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Victoria Parr Date

The Association between Type 2 Diabetes and
Sexually Transmitted Infections in the United States, NHANES 2007-2014

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By

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B.S., Georgetown University, 2015

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Master of Public Health
in Epidemiology
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Abstract

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By Victoria Parr

Diabetes (DM) and sexually transmitted infections (STIs) are both growing problems in the United States, with prevalences of 22 million and 110 million, respectively. The immunopathology of DM and the propensity towards infection make it very likely that these mounting burdens will begin to overlap, resulting in a higher burden of STIs among those with diabetes. We performed a cross-sectional analysis of 2007-2014 National Health and Nutrition Examination Survey (NHANES) data to determine the association between DM and STI. After exclusions, the study population consisted of 16,696 individuals. DM, the exposure, was determined by a combination of glycohemoglobin testing and self-report. STI status was determined by self-reporting any of: chlamydia (last 12 months), gonorrhea (last 12 months), herpes (ever), and human papillomavirus (HPV) (ever). Results were produced using univariate and multivariate logistic regression models. With few exceptions, the odds of being STI positive among people with diabetes were consistently lower than those of people without diabetes. Notably, the odds of having herpes among people with diabetes were 0.48 times those of people without diabetes, adjusting for age, race, sex, risky sexual behavior, HIV, sexual orientation, health insurance coverage, and BMI (95%CI: 0.25-0.90). Interestingly, when herpes laboratory testing was used as the outcome, the odds of having herpes among people with diabetes was 1.79 (95%CI: 1.34-2.38) times that of people without diabetes, adjusting for the same covariates. Using self-report as a proxy for symptomatic disease, the discrepancy in the self-report versus laboratory test modeling results may indicate that although people with diabetes have significantly higher odds of being herpes positive upon testing, they have lower odds of being symptomatic.

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CHAPTER I: Background and Literature Review

Diabetes

Diabetes is a chronic metabolic disease characterized by disordered metabolism of blood sugar and lipids. Diabetes results from a relative imbalance between insulin secretion and need (K.M. Narayan 2006). Insulin is produced by the pancreas to facilitate glucose absorption into cells. As the body's insulin imbalance emerges (either due to decreased insulin secretion or the body becoming less sensitive to insulin [insulin resistance] or both), glucose builds up in the bloodstream, leading to hyperglycemia. Untreated hyperglycemia can lead to vision loss, kidney damage, or nerve damage that could require amputation as well as potentiate the risk of cardiovascular disease and events (American Diabetes Association 2015). Type 2 diabetes (T2D), which tends to exhibit an insulin resistance phenotype, represents up to 95 percent of all diabetes diagnoses (K.M. Narayan 2006).

The most recent surveillance data from the Centers for Disease Control and Prevention (CDC) estimate that 29 million people are currently living with diabetes in the United States; 22 million are currently diagnosed. That is approximately a 4-fold increase since 1980 (Centers for Disease Control and Prevention 2015). As of 2015, the US diabetes (DM) prevalence was 6.5 per 100 people, a burden that seems to have plateaued over the last six years (Centers for Disease Control and Prevention 2015). A recent study analyzing a large US claims database supported this conclusion, finding that the prevalence of diagnosed DM has stabilized at around 8.2-8.3%, with the plateau beginning in 2007 (Weng, Liang et al. 2016). Even though this data appears to show a public health win in terms of halting the

rising DM incidence, DM still has considerable effects on the overall health of the US population.

A 2010 analysis found that in the US, 3.2% of deaths were attributable to DM, making it the sixth leading cause of death. Furthermore, DM resulted in 1,392,000 years of life lost and 1,165,000 years lived with disability (Murray and Lopez 2013). DM is not only prolific but also very expensive; each year, the US loses approximately $750 billion due to diabetes and heart disease-associated medical care and loss of productivity (Narayan, Ali et al. 2010). More specifically, in 2013 alone, the US spent $101.4 billion on diabetes care, making it the most costly health condition on a national scale (Dieleman, Baral et al. 2016).

Sexually Transmitted Infections

A sexually transmitted infection (STI) is any infection with sexual contact as a primary transmission route; however, STIs can also be spread through contact with blood products or from mother to child. There are over thirty types of STIs, including infections caused by parasites, viruses, and bacteria. The most common STIs are HIV, gonorrhea, chlamydia, syphilis, herpes, HPV, and hepatitis B (World Health Organization 2016).

Among all infectious diseases in the United States, STIs are the most common. The estimated prevalence of US STIs is 110 million cases, with an annual incidence of 20 million cases. Although not as costly as diabetes, STI health care costs are not trivial; each year, $16 billion is spent on STI care (Mark, Dhir et al. 2015). While younger adults do represent a disproportionately large share of STI diagnoses (50% of cases occur in people aged 15-24), national and global surveillance data indicates that STI rates in adults over age 50 are increasing, most likely due to increased sexual activity later in life, risky sexual behaviors, and inadequate condom usage (Mark, Dhir et al. 2015, Tuddenham, Page et al. 2016).

Surveillance data from 2015 indicates that STI rates are on the rise. Compared to 2014, chlamydia rates increased by 5.9%, gonorrhea rates increased by 12.8%, syphilis rates

increased by 19.0%, and congenital syphilis rates increased by 6.0%. The prevalence of genital warts, which can be caused by several types of HPV, is estimated at 0.9% for women, 3.3% for men who have sex with men, and 4.3% for men who have sex with women. With the HPV vaccine becoming more widely used, HPV prevalence has either decreased or stayed the same over the past decade in all age groups. The seroprevalence of herpes simplex virus-2 (HSV-2) has been slowly decreasing for the past three decades, whereas herpes simplex virus-1 (HSV-1) seroprevalence has been increasing in young adults. Despite these opposing trends, herpes overall remains one of the most prevalent STIs (Centers for Disease Control and Prevention 2016).

Diabetes and STIs

Besides the previously discussed complications, DM can also cause chronic low-level inflammation. This state of chronic inflammation disrupts the immune system and makes individuals with DM more susceptible to infections (H Hu 2015). Recent research has shown that the hyperglycemic state of DM increases production of two dicarbonyls, methylgloxal (MGO) and glyoxal (GO), which in turn attach to and reduce the antimicrobial effectiveness of immune molecules called beta-defensins. It is this molecular immune disruption that underlies the increased infection susceptibility, chronic inflammation, and slow wound healing in those with DM (Kiselar, Wang et al. 2015). Furthermore, a retrospective cohort study in Canada found that those with diabetes were more likely to have serious bacterial infections than those without diabetes. The contrast was so stark that the researchers recommended that healthcare providers view infections as another natural complication of DM (Shah and Hux 2003).

Given the high prevalence and incidence of both DM and STIs in the United States, combined with the high risk of infection in those with diabetes, some comorbidity overlap is expected. However, very little is known about the relationship between DM and STIs.

The interaction between DM and STIs likely depends on a variety of factors, including health care insurance coverage, sexual behavior, and age (Figure 1). In compiling this directed acyclic graph (DAG), a literature review involving the various relationships presented in the DAG was undertaken. Table 1 shows the top twelve most relevant publications.

Due to the dearth of literature concerning these relationships, it is difficult to estimate how diabetes affects STI risk, and vice versa. One of very few studies directly looking at the relationship between DM and STIs involved examining the blood glucose levels of those with and those without neurosyphilis (NS). The researchers found that those with NS had significantly higher fasting plasma glucose levels than those without NS, leading to the hypothesis that other STIs might also influence blood glucose levels (Yang, Tong et al. 2014). In a different study, researchers examined the prevalence of HSV-1 infection in those with and without type 2 diabetes. They found that HSV-1 prevalence was significantly higher in the diabetes group, and suggested that having diabetes is a risk factor for viral infection (Sun, Pei et al. 2005). In a similar study, researchers in China found that the prevalence of chronic hepatitis B infection was higher in those with DM compared to those without DM (Lu, Hou et al. 2016).

