



Risk of Type 2 Diabetes Among Lesbian, Bisexual, and Heterosexual Women: Findings From the Nurses' Health Study II

Heather L. Corliss,^{1,2} Nicole A. VanKim,³
Hee-Jin Jun,¹ S. Bryn Austin,^{2,4,5}
Biling Hong,⁶ Molin Wang,^{2,6,7} and
Frank B. Hu^{2,6,8}

<https://doi.org/10.2337/dc17-2656>

OBJECTIVE

Lesbian and bisexual (LB) women are more likely than heterosexual women to exhibit risk factors for type 2 diabetes, but studies estimating the burden of type 2 diabetes among LB women are uncommon and limited to cross-sectional designs. This study investigated incidence of type 2 diabetes in LB women and heterosexual women in a large, longitudinal U.S. cohort.

RESEARCH DESIGN AND METHODS

Women participating in the Nurses' Health Study II ages 24–44 years in 1989 were prospectively followed through 2013. Self-reported clinician diagnosis of type 2 diabetes was assessed every other year to identify incidence. Of the participants, 1,267 identified as lesbian or bisexual and 92,983 identified as heterosexual. Cox proportional hazards regression was used to model incidence of type 2 diabetes.

RESULTS

LB women had a 27% higher risk of developing type 2 diabetes than heterosexual women (adjusted incidence rate ratio [IRR] 1.27, 95% CI 1.05–1.54). Differences between LB women and heterosexual women in risk of type 2 diabetes were greater during younger ages (sexual orientation–by-age interaction, $P < 0.001$). BMI mediated the relationship between sexual orientation and type 2 diabetes; the IRR was completely attenuated when BMI was added to the model (IRR 0.85, 95% CI 0.70–1.03).

CONCLUSIONS

Findings indicate that LB women develop type 2 diabetes at younger ages than heterosexual women. Higher BMI in LB women is an important contributor to this disparity. Public health and clinical efforts to prevent, detect, and manage obesity and type 2 diabetes among LB women are warranted.

Although the majority of lesbian and bisexual (LB) women living in the U.S. are no less healthy than their heterosexual female counterparts, the population of LB women has health disparities and unique health needs (1). For example, extensive research demonstrates that LB women are more likely than heterosexual women to experience mental health and substance use problems (2–4). Less extensive is research examining potential differences between LB women and heterosexual women in their risk of developing chronic physical health problems; results from such studies have been inconclusive thus far (5,6). For example, findings from cross-sectional studies investigating differences between LB women and heterosexual women in risk for type 2 diabetes have

¹Graduate School of Public Health and Institute for Behavioral and Community Health, San Diego State University, San Diego, CA

²Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

³Department of Biostatistics and Epidemiology, School of Public Health and Health Sciences, University of Massachusetts Amherst, Amherst, MA

⁴Division of Adolescent and Young Adult Medicine, Boston Children's Hospital, Boston, MA

⁵Department of Social and Behavioral Sciences, Harvard T.H. Chan School of Public Health, Boston, MA

⁶Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA

⁷Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA

⁸Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA

Corresponding author: Heather L. Corliss, hcorliss@mail.sdsu.edu.

Received 20 December 2017 and accepted 5 April 2018.

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been mixed, with some studies finding differences by sexual orientation (7–9) and other studies finding no difference (10–15). Most studies detecting sexual orientation differences found higher risk for type 2 diabetes in LB women compared with heterosexual women (7,8).

Despite inconclusive findings, there is reason to suspect that LB women may have disparities in chronic physical health conditions, including type 2 diabetes, because they are more likely than heterosexual women to have risk factors such as obesity (16), tobacco smoking (3,16), heavy alcohol drinking (3,16), and stress-related exposures (e.g., discrimination, violence victimization, and psychological distress) (3,17–19). Consistent with findings from population-based studies, analyses with data from the Nurses' Health Study II (NHS II), the longitudinal cohort examined in the current study, have found that LB women are more likely than heterosexual women to report obesity, cigarette smoking, heavy alcohol use, depression, and childhood victimization (20–22).

