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Identifying Risk Factors Associated With Cardiovascular Disease Risk In Lesbians

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IDENTIFYING RISK FACTORS ASSOCIATED WITH CARDIOVASCULAR DISEASE RISK IN LESBIANS

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IDENTIFYING RISK FACTORS ASSOCIATED WITH CARDIOVASCULAR DISEASE RISK IN LESBIANS

by

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IDENTIFYING RISK FACTORS ASSOCIATED WITH CARDIOVASCULAR DISEASE RISK IN LESBIANS

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Cardiovascular disease (CVD) is the leading cause of female deaths in the United States (1). While women, in general, are at risk for CVD, current research indicates that sexual minority women (i.e. lesbians and bisexual women [SMW]) may be at greater risk for CVD than heterosexual women. This heightened risk potentially stems from an increased prevalence of traditional CVD risk factors in SMW, creating health disparities between SMW and their heterosexual counterparts (2). Further research into this high-risk population is needed, in order to minimize these disparities.

The purpose of this study was to establish differences in the prevalence of modifiable CVD risk factors among lesbians and heterosexual women and compare their risks for coronary heart disease. This study also sought to identify best practices for obtaining higher rates of sexual orientation (SO) disclosure in questionnaire settings.

Data collected through the Houston HeartReach Registry from 2013-2017 was used for the creation of a lesbian cohort. A cohort of heterosexual women was aggregated from the 2015-2016 National Health and Nutrition Examination Surveys. Both cohorts contained

information on sociodemographic data and traditional CVD risk factors. A 10-year risk score for developing coronary heart disease was calculated for all women and compared by SO. Differences in the prevalence of traditional cardiovascular disease risk factors were also examined by SO. Lesbians were more likely to be current or ever smokers, to be depressed or have hypertension, to have an education level past high school, and to earn less income than their heterosexual counterparts. On average, lesbian participants had a 0.60% (95% confidence interval [CI] = -0.25%, 1.44%) greater chance of developing coronary heart disease over the next ten years than their heterosexual counterparts, but this difference was not significant ($p = 0.167$). Neither income, glucose, family history of cardiovascular disease, or depression accounted for this difference, but education and body mass index (BMI) partially intensified this difference.

Lesbians have an increased prevalence of various CVD risk factors compared to their heterosexual counterparts, but future research is needed to fully understand the causes of these increased risk factors and their effect on CVD risk. With lesbians comprising a uniquely high-risk subgroup for CVD, attention must be paid to their CVD risk profile. The identification of CVD risk factors unique to and/or heightened in lesbians will allow for more targeted interventions that can lead to a reduction in disparities of CVD risk for lesbians and reduce the morbidity of CVD in women overall. A literature review of PubMed, conducted as a part of this thesis, indicates that future epidemiologic studies working with SMW should create an LGBT-welcoming environment, use accepting and inclusive language, and demonstrate a knowledge of lesbian-specific health at recruiting events and in questionnaires, in order to facilitate SO disclosure and increase the likelihood of successful recruitment.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

BACKGROUND

Literature Review

In the United States, there are currently more than 12 million American adults identifying as lesbian, gay, bisexual, or transgender (LGBT), of which nearly 4 million are estimated to be lesbians (3,4). Individuals belonging to this population tend to experience unique stressors that may stem from facing a hostile and stressful social environment as a result of their sexual identity (2). This added stress, coined 'minority stress' by Meyer in 2003, has been associated with negative coping behaviors such as smoking, excessive alcohol use, and drug use, as well as increased risk of mental disorders, all of which are important risk factors for many adverse health conditions (2). Due to this increased prevalence of risk factors, the LGBT community comprises a high-risk subgroup for both mental health issues and chronic conditions, creating health disparities between the LGBT population and their heterosexual counterparts. In order to try and minimize these disparities, further research into sexual minority populations (i.e., LGBT individuals) is needed.

With the inclusion of sexual orientation questions in large-scale surveys in recent years, opportunities for research concerning sexual minorities are growing. However, capturing sexual orientation can be difficult, as there is currently no normed method for doing so, and various barriers can prevent a sexual minority individual from disclosing their sexual orientation (5-21). These impediments lead to most studies focusing on sexual minorities having small sample sizes and limited statistical power. In order to be able to perform more effective research regarding health disparities between sexual minorities and heterosexual people, future data collection practices must employ best practices in the design

of recruiting events and the creation and administration of effective questionnaires that will facilitate sexual orientation disclosure to gather reliable sexual orientation information with a high response rate. The identification of modifiable factors (i.e., facilitators) that improve disclosure can help to strengthen research in sexual minority populations.

Currently, there is a paucity of research focused on sexual minorities. From 1989–2011, the National Institutes of Health (NIH) funded 628 studies concerning LGBT health, making up 0.1% of all NIH-funded studies in the same timeframe, when excluding HIV/AIDS and other sexual matters as the topic of research (22). Of the NIH-funded research involving sexual minorities, the majority focused on sexually transmitted infections (79.1%), substance abuse (43.8%), and mental health disorders (23.2%), with little research dedicated to chronic, non-infectious diseases, such as cardiovascular disease (CVD) (22). Because most studies had more than one focus, the percentages above add up to more than 100%.

Claiming approximately 1 of every 3 deaths in the United States, CVD is the leading cause of mortality in the United States (1,23). While much research has been devoted to CVD, few CVD studies focus on sexual minorities as their study population. As a result of minority stress, sexual minorities are more likely to have an increased prevalence of traditional CVD risk factors, such as smoking, diabetes, obesity, depression, hypertension, alcohol consumption, and drug use (24-27). This increased prevalence of risk factors places sexual minorities at higher risk for CVD than their heterosexual counterparts. Studies have found sexual minorities to have a higher risk of being overweight or obese, with one study finding lesbians to have more than twice the odds of overweight (odds ratio [OR] = 2.69; CI

1.40, 5.18) and obesity (OR = 2.47; CI 1.19, 5.09) as heterosexual women (28). A Swedish national population-based study found sexual minorities to have a significantly elevated risk of high-risk alcohol consumption (adjusted odds ratio [AOR] = 1.33; CI 1.11, 1.58), drug use (AOR = 1.91; CI 1.37, 2.66), and daily tobacco smoking (AOR = 1.72; CI 1.39, 2.12), when compared to their heterosexual counterparts (29). A cross-sectional study published this year examined cardiovascular health disparities for sexual minorities, using self-reported CVD outcomes and sexual orientation and identified a 50% increased prevalence of CVD for LGB individuals as compared to heterosexuals, mediated, in part, by increased mental health problems (30). Because of the increased prevalence of CVD risk factors in sexual minorities, disparities in CVD exist for this population.

Disparities seen in CVD risk between sexual minorities and their heterosexual counterparts are further compounded by gender differences. While men and women are known to share many of the traditional risk factors for CVD, women have been found to have additional, or heightened, risk factors due to their sex (31-33). Certain female-specific risk factors, such as menopause and pregnancy complications (e.g. preeclampsia and gestational diabetes), are associated with an increased incidence of CVD (33). Furthermore, there are also various CVD risk factors, including smoking and diabetes, that have been found to be more strongly associated with CVD risk in women than in men (31,32). A recent study showed that women who smoke had a 50% higher risk for coronary heart disease (CHD) than male smokers, and diabetic women were at 44% greater CHD risk than diabetic men (31). Drawing from the aforementioned Swedish national population-based study, while both sexual-minority women (i.e. lesbians and bisexual women [SMW]) and sexual-minority men

(i.e. gay and bisexual men [SMM]) were at increased risk of high-risk alcohol consumption and drug use over their heterosexual counterparts, the risks in SMW were nearly five times that of SMM (29). Bearing in mind these gender differences, there is reason to believe that CVD disparities exist even within sexual minorities, with SMW comprising a higher-risk subgroup than SMM. Furthermore, some studies have found that individuals who identify as non-heterosexual (i.e. lesbians and gay men) have greater prevalence for various CVD risk factors than bisexual individuals (2,34). This was demonstrated in a population-based study of CVD risk in SMW, where a marked increase in CVD risk was noted when the definition of SMW was narrowed down from lesbians and bisexual women to only lesbians (34), as well as in another population-based study where lesbian women were found to have a higher prevalence of both overweight and obesity than bisexual or heterosexual women (28). Logically, it follows that lesbians may comprise a uniquely high-risk subgroup of the population at risk for developing CVD.