Diabetes and Sexual Behavior

Research concerning diabetes and sexual behavior is less sparse, but the results among these studies often differ. While almost all of the studies indicate that those with diabetes have issues with sexual health or dysfunction, many studies differ as to the underlying cause of the dysfunction. A study examining vaginal blood flow and arousal among women with type 1 diabetes found no significant differences in these measures between those with and without diabetes (Both, Ter Kuile et al. 2015). A study of gestational diabetes and sexual function found that although those with diabetes had a higher prevalence

of sexual dysfunction, those with diabetes and those without did not differ significantly in terms of degree of desire, lubrication, or pain (Souza Fde, Dias et al. 2013). In contrast, a cross-sectional study among women aged 40 to 80 years found that women with T2D who also take insulin were at greater risk for issues with lubrication and orgasm than women without T2D (Copeland, Brown et al. 2012).

In a study of Nigerian men, researchers compared sexual dysfunction and reproductive hormone levels among men with normal BMI to men with metabolic syndrome (MS, the precursor to diabetes), and men with T2D. They found that men with MS had both lower testosterone levels than controls and lower libido than controls or men with T2D. They concluded that the differences in sexual function in men with MS and T2D could be due to the testosterone-converting effect of excess adipose tissue (Fabian, Charles-Davies et al. 2016).

Danish researchers found that both men and women with T2D reported low sexual desire, low sexual satisfaction, and sexual dysfunction more often than those without T2D (Pedersen, Giraldi et al. 2015, Rutte, van Splunter et al. 2015). Sexual inactivity was much more highly prevalent among women with T2D (47%) than men with T2D (17%), but that trend reversed when examining sexual distress, with only 11% of women compared to 32% of men with T2D reporting sexual distress (Bjerggaard, Charles et al. 2015). In contrast, a Spanish case-control study found no significant difference in sexual activity measures between those with and without diabetes, but they did find that those with T2D reported significantly worse sexual health than those without diabetes (Jimenez-Garcia, Martinez-Huedo et al. 2012).

Overall, the patchwork of research makes it very difficult to tease out the typical sexual behavior among those with DM—are those with DM more sexually inactive? Do they

have greater difficulty with lubrication or physiological arousal? Are adipose-tissue related hormones to blame?

BMI and STI Risk

In a study of young mothers, researchers found that the odds of having an STI among overweight women was 1.79 times that of normal weight women. Interestingly, obesity appeared to be protective against STIs, with the odds of having an STI among obese women being 0.57 times that of normal weight women. Although causation cannot be determined given this study design, there is a significant association between weight/BMI and STI incidence (Kershaw, Arnold et al. 2011).

Age, Sexual Behavior, and STIs

In an analysis of survey data from US adults ages 18-44, researchers found that 92.0% of men and 94.2% of women had engaged in intercourse at least once. Sexual behavior varies based on not only age, but also relationship status, educational level, and race/ethnicity (Copen, Chandra et al. 2016).

The younger generation is, in general, at greater risk for STIs. For example, HPV prevalence ranges from approximately 20% in 14-19 year old women to 42% in women ages 20-24. Surveillance data from 2014 indicates that STI rates are on the rise; compared to 2013, chlamydia rates increased by 2.8%, gonorrhea rates by 5.1%, syphilis rates by 15.1%, and congenital syphilis rates by 27.5%. Genital herpes prevalence has been steadily increasing for the past five decades, and is one of the most prevalent STIs (Centers for Disease Control and Prevention 2015).

Despite high STI prevalence rates among younger adults, the rise in STI rates has also affected the older population. In US adults over age 65, chlamydia diagnoses increased by 31% and syphilis diagnoses by 52% between 2007 and 2011, putting seniors on par with adults aged 20-24 (Emanuel 2014). Researchers suggest that the main factors contributing to

the unexpected rise in STIs among older adults are the close proximity afforded by nursing homes and senior living facilities, better overall health, the prevalence of drugs such as Viagra, and poor condom usage (Emanuel 2014, Tuddenham, Page et al. 2016). In one retrospective cohort study, researchers found that 24.1% of younger adults reported no condom usage compared to 32.6% of adults aged 50 and older (Tuddenham, Page et al. 2016).

Scope of Analysis

Overall, very little is known about the relationship between diabetes (DM) and STIs, or about the other relationships surrounding this association. Of the research that has been done, these are the main conclusions: STIs may be related to blood glucose levels; the sexual behavior of people with diabetes is poorly characterized, however, several studies do support the conclusion that those with diabetes have poorer sexual health, greater sexual dysfunction, and lower sexual satisfaction than those without diabetes; a higher BMI/being overweight can increase STI risk; STI rates are increasing, even in older (>50 years) populations; having diabetes increases infection risk.

Due to these mixed findings in the literature, relationships between diabetes and STIs remain unclear. Because of these considerable research gaps and the widespread and/or increasing prevalence of both DM and STIs, an investigation into the relationship between DM and STIs is warranted. This analysis will use the National Health and Nutrition Examination Survey (NHANES) dataset, which is survey data that is representative of the overall health and nutrition of the non-institutionalized civilian American population. Due to variations in data collection from year to year, the STIs being examined are limited to gonorrhea, chlamydia, herpes, and HPV. Using various regression analyses, we examined the associations between DM and these STIs, while controlling for the potential confounders pictured in Figure 1.

Both diabetes and STIs are growing problems. If diabetes is significantly associated with STIs, then public health and prevention programs need to be established. STI-prevention programs in particular would need to take special consideration of those with diabetes. Targeted interventions for STIs and/or enhanced STI screening for those with diabetes may be warranted if they are at greater risk.

