EXAMINING CARDIOVASCULAR DISEASE AND HUMAN PAPILLOMA VIRUS

AMONG A NATIONALLY REPRESENTATIVE SAMPLE OF

LESBIAN AND BISEXUAL WOMEN

IN THE UNITED STATES

by

Vanessa Cox, MS

APPROVED:

George Delclos, MD, MPH, PhD

Stacia DeSantis, PhD

Carol Etzel, PhD

Vanessa Schick, PhD

DEAN, THE UNIVERSITY OF TEXAS
SCHOOL OF PUBLIC HEALTH

DEDICATION

To My Family and Friends

EXAMINING CARDIOVASCULAR DISEASE AND HUMAN PAPILLOMA VIRUS AMONG A NATIONALLY REPRESENTATIVE SAMPLE OF LESBIAN AND BISEXUAL WOMEN IN THE UNITED STATES

by

VANESSA COX
MS, Texas A&M University, 2003

Presented to the Faculty of The University of Texas

School of Public Health

in Partial Fulfillment

of the Requirements

for the Degree of

DOCTOR OF PHILOSOPHY

THE UNIVERSITY OF TEXAS
SCHOOL OF PUBLIC HEALTH
Houston, Texas
August 2017

PREFACE

This work was inspired by my own interests in examining the causes for health disparities in lesbian, gay, and bisexual populations, leading me to research the Minority Stress Theory proposed by Dr. Ilan Meyer. This theory has provided me with a framework to research health disparities and ultimately led me back to pursue my PhD in Epidemiology from UT School of Public Health. I am fortunate to have met many amazing researchers and colleagues along the way.

ACKNOWLEDGEMENTS

I would like to acknowledge Dr. George Delclos for his continuous support as both my Academic Advisor and Dissertation Chair.

EXAMINING CARDIOVASCULAR DISEASE AND HUMAN PAPILLOMA VIRUS AMONG A NATIONALLY REPRESENTATIVE SAMPLE OF LESBIAN AND BISEXUAL WOMEN IN THE UNITED STATES

Vanessa Cox, MS, PhD
The University of Texas
School of Public Health, 2017

Dissertation Chair: George Delclos, MD, MPH, PhD

Background: Sexual minority women (including lesbian and bisexual women) are at a higher risk for numerous diseases. It was previously unknown if this increase in risk translated into higher disease burden. The aim of this dissertation was to compare the prevalence of oral HPV, the risk of cardiovascular disease (CVD), and the incidence of CVD between sexual minority and heterosexual women in a nationally representative sample of adult women.

Methods: Data were obtained from the National Health and Nutrition Examination Survey from 2001-2014. All participants who completed the sexual behavior module and specified their sexual orientation was "lesbian," "bisexual," or "heterosexual" were eligible for analysis. Participants were included classified as sexual minority women by either identification as lesbian or bisexual. Each group was compared to heterosexual women when sample size allowed. Sensitivity analysis were conducted to compare heterosexual women

who had ever had sex with a woman (hetero-WSW) with heterosexual women who had never had sex with a woman (hetero-NSW).

Oral HPV prevalence was obtained from laboratory tests using an oral rinse and strain was classified into high-risk and low-risk for causing cancer. Univariate and multivariate logistic regression models were used to compare lesbian versus heterosexual and bisexual versus heterosexual prevalence of oral HPV. Sensitivity models compared oral HPV prevalence between hetero-WSW with hetero-NSW.

Risk of CVD was obtained by computing the Framingham Risk Score (FRS) based on age, high-density cholesterol (HDL), total cholesterol, systolic blood pressure (SBP), use of hypertensive medications, smoking status, and diabetes status. An alternative risk score (FRS-BMI) utilized body mass index (BMI) in place of laboratory measurements. Weighted univariate and multivariable regression models were used to compare risk of CVD between sexual minority women (defined as lesbian, bisexual, or hetero-WSW) versus hetero-NSW.

Incidence of CVD was obtained by calculating person-time to CVD event defined as heart attack or stroke. Participants were censored at current age if they had never had a CVD. Univariate and multivariate Cox proportional hazards models were used to compare incidence of CVD between lesbian and heterosexual and bisexual versus heterosexual participants.

Results: Sexual minority women experienced a higher burden of disease including: prevalence of oral HPV in bisexual versus heterosexual women, higher risk of CVD in bisexual and hetero-WSW versus heterosexual women, and higher incidence of CVD in combined lesbian and bisexual versus heterosexual women. Current smokers and black and

Hispanic women who identified as lesbian or heterosexual experienced even higher disease burden. However, nearly all of these results were attenuated by either smoking status.

Conclusions: We determined sexual minority women are at increased risk and experience a higher burden of disease including oral HPV, and CVD risk and incidence. Even within this high-risk group, we identified other characteristics, most notably current smokers, who represent the highest risk of disease. These findings provide information on burden of disease and also point to groups which would most benefit from tailored interventions.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER 1: BACKGROUND

National statistics for cardiovascular disease (CVD) and human papillomavirus (HPV) are almost entirely unknown and undocumented for lesbian and bisexual (LB) women, despite CVD being the leading cause of death in women and HPV the most common sexually transmitted infection (STI).[1-3] Additionally, a large body of literature has consistently documented that LB women are at an increased risk for these and other chronic diseases based on higher rates of smoking, drinking, obesity, and other risk factors compared to heterosexual women.[4-5] This study will estimate the prevalence of HPV, risk of CVD, and incidence of CVD in LB women using a nationally representative sample of women in the United Status (US). Secondly, this study will compare the occurrence of these diseases between both lesbian and bisexual women to heterosexual women to determine if there is evidence of a health disparity among these sexual minority women. If sample size allows, risk factors (e.g. race/ethnicity, smoking status) will be compared with post-hoc testing to determine high-risk groups for each disease. Lastly, sensitivity analysis will compare the differential contribution of sexual behavior and sexual identity in operationalizing sexual orientation in the examination of health disparities.

Sexually Transmitted Infections

Nearly 60 million cases of sexually transmitted infections (STIs) were detected in US women in 2008, with approximately 40 million cases of HPV, and up to 85% of sexual active adults have had HPV during their lifetimes.[1] Typically the body is able to contain the HPV infection, although some infections do become persistent.[2] About 15 of 100 strains of HPV are high-risk for causing cancer, and when a high risk strain is also persistent, is causally linked to cervical cancer, anal cancer, oral cancer, vaginal cancer, and vulva cancer.[6-8]

Risk of HPV is associated with number of sexual partners and not using a contraceptive barrier and persistent infection is associated with smoking or chewing tobacco, weak immune system, parity, birth control use, and poor oral hygiene.[3] National prevalence rates for the majority of STIs are not available for LB women, despite these rates being frequently available for men who have sex with men (MSM). Lesbian and bisexual women might be at greater risk for HPV infection due to a higher preponderance of risk factors for cancer and chronic diseases including obesity, smoking, binge drinking, stress, and less likely to undergo screenings or utilize preventive health services.[4,5]

Several studies have begun to investigate the burden of STI's among sexual minority women (including heterosexual women who have had sex with a woman (hetero-WSW), lesbian, and bisexual). Prevalence of detected herpes simplex virus type 2 (HSV2) in women was found to be higher in hetero-WSW and bisexual, and lower in lesbian, versus heterosexual women who had never had sex with a woman (hetero-NSW).[9] Prevalence of bacterial vaginosis was approximately 50% higher in hetero-WSW versus hetero-NSW.[10] A recent study found higher prevalence of vaginal HPV among lesbian, bisexual, and hetero-WSW versus hetero-NSW.[11] This study will fill a critical gap by examining prevalence of oral HPV in lesbian, bisexual, and hetero-WSW to examine the importance for screening and early detection of HPV to prevent HPV related cancers.

Cardiovascular Disease

CVD, or disease of the heart and blood vessels, is the leading cause of death in both women and men in the US.[1,2] CVD includes coronary artery disease, arrhythmia, congenital heart defects, heart attack, chest pain (angina), and stroke.[1,2] Risk factors for heart disease include high

blood pressure, high blood cholesterol, diabetes, pre-diabetes, smoking, being overweight or obese, being physically inactive, family history of heart disease, history of preeclampsia during pregnancy, unhealthy diet, and age (55 or older for women).[12]

LB women have higher rates of obesity, smoking, binge drinking and stress and are less likely to have health insurance and get routine screenings (e.g. Pap test, mammograms, and clinical breast exams), or have a usual place of medical care than heterosexual women.[4,5,13] Reliable and nationally representative prevalence rates of CVD are not available for lesbian or bisexual women. Proportions for self-reported diagnosis are available from National Health Interview Survey (NHIS) 2013 for chronic obstructive pulmonary disease (COPD), coronary heart disease (CHD), and stroke but because the sample size was limited to a single year of data with sexual orientation, the relative standard error of these estimates makes them unreliable (relative standard error >30%).[14] Similarly, self-reported prevalence rates from multi-state data including 10 out of 50 states using data from Behavioral Risk Factor Surveillance System (BRFFS) 2010, which captures sexual orientation, did not have a large enough sample size to reliably approximate CVD prevalence in lesbian or bisexual women when combining heart attack, angina/CHD, and stroke. Other studies have either combined lesbian and bisexual women versus heterosexual women[15]; combined genders to compare gay and lesbian men and women versus heterosexual men and women[16]; or combined outcomes into a composite[17] (e.g. CVD defined as heart attack, angina/CHD, or stroke). Disease risk factors (e.g. obesity, smoking status) were not included in the analysis for any of the previously mentioned studies.

In addition to examining individual risk factors, several studies have examined the 10-year risk of CVD event and vascular age using the Framingham Risk Model[18] and the majority

have found that lesbian and bisexual women are at a greater risk for CVD or higher vascular age than heterosexual women. [19,20] All but one study looked exclusively at risk factors, while the one study which did examine prevalence of CVD as an outcome combined lesbian and bisexual women into a single group compared to heterosexual women. This study will provide nationally representative incidence rates and risk of CVD based on lab-work (and self-reported data when available) among LB women by combining 7 cycles of National Health and Nutrition Examination Survey (NHANES) data from 2001-2014and compare these estimates to heterosexual women to determine if the risk factors previously documented in LB women correspond with an increased prevalence of CVD.

Minority Stress Theory

The Minority Stress Theory is one of the first, and perhaps the most widely accepted theories to explain health disparities among sexual minorities, or those who do not identify as heterosexual.[21-24] Based on the Minority Stress Theory[25], lesbian and bisexual women experience chronic stressors unique to being a sexual minority. These stressors may, in turn, influence mental health and contribute to engagement in high risk behavior (e.g. smoking, drinking) in order to cope with the corresponding negative affect. Numerous studies have demonstrated worse mental health in sexual minorities including higher rates of depression, stress, anxiety, and suicidality than their heterosexual counterparts.[26-28] The Minority Stress Theory might explain risky behaviors in LB women (e.g. smoking, drinking), which might in turn increase health disparities in chronic conditions linked to these risk factors.

Public Health Significance

Historically, LB sexual health has been understudied and underfunded, despite representing between 3-11% of the adult female population.[29] Further, the availability of oral, and vaginal lab data for HPV makes NHANES useful in examining the burden of STIs among LB women.

Findings from this study should help inform the planning and implementation of health services, by providing new information on basic demographic predictors as well as risk and incidence rates for CVD and prevalence of HPV for LB women. This basic information is needed to design tailored interventions for LB women. In addition, this study examines a medically underserved population, and findings may help target future disease-specific interventions for cancer and heart disease. For example, researchers have noted that interventions within the lesbian community that focus on weight loss rather than emphasizing overall health as an outcome may actually contradict some social norms of this population. Its ultimate goal is to reduce minority health disparities of LB women by identifying modifiable risk factors and high-risk groups, in hopes of preventing or minimizing disease prevalence and mortality. Additionally, the knowledge gained should help inform local organizations and health policy decision makers. Results will be presented to academic and research groups, also in addition to organizations serving LB communities, in hopes of informing those who would be most directly impacted by any research findings.

Specific Aims

Lesbian and bisexual women (LB) have been identified as potentially facing health disparities due to of increased risk and delayed screening practices. Despite these risk factors and national calls to action[46], the burden of cardiovascular disease (CVD) and sexually transmitted infections (STI) in this collective is largely unknown.

The purpose of this study is to compare the prevalence of HPV as well as risk and incidence of CVD between lesbian and bisexual (LB) women versus heterosexually identified women in the U.S.

Aim 1. To compare prevalence of HPV between LB and heterosexual women using self-report and lab results.

Aim 2. To compare risk of cardiovascular disease (CVD) between LB and heterosexual women using self-report and physical exam measurements.

Aim 3. To compare incidence of cardiovascular disease (CVD) between LB and heterosexual women using self-report and physical exam measurements.

CHAPTER 2: METHODS

Study Design

This study will utilize and combine NHANES 2001-2014 public data to obtain a large and nationally representative sample of non-institutionalized US adult women, cross-sectional by design, to examine prevalence of HPV, as well as risk and incidence of CVD in 3 separate manuscripts. Data were downloaded by survey cycle (2001-2002, 2003-2004, 2005-2006, 2007-2008, 2009-2010, 2011-2012, and 2013-2014) from the NHANES website (https://wwwn.cdc.gov/nchs/nhanes/). Each survey cycle contains numerous datasets (e.g. Demographics, Examination, Laboratory, and Questionnaire) which can be merged together by a unique sequence number (SEQN). After linking datasets within each survey year, the datasets were concatenated by year to form one dataset with one observation for SEQN from 2001-2014.

Data collection by NHANES is designed to capture a nationally representative of non-institutionalized citizens in the United States, excludes active military, and oversamples older (over 60 years old), Hispanic, African-American participants, and persons living below 130% of the federal poverty level, using a multistage sample design (National Center for Health Statistics).[30-32] Due to the sampling method, in order to obtain reliable estimates for standard error, statistical analysis must take into account primary sampling unit (PSU), as well as survey weight and strata.[30-32]

In Manuscript 1 (Chapter 3), weighted proportions and logistic regression models were used to compare risk factors and morbidity distinct groups of lesbian and bisexual versus heterosexual women using NHANES 2009-2014. Sensitivity models examined any difference in prevalence of HPV by sexual behavior between women who have had sex with women only

(WSW), women who have had sex with women and men (WSWM) versus women who have had sex with men only (WSM). Weighted regression models were used to compare the 10-year risk of CVD in lesbian, bisexual and heterosexual women who have had sex with women (hetero-WSW) versus heterosexual women who have never had sex with women (hetero-NSW) in Manuscript 2 (Chapter 4) using NHANES 2001-2014. Lastly, Manuscript 3 (Chapter 5) utilizes NHANES 2001-2014 in weighted Cox-regression models were used to compare incidence of CVD in sexual minority (lesbian or bisexual women) versus heterosexual women. All analysis was performed as 2 sided tests with α=0.05 level of significance using STATA (Version 14). Variances were estimated using Taylor series linearization, and analysis takes into account survey weights in accordance with NHANES guidelines.

Study Subjects

All female respondents who completed the sexual behavior module and specify their sexual orientation is "heterosexual", "lesbian", or "bisexual" will be included in the analysis. Unrestricted data is available for women 18 years or older. Sexual orientation was asked of participants 18-59 years old beginning in 2001. Oral-HPV laboratory testing was available during 2009-2014 survey cycles. Data utilized for CVD risk and incidence were available in 2001-2014 survey cycles.

Measures

HPV Prevalence

History of HPV ("Ever been told by a doctor you had HPV?") as well as lab results for HPV (oral and vaginal) were tabulated. Samples were collected by oral or vaginal swab and then genotyped by using Roche Linear Array.[33] HPV strain was then classified into high-risk and low-

risk for causing cancer; high-risk strains were HPV types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 64, 66, 68, 67, 69, 70, 73, and 82.[6,8-11]

Survey-weighted logistic regression models compared prevalence of any, high-risk, and low risk types of oral or vaginal HPV between lesbian versus heterosexual and bisexual versus heterosexual respondents. Multivariate models were used to examine the difference in any-strain and high risk strain after adjustment for age, race (white, black, Hispanic, or other), smoking status (current smoker versus former or never), education (at least college degree versus less than college degree), number of lifetime sexual partners, and relationship status (married or partnered versus not).

CVD Risk

Framingham Risk Score (FRS) is calculated based on lab values (high-density lipoprotein cholesterol, total cholesterol, and systolic blood pressure), physical exam (height and weight), and self-reported (current use of high blood pressure medications, diabetes, smoking status) characteristics to predict 10-year risk of CVD.[18] A second risk score (FRS-BMI) is calculated utilizing body mass index (BMI) in place of laboratory risk-factors. For each score, FRS or FRS-BMI, each risk factor contributes a point value to the total of the points, corresponding to a vascular age for each participant. Vascular age corresponds to the age of a person with similar risk, but with all of the risk factors within the normal range. The ratio of the FRS or FRS-BMI vascular age to the woman's chronological age determines the FRS or FRS-BMI vascular ratio, a metric to estimate the risk of a person relative to their age.[18] For example, a 40 year-old woman with diabetes and total cholesterol of 240 has a vascular age of 68, and the ratio of her vascular

age to chronological age is 1.70, indicating her vascular system is approximately 70% older than a woman her age without any risk factors.