Public Health Significance

Because of the significant morbidity and mortality associated with CVD, leading government and health care organizations have urged for more CVD research (35). However, despite the vast amount of CVD research that has taken place in previous years, gaps remain in risk-assessment and prevention strategies specific to women, especially SMW. Of the 628 NIH-funded studies from 1989-2011 concerning sexual minorities, 92.9% used sexual-minority men or transgender individuals as their study population, with little research focusing on SMW (22). To the best of my knowledge, only one study has been conducted

regarding CVD risk specifically in lesbians, focusing on waist-to-hip ratio (WHR) as the main risk factor and having fewer than 650 women in the study (24). The purpose of the current study was to establish differences in the prevalence of modifiable CVD risk factors among lesbians and heterosexual women and to compare their risks for predicted 10-year CHD risk, so that future prevention strategies can better target the SMW high-risk population. Implementation of more specific interventions to reduce lesbians' CVD risk will address disparities in CVD for the millions of women belonging to this population and lead to a reduction in their overall CVD morbidity. This study also sought to establish best practices for obtaining higher rates of sexual orientation disclosure, in order to increase the likelihood of successful recruitment for future epidemiologic studies of SMW.

Hypothesis, Research Question, and Specific Aims

Claiming almost as many women's lives as cancer, chronic lower respiratory disease, and diabetes combined, CVD is the biggest killer of women in the United States (23). While CVD is highly prevalent in both sexes, gender differences in CVD risk factors place women at greater risk for CVD than men (31-33). Within the female gender, the prevalence of several CVD risk factors is higher among SMW than heterosexual women. Studies have found SMW more likely to smoke, be overweight or obese, and have increased rates of alcohol consumption and drug use as compared to heterosexual women (29,31,32). The increased prevalence of CVD risk factors in SMW creates a high-risk subgroup of women. Furthermore, because lesbians tend to experience increased and unique types of stress that

affect CVD risk factors when compared to bisexual women, lesbians form a particularly high-risk subgroup (2).

Currently, the majority of the literature regarding sexual minorities and CVD risk focuses on HIV-infected individuals and transgender persons utilizing sex hormones. Of the few studies that have examined CVD prevalence in SMW, to my knowledge, only one has been specific to lesbians alone. The dearth of research on this high-risk group of lesbian women has left a gap in knowledge, impeding our ability to effectively address CVD health disparities among women. The central hypothesis guiding this research was that lesbians would have different frequencies of the following CVD risk factors: smoking, diabetes, obesity, depression, hypertension, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and total cholesterol levels, systolic blood pressure, and family history of CVD when compared to their heterosexual counterparts, placing them at increased risk for CVD.

The setting for the lesbian cohort in this study is the Texas Heart Institute (THI) Center for Women's Heart & Vascular Health. The Center for Women's Heart & Vascular Health offers Houston HeartReach programs through local community centers, employer health fairs, and doctor offices that provide individuals free opportunities to learn more about their health. Participants volunteer their information from health screenings, detailed past medical history, and physical examination data to a community-wide registry research study that aims to make improvements in heart disease prevention, diagnosis, and treatment for all women. The cohort of heterosexual women was created using a subset of the 2015-2016 National Health and Nutrition Examination Survey (NHANES), a survey research program conducted by the National Center for Health Statistics designed to assess the health and

nutritional status of adults and children in the United States through a combination of interviews, physical examinations, and laboratory tests (36). With over 100 participants identifying as lesbians and hundreds of heterosexual women included, estimates of the prevalence of various CVD risk factors within these populations could be compared and explored.

Specific Aim 1: Establish and compare the prevalence of CVD risk factors between lesbians and heterosexual women and compute and compare their risk for CHD

As previous research suggests that the burden of CVD risk factors may be higher in sexual minority women, this study evaluated the role of sexual orientation (specifically lesbianism) on the prevalence of various CVD risk factors and demographic characteristics in women, as well as their predicted 10-year risk for CHD. Potential confounders were explored in order to further explore the role of these characteristics on CVD risk.

Specific Aim 2: Develop best practices to increase sexual orientation disclosure for use in future health screenings

In order to identify best practices, a literature review was performed to investigate the major facilitators for sexual orientation disclosure by sexual minorities. Suggestions for the implementation of best practices in future data collection focused on easily modifiable practices found in the literature review.

METHODS

Study Design, Population, and Sampling for Specific Aim 1

The THI Center for Women's Heart & Vascular Health (CWHVH) developed the infrastructure necessary to collect and store data from participants who have given written

consent to include their data in the CWHVH database registry (Houston HeartReach Registry WIRB #1172298). The cohort of lesbian women used in this study came from data collected in the Houston HeartReach Registry between June 2013 and September 2017, which yielded 128 lesbian participants aged between 22 and 70 years. Houston HeartReach is a collaborative effort joining the cardiovascular clinical and research expertise of the Texas Heart Institute's CWHVH with the community outreach of Greater Houston area organizations. The primary purpose of the Houston HeartReach Registry is to identify the disparities and trends in heart-health risks across an ethnically and culturally diverse population of women, including women who are medically underserved and/or women who lack appropriate medical health insurance. In order to be eligible for the Houston HeartReach Registry, the participant must be at least 18 years old, not pregnant, and have been born biologically a woman or gender-identify as a woman. Women from all racial, ethnic, and cultural backgrounds are included, with no restrictions. Recruitment occurs through the CWHVH's Houston HeartReach for Women programs. Potential participants are invited to take part in the study through community events, health fairs, employer events, collaborating physicians' offices, website referrals, online surveys, and/or email communications. Research information is collected during a patient's standard of care visit and/or during a hospital clinic visit at an approved institution and/or in connection with a Houston HeartReach for Women community partnership and/or event. After written informed consent has been obtained, the hospital, clinic, or research personnel collects related information through a surveyor-assisted, one-hour questionnaire fully developed by Dr. Stephanie Coulter of THI. Questionnaires are offered in either English or Spanish.

While most of the lesbian participants in the Houston HeartReach Registry between June 2013 and September 2017 were Non-Hispanic White, the majority of heterosexual participants were Hispanic. In order to create a more comparable heterosexual cohort to be used in this study, publicly available data from the 2015-2016 NHANES was used (36). NHANES is a nationally representative cross-sectional survey aimed at assessing health and nutritional status of U.S. children and adults through a combination of interviews, physical examinations, and laboratory tests used to gather demographic, socioeconomic, dietary, and health-related information on participants (37). Each year, nearly 7,000 residents from across the United States are randomly selected and invited to participate in the annual NHANES, with survey results being continuously added to existing data in order to provide a longitudinal representation of the health of the U.S. population (37). From 2015-2016, 1516 heterosexual women aged 18 to 59 years completed the survey. Heterosexual women were individually matched to lesbian participants on race and age (+/– 5 years), at a 3:1 ratio. Four lesbian participants were excluded from analysis due to their extreme age (65-70 years) not permitting matching, resulting in a final sample of 124 lesbians and 372 heterosexual women for the study.

CVD Risk Factor Collection for the Parent Studies for Specific Aim 1

The Houston HeartReach Registry and NHANES have consistent data collection approaches for the CVD risk factors considered in this thesis. In the Houston HeartReach Registry, the questionnaire covers information concerning the participant's sexual orientation, sociodemographics, age, smoking behaviors, and personal and family medical history with a focus on cardiovascular risk factors and disease (i.e. hypertension, diabetes,

family history of CVD, and mental health). In addition, a trained professional conducts a health screening to gather data on blood pressure, body mass index (BMI), glucose, triglycerides, and HDL, LDL, and total cholesterol. Participants may provide their medical records and relevant health data prior to, during, or after the health screenings. NHANES reports data and makes it publicly available every two years, with the 2015-2016 survey data being the most recent data available. Data files matching the variables included in the Houston HeartReach Registry were pulled from the 2015-2016 NHANES and merged by identification number for the creation of the heterosexual cohort.