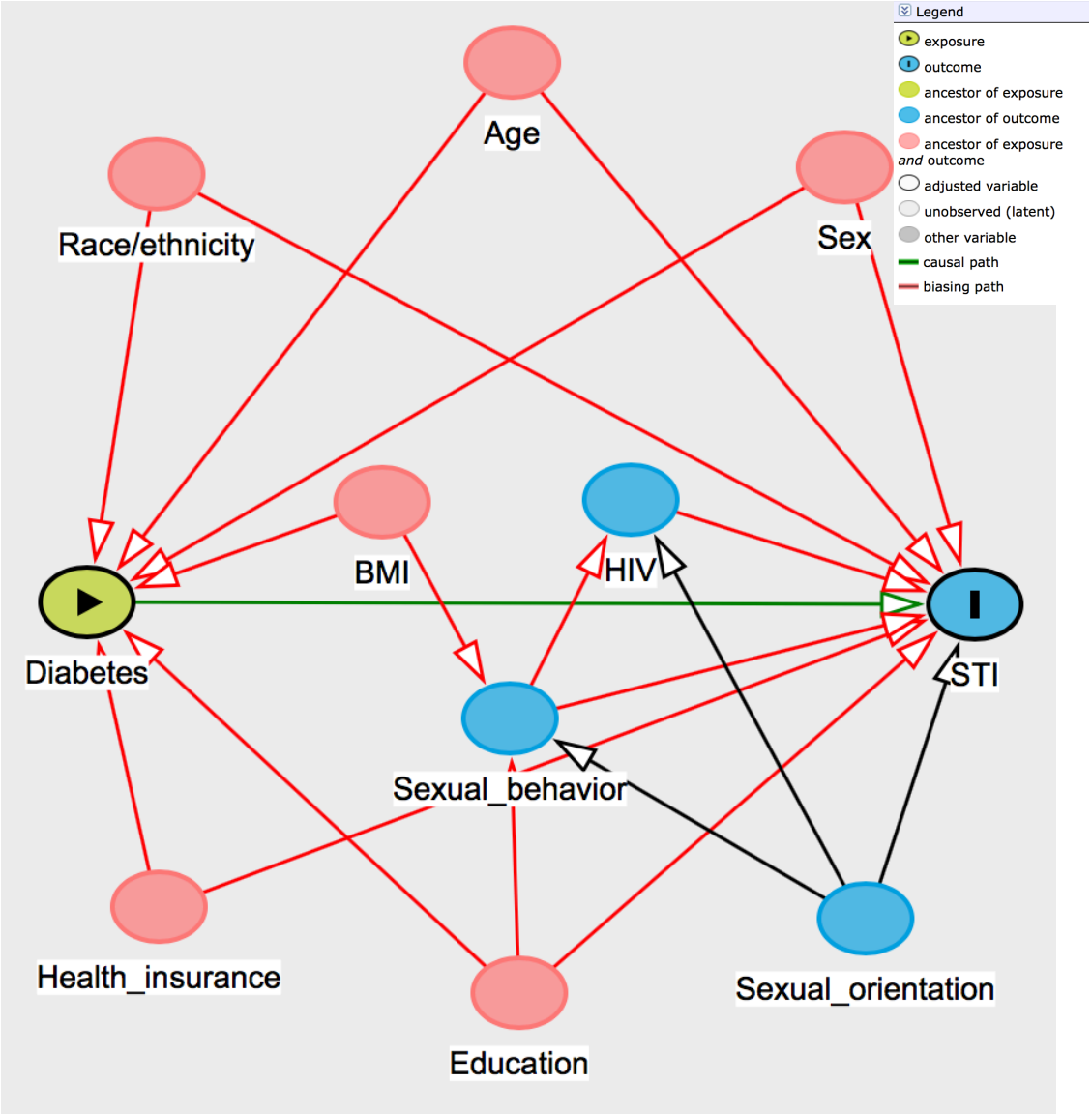

Figure 1. Directed acyclic graph (DAG) showing the hypothesized relationships surrounding the DM/STI association. DAG made using DAGitty v2.3.

Table 1. Top Twelve Publications Related to Diabetes and STIs.

Publication	Main Topics	Results/Conclusions
Yang et al. 'Association between neurosyphilis and diabetes mellitus: resurgence of an old problem' J. Diabetes 2014.	STIs, blood glucose levels	Fasting plasma glucose was significantly higher in patients with neurosyphilis (NS) compared to patients with non-NS syphilis and healthy control patients.
Sun et al. 'An association of herpes simplex virus type 1 infection with type 2 diabetes.' Diabetes Care. 2005.	Diabetes, herpes	In a cross-sectional study of those with and without diabetes, those with T2D were found to have a significantly higher prevalence of HSV-1 infection compared to the group without diabetes.
Lu et al. 'Hepatitis B virus infection status is more prevalent in patients with type 2 diabetes.' J. Diabetes Investigation 2016.	Diabetes, hepatitis B	In a cross-sectional study of those with and without type 2 diabetes, the prevalence of chronic hepatitis B infection was found to be significantly higher in those with diabetes than in those without diabetes.
Pedersen et al. 'Prevalence of sexual desire and satisfaction among patients with screen-detected diabetes and impact of intensive multifactorial treatment: results from the ADDITION-Denmark study' Scand J Prim Health Care. 2015.	Diabetes, sexual behavior	A cross-sectional study of 968 men and women with screen-detected T2D in Denmark found that low sexual desire and low sexual satisfaction were common in patients with T2D, with 53-54% of women and 24-25% of men reporting low sexual desire and 18-23% of women and 27-37% of men reporting low sexual satisfaction.
Jiménez-Garcia et al. 'Sexuality among Spanish adults with diabetes: a population-based case control study' Prim Care Diabetes. 2012.	Diabetes, sexual behavior	Spanish researchers performed a 1:2 type 2 diabetes case-healthy control study matched on age, sex, and type of sexual partner. The researchers found no significant difference in sexual activity measures between those with and without diabetes, but they did find that those with T2D reported significantly worse sexual health than those without diabetes (aOR for women 1.74 (95% CI 1.15-2.63); aOR for men 1.88 (95% CI 1.29-2.75)).
Bal et al. 'Does the diabetes of type 2 affect the sexual functions of women?' J Sex Marital Ther. 2015.	Diabetes, sexual behavior	A case-control study was performed to examine sexual behavior of women with DM vs. women without DM. Those with diabetes had higher prevalence of sexual dysfunction than women without diabetes. The researchers also found that higher HbA1c, higher BMI, and longer DM duration are associated with increased prevalence of sexual dysfunction.

Publication	Main Topics	Results/Conclusions
Copeland et al. 'Diabetes mellitus and sexual function in middle-aged and older women' Obstet Gynecol. 2012.	Diabetes, sexual behavior, medications	Researchers administered a cross-sectional questionnaire to a group of 2,270 women between the ages of 40 and 80 years. They found that women with diabetes were more likely to report lower sexual satisfaction. Women with diabetes who were being treated with insulin reported greater difficulty with lubrication and orgasm.
Souza et al. 'Assessment of female sexual function in pregnant women with gestational diabetes mellitus' J Sex Med. 2013.	Gestational diabetes, sexual behavior	The researchers examined pregnant female sexual function by comparing women with gestational diabetes to women with low-risk pregnancies using questionnaires. They found that the women with gestational diabetes had a significantly higher prevalence of sexual dysfunction, but the two groups did not differ significantly in terms of degree of desire, lubrication, or pain.
Kershaw et al. 'The Skinny on Sexual Risk: The Effects of BMI on STI Incidence and Risk' AIDS Behav. 2011.	BMI/weight, STI risk	By examining 704 mothers aged 14-25, the researchers found that the odds of having an STI among overweight women was 1.79 times that of normal weight women (95% CI: 1.11-2.89). Interestingly, the odds of having an STI among obese women were 0.57 times that of normal weight women (95% CI: 0.34-0.96).
Tuddenham et al. 'Patients fifty years and older attending two sexually transmitted disease clinics in Baltimore, Maryland.' Int J STD AIDS. 2016.	Age, sexual behavior, STIs	While younger adults do represent a disproportionately large share of STI diagnoses, national and global surveillance data indicates that STI rates in adults over age 50 are increasing, most likely due to increased sexual activity later in life, risky sexual behaviors, and inadequate condom usage. Based on the results of a retrospective cohort study, the researchers found that 32.6% of patients 50 and older reported no condom usage, compared to 24.1% of younger adults.
Shah and Hux. 'Quantifying the risk of infectious diseases for people with diabetes.' Diabetes Care. 2003.	Diabetes, infections	Using data from a retrospective cohort study in Ontario, Canada, researchers found that the risk of hospitalization due to infectious disease was 2.17 times higher for those with diabetes compared to those without diabetes (99% CI: 2.10-2.23). Furthermore, those with diabetes had a 1.92 times higher risk of dying from an infection compared to those without diabetes (99% CI: 1.79-2.05). Most of these infections were bacterial.

Publication	Main Topics	Results/Conclusions
CDC Report. 2015.	STIs	Surveillance data from 2014 indicates that STI rates are on the rise. Compared to 2013, chlamydia rates increased by 2.8%, gonorrhea rates increased by 5.1%, syphilis rates increased by 15.1%, and congenital syphilis rates increased by 27.5%. The prevalence of HPV ranges from approximately 20% in women aged 14-19 to approximately 42% in women aged 20-24. With the HPV vaccine becoming more widely used, HPV prevalence has either decreased or stayed the same over the past decade in all age groups. Genital herpes prevalence has been steadily increasing for the past five decades, and is one of the most prevalent STIs.