CVD Incidence

Participants were asked if they had ever been told they had: congestive heart failure (CHF), coronary heart disease (CHD), angina/angina pectoris (angina), heart attack, or stroke. Those who answered "Yes" to any of these questions were classified as having a cardiovascular event. Participants who answered "No" to all of these questions were classified as never having a cardiovascular event. Age when told you had CHF, CHD, angina, heart attack or stroke was collected from respondents who reported having any CVD event. Age at first cardiac event was defined as the youngest age reported for any cardiac event.

Participants contributed person-time to the analysis until the first event: (1) Age at first cardiac event or (2) Age at study enrollment for those who have never had a cardiac event. Survey weighted Cox regression models were used to calculate hazard ratios, confidence intervals, and Wald-test p-value. The proportional hazards assumption was evaluated by testing for an interaction between each factor (sexual orientation, race, and smoking status) by time in the model.

Sexual Identity and Sexual Behavior

Sexual orientation was defined for this project by a single item question asked of female respondents by NHANES "Do you think of yourself as…" with the following choices: heterosexual or straight (attracted to men), homosexual or lesbian (attracted to women), bisexual (attracted to men and women), something else, not sure, refused, or don't know. All participants who answered "heterosexual", "lesbian", or "bisexual" will be included in the analysis.

NHANES participants were asked how many men and women they had sex with in the last year. Heterosexual women who have had sex with at least one woman during the past year will be considered as sexual minority women in a sensitivity analysis to examine a possible interaction between sexual identity and sexual behavior. To compare the differential contribution of sexual behavior and sexual identity to sexual health risk factors and morbidity, sexual behavior (sex with a woman during the last year, yes/no) will be tabulated by sexual identity (lesbian, bisexual, or heterosexual) to identify sexual minority women (SMW) who identify as heterosexual but have had sex with women during the last year.

Study Power

Approximately 11183 women completed the sexual behavior portion of NHANES and identified as lesbian, bisexual, or heterosexual from 2001-2014, including144 (1.3%) lesbian, 403 (3.6%) bisexual, and 10636 (95.1%) heterosexual women. All power calculations are based on unweighted data frequencies and peer-reviewed prevalence estimates of adult women in the US to test the difference in proportion of CVD, cancer, or STIs between lesbian versus heterosexual and bisexual versus heterosexual women.

Approximately 35% of women in the US have some kind of cardiovascular disease (including CHD, heart failure, stroke, or hypertension), ranging from 10% in 20-39 year olds to 87% in women over 80 years old.[47] Excluding hypertension, 4.2% of women aged 45-54 were found to have CVD, and 40% of women aged 75-84.[47] The power to detect an odds ratio of CVD comparing lesbian to heterosexual women of 2 with 18% of heterosexuals having CVD was 0.94 using PASS version 13.0.1 (NCSS, Inc, Kaysville, UT, USA). Refer to Table 1 and Figure 1 for detailed estimates. Among bisexual versus heterosexual women, we will achieve 77% power to

detect an odds ratio of 1.5 if 10% of heterosexual women have CVD. To account for the effect of weighted observations on power calculations, a design factor of 2 was also utilized to obtain more conservative estimates (Table 1 and Figure 1).

Data Collection

Publicly available, de-identified data will be obtained for NHANES 2001-2014 survey years and combined for analysis. Analysis is limited to unrestricted data. Oral HPV labs were only available for 2009-2014, limiting analysis for the HPV study to these years. Risk and incidence of CVD were examined from 2001-2014.

Data Analysis

Prevalence of, and risk factors for HPV, CVD incidence, and risk models for CVD will be compared between lesbian and heterosexual women and bisexual and heterosexual women using weighted logistic regression models and Rao-Scott chi-squared test. Crude and age-adjusted prevalence will be tabulated by sexual orientation. All testing will be done at the 2-sided α=0.05 level of significance using heterosexual women as the reference. All missing data will be assumed to be missing at random.

Potential covariates the logistic regression models will be added using a stepwise approach, first adding demographic (age, race/ethnicity, income, and education); second adding disease specific risk factors (e.g. measured cancer risk factors include: obesity, smoking status, tobacco exposure, alcohol overuse, family history of cancer, physical activity, HPV vaccine, history of HPV, history of birth control usage, and detection of high-risk HPV strain from lab testing). All covariates with a univariate p-value $\leq$ 0.20 will be included in the stepwise models for the outcomes. In addition, confounding will be assessed by examining a change in excess of

10% in the outcome for covariates associated with both the exposure (sexual orientation) and the outcome (cardiovascular disease, cancer, or STI). All potential confounders will be adjusted for in the final models.

A sensitivity analysis will be conducted using sexual behavior during the last year to classify heterosexually identified women into categories: women who have sex with women (hetero-WSW), women who have sex with women and men (hetero-WSWM), women who have sex with men (hetero-WSM), and women who have no sexual partners (hetero-WSX). Heterosexual women with only male partners will be the reference group versus lesbian, bisexual, and other heterosexual based on sexual behavior (WSW, WSWM, and X). The hierarchical models will again be constructed with both sexual orientation and sexual behavior in the models to determine if sexual behavior is confounding the relationship between sexual orientation and the outcomes. Additionally, univariate association between the exposure and the outcomes will be stratified by sexual behavior to determine any potential effect modification of sexual behavior. Power for these analysis should be at least as high as the main analysis since the number of sexual minority women will either stay the same or increase when combined with sexual behavior.

Human Subjects, Animal Subjects, or Safety Considerations

All data obtained from NHANES are publicly available and de-identified. No attempt will be made to identify subjects or match with any other dataset. This protocol will be reviewed by the UT School of Public Health Office of Research, who will determine whether review by the full IRB (UTHealth Committee for the Protection of Human Subjects) is indicated to ensure compliance with local and state guidelines.

CHAPTER 3: JOURNAL ARTICLE 1

Comparing Prevalence of Human Papilloma Virus Infection Between Bisexual, Lesbian, and Heterosexual-Identified Women: National Health and Nutrition Examination Survey 2009-2014

Prepared for American Journal of Public Health

Abstract

Objectives. Burden of oral-HPV is unknown for lesbian and bisexual women. We aimed to estimate and compare the proportion of oral and vaginal human papilloma virus (HPV) infection between US female adults who identify as lesbian, bisexual, or heterosexual.

Methods. Data from the 2009-2014 National Health and Nutritional Examination Study were utilized. Respondents were classified by sexual identity. Age-adjusted prevalence of oral and vaginal HPV was compared between lesbian and heterosexual women, as well as between bisexual and heterosexual women.

Results. We found age-adjusted prevalence was statistically significantly higher in bisexual women for any oral and high-risk oral HPV infection (any-oral: 7.4% lesbian, 4.9% bisexual, 3.1% heterosexual women; high-risk oral: 1.4% lesbian, 2.9% bisexual, 1.6% heterosexual). These differences were attenuated in multivariate models that adjusted for race/ethnicity, smoking status, education, birth control, number of sexual partners, and frequency of condom use. Women who were current smokers were more likely to have oral or high-risk oral HPV. No difference was detected in the prevalence of any-oral or high-risk oral HPV between lesbian and heterosexual women in age-adjusted or fully adjusted models.

Conclusion. Oral HPV is more common among lesbian and bisexual than heterosexual women. We found a higher prevalence of any-oral and high-risk oral HPV among bisexual women,

which was attenuated by other risk factors. These risk factors might indicate a group who would benefit most from a tailored HPV intervention. Based on these results, HPV screening should be part of the preventive health message targeting women in the lesbian and bisexual community.

Introduction

Human Papilloma Virus (HPV) is a common sexually transmitted infection (STI), with approximately 85% of all sexually active adults ever having HPV, resulting in 40 million cases in the United States (US) women in 2008.[1] Typically the body is able to contain the HPV infection, although some infections do become persistent.[2] There are over 100 known strains of HPV, and approximately 15 of those are classified as high-risk for causing cancer.[3] In cases where HPV infection is both persistent and a high-risk strain, HPV is causally linked to nearly all cervical cancers, 95% of anal cancers, 70% of oral cancers, 65% of vaginal cancers, and 50% of vulva cancers.[4,5]

Risk of HPV infection has been linked to number of sexual partners and not using a contraceptive barrier.[1] Risk factors for a persistent HPV infection include smoking or chewing tobacco, a weakened immune system, number of child births, long term birth control pill use, and poor oral hygiene.[6] National prevalence rates of HPV infection are poorly documented for lesbian and bisexual women, despite potential for HPV infection based on increased number of sexual partners during the last year[7] and higher smoking prevalence[8]. Detecting an increase in HPV infection would contribute to a large body of literature that has documented lesbian and bisexual women are at a higher risk for cancer due to a preponderance of risk factors including higher rates of obesity, smoking, binge drinking and stress.[9,10] They are also less likely to have health insurance, undergo routine screening (e.g. Pap test, mammograms, and clinical breast exams) and gynecological care, or have a usual place of care than heterosexual women which could cause cancer to go undetected.[9,10] A recent study found higher prevalence of vaginal HPV among non-heterosexual versus heterosexual women when grouped by sexual orientation

identity and gender of sexual partners.[11] We now fill a critical gap by providing prevalence of oral HPV by sexual orientation identity, to examine the importance for oral HPV screening for early detection and prevention of HPV related cancers in lesbian and gay women.

Methods

In the present study, we used data from the National Health and Nutrition Examination Survey (NHANES), conducted by the National Center for Health Statistics, a part of the Centers for Disease Control and Prevention. NHANES data collection has been described extensively elsewhere.[12,13] Briefly, data collection cycles span two year increments, oversample older, Hispanic, and African-American participants, and use a multi-stage sampling design to obtain nationally representative estimates of health characteristics and disease among non-institutionalized children and adults in the US.[14]

All female respondents ages 18-59 from 2009-2014 NHANES who completed the sexual behavior module, indicated ever having had sex, and with valid HPV laboratory results for either vaginal or oral HPV were included in the analysis. Sensitivity analyses were conducted to compare demographic characteristics and risk factors to respondents who were not tested for HPV infection. All results were age-adjusted to avoid confounding of health characteristics by age, and standardized to the 2000 US Census as a recommended practice for NHANES data.[14]

Sexual orientation was defined by a single item question asked of female respondents, "*Do you think of yourself as…?*" with the following choices: heterosexual or straight (attracted to men), homosexual or lesbian (attracted to women), bisexual (attracted to men and women), something else, not sure, refused, or don't know. All participants who answered heterosexual, lesbian, or bisexual were included in the analysis. Those who answered "something else," "not

sure," "don't know" or refused to answer their sexual orientation identity were excluded due to small sample size, as were women who reported never having sex before or who refused to answer.

Respondents were asked how many men and women they had sex with during their lifetime, calculated as a sum of the number of males and females, by the following questions: 1) *In your lifetime, with how many men have you had any kind of sex?* 2) *In your lifetime with how many women have you had sex? By sex, we mean sexual contact with another woman's vagina or genitals*. Participants were asked how often they used protection during the last year when performing oral sex (never, rarely, usually, or always) and how often they had vaginal or anal sex without using a condom (never, < ½ time, ½ time, > ½ time, or always).

Respondents were classified into those who reported ever having been diagnosed with HPV (yes/no) based on the question "*Ever been told by a doctor you had HPV?*" Additionally, laboratory results for HPV (oral and vaginal), were tabulated overall and by high risk strain. Oral and cervicovaginal swabs were collected in each cycle spanning 2009-2014 years, and DNA was tested using the Roche Linear Array.[15] HPV strain was categorized into high-risk and low-risk strain; high-risk strains were HPV types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 64, 66, 68, 67, 69, 70, 73, and 82.[3,16]

Age-adjusted demographic characteristics (income, insurance, race/ethnicity, education, smoking status, HPV vaccination, and relationship status) were tabulated by sexual orientation. Prevalence of HPV, lifetime number of sexual partners, and use of protection for oral, and vaginal/anal sex were compared between lesbian and heterosexual women and bisexual and heterosexual women using weighted logistic regression models. All testing was performed at the

2-sided α=0.05 level of significance using heterosexual identified women as the reference group. Missing data were assumed to be missing at random.

Potential covariates were added to the logistic regression models using a stepwise approach. First, we added demographic characteristics; second, we added disease-specific risk factors. All covariates with a univariate p-value ≤ 0.20 were included in the stepwise models for the outcomes. To examine the effect of condom usage on HPV prevalence, participants who had sex with at least one man or one woman were included in models for oral and vaginal HPV including a term for oral protection or condom for vaginal/anal sex, respectively. Due to the high degree of missingness about use of a contraceptive barrier (approximately 30% missing), the final models were created with and without this covariate.

A number of risk factors for HPV are behaviorally based, therefore in addition to sexual orientation identity, we conducted a sensitivity analysis using lifetime sexual behavior to classify participants into sexual behavior categories: women who have sex with women (WSW), women who have sex with women and men (WSWM), and women who have sex with men (WSM). WSM were the reference group versus women with any same sex partners (WSW and WSWM). Models were similarly constructed with sexual behavior to determine if sexual behavior and sexual identities had a similar prevalence of HPV.

Results

7781 women completed the sexual behavior portion of NHANES from 2009-2014. Women who either refused to answer their sexual orientation or answered "something else," "not sure," "don't know" (n=210), did not respond to the question (n=2385), and women who reported never having sex before (n=224) were excluded. An additional 42 women did not have

HPV labs available, leaving an eligible sample of 4918 including 71 (1.4%) lesbian, 247 (4.9%) bisexual, and 4600 (93.7%) heterosexual women.

Demographic Characteristics

Eligible participants were an average of 39.1 years old, and bisexual women were younger than heterosexual women (38.1, 31.2, 39.5 years for lesbian, bisexual and heterosexual respectively, results not shown). Thus, all study results are age adjusted. Lesbian and bisexual were less likely to be Hispanic, more likely to be current or ever smokers, and less likely to be married or living with a significant other than heterosexual women (Table 1, $p<0.05$). Lesbian and bisexual were less likely to have ever had sex with men only, have a greater number of lifetime sexual partners, were less likely to have sex with men only during the last year, and were more likely to have sex with 2 or more people during the last year than heterosexual women (Table 2, $p<0.05$). However, the majority of lesbian women who had sex with more than 2 partners during the last year were among the unmarried/not living with partner group. Bisexual women were more likely to use protection during oral sex, and lesbian women were less likely to use a condom for vaginal or anal sex than heterosexual women ($p<0.05$).

HPV Prevalence

Self-reported HPV lifetime prevalence did not significantly differ between lesbian or bisexual versus heterosexual women (10.3% heterosexual, 5.5% lesbian and 9.9% bisexual, $p=0.444$ and 0.800 respectively). However, bisexual women had a higher prevalence of HPV from laboratory testing compared to heterosexual women, including any oral HPV (4.9% vs. 3.1%), high-risk oral HPV (2.9% vs. 1.6%), any vaginal HPV (54.6% vs. 41.7%), and low-risk vaginal HPV (45.1% vs. 28.4%, Table 3, all $p<0.05$ respectively). Prevalence of oral HPV

ranged from 2.7-4.8% by sexual orientation. No statistically significant difference was detected in vaginal or oral HPV between lesbian and heterosexual women, although the prevalence of any oral HPV was more than twice as high in lesbian (7.4%) relative to heterosexual women (3.1%, p=0.680, Table 3).

Oral HPV

Multivariate models for oral HPV did not detect a statistically significant difference between lesbian or bisexual women relative to heterosexual women. Current smokers were at higher risk for any-oral HPV and high-risk oral HPV [OR (95% CI): 2.8 (2.0, 4.1) and 2.5 (1.5, 4.4) respectively]. Being married or partnered was a protective risk factor for oral HPV. Among women who had sex during the last year, models that included a term for protection during oral sex had similar results for prevalence of any oral for lesbian and bisexual versus heterosexual [OR (95% CI): 0.8 (0.2, 3.0) and 1.6 (0.8, 3.1)] and high risk oral HPV for lesbian and bisexual versus heterosexual [OR (95% CI): 0.7 (0.1, 3.7) and 2.2 (0.9, 5.2)].

Vaginal HPV

In multivariable models examining the prevalence of vaginal HPV in lesbian and bisexual respondents, the higher prevalence in age-adjusted vaginal HPV and high-risk vaginal HPV among bisexual women was attenuated by race (black vs. white), current smoking status, lower education, not being married or partnered. Lesbian women were at a reduced risk for any or high-risk vaginal HPV as compared to heterosexual women.

Sensitivity Models

Multivariable models for oral and vaginal HPV using sexual behavior as a proxy for sexual identity indicated similar prevalence of vaginal HPV between WSW and WSWM

compared to WSM (results not shown). There was a slight increase in the prevalence of oral HPV (OR and 95% CI 1.7 (1.0, 2.9)) but not high-risk oral, although the results were not statistically significant. Similarly, there was not a detectible difference in high-risk vaginal HPV between WSW or WSWM compared to WSM.