Study Definitions for Specific Aim 1

Sexual orientation was measured for all heterosexual participants (i.e. NHANES cohort) through the question, "Do you think of yourself as… lesbian or gay; straight, that is, not lesbian or gay; bisexual; something else; or you don't know the answer?" For lesbian participants (i.e. Houston HeartReach Registry), sexual orientation was measured through participants' selection of "Heterosexual/Straight, Lesbian, Gay (male), Gay (female), Bisexual, Something Else, or Prefer not to answer" for Sexual Orientation. Heterosexual participants were classified as ever smokers if they answered "Yes" to the question "Have you smoked at least 100 cigarettes in your life?" while lesbian participants were classified as ever smokers if they answered "Yes" to the question "Did you smoke in the past?" Heterosexual participants were classified as current smokers if they answered "Yes" to the question "Do you now smoke cigarettes?", while lesbian participants were classified as current smokers if they answered "Yes" to the question "Do you currently smoke on a daily

basis (even socially)?" Heterosexual participants were considered diabetic if they answered "Yes" to the question "Other than during pregnancy, have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes?", while lesbian participants were classified as diabetic if they answered "Yes" to the question "Do you have or have you ever had diabetes?" Heterosexual participants were considered to have a family history of cardiovascular disease if they answered "Yes" to the question "Ever had a close biological relative told they had a heart attack before age 50?", while lesbian participants were considered to have a family history of cardiovascular disease if they answered "Yes" to the question "Do you have a family history of coronary artery disease or peripheral vascular disease?" Both lesbian and heterosexual participants were classified as depressed if they answered "More than half the days" or "Nearly every day" to both "Over the last two weeks, how often have you been bothered by the following problems: little interest or pleasure in doing things?" and "Over the last two weeks, how often have you been bothered by the following problems: feeling down, depressed, or hopeless?"

For both lesbians and heterosexual participants, HDL and total cholesterol were measured in milligrams per deciliter (mg/dL) and blood pressure was measured in millimeters of mercury (mmHg). NHANES implemented enzymatic assays for the measurement of HDL and total cholesterol. Both the Houston HeartReach Registry and NHANES used the average of three consecutive blood pressure readings after five minutes of resting quietly in a seated position for blood pressure measurement. All participants had their BMI measured in kilograms per meters squared (kg/m^2), which was then classified into four groups, based on the World Health Organization's categories: underweight (BMI < 18.5),

normal weight (BMI 18.5 – 24.9), overweight (BMI 25.0 – 29.9), or obese (BMI ≥ 30). Both lesbian and heterosexual respondents were considered hypertensive if they met any of the following criteria: 1) measured systolic blood pressure exceeding 140 mmHg and/or diastolic blood pressure exceeding 90 mmHg or 2) measured diastolic or systolic blood pressure not exceeding the respective threshold but the respondent reports previous and/or current use of blood pressure medication. While the heterosexual cohort had complete data for LDL cholesterol values, lesbian participants were missing data on LDL cholesterol. LDL cholesterol was measured in mg/dL for heterosexual participants and imputed in mg/dL for lesbian participants using the Friedewald formula (i.e. LDL = total cholesterol – (triglycerides/5) – HDL). In order to test the accuracy of the Friedewald formula, predicted LDL cholesterol values were computed for heterosexual participants in this study and compared to their recorded LDL cholesterol. All predicted values were within 0.4 mg/dL of recorded values.

In addition to the main CVD risk factors considered, the study also assessed participants' age, education, annual household income, and race/ethnicity. For consistency in the categorization of education level between lesbian and heterosexual participants, education was recoded into four categories: less than high school, high school graduate, some college or Associate's degree, or college graduate or more. Similarly, for both cohorts, race/ethnicity was coded as non-Hispanic White, non-Hispanic Black, Hispanic, and Other Race (including multiracial). For annual household income, both cohorts recoded annual household income into five categories: less than $24 999, $25 000 to $34 999, $35 000 to $49 999, $50 000 to $75 000, and $75 000 or more.

CVD risk was assessed by using a 10-year CHD risk score. The 10-year CHD risk score is a sex-specific, multivariable, risk factor algorithm that uses various traditional cardiovascular risk factors to predict the chance of developing CHD over 10 years (37). The 10-year CHD risk score of an individual is calculated based on six different CVD risk factors and uses either total cholesterol or LDL cholesterol point allocations. Because LDL cholesterol values were imputed for lesbians but not for heterosexuals, 10-year CHD risk scores for this study were built using total cholesterol point values. When calculating a participant's CHD risk score, the participant's age, total cholesterol, HDL cholesterol, blood pressure, diabetes status, and smoking status are all assigned a total cholesterol point value. For age, total cholesterol, and HDL cholesterol, there is a direct relationship between the CVD risk factor and the total cholesterol point value assigned (i.e. the greater the value for the CVD risk factor, the greater the amount of total cholesterol points given). For blood pressure, diastolic and systolic blood pressure are assessed simultaneously, with higher values of either blood pressure reading being associated with a higher total cholesterol point value. Both diabetes and smoker status result in a higher total cholesterol point value versus non-diabetic and non-smoker status. Once all total cholesterol point values have been allocated for each CVD risk factor, the sum of the six values is taken to create a final point total. The final point total is then looked up in a CHD risk table (see Appendix B) and matched with a predicted 10-year CHD risk.

Data Analysis for Specific Aim 1

Data was analyzed using STATA version 15.1, without weights incorporated for the NHANES cohort, in order to maintain crude, unadjusted mean and percentage values such as

those found in the Houston HeartReach Registry dataset. Demographic characteristics and CVD risk factors were compared by sexual minority status at a significance level of $\alpha = 0.05$ by using χ^2 tests for categorical variables and Mann-Whitney tests for continuous variables.

Linear regression was used to examine whether 10-year CHD risk varied by sexual orientation status. A multivariable linear regression model was used to adjust for differences in demographic characteristics and other covariates that were not included in the calculation of the 10-year CHD risk score. Hypertension was not considered for possible adjustment, due to being highly correlated with blood pressure, which was used in the 10-year CHD risk score calculation. Variables found to demonstrate a statistically significant difference in prevalence by sexual orientation at the $\alpha = 0.10$ level were considered potential confounders for inclusion in the multivariable linear regression model. For each potential confounder, separate linear regression models were run to assess their impact on the parameter estimate for the effect of sexual orientation status on 10-year CHD risk. Rather than using a significance level as the criterion for determining which potential confounders to retain as covariates for the final model, a 10% change in the parameter estimate for sexual orientation status was used. This method for model creation was employed in a similar study published in the American Journal of Public Health in 2013 (34).

Study Power for Specific Aim 1

Because of the limited sample size of lesbian participants, stratified analysis by sexual orientation and demographic characteristics and/or other covariates was not possible (e.g. low-income lesbians vs. low-income heterosexual women), due to insufficient power.

Human Subjects

The UTHealth institutional review board reviewed this study and determined that it did not meet the criteria of human participant research. Data were kept on a secure server, with no paper material being used. All data was de-identified before receipt and destroyed at the completion of the project. This project has UTHealth IRB approval (HSC-SPH-18-0702).

Study Design, Population, and Sampling for Specific Aim 2

An in-depth review of the literature available on PubMed concerning sexual orientation disclosure was performed in order to determine best practices for gathering sexual orientation data. Only articles published after 2000 with samples including at least some lesbian or bisexual women were considered for review. For each article, facilitators for sexual orientation disclosure were identified. Final suggestions for best practices focused on factors that can be easily modified and implemented in a self-administered questionnaire setting.

RESULTS

Specific Aim 1

Table 1 provides a summary of demographic characteristics by sexual orientation status. Due to matching, lesbians and heterosexual women were similar with regard to age and race, but differed in regard to education ($p = 0.002$) and income levels ($p < 0.001$). Lesbians were more likely to have higher than a high school education (82% vs. 69.9%) and were more likely to earn less than their heterosexual counterparts.

