). One of the essential biological markers for inflammation for CVDs is CRP—a hepatic protein produced in response to acute and chronic inflammation. At population level, a high-sensitive CRP (hs-CRP) test is used to assess CVD risk.

Multiple studies have examined the relation between SHS and inflammation, and all of them have shown a positive correlation between SHS and inflammation (Jefferis et al., 2010; Venn & Britton, 2007). For example, in a cross-sectional, population-based study of more than 5,000 participants, investigators looked at multiple biological markers for inflammation, including CRP, WBC count, triglycerides, fibrinogen, and blood viscosity (Jefferis et al., 2010). Compared to nonsmokers, participants who were current smokers or nonsmokers with SHS exposure had higher circulating levels of CRP, WBC count, triglycerides, and fibrinogen. The authors concluded that inflammatory markers related to CVDs risk showed an independent association with SHS exposure in a similar way as active smoking (Jefferis et al., 2010).

Furthermore, using data from the third National Health and Nutrition Examination Survey (NHANES III), Venn & Britton (2007) examined the relationship between SHS and inflammation levels using participants' cotinine levels. They found that participants exposed to a small amount of SHS had increased levels of two biological markers for CVDs, which were fibrinogen and homocysteine (Venn & Britton, 2007). However, there was no evidence that CRP increased in relation to cotinine levels (Venn & Britton, 2007). Yet, a different study that also used NHANES III data to examine the relation between SHS and CRP levels in never smokers 6-18 years old found that there was an association between the increase in serum cotinine and an increase in CRP (Wilkinson, Lee, & Arheart, 2007). In conclusion, there is strong evidence of a relation between exposure to SHS and an increase in CVD inflammation biomarkers.

Lipid Profile

Secondhand smoke exposure may promote atherosclerosis due to its effects on endothelial cells and lipid profile. In an animal study, investigators used a mouse model and smoking systems that closely simulated exposure of SHS. The mice had moderate lipid levels that mimicked human lipid levels that led to atherosclerosis plaque formation. They found that exposure to SHS decreased plasma high-density lipoprotein (HDL) cholesterol levels in the blood and decreased the ratio between HDL and low-density lipoprotein (LDL) cholesterol, HDL cholesterol and triglycerides, and HDL cholesterol and total cholesterol (Yuan et al., 2007). In a similar study with humans, investigators took blood samples from 10 nonsmokers (5 male and 5 female) with normal lipid levels. Then subjects were exposed to 30 minutes of SHS. They found that exposure to SHS accelerated lipid peroxidation and LDL cholesterol modification. Additionally, there was an association between an increased accumulation of LDL cholesterol in human macrophages (Valkonen & Kuusi, 1998).

Furthermore, a study examined 12 healthy, nonsmoker males to determine the influence of a 6-hour exposure to SHS on lipoprotein levels. Baseline blood samples were drawn before SHS exposure and after 6, 8, 16, and 24 hours of SHS exposure. Investigators found that exposure to SHS can reduce HDL cholesterol levels by 18%. Additionally, there was a negative impact on HDL cholesterol levels and remained depressed for at least 24 hours (Moffatt, Chelland, Pecott, & Stamford, 2004). Therefore, short-term exposure to SHS led to inflammation and an imbalance in the lipid profile, which leads to lipid accumulation in the liver and the blood vessels of the heart that leads to more severe types of CVDs.

Thrombosis

Thrombosis is the formation of a thrombus—a blood clot, within a blood vessel. Thrombocytes are cell derivatives that circulate in the blood and play a role in thrombosis. Secondhand smoke exposure can cause alteration in the function of platelets and antithrombotic, prothrombotic, and fibrinolytic factors (Ambrose & Barua, 2004). Additionally, SHS exposure may decrease availability of platelet-derived NO and decrease platelet sensitivity to exogenous NO, leading to increased activation and adhesion (Ambrose & Barua, 2004; Ichiki, Ikeda, Haramaki, Ueno, & Imaizumi, 1996). Increased platelet adhesion will increase thrombus formation, which disrupts the endothelium, speed progression of atherosclerosis, and increase risk of ischemic heart disease (Law & Wald, 2003).

A study by Burghuber et al (1986) concurs with the findings reported by Ambrose & Baru (2004) regarding platelet sensitivity and SHS exposure. This study had 9 healthy male nonsmokers sit in a room for 20 minutes where 30 heavy band cigarettes had just been smoked. Blood was drawn before and 15 minutes after participants had been exposed to SHS. Investigators found that platelets sensitivity nonsmokers decreased due to SHS exposure.

Therefore, exposure to SHS decrease platelets sensitivity, which can increase platelets activation and thrombosis that can leads to more severe types of CVDs such as CHD and stroke.

Hypertension

Secondhand smoke exposure shows multiple effects on blood pressure; however, the literature suggests these effects may primarily occur in males (Flouris, Metsios, Jamurtas, & Koutedakis, 2008). For example, in a study that examined the effects of exposure to SHS on blood pressure, 14 men and 14 women were exposed to a simulated SHS in bar-restaurant environment for 60 minutes. Even though the study included a small sample size, the investigator found that systolic blood pressure significantly increased in men but not in women (Flouris et al., 2008). Similarly, in a study examined the effects of a 60-minute exposure to SHS on blood pressure and aortic pressure waveform in 10 healthy men, 11 women, and 12 controls (6 men, 6 women). The investigators found that, in men only, there was an association between SHS and increased brachial and aortic systolic blood pressure after 60 minutes. About half of the blood pressure increase happened at 15 minutes and it reached steady state after 30 minutes. Additionally, the authors found an increase in arterial stiffness, which could be the cause of increased blood pressure. However, brachial and aortic diastolic blood pressure and heart rate did not change in either male or females subjects (Mahmud & Feely, 2004). Therefore, an acute exposure to SHS has a deleterious effect on blood pressure in healthy males but not females.

Coronary Heart Disease

Also known as coronary artery disease or ischemic heart disease, CHD is the most common type of heart disease in the United States, killing more than 365,900 people in 2017. Additionally, about 18.2 million adults age 20 and older have CHD (Centers for Disease Control and Prevention, 2019a). Coronary heart disease is caused by plaque buildup in the wall of the

coronary artery of the heart. Plaque is made up of deposits of cholesterol and overtime it can become atherosclerosis.

The effect of SHS on the risk of CHD is controversial. Although several meta-analyses have concluded that exposure to SHS increases the risk of CHD by 25% among nonsmokers, a study by Enstrom and Kabat (2006) disputed the results of these studies, suggesting that selection bias of results may have skewed findings (Enstrom & Kabat, 2006). Their study focused on the United States cohort studies which provided the most available evidence about the association between CHD and SHS. They concluded that there is about 5% increase risk of death from CHD in nonsmokers exposed to SHS (Enstrom & Kabat, 2006). Similarly, in a different meta-analysis that reviewed epidemiological studies published between 1966 and 1998, He and colleagues (1999) looked at 10 prospective cohort studies and 8 case-control studies on the association between SHS and CHD. This study found that SHS exposure is associated with a greater risk of CHD (relative risk [RR] 1.25; 95% confidence interval [CI] [1.17, 1.32]) compared to unexposed nonsmokers. Specifically, there was a, 21% increased risk of CHD in cohort studies, and a 51% increased risk of CHD case control studies (J. He et al., 1999).

Angina

Also known as angina pectoris and acute coronary syndrome, angina is chest pain or discomfort that occurs when the heart muscle does not get enough oxygenated blood. It is a common symptom of CHD, which narrows the blood vessels to limit blood flow to the heart and increases the risk of a heart attack (National Heart Lung and Blood Institute, n.d.). Early work by Aronow (1978) examined the association between angina and exposure to SHS in a sample of ten male patients who experienced exercise-induced angina, after exposure to the smoke of 15 cigarettes within two hours in a ventilated room and unventilated room. The study found that

exposure to SHS lead subjects to elevated venous carboxyhemoglobin, increased heart rate, systolic and diastolic blood pressure while resting, and decreased heart rate and systolic blood pressure at angina. Additionally, the study concluded that exposure to SHS aggravates angina (Aronow, 1978). However, this is the only study that has been done to examine the association between angina and exposure to SHS. Thus, it is a reason for more research to be done to examine SHS and chronic angina.