CHAPTER II: Manuscript

Viggy Parr, Matthew J. Magee, Mohammed K. Ali

ABSTRACT. Diabetes (DM) and sexually transmitted infections (STIs) are both growing problems in the United States, with prevalences of 22 million and 110 million, respectively. The immunopathology of DM and the propensity towards infection make it very likely that these mounting burdens will begin to overlap, resulting in a higher burden of STIs among those with diabetes. We performed a cross-sectional analysis of 2007-2014 National Health and Nutrition Examination Survey (NHANES) data to determine the association between DM and STI. After exclusions, the study population consisted of 16,696 individuals. DM, the exposure, was determined by a combination of glycohemoglobin testing and self-report. STI status was determined by self-reporting any of: chlamydia (last 12 months), gonorrhea (last 12 months), herpes (ever), and human papillomavirus (HPV) (ever). Results were produced using univariate and multivariate logistic regression models. With few exceptions, the odds of being STI positive among people with diabetes were consistently lower than those of people without diabetes. Notably, the odds of having herpes among people with diabetes were 0.48 times those of people without diabetes, adjusting for age, race, sex, risky sexual behavior, HIV, sexual orientation, health insurance coverage, and BMI (95%CI: 0.25-0.90). Interestingly, when herpes laboratory testing was used as the outcome, the odds of having herpes among people with diabetes was 1.79 (95%CI: 1.34-2.38) times that of people without diabetes, adjusting for the same covariates. Using self-report as a proxy for symptomatic disease, the discrepancy in the self-report versus laboratory test modeling results may indicate that although people with diabetes have significantly higher odds of being herpes positive upon testing, they have lower odds of being symptomatic.

Introduction

The Centers for Disease Control and Prevention (CDC) estimate that 22 million people are currently living with diagnosed DM in the United States (Centers for Disease Control and Prevention 2015). Diabetes (DM) is a systemic disease resulting from dysglycemia that can lead to kidney damage, vision loss, and amputation, and it is also associated with chronic, low-level inflammation (H Hu 2015). Given that people with DM have an estimated twice the risk of dying from an infection compared to people without diabetes (Shah and Hux 2003), it is surprising that few studies have examined the link between DM and sexually transmitted infections (STIs), the most common infectious diseases in the United States (Mark, Dhir et al. 2015). STIs can affect people at any age, and have the abilities to be often asymptomatic, easily transmitted, and result in costly and painful sequelae. The estimated prevalence of US STIs is 110 million cases, with an annual incidence of 20 million cases (Mark, Dhir et al. 2015). While younger adults do represent a disproportionately large share of STI diagnoses (50% of cases occur in people aged 15-24), national and global surveillance data indicates that STI rates in adults over age 50 are increasing, most likely due to increased sexual activity later in life, risky sexual behaviors such as a high number of sexual partners, and inadequate condom usage (Mark, Dhir et al. 2015, Tuddenham, Page et al. 2016). Furthermore, studies investigating the risk for STIs in populations such as those with HIV or cancer indicate that immunocompromise could increase STI risk (Nordfors, Vlastos et al. 2014, Brownstein, Gillespie et al. 2015, Torres, Gheit et al. 2015). As a disease with associated immunopathology, diabetes' association with STIs should be investigated.

Given the high prevalence and incidence of both DM and STIs in the United States, combined with the high risk of infection in those with diabetes, some comorbidity overlap is expected. However, very little is known about the relationship between DM and STIs. Due

to the dearth of literature concerning this relationship, it is difficult to estimate how diabetes affects STI risk, and vice versa. In one study examining diabetes and neurosyphilis (NS), those with NS had significantly higher fasting plasma glucose levels than those without NS, leading to the hypothesis that other STIs might also influence blood glucose levels (Yang, Tong et al. 2014). In a different study, HSV-1 prevalence was significantly higher in those with diabetes versus those without, suggesting that having diabetes is a risk factor for viral infection (Sun, Pei et al. 2005).

Given the greater risk of infection associated with DM, it is expected that the prevalence of STIs will be higher among those with diabetes compared to those without. Using a cross-sectional study design, we aimed to examine the relationship between STIs and diabetes using nationally representative survey data collected through the National Health and Nutrition Examination Survey (NHANES) from 2007-2014.

Methods

We performed a cross-sectional analysis using data from the 2007-2014 National Health and Nutrition Examination Survey (NHANES) cycles. Every two years, NHANES collects data from a sample of the US population that is representative of the non-institutionalized civilian American population (Centers for Disease Control and Prevention 2017). Data collected include questionnaires, health examinations, and biochemical samples. In order to be representative, NHANES data is weighted using a stratified probability sampling method (Centers for Disease Control and Prevention 2015).

Individuals included in the 2007-2014 NHANES survey cycles were eligible for inclusion in this study if they were between the ages of 18 and 59, had been tested for glycohemoglobin levels and HIV, had undergone a health examination (which includes measurements such as body mass index (BMI), height, and weight), and had answered questionnaires regarding diabetes, sexual behavior, healthcare access, and demographics.

Individuals were excluded from the study population if they had never had sex before, were outside the age range, or were missing data regarding important covariates of interest (Figure 1). After exclusions, the study population included 16,696 individuals.

Diabetes status was categorized into three levels: no diabetes (negative self-report and A1c < 5.7); prediabetes (negative self-report and 5.7% ≤ A1c ≤ 6.4); diabetes (positive self-report or A1c ≥ 6.5%). We defined STI status using a combination of four NHANES questions requiring the participant to self-report their status. STI status was considered positive if the participant had responded 'yes' to any of the following questions: have you ever been diagnosed with genital warts (a proxy for HPV); have you ever been diagnosed with genital herpes; in the past 12 months, have you been diagnosed with gonorrhea; in the past 12 months, have you been diagnosed with chlamydia. We defined risky sexual behavior based on answers to the following NHANES questions: in the past 12 months, with how many men/women have you had vaginal, anal, or oral sex; in the past 12 months, about how often have you had vaginal or anal sex without using a condom. We categorized the risky sex variable into three levels: low risk (had sex with 1 or fewer people in the last year regardless of condom use or had sex with more than one person in the last year but always used condoms); moderate risk (had sex with more than one person in the last year and sometimes used condoms) and high risk (had sex with more than one person in the last year and never used condoms). We partitioned age into three categories, based loosely on Centers for Disease Prevention and Control (CDC) age groups for STI surveillance reporting (Centers for Disease Control and Prevention 2016). We categorized body mass index (BMI) into the four groups of underweight (BMI <18.5), normal weight (18.5 ≤ BMI ≤ 24.99), overweight (25.0 ≤ BMI ≤ 29.99), and obese (BMI ≥ 30.0) per internationally recognized standards (Centers for Disease Control and Prevention 2015).

We estimated the association between diabetes and STI using bivariate and multivariate analyses. All analyses were carried out using SAS 9.4 (Cary, NC). Both descriptive statistics and odds ratios were produced using SAS survey procedures to account for the complex probability sampling of NHANES data. For the descriptive analyses, P-values were calculated using the Rao-Scott chi-square test for categorical variables and a F-test for continuous variables. An alpha of 0.05 was used as the threshold for significance. First, descriptive statistics based on diabetes status and STI status were produced. For continuous variables, there was no gross departure from normality. Next, clinical characteristics for only those with diabetes were described. For the modeling, STI self-report was used as the outcome (both aggregated as 'Any STI' and by specific STI), and diabetes was the exposure. Both univariate and multivariable no-interaction logistic regression models were run. Potential variables for the multivariate analyses were chosen based on bivariate associations and Directed Acyclic Graph (DAG) theory (Greenland, Pearl et al. 1999). These variables included race, sex, age, body mass index (BMI), education, HIV status, risky sexual behavior, health insurance coverage, and sexual orientation. Finally, the same variables used in the STI self-report models were run with laboratory-confirmed specific STIs (herpes and HPV) as the outcome. Due to insufficient data, the laboratory-confirmed chlamydia and gonorrhea data could not be incorporated into a model. All analyses included methods to account for the complex sample survey design of NHANES.