Discussion

We found that bisexual women have an increased age-adjusted prevalence for both oral and vaginal HPV as compared to heterosexual women. Lesbian women have a similar prevalence of vaginal HPV, but higher oral HPV prevalence compared to heterosexual women, although not statistically significant due to low sample size. However, any differences in HPV prevalence, especially oral HPV, due to sexual orientation or behavior were attenuated after adjusting for other risk factors. These findings suggest that differences in prevalence are being driven by a different distribution of known risk factors for HPV rather than directly by sexual identity. To our knowledge, this is the first study to examine nationally representative data on prevalence of oral HPV infection in lesbian and bisexual women.

Our findings are consistent with prior research.[11] The attenuation of both oral and vaginal HPV prevalence is consistent with Minority Stress Theory, and suggests that health disparities among sexual minorities (including lesbian and bisexual women) may be to the result of mechanisms unhealthy behaviors used as coping mechanisms specific to sexual-minority stressors (e.g. homophobia).[17] According to this theory, the unique and chronic stressors experienced by lesbian and bisexual women may negatively impact their mental health and wellbeing, thereby increasing risky behaviors in order to cope with the stressors. In the present study, current smokers were 2.5 and 2.8 times more likely to have any-oral and high-risk oral

HPV, respectively, and appear to be the main driving factor behind the apparent increased risk in HPV infection among bisexual women. Lesbian and bisexual women were more than twice as likely to be current smokers as heterosexual women (20% heterosexual, 54% lesbian, and 43%, Table 1). Previous research has shown that stress and psychological distress contribute to the relationship between sexual orientation and increased smoking rates among lesbian, bisexual, and gay men and women.[18,19]

Participants in the present study who were single or not living with their partner, were less than college educated, and those who were black or Hispanic were more likely to have oral or vaginal HPV, all of which is consistent with prior HPV research.[16,20,21] These characteristics have also been associated with increased stress among lesbian and bisexual populations, and in particular with research indicating the intersectionality of belonging to more than one minority group (e.g. black and Hispanic bisexual women).[18,22,17]

Strengths of this study include use of a large, nationally representative dataset with well-documented laboratory procedures to examine prevalence of oral and vaginal HPV as well as the availability of measures for sexual orientation and behavior. Limitations include cross-sectional study design (associations are reported), the lack of further information for women who indicated "something else" or "not sure" for their sexual orientation, and missing data for contraceptive barrier use. Research probing "something else" and "not sure" responses has found some of these respondents identify as other non-heterosexual orientations, while others are transgender or non-binary gender.[23] Gender is captured by a dichotomous choice for male and female in NHANES surveys, not allowing for inclusion of intersex, transgender, or non-binary gender individuals in these analysis. The number of these respondents who were either non-heterosexual or

transgender produced a small misclassification error.[23] Additionally, we are unable to determine which infections are persistent. Further research is needed to determine if lesbian and bisexual women are at increased risk for persistent HPV infection compared to heterosexual women. Women excluded from the study who were missing either sexual orientation or HPV labs tended to be older (50 vs. 39 years, $p<0.001$), less often current smokers (16% vs. 21%, $p<0.001$), and less often white (61% vs. 65%, $p=0.019$).

Use of a contraceptive barrier has been associated with a reduction in HPV risk. However, we were unable to create models incorporating use of a condom for vaginal sex or oral sex during the past year due to the high degree of missing values for this item. To examine possible confounding by contraceptive barriers, we examined sensitivity models including contraceptive barriers which yielded similar results. Additionally, thirty women who reported never having sex tested positive for oral or vaginal HPV. This is plausible since HPV is spread by direct skin to skin contact. However, it is possible that these women were at risk for HPV due to other sexual behaviors, such as using sex toys with a partner, or that the questions asked did not elicit a sexual history that would capture risk among non-heterosexual women.

Our results indicate that both oral and vaginal HPV occur within the lesbian and bisexual community at higher rates than the heterosexual population, which is an important public health message for these populations to encourage HPV screening. Further, we identified characteristics associated with increased risk within these populations, most notably with smoking. It is critical for lesbian and bisexual women to know prevalence of HPV infection is increased in current smokers, since this is a modifiable risk factor for persistent HPV infection. However, since smoking is often associated with other risky behaviors among lesbian and bisexual women (e.g.

binge drinking and greater number of sexual partners), further research is needed to determine if smoking interventions or more comprehensive risk-reduction interventions would best prevent HPV in these populations. Findings from this study should help inform the planning and implementation of health services, by providing data on the prevalence of oral and vaginal HPV for lesbian and bisexual women. Along with information about risk factors, this information can be used to design tailored interventions for lesbian and bisexual women.

Tables

Table 1. Age Adjusted Demographic Characteristics and HPV Risk Factors by Sexual Orientation, Female NHANES 2009-2014 Participants who ever had sex, % (SE)

Variable	Heterosexual N=4600	Lesbian N=71	Bisexual N=247
Overall	93.7 (0.4)	1.4 (0.3)	4.9 (0.3)
Income,			
<$25k	20.5 (1.3)	40.4 (3.0)	33.9 (2.9)
$25k-$74.9k	38.3 (1.2)	40.6 (3.7)	36.5 (2.3)
≥$75k[a]	41.1 (1.4)	19.0 (2.6)	29.5 (2.4)$^{+}$
Insurance,			
Insured	79.5 (0.9)	60.7 (3.2)	72.1 (2.3)
Uninsured	20.5 (0.9)	39.3 (3.2)	27.9 (2.3)$^{+}$
Race/Ethnicity			
White, non-Hispanic[b]	63.3 (2.1)	54.6 (3.7)	57.3 (3.7)
Black, non-Hispanic[c]	13.0 (1.1)	34.1 (3.3)$^{+}$	23.7 (3.5)
Hispanic[d]	16.4 (1.6)	8.7 (1.9)*	9.9 (1.7)*
Other/multiple races	7.3 (0.5)	2.6 (1.5)	9.1 (1.8)
Education			
< College graduate	68.4 (1.4)	74.0 (3.7)	78.3 (2.6)
≥College graduate	31.6 (1.4)	26.0 (3.7)	21.7 (2.6)*
Tobacco Exposure			
Current smoker[e]	19.6 (1.0)	54.4 (2.1)*	43.0 (2.8)*
Former smoker	16.4 (1.0)	19.4 (1.7)	19.6 (2.0)
Ever smoker[f]	36.0 (1.2)	73.8 (2.5)*	62.5 (2.6)*
Never smoker	64.0 (1.2)	26.2 (2.5)	37.5 (2.6)
Ever HPV vaccine	10.8 (0.6)	13.1 (1.7)	15.8 (1.8)$^{+}$
Relationship Status			
Married/Living with Partner[h]	64.9 (1.0)	29.6 (2.6)*	38.8 (2.9)*
Widowed	1.5 (0.2)	0.0 (0.0)	6.1 (0.9)
Divorced	11.2 (0.6)	10.3 (2.0)	17.1 (2.8)
Separated	3.0 (0.3)	4.0 (0.0)	4.3 (1.3)
Never Married	19.4 (0.8)	56.0 (2.5)	33.7 (2.8)

Note: % (SE) unless otherwise noted; * denotes $p<0.05$ (vs. heterosexual reference group); $^{+}$ denotes $p<0.10$;
a. <$75k vs ≥$75k; b. White vs non-White; c. Black vs non-Black; d. Hispanic vs non-Hispanic; e. Current vs former/never smoker; f. Ever vs never smoker; g. Excluded from 2013-2014 survey; h. Married/Living with Partner vs not married or living with partner

Table 2. Sexual Behavior Characteristics by Sexual Orientation, Female NHANES 2009-2014 Participants who ever had sex, % (SE)

Variable	Heterosexual	Lesbian	Bisexual
Lifetime Gender of Sexual Partner			
Women only	--	24.5 (2.3)	--
Men only	94.8 (0.3)	0.7 (0.5)*	21.7 (2.7)*
Men and Women	5.2 (0.3)	74.8 (2.4)	78.3 (2.7)
Lifetime Number of sexual partners, mean (SE)			
Total	8.0 (0.3)	25.7 (1.7)*	33.2 (7.0)*
Female	0.1 (0.0)	11.7 (1.7)*	11.4 (6.1)$^{+}$
Male	7.9 (0.3)	13.4 (1.0)	21.8 (3.8)*
Past Year Behavior			
Use protection performing oral sex			
Never[a]	58.9 (1.0)	55.7 (2.9)	54.0 (3.2)*
Rarely	2.8 (0.3)	--	6.3 (1.3)
Usually	1.6 (0.2)	0.3 (0.4)	4.3 (1.3)
Always	2.8 (0.2)	9.9 (1.8)	6.3 (1.4)
Missing	34.0 (0.9)	34.1 (2.4)	29.1 (2.4)
Vaginal or anal sex without using a condom			
Never[a]	18.4 (0.7)	14.8 (2.7)*	22.8 (2.8)
< ½ time	10.1 (0.5)	1.8 (0.9)	12.8 (2.2)
½ time	4.3 (0.3)	2.0 (0.8)	6.4 (1.4)
>½ time	8.0 (0.5)	--	3.9 (0.8)
Always	46.1 (0.9)	9.3 (2.1)	33.8 (3.3)
Missing	13.2 (0.6)	72.0 (2.9)	20.3 (2.3)

Age-adjusted prevalence of women from the 2009-2014 NHANES who have ever had sex
Note: % (SE) unless otherwise noted; * denotes $p<0.05$ (vs. heterosexual reference group); $^{+}$ denotes $p<0.10$
a: never vs. >never excluding missing values

Table 3. Prevalence of HPV Infection by Sexual Orientation, Female NHANES 2009-2014 Participants % (SE)

	Heterosexual N=4600	**Lesbian N=71**		**Bisexual N=247**	
	% (SE)	% (SE)	p-value (L vs. H)	% (SE)	p-value (B vs. H)
Self Reported					
	n=4,599	n=71		n=247	
Any type	10.3 (0.6)	5.5 (2.1)	0.444	9.9 (2.0)	0.800
Laboratory Testing					
Vaginal (37 strains)	n=4,331	n=65		n=233	
Any	41.7 (1.1)	41.5 (2.3)	0.157	54.6 (2.7)	0.004*
Low risk[a]	28.4 (0.8)	33.5 (3.1)	0.979	45.1 (2.9)	0.000*
High risk[b]	28.5 (1.1)	25.7 (2.3)	0.130	33.5 (2.8)	0.087[+]
Oral (37 strains)	n=4,427	n=69		n=238	
Any	3.1 (0.3)	7.4 (1.5)	0.680	4.9 (1.5)	0.009*
Low risk[a]	1.7 (0.2)	6.6 (1.3)	0.270	2.0 (0.9)	0.457
High risk[b]	1.6 (0.2)	1.4 (1.0)	0.852	2.9 (1.1)	0.004*

Age-adjusted prevalence of HPV among women from the 2009-2014 NHANES who have ever had sex
Self reported HPV indicates having ever been told by a doctor or medical professional they have HPV.
Positive HPV laboratory test indicates current HPV infection at the time of the survey.
* denotes $p<0.05$; [+] denotes $0.10>p>0.05$; heterosexual reference group
a. Low risk strains include HPV types 6, 11, 40, 42, 54, 55, 61, 62, 64, 67, 69, 70, 71, 72, 81, 83, 84, 89
b. High risk strains include HPV types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82

Table 4. Multivariable logistic regression models for HPV, Female NHANES 2009-2014 Participants Odds Ratio (95% Confidence Interval)

	Vaginal HPV, N=4393			Oral HPV, N=4300	
	Any Strain[a] OR (CI)	High Risk Strain[b] OR (CI)		Any Strain[a] OR (CI)	High Risk Strain[b] OR (CI)
Sexual Orientation			Sexual Orientation		
Heterosexual	1 (Ref)	1 (Ref)	Heterosexual	1 (Ref)	1 (Ref)
Lesbian	0.3 (0.1 ,0.5)*	0.3 (0.1 ,0.6)*	Lesbian	0.7 (0.2 ,2.5)	0.6 (0.1 ,3.0)
Bisexual	1.0 (0.7 ,1.5)	0.9 (0.6 ,1.4)	Bisexual	1.7 (0.8 ,3.3)	2.0 (0.9 ,4.7)[+]
Age	1.0 (1.0 ,1.0)*	1.0 (1.0 ,1.0)*	Age	1.0 (1.0 ,1.0)	1.0 (1.0 ,1.0)
Race			Race		
White	1 (Ref)	1 (Ref)	White	1 (Ref)	1 (Ref)
Black	2.1 (1.7 ,2.6)*	1.4 (1.2 ,1.8)*	Black	1.3 (0.8 ,2.2)	1.2 (0.6 ,2.2)
Hispanic	1.3 (1.0 ,1.5)*	1.1 (0.9 ,1.4)	Hispanic	1.4 (0.9 ,2.3)	1.2 (0.7 ,2.1)
Other	1.0 (0.8 ,1.3)	0.9 (0.6 ,1.2)	Other	1.1 (0.5 ,2.7)	0.7 (0.3 ,2.0)
Smoking Status			Smoking Status		
Never smoker	1 (Ref)	1 (Ref)	Never smoker	1 (Ref)	1 (Ref)
Current smoker	1.8 (1.5 ,2.3)*	1.7 (1.4 ,2.2)*	Current smoker	2.8 (2.0 ,4.1)*	2.5 (1.5 ,4.4)*
Education level			Education level		
< College	1 (Ref)	1 (Ref)	< College	1 (Ref)	1 (Ref)
≥ College	0.7 (0.6 ,0.9)*	0.8 (0.6 ,1.0)*	≥ College	0.6 (0.3 ,1.4)	0.7 (0.3 ,1.6)
Number of Lifetime Sexual Partners	1.0 (1.0 ,1.0)[+]	1.0 (1.0 ,1.0)	Number of Lifetime Sexual Partners	1.0 (1.0 ,1.0)	1.0 (1.0 ,1.0)
Relationship Status			Relationship Status		
Single	1 (Ref)	1 (Ref)	Single	1 (Ref)	1 (Ref)
Married/Partnered	0.4 (0.4 ,0.5)*	0.4 (0.4 ,0.5)*	Married/Partnered	0.6 (0.4 ,1.0)*	0.6 (0.3 ,1.2)

* denotes $p<0.05$, heterosexual reference group

[+] denotes $0.10>p>0.05$, heterosexual reference group

a. Any strain include HPV types 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73 ,81, 83, 84, 89

b. High risk strains include HPV types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82

References

1. Satterwhite, C. L., Torrone, E., Meites, E., Dunne, E. F., Mahajan, R., Ocfemia, M. C., Su, J., Xu, F, Weinstock, H. (2013). Sexually transmitted infections among US women and men: Prevalence and incidence estimates, 2008. *Sexually Transmitted Diseases, 40*(3), 187-193.

2. De Villiers, E., Fauquet, C., Broker, T. R., Bernard, H., & zur Hausen, H. (2004). Classification of papillomaviruses. *Virology, 324*(1), 17-27.
3. Cogliano, V., Baan, R., Straif, K., Grosse, Y., Secretan, B., & El Ghissassi, F. (2005). Carcinogenicity of human papillomaviruses. *Lancet Oncology, 6*(4), 204.
4. Chaturvedi, A. K., Engels, E. A., Pfeiffer, R. M., Hernandez, B. Y., Xiao, W., Kim, E., Jiang, B., Goodman, M., Sibug-Saber, M. Cozen, W, Liu, L., Lynch, C., Wenterzensen, Br., Altekruse, S., Anderson, W., Rosenberg, P., Gillison, M. (2011). Human papillomavirus and rising oropharyngeal cancer incidence in the United States. *Journal of Clinical Oncology, 29*(32), 4294-4301.
5. Gillison, M. L., Chaturvedi, A. K., & Lowy, D. R. (2008). HPV prophylactic vaccines and the potential prevention of noncervical cancers in both men and women. *Cancer, 113*(S10), 3036-3046.
6. National Institutes of Health. (1996). NIH consensus development panel. consensus development conference statement: Cervical cancer. *J Natl Cancer Inst Monographs, 21.*
7. Koh, A. S., Gómez, C. A., Shade, S., & Rowley, E. (2005). Sexual risk factors among self-identified lesbians, bisexual women, and heterosexual women accessing primary care settings. *Sexually Transmitted Diseases, 32*(9), 563-569.

8. Gruskin, E. P., Greenwood, G. L., Matevia, M., Pollack, L. M., & Bye, L. L. (2007). Disparities in smoking between the lesbian, gay, and bisexual population and the general population in california. *American Journal of Public Health, 97*(8), 1496-1502.
9. Ward, B. W., Dahlhamer, J. M., Galinsky, A. M., & Joestl, S. S. (2014). Sexual orientation and health among US adults: National health interview survey, 2013. *Natl Health Stat Report, 77*, 1-12
10. Matthews, A. K., Brandenburg, D. L., Johnson, T. P., & Hughes, T. L. (2004). Correlates of underutilization of gynecological cancer screening among lesbian and heterosexual women. *Preventive Medicine, 38*(1), 105-113.
11. Reiter, P. L., & McRee, A. L. (2017). HPV infection among a population-based sample of sexual minority women from USA. *Sexually Transmitted Infections, 93*(1), 25-31.
12. National Center for Health Statistics. (a). *National health and nutrition examination survey (NHANES): MEC laboratory procedures manual.* Retrieved 04/14, 2017, from https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/manuals/2013_MEC_Laboratory_Procedures_Manual.pdf
13. National Center for Health Statistics. (b). *National health and nutrition examination survey: Sample design, 2011–2014.* Retrieved 04/14, 2017, from https://wwwn.cdc.gov/nchs/data/series/sr02_162.pdf
14. Klein, R. J., & Schoenborn, C. A. (2001). Age adjustment using the 2000 projected US population.