Table 1: Demographic Characteristics of Lesbian and Heterosexual Cohorts

	Lesbians (n = 124), n (%) or Mean (SE)	Heterosexual Women (n = 372), n (%) or Mean (SE)	*P*
Age (years)	42.32 (10.8)	42.35 (10.6)	0.915
Race			1.000
Non-Hispanic White	60 (48.4)	180 (48.4)	
Non-Hispanic Black	32 (25.8)	96 (25.8)	
Hispanic	22 (17.7)	66 (17.7)	
Other[1]	10 (8.1)	30 (8.1)	
Education			0.002
< High School	4 (3.1)	41 (11.0)	
High School	19 (14.8)	71 (19.1)	
Some College	66 (53.9)	134 (36.0)	
≥ College Graduate	35 (28.1)	126 (33.9)	
Income			< 0.001
< 25 000	64 (51.6)	105 (28.2)	
25 000 – 34 999	17 (13.7)	27 (7.3)	
35 000 – 49 999	16 (12.9)	35 (9.4)	
50 000 – 75 000	7 (5.7)	102 (27.4)	
> 75 000	7 (5.7)	92 (24.7)	
Missing	13 (10.4)	11 (3.0)	

[1]Including multiracial

Table 2 provides a summary of CVD risk factors by sexual orientation status. Lesbians were more likely to be current smokers (35.5% vs. 21.7%) or ever smokers (55.3% vs. 39.9%), were more likely to have a greater BMI (31.7 kg/m^2 vs. 30.1 kg/m^2) and be overweight or obese (77.5% vs. 68.9%), were more likely to be depressed (17.7% vs. 8.3%), and were more likely to have hypertension (9.7% vs. 2.4%). Heterosexual women were more likely to have diabetes (10.2% vs. 3.2%), were more likely to have a family history of cardiovascular disease (67.7% vs. 36.4%), and were more likely to have higher total cholesterol (193.8 mg/dL vs. 186.0 mg/dL) and HDL cholesterol (58.9 mg/dL vs. 53.8 mg/dL). There were no statistically significant differences by sexual orientation for LDL cholesterol, systolic blood pressure, glucose, or triglycerides.

Table 2: Cardiovascular Disease Risk Factors of Lesbian and Heterosexual Cohorts

	Lesbians (n = 124), n (%) or Mean (SE)	Heterosexual Women (n = 372), n (%) or Mean (SE)	*P*
CHD[1] Risk (%)	4.08 (4.70)	3.55 (3.85)	0.322
Total Cholesterol, mg/dL	186.0 (41.1)	193.8 (40.2)	0.032
HDL[2] Cholesterol, mg/dL	53.8 (15.7)	58.9 (17.3)	0.006
LDL[3] Cholesterol, mg/dL	107.8 (37.0)	108.2 (34.8)	0.970
Systolic Blood Pressure, mmHg	119.6 (16.2)	119.3 (15.4)	0.999
Body Mass Index, kg/m^2	31.7 (8.3)	30.1 (8.3)	0.026
Glucose	92.4 (27.7)	98.8 (40.9)	0.088
Triglycerides	122.6 (78.4)	133.9 (90.9)	0.323
Current Smoker			0.005
Yes	44 (35.5)	80 (21.7)	
No	80 (64.5)	289 (78.3)	
Ever Smoker			0.003
Yes	68 (55.3)	148 (39.9)	
No	55 (44.7)	223 (60.1)	
Diabetes			0.015
Yes	4 (3.2)	38 (10.2)	
No	120 (96.8)	334 (89.8)	
BMI[4] Categories			0.028
Underweight (<18.5)	2 (1.6)	5 (1.3)	
Normal (18.5 – 24.9)	26 (21.0)	111 (29.8)	
Overweight (25-29.9)	25 (20.2)	100 (27.0)	
Obese (≥30)	71 (57.3)	156 (41.9)	
Family History of CVD[5]			<0.001
Yes	44 (36.4)	252 (67.7)	
No	77 (63.6)	120 (32.3)	
Depression			<0.001
Yes	22 (17.7)	31 (8.3)	
No	102 (82.3)	341 (91.7)	
Hypertension			0.001
Yes	12 (9.7)	9 (2.4)	
No	112 (90.3)	363 (97.6)	

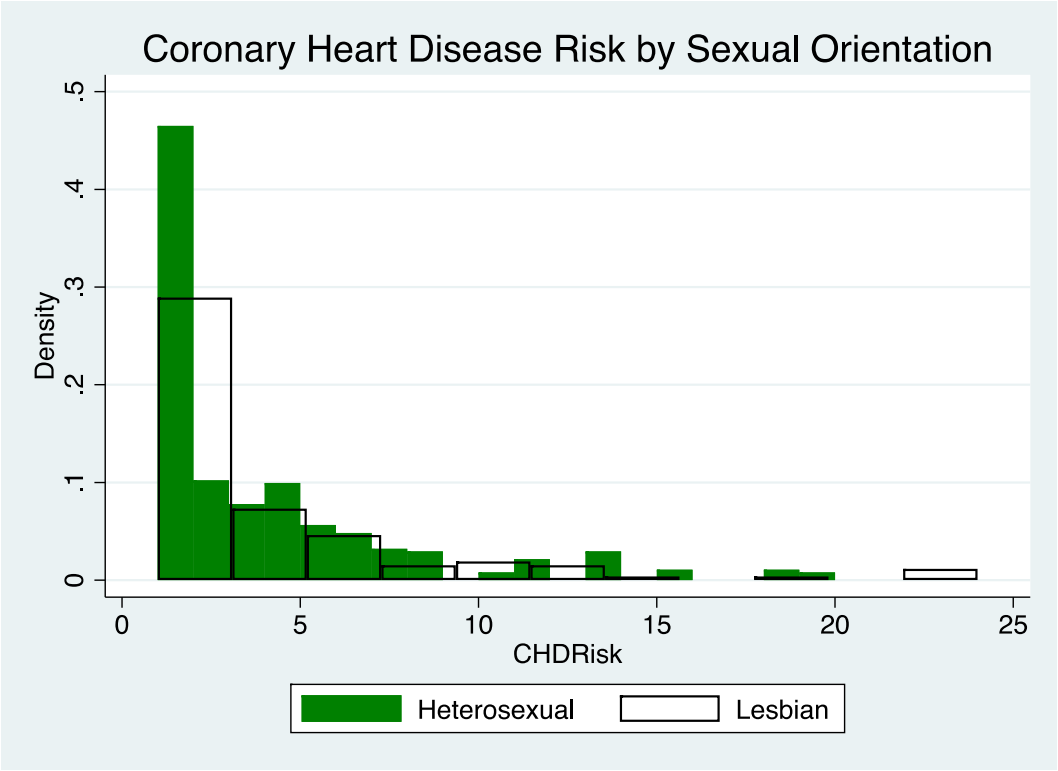
[1]Coronary Heart Disease; [2]High-Density Lipoprotein; [3]Low-Density Lipoprotein; [4]Body Mass Index; [5]Cardiovascular Disease

Figure 1 shows the distribution of predicted 10-year CHD risk by sexual orientation.

The average predicted 10-year CHD risk was higher for lesbians than heterosexual women

(4.08% vs. 3.55%), but the difference was not found to be statistically significant (p-value = 0.322). Nevertheless, model building for an adjusted model was still performed. Seven variables met the criteria to be potential confounders: education, income, glucose, BMI, BMI categories, family history of CVD disease, and depression all showed a statistically significant difference in prevalence by sexual orientation at the α = 0.10 level. To avoid multicollinearity between BMI and the categorical version of BMI, the categorical version of BMI was dropped, as it was more highly correlated with the variables used for the 10-year CHD risk calculation. The six remaining potential confounders were tested for multicollinearity with the variables used for the 10-year CHD risk calculation and the other potential confounders, and no multicollinearity issues were identified. Linear regression analysis was performed with each potential confounder, to assess the impact of its inclusion on the parameter estimate for the effect of sexual orientation status on 10-year CHD risk. Of the six potential confounders, only education (p = 0.018) and BMI (p < 0.001) produced more than a 10% change in the parameter estimate for sexual orientation status. A final linear regression model adjusted for education ($\beta_{educ} = -0.40$; CI -0.79, -0.15; p = 0.042) and BMI ($\beta_{BMI} = 0.08$; CI 0.04, 0.12; p < 0.001) was created to model the effect of sexual orientation status on predicted 10-year CHD risk. After adjustment for the potential confounders, the effect of sexual orientation status on predicted 10-year CHD risk increased by 15.38% from 0.52% to 0.60%, but failed to achieve statistical significance (p = 0.167).