Results

From an initial dataset of 70,300 observations for NHANES cycles between 2007 and 2014, 40,611 individuals were excluded (57.8%) because they either were missing data on sexual behavior such as condom use or they had never had sex before (2.9%). Of the 29,689 individuals remaining in the dataset, an additional 49 (0.07%) were excluded because they were missing information about STI status. 1,179 individuals (1.7%) were further excluded

because they were missing information about diabetes status. Finally, an additional 8,429 individuals (12.0%) were excluded because they were 60 years of age or older. An additional 675 (1.0%) were excluded because they had information missing for any or all of the following variables: BMI, sexual orientation, health care insurance coverage, education level, or risky sexual behavior. Finally, an additional 2,022 (2.9%) were excluded because they were missing information for HIV status and 366 (0.5%) were excluded because they had diabetes but were missing information about diabetes duration. After exclusions, the dataset contained 16,969 observations (Figure 1).

Descriptive Analyses

Table 1 shows the distribution of basic demographic characteristics by diabetes status. The proportions for different levels of race, age, education, risky sexual behavior, and BMI were significantly different among the three categories of diabetes status. In contrast, the distributions for different levels of sex (male or female), sexual orientation, health insurance coverage, and HIV status were not significantly different by diabetes status. Those with diabetes were more often white, older, engaging in low risk sexual behavior, and had higher BMIs than those with prediabetes or no diabetes.

Demographic characteristic distributions were also calculated based on STI status (Table 2). 10.5% (95%CI: 9.0-11.9) of the study population was STI positive, per self-report. As with Table 1, Table 2 shows that the distribution of race was significantly different between those with and those without STIs. With the exception of race, every variable that was not significantly differently distributed by diabetes status is significant by STI status. Those variables include sex, sexual orientation, health insurance coverage, and HIV status. The STI positive group as a whole was more often white, female, gay, bisexual, or other, covered by health insurance, and HIV positive compared to the STI negative group.

To better measure the descriptive relationship between diabetes and STIs, a sub-analysis of only those with diabetes was performed (Table 3). Table 3 shows the distribution of various clinical and demographic characteristics by STI status, among those with diabetes only. Although no variables showed statistically significantly different distributions by STI status, it is worth noting that higher proportions of STI positive people with diabetes were female and in the oldest age category. Additionally, the STI positive group had overall longer diabetes duration than the STI negative group. An estimated 10% of individuals taking pills only were STI positive, which was the highest proportion across all medication categories. Additionally, those with STIs had nearly ten times the HIV infections compared to those without STIs.

Regression Analyses

Univariate Models

Univariate regression models with STI as the outcome and a variety of variables as the exposure were run. Variables with STI odds ratios that did not contain the null included race, sex, health insurance coverage, sexual orientation, risky sexual behavior, and HIV status. Of note, the odds of being STI positive for those with HIV were 8.02 times that of those without HIV (95%CI: 2.61-24.65). All sexual orientation groups with the exception of straight/heterosexual had elevated odds of being STI positive, ranging from 1.72 (95% CI: 1.09-2.71) for the bisexual group to 2.23 (95%CI: 1.12-4.41) for the gay/homosexual group. The odds of having an STI for those not covered by health insurance were 0.69 times that of those covered by health insurance. The odds of being STI positive for females were 2.56 (95%CI: 1.90-3.44) times that of males. Finally, all race categories except for Blacks had reduced odds of being STI positive compared to Whites, ranging from 0.43 (95%CI: 0.29-0.64) for Mexican-Americans to 0.63 (95%CI: 0.45-0.89) for other Hispanics. With an

odds ratio of 1.25 (95%CI: 0.93-1.69), Blacks had slightly elevated odds of being STI positive compared to Whites, but this result was not significant.

Multivariate Models

Building upon the univariate models, multivariate models with both 'Any STI' and specific STIs were run (Table 4). For any STI, chlamydia, gonorrhea, and HPV, the odds of being STI positive among people with prediabetes were either equal to or slightly above those of people without diabetes in the adjusted models. With one exception (the STI odds ratio for chlamydia in model 2), the odds of being STI positive among people with diabetes were consistently lower than those of people without diabetes. The only significant results were produced by modeling herpes. The odds of having herpes among people with diabetes were 0.48 times those of people without diabetes, adjusting for age, race, sex, risky sexual behavior, HIV, sexual orientation, health insurance coverage, and BMI (95%CI: 0.25-0.90).

A sensitivity analysis using laboratory-confirmed herpes and HPV was performed. When herpes laboratory results were used as the outcome variable in logistic regression models, with a positive herpes outcome defined as having positive NHANES laboratory test results for either HSV-1 or HSV-2, 4,035 observations were deleted due to missing data for the herpes outcome variable. With those exclusions, a univariate logistic regression model with diabetes status as the exposure variable and herpes test result as the outcome produced the following results: the odds of being herpes positive among those with diabetes was 2.87 (95%CI: 1.94-4.24) times that of those without diabetes. Further, the odds of being herpes positive among those with prediabetes was 2.32 (95%CI: 1.81-2.98) times that of those without diabetes (Table 5).

Interestingly, when using the laboratory test results for herpes instead of the self-report, the previously noted trend from Table 4 is reversed. No significant results were produced from the HPV laboratory test models.

Discussion

Overall, these findings are semi-consistent with the hypothesis for this study: the odds of having had an STI are higher for those with diabetes than those without diabetes. While self-report of STI indicates that those with diabetes actually have lower odds of being STI positive than those without diabetes, laboratory testing indicates the opposite result. Interestingly, some of the results of this study disagree with the conclusions from the literature, particularly surrounding herpes. Whereas Sun et al. found that laboratory-tested HSV-1 infection was more prevalent in those with diabetes, this study has found that self-reported herpes is more prevalent in those without diabetes than in those with diabetes (5.8% vs. 3.3%, respectively) (Sun, Pei et al. 2005). However, when laboratory-tested herpes was used as the outcome, adjusted models indicated that people with diabetes have nearly twice the odds of being herpes positive compared to those without diabetes. The stark contrast between these two sets of results highlights the disparity between results from self-report and results from laboratory testing. We found that the agreement between laboratory testing and self-report for STIs that are often symptomatic and require treatment, such as chlamydia and gonorrhea, was very high (>96%). In contrast, for chronic STIs like herpes or STIs that are frequently asymptomatic and do not require treatment like HPV, the agreement between lab oratory testing and self-report was considerably lower (32-67%). However, the cases of herpes and HPV that are self-reported are most likely symptomatic and acute. If we consider self-report as a proxy for symptomatic disease, then perhaps the discrepancy in the self-report versus laboratory test modeling results indicates that although people with dysglycemia (either prediabetes or diabetes) have significantly higher odds of being herpes positive upon testing, they have lower odds of being symptomatic.