15. Dunne, E. F., Unger, E. R., Sternberg, M., McQuillan, G., Swan, D. C., Patel, S. S., et al. (2007). Prevalence of HPV infection among females in the United States. *Jama, 297*(8), 813-819.

16. Gillison, M. L., Broutian, T., Pickard, R. K., Tong, Z., Xiao, W., Kahle, L., et al. (2012). Prevalence of oral HPV infection in the united states, 2009-2010. *Jama, 307*(7), 693-703.

17. Meyer, I. H., Schwartz, S., & Frost, D. M. (2008). Social patterning of stress and coping: Does disadvantaged social statuses confer more stress and fewer coping resources? *Social Science & Medicine, 67*(3), 368-379.

18. Balsam, K. F., Beadnell, B., & Riggs, K. R. (2012). Understanding sexual orientation health disparities in smoking: A Population-Based analysis. *American Journal of Orthopsychiatry, 82*(4), 482-493.

19. Rosario, M., Reisner, S. L., Corliss, H. L., Wypij, D., Calzo, J., & Austin, S. B. (2014). Sexual-orientation disparities in substance use in emerging adults: A function of stress and attachment paradigms. *Psychology of Addictive Behaviors, 28*(3), 790.

20. Sellors, J. W., Mahony, J. B., Kaczorowski, J., Lytwyn, A., Bangura, H., Chong, S., et al. (2000). Prevalence and predictors of human papillomavirus infection in women in ontario, canada. survey of HPV in ontario women (SHOW) group. *CMAJ : Canadian Medical Association Journal = Journal De l'Association Medicale Canadienne, 163*(5), 503-508.

21. Wheeler, C. M., Parmenter, C. A., Hunt, W. C., Becker, T. M., Greer, C. E., Hildesheim, A., et al. (1993). Determinants of genital human papillomavirus infection among

cytologically normal women attending the university of new mexico student health center. *Sexually Transmitted Diseases, 20*(5), 286-289.

22. Bowleg, L. (2008). When black lesbian woman≠ black lesbian woman: The methodological challenges of qualitative and quantitative intersectionality research. *Sex Roles, 59*(5-6), 312-325.
23. Dahlhamer, J. M., Galinsky, A. M., Joestl, S. S., & Ward, B. W. (2014). Sexual orientation in the 2013 national health interview survey: A quality assessment. *Vital and Health Statistics.Series 2, Data Evaluation and Methods Research, (169)*(169), 1-32.

CHAPTER 4: JOURNAL ARTICLE 2

Comparing Risk of Cardiovascular Disease Between Lesbian, Bisexual, and Heterosexual-Identified Women: National Health and Nutrition Examination Survey 2001-2014

Prepared for American Journal of Public Health

Abstract

Comparing Risk of Cardiovascular Disease Between Lesbian, Bisexual, and Heterosexual-Identified Women in a Nationally Representative Sample of Adult Women: National Health and Nutrition Examination Survey 2001-2014

Background: Previous research indicates sexual minority women including lesbian and bisexual women might be at increased risk for cardiovascular disease (CVD) due to an accumulation of risk factors. In contrast to two studies that examined the Framingham Risk Score (FRS), a 10 year prediction algorithm for CVD, in a combined grouping of non-heterosexual women, we compared risk of CVD of distinct sexual minority groups (lesbian, bisexual, and heterosexual women who have ever had sex with a woman (hetero-WSW)) to heterosexual women who had never had sex with a woman (hetero-NSW).

Methods: Data from the National Health and Nutrition Examination Survey (NHANES) 2001-2014 were used to calculate FRS for all female respondents who identified as lesbian, bisexual, or heterosexual. FRS is based on age, high-density cholesterol (HDL), total cholesterol, systolic blood pressure (SBP), use of hypertensive medications, smoking status, and diabetes status. We also calculated an alternative risk score (FRS-BMI) that incorporates body mass index (BMI) instead of laboratory measurements. FRS and FRS-BMI were used to determine vascular age,

and used to calculate the ratio of vascular age to chronological age. We then fit weighted regression models to compare the FRS and FRS-BMI vascular ratios of lesbian, bisexual, and hetero-WSW with hetero-NSW.

Results: Lesbian, bisexual, and hetero-WSW tended to be younger, more often smokers, less often married or partnered, with lower HDL and total cholesterol than hetero-NSW. We found an increased vascular ratio by both FRS and FRS-BMI, by a magnitude of 6-7% in bisexual and 4-5% in hetero-WSW compared to hetero-NSW (all $p<0.05$). Lesbian women had a 3% higher risk of CVD by FRS and FRS-BMI than hetero-NSW, though neither result was statistically significant. Excess CVD risk in bisexual and hetero-WSW remained statistically significant in models adjusted for race (white vs. non-white), education (college or higher vs. less than college) and relationship status (married or partnered vs. not). Current smoking status appeared to drive the difference in vascular ratio between bisexual and hetero-WSW versus hetero-NSW.

Conclusion: Lesbian, bisexual, and hetero-WSW had higher 10-year risk of CVD using FRS and FRS-BMI vascular ratios, even after adjusting for other risk factors. These results suggest CVD screening and interventions are critical for improving health among sexual minority women.

Comparing Risk of Cardiovascular Disease Between Lesbian, Bisexual, and Heterosexual-Identified Women in a Nationally Representative Sample of Adult Women: National Health and Nutrition Examination Survey 2001-2014

BACKGROUND

Cardiovascular disease (CVD), or diseases of the heart and blood vessels, are the leading cause of death in both women and men in the US.[1,2] Among others, CVD includes coronary artery disease, arrhythmia, congenital heart defects, heart attack, chest pain (angina), and stroke.[1,2] Well-established risk factors for heart disease include high blood pressure, high blood cholesterol, diabetes, pre-diabetes, smoking, being overweight or obese, being physically inactive, family history of heart disease, history of preeclampsia during pregnancy, unhealthy diet, and age.[3]

Sexual minority women, including lesbian and bisexual identified women or heterosexual-identified women who have sex with women (hetero-WSW), experience higher prevalence of CVD risk factors than heterosexual women who have never had sex with a woman (hetero-NSW) including tobacco use, alcohol consumption, drug use, worse mental health, and obesity.[4-6] In addition to individual risk factors, two studies have examined the risk of CVD event and vascular age using the Framingham Risk Score (FRS), a score developed to provide a 10-year risk of CVD based on a set of factors (i.e., age, high-density lipoprotein cholesterol (HDL), total cholesterol, systolic blood pressure, use of hypertensive medications, smoking status, and diabetes).[7,8] Both studies found that non-heterosexual women are at a greater risk for CVD than heterosexual women. One study compared an aggregate group of sexual minority

women (lesbian, bisexual, and hetero-WSW) to hetero-NSW but were unable to make between group comparisons due to small sample size.[7] The second study compared the risk among 24-34 year olds by sexual identity: heterosexual, mostly heterosexual, bisexual, mostly homosexual, and homosexual.[8] In the present study we will be able to address limitations of each of these studies, aggregation of sexual minority groups and lack of older participants. First, although lesbian, bisexual, and hetero-WSW are collectively part of the general umbrella of sexual minority women, previous research has detected differences in health outcomes between these groups who have distinctive characteristics including behavior, risk factors, and social support that warrant sufficiently powered risk analysis for each sexual minority group.[9,10] Our study will examine sexual minority groups distinctively, based on both sexual orientation and behavior, and compare lesbian, bisexual, and heterosexual women who have sex with women (hetero-WSW) to heterosexual women who have never had sex with a woman (hetero-NSW). The differential contribution of sexual orientation and behavior has not been previously measured in terms of CVD risk. Secondly, this study utilizes information from participants 18-59, allowing for the study of CVD risk in older populations.

METHODS

This study used public data from the National Health and Nutrition Examination Survey (NHANES), collected by the National Center for Health Statistics, from years 2001-2014. Data were collected in two-year cycles and inquiry on sexual orientation among female participants began in 2001. Data were collected through a multi-stage sampling to yield a nationally representative sample of non-institutionalized respondents, and oversampled black, Hispanic, and older (>60 years old) participants.[11-13]

Sexual orientation was defined by a single item question asked of female respondents by NHANES "*Do you think of yourself as…?*" with the following choices: heterosexual or straight (attracted to men), homosexual or lesbian (attracted to women), bisexual (attracted to men and women), something else, not sure, refused, or don't know. All participants who answered heterosexual, lesbian, or bisexual were included in the analysis, thereby excluding those who answered "something else," "not sure," "don't know" or refused to answer their sexual orientation identity. Further, heterosexual women were subdivided into those who had ever had sex with a woman by those who responded yes to *"Have you ever had any kind of sex with a woman? By sex, we mean sexual contact with another woman's vagina or genitals."* Hetero-NSW served as the reference group, compared with lesbian, bisexual, and hetero-WSW.

The FRS, a 10-year prediction algorithm for CVD in adults without prior history of CVD, was calculated based on the following risk factors: age, HDL, total cholesterol, SBP, use of hypertensive medications, smoking status and diabetes status.[14] A second risk score (FRS-BMI) was calculated using body mass index (BMI) in place of laboratory-based predictors.[14] In each scoring scheme (FRS and FRS-BMI), each risk factor contributes a point value and the total of the points corresponds to a vascular age for each woman. Vascular age reflects the age of a person with similar risk, but with all risk factors within the normal range. The ratio of the FRS and FRS-BMI vascular age to the woman's chronological age determine the FRS and FRS-BMI vascular ratio, and provides a metric to understand the accumulated risk of a person relative to their age.[14] For example, a 40 year- old woman with diabetes, and total cholesterol level of 240 has a vascular age of 68, and the ratio of her vascular age to chronological age is 1.70, indicating her vascular system is approximately 70% older than her age.

Vascular ratio and prevalence of risk factors for cardiovascular disease and demographic characteristics were compared between lesbian, bisexual, and hetero-WSW, with hetero-NSW using weighted regression models. All testing was performed at the 2-sided α=0.05 level of significance with hetero-NSW as the reference, using STATA 13.0. Missing data were assumed to be missing at random.

Additionally, to determine which risk factors contribute to the difference in CVD risk by sexual orientation identity, we constructed models for FRS and FRS-BMI, with an additional covariate in the model for each of the component risk factors. We considered an individual predictor to account for the CVD risk if the adjusted models attenuated the difference between lesbian, bisexual or hetero-WSW with hetero-NSW.

RESULTS

From 2001-2014, 15279 women completed the sexual behavior questionnaire and 11531 responded to the question about their sexual orientation. We excluded 348 responses who answered “something else”, “not sure”, or “don’t know”, or who refused to answer their sexual orientation. Women who had ever had any cardiovascular event, including congestive heart failure, coronary heart disease, angina/angina pectoris, heart attack, or stroke (n=417), or who were missing information on history of a cardiac event (n=405) were excluded from the analysis. FRS is a validated predictor of 10-year risk of CVD among individuals without previous CVD. Additionally, 2853 women were missing components of the FRS and excluded from analysis. The final analytic sample of 7508 was composed of 97 lesbian, 256 bisexual, 162 hetero-WSW and 6993 hetero-NSW.

Bisexual and hetero-WSW had lower income than hetero-NSW ($p<0.05$, Table 1). Lesbian, bisexual, and hetero-WSW were less likely to be insured than hetero-NSW (30%, 25%, and 29% vs 19%, $p<0.05$ for all), and were less often married or living with a partner (33%, 46%, 49%, vs. 66%, $p<0.05$ for lesbian and bisexual, $p<0.10$ for hetero-WSW). Bisexual women were more often white, less often Hispanic, and less likely to have graduated from college ($p<0.05$ for all).

Of the eight risk factors incorporated in the FRS, sexual minority women tended to be younger age, have a lower risk for total cholesterol, and higher risk for smoking status and HDL cholesterol ($p<0.05$ for each, Table 2). Bisexual and hetero-WSW were younger than hetero-NSW and lesbian, bisexual, and hetero-WSW had lower total cholesterol than hetero-NSW ($p<0.05$ for all). Lesbian, bisexual, and hetero-WSW were approximately twice as likely to be smokers as hetero-NSW (40%, 42%, 38% vs. 21%, respectively), and lesbian and bisexual women had lower total cholesterol levels ($p<0.05$ for all). Additionally, we investigated the difference between groups in triglycerides and low-density lipoprotein cholesterol (LDL) as components of total cholesterol (results not shown). We found that lesbians had significantly lower LDL than hetero-NSW (100mg/L vs 114 mg/L, $p=0.048$), which likely drives their lower total cholesterol levels. Hetero-WSW had significantly lower triglycerides than hetero-NSW (98 mg/dL vs 116 mg/dL, $p=0.030$), contributing to their lower total cholesterol levels.

Both FRS and FRS-BMI vascular ratio were higher for bisexual and hetero-WSW than hetero-NSW ($p<0.05$ for all). Bisexual women were 6-7% older in terms of FRS and FRS-BMI vascular ratio and hetero-WSW were 4-5% older than hetero-NSW by the two measures (Table

3). Lesbian women had an increased vascular age by approximately 3% compared to hetero-NSW by both measures, although this result was not statistically significant.

Multivariate models for FRS vascular ratio indicated an excess in CVD risk for lesbian (2%, p=0.462, Table 3), bisexual (4%, p=0.034) and hetero-WSW (4%, p=0.042) compared to hetero-NSW. Similarly, multivariate models for FRS-BMI vascular ratio indicate similar excess risk for lesbian (2%, p=0.265), bisexual (6%, p=0.003), and hetero-WSW (3%, p=0.086).

In exploratory models to examine the most significant determinants of CVD risk, we found that current smoking status attenuated the excess risk in FRS in both bisexual and hetero-WSW versus hetero-NSW (Table 4). Similarly, the excess CVD risk was attenuated for hetero-WSW in FRS-BMI models. However, CVD risk using the FRS-BMI models was still 3% higher for bisexual versus hetero-NSW.

DISCUSSION

To our knowledge, this is the first study to compare vascular age of women based on sexual orientation using nationally representative data. We found that bisexual and hetero-WSW were older in terms of the FRS vascular ratios than hetero-NSW, which incorporates risk due to age, HDL, total cholesterol, SBP, hypertension medications, current smoking status, and diabetes. Similar excess risk was detected using FRS-BMI, which incorporates risk due to BMI in place of laboratory measurements. These results remained consistent in multivariable models adjusting for race, education, and relationship status. Lesbian women tended have increased risk indicated by FRS and FRS-BMI vascular ratio, although the increase was not statistically significant. Additionally, the increase in vascular ratios among bisexual and hetero-WSW appears to be primarily driven by smoking status more-so than any of the other FRS components.

These results are consistent with previous research that estimated the vascular ratio of sexual minority women to be approximately 6% greater than heterosexual women.[9,10] This study expands previous research by providing estimates for subgroups of sexual minority women for which the NHANES study was adequately powered, and found an excess risk of CVD as defined by FRS and FRS-BMI vascular age of 3% for lesbian, 6% for bisexual, and 5% for hetero-WSW compared to hetero-NSW. Several studies have found that health disparities might be highest in bisexual women due to stigma even among their sexual minority peers, possibly limiting the positive impact of social support. Further, this study adds to the literature by determining smoking status was the most significant risk factors driving the FRS in each of these subgroups. However, bisexual women experienced 3% higher risk in CVD beyond any risk attributed to smoking status. There was a marginal decrease in difference of magnitude between FRS when adjusted for HDL, although adjusting did completely attenuate the difference between bisexual and hetero-WSW with hetero-NSW. More research is needed to further explore all of the contributors to CVD risk, and in particular, for bisexual women.

Strengths of this study include a large enough dataset to compare each sexual orientation/behavior group to hetero-NSW, as well as laboratory measurements for cholesterol and blood sugar levels, and a nationally representative sample. CVD risk was computed using two validated measures, FRS and FRS-FMI. Limitations include self-reported use of hypertensive medications and smoking status. We were unable to include women who were not asked about their sexual orientation (participants older than 59), or those who indicated their sexual orientation was “something else” or “not sure”. Future research is needed to examine the CVD risk in sexual minority women older than 59. However, researchers have been able to

probe respondents who answered “something else” or “not sure” and found that some respondents did not identify with the labels of “lesbian” or “bisexual” but identified as other sexual minorities, and other respondents did not understand the question.[15] Additionally, we identified sexual minority behavior based on ever having sex with a woman. Sexual behavior varies across a lifetime, and this single point in time measure might not identify women who are currently experiencing stress due to being a sexual minority.