Heart Attack

Heart attack, also called a myocardial infarction (MI), happens when a part of the myocardium does not get enough blood. The leading cause of death in the United States is heart diseases which can lead to heart attack. In the United States, about 805,000 Americans have a heart attack every year, and about one in five heart attacks is silent—the person is not aware of it (Centers for Disease Control and Prevention, 2019a). It is unknown, however, the percentage of heart attacks that may have been a result of SHS, as SHS exposure can cause cellular dysfunction through endothelial dysfunction, inflammation, and thrombosis, which may lead to more serious heard diseases, and result in a heart attack.

Based on this findings, results from multiple studies support the suggestion that exposure to SHS increases the risk of a heart attack across the world (Attard et al., 2017; Iversen, Jacobsen, & Lochen, 2013). For example, Iversen and collaborators (2013) looked at active and passive smoking as a risk factor for heart attack in an 11-year follow-up of 11,762 men and 13,206 women using data from the Tromsø Study in Norway. Out of 453 cases of heart attack in women, 20% of these cases were attributed to SHS. Additionally, the study concluded that women who are living with a smoker for 30 years or more after the age of 20 had increased risk

of heart attack by 40% due to SHS. However, there was no effect of living with a smoker in men (Iversen et al., 2013).

Similarly, the Maltese Acute Myocardial Infarction (MAMI) case-control study examined 423 cases with a first heart attack and 465 population controls. The study used a questionnaire and morning fasting blood samples to investigate the effect of SHS and the risk of a heart attack. The study concluded that exposure to SHS increased the risk of heart attack, and reported that there was a higher risk of heart attack from SHS in the home rather than in public settings (Attard et al., 2017). These findings suggest that exposure to SHS in nonsmokers does increase the risk of a heart attack, and that this risk may be particularly high in nonsmokers living in households with other smokers.

Stroke

Stroke is one of the leading causes of death in the United States. Every year, stroke kills about 140,000 people in the United States and 8,000 of those deaths due to SHS exposure. Additionally, about 87% of all strokes are ischemic stroke—when blood flow to the brain is blocked, usually by a thrombus (Centers for Disease Control and Prevention, 2019c, 2020). The current literature suggests an increased risk for stroke when there is SHS exposure. For example, in a national population-based case-control study in China, investigators used the Nationwide Retrospective Mortality Survey, conducted from 1989 through 1991. The study included 16,205 cases (12,579 with hemorrhagic stroke and 3626 with ischemic stroke). The study concluded that, compared with nonsmokers without any exposure to SHS, exposure to SHS significantly increased the likelihood of death by 10% for all strokes (odds ratio [OR] 1.10; 95% CI [1.05, 1.16]), by 10% for hemorrhagic stroke (OR 1.10; 95% CI [1.04, 1.16]), and by 12% for ischemic stroke (OR 1.12; 95% CI [1.03, 1.23]), (Hou et al., 2017).

Furthermore, a meta-analysis included 14 studies involving 30,3134 subjects and 4,050 stroke events, compared to smokers and nonsmokers with exposure to SHS for the risk of stroke. The study concluded that smokers had an overall significantly increased likelihood of stroke compared with nonsmokers (OR 1.61; 95% CI [1.34, 1.93]). There was a statically significant difference by sex among males (OR 1.54; 95% CI [1.11, 2.13]) and in females (OR 1.88; 95% CI [1.45, 2.44]). Additionally, exposure to SHS significantly increased the overall likelihood of stroke by 45% (OR 1.45; 95% CI [1.0, 2.11]) (Pan et al., 2019). All 14 studies found that there was an association between both smoking and exposure to SHS with increased risk of stroke (Pan et al., 2019). Therefore, exposure to SHS in nonsmokers increases the risk of stroke.

Heart Failure

Heart failure happens when the heart cannot pump enough blood to support other organs in the body. There are about 6.5 million adults with heart failure in the United States and it costs the nation about $30.7 billion in 2012 (Centers for Disease Control and Prevention, 2019b). Multiple studies examined the association of mortality with SHS exposure for patients with heart failure. For example, in one study that used NHANES III, there was a total of 19,592 adults, including 572 participants who had a diagnosis of heart failure, included in their analysis. The study looked at the household SHS exposure and mortality status of participants from the 2011 Public-Use Mortality Linked File. After analysis, the investigators concluded that there was an association between the household SHS exposure and an increased risk of death among heart failure patients (X. He, Zhao, He, Dong, & Liu, 2019).

Similarly, in a longitudinal cohort study, a questionnaire and urinary cotinine levels were used to define people with SHS to examine its impact on heart failure in 197 participants. After a

median follow up of 4.3 years, the mean mortality rate was 9 deaths per 100 patient-years (95% CI [8, 11]), and they concluded that SHS exposure is associated with increase in mortality of patients with heart failure (Psotka, Rushakoff, Glantz, De Marco, & Fleischmann, 2020). Therefore, exposure to SHS can increase the mortality rates of patients with heart failure but it does not increase the risk of heart failure itself.

Overall, the literature demonstrates a meaningful relation between exposure to SHS and CVDs. The present study addresses a gap in the literature by using a larger sample size from a national survey to generate more generalizable results that pertain to cardiovascular outcomes in nonsmokers exposed to SHS.

METHODS

Participants

Data in this study were obtained from the National Health and Nutrition Examination Survey (NHANES) 2015-2016 cycle, which targeted the noninstitutionalized United States civilian population and is administrated by the National Center for Health Statistics (NCHS), part of the CDC. The annual NHANES collects information on a range of topics pertaining to health using interviews, physical examination, and laboratory work (Centers for Disease Control and Prevention, 2017). Relevant contents to this study include current and former smoking status, exposure to SHS, CVDs, disease prevalence, and blood draw used to determine serum cotinine levels, among other variables.

The sample size completing the annual NHANES interviews is approximately 5,000 individuals of all ages (Centers for Disease Control and Prevention, 2017). Although the NHANES has collected data since 1960, this study specifically investigated the sample form the years 2015 to 2016, which had 9,971 persons who completed the interview, among which

9,544 (95.7%) participants completed interview and provided biological specimens. Data collected from these years are the most recently published data after the change in the initial sample design that happened in 2011, which implemented NHANES to oversample non-Hispanic (NH) Asians. Additionally, the oversample subgroups in the 2015-2016 survey cycle included: Hispanics, NH black, NH white, and other races, including multiracial backgrounds (Centers for Disease Control and Prevention, 2018b).

Procedure

Demographics

The sample population comprised of 13,164 subjects who answered questions on tobacco usage, had recorded laboratory values for serum cotinine in blood, and answered specific questions about CVDs. Demographic data included age, gender, and race/ethnicity and were self-reported by participants. For this study, the sample population was categorized by decades, starting at age 10 up to a last group comprising 80 years old and above. The race/ethnicity variables were also categorized into six groups: Mexican American, other Hispanic, non-Hispanic white, non-Hispanic black, non-Hispanic Asian, and other races, including multi-racial.

Exposure Groups

Participants were divided into three groups: nonsmokers, nonsmokers exposed to SHS, and current smokers (CS). Nonsmokers responded "no" to the question "During the past 5 days, including today, did you smoke cigarettes, pipes, cigars, little cigars or cigarillos, water pipes, hookahs, or e-cigarettes?" and had blood serum cotinine levels ≤0.050 ng/ml. Participants exposed to SHS responded "no" to the question "During the past 5 days, including today, did you smoke cigarettes, pipes, cigars, little cigars or cigarillos, water pipes, hookahs, or e-cigarettes?" and had blood serum cotinine levels >0.050 ng/ml. Finally, participants were defined as CS if they responded "yes" to the question "During the past 5 days, including today, did you smoke cigarettes, pipes, cigars, little cigars or cigarillos, water pipes, hookahs, or e-cigarettes?" and if they had blood serum cotinine levels >3.0 ng/ml. Participants must have responded to the questions and have blood serum cotinine levels reported to be considered in this study. Participants were excluded if they did not answer the questions above or if they did not have a blood serum cotinine levels reported.