There are a few possible explanations for these results. Perhaps those with diabetes have milder STI symptoms, or simply attribute any new symptoms to their underlying

chronic condition and therefore do not seek care for the infection. At least in the case of herpes, perhaps the chronic inflammatory environment created by diabetes discourages the herpes virus from leaving its sequestered location of dormancy in the nerve cells, and therefore prevents symptomatic infection. A greater understanding of how DM and particular STIs interact at a cellular level could go a long way towards reducing both the severity and prevalence of both conditions. Furthermore, greater research into this area could help tease apart the associations between diabetes and symptomatic versus asymptomatic STIs.

Due to the severe dearth of previous work on the association between diabetes and STIs, this research is venturing into new territory, and could have important public health implications. Assuming self-report is a proxy for symptomatic STI, then these results indicate that it is possible that people with diabetes are at greater risk for asymptomatic STI, especially herpes. This is dangerous, given both that herpes can be transmitted even from asymptomatic carriers and that people with diabetes are immunocompromised. STI-prevention programs in particular should take special consideration of those with diabetes., and clinicians treating patients with diabetes should encourage routine STI screening. Furthermore, targeted interventions for STIs for those with diabetes may be warranted.

Strengths and Limitations

This study has many strengths. By using an NHANES dataset, these results are applicable to the entire non-institutionalized, civilian United States population. The thorough and varied set of variables in the dataset allowed for the creation of concrete variables to describe concepts like risky sexual behavior. Finally, data on a variety of STIs was collected, allowing for both individual examination of specific STIs and a comprehensive look at STIs in general.

Despite the strengths of using NHANES, it also has its limitations. NHANES is a collection of survey and surveillance data, so these conclusions can only describe association, not causation. For sensitive questions, such as those regarding sexual behavior, there may be self-reporting bias if respondents are uncomfortable discussing their sexuality. Furthermore, with STIs and DM being self-reported, respondents might not yet know if they have the diseases or may be asymptomatic and therefore underreport. Given that STI-related questions were asked in the form of "Has a doctor or health care professional ever told you that you had X?" (in the case of herpes and HPV) or "In the past 12 months, has a doctor or health care professional told you that you had gonorrhea?" (in the case of gonorrhea and chlamydia), understanding temporality can be tricky.

CHAPTER III: Public Health Implications and Future Directions

Public Health Implications

Ultimately, this study has found that people with diabetes may be more likely to have asymptomatic STIs that could potentially be transmitted to their partners. This study also highlights the chasm between self-report and laboratory-confirmed disease. The complicated etiology and biology of diabetes makes it difficult to elucidate exactly how STIs affect this population; however, targeted prevention efforts and increased STI screenings could be considered for the population with diabetes.

When prevention efforts are unsuccessful, treatment and care management should be initiated as quickly as possible. STI testing should be offered to high-risk groups, such as patients with diabetes, at both routine physicals and annual gynecological exams. The best way to break the network of STI transmission is to diagnose and treat cases (as well as their partners) early.

Future Directions

As previously mentioned, this research provides a concrete jumping off point for future studies. Further investigations should focus on providing stronger evidence to link diabetes and STIs, using cohort or case-control study designs. For example, performing a cohort study in a population of people with and without diabetes and assessing STI diagnoses could better define the differences in STI risk by diabetes status. Beyond epidemiology, studies regarding the biological underpinnings of the interactions of diabetes and STIs should be performed to better understand both immune function in patients with diabetes and the best treatment strategies in a world where antibiotics are becoming increasingly obsolete.

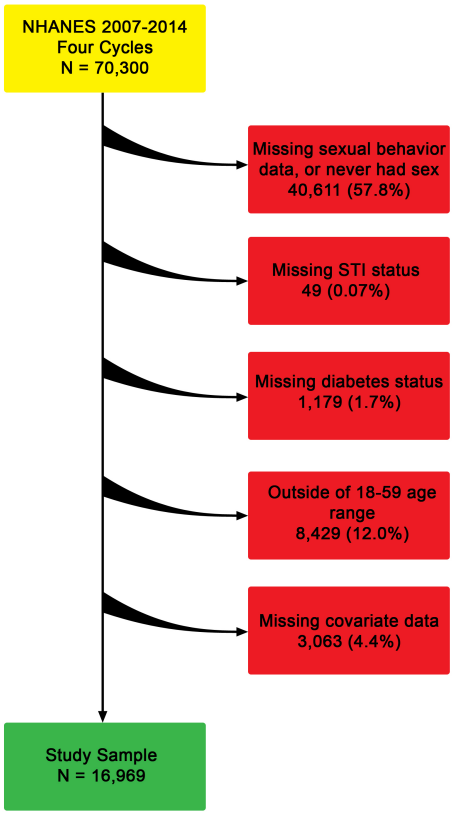

Figure 1. Diagram of sample exclusions. Diabetes status was classified in the following way: no diabetes: negative self-report and A1c < 5.7; prediabetes: negative self-report and 5.7% ≤ A1c ≤ 6.4; diabetes: positive self-report or A1c ≥ 6.5%. Those missing information on self-report or A1c were excluded. Covariates of interest for a multivariable model included BMI, sexual orientation, health care insurance coverage, education level, risky sexual behavior, diabetes duration, and HIV status. Those missing information on any of these covariates were excluded. STI status was determined by self-report, and was a combination of chlamydia, gonorrhea, herpes, and HPV self-report.

Table 1. Demographic characteristics of sample by diabetes status,[1] NHANES 2007-2014.

Characteristic	Diabetes 11.0 (9.6-12.3) % (95% CI)[2]	Prediabetes 17.8 (15.8-19.8) % (95% CI)[2]	No diabetes 71.2 (69.2-73.2) % (95% CI)[2]	TOTAL % (95% CI)[2]	P-value[3]
Race					
Mexican-American	8.6 (4.4-12.9)	7.4 (5.3-9.5)	7.6 (5.9-9.2)	7.6 (5.8-9.5)	
Other Hispanic	5.2 (3.2-7.2)	5.3 (3.6-6.9)	5.1 (3.8-6.3)	5.1 (3.9-6.3)	
White	61.6 (55.1-68.2)	63.3 (56.0-70.5)	73.8 (70.4-77.2)	70.6 (66.8-74.3)	**<0.0001**
Black	18.9 (13.9-23.8)	18.3 (13.3-23.2)	8.3 (6.9-9.8)	11.3 (9.2-13.3)	
Other	5.6 (3.5-7.8)	5.8 (4.4-7.2)	5.3 (4.5-6.0)	5.4 (4.7-6.1)	
Sex					
Male	46.7 (39.6-53.8)	47.5 (43.8-51.2)	45.6 (43.7-47.4)	46.1 (44.6-47.5)	0.723
Female	53.3 (46.2-60.4)	52.5 (48.8-56.2)	54.4 (52.6-56.3)	53.9 (52.5-55.4)	
Age, continuous[4] ***Range 18-59***	47.8 (46.8-48.9)	45.8 (45.1-46.5)	38.4 (37.7-39.0)	40.7 (40.2-41.3)	**<0.0001**
Age, categorized					
18-24	0.9 (0.1-1.7)	3.6 (2.9-4.3)	15.2 (13.4-17.0)	11.6 (10.2-12.9)	
25-39	13.3 (9.9-16.7)	21.3 (18.1-24.6)	37.0 (35.3-38.6)	31.6 (30.2-33.0)	**<0.0001**
40-59	85.8 (82.4-89.2)	75.0 (71.8-78.3)	47.9 (45.4-50.3)	56.9 (54.9-58.9)	
Education					
Less than 9th grade	6.6 (4.2-9.0)	3.8 (2.7-4.8)	2.5 (2.1-3.0)	3.2 (2.6-3.8)	
9-12th, no diploma	12.7 (9.2-16.2)	18.0 (12.3-23.6)	10.9 (9.4-12.5)	12.4 (10.4-14.4)	
High school graduate/GED	20.6 (15.6-25.7)	25.1 (20.1-30.1)	20.9 (18.7-23.1)	21.6 (19.6-23.6)	**<0.0001**
Some college or AA degree	39.3 (32.6-46.0)	30.1 (26.3-33.8)	33.8 (31.7-35.8)	33.7 (31.6-35.8)	