Lesbian, bisexual, and hetero-WSW had higher 10-year risk of CVD using FRS and FRS-BMI vascular ratios, even after adjusting for other risk factors. Smoking status was the most significant contributor to FRS vascular age. Demographic characteristics did not mitigate differences in CVD risk between sexual minority and hetero-NWW. The results, higher CVD risk for sexual minority compared to heterosexual women, suggest CVD screening are critical for improving health in sexual minority women. Further, the identification of smoking as the driving characteristic behind the excess risk points to smoking cessation in sexual minority women as a high-impact intervention to reduce CVD risk.

TABLES

Table 1. Demographic Characteristics by Sexual Orientation, Female National Health and Nutrition Examination Survey 2001-2014, % (SE)

Variable	Hetero-NSW[e] N=6993	Lesbian N=97	Bisexual N=256	Hetero-WSW[f] N=162
Overall	93.3 (0.4)	1.4 (0.2)	3.5 (0.2)	1.9 (0.2)
Income,				
<$25k	18.9 (0.7)	30.5 (3.1)	29.2 (2.8)	36.3 (3.7)
$25k-$74.9k	42.5 (0.9)	46.5 (3.6)	38.2 (3.2)	41.3 (3.2)
≥$75k[a]	38.6 (1.1)	23.0 (3.6)	32.5 (2.4)*	22.4 (2.7)*
Insurance,				
Insured	80.8 (0.7)	69.9 (2.0)	74.6 (2.7)	71.2 (2.8)
Race/Ethnicity				
White, non-Hispanic[b]	67.8 (1.3)	65.2 (3.3)	69.0 (2.6)*	61.0 (3.8)
Black, non-Hispanic[c]	12.1 (0.8)	20.2 (2.7)$^{+}$	19.3 (2.5)	20.6 (3.0)$^{+}$
Hispanic[d]	14.1 (0.9)	10.8 (1.9)	8.3 (1.3)*	10.8 (2.2)
Other/multiple races	6.0 (0.4)	3.7 (1.8)	3.4 (0.9)	7.7 (1.7)
Education				
< College graduate	68.9 (1.0)	72.3 (3.0)	74.5 (3.0)	74.1 (3.4)
≥College graduate	31.0 (1.0)	27.7 (3.0)	25.5 (3.0)*	25.9 (3.4)
Relationship Status				
Married/Living with Partner	65.7 (0.8)	33.1 (2.9)*	45.5 (2.5)*	49.2 (3.7)$^{+}$
Not married/living with partner	34.3 (0.8)	66.9 (2.9)	54.5 (2.5)	50.8 (3.7)

Note: % (SE) unless otherwise noted;
* denotes $p<0.05$ (vs. heterosexual reference group); $^{+}$ denotes $p<0.10$;
a. <$75k vs ≥$75k; b. White vs non-White; c. Black vs non-Black; d. Hispanic vs non-Hispanic
e. Hetero-NSW: heterosexual woman who has never had sex with a woman (Reference group)
f. Hetero-WSW indicates a heterosexual woman who has ever had sex with a woman

Table 2. Framingham Risk Factors among National Health and Nutrition Examination Survey 2001-2014 Female Participants by Sexual Orientation and Behavior, % (SE)

Variable	Hetero-NSW [f]	Lesbian	Bisexual	Hetero-WSW [g]
Age (years), mean(SE)	39.4 (0.2)	37.4 (1.3)	33.0 (0.8)*	37.0 (1.1)*
18-29[a]	24.9 (0.9)	28.5 (5.2)	46.1 (4.0)*	33.1 (5.0)[+]
30-34	11.7 (0.4)	12.1 (3.6)	15.6 (2.5)	13.5 (3.3)
35-39	12.5 (0.6)	14.3 (3.5)	10.6 (2.6)	14.5 (3.3)
40-44	13.7 (0.6)	19.5 (5.2)	7.9 (2.0)	13.2 (3.4)
45-49	14.0 (0.6)	9.1 (3.5)	8.5 (1.7)	5.7 (1.6)
50-54	12.6 (0.6)	7.8 (2.8)	8.9 (2.5)	10.3 (3.1)
55-59	10.6 (0.5)	8.6 (4.4)	2.5 (1.2)	9.8 (2.7)
Smoking Status				
Smoker	21.1 (0.7)	40.1 (6.5)*	42.3 (3.2)*	37.9 (3.8)*
Non-smoker	78.9 (0.7)	59.9 (6.5)	57.7 (3.2)	62.1 (3.8)
Body Mass Index (kg/m^2), mean(SE)	26.9 (0.1)	25.8 (0.8)	26.8 (0.5)	27.2 (0.7)
Normal (<25)	42.8 (0.7)	53.0 (6.4)	45.2 (3.0)	43.8 (4.8)
Overweight (25-29.9)	29.5 (0.6)	23.9 (5.4)	26.2 (3.2)	26.3 (4.5)
Obese (≥30) [b]	27.7 (0.7)	23.0 (5.0)	28.6 (3.5)	29.9 (4.7)
Diabetes				
Yes	4.1 (0.2)	1.0 (0.7)[+]	3.7 (1.4)	2.0 (1.1)
No	95.9 (0.2)	99.0 (0.7)	96.3 (1.4)	98.0 (1.1)
HDL Cholesterol (mg/dL), mean(SE)	58.1 (0.3)	54.7 (1.7)*	54.8 (1.2)*	56.5 (1.6)
≥45[c]	79.9 (0.7)	77.9 (5.0)	74.3 (3.2)[+]	77.6 (3.8)
35-44	16.3 (0.6)	16.8 (4.7)	18.6 (3.0)	18.2 (3.7)
<35	3.8 (0.3)	5.4 (2.2)	7.0 (1.8)	4.3 (2.0)
Total Cholesterol (mg/dL) , mean(SE)	197.4 (0.8)	186.4 (4.4)*	189.4 (3.3)*	190.3 (3.3)*
<160[d]	16.4 (0.6)	25.0 (5.7)	26.4 (3.5)*	28.9 (4.4)*
160-199	40.0 (0.8)	42.4 (5.8)	37.5 (3.8)	26.6 (3.7)
200-239	30.4 (0.8)	21.8 (5.7)	22.0 (3.2)	32.9 (5.0)
240-279	9.9 (0.5)	9.7 (3.0)	10.4 (2.8)	10.2 (2.6)
≥280	3.4 (0.3)	1.1 (0.8)	3.7 (1.5)	1.4 (0.8)
Systolic Blood Pressure (mm Hg) , mean(SE)	119.3 (0.3)	120.3 (2.4)	119.1 (1.5)	118.9 (1.8)
<130[e]	76.4 (0.6)	75.4 (4.8)	75.3 (3.3)	82.3 (3.7)
130-139	10.5 (0.4)	9.1 (3.5)	8.4 (2.1)	4.5 (1.4)
140-149	6.0 (0.4)	9.7 (3.2)	7.9 (2.3)	4.0 (1.7)
150-159	3.2 (0.2)	1.0 (0.7)	3.2 (1.3)	5.8 (2.3)
≥160	3.9 (0.3)	4.9 (2.3)	5.1 (1.7)	3.5 (2.2)
Hypertensive Medications				
Yes	15.8 (0.6)	12.2 (3.7)	10.3 (2.4)	12.4 (3.0)
No	84.2 (0.6)	87.8 (3.7)	89.7 (2.4)	87.6 (3.0)

Note: % (SE) unless otherwise noted; * denotes p<0.05 (vs. heterosexual who have never had sex with a woman reference group); [+] denotes p<0.10; Reference categories- a: <35 vs ≥35; b: <30 vs ≥30; c: ≥45 vs <45; d: <160 vs ≥160; e: <130 vs ≥130; f. Hetero-NSW: heterosexual woman who has never had sex with a woman; g. Hetero-WSW indicates a heterosexual woman who has ever had sex with a woman

Table 3. Framingham Risk Score (FRS) Vascular Ratio of National Health and Nutrition Examination Survey 2001-2014 Female Participants by Sexual Orientation and Behavior, % (SE)

	Ratio (SE)	Unadjusted Difference (95% CI)	Adjusted Difference (95% CI)
FRS Vascular Ratio, N=7179			
Hetero-NSW[a]	1.046 (0.004)		
Lesbian	1.071 (0.026)	0.025 (-0.026, 0.076)	0.018 (-0.031, 0.067)
Bisexual	1.104 (0.018)	0.058 (0.021, 0.094)*	0.038 (0.003, 0.073)*
Hetero-WSW[b]	1.100 (0.023)	0.053 (0.007, 0.099)*	0.043 (0.001, 0.084)*
FRS-BMI Vascular Ratio, N=7410			
Hetero-NSW[a]	1.046 (0.003)		
Lesbian	1.080 (0.022)	0.033 (-0.009, 0.076)	0.022 (-0.017, 0.062)
Bisexual	1.116 (0.019)	0.070 (0.032, 0.108)*	0.055 (0.020, 0.091)*
Hetero-WSW[b]	1.086 (0.019)	0.039 (0.001, 0.077)*	0.031 (-0.005, 0.066)$^{+}$

* denotes p<0.05; heterosexual women who have never had sex with a woman reference group
FRS Vascular Ratio includes: age, HDL, total cholesterol, systolic blood pressure and medications, current smoking status, and diabetes status
FRS-BMI Vascular Ratio includes: age, BMI, systolic blood pressure and medications, current smoking status, and diabetes status
Heterosexual WSW indicates a heterosexual woman who has ever had sex with a woman
Adjusted models include race (white vs. non-white), education (college or higher vs. less than college education), and relationship status (married or partnered vs. not)
a. Hetero-NSW: heterosexual woman who has never had sex with a woman (Reference group)
b. Hetero-WSW indicates a heterosexual woman who has ever had sex with a woman

Table 4. Framingham Risk Score (FRS) and FRS-BMI Vascular Ratio of NHANES 2001-2014 Female Participants by Sexual Orientation and Behavior – Adjusted for Risk Factors, % (SE)

	Lesbian Diff (95% CI)	**Bisexual** Diff (95% CI)	**Hetero-WSW**[c, d] Diff (95% CI)
FRS[a], N=7179			
Unadjusted	0.03 (-0.03, 0.08)	0.06 (0.02, 0.09)*	0.05 (0.01, 0.10)*
Age	0.02 (-0.03, 0.07)	0.05 (0.01, 0.08)*	0.05 (0.00, 0.09)*
HDL	0.01 (-0.03, 0.06)	0.04 (0.01, 0.07)*	0.04 (0.01, 0.08)*
Total Cholesterol	0.04 (-0.01, 0.09)	0.07 (0.03, 0.11)*	0.06 (0.02, 0.10)*
SBP and Treatment	0.02 (-0.02, 0.06)	0.07 (0.04, 0.10)*	0.06 (0.02, 0.09)*
Smoker	-0.01 (-0.06, 0.04)	0.01 (-0.02, 0.04)	0.02 (-0.03, 0.06)
Diabetes	0.04 (-0.01, 0.09)	0.06 (0.02, 0.09)*	0.06 (0.01, 0.11)*
FRS-BMI[b], N=7410			
Unadjusted	0.03 (-0.01, 0.08)	0.07 (0.03, 0.11)*	0.04 (0.00, 0.08)*
Age	0.02 (-0.01, 0.06)	0.04 (0.01, 0.08)*	0.03 (-0.01, 0.06)
SBP and Treatment	0.04 (0.00, 0.07)*	0.08 (0.06, 0.10)*	0.04 (0.02, 0.07)*
Smoker	0.00 (-0.04, 0.04)	0.03 (0.00, 0.07)*	0.01 (-0.03, 0.05)
Diabetes	0.04 (0.00, 0.08)+	0.07 (0.04, 0.11)*	0.04 (0.01, 0.08)*
BMI	0.05 (0.01, 0.09)*	0.07 (0.04, 0.11)*	0.04 (0.00, 0.07)*

* denotes p<0.05; + denotes 0.05 ,p<0.10; hetero-NSW

a. FRS Vascular Ratio includes: age, HDL, total cholesterol, systolic blood pressure and medications, current smoking status, and diabetes status

b. FRS-BMI Vascular Ratio includes: age, BMI, systolic blood pressure and medications, current smoking status, and diabetes status

c. Hetero-NSW: heterosexual woman who has never had sex with a woman (Reference group)

d. Hetero-WSW indicates a heterosexual woman who has ever had sex with a woman

Adjusted models include race (white vs. non-white), education (college or higher vs. less than college education), and relationship status (married or partnered vs. not)

References

1. Centers for Disease Control and Prevention (CDC). (2008). Heart disease facts and statistics. Retrieved: April, 30
2. National Heart Lung and Blood Institute. (2006). Incidence and prevalence: 2006 chart book on cardiovascular and lung diseases. Bethesda, MD: National Institutes of Health.
3. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). (2002). Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. Circulation, 106(25), 3143-3421.
4. Caceres, B., Primiano, J., Luscombe, R., & Brody, A. (2017). Patient and providers perspectives on lesbian, gay, bisexual and transgender issues in long-term care: A systematic review. *Nursing Research, , 66*(2) E84-E84.
5. Ward, B. W., Dahlhamer, J. M., Galinsky, A. M., & Joestl, S. S. (2014). Sexual orientation and health among US adults: National health interview survey, 2013. *Natl Health Stat Report, 77*, 1-12
6. Matthews, A. K., Brandenburg, D. L., Johnson, T. P., & Hughes, T. L. (2004). Correlates of underutilization of gynecological cancer screening among lesbian and heterosexual women. *Preventive Medicine, 38*(1), 105-113.
7. Farmer, G. W., Jabson, J. M., Bucholz, K. K., & Bowen, D. J. (2013). A population-based study of cardiovascular disease risk in sexual-minority women. American Journal of Public Health, 103(10), 1845-1850.

8. Clark, C. J., Borowsky, I. W., Salisbury, J., Usher, J., Spencer, R. A., Przedworski, J. M., et al. (2015). Disparities in long-term cardiovascular disease risk by sexual identity: The national longitudinal study of adolescent to adult health. Preventive Medicine, 76, 26-30.
9. Matthews, D. D., Blosnich, J. R., Farmer, G. W., & Adams, B. J. (2014). Operational definitions of sexual orientation and estimates of adolescent health risk behaviors. *LGBT Health, 1*(1), 42-49.
10. Bostwick, W. B., Boyd, C. J., Hughes, T. L., & McCabe, S. E. (2010). Dimensions of sexual orientation and the prevalence of mood and anxiety disorders in the united states. *American Journal of Public Health, 100*(3), 468-475.
11. National Center for Health Statistics. (a). *National health and nutrition examination survey (NHANES): MEC laboratory procedures manual.* Retrieved 04/14, 2017, from https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/manuals/2013_MEC_Laboratory_Procedures_Manual.pdf
12. National Center for Health Statistics. (b). *National health and nutrition examination survey: Sample design, 2011–2014.* Retrieved 04/14, 2017, from https://wwwn.cdc.gov/nchs/data/series/sr02_162.pdf
13. Klein, R. J., & Schoenborn, C. A. (2001). Age adjustment using the 2000 projected US population.
14. D'Agostino RB, S., Vasan, R. S., Pencina, M. J., Wolf, P. A., Cobain, M., Massaro, J. M., et al. (2008). General cardiovascular risk profile for use in primary care: The framingham heart study. Circulation, 117(6), 743-753.

15. Dahlhamer, J. M., Galinsky, A. M., Joestl, S. S., & Ward, B. W. (2014). Sexual orientation in the 2013 national health interview survey: A quality assessment. *Vital and Health Statistics.Series 2, Data Evaluation and Methods Research, (169)*(169), 1-32.

CHAPTER 5: JOURNAL ARTICLE 3

Comparing Incidence of Cardiovascular Disease Between Lesbian, Bisexual, and Heterosexual-Identified Women: National Health and Nutrition Examination Survey 2001-2014

Prepared for American Journal of Public Health

Abstract

Comparing Incidence of Cardiovascular Disease Between Sexual Minority and Heterosexual Women: National Health and Nutrition Examination Survey (NHANES) 2001-2014

Objective: Previous research suggests that sexual minority women, including lesbian and bisexual women, have an increased risk of cardiovascular disease (CVD). We investigated whether these high-risk groups experienced an increased incidence of CVD in a nationally representative sample of adult women.

Methods: Data were obtained from the National Health and Nutrition Examination Survey (NHANES), 2001-2014. Cox regression analyses and Hazard Ratios (HR) of CVD incidence of lesbian and bisexual (LB) participants were compared to heterosexual-identified women. Final models were adjusted for race and smoking status.

Results: We found an increased risk of CVD in LB women compared to heterosexual women (HR = 1.7; 95% confidence interval (CI) 1.0-2.9). These results were partially attenuated by race adjusted (HR=1.6; 95% CI: 0.9-2.8) and race plus current smoking adjusted (HR=1.4; 95% CI 0.8-2.5) models.

Conclusions: This study is the first to examine incidence of CVD among LB compared to heterosexual women, and found that sexual minority women have higher incidence of CVD. This is consistent with literature which has identified increased risk of CVD among sexual minority

women. These results were attenuated by race and smoking status, allowing the identification of high-risk and high-impact groups that might benefit from targeted interventions.