Figure 1: Coronary Heart Disease Risk by Sexual Orientation



Histograms were created comparing predicted 10-year CHD risk by hypertension, education, depression, ever smoker and current smoker status, race, diabetes, BMI categories, and income, independently (see Appendix A). Under the adjusted model for predicted 10-year CHD risk, an obese lesbian with less than a high school education (i.e. high-risk) would have a 2.6% chance of developing CHD over the next years, while a lesbian with normal weight and a college degree or higher (i.e. low-risk) would have a 10-year CHD risk of 0.48%. For heterosexual women, a high-risk profile would result in a 10-year CHD risk of 2% and a low-risk profile would produce a 10-year CHD risk of 0% (raw value of -0.12%).

Specific Aim 2

A total of 17 papers from PubMed were included in the literature review, with four having sexual minority women as their study population and five focused on lesbians alone. Over half of the papers included used a mostly White or all White study population, and only three used an ethnically diverse study population. Summary characteristics were ascertained for each article in the literature review and are displayed in Table 3.

Table 3: Characteristics of Studies Included in Literature Review

Authors (Year) [Ref]	**Study Population**	**Sample Characteristics**	**Sample Size**
Barbara AM, Quandt SA, Anderson RT (2001) [5]	Lesbian women	Age range 24-65 Mostly White[1]	32
Bjorkman M, Malterud K (2007) [6]	Lesbian women	Age range 20-71 Mostly White[1]	47
Mitchell M, Howarth C, Kotecha M, et al (2008) [7]	Lesbian, gay, and bisexual men and women	Research review	N/a
Bjorkman M, Malterud K (2009) [8]	Lesbian women	Age range 18-60+ Mostly White[1]	121
Almazan E, Conron K, Ayala G, et al (2009) [9]	Lesbian, gay, and bisexual men and women	Research review	N/a
Lindley LL, Walsemann KM, Carter JW (2012) [10]	Men and women of any sexual orientation	Age range 24-32 Mostly White[1]	14,412
Kim H, Fredriksen-Goldsen KI (2013) [11]	Men and women of any sexual orientation	Age range 18+ Ethnically diverse[2]	161,600
Durso LE, Meyer IH (2013) [12]	Lesbian, gay, and bisexual men and women	Age range 18-59 Ethnically diverse[2]	396
Johnson MJ, Nemeth LS (2014) [13]	Lesbian and bisexual women	Age range 18-24 Mostly White[1]	9
Badgett MV, Baker K, Conron K (2014) [14]	Lesbian, gay, and bisexual men and women	Research review	N/a
Marques AM, Noguieira C, de Oliveira JM (2015) [15]	Lesbian women	Age range 21-63 Portuguese	30

Authors (Year) [Ref]	Study Population	Sample Characteristics	Sample Size
Mattocks KM, Sullivan JC, Bertrand C, et al (2015) [16]	Lesbian women	Age range 41-50 Ethnically diverse[2] Military veterans	20
Munson S, Cook C (2016) [17]	Lesbian and bisexual women	Age range 23-47 Mostly White[1]	6
Roller GG, Sedlak CA, Draucker CB, et al (2016) [18]	Lesbian and bisexual women	Age range 21-59 All White	13
Eliason MJ, Radix A, McElroy JA, et al (2016) [19]	Lesbian and bisexual women	Age range 40-84 Mostly White[1] Overweight	376
Hadland SE, Yehia BR, Makadon HJ (2017) [20]	Lesbian, gay, and bisexual men and women	Research review	N/a
Brooks H, Llewellyn CD, Nadarzynski T, et al. (2018) [21]	Lesbian, gay, bisexual, or transgender men and women	Research review	N/a

[1] >50% White/Caucasian; [2]at least two race/ethnicities having similar proportions and no race/ethnicity being over 40% of sample

The different facilitators to sexual orientation disclosure that were identified in the literature review are presented in Table 4, along with a list of their supporting articles. Of the 17 studies included, eleven commented on the participants' belief that an LGBT-welcoming environment served as a facilitator for disclosure of sexual orientation (5-8,12,15-18,20,21). Five studies mentioned the use of accepting and inclusive language as facilitators (5,8,19,20,21), four emphasized the importance of confidentiality and anonymity measures for sexual orientation disclosure (7,14,15,20), and two stated that a knowledge of lesbian-specific health issues can serve as a facilitator for sexual orientation disclosure (8,13). In regards to the way that sexual orientation is asked, three studies found the inclusion of ethnically-diverse terms as response options to serve as a facilitator for sexual orientation disclosure (7,9,11), two studies found that excluding opt-out categories as response options

facilitated disclosure (9,19), two studies proposed that the placement of the sexual orientation question at the end of the standard demographics section serves as a facilitator (9,14), and specifics on what to include in the sentence stem itself had mixed reviews (9,19).

Table 4: Facilitators for Sexual Orientation Disclosure

Facilitator	**References**
LGBT-welcoming environment	5, 6, 7, 8, 12, 15, 16, 17, 18, 20, 21
Accepting and inclusive language	5, 8, 18, 20, 21
Confidentiality and anonymity measures	7, 14, 15, 20
Ethnically-diverse terms in questionnaire	7, 9, 11
Knowledge of lesbian-specific health issues	8, 13
Exclusion of "Other/Prefer not to answer/Not sure"	9, 19
Place sexual orientation question at the end of the standard "Demographics" section	9, 14
Not including "Sexual Orientation" in question stem	9
Include definition of "Sexual Identity" in question stem	19

DISCUSSION

Specific Aim 1

The results of this study suggest that lesbians are at increased risk of certain CVD risk factors when compared with their heterosexual counterparts. On average, lesbian participants had a 0.53% greater chance of developing CHD over the next ten years than their heterosexual counterparts. Neither income, glucose, family history of cardiovascular disease, or depression accounted for this difference, but education and BMI did partially enlarge this difference, with lesbians having a 0.60% greater chance of developing CHD over the next ten years than their heterosexual counterparts, after adjusting for both confounders. Higher levels

of education were associated with decreased 10-year CHD risk ($\beta_{educ} = -0.40$; CI -0.79, -0.15), while increased BMI placed individuals at greater 10-year CHD risk ($\beta_{BMI} = 0.08$; CI 0.04, 0.12). Both findings are consistent with current literature.

In terms of demographics, a novel finding in this study is that lesbians were more likely to be more educated, while also being likelier to have a smaller annual household income than their heterosexual counterparts. These findings differ with recent studies that have compared education and income levels between lesbians and heterosexual women and failed to find statistically significant differences between the two groups (4,31). Because marital and employment status were not considered in this study and income was measured for the entire household, the differences found in this study could be due to more individuals from the heterosexual cohort having their annual household income being supplemented by another individual (i.e. it could be that more spouses of heterosexual women work versus spouses of lesbians).

The increased prevalence of smoking, obesity, depression, and hypertension in lesbians versus heterosexual women in this study is consistent with the literature. However, contrary to other studies of sexual minority women, heterosexual women were found to have an increased prevalence for diabetes when compared to lesbian participants. This was further substantiated by heterosexual women in this study having higher levels of glucose. It is interesting to note that heterosexual women were asked to exclude gestational diabetes when answering if they had ever been diabetic, while lesbian participants were not given such a clarification. The difference in diabetes prevalence could potentially be more pronounced, given the same questioning.

While lesbians having increased rates of hypertension is consistent with previous literature, the fact that this increase occurred in conjunction with lesbians having lower HDL and total cholesterol values, a smaller prevalence for diabetes, and nearly identical SBP values is noteworthy. Because classification of hypertension status included self-report of taking medication for hypertension, it could be that a significant number of the lesbians were classified as hypertensive because they were being medicated for it, controlling their SBP levels.