Blood cotinine levels cut-offs were ≤0.050 ng/ml for nonsmokers and >0.050 ng/ml for nonsmokers exposed to SHS. These values were based on methods reported by previous studies examining blood cotinine levels in nonsmokers and people exposed to SHS (Agarwal, 2009; Fabry et al., 2011). As for CS, the blood cotinine level cut-off was >3.0 ng/ml based on previous studies examining blood cotinine levels in CS (Fabry et al., 2011; Saxena et al., 2017).

Outcomes

There were 11 questions assessing CVDs among NHANES respondents, including six questions from the Blood Pressure & Cholesterol and five questions from the Medical Conditions questionnaires. All the answers to these questions were binary (yes/no) and self-reported. Participants who refused to answer the questions, were not provided with questionnaire, or who did not know the answer were excluded from the study. The questions from Blood Pressure & Cholesterol questionnaire were:

- Have you ever been told by a doctor or other health professional that you had hypertension, also called high blood pressure?
- Were you told on 2 or more different visits that you had hypertension, also called high blood pressure?
- Because of your high blood pressure/hypertension, have you ever been told to take prescribed medicine?
- Are you now taking prescribed medicine for high blood pressure?
- Have you ever been told by a doctor or other health professional that your blood cholesterol level was high?
- To lower your blood cholesterol, have you ever been told by a doctor or other health professional to take prescribed medicine?

The questions from the Medical Conditions questionnaires were:

- Has a doctor or other health professional ever told you that you had congestive heart failure?
- Has a doctor or other health professional ever told you that you had coronary heart disease?
- Has a doctor or other health professional ever told you that you had angina, also called angina pectoris?
- Has a doctor or other health professional ever told you that you had a heart attack also called myocardial infarction?
- Has a doctor or other health professional ever told you that you had a stroke?

Statistical Analyses

Data on demographics, blood serum cotinine levels, questionnaire about blood pressure and cholesterol and medical conditions, were downloaded from the CDC website. Each dataset was opened and match-merged one-to-one by participant identification number using the Statistical Analysis System (SAS) (The SAS Institute; Cary, NC) software. The full dataset was then exported to the Statistical Package for Social Sciences (SPSS) software (The IBM Corporation; Armonk, NY) for further analyses.

Chi-square tests were performed to examine the responses to the 11 health questions related to CVD by the three groups of interest (i.e., CS, exposed to SHS, nonsmokers). Significance level was established at α=.05.

Additionally, ORs with 95% CIs were calculated using two logistic regression models to estimate the strength of association between exposure to SHS and cardiovascular outcomes. Model 1 yielded raw ORs and Model 2 was adjusted for gender, race/ethnicity, and age. In both models, nonsmokers with no exposure to SHS were used as a reference group and Nagelkerke's

R^2 was reported as a measure of model fit. This coefficient can be interpreted as the percentage of variance in the CVD outcomes that can be accounted for by the variables in the models.

Ethical Considerations

The NHANES is a publicly available dataset without any identifiable information available for use by the research community. Therefore, the Institutional Review Board approval was not necessary for these secondary analyses.

RESULTS

The sample population comprised of 13,164 subjects who answered questions on tobacco usage, had recorded laboratory values for serum cotinine in blood, and answered various questions about CVDs. Of the 13,164 subjects in the dataset, 7,455 (56.6%) were excluded because they did not complete portions of the questionnaire about tobacco use or CVDs, leaving 5,709 subjects in the analytic sample.

Demographic Characteristics

The demographic data for the study participants is presented in Table 1.

Table 1. Demographic characteristics of the studied population

Demographic Variables	Smokers (*N*=1054)		Secondhand smokers (*N*=1347)		Nonsmokers (*N*=3308)		Total (*N*=5709)		χ^2 (df)[a]
	n	Col %	*n*	Col %	*n*	Col %	*n*	Col %	
Gender									87.88 (2)
Male	652	61.9	661	49.1	1498	45.3	2811	49.2	
Female	402	38.1	686	50.9	1810	54.7	2898	50.8	
Age Groups, years									322.79 (14)
10-19	56	5.3	356	26.4	626	18.9	1038	18.2	
20-29	191	18.1	206	15.3	350	10.6	747	13.1	
30-39	199	18.9	140	10.4	417	12.6	756	13.2	
40-49	162	15.4	154	11.4	457	13.8	773	13.5	
50-59	200	19.0	142	10.5	419	12.7	761	13.3	
60-69	168	15.9	164	12.2	505	15.3	837	14.7	
70-79	61	5.8	114	8.5	314	9.5	489	8.6	
80 and older	17	1.6	71	5.3	220	6.7	308	5.4	
Race/Ethnicity									361.48 (10)
Mexican-American	126	12.0	190	14.1%	769	23.2	1085	19.0	
Other Hispanic	107	10.2	137	10.2	493	14.9	737	12.9	
NH white	381	36.1	456	33.9	1048	31.7	1885	33.0	
NH black	329	31.2	404	30.0	456	13.8	1189	20.8	
NH Asian	55	5.2	102	7.6	431	13.0	588	10.3	
Other[b]	56	5.3	58	4.3	111	3.4	225	3.9	

Abbreviations: col, column; df, degrees of freedom; NH, non-Hispanic

[a] $P<0.001$ for all χ^2 distributions tested.

[b] Includes multi-racial

Among smokers, typical participants were males (61.9%), non-Hispanic whites (36.1%), in the 50-59 years old (19.0%) and 30-39 years old (18.9%) groups and compared to secondhand smokers which had typical participants as females (50.9%), non-Hispanic whites (33.9%), in the 10-19 years old (26.4%) and 20-29 years old group (15.3%). While among nonsmokers, typical participants were females (50.8%), non-Hispanics whites (31.7%), in the 10-19 years old (18.9%) group. Chi-square tests for all three demographic characteristics showed that these distributions were statistically significantly different from a distribution that would occur at random ($P<0.001$ for the three distributions).

Cardiovascular Outcomes

Chi-square tests results for the distribution of the 11 CVD outcomes by the three smoking statuses are presented in Table 2. It can be observed that among nonsmokers, nonsmokers exposed to SHS, and smokers in the sample, there were statistically significantly different distributions for the outcomes of hypertension ($P=0.04$ for taking prescription and $P<0.001$ for ever been diagnosed), high cholesterol levels ($P<0.001$), heart failure ($P=0.01$), and angina ($P=0.006$). However, the distribution by smoking groups was not statistically significantly different for the outcomes of CHD, heart attack, and stroke.

Table 2. Cardiovascular Outcomes

Cardiovascular Outcomes	*N*	χ^2 with 2 df	*P*
Ever told you had high blood pressure	5166	1.674	0.43
Told had high blood pressure >2 times	1768	1.969	0.37
Taking prescription for hypertension	1780	6.602	0.04
Now taking prescribed medicine for high blood pressure	1583	20.211	<0.001
Doctor told you -high cholesterol level	5135	27.054	<0.001
Told to take prescription for cholesterol	3809	5.274	0.07
Ever told had congestive heart failure	4662	8.483	0.01
Ever told you had coronary heart disease	4648	0.456	0.80
Ever told you had angina/angina pectoris	4657	10.158	0.006
Ever told you had heart attack	4664	4.273	0.12
Ever told you had a stroke	4668	4.010	0.14

Abbreviation: df, degrees of freedom

Further, we analyzed and tested the chi-square distributions of CVD outcomes by demographic characteristics. The results are presented in Table 3 for gender, Table 4 for age groups, and Table 5 for race/ethnicity.

Table 3 displays the chi-square results based on CVD outcomes by gender. There was a statistically significantly different distribution for males compared to that of females. Males had a statistically significantly higher distribution in the group exposed to SHS and two measures of hypertension and high cholesterol while females exposed to SHS only had statistically significantly higher distribution angina. There were no other statistically significantly different distributions for the rest of the CVDs analyzed.

Table 4 presents the chi-square results based on CVD outcomes by age groups. There were statistically significantly different distributions in hypertension, CHD, angina, heart attack, and stroke in individuals between 50-59 years old. While individuals between 40-49 years old had statistically significantly different distributions for hypertension, heart failure, angina, and stroke. The rest of age groups had two to no CVDs as statistically significant.