Comparing Incidence of Cardiovascular Disease Between Sexual Minority and Heterosexual Women: National Health and Nutrition Examination Survey (NHANES) 2001-2014

BACKGROUND

Cardiovascular disease (CVD) is the leading cause of death and approximately 1/3 of adults have at least one type of CVD in the United States (US).[1] CVD is defined as diseases of the heart and blood vessels and includes coronary artery disease, arrhythmia, congenital heart defects, chest pain (angina), heart attack, heart failure, and stroke. CVD is more common in men than women, and varies by race/ethnicity, socioeconomic status, and family history of heart disease, as well as several modifiable risk factors including smoking status, physical activity, obesity, cholesterol, and diabetes.[2]

After dietary risks, smoking is the second leading risk factor for death in the US, and although men are more often smokers than women, sexual minority women (including lesbian and bisexual women) are nearly twice as likely to smoke as heterosexual women.[3,4] In fact, lesbian and bisexual women are not only more likely to be current smokers, but also experience higher levels of stress, are less likely to have health insurance or undergo regular health screenings.[5] Several recent studies have documented an excess risk of CVD among sexual minority women.[6-8] However, to date, no study has examined incidence of CVD in sexual minority women. We used data from a nationally representative sample to compare incidence of CVD in lesbian and bisexual women to heterosexual women.

METHODS

We used data from the National Health and Nutrition Examination Survey (NHANES), collected by the National Center for Health Statistics. Data are collected in 2 year cycles,

oversample older, Hispanic and African-Americans, through multi-stage sampling methods to obtain nationally representative samples of non-institutionalized children and adults.[9-11] All female respondents ages 18-59 years from NHANES 2001-2014 who completed the sexual behavior module and identified their sexual orientation as lesbian, bisexual, or heterosexual were included in the analysis. Sensitivity analyses were conducted to compare characteristics of women who did not complete the module, refused to provide sexual orientation, or specified their sexual orientation as "don't know" or "something else".

Participants were asked if they had ever been told by a doctor or health professional that they had congestive heart failure (CHF), coronary heart disease (CHD), angina/angina pectoris (angina), heart attack, or stroke. Those who answered "Yes" to any of these questions were classified as having a CVD (event). Age at which they were told they had CHF, CHD, angina, heart attack or stroke was collected from respondents who reported each event. Age at first CVD was defined as the youngest age reported for any event. Participants who answered "No" to all CVD event questions were classified as never having a CVD event and censored at study enrollment age. Participants contributed person-time to the analysis until age at first CVD or age at study enrollment (censored). All events reported to occur prior to 16 years of age were considered likely due to congenital anomalies and excluded from further analysis.

Participants were classified by ethnicity and race into Hispanic, non-Hispanic white (white), non-Hispanic black (black), and other race or multiple races (other). Participants were asked at what age they started smoking cigarettes regularly, and the age at which they last smoked cigarettes regularly. Due to the restrictions for analysis of survey data, we were unable to consider smoking status as a time-varying covariate. Therefore participants were classified as

current, former, or never smokers based on whether CVD event or censoring occurred within the window of smoking exposure (start age to stop age). Age at enrollment was considered smoking stop age for those who reported a start age but did not report a stop age and were current smokers at study enrollment.

Race and smoking status at time of event or censor were tabulated by sexual orientation. Univariate and multivariate survey weighted Cox proportional hazards regression models were used to calculate hazard ratios, confidence intervals, and Wald-test p-value. All analyses were performed at the 2-sided α=0.05 level of significance with heterosexual identified women as the reference group using STATA 14.0. Variances were estimated using Taylor series linearization, were age-adjusted, and the analysis took into account survey weights in accordance with NHANES guidelines. [9-11] Due to the structure of the survey data design, we were unable to test the proportional hazards assumption based on Schoenfeld residuals. Instead, the proportional hazards assumption was evaluated by plots of –ln{-ln(survival)} by ln(age) (log-log plots) for each factor (sexual orientation, race, and smoking status). The proportional-hazards assumption was assumed to be violated when the log-log plots crossed each other. We constructed Kaplan Meier graphs for race and smoking status and included terms in the model with log-rank p-value<0.05. We examined possible interactions between sexual orientation with race and smoking status by adding an interaction term to the models in addition to main effects. To further examine heterogeneity, models were stratified by race and smoking status with sexual orientation. Multiple comparisons are not supported for survey data, so 99% CI's were constructed to penalize the stratified estimates.

Data were de-identified and no attempt was made to link to external data sources. The study protocol was reviewed and approved by The University of Texas Health Science Center at Houston Committee for the Protection of Human Subjects prior to conducting the analysis.

RESULTS

Overall, 3.3% of both heterosexual and lesbian and bisexual (LB) women reported ever having CVD. Median age and interquartile range (IQR) of participants were 32 (IQR: 24-43) and 40 years (IQR: 30-49, $p<0.001$, Table 1) for LB and heterosexual women, respectively. The proportional hazards assumption was violated between lesbian and bisexual women, current and former smokers, and white, Hispanic and other race, and therefore categories were combined as lesbian and bisexual (LB) versus heterosexual, former and never smoker (not current) versus current smoker, and white, Hispanic or other race (white*) versus black for analysis (results not shown).

First CVD occurred 5 years earlier in LB women versus heterosexual women (LB 38 vs. heterosexual 43 years, $p=0.07$, Table 1). LB women were more often regular smokers than heterosexual women (42.7% vs. 22.2%, respectively, $p<0.001$). Additionally, a higher proportion of LB were black and a lower proportion were Hispanic than heterosexual women.

The overall incidence of CVD was higher among LB (HR 1.7; 95% CI 1.0-2.9, Table 2) compared to heterosexual respondents. CVD incidence was also higher for black women versus white* (HR 1.9; 95% CI 1.4-2.4), and for current smokers versus non-smokers (HR 3.3; 95% CI 2.5-4.2). Kaplan-Meier survival estimates by sexual orientation, race, and smoking status are shown in Figures 1a-1c. In multivariable models adjusting for race, LB women experienced higher CVD incidence (HR 1.6; 95% CI 0.9-2.8, Table 2). In models adjusted for current

smoking status, the difference between LB with heterosexual women in CVD risk was attenuated by smoking status (HR: 1.5, 95% CI 0.2-2.6). There was no interaction between sexual orientation with race or sexual orientation with smoking status (p=0.898 and p=0.801 respectively for interaction term, results not shown).

We further examined CVD incidence to identify highest risk groups by stratifying by race, smoking status, and race by smoking status as subgroups within sexual orientation. First, stratified by race, women who were black and LB had the highest CVD incidence (HR 2.9; 99% CI 1.1-7.7, Figure 2), followed by black and heterosexual (HR 1.9; 99% CI 1.3-2.7) and white*-LB women (HR 1.7; 99% CI 0.7, 4.1) versus white-heterosexual women. Second, stratified by smoking status, CVD incidence among LB women who smoke was highest (HR 5.0; 99% CI 2.0-12.7), followed by heterosexual smokers (HR 3.2; 99% CI 2.3-4.6), and LB non-smokers (HR 1.3; 99% CI 0.4, 4.7) versus heterosexual non-smokers. Third, simultaneously stratifying by race and smoking status within sexual orientation varied little by race. The greatest risk of CVD incidence was found among LB women who smoke (HR 5.5 for black and 5.2 for white*), heterosexual women who smoked (HR 3.9 for black and 3.1 for white*), LB women who were non-smokers (HR 3.2 for black and 1.2 for white*) and heterosexual black women who were non-smokers (HR 2.3) compared to white*, heterosexual, non-smokers.

DISCUSSION

Previous research has documented an excess risk for CVD among sexual minority women, yet none have examined incidence of CVD.[6-8] We found that lesbian and bisexual women experienced an increase of about 1.7 times incidence of CVD compared to heterosexual women in a nationally representative sample. Moreover lesbian and bisexual women experienced

their first CVD approximately 5 years earlier than heterosexual women. CVD is the leading cause of death, and these results present a first examination into the CVD burden of sexual minority women.[1]

This study, to the best of our knowledge, is the first to examine the hazard ratio for CVD based on sexual orientation. Although NHANES is cross-sectional by design, we were able to utilize reported age of first onset of CVD to compare incidence between lesbian and bisexual with heterosexual women, and to examine interactions with race and smoking status. The greatest risk for CVD occurred in sexual minority women who were current smokers or black, pointing to subgroups which would benefit most from interventions.

Smoking is an established risk factor for CVD and sexual minority women are twice as likely to smoke as heterosexual women[2-4]. We identified lesbian and bisexual women who smoke are over 5 times higher risk for CVD. This might be explained by higher levels of stress experience by sexual minority women, another known risk factor for CVD[2-4]. Our results indicate that smoking attenuates but does not fully eliminate the difference in CVD incidence by sexual orientation. Future studies are needed to examine the full relationship between smoking, stress, and CVD in sexual minority women. Additionally, we identified women who were black and lesbian or bisexual had over 3 times the risk of CVD compared to white heterosexual women. One possible explanation for the excess risk of women who are both black and lesbian or bisexual is examining this health disparity through the theoretical framework of intersectionality. Some researchers have found that individuals who belong to more than one group which has been historically oppressed (e.g. based on race, sexual orientation, gender, socio-economic status (SES)) will manifest as worse health.[14,15] However, health disparities

among individuals belonging to more than one minority group have been mixed, and a recent study found similar prevalence of mental health issues when comparing lesbian, bisexual, and gay men and women by race (black versus white).[14-16]

There are some limitations to our study including self-reported information on history and age of CVD which is subject to recall bias. Further, sexual identity was measured by a single question regarding sexual orientation with limited fixed categories of lesbian, bisexual, and heterosexual. Due to small sample size, those who specified their sexual orientation was something else or did not know were excluded from analysis. Our sensitivity analysis detected that women excluded from analysis who were eligible for the sexual orientation question (<60 years old) tended to be younger and black, but did not differ in current smoking status from those included in analysis. Lastly, sexual orientation was obtained at the time of the survey, and assumed to be constant for participants with CVD. It is possible that sexual orientation at the time of CVD could differ from that ascertained at the time of the survey. However, misclassification of exposure would most likely bias results towards the null.

To our knowledge, this is the first study to examine lifetime incidence of CVD by sexual orientation in a nationally representative sample. It adds to the growing body of literature documenting health disparities among sexual minority women by providing insight into the increased risk of CVD and in particular, the greater burden among black and current smokers. Further investigation among sexual minority women is needed to validate these results across a spectrum of sexual minority identities and racial groups.

Table 1. Demographic Characteristics by Sexual Orientation, Female NHANES 2001-2014, % (SE)

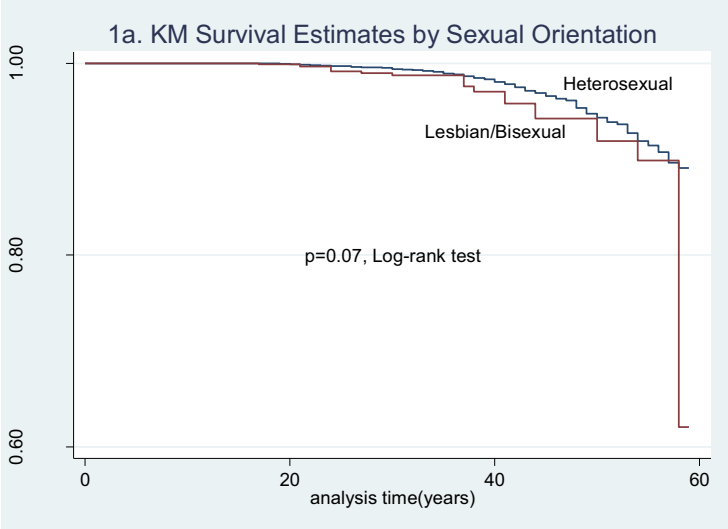
Variable	Heterosexual N=10207	Lesbian or Bisexual N=513	p-value
Age (censored), years			
Median [p25, p75]	40 [30, 49]	32 [24, 43]	<0.001
Mean (SE)	39.7 (0.1)	34.2 (0.5)	<0.001
Smoking Status,			
Current smoker (censored)	22.2 (0.7)	42.7 (2.2)	<0.001
Race/Ethnicity			
White, non-Hispanic[b]	67.9 (1.3)	70.5 (2.4)	0.212
Black, non-Hispanic[c]	12.2 (0.8)	15.8 (1.9)	0.020
Hispanic[d]	13.7 (0.9)	8.7 (1.1)	<0.001
Other/multiple races	6.1 (0.4)	5.0 (1.0)	--
Proportion of CVD Events	3.3 (0.3)	3.3 (0.9)	0.988
Age at CVD,			
Median [p25, p75]	43 [35, 49]	38 [27, 50]	<0.001

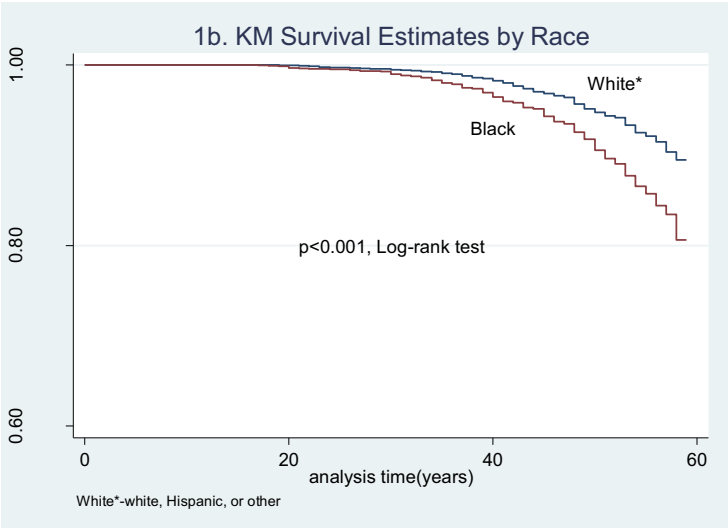
Note: % (SE) unless otherwise noted;

* denotes p<0.05 (vs. heterosexual reference group); $^{+}$ denotes p<0.10;

a. <$75k vs ≥$75k; b. White vs non-White; c. Black vs non-Black; d. Hispanic vs non-Hispanic

Figure 1. Kaplan-Meier (KM) Survival Estimates by Sexual Orientation (1a), Race (1b), and Smoking Status (1c)





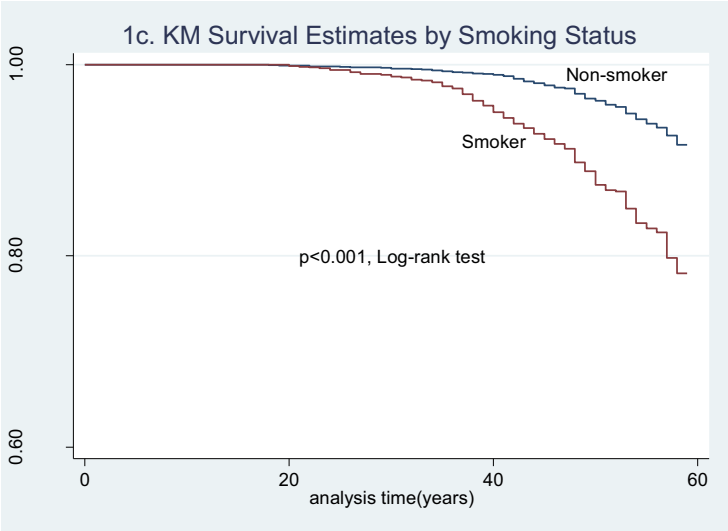
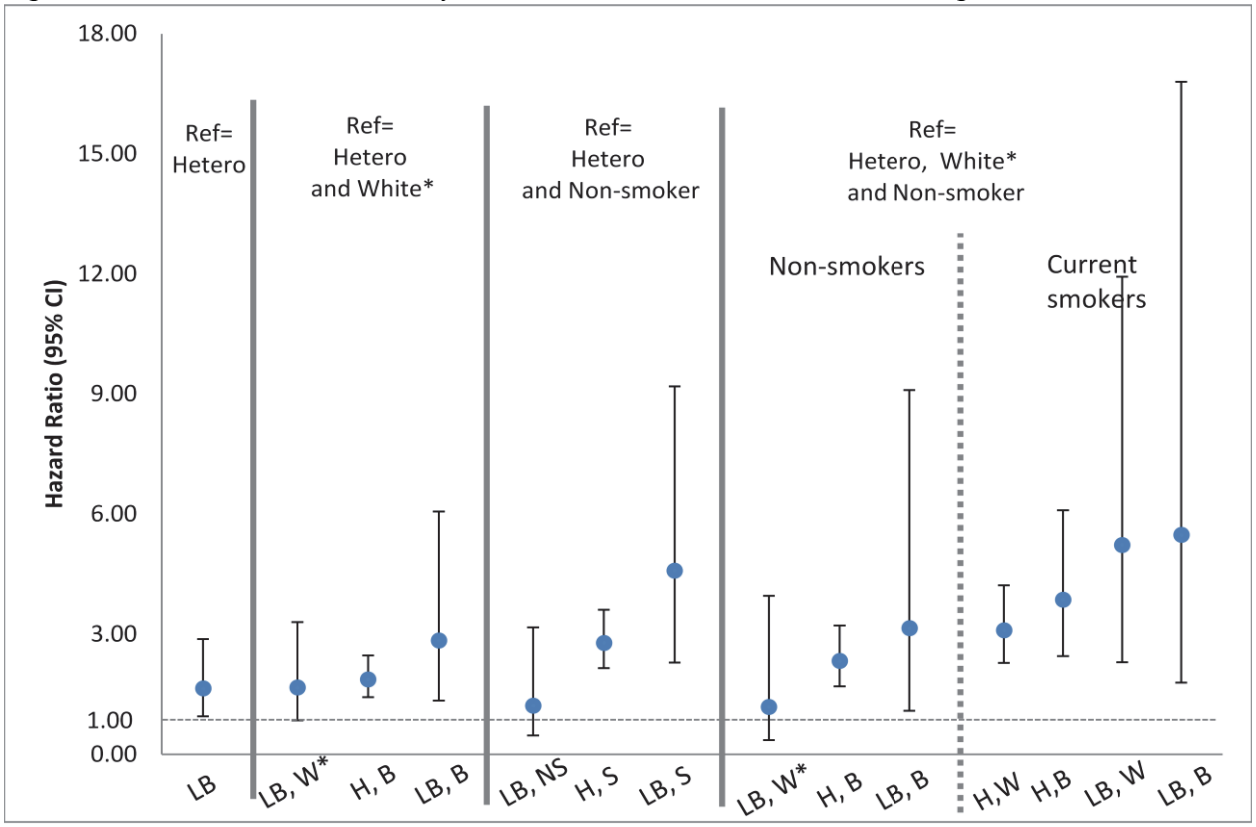