Strengths of this study are the ability to match on age and race, due to the established link between both risk factors and cardiovascular disease. As for limitations, the current study was limited to an assessment of sexual identity alone, without considering sexual attraction or sexual behavior, which sometimes differ with sexual identity and could lead to differential misclassification (10,15,20). Also, the sample size for the lesbian cohort may have been too small to detect differences of CVD risk factors and 10-year CHD risk score between sexual orientation status. The limited sample size also did not allow for stratification by sexual minority status and age, race, educational level, income, or smoking status because of limited power. The 10-year CHD risk equation used in this study is aimed at predictions for middle-aged, White females and may have over- or underestimated the 10-year CHD risk in the younger women and/or racial/ethnic minorities in the study (40). The implementation of the 10-year CHD risk calculations also limited the ability to test for the effects of smoking, diabetes, and hypertension as potential confounders. In addition, heterosexual and lesbian women might differ on CVD risks not measured in the 10-year CHD risk calculation. A big limitation is the fact that the two cohorts underwent different questionnaires and

examinations for data collection. Future research should employ a heterosexual cohort collected through the Houston HeartReach program, in order to increase comparability between the two groups. This would also address the issue that the NHANES cohort was limited to crude, unadjusted values, in order to maintain more comparability with the Houston HeartReach Registry, which could result in biased estimates and overstating significance levels.

Specific Aim 2

In order to increase the sample size of the lesbian cohort for future research, facilitators for sexual orientation disclosure identified by the literature review should be implemented. These implementations call for changes to how the recruiting events are run, as well as for modifications to the survey instrument.

For recruiting events, creating an LGBT-welcoming environment, the use of accepting and inclusive language, and demonstrating a knowledge of lesbian-specific health issues are the main facilitators to focus on. Ensuring the latter two facilitators would simultaneously work towards creating an LGBT-welcoming environment. To address all three facilitators, some potential changes moving forward could be the presence of pamphlets and literature specific to sexual minority health at recruiting events along with proper training for all personnel on how to avoid heteronormative assumptions and language when interacting with participants.

The majority of the facilitators for sexual orientation disclosure would be implemented in the survey instrument. For many sexual minorities, the main deterrent for

disclosure is a fear that confidentiality and anonymity will not be guaranteed (5,8,18,20,21). Future survey versions can benefit from briefly reiterating that any and all data collected would remain confidential and anonymous, immediately before sexual orientation questions. Best practice would be to place sexual orientation questions at the end of the standard demographics section of the survey (9,14), and to ensure that said section is not be located on the front page of the survey, so as to grant the participant more privacy.

The final facilitators considered were specific to the sexual orientation question itself. Studies found that traditional answer options for sexual orientation (i.e. "Heterosexual", "Lesbian", "Gay", "Bisexual") were geared towards White participants, with participants from other ethnicities potentially selecting "Other," "Prefer not to answer," or "Not sure" due to not understanding the options (7,9,11). Some common terms for non-White ethnicities that could be included are "Two-spirit", "Same gender loving", "Homosexual", "Down low", or "Queer" (7,9,11). With the inclusion of more ethnically-diverse terms in the sexual orientation question, the amount of participants selecting "Other," "Prefer not to answer," or "Not sure" should be minimized, allowing for those response categories to be excluded altogether. While most participants would fall into one of the response categories provided for sexual orientation, individuals who might prefer less conventional labels might choose "Other", "Prefer not to answer", or "Not sure" if they are available, whereas they would likely choose from the offered response categories if they were excluded from the questionnaire (9,19). Evidence from previous research also shows that the majority of people who indicate "Not sure" typically do so out of failure to understand the question and not because they are actually uncertain of their sexual orientation (9). The exclusion of this

option would push for participants to potentially seek out clarification on the question, which would allow them to give an accurate and informed response.

It is important to note that the majority of the articles included in the literature review were aimed at sexual orientation disclosure to a healthcare professional, not in a survey setting. The inclusion of sexual orientation questions in large-scale surveys is still relatively new, so there is currently a dearth in research regarding capturing sexual orientation through questionnaires. Also, of the studies included in the literature review, only those that included men and women of all sexual orientations had particularly large sample sizes. Because of the small percentage of people identifying as LGBT and the difficulties in capturing their sexual orientation, most of the studies with only sexual minorities in their sample had very small sample sizes. Furthermore, most of the sexual minority samples considered were comprised of mostly White and middle-aged individuals, whose disclosure patterns might differ from other ethnicities and age groups.

CONCLUSION

The findings from this study indicate that lesbians have an increased prevalence of various CVD risk factors compared to their heterosexual counterparts, but future research is needed to fully understand the causes of these increased risk factors and their effect on cardiovascular disease risk. Future work should employ best practices when collecting sexual orientation, in order to increase the amount and reliability of data on sexual minorities. This study helps to begin filling the gap in knowledge on health disparities by sexual orientation. With the knowledge to be gained, the identification of CVD risk factors unique to and/or

heightened in lesbians will allow for more targeted interventions for this high-risk subgroup, improving their health status and health care. Informed prevention strategies will lead to a reduction in disparities of CVD risk for lesbians and reduce the morbidity of CVD in women overall.

APPENDICES

Appendix A: CHD Risk by Sexual Orientation and Categorical Variables

Figure 2: Coronary Heart Disease Risk by Sexual Orientation and Depression Status

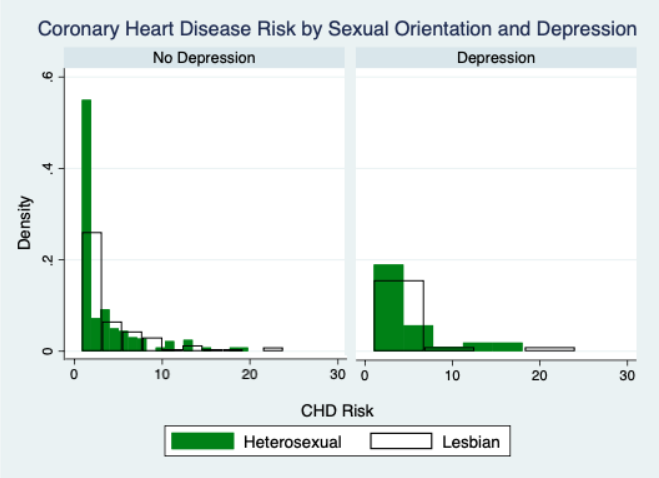


Figure 3: Coronary Heart Disease Risk by Sexual Orientation and Hypertension Status

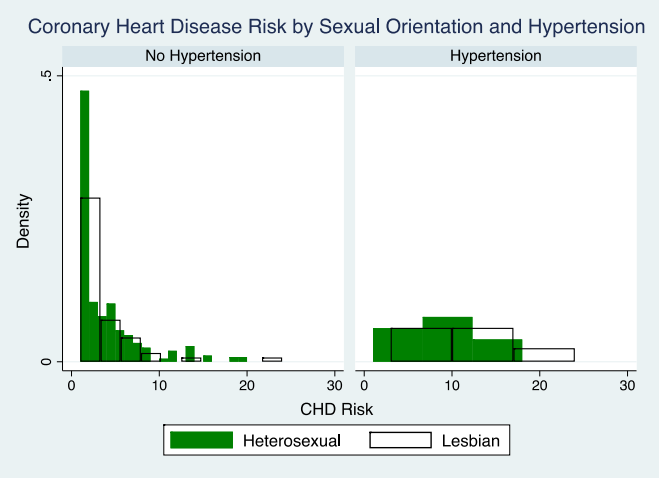


Figure 4: Coronary Heart Disease Risk by Sexual Orientation and Education Level

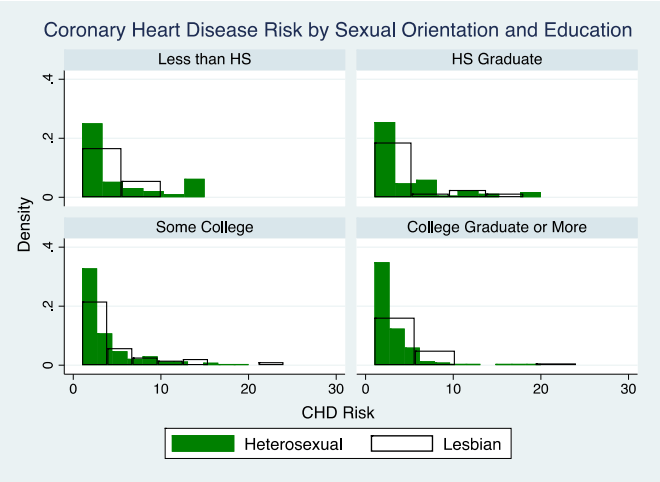


Figure 5: Coronary Heart Disease Risk by Sexual Orientation and Ever Smoker Status