Additionally, Table 5 displays the chi-square results based on cardiovascular outcomes by race/ethnicity groups. Among the six race/ethnicity groups, non-Hispanic blacks tend to have most CVDs outcomes (4 out of 7 were statistically significant) while non-Hispanic whites tended to have the second most CVDs outcomes (3 out of 7 were statistically significant) and Mexican Americans did not have statistically significantly different distribution for any of the seven CVDs that were examined in this study.

Table 3. Cardiovascular Outcomes by Gender

Cardiovascular Outcomes	**Males**			**Females**		
	N	**χ^2 with 2 df**	***P***	***N***	**χ^2 with 2 df**	***P***
Ever told you had high blood pressure	2515	0.695	0.707	2651	1.604	0.448
Told had high blood pressure >2 times	856	3.548	0.170	912	2.508	0.285
Taking prescription for hypertension	861	2.353	0.308	919	2.869	0.238
Now taking prescribed medicine for high blood pressure	744	13.578	0.001	839	5.066	0.079
Doctor told you -high cholesterol level	2502	29.234	<0.001	2633	5.019	0.081
Told to take prescription for cholesterol	1805	6.455	0.040	2004	3.827	0.148
Ever told had congestive heart failure	2267	3.294	0.193	2395	5.244	0.073
Ever told you had coronary heart disease	2255	0.678	0.713	2393	0.795	0.672
Ever told you had angina/angina pectoris	2266	3.098	0.212	2391	7.725	0.021
Ever told you had heart attack	2269	0.279	0.870	2395	5.519	0.063
Ever told you had a stroke	2272	3.218	0.200	2396	4.555	0.103

Abbreviation: df, degrees of freedom

Table 4. Cardiovascular Outcomes by Age Groups

	10-19			20-29			30-39			40-49		
Outcome	*N*	χ^2 with 2 df	*P*	*N*	χ^2 with 2 df	*P*	*N*	χ^2 with 2 df	*P*	*N*	χ^2 with 2 df	*P*
Ever told you had high blood pressure	500	5.170	0.08	747	0.466	0.79	753	18.004	<0.001	773	9.088	0.01
Told had high blood pressure >2 times	18	0.450	0.80	58	0.214	0.90	143	0.238	0.89	215	0.959	0.62
Taking prescription for hypertension	19	0.262	0.89	58	0.110	0.95	143	0.966	0.62	215	7.040	0.03
Now taking prescribed medicine for high blood pressure	5	2.917	0.23	25	1.176	0.56	99	0.495	0.78	173	7.364	0.02
Doctor told you -high cholesterol level	500	1.036	0.60	746	0.152	0.93	752	4.343	0.14	771	0.607	0.74
Told to take prescription for cholesterol	171	2.636	0.27	370	3.834	0.15	497	5.174	0.08	624	3.823	0.15
Ever told had congestive heart failure	0	—	—	747	—	—	756	1.630	0.44	773	6.753	0.03
Ever told you had coronary heart disease	0	—	—	747	—	—	756	0.808	0.67	771	0.054	0.97
Ever told you had angina/angina pectoris	0	—	—	747	2.63	0.27	755	3.299	0.19	772	7.063	0.03
Ever told you had heart attack	0	—	—	747	—	—	755	1.567	0.46	772	4.493	0.10
Ever told you had a stroke	0	—	—	747	5.737	0.06	756	1.378	0.50	773	15.933	<0.001

Abbreviation: df, degrees of freedom

	50-59			60-69			70-79			≥80		
Outcome	*N*	χ^2 with 2 df	*P*	*N*	χ^2 with 2 df	*P*	*N*	χ^2 with 2 df	*P*	*N*	χ^2 with 2 df	*P*
Ever told you had high blood pressure	761	15.968	<0.001	837	3.576	0.17	489	2.386	0.30	306	3.863	0.14
Told had high blood pressure >2 times	331	3.158	0.21	498	4.527	0.10	302	0.735	0.69	203	0.483	0.78
Taking prescription for hypertension	331	0.335	0.85	502	4.62	0.10	304	1.711	0.42	208	0.352	0.84
Now taking prescribed medicine for high blood pressure	312	0.004	>0.99	476	5.712	0.06	290	1.445	0.48	203	1.199	0.55
Doctor told you -high cholesterol level	750	2.236	0.33	832	3.362	0.19	483	0.435	0.80	301	4.832	0.09
Told to take prescription for cholesterol	652	0.138	0.93	760	3.072	0.22	455	0.072	0.96	280	0.802	0.67
Ever told had congestive heart failure	760	4.540	0.10	834	5.931	0.05	485	15.707	<0.001	307	0.034	0.98
Ever told you had coronary heart disease	759	8.306	0.02	831	3.085	0.21	481	4.892	0.09	303	1.467	0.48
Ever told you had angina/angina pectoris	759	9.995	0.007	836	13.784	0.001	486	0.547	0.76	302	2.102	0.35
Ever told you had heart attack	761	13.128	0.001	837	9.013	0.01	488	3.008	0.22	304	1.237	0.54
Ever told you had a stroke	760	10.116	0.006	836	1.315	0.52	489	5.743	0.06	307	1.596	0.45

Abbreviation: df, degrees of freedom

Table 5. Cardiovascular Outcomes by Race

	Mexican American			Other Hispanic			Non-Hispanic White		
Outcome	*N*	χ^2 with 2 df	*P*	*N*	χ^2 with 2 df	*P*	*N*	χ^2 with 2 df	*P*
Ever told you had high blood pressure	968	0.694	0.71	658	5.188	0.08	1730	1.641	0.44
Told had high blood pressure >2 times	287	5.771	0.06	223	3.595	0.17	614	3.373	0.18
Taking prescription for hypertension	289	1.704	0.43	223	17.686	<0.001	620	0.622	0.73
Now taking prescribed medicine for high blood pressure	251	5.257	0.07	195	6.911	0.03	556	6.791	0.03
Doctor told you -high cholesterol level	957	1.926	0.38	654	3.204	0.20	1720	11.264	0.004
Told to take prescription for cholesterol	614	3.465	0.18	488	2.464	0.29	1370	1.698	0.43
Ever told had congestive heart failure	842	0.226	0.89	602	2.697	0.26	1605	0.424	0.81
Ever told you had coronary heart disease	839	2.224	0.33	601	0.698	0.70	1599	1.503	0.47
Ever told you had angina/angina pectoris	843	0.850	0.65	599	0.358	0.84	1604	6.831	0.03
Ever told you had heart attack	843	0.328	0.85	604	0.568	0.75	1605	0.025	0.99
Ever told you had a stroke	842	4.817	0.09	604	0.686	0.71	1608	0.608	0.74

Abbreviation: df, degrees of freedom

	Non-Hispanic Black			Non-Hispanic Asian			Other, including multiracial		
Outcome	*N*	χ^2 with 2 df	*P*	*N*	χ^2 with 2 df	*P*	*N*	χ^2 with 2 df	*P*
Ever told you had high blood pressure	1071	2.309	0.32	545	0.334	0.85	194	6.954	0.03
Told had high blood pressure >2 times	447	0.157	0.92	125	1.185	0.55	72	0.657	0.72
Taking prescription for hypertension	449	2.850	0.24	126	2.680	0.26	73	2.571	0.2877
Now taking prescribed medicine for high blood pressure	414	7.359	0.02	105	4.171	0.12	62	0.210	0.90
Doctor told you -high cholesterol level	1066	16.584	<0.001	544	4.428	0.11	194	9.859	0.007
Told to take prescription for cholesterol	802	2.355	0.31	394	0.712	0.70	141	7.976	0.02
Ever told had congestive heart failure	957	8.537	0.01	488	4.543	0.10	168	3.405	0.18
Ever told you had coronary heart disease	954	3.952	0.14	488	3.991	0.14	167	1.075	0.58
Ever told you had angina/angina pectoris	956	4.363	0.11	488	6.493	0.04	167	0.425	0.81
Ever told you had heart attack	956	9.206	0.01	489	7.362	0.02	167	0.905	0.64
Ever told you had a stroke	957	0.351	0.84	489	0.756	0.69	168	0.786	0.68

Abbreviation: df, degrees of freedom

Moreover, ORs with 95% CIs were calculated from logistic regression models for estimating the effects of exposure to SHS on cardiovascular outcomes.