Table 2. Hazard Ratios of CVD; NHANES 2001-2014 Female Participants by Sexual Orientation, % (SE)

	Unadjusted (95% CI)	Race Adjusted (95% CI)	Fully Adjusted (95% CI)
Race/Ethnicity, N=10720			
White/Hispanic/Other	1 (Ref)	--	--
Black	1.9 (1.4, 2.4)*	--	--
Smoking Status, N=10719			
Non-smoker	1 (Ref)	--	--
Current smoker	3.3 (2.5, 4.2)*	--	--
Sexual Orientation, N=10720	N=10720	N=10720	N=10719
Heterosexual	1 (Ref)	1 (Ref)	1 (Ref)
Lesbian/Bisexual	1.7 (1.0, 2.9)$^{+}$	1.6 (0.9, 2.8)$^{+}$	1.4 (0.8, 2.5)

* denotes p<0.05; heterosexual women who have never had sex with a woman reference group
Standard Vascular Ratio includes: age, HDL, total cholesterol, systolic blood pressure and medications, current smoking status, and diabetes status
BMI Vascular Ratio includes: age, BMI, systolic blood pressure and medications, current smoking status, and diabetes status
Adjusted models include race (black, Hispanic, other vs. white), and current smoking status at time of CVD or censored age (current smoker vs non-smoker), and family history of heart attack

Figure 2. Hazard Ratios of CVD by Sexual Orientation, Race, and Smoking Status



Sexual orientation groups: LB-lesbian or bisexual; H-heterosexual
Race/ethnicity groups: B-black, W*-white, Hispanic, or other
Smoking groups: S-current smoker, NS-Former or never smoker
Hetero denotes heterosexual women

References

1. Murray, C. J., Abraham, J., Ali, M. K., Alvarado, M., Atkinson, C., Baddour, L. M., . . . Birbeck, G. (2013). The state of US health, 1990-2010: Burden of diseases, injuries, and risk factors. *Jama, 310*(6), 591-606.
2. Writing Group Members, Mozaffarian, D., Benjamin, E. J., Go, A. S., Arnett, D. K., Blaha, M. J., . . . Stroke Statistics Subcommittee. (2016). Heart disease and stroke statistics-2016 update: A report from the american heart association. *Circulation, 133*(4), e38-360.
3. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). (2002). Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. *Circulation, 106*(25), 3143-3421.
4. Jamal, A., Agaku, I. T., O'Connor, E., King, B. A., Kenemer, J. B., & Neff, L. (2014). Current cigarette smoking among adults--united states, 2005-2013. *MMWR.Morbidity and Mortality Weekly Report, 63*(47), 1108-1112.
5. Conron, K. J. (2008). *A Health Profile of Massachusetts Adults by Sexual Orientation Identity: Results from the 2001-2006 Behavioral Risk Factor Surveillance System Surveys.*
6. Clark, C. J., Borowsky, I. W., Salisbury, J., Usher, J., Spencer, R. A., Przedworski, J. M., et al. (2015). Disparities in long-term cardiovascular disease risk by sexual identity: The national longitudinal study of adolescent to adult health. Preventive Medicine, 76, 26-30.

7. Farmer, G. W., Jabson, J. M., Bucholz, K. K., & Bowen, D. J. (2013). A population-based study of cardiovascular disease risk in sexual-minority women. American Journal of Public Health, 103(10), 1845-1850.

8. Ward, B. W., Dahlhamer, J. M., Galinsky, A. M., & Joestl, S. S. (2014). Sexual orientation and health among US adults: National health interview survey, 2013. *Natl Health Stat Report, 77*, 1-12

9. National Center for Health Statistics. (a). *National health and nutrition examination survey (NHANES): MEC laboratory procedures manual.* Retrieved 04/14, 2017, from https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/manuals/2013_MEC_Laboratory_Procedures_Manual.pdf

10. National Center for Health Statistics. (b). *National health and nutrition examination survey: Sample design, 2011–2014.* Retrieved 04/14, 2017, from https://wwwn.cdc.gov/nchs/data/series/sr02_162.pdf

11. Klein, R. J., & Schoenborn, C. A. (2001). Age adjustment using the 2000 projected US population.

12. Centers for Disease Control and Prevention. Compressed mortality file: underlying cause-of-death 1999–2013. CDC WONDER Online Database. Released October 2014. Atlanta, GA: Centers for Disease Control and Prevention. http://wonder.cdc.gov/mortSQl.html. Accessed September 1, 2015.

13. US Department of Health and Human Services. How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease: A Report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease

Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2010.

14. Bowleg, L. (2008). When black lesbian woman≠ black lesbian woman: The methodological challenges of qualitative and quantitative intersectionality research. *Sex Roles, 59*(5-6), 312-325.

15. Bowleg, L. (2012). The problem with the phrase women and minorities: Intersectionality—an important theoretical framework for public health. *American Journal of Public Health, 102*(7), 1267-1273.

16. Kertzner, R. M., Meyer, I. H., Frost, D. M., & Stirratt, M. J. (2009). Social and psychological Weil-Being in lesbians, gay men, and bisexuals: The effects of race, gender, age, and sexual identity. *American Journal of Orthopsychiatry, 79*(4), 500-510.

CHAPTER 6: CONCLUSIONS

The aim of this dissertation was to investigate health disparities between sexual minorities and heterosexual women. To our knowledge, this is the first study to compare prevalence of oral HPV and incidence of CVD in sexual minority women using nationally representative data. Additionally, we were the first to compare risk of CVD between distinctive groups of sexual minority women (e.g. lesbian vs. heterosexual and bisexual vs. heterosexual).

We identified higher prevalence of oral and vaginal HPV, risk of CVD, and incidence of CVD in sexual minority versus heterosexual women. Prevalence of oral HPV was approximately twice as high for both lesbian and bisexual women, and prevalence of vaginal HPV was 30% higher in bisexual than in heterosexual women. Risk of CVD, measured by FRS, was 3% higher in lesbian and 6% higher in bisexual compared to heterosexual women. The incidence of CVD was 67% higher in lesbian and bisexual women versus heterosexual. All estimates were in the expected direction, and add to the literature documenting that sexual minority women experience a higher risk for and burden of disease compared to heterosexual women.

These results of this study are broadly consistent with previous studies examining health disparities among sexual minority women. Our vaginal-HPV results were similar in magnitude and direction to a recent study which found higher prevalence in bisexual and lower prevalence in lesbian versus heterosexual women.[11] Increased risk of CVD for lesbian, bisexual, and hetero-WSW is also consistent with the increase in vascular age previously detected in disaggregated sexual orientation and behavior groups.[19,20] Further research is needed to examine characteristics that might explain differences between these groups.

One theme throughout this study was the increase in health disparities among women who were current smokers or racial minorities, in addition to being sexual minority women. For instance, in fully adjusted models, bisexual women had twice the odds and current smokers had 2.5 times the odds of high-risk oral HPV. Smoking was also the primary factor driving the excess CVD risk between sexual minority and heterosexual women. Additionally, black women experienced higher risk of CVD, although not statistically significant, and had twice the incidence of CVD. Although these were secondary findings, they serve to identify the most high-risk groups for future studies to confirm. Being black or Hispanic has been associated with higher levels of stress among lesbian and bisexual populations, possibly due to the intersectionality of belonging to more than one minority group (e.g. black lesbian women).[21,34-36] Intersectionality provides a framework to view individuals who belong to more than one marginalized population (e.g. based on race, sexual orientation, gender, and socio-economic status), which sometimes manifests as worse health outcomes.[34-36] However, research involving sexual minorities who are also black or Hispanic have shown mixed results, including a recent study detecting similar prevalence of mental health issues comparing lesbian, bisexual, and gay men and women by race (black versus white).[37] Graphs were created to view each of the primary outcomes (prevalence of oral HPV, risk of CVD, and incidence of CVD) by sexual orientation and race/ethnicity (Figures 2a-2c). The majority of these graphs illustrate better outcomes for white and worse outcomes for black and Hispanic, with a few exceptions. No testing was done to compare these groups. Further research is needed to determine the variation of health disparities of sexual minority women across race and ethnic groups. Additionally, if women of minority race/ethnicity used smoking as a coping mechanism, this could explain some of the added health

burden within the context of the Minority Stress Theory.[17] This theory suggests that health disparities among sexual minority groups are the result of chronic stress due to being a sexual minority as well as unhealthy coping mechanisms (e.g. smoking).[17] The extent to which these stressors drive the difference detected in the health outcomes measured in the current study (HPV prevalence, CVD risk, and CVD incidence) could be further examined by comparing stress levels between sexual minority versus heterosexual women.

Strengths of this study include a large enough dataset to compare each outcome by sexual orientation/behavior group, as well as laboratory measurements for HPV strain, cholesterol, and blood sugar levels. Moreover, this dataset is nationally representative. Limitations include the use of cross-sectional data and of self-reported measures for smoking status, hypertensive medications, and age at first CVD event.

This study is the first to compare prevalence of oral HPV or incidence of CVD in sexual minority to heterosexual women. It expands research in health disparities by moving beyond excess risk to identifying the burden of disease in sexual minority women. Further, this research further underscores the importance of treating distinctive groups by sexual orientation and behavior as such, by documenting the varying impact of some diseases more to one group than another. Previous studies lacked sufficient sample size to disaggregate these groups for comparison, which might have several causes including lack of participation in research by sexual minorities, lack of proper methods to capture information on sexual orientation and behavior, and lack of knowledge of the existence of these health disparities. Our hope is that it will serve to provide robust measures of health disparities that might add to the importance of the collection of sexual identity measures in healthcare data.

Heart disease and cancer account for over half of female deaths in the United States.[1] After dietary risks, smoking is the second leading risk factor for death in the US. This research adds to the growing body of literature documenting health disparities among sexual minority women by providing insight into increased prevalence of HPV, risk of CVD, and incidence of CVD finding the greatest burden among black and current smokers. Further investigation among sexual minority women is needed to validate these results across a spectrum of sexual orientation and behaviors, ideally through a cohort design. Lesbian, bisexual, and hetero-WSW would benefit from interventions for HPV and CVD including smoking cessation and need to be inclusive of race/ethnic minority groups to target the most at-risk populations.

TABLES

Table 1. Power estimates for Lesbian and Bisexual versus Heterosexual prevalence of diseases

Power = 0.80; N-heterosexual=10635; α=0.05								
Heterosexual	Bisexual, n=403				Lesbian, n=144			
	Design Factor = 1		Design Factor = 2		Design Factor = 1		Design Factor = 2	
Cntrl	Trt|H1	Diff	Trt|H1	Diff	Trt|H1	Diff	Trt|H1	Diff
P2	P1	D1	P1	D1	P1	D1	P1	D1
0.100	0.145	0.045	0.165	0.065	0.176	0.076	0.211	0.111
0.150	0.203	0.053	0.226	0.076	0.239	0.089	0.278	0.128
0.200	0.259	0.059	0.284	0.084	0.298	0.098	0.341	0.141
0.250	0.313	0.063	0.340	0.090	0.355	0.105	0.400	0.150
0.300	0.366	0.066	0.394	0.094	0.410	0.110	0.457	0.157
0.350	0.419	0.069	0.447	0.097	0.464	0.114	0.511	0.161
0.400	0.470	0.070	0.499	0.099	0.516	0.116	0.564	0.164
0.450	0.521	0.071	0.550	0.100	0.567	0.117	0.614	0.164
0.500	0.571	0.071	0.600	0.100	0.617	0.117	0.664	0.164
0.550	0.620	0.070	0.649	0.099	0.665	0.115	0.711	0.161
0.600	0.669	0.069	0.697	0.097	0.713	0.113	0.757	0.157
0.650	0.717	0.067	0.744	0.094	0.759	0.109	0.801	0.151
0.700	0.764	0.064	0.789	0.089	0.803	0.103	0.843	0.143
0.750	0.810	0.060	0.833	0.083	0.847	0.097	0.883	0.133
0.800	0.855	0.055	0.876	0.076	0.888	0.088	0.920	0.120
0.850	0.898	0.048	0.917	0.067	0.927	0.077	0.954	0.104
0.900	0.940	0.040	0.955	0.055	0.963	0.063	0.983	0.083

FIGURES

Figure 1. Power estimates for Lesbian and Bisexual versus Heterosexual prevalence of diseases

Figure 1: Power estimates for Lesbian and Bisexual versus Heterosexual prevalence of diseases