Characteristic	Diabetes 11.0 (9.6-12.3) % (95% CI)[2]	Prediabetes 17.8 (15.8-19.8) % (95% CI)[2]	No diabetes 71.2 (69.2-73.2) % (95% CI)[2]	TOTAL % (95% CI)[2]	P-value[3]
College graduate or above	20.8 (13.5-28.1)	23.1 (19.1-27.1)	31.9 (28.7-35.0)	29.1 (26.3-31.9)	
Sexual orientation					0.264
Gay/homosexual	0.4 (0.01-0.7)	1.5 (0.4-2.6)	2.0 (1.3-2.7)	1.7 (1.2-2.3)	
Straight/heterosexual	94.9 (91.8-97.9)	94.6 (93.0-96.2)	93.6 (92.6-94.6)	93.9 (93.1-94.8)	
Bisexual	2.9 (0.2-5.6)	2.6 (1.6-3.6)	3.2 (2.6-3.8)	3.1 (2.6-3.6)	
Other	1.9 (0.6-3.2)	1.3 (0.7-1.9)	1.2 (0.9-1.5)	1.3 (1.0-1.6)	
Covered by health insurance	81.8 (76.8-86.9)	80.2 (76.8-83.6)	81.3 (79.6-82.9)	81.1 (79.5-82.8)	0.796
Risky sexual behavior[5]					**0.001**
Low risk	93.9 (91.7-96.1)	91.8 (90.0-93.7)	89.0 (87.9-90.1)	90.0 (89.1-91.0)	
Moderate risk	4.1 (2.5-5.7)	4.8 (3.4-6.1)	8.2 (7.3-9.1)	7.1 (6.3-7.9)	
High risk	2.1 (0.7-3.4)	3.4 (1.7-5.1)	2.8 (2.3-3.3)	2.8 (2.3-3.3)	
BMI, continuous[4] ***Range 13.6-81.25***	36.1 (35.0-37.3)	32.2 (31.2-33.3)	28.2 (27.9-28.5)	29.8 (29.4-30.1)	**<0.0001**
BMI, categorized					**<0.0001**
Underweight	0.03 (0.0-0.1)	0.6 (0.1-1.0)	1.8 (1.4-2.2)	1.4 (1.1-1.7)	
Normal weight	9.6 (5.9-13.3)	14.5 (11.4-17.7)	31.4 (29.5-33.4)	26.0 (24.4-27.7)	
Overweight	15.1 (11.5-18.6)	31.6 (27.3-35.8)	34.5 (32.4-36.6)	31.9 (29.9-33.8)	
Obese	75.3 (69.6-81.0)	53.3 (47.7-59.0)	32.3 (30.2-34.3)	40.7 (38.7-42.8)	
HIV					0.334
Yes	1.3 (0.0-2.9)	0.7 (0.2-1.2)	0.5 (0.2-0.7)	0.6 (0.3-0.9)	
No	98.7 (97.1-100.0)	99.3 (98.8-99.8)	99.5 (99.3-99.8)	99.4 (99.1-99.7)	
TOTAL[6]	**2,239**	**3,393**	**11,337**	**16,969**	

[1]: Diabetes status was categorized in the following way: no diabetes: negative self-report and A1c <

5.7; prediabetes: negative self-report and 5.7% ≤ A1c ≤ 6.4; diabetes: positive self-report or A1c ≥ 6.5%.
[2]: Weighted percentages and confidence intervals, unadjusted.
[3]: P-values were calculated using the Rao-Scott chi-square test for categorical variables and a F-test for continuous variables, both of which took weighting into account. Significant (<0.05) values in bold.
[4]: Weighted mean and 95% CI presented. Total indicates overall weighted mean and weighted 95% CI.
[5]: Risky sexual behavior was defined in the following way: low risk (had sex with 1 or fewer people in the last year regardless of condom use or had sex with more than one person in the last year but always used condoms); moderate risk (had sex with more than one person in the last year and sometimes used condoms) and high risk (had sex with more than one person in the last year and never used condoms).
[6]: Unweighted frequency.

Table 2. Demographic characteristics of sample by STI status,[1] NHANES 2007-2014.

Characteristic	STI Positive 10.5 (9.0-11.9) % (95% CI)[2]	STI Negative 89.5 (88.1-91.0) % (95% CI)[2]	P-value[3]
Race			
Mexican-American	5.1 (3.3-7.0)	94.9 (93.0-96.7)	**<0.0001**
Other Hispanic	7.4 (5.3-9.4)	92.6 (90.6-94.7)	
White	11.2 (9.3-13.1)	88.8 (86.9-90.7)	
Black	13.6 (10.8-16.4)	86.4 (83.6-89.2)	
Other	5.2 (3.5-7.0)	94.8 (93.0-96.5)	
Sex			
Male	6.1 (4.6-7.6)	93.9 (92.4-95.4)	**<0.0001**
Female	14.2 (12.1-16.4)	85.8 (83.6-87.9)	
Age, continuous[4]	41.6 (40.3-43.0)	40.6 (40.1-41.2)	0.135
Age, categorized			
18-24	9.1 (6.6-11.7)	90.9 (88.3-93.4)	0.169
25-39	9.5 (7.8-11.2)	90.5 (88.8-92.2)	
40-59	11.3 (9.2-13.4)	88.7 (86.6-90.8)	
Education			
Less than 9th grade	6.5 (2.6-10.5)	93.5 (89.5-97.4)	0.348
9-12th, no diploma	11.5 (6.6-16.3)	88.5 (83.7-93.4)	
High school graduate/GED	9.3 (7.1-11.6)	90.7 (88.4-92.9)	
Some college or AA degree	10.1 (8.3-11.8)	89.9 (88.2-91.7)	
College graduate or above	11.9 (9.3-14.4)	88.1 (85.6-90.7)	
Sexual orientation			
Gay/homosexual	19.9 (8.7-31.1)	80.1 (68.9-91.3)	**0.044**
Straight/heterosexual	10.0 (8.6-11.5)	90.0 (88.5-91.4)	
Bisexual	16.1 (10.4-21.8)	83.9 (78.2-89.6)	
Other	17.2 (8.3-26.1)	82.8 (73.9-91.7)	
Covered by health insurance	11.1 (9.4-12.7)	88.9 (87.3-90.6)	**0.004**
Risky sexual behavior[5]			
Low risk	10.0 (8.5-11.5)	90.0 (88.5-91.5)	0.063
Moderate risk	14.9 (11.9-18.0)	85.1 (82.0-88.1)	
High risk	14.7 (5.7-23.6)	85.3 (76.4-94.3)	
BMI, continuous[4]	29.1 (28.3-29.9)	29.9 (29.5-30.2)	0.090
BMI, categorized			
Underweight	9.9 (2.0-17.9)	90.1 (82.1-98.0)	0.316
Normal weight	10.6 (8.9-12.3)	89.4 (87.7-91.1)	
Overweight	11.9 (8.8-15.0)	88.1 (85.0-91.2)	
Obese	9.3 (7.4-11.2)	90.7 (88.8-92.6)	
HIV			
Yes	47.8 (20.1-79.9)	52.2 (24.4-79.9)	**0.032**
No	10.3 (8.8-11.7)	89.7 (88.3-91.2)	
TOTAL[6]	**1,634**	**15,335**	

[1]: STI status determined by self-report; includes chlamydia, gonorrhea, herpes, and HPV self-report.
[2]: Weighted percentages and confidence intervals, unadjusted.
[3]: P-values were calculated using the Rao-Scott chi-square test for categorical variables and a F-test for continuous variables, both of which took weighting into account. Significant (<0.05) values in bold.
[4]: Weighted mean and 95% CI presented.
[5]: Risky sexual behavior was defined in the following way: low risk (had sex with 1 or fewer people in the last year regardless of condom use or had sex with more than one person in the last year but always used condoms); moderate risk (had sex with more than one person in the last year and sometimes used condoms) and high risk (had sex with more than one person in the last year and never used condoms).
[6]: Unweighted frequency.
*Note: percentages represent row totals, not column totals.