In Model 1 (Table 6), compared to nonsmokers not exposed to SHS, secondhand smokers had statistically significant association between exposure to SHS and both hypertension and high cholesterol levels. Secondhand smokers are 43% more likely to report being told to take prescribed medication for hypertension and twice as likely to report that they were taking medication for hypertension during the time they answered the questionnaire. Also, secondhand smokers are 31% more likely to report that they were told by a physician about having high cholesterol levels, and 23% more likely to report taking medication for cholesterol levels. Additionally, Model 1 found a statistically significant association between exposure to SHS and a reduced likelihood of angina (OR 0.545; 95% CI [0.361, 0.824]) but there was no other statistically significant likelihood of having other types of CVDs when exposed to SHS.

Furthermore, compared to nonsmokers exposed to SHS, smokers are 41.5% more likely of having high cholesterol and there was statistically significant association between smoking and high cholesterol levels. However, there was no statistically significant association between smoking and any of the other CVD outcomes that were examined through Model 1.

Nagelkerke's R_2 were also calculated for Model 1 which is a measure of the model fit that range from 0.00 to 1.00. The values in Model 1 were between 0% and 2% which indicate that there are 98% unaccounted variables for the model's variability and fit. This model was not a good fit for the data.

Table 6. Unadjusted odds ratios and 95% confidence intervals (CIs) for cardiovascular study outcomes.

Cardiovascular Outcomes	Nagelkerke's R_2	Nonsmokers Exposed to Secondhand Smoke		Smokers	
		OR_a	95% CI	OR_a	95% CI
Ever told you had high blood pressure	0.000	0.908	0.783, 1.052	0.980	0.849, 1.130
Told had high blood pressure >2 times	0.002	0.923	0.682, 1.250	1.172	0.884, 1.553
Taking prescription for hypertension	0.007	1.430	1.008, 2.029	0.829	0.557, 1.233
Now taking prescribed medicine for high blood pressure	0.021	2.099	1.508, 2.922	1.189	0.831, 1.702
Doctor told you -high cholesterol level	0.007	1.317	1.130, 1.535	1.415	1.129, 1.641
Told to take prescription for cholesterol	0.002	1.229	1.031, 1.467	1.052	0.888, 1.247
Ever told had congestive heart failure	0.006	0.699	0.482, 1.014	0.609	0.426, 0.871
Ever told you had coronary heart disease	0.000	0.905	0.640, 1.281	1.039	0.722, 1.495
Ever told you had angina/angina pectoris	0.009	0.545	0.361, 0.824	1.071	0.641, 1.790
Ever told you had heart attack	0.003	0.719	0.517, 1.000	0.805	0.572, 1.134
Ever told you had a stroke	0.003	0.704	0.495, 1.003	0.965	0.652, 1.427

[a]Nonsmokers not exposed to secondhand smoke are the reference group.

Model 2 (Table 7) adjusted the ORs and 95% CI for CVD study outcomes by gender, race/ethnicity, and age groups. Compared to nonsmokers not exposed to SHS, secondhand smokers were 55% more likely to take prescribed medication for hypertension and 21% more likely having high cholesterol levels. Additionally, secondhand smokers were significantly less likely to report hypertension, congestive heart failure, CHD, angina, heart attack, and stroke. Furthermore, compared to nonsmokers exposed to SHS, smokers were 21% more likely of having high cholesterol and smokers were 43% less likely for reporting heart failure.

Like Model 1, Nagelkerke's R2 were also calculated for Model 2. However, Model 2 had a much better model fit compared to Model 1. All the values in Model 2 were between 4% and 32%. Although Model 2 had higher values than Model 1, Nagelkerke's R2 showed that Model 2 still did not account for 68% of the variables for the model's variability and fit; however, it is still considered a moderate fit that improved the fit of Model 1.

Table 7. Adjusted[a] odds ratios and 95% confidence intervals (CIs) for CVD study outcomes.

Outcomes	Nagelkerke's R_2	Nonsmokers Exposed to Secondhand Smoke		Smokers	
		AOR[a,b]	95% CI	AOR[a,b]	95% CI
Ever told you had high blood pressure	0.314	0.768	0.645, 0.914	0.803	0.677, 0.951
Told had high blood pressure >2 times	0.042	0.921	0.664, 1.278	1.181	0.883, 1.580
Taking prescription for hypertension	0.285	1.060	0.697, 1.612	0.698	0.442, 1.102
Now taking prescribed medicine for high blood pressure	0.156	1.554	1.066, 2.265	1.098	0.749, 1.610
Doctor told you -high cholesterol level	0.272	1.213	1.017, 1.446	1.206	1.019, 1.428
Told to take prescription for cholesterol	0.324	0.966	0.783, 1.191	0.905	0.742, 1.105
Ever told had congestive heart failure	0.195	0.462	0.307, 0.696	0.568	0.390, 0.828
Ever told you had coronary heart disease	0.231	0.585	0.397, 0.862	0.929	0.632, 1.364
Ever told you had angina/angina pectoris	0.119	0.421	0.269, 0.659	1.007	0.596, 1.699
Ever told you had heart attack	0.201	0.489	0.339, 0.706	0.730	0.509, 1.048
Ever told you had a stroke	0.124	0.543	0.369, 0.798	0.934	0.624, 1.399

[a]Adjusted for gender, race/ethnicity, and age groups.

[b]Nonsmokers not exposed to secondhand smoke are the reference group.

DISCUSSION

The purpose of this study was to assess the distribution and likelihood of CVDs in nonsmokers exposed to SHS. It was originally hypothesized that nonsmokers exposed to SHS would have similar likelihood of having CVDS compared to firsthand smokers. The results showed that secondhand smokers were significantly more likely to take medication for hypertension and having high cholesterol levels compared to nonsmokers.

Based on the results adjusted by demographics in Model 2, this study showed that SHS exposure in self-reported nonsmokers was significantly associated with higher likelihood of hypertension and cholesterol levels. Both hypertension and cholesterol levels were examined using two types of questions. While the first set of questions asks participants if they were told before that they have high blood pressure or high cholesterol levels, the second set of questions asks participants about medication use for either condition. Results showed that, compared to nonsmokers not exposed to SHS, secondhand smokers had significantly higher likelihood of taking prescribed medication for hypertension and having high cholesterol levels. However, these results were inconsistent with the results of the other questions about hypertension and cholesterol levels as they showed no statistically significant association between exposure to SHS and having hypertension (OR 0.921; 95% CI [0.664, 1.612]) or taking medication for high cholesterol levels (OR 0.966; 95% CI [0.783, 1.191]). Since these answers are self-reported, the biases associated with self-report cannot be ruled out. On one hand, recall bias—when participants do not recall specific facts or events related to their medical records—can be a result of recall error and are common in epidemiology and medical research (Althubaiti, 2016). On the other hand, social desirability bias may also play a role: participants answer questions how they think the researcher would like them to answer. Social desirability bias is also ubiquitous in

epidemiology research especially when researchers are using data based on survey or questionnaire and do not have a way to know if participants underestimate or overestimate their answers (Althubaiti, 2016).

Few previous studies have explored the effects of SHS on hypertension, although these studies are consistent with the our results, they were gender-specific and typically involved a small sample size (Flouris et al., 2008; Li et al., 2015; Mahmud & Feely, 2004). Also, most of these studies found that males are more likely to have hypertension than females (Flouris et al., 2008; Mahmud & Feely, 2004). However, other studies that used larger datasets supported our results (Kim et al., 2019; Park et al., 2018; Yang et al., 2017). On one hand, Kim and collaborators (2019), examined the association between SHS exposure and hypertension in 106,268 Korean nonsmokers using both self-reported questionnaire and urine cotinine levels, similar to our methods. However, they also used an average of two blood pressure measurements and antihypertensive medication intake to examine the association between SHS and hypertension. The results concluded that there was a significant association between SHS exposure and hypertension even with lower levels of frequent and duration of SHS exposure (OR 1.16; 95% CI [1.05, 1.24]) (Kim et al., 2019).