Minority stress is theorized to be a central reason why LB women are at elevated risk for physical health problems including type 2 diabetes (23). Minority stress, or the external (e.g., discrimination) and internal (e.g., expectations of rejection) stressors resulting from a socially stigmatized sexual orientation (18), can negatively affect coping, emotion regulation, and social, interpersonal, and cognitive processes (24). Both physiological and behavioral pathways link minority stress to type 2 diabetes risk. Regarding physiological pathways, high allostatic load, or the cumulative wear and tear on the body resulting from chronic exposure to stress, can increase risk for disease (25). Chronic stress is associated with type 2 diabetes through dysregulation of at least three biological pathways: the hypothalamic-pituitary-adrenal axis, the autonomic nervous system, and the inflammatory system (26). Dysregulation of the hypothalamic-pituitary-adrenal axis results in elevated cortisol, which leads to intra-abdominal adiposity and insulin resistance, both factors contributing to increased risk of type 2 diabetes. Also, overactivation of both the autonomic nervous system and the inflammatory response can lead to insulin resistance. Regarding behavioral pathways, exposure to minority stress may be associated with a

greater likelihood of engaging in maladaptive coping behaviors such as cigarette smoking or stress-related eating, which may increase risk for type 2 diabetes (27–29).

According to an Institute of Medicine report published in 2011 (1), research is needed to understand how minority sexual orientation intersects with other sociodemographic factors to influence health. Age and rural residence are two such factors that could modify sexual orientation-related differences in risk for type 2 diabetes. Regarding age, exposure to minority stress and resulting risk factors for type 2 diabetes may be heightened during adolescence and young adulthood when LB women typically become aware of their minority sexual orientation (30). Thus, differences between LB women and heterosexual women in risk of developing type 2 diabetes may be accentuated during younger ages. In support of this hypothesis, research suggests that when age modifies relationships between minority sexual orientation and behavioral, mental, or physical health outcomes, disparities are larger during younger versus older ages (31,32). However, there is some inconsistency, as an analysis of the representative California Health Interview Survey found that compared with heterosexual women of similar age, lesbian women aged 60 years or older had elevated risk for type 2 diabetes, but lesbian women younger than aged 60 years did not (31). Regarding rural residence, LB women living in rural areas may have unique challenges related to minority stress that have the potential to exacerbate risk for type 2 diabetes. Although research is inconclusive, rural-residing LB women may have lower social support, less access to affirming health care providers, and less comfort disclosing their minority sexual orientation to others compared with LB women living in urban areas (1,33). A previous study found that rural-residing lesbian women had significantly higher BMIs than urban-residing lesbian women (34).

A limitation of previous studies investigating differences between LB and heterosexual women in risk for type 2 diabetes is a lack of longitudinal designs. Another limitation is that studies frequently had low power to detect statistically significant differences between LB women and heterosexual women. As a consequence, effect sizes in some studies

have suggested potential elevated risk for type 2 diabetes in lesbian or bisexual women, but estimates were not statistically significant and crossed the null value (12,14). To address these limitations and build on the current literature, we analyzed longitudinal data from the NHS II to compare age-specific incidence of type 2 diabetes during ages 24–68 years among LB and heterosexual women. We also examined intersections of sexual orientation with age and rural living status to assess potential differences in type 2 diabetes risk by these factors. Lastly, because of the robust evidence that LB women have higher BMI than heterosexual women and BMI's strong positive relationship with risk of type 2 diabetes, we examined its mediating influence in explaining the relationship between sexual orientation and type 2 diabetes.

RESEARCH DESIGN AND METHODS

Study Population

The NHS II is a prospective cohort of female registered nurses established in 1989. Participants aged 24–44 years were recruited from 15 of the most populous states in the U.S. using state nursing boards. The baseline questionnaire was mailed to 517,000 women, of which 123,000 (24%) responded. Those who had incomplete surveys or were ineligible (including those who reported breast cancer) were excluded, yielding a total of 116,671 in the cohort. Biennial mailed questionnaires were used for follow-up. The follow-up rate has exceeded 90% for every 2-year period. Data collected from 1989 to 2013 comprised the analyses.

Analytic Sample

Participants were excluded from analyses if they had a diagnosis of diabetes before 1989, self-reported diabetes in 1989, reported a history of gestational diabetes in 1989, had type 1 diabetes, or reported type 2 diabetes without providing a date of diagnosis. Participants were also excluded if they did not report a heterosexual, lesbian, or bisexual sexual orientation. After exclusions, a total of 94,250 women remained in the analytic sample; 1,267 lesbian or bisexual women contributed 29,984 person-years and 92,983 heterosexual women contributed 2,230,488 person-years during ages 24–68 years to the analytic models.