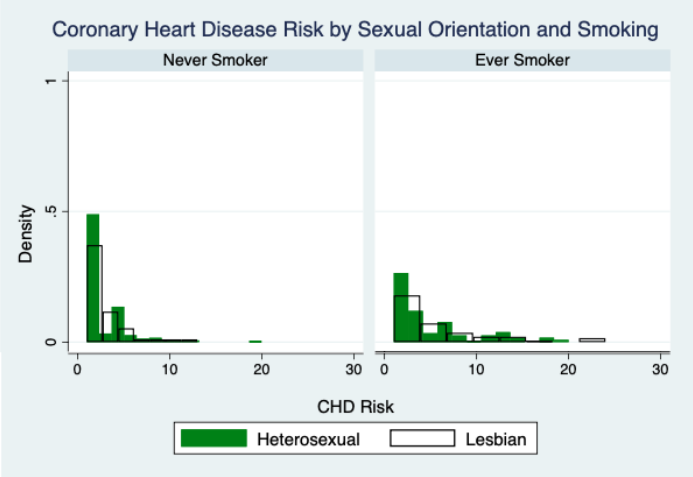


Figure 6: Coronary Heart Disease Risk by Sexual Orientation and Current Smoker Status

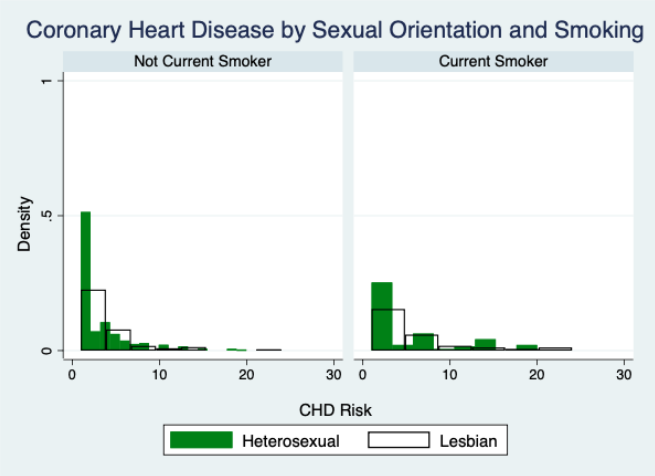


Figure 7: Coronary Heart Disease Risk by Sexual Orientation and Race

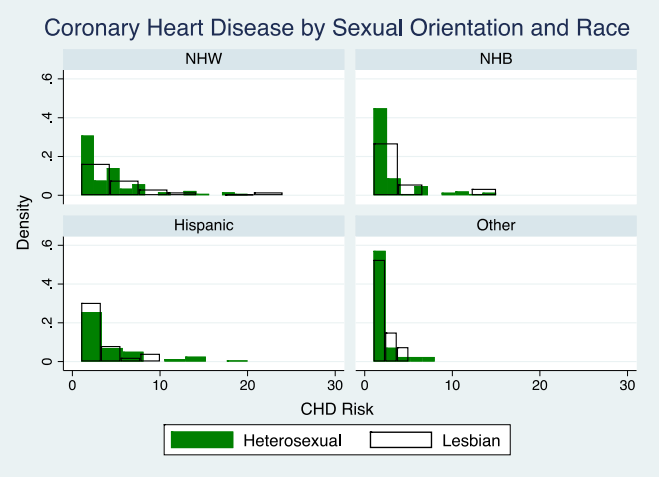


Figure 8: Coronary Heart Disease Risk by Sexual Orientation and Diabetes Status

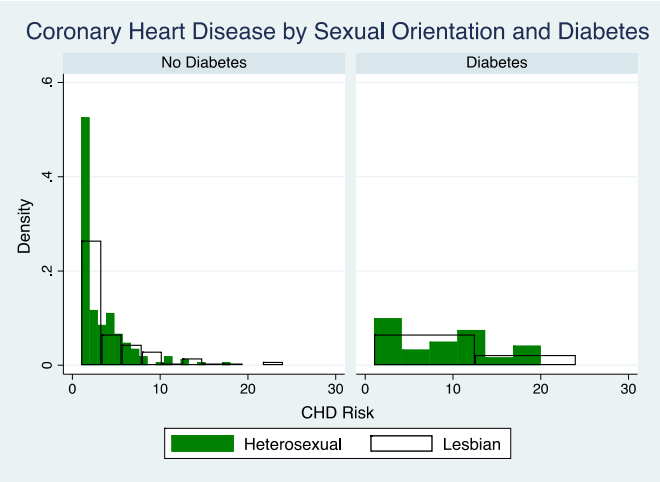


Figure 9: Coronary Heart Disease Risk by Sexual Orientation and BMI Category

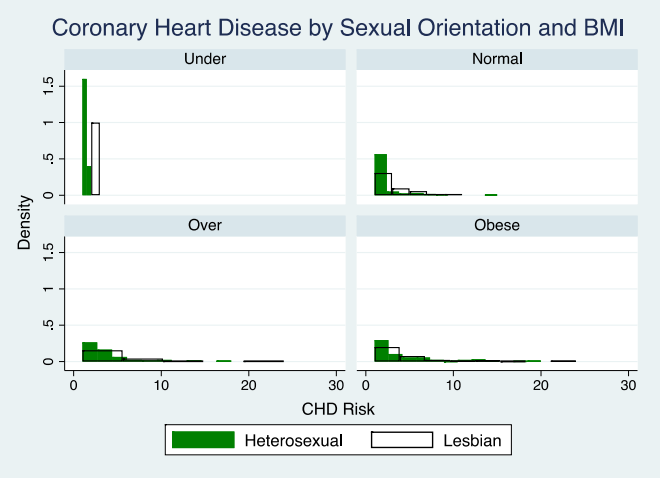


Figure 10: Coronary Heart Disease Risk by Sexual Orientation and Income Category

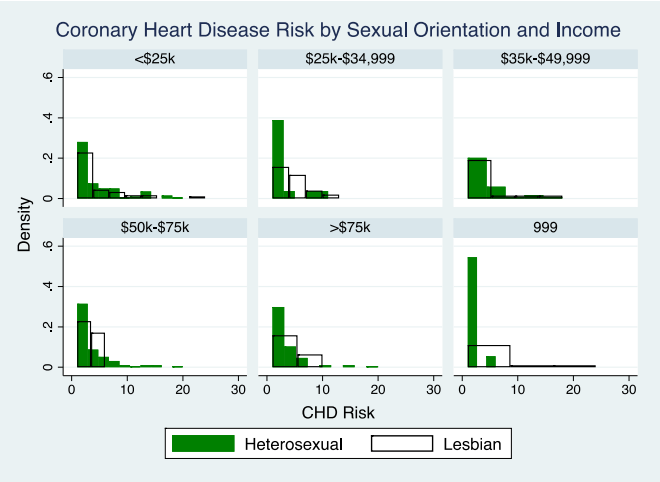
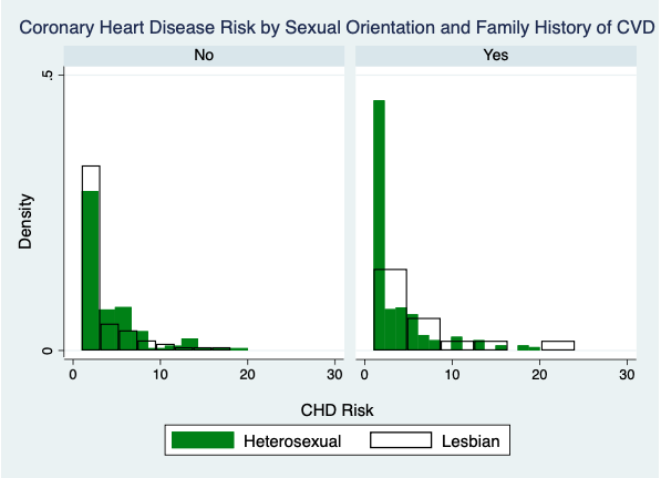
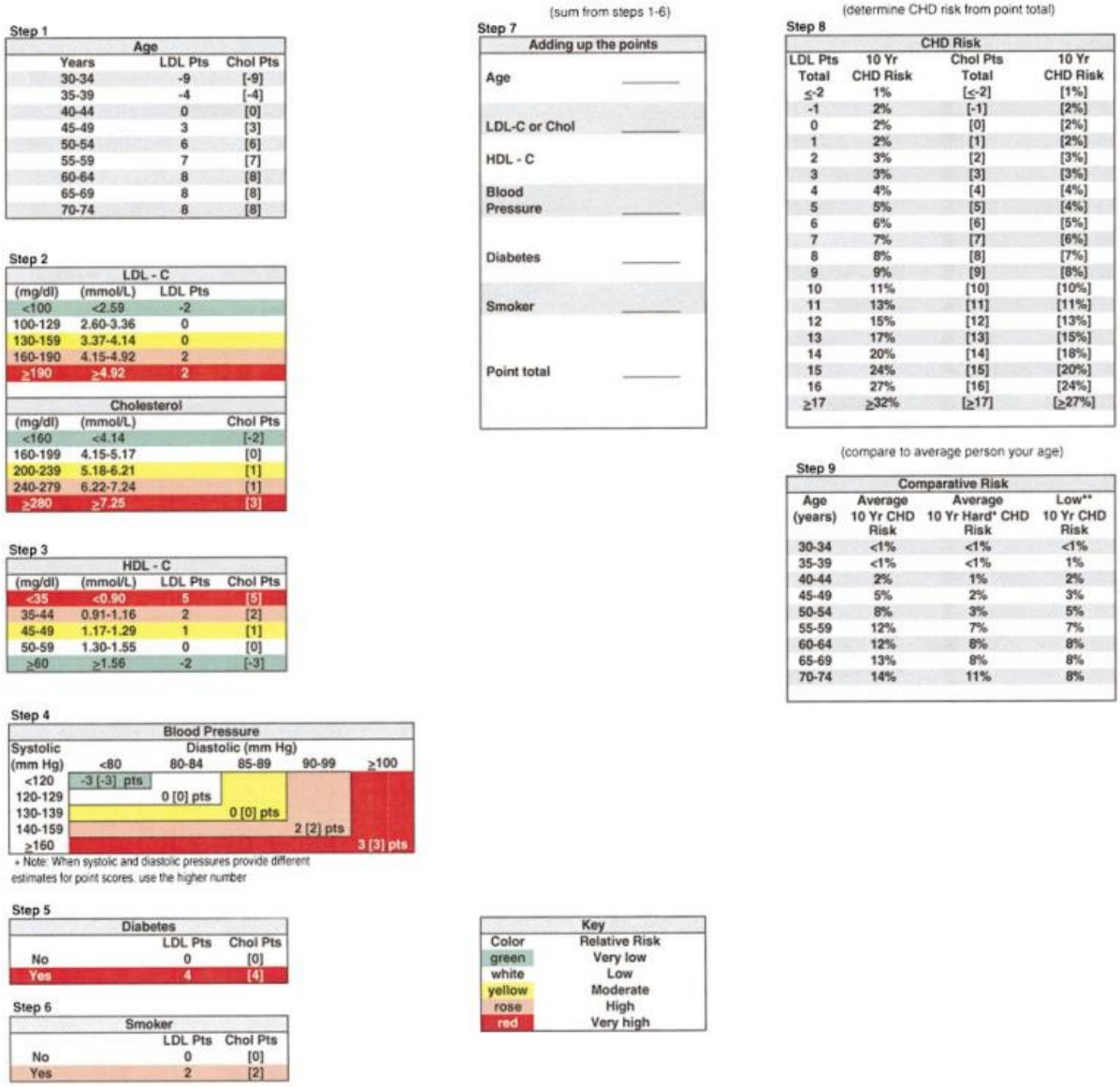


Figure 11: Coronary Heart Disease Risk by Sexual Orientation and History of CVD



Appendix B: CHD Score Sheet for Women



Step 1

Age		
Years	LDL Pts	Chol Pts
30-34	-9	[-9]
35-39	-4	[-4]
40-44	0	[0]
45-49	3	[3]
50-54	6	[6]
55-59	7	[7]
60-64	8	[8]
65-69	8	[8]
70-74	8	[8]

Step 2

LDL - C		
(mg/dl)	(mmol/L)	LDL Pts
<100	<2.59	-2
100-129	2.60-3.36	0
130-159	3.37-4.14	0
160-190	4.15-4.92	2
≥190	≥4.92	2

Cholesterol		
(mg/dl)	(mmol/L)	Chol Pts
<160	<4.14	[-2]
160-199	4.15-5.17	[0]
200-239	5.18-6.21	[1]
240-279	6.22-7.24	[1]
≥280	≥7.25	[3]

Step 3

HDL - C			
(mg/dl)	(mmol/L)	LDL Pts	Chol Pts
<35	<0.90	5	[5]
35-44	0.91-1.16	2	[2]
45-49	1.17-1.29	1	[1]
50-59	1.30-1.55	0	[0]
≥60	≥1.56	-2	[-3]

Step 4

Blood Pressure					
Systolic (mm Hg)	Diastolic (mm Hg) <80	80-84	85-89	90-99	≥100
<120	-3 [-3] pts				
120-129		0 [0] pts			
130-139			0 [0] pts		
140-159				2 [2] pts	
≥160					3 [3] pts

+ Note: When systolic and diastolic pressures provide different estimates for point scores, use the higher number

Step 5

Diabetes		