Similarly, Park and collaborators (2018), using data from the Korean National Health and Nutrition Examination Survey (KNHANES) V 2010-2012, examined the association between SHS exposure and hypertension in 10,532 (8987 women and 1545 men) never smokers. They used duration of SHS exposure, blood pressure measurements, and antihypertensive medication intake to define the exposure groups. They concluded that there was a significant association between SHS exposure and hypertension in women only (adjusted OR 1.50; 95% CI [1.10, 2.04]) (Park et al., 2018). Additionally, in another study that included more than 5 million

females along with their husbands from the National Free Pre-pregnancy Checkup Projects conducted across 31 provinces in China in 2014 examined the association between SHS exposure and hypertension. The data were collected using face-to-face interviews and serum cotinine levels to define the exposure groups. The investigators found statistically significant association between SHS exposure and hypertension in males (OR 1.28; 95% CI [1.27, 1.30]), females (OR 1.53; 95% CI [1.30, 1.79]), and mix group of both females and males (OR 1.50; 95% CI [1.36, 1.67]) (Yang et al., 2017). With the literature supporting the results of the present study, it can be concluded that hypertension is significantly associated with exposure to SHS in males' nonsmokers. Thus, nonsmokers who reduce their exposure to SHS reduce their odds of developing hypertension.

Furthermore, previous studies have examined the impact of SHS exposure on cholesterol levels in both animal and human studies (Moffatt et al., 2004; Valkonen & Kuusi, 1998; Yuan et al., 2007). However, similar to the previous studies reporting hypertension outcomes, most studies examined small sample sizes and showed negative effects of SHS exposure at the cellular levels that decrease HDL and increase LDL cholesterol (Valkonen & Kuusi, 1998; Yuan et al., 2007). Although the present study examined self-reported hypercholesterolemia and medication intake in general, it still adds value to the current literature on the association between SHS exposure and cholesterol levels due to the analysis of a large sample size of a human population. The increased likelihood of nonsmokers exposed to SHS to develop high cholesterol levels might be due to the negative effect of SHS at the cellular level. For example, it has been established that exposure to SHS can cause endothelial dysfunction which can lead to the development of atherosclerosis (Glantz & Parmley, 2001; Otsuka et al., 2001). Atherosclerosis is associated with

both hypertension and hyperlipidemia (Alexander, 1995). Therefore, exposure to SHS has an impact at the cellular level that can lead to further advance the severity of different CVD types.

Surprisingly, compared to nonsmokers, secondhand smokers are significantly less likely of having congestive heart failure CHD, angina, heart attack, and stroke. Although, these results contradict the current literature regarding stroke and heart attack, they are considered accurate due to the fact that 26% (*N*=356) of nonsmokers are in the 10-19 years old and 15% (*N*= 206) are in the 20-29 years old group. Typically, these age groups do not develop higher rates of CVDs such as CHD, angina, heart attack, and stroke. Additionally, our results do not account for the duration of SHS exposure in each age group. These two conditions make a strong argument for a dose-response association that cannot be observed in samples with a high proportion of youth, as it is the case.

Limitations

Several limitations of the study are worth noting. First, there is a possibility of self-reporting biases, such as social desirability and recall biases (Althubaiti, 2016). Second, a large number of participants were excluded from the study due missing variables on SHS exposure and CVDs. Third, although the proposed demographic-adjusted Model 2 found some differences compared to crude Model 1, the overall model fit (Nagelkerke's R^2) was relatively low for both. This means that there are still other variables unaccounted for both models' variability and fit. Those unaccounted variables—such as other health conditions, obesity, genetic composition, socioeconomic status (SES), and duration of exposure to secondhand smoke—might have further mediation and moderation effects that were not considered in the models. Therefore, future studies should consider exploring how other health conditions related to CVDs may attenuate or increase the magnitude of the association of SHS with CVDs.

Despite these limitations aside, there are notable strengths in this study. First, to the best of our knowledge, this is the first study to use the NHANES database to explore the association between exposure to SHS and cardiovascular outcomes. The NHANES database included a large sample size which is a representative of the demographics in the United States. Second, the present study used cotinine measurements to define the three smoker groups including the nonsmokers exposed to secondhand smoke in addition to self-reported responses. Using the cotinine levels yields an accurate cut-off value to separate the three smoker groups and reduce the self-report biases of participants regarding exposure to SHS. Thus, this study further advances research on secondhand smoke and cardiovascular disease. Last, this study used a solid and widely accepted methodology to investigate both distributional assumptions through chi-square test and strength of association through logistic regression.

Implications for Research and Policy

Future studies should use matched data from secondary sources that explore exposure to SHS and cardiovascular outcomes to analyze change over time. This could highlight the effects of changes in policies that impact smoking bans in public places as there are 12 states in the United States that do not have 100% smoke-free state law (American Nonsmokers' Rights Foundation, 2020). Future research should also target the effects of variables not accounted for in this study, such as other health conditions, obesity, genetic composition, SES, and duration of exposure to secondhand smoke on the cardiovascular outcomes. This study only determined whether CVDs were more likely after exposure to SHS but was not able to determine a dose-response by any of the above variables.

Furthermore, there are 28 states in the United States that have statewide comprehensive smoke-free law in effect, prohibiting smoking in all indoor areas of workplaces, restaurants, and

bars (American Lung Association, 2020). Multiple studies have looked at the impact of policies implication to regulate SHS exposure among nonsmokers in the United States (Farrelly et al., 2005; Wilson, Shamo, Boynton, & Kiley, 2012). One study based in Michigan, found that urine cotinine levels among nonsmoking bar employees decreased from 35.9 ng/ml to a level that could not be measured within 2 months after the have statewide comprehensive smoke-free law went into effect. Also, the majority of bar employees reported a significant improvement in general health and in six respiratory symptoms (Wilson et al., 2012). Another study based in New York, found that salivary cotinine levels among nonsmoking adult workers in restaurants, bars, and bowling facilities decreased by 85% within 1 year after the smoke-free law went into effect 2003 (Farrelly et al., 2005). Therefore, it is important to have statewide smoke-free law in effect in every state in the United States to reduce the SHS exposure among nonsmokers which will reduce future CVDs.

Implications for Clinical Practice

Considering the strong association between exposure to SHS and both hypertension and cholesterol levels, clinicians have the opportunity to start educating patients about the impact of SHS exposure on their health. Currently, clinicians do not use any screening test to examine SHS exposure. Therefore, we can start screening patients for SHS exposure by including question about SHS exposure in home, workplaces, and public places. By doing so, clinicians can add this information to the patients' medical history and implement preventive measure.

Additionally, clinicians can promote behavior modification plans for nonsmokers exposed to SHS or have a family history of CVDs. Past research demonstrates that interventions focused on promoting healthy diets have proven effective for reducing the risk of hypertension and non-fatal CVDs (Jackson et al., 2020). Additional study concluded that physical training

have proven to be an effective method for reducing total serum cholesterol levels (Golding, 2013). Therefore, more evidence-based interventions need to be developed to target behavior and lifestyle modifications. Additional research is needed to identify barriers among different populations to develop culturally appropriate preventive programs since not all races/ethnicities are exposed to SHS equally.

Clinician should also consider other variables not accounted for in this study that are well-known factors for CVDs among nonsmokers exposed to SHS such as other health conditions, obesity, genetic composition, and duration of exposure to secondhand smoke. Previous studies have proven that individuals with diabetes mellitus at higher risk if developing CVDs such as hypertension and high cholesterol levels (Leon & Maddox, 2015). Additionally, obesity is common in patients with diabetes especially Type II diabetes and is associated with an increased risk of CVDs (Leon & Maddox, 2015). Thus, other health conditions may affect a nonsmoker exposed to SHS health outcomes by increasing the risk of having CVDs.

CONCLUSION

This study demonstrated a statistically significant distribution and likelihood of cardiovascular disease after exposure to second-hand smoke. After controlling for age, sex, and race/ethnicity, nonsmokers exposed to second-hand smoke had a significantly higher likelihood of reporting hypertension and elevated blood cholesterol levels. Additionally, the present study addresses a gap in the literature by using a larger sample size from a nationally representative survey to generate more generalizable results pertaining to cardiovascular outcomes in nonsmokers exposed to second-hand smoke. This study adds to the literature supporting the need to develop health interventions to reduce second-hand smoke exposure. Clinicians and researchers should educate, respectively, patients and populations exposed to second-hand smoke on meaningful, evidence-based ways to reduce their SHS exposure to reduce the burden of cardiovascular disease.