Measures

Type 2 Diabetes

Participants were asked if and when they had been diagnosed with type 2 diabetes by a clinician on each biennial questionnaire. Participants reporting diabetes were mailed a supplementary questionnaire assessing symptoms, diagnostic tests, and hypoglycemic therapy to confirm self-reported diagnoses. As recommended (35), confirmation of diabetes required at least one of the following: 1) at least one classic symptom (e.g., excessive thirst, polyuria) plus fasting plasma glucose (PG) ≥ 126 mg/dL or random PG ≥ 200 mg/dL; or 2) at least two elevated PG levels on different occasions (fasting PG ≥ 126 mg/dL and/or random PG ≥ 200 and/or PG ≥ 200 at 2 h on oral glucose tolerance testing) in the absence of symptoms; or 3) treatment with hypoglycemic medication (insulin or oral hypoglycemic agent). This is a validated method of identifying type 2 diabetes in the NHS II, as assessed via a substudy that confirmed by medical record review more than 98% of self-reported diabetes cases (36). Because participants are nurses who virtually all have access to health care, prevalence of undiagnosed diabetes in the NHS II is rare. Another validation substudy found that only 1 out of 200 randomly selected participants not previously reporting a diabetes diagnosis had an elevated fasting PG or plasma fructosamine level in the diabetic range (37).

Sexual Orientation

Participants identified their sexual orientation in 1995 and 2009 using the following question: "Whether or not you are currently sexually active, what is your sexual orientation or identity? (Please choose one answer)." Response options included "Heterosexual"; "Lesbian, gay, or homosexual"; "Bisexual"; "None of these"; and "Prefer not to answer." Consistent with our previous work (38,39), reported sexual orientation in 2009 was used, except where there was missing information (i.e., not identifying as heterosexual, lesbian, or bisexual), in which case sexual orientation reported in 1995 was used. A sensitivity analysis using an alternative assignment of sexual orientation, where sexual orientation reported in 1995 was used for waves 1991 to 2007 and sexual orientation reported in 2009 was used for the 2011 and 2013 waves, was performed (data not shown). Results of two different sexual orientation

categorizations were consistent, thus analyses based on most recent report of sexual orientation are presented. For this study, we also combined women reporting their sexual orientation as lesbian or bisexual into one category to increase the statistical power to detect differences by sexual orientation. Prior to collapsing lesbian and bisexual women into one category, preliminary analyses keeping these groups separate were performed. Because effect estimates were consistent for these groups, they were combined in analyses.

BMI

NHS II participants reported their height and weight at baseline and in each follow-up questionnaire, and those reports were used to calculate their BMI (kg/m^2). For analysis, BMI was updated at each assessment and modeled as a continuous variable. Because BMI is a causal factor for type 2 diabetes, it was conceptualized and modeled as a mediator in the relationship between minority sexual orientation and type 2 diabetes.

Covariates

Age (continuous), family history of diabetes (assessed at baseline), race/ethnicity (non-Hispanic white vs. all other race/ethnicities), region of residence (Northeast, Midwest, South, and West), rural status (rural, defined as population density < 500 people per square mile, vs. nonrural), menopausal status (premenopausal, postmenopausal and never used postmenopausal hormones, postmenopausal and previously used postmenopausal hormones, and postmenopausal and currently using postmenopausal hormones), and whether a participant visited a health care provider during the past 2 years were all included as potential confounders in analyses. Time-varying confounders (e.g., region of residence, menopausal status, visited health care provider during the past 2 years) were updated with each new data collection. Behaviors such as physical activity, diet, smoking, and alcohol use were not included as covariates because these factors are likely on the causal pathway between sexual orientation and incident type 2 diabetes. Inclusion of these factors as covariates would have yielded overadjustment bias (40).

Data Analysis

Distributions of the independent variables were computed for LB women and

heterosexual women. Age-specific Cox proportional hazards regression models were then fit to examine the association between sexual orientation and incident type 2 diabetes. Study time for these models began in 1989 (baseline) and continued until age of type 2 diabetes diagnosis, death, loss to follow-up, or end of follow-up. The Wald test and likelihood ratio test were used to compute *P* values. We tested for departures from the proportional hazards assumption (i.e., effect modification by age) using likelihood ratio tests comparing models with and without age interaction terms. In addition to examining effect modification by age, we examined effect modification by rural living status using a sexual orientation-by-rural term in the model. To test whether BMI mediated the relationship between sexual orientation and type 2 diabetes, we compared estimates from models that included and excluded BMI updated at each assessment to assess for changes in model parameter estimates. Incidence rate ratios (IRR) and 95% CIs comparing LB women to heterosexual women are reported.

Analyses were conducted using SAS software, version 9.3, with a significance level of 0.05. Participants provided informed consent for this study, which was approved by the Institutional Review Board at Brigham and Women's Hospital and the Human Subjects Committee at the Harvard T. H. Chan School of Public Health. Analyses for this study were performed between 2016 and 2018.

RESULTS

Sociodemographic characteristics of the study sample are presented in Table 1. The average age of women during follow-up was about 46 years. The majority of women were non-Hispanic white and were premenopausal during most of the follow-up period. Compared with heterosexual women, LB women were less likely to have lived in the Midwest and in rural areas and they had a higher mean BMI.