	LDL Pts	Chol Pts
No	0	[0]
Yes	4	[4]

Step 6

Smoker		
	LDL Pts	Chol Pts
No	0	[0]
Yes	2	[2]

(sum from steps 1-6)

Step 7

Adding up the points	
Age	_____
LDL-C or Chol	_____
HDL - C	
Blood Pressure	_____
Diabetes	_____
Smoker	_____
Point total	_____

Key	
Color	Relative Risk
green	Very low
white	Low
yellow	Moderate
rose	High
red	Very high

(determine CHD risk from point total)

Step 8

CHD Risk			
LDL Pts Total	10 Yr CHD Risk	Chol Pts Total	10 Yr CHD Risk
≤-2	1%	[≤-2]	[1%]
-1	2%	[-1]	[2%]
0	2%	[0]	[2%]
1	2%	[1]	[2%]
2	3%	[2]	[3%]
3	3%	[3]	[3%]
4	4%	[4]	[4%]
5	5%	[5]	[4%]
6	6%	[6]	[5%]
7	7%	[7]	[6%]
8	8%	[8]	[7%]
9	9%	[9]	[8%]
10	11%	[10]	[10%]
11	13%	[11]	[11%]
12	15%	[12]	[13%]
13	17%	[13]	[15%]
14	20%	[14]	[18%]
15	24%	[15]	[20%]
16	27%	[16]	[24%]
≥17	≥32%	[≥17]	[≥27%]

(compare to average person your age)

Step 9

Comparative Risk			
Age (years)	Average 10 Yr CHD Risk	Average 10 Yr Hard* CHD Risk	Low** 10 Yr CHD Risk
30-34	<1%	<1%	<1%
35-39	<1%	<1%	1%
40-44	2%	1%	2%
45-49	5%	2%	3%
50-54	8%	3%	5%
55-59	12%	7%	7%
60-64	12%	8%	8%
65-69	13%	8%	8%
70-74	14%	11%	8%

*Hard CHD events exclude angina pectoris

** Low risk was calculated for a person the same age, optimal blood pressure, LDL-C 100-129 mg/dL or cholesterol 160-199 mg/dL, HDL-C 55 mg/dL for women, non-smoker, no diabetes.

Risk estimates were derived from the experience of the Framingham Heart Study, a predominantly Caucasian population in Massachusetts, USA.

Note. Reprinted from Prediction of Coronary Heart Disease Using Risk Factor Categories, by Wilson PWF, D'Agostino RB, Levy D, et al. Retrieved from https://www.ahajournals.org/doi/pdf/10.1161/01.CIR.97.18.1837. Copywrite 1998 by American Heart Association, Inc.

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