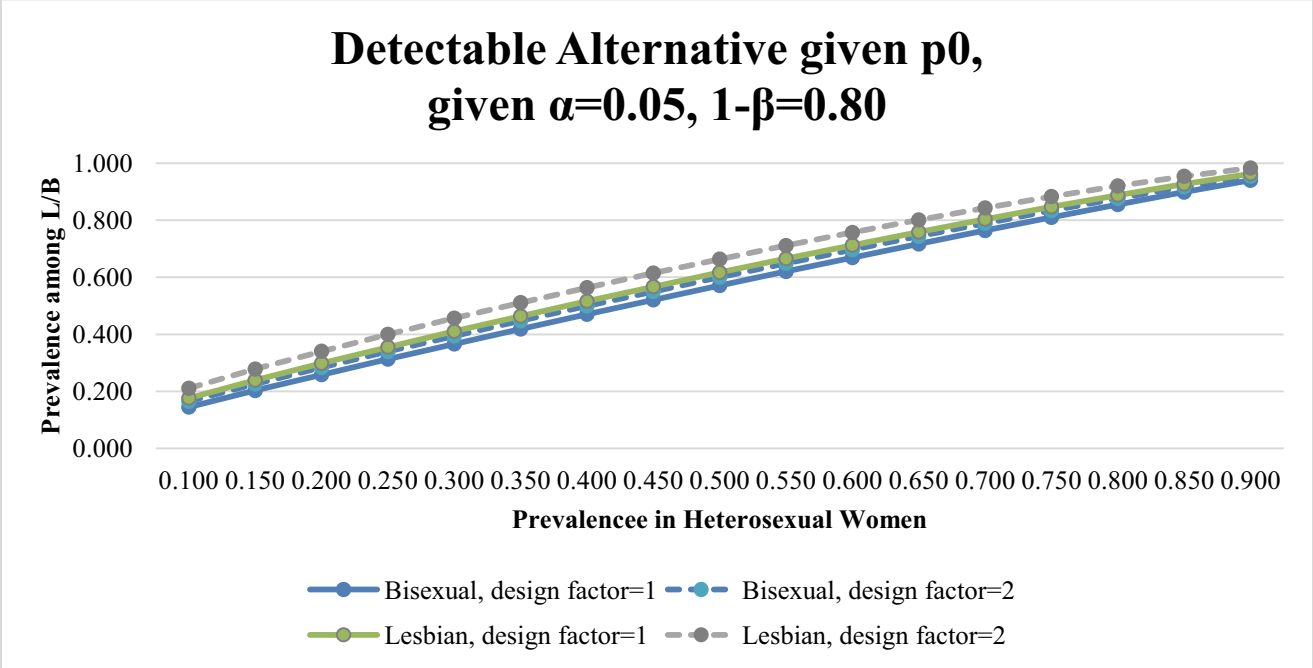
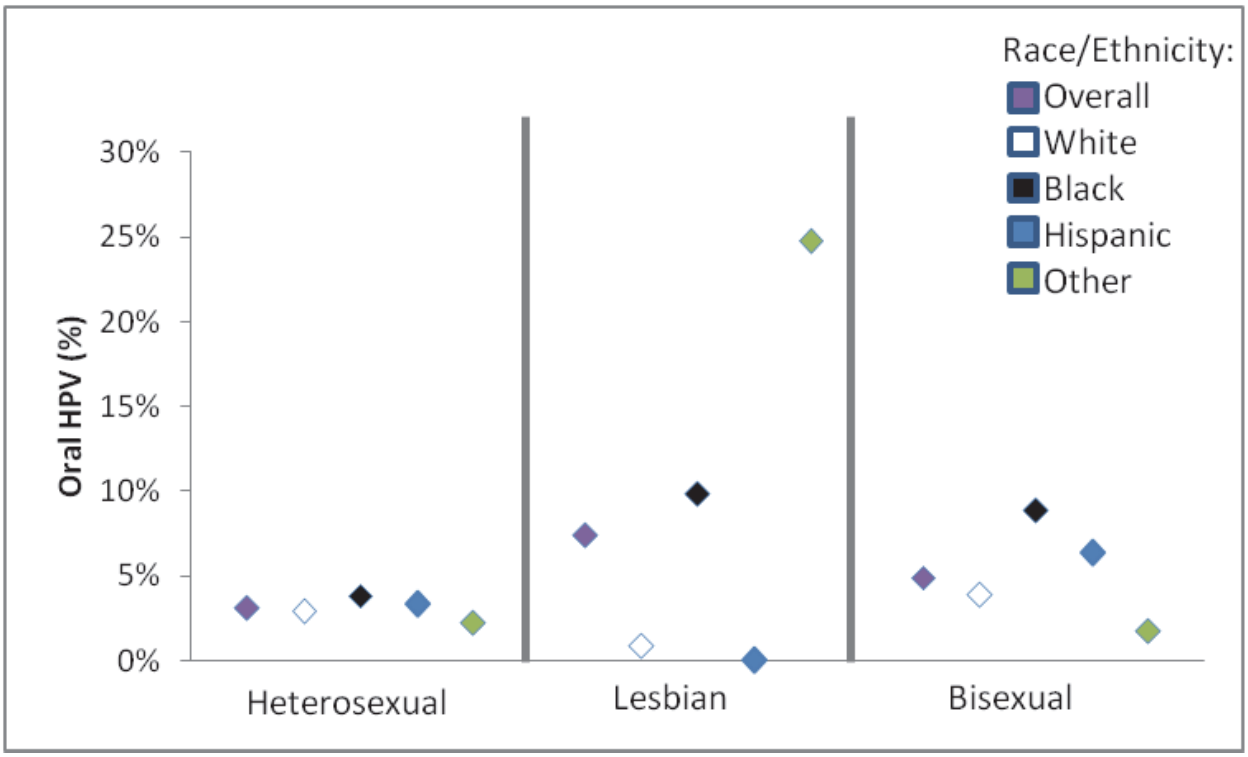
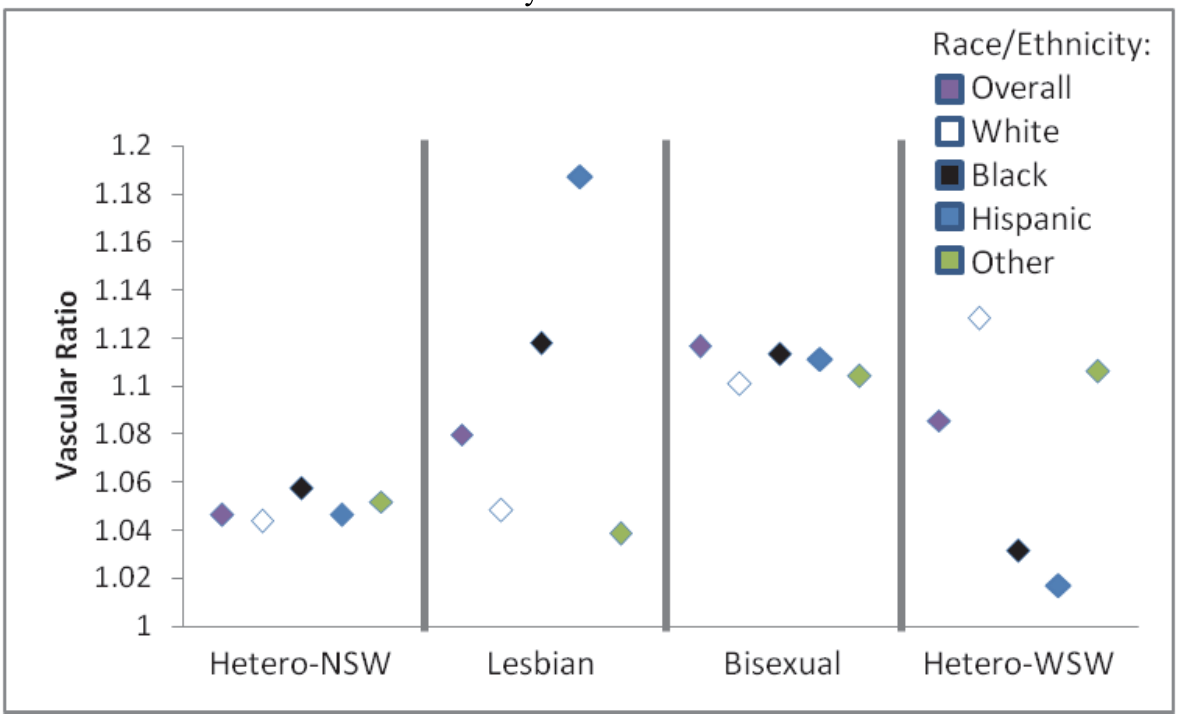


Figure 2a: Prevalence of Oral HPV Infection (%) by Sexual Orientation and Race/Ethnicity, National Health and Nutrition Examination Survey (NHANES) 2009-2014 Female Participants



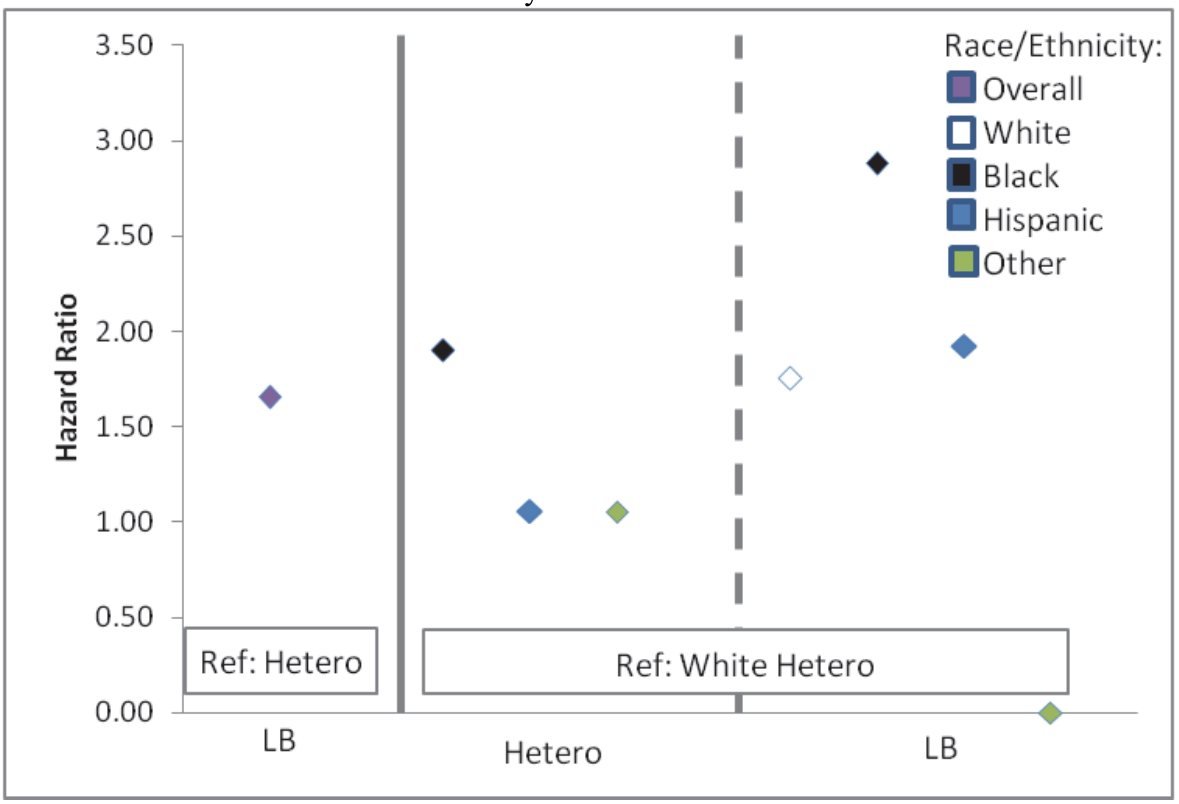
Age-adjusted prevalence of oral HPV infection among women from the 2009-2014 NHANES who have ever had sex. Positive HPV laboratory test indicates current HPV infection at the time of the survey.

Figure 2b: Framingham Risk Score (FRS) Vascular Ratio of National Health and Nutrition Examination Survey (NHANES) 2001-2014 Female Participants by Sexual Orientation and Race/Ethnicity



FRS Vascular Ratio includes: age, HDL, total cholesterol, systolic blood pressure and medications, current smoking status, and diabetes status

Figure 2c: Hazard Ratios of Cardiovascular Disease (CVD), National Health and Nutrition Examination Survey (NHANES) 2001-2014 Female Participants by Sexual Orientation and Race/Ethnicity



LB denotes lesbian or bisexual
Hetero denotes heterosexual

REFERENCES

1. Centers for Disease Control and Prevention (CDC). (2008). Heart disease facts and statistics. Retrieved: April, 30
2. National Heart Lung and Blood Institute. (2006). Incidence and prevalence: 2006 chart book on cardiovascular and lung diseases. Bethesda, MD: National Institutes of Health.
3. Satterwhite, C. L., Torrone, E., Meites, E., Dunne, E. F., Mahajan, R., Ocfemia, M. C., Su, J., Xu, F, Weinstock, H. (2013). Sexually transmitted infections among US women and men: Prevalence and incidence estimates, 2008. *Sexually Transmitted Diseases, 40*(3), 187-193.
4. Ward, B. W., Dahlhamer, J. M., Galinsky, A. M., & Joestl, S. S. (2014). Sexual orientation and health among US adults: National health interview survey, 2013. *Natl Health Stat Report, 77*, 1-12
5. Matthews, A. K., Brandenburg, D. L., Johnson, T. P., & Hughes, T. L. (2004). Correlates of underutilization of gynecological cancer screening among lesbian and heterosexual women. *Preventive Medicine, 38*(1), 105-113.
6. Cogliano, V., Baan, R., Straif, K., Grosse, Y., Secretan, B., & El Ghissassi, F. (2005). Carcinogenicity of human papillomaviruses. *Lancet Oncology, 6*(4), 204.
7. Chaturvedi, A. K., Engels, E. A., Pfeiffer, R. M., Hernandez, B. Y., Xiao, W., Kim, E., Jiang, B., Goodman, M., Sibug-Saber, M. Cozen, W, Liu, L., Lynch, C., Wenterzensen, Br., Altekruse, S., Anderson, W., Rosenberg, P., Gillison, M. (2011). Human papillomavirus and rising oropharyngeal cancer incidence in the United States. *Journal of Clinical Oncology, 29*(32), 4294-4301.

8. Gillison, M. L., Chaturvedi, A. K., & Lowy, D. R. (2008). HPV prophylactic vaccines and the potential prevention of noncervical cancers in both men and women. *Cancer, 113*(S10), 3036-3046.
9. Xu F, Sternberg MR, Markowitz LE. Women who have sex with women in the united states: Prevalence, sexual behavior and prevalence of herpes simplex virus type 2 infection-results from national health and nutrition examination survey 2001-2006. *Sex Transm Dis*. 2010;37(7):407-413.
10. Koumans EH, Sternberg M, Bruce C, et al. The prevalence of bacterial vaginosis in the united states, 2001-2004; associations with symptoms, sexual behaviors, and reproductive health. *Sex Transm Dis*. 2007;34(11):864-869.
11. Reiter, P. L., & McRee, A. L. (2017). HPV infection among a population-based sample of sexual minority women from USA. *Sexually Transmitted Infections, 93*(1), 25-31.
12. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III) final report. *Circulation*. 2002;106(25):3143-3421.
13. Caceres, B., Primiano, J., Luscombe, R., & Brody, A. (2017). Patient and providers perspectives on lesbian, gay, bisexual and transgender issues in long-term care: A systematic review. *Nursing Research, , 66*(2) E84-E84.
14. Ward BW, Joestl SS, Galinsky AM, Dahlhamer JM. Selected diagnosed chronic conditions by sexual orientation: A national study of US adults, 2013. *Prev Chronic Dis*. 2015;12:E192.

15. Matthews DD, Lee JG. A profile of north carolina lesbian, gay, and bisexual health disparities, 2011. *Am J Public Health*. 2014;104(6):e98-e105.

16. Conron KJ. *A health profile of Massachusetts adults by sexual orientation identity: Results from the 2001-2006 Behavioral Risk Factor Surveillance System Surveys*. 2008.

17. Blosnich JR, Farmer GW, Lee JG, Silenzio VM, Bowen DJ. Health inequalities among sexual minority adults: Evidence from ten US states, 2010. *Am J Prev Med*. 2014;46(4):337-349.

18. D'Agostino RB S, Vasan RS, Pencina MJ, et al. General cardiovascular risk profile for use in primary care: The framingham heart study. *Circulation*. 2008;117(6):743-753.

19. Farmer, G. W., Jabson, J. M., Bucholz, K. K., & Bowen, D. J. (2013). A population-based study of cardiovascular disease risk in sexual-minority women. American Journal of Public Health, 103(10), 1845-1850.

20. Clark, C. J., Borowsky, I. W., Salisbury, J., Usher, J., Spencer, R. A., Przedworski, J. M., et al. (2015). Disparities in long-term cardiovascular disease risk by sexual identity: The national longitudinal study of adolescent to adult health. Preventive Medicine, 76, 26-30.

21. Meyer IH. Prejudice, social stress, and mental health in lesbian, gay, and bisexual populations: Conceptual issues and research evidence. *Psychol Bull*. 2003;129(5):674.

22. Meyer IH. Minority stress and mental health in gay men. *J Health Soc Behav*. 1995;36(1):38-56.

23. Meyer IH, Wilson PA. Sampling lesbian, gay, and bisexual populations. *Journal of Counseling Psychology*. 2009;56(1):23-31.

24. Meyer IH, Northridge ME, SpringerLink (Online service). *The health of sexual minorities: Public health perspectives on lesbian, gay, bisexual, and transgender populations.* New York: Springer; 2007. 10.1007/978-0-387-31334-4.

25. Meyer IH. Prejudice, social stress, and mental health in lesbian, gay, and bisexual populations: Conceptual issues and research evidence. *Psychol Bull*. 2003;129(5):674.

26. Fitzpatrick KK, Euton SJ, Jones JN, Schmidt NB. Gender role, sexual orientation and suicide risk. *J Affect Disord*. 2005;87(1):35-42.

27. Katz-Wise SL, Hyde JS. Victimization experiences of lesbian, gay, and bisexual individuals: A meta-analysis. *J Sex Res*. 2012;49(2-3):142-167.

28. Cochran SD, Sullivan JG, Mays VM. Prevalence of mental disorders, psychological distress, and mental health services use among lesbian, gay, and bisexual adults in the united states. *J Consult Clin Psychol*. 2003;71(1):53.

29. Gary J. Gates, how many people are lesbian, gay, bisexual, and transgender. *The Williams Institute, UCLA School of Law*. 2011:3.

30. National Center for Health Statistics. (a). *National health and nutrition examination survey (NHANES): MEC laboratory procedures manual.* Retrieved 04/14, 2017, from https://wwwn.cdc.gov/nchs/data/nhanes/2013-2014/manuals/2013_MEC_Laboratory_Procedures_Manual.pdf

31. National Center for Health Statistics. (b). *National health and nutrition examination survey: Sample design, 2011–2014.* Retrieved 04/14, 2017, from https://wwwn.cdc.gov/nchs/data/series/sr02_162.pdf

32. Klein, R. J., & Schoenborn, C. A. (2001). Age adjustment using the 2000 projected US population.

33. Dunne, E. F., Unger, E. R., Sternberg, M., McQuillan, G., Swan, D. C., Patel, S. S., & Markowitz, L. E. (2007). Prevalence of HPV infection among females in the united states. *Jama, 297*(8), 813-819.

34. Balsam, K. F., Beadnell, B., & Riggs, K. R. (2012). Understanding sexual orientation health disparities in smoking: A Population-Based analysis. *American Journal of Orthopsychiatry, 82*(4), 482-493.

35. Bowleg, L. (2008). When black lesbian woman≠ black lesbian woman: The methodological challenges of qualitative and quantitative intersectionality research. *Sex Roles, 59*(5-6), 312-325.

36. Bowleg, L. (2012). The problem with the phrase women and minorities: Intersectionality—an important theoretical framework for public health. *American Journal of Public Health, 102*(7), 1267-1273.

37. Kertzner, R. M., Meyer, I. H., Frost, D. M., & Stirratt, M. J. (2009). Social and psychological Weil-Being in lesbians, gay men, and bisexuals: The effects of race, gender, age, and sexual identity. *American Journal of Orthopsychiatry, 79*(4), 500-510.