REFERENCES

Adams, T., Wan, E., Wei, Y., Wahab, R., Castagna, F., Wang, G., . . . Jelic, S. (2015). Secondhand Smoking Is Associated With Vascular Inflammation. *Chest, 148*(1), 112-119. doi:10.1378/chest.14-2045

Agarwal, S. (2009). The association of active and passive smoking with peripheral arterial disease: results from NHANES 1999-2004. *Angiology, 60*(3), 335-345. doi:10.1177/0003319708330526

Alexander, R. W. (1995). Theodore Cooper Memorial Lecture. Hypertension and the pathogenesis of atherosclerosis. Oxidative stress and the mediation of arterial inflammatory response: a new perspective. *Hypertension, 25*(2), 155-161. doi:10.1161/01.hyp.25.2.155

Althubaiti, A. (2016). Information bias in health research: definition, pitfalls, and adjustment methods. *J Multidiscip Healthc, 9*, 211-217. doi:10.2147/JMDH.S104807

Ambrose, J. A., & Barua, R. S. (2004). The pathophysiology of cigarette smoking and cardiovascular disease: an update. *J Am Coll Cardiol, 43*(10), 1731-1737. doi:10.1016/j.jacc.2003.12.047

American Lung Association. (2020). Smokefree Air Laws. Retrieved from https://www.lung.org/policy-advocacy/tobacco/smokefree-environments/smokefree-air-laws

American Nonsmokers' Rights Foundation. (2020). United States 100% Smokefree Laws Map. *Smokefree Workplace Lists and Maps.* Retrieved from https://no-smoke.org/materials-services/lists-maps/#1518200878061-ebc83fdc-2d6c

Aronow, W. S. (1978). Effect of passive smoking on angina pectoris. *N Engl J Med, 299*(1), 21-24. doi:10.1056/NEJM197807062990105

Asfar, T., Koru-Sengul, T., Ruano-Herreria, E. C., Sierra, D., Lee, D. J., & Arheart, K. L. (2019). Secondhand Smoke Exposure Among High-Risk Patients in the United States (NHANES 2001-2012): Implications for Clinical Practice. *Nicotine Tob Res, 21*(4), 551-556. doi:10.1093/ntr/nty060

Attard, R., Dingli, P., Doggen, C. J. M., Cassar, K., Farrugia, R., & Wettinger, S. B. (2017). The impact of passive and active smoking on inflammation, lipid profile and the risk of myocardial infarction. *Open Heart, 4*(2), e000620. doi:10.1136/openhrt-2017-000620

Benowitz, N. L. (1999). The biology of nicotine dependence: from the 1988 Surgeon General's Report to the present and into the future. *Nicotine Tob Res, 1 Suppl 2*, S159-163. doi:10.1080/14622299050012001

Benowitz, N. L., Bernert, J. T., Caraballo, R. S., Holiday, D. B., & Wang, J. (2009). Optimal serum cotinine levels for distinguishing cigarette smokers and nonsmokers within different racial/ethnic groups in the United States between 1999 and 2004. *Am J Epidemiol, 169*(2), 236-248. doi:10.1093/aje/kwn301

Centers for Disease Control and Prevention. (2017, September 15, 2017). About the National Health and Nutrition Examination Survey. Retrieved from https://www.cdc.gov/nchs/nhanes/about_nhanes.htm

Centers for Disease Control and Prevention. (2018a, January 17). Health Effects of Secondhand Smoke. Retrieved from https://www.cdc.gov/tobacco/data_statistics/fact_sheets/secondhand_smoke/health_effects/index.htm

Centers for Disease Control and Prevention. (2018b, October 30). NHANES 2015-2016 Overview. Retrieved from https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/overview.aspx?BeginYear=2015

Centers for Disease Control and Prevention. (2018c, January 18). Secondhand Smoke (SHS) Facts. Retrieved from https://www.cdc.gov/tobacco/data_statistics/fact_sheets/secondhand_smoke/general_facts/index.htm

Centers for Disease Control and Prevention. (2018d). Smoking is down, but almost 38 million American adults still smoke. Retrieved from https://www.cdc.gov/media/releases/2018/p0118-smoking-rates-declining.html

Centers for Disease Control and Prevention. (2019a). Heart Disease Facts . Retrieved from https://www.cdc.gov/heartdisease/facts.htm

Centers for Disease Control and Prevention. (2019b). Heart Failure. Retrieved from https://www.cdc.gov/heartdisease/heart_failure.htm

Centers for Disease Control and Prevention. (2019c). Smoking and Heart Disease and Stroke. Retrieved from https://www.cdc.gov/tobacco/campaign/tips/diseases/heart-disease-stroke.html

Centers for Disease Control and Prevention. (2020). Stroke Facts. Retrieved from https://www.cdc.gov/stroke/facts.htm

Enstrom, J. E., & Kabat, G. C. (2006). Environmental tobacco smoke and coronary heart disease mortality in the United States--a meta-analysis and critique. *Inhal Toxicol, 18*(3), 199-210. doi:10.1080/08958370500434255

. Evaluating Exposure to Secondhand Smoke. (2010). In *Secondhand Smoke Exposure and Cardiovascular Effects: Making Sense of the Evidence* (pp. 31-58). Washington (DC): The National Academies Press.

. Experimental Studies Relevant to the Pathophysiology of Secondhand Smoke. (2010). In *Secondhand Smoke Exposure and Cardiovascular Effects: Making Sense of the Evidence* (pp. 59-94). Washington (DC): The National Academies Press.

Fabry, D. A., Davila, E. P., Arheart, K. L., Serdar, B., Dietz, N. A., Bandiera, F. C., & Lee, D. J. (2011). Secondhand smoke exposure and the risk of hearing loss. *Tob Control, 20*(1), 82-85. doi:10.1136/tc.2010.035832

Farrelly, M. C., Nonnemaker, J. M., Chou, R., Hyland, A., Peterson, K. K., & Bauer, U. E. (2005). Changes in hospitality workers' exposure to secondhand smoke following the implementation of New York's smoke-free law. *Tob Control, 14*(4), 236-241. doi:10.1136/tc.2004.008839

Flouris, A. D., Metsios, G. S., Jamurtas, A. Z., & Koutedakis, Y. (2008). Sexual dimorphism in the acute effects of secondhand smoke on thyroid hormone secretion, inflammatory markers and vascular function. *Am J Physiol Endocrinol Metab, 294*(2), E456-462. doi:10.1152/ajpendo.00699.2007

Glantz, S. A., & Parmley, W. W. (2001). Even a little secondhand smoke is dangerous. *JAMA, 286*(4), 462-463. doi:10.1001/jama.286.4.462

Golding, L. A. (2013). Effects of Physical Training upon Total Serum Cholesterol Levels. *Research Quarterly. American Association for Health, Physical Education and Recreation 32*(4), 499-506. doi:10.1080/10671188.1961.10613177

He, J., Vupputuri, S., Allen, K., Prerost, M. R., Hughes, J., & Whelton, P. K. (1999). Passive smoking and the risk of coronary heart disease--a meta-analysis of epidemiologic studies. *N Engl J Med, 340*(12), 920-926. doi:10.1056/NEJM199903253401204

He, X., Zhao, J., He, J., Dong, Y., & Liu, C. (2019). Association of household secondhand smoke exposure and mortality risk in patients with heart failure. *BMC Cardiovasc Disord, 19*(1), 280. doi:10.1186/s12872-019-1269-y

Homa, D. M., Neff, L. J., King, B. A., Caraballo, R. S., Bunnell, R. E., Babb, S. D., . . . Prevention. (2015). Vital signs: disparities in nonsmokers' exposure to secondhand smoke--United States, 1999-2012. *MMWR Morb Mortal Wkly Rep, 64*(4), 103-108. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/25654612

Hou, L., Han, W., Jiang, J., Liu, B., Wu, Y., Zou, X., . . . Li, J. (2017). Passive smoking and stroke in men and women: a national population-based case-control study in China. *Sci Rep, 7*, 45542. doi:10.1038/srep45542