Table 3. Clinical and demographic characteristics of those with diabetes[1] in the sample, by STI status,[2] NHANES 2007-2014.

Characteristic	STI Positive 7.4 (3.5-11.3) % (95% CI)[3]	STI Negative 92.6 (88.7-96.5) % (95% CI)[3]	P-value[4]
Sex			
Male	5.7 (0.0-11.6)	94.3 (88.4-100.0)	0.365
Female	8.9 (4.3-13.5)	91.1 (86.5-95.7)	
Age, categorized			
18-24	0	100.0 (100.0-100.0)	N/A*
25-39	2.2 (0.0-4.8)	97.8 (95.2-100.0)	
40-59	8.3 (3.9-12.7)	91.7 (87.3-96.1)	
Diabetes duration, in years			
0-5	5.9 (1.8-10.0)	94.1 (90.0-98.2)	0.624
6+	8.9 (2.5-15.3)	91.1 (84.7-97.5)	
Diabetes medications			
No medications	6.2 (0.7-11.6)	93.8 (88.4-99.3)	0.289
Insulin	6.5 (0.0-14.8)	93.5 (85.2-100.0)	
Pills	10.0 (3.1-16.9)	90.0 (83.1-96.9)	
Insulin and Pills	2.4 (0.0-5.7)	97.6 (94.3-100.0)	
Any medication	7.5 (3.2-11.9)	92.5 (88.1-96.8)	
A1c			
< 7.0%	6.5 (2.2-10.9)	93.5 (89.1-97.8)	0.667
≥ 7.0%	8.1 (2.2-13.9)	91.9 (86.1-97.8)	
Two hour glucose tolerance test			
< 140 mg/dL	7.4 (3.5-11.4)	92.6 (88.6-96.5)	0.722
≥ 140 mg/dL	5.3 (0.0-16.0)	94.7 (84.0-100.0)	
BMI, categorized			
Underweight	0	100.0 (100.0-100.0)	N/A*
Normal weight	3.1 (0.0-6.8)	96.9 (93.2-100.0)	
Overweight	6.3 (1.6-11.1)	93.7 (88.9-98.4)	
Obese	8.2 (3.5-12.8)	91.8 (87.2-96.5)	
HIV			
Yes	54.0 (0.0-100.0)	46.0 (0.0-100.0)	0.338
No	6.8 (3.0-10.5)	93.2 (89.5-97.0)	
TOTAL[5]	**188**	**2,051**	

[1]: Diabetes status was categorized in the following way: no diabetes: negative self-report and A1c < 5.7; prediabetes: negative self-report and 5.7% ≤ A1c ≤ 6.4; diabetes: positive self-report or A1c ≥ 6.5%.

[2]: STI status determined by self-report; includes chlamydia, gonorrhea, herpes, and HPV.

[3]: Weighted percentages and confidence intervals, unadjusted.

[4]: P-values were calculated using the Rao-Scott chi-square test for categorical variables, which takes weighting into account. Significant (<0.05) values in bold.

[5]: Unweighted frequency.

*Insufficient data present to perform a chi-square test.

** Note: percentages reflect the row percentage instead of the column percentage; i.e. what percentage of the population on pills was STI positive.

Table 4. Specific and overall STI[1] odds ratios produced by several multivariable models, NHANES 2007-2014.

		Model		
STI Outcome	**Comparison***	**Diabetes[2] OR (95% CI)**	**Diabetes, age, race, sex OR (95% CI)**	**Diabetes, age, race, sex, risky sexual behavior, HIV, sexual orientation, health insurance, BMI OR (95% CI)**
Any STI	***Prediabetes***	0.89 (0.68-1.16)	1.04 (0.64-1.68)	1.09 (0.69-1.72)
	Diabetes	0.79 (0.47-1.35)	0.61 (0.35-1.08)	0.67 (0.37-1.21)
Chlamydia	***Prediabetes***	0.77 (0.40-1.48)	1.13 (0.53-2.39)	1.11 (0.49-2.52)
	Diabetes	0.64 (0.15-2.79)	1.08 (0.24-4.85)	0.96 (0.19-4.72)
Gonorrhea	***Prediabetes***	0.73 (0.25-2.14)	0.90 (0.28-2.93)	1.00 (0.23-4.39)
	Diabetes	0.56 (0.09-3.54)	0.79 (0.12-5.40)	0.91 (0.10-8.55)
Herpes	***Prediabetes***	1.08 (0.71-1.65)	0.97 (0.62-1.51)	0.98 (0.62-1.54)
	Diabetes	0.56 (0.29-1.08)	**0.48 (0.24-0.94)**	**0.48 (0.25-0.90)**
HPV	***Prediabetes***	1.14 (0.61-2.12)	1.00 (0.54-1.88)	1.05 (0.54-2.02)
	Diabetes	0.77 (0.32-1.85)	0.65 (0.27-1.56)	0.70 (0.28-1.76)

[1]: STI determined by self-report. 'Any STI' includes chlamydia, gonorrhea, herpes, and HPV.
[2]: Diabetes status was categorized in the following way: no diabetes: negative self-report and A1c < 5.7; prediabetes: negative self-report and 5.7% ≤ A1c ≤ 6.4; diabetes: positive self-report or A1c ≥ 6.5%.
*The first OR presented is for prediabetes, and the second OR is for diabetes.
ORs with 95% confidence intervals not containing the null are in bold.

Table 5. Specific STI[1] odds ratios produced by several multivariable models, NHANES 2007-2014.

		Model		
STI Outcome	**Comparison***	**Diabetes[2] OR (95% CI)**	**Diabetes, age, race, sex OR (95% CI)**	**Diabetes, age, race, sex, risky sexual behavior, HIV, sexual orientation, health insurance, BMI OR (95% CI)**
Herpes[3]	***Prediabetes***	**2.32 (1.81-2.98)**	**1.97 (1.53-2.55)**	**1.79 (1.34-2.38)**
	Diabetes	**2.87 (1.94-4.24)**	**2.17 (1.48-3.19)**	**1.95 (1.34-2.85)**
HPV[4]	***Prediabetes***	0.84 (0.63-1.11)	0.97 (0.69-1.38)	0.96 (0.69-1.35)
	Diabetes	1.25 (0.84-1.87)	1.41 (0.84-2.38)	1.43 (0.89-2.32)

[1]: STI determined by laboratory testing.
[2]: Diabetes status was categorized in the following way: no diabetes: negative self-report and A1c < 5.7; prediabetes: negative self-report and 5.7% ≤ A1c ≤ 6.4; diabetes: positive self-report or A1c ≥ 6.5%.
[3]: 4,035 observations were deleted due to missing information about herpes lab testing; therefore, the total sample size being used for these models was 12,661.
[4]: 8,063 observations were deleted due to missing information about HPV lab testing; therefore, the total sample size being used for these models was 8,633.
*The first OR presented is for prediabetes, and the second OR is for diabetes.
ORs with 95% confidence intervals not containing the null are in bold.

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