Hukkanen, J., Jacob, P., 3rd, & Benowitz, N. L. (2005). Metabolism and disposition kinetics of nicotine. *Pharmacol Rev, 57*(1), 79-115. doi:10.1124/pr.57.1.3

Ichiki, K., Ikeda, H., Haramaki, N., Ueno, T., & Imaizumi, T. (1996). Long-term smoking impairs platelet-derived nitric oxide release. *Circulation, 94*(12), 3109-3114. doi:10.1161/01.cir.94.12.3109

Iversen, B., Jacobsen, B. K., & Lochen, M. L. (2013). Active and passive smoking and the risk of myocardial infarction in 24,968 men and women during 11 year of follow-up: the Tromso Study. *Eur J Epidemiol, 28*(8), 659-667. doi:10.1007/s10654-013-9785-z

Jackson, J. K., MacDonald-Wicks, L. K., McEvoy, M. A., Forder, P. M., Holder, C., Oldmeadow, C., . . . Patterson, A. J. (2020). Better diet quality scores are associated with

a lower risk of hypertension and non-fatal CVD in middle-aged Australian women over 15 years of follow-up. *Public Health Nutr, 23*(5), 882-893. doi:10.1017/S1368980019002842

Jefferis, B. J., Lowe, G. D., Welsh, P., Rumley, A., Lawlor, D. A., Ebrahim, S., . . . Whincup, P. H. (2010). Secondhand smoke (SHS) exposure is associated with circulating markers of inflammation and endothelial function in adult men and women. *Atherosclerosis, 208*(2), 550-556. doi:10.1016/j.atherosclerosis.2009.07.044

Kim, B. J., Kang, J. G., Kim, J. H., Seo, D. C., Sung, K. C., Kim, B. S., & Kang, J. H. (2019). Association between Secondhand Smoke Exposure and Hypertension in 106,268 Korean Self-Reported Never-Smokers Verified by Cotinine. *J Clin Med, 8*(8). doi:10.3390/jcm8081238

Kritz, H., Schmid, P., & Sinzinger, H. (1995). Passive smoking and cardiovascular risk. *Arch Intern Med, 155*(18), 1942-1948. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/7575047

Law, M. R., & Wald, N. J. (2003). Environmental tobacco smoke and ischemic heart disease. *Prog Cardiovasc Dis, 46*(1), 31-38. doi:10.1016/s0033-0620(03)00078-1

Leon, B. M., & Maddox, T. M. (2015). Diabetes and cardiovascular disease: Epidemiology, biological mechanisms, treatment recommendations and future research. *World J Diabetes, 6*(13), 1246-1258. doi:10.4239/wjd.v6.i13.1246

Li, N., Li, Z., Chen, S., Yang, N., Ren, A., & Ye, R. (2015). Effects of passive smoking on hypertension in rural Chinese nonsmoking women. *J Hypertens, 33*(11), 2210-2214. doi:10.1097/HJH.0000000000000694

Mahmud, A., & Feely, J. (2004). Effects of passive smoking on blood pressure and aortic pressure waveform in healthy young adults--influence of gender. *Br J Clin Pharmacol, 57*(1), 37-43. doi:10.1046/j.1365-2125.2003.01958.x

Max, W., Sung, H. Y., & Shi, Y. (2012). Deaths from secondhand smoke exposure in the United States: economic implications. *Am J Public Health, 102*(11), 2173-2180. doi:10.2105/AJPH.2012.300805

Moffatt, R. J., Chelland, S. A., Pecott, D. L., & Stamford, B. A. (2004). Acute exposure to environmental tobacco smoke reduces HDL-C and HDL2-C. *Prev Med, 38*(5), 637-641. doi:10.1016/j.ypmed.2003.12.002

National Heart Lung and Blood Institute. (n.d.). Angina. Retrieved from https://www.nhlbi.nih.gov/health-topics/angina

Otsuka, R., Watanabe, H., Hirata, K., Tokai, K., Muro, T., Yoshiyama, M., . . . Yoshikawa, J. (2001). Acute effects of passive smoking on the coronary circulation in healthy young adults. *JAMA, 286*(4), 436-441. doi:10.1001/jama.286.4.436

Pan, B., Jin, X., Jun, L., Qiu, S., Zheng, Q., & Pan, M. (2019). The relationship between smoking and stroke: A meta-analysis. *Medicine (Baltimore), 98*(12), e14872. doi:10.1097/MD.0000000000014872

Park, Y. S., Lee, C. H., Kim, Y. I., Ahn, C. M., Kim, J. O., Park, J. H., . . . Yoo, K. H. (2018). Association between secondhand smoke exposure and hypertension in never smokers: a cross-sectional survey using data from Korean National Health and Nutritional Examination Survey V, 2010-2012. *BMJ Open, 8*(5), e021217. doi:10.1136/bmjopen-2017-021217

Psotka, M. A., Rushakoff, J., Glantz, S. A., De Marco, T., & Fleischmann, K. E. (2020). The Association Between Secondhand Smoke Exposure and Survival for Patients With Heart Failure. *J Card Fail*. doi:10.1016/j.cardfail.2019.12.008

Saxena, K., Liang, Q., Muhammad-Kah, R., & Sarkar, M. (2017). Evaluating the relationship between biomarkers of potential harm and biomarkers of tobacco exposure among current, past, and nonsmokers: data from the National Health and Nutrition Examination Survey 2007-2012. *Biomarkers, 22*(5), 403-412. doi:10.1080/1354750X.2016.1201536

Schick, S., & Glantz, S. (2005). Philip Morris toxicological experiments with fresh sidestream smoke: more toxic than mainstream smoke. *Tob Control, 14*(6), 396-404. doi:10.1136/tc.2005.011288

Tsai, J., Homa, D. M., Gentzke, A. S., Mahoney, M., Sharapova, S. R., Sosnoff, C. S., . . . Trivers, K. F. (2018). Exposure to Secondhand Smoke Among Nonsmokers - United States, 1988-2014. *MMWR Morb Mortal Wkly Rep, 67*(48), 1342-1346. doi:10.15585/mmwr.mm6748a3

U.S. Department of Health and Human Services. (2014). *The health consequences of smoking--50 years of progress: A report of the Surgeon General*. Retrieved from Rockville, MD: https://www.cdc.gov/tobacco/data_statistics/sgr/50th-anniversary/index.htm

Valkonen, M., & Kuusi, T. (1998). Passive smoking induces atherogenic changes in low-density lipoprotein. *Circulation, 97*(20), 2012-2016. doi:10.1161/01.cir.97.20.2012

Venn, A., & Britton, J. (2007). Exposure to secondhand smoke and biomarkers of cardiovascular disease risk in never-smoking adults. *Circulation, 115*(8), 990-995. doi:10.1161/CIRCULATIONAHA.106.648469

Wilkinson, J. D., Lee, D. J., & Arheart, K. L. (2007). Secondhand smoke exposure and C-reactive protein levels in youth. *Nicotine Tob Res, 9*(2), 305-307. doi:10.1080/14622200601080299

Wilson, T., Shamo, F., Boynton, K., & Kiley, J. (2012). The impact of Michigan's Dr Ron Davis smoke-free air law on levels of cotinine, tobacco-specific lung carcinogen and severity of self-reported respiratory symptoms among non-smoking bar employees. *Tob Control, 21*(6), 593-595. doi:10.1136/tobaccocontrol-2011-050328

World Health Organization. (n.d.). Global Health Observatory (GHO) data: Second-hand smoke. Retrieved from https://www.who.int/gho/phe/secondhand_smoke/en/

Yang, Y., Liu, F., Wang, L., Li, Q., Wang, X., Chen, J. C., . . . Ma, X. (2017). Association of Husband Smoking With Wife's Hypertension Status in Over 5 Million Chinese Females Aged 20 to 49 Years. *J Am Heart Assoc, 6*(3). doi:10.1161/JAHA.116.004924

Yuan, H., Wong, L. S., Bhattacharya, M., Ma, C., Zafarani, M., Yao, M., . . . Martins-Green, M. (2007). The effects of second-hand smoke on biological processes important in atherogenesis. *BMC Cardiovasc Disord, 7*, 1. doi:10.1186/1471-2261-7-1