During the follow-up period (1989–2013), 6,399 out of 94,250 women developed type 2 diabetes. Table 2 presents the IRR for type 2 diabetes comparing LB women to heterosexual women. Before adjusting for potential confounders, the crude IRR suggested that LB women had a 22% greater risk of developing type 2 diabetes than heterosexual women. After

Table 1—Sociodemographic characteristics of heterosexual and LB women in the NHS II, 1989–2013

	Heterosexual	LB
Sample size, <i>n</i>	92,983	1,267
Person-years, <i>n</i>	2,230,488	29,984
Age in years during follow-up	45.7 (8.8)	46.3 (8.8)
Non-Hispanic white	95	95
Region of residence		
Northeast	33	33
Midwest	33	22
South	19	18
West	15	27
Rural status (population density <500 people/mi ²)	32	24
Menopausal status		
Premenopausal	69	66
Postmenopausal, never used postmenopausal hormones	9	11
Postmenopausal, previously used postmenopausal hormones	12	13
Postmenopausal, currently using postmenopausal hormones	10	10
Visited health care provider during past 2 years	94	93
Family history of diabetes	15	16
BMI, kg/m ²	26.0 (5.8)	27.5 (6.8)

Data are mean (SD) or percent unless otherwise indicated.

adjusting for family history of diabetes, race/ethnicity, region of residence, rural status, and menopausal status, LB women continued to have a significantly higher incidence of type 2 diabetes than heterosexual women (IRR 1.27, 95% CI 1.05–1.54; $P = 0.014$).

Results of the mediation analysis shown in Table 2 indicated that the relationship between sexual orientation and type 2 diabetes was completely attenuated after BMI was added to the model. This finding suggests that higher BMI among LB women completely explained their greater incidence of type 2 diabetes.

Figure 1 illustrates the sexual orientation-by-age interaction on incident type 2 diabetes. According to the figure, the incidence of type 2 diabetes for LB women was significantly higher than for heterosexual women until approximately age 50, after which risk among LB and

heterosexual women became more similar. A statistical test of the sexual orientation-by-age interaction indicated it was significant ($P = 0.0007$). Results of age-stratified models are shown in Table 3. When women were younger than age 40, incidence of type 2 diabetes was more than two times higher among LB women compared with heterosexual women, whereas incidence was approximately 30% higher among LB women during ages 40–49 years. After age 50, incidence of type 2 diabetes was similar for both sexual orientation groups. Adjustment for BMI attenuated associations between sexual orientation and incidence of type 2 diabetes during ages 24–39 years and ages 40–49 years. A test of a sexual orientation-by-rural statistical interaction indicated that differences between LB women and heterosexual women in risk of type 2 diabetes were

similar irrespective of rural status (sexual orientation-by-rural interaction, $P = 0.21$).

CONCLUSIONS

Findings from the NHS II cohort suggest that LB women have a higher incidence of type 2 diabetes than heterosexual women. Our study also found that differences between LB women and heterosexual women in risk of type 2 diabetes were greater during younger ages than older ages. When participants were ages 24–39 years, LB women had more than twice the risk of developing type 2 diabetes than heterosexual women, whereas risk for developing type 2 diabetes was similar for both groups of women by the time they reached age 50 years. In contrast, we did not find evidence that rural LB women were especially vulnerable to developing type 2 diabetes. Findings indicated that differences between LB women and heterosexual women in risk for developing type 2 diabetes were similar in rural and nonrural settings. Finally, our study found that greater BMI among LB women prospectively explained their elevated risk for type 2 diabetes. This finding helps to establish the critical role of obesity in contributing to LB women's greater risk of developing type 2 diabetes.

Our study has important advantages compared with previous studies examining type 2 diabetes among LB women. First, prior studies have been limited to cross-sectional designs (7–15) that were only able to examine prevalence of disease. In contrast, our study followed women over a significant portion of adulthood to identify sexual orientation differences in the development of new cases of type 2 diabetes. Second, our study had greater statistical power than prior studies, which strengthened the ability to detect differences. Third, in contrast to prior studies, which had a significant portion of participants who were relatively young, our study followed a substantial proportion of women into their 60s. Because type 2 diabetes is a disease that develops with age, it may be difficult to detect sexual orientation-related differences in existing cross-sectional samples.

The results of this study have important clinical and public health implications. Clinically, type 2 diabetes is a complex condition requiring careful management, which can include lifestyle therapy, medication adherence, and personal monitoring

Table 2—Results of Cox proportional hazards regression models estimating the IRR for type 2 diabetes comparing LB women to heterosexual women in the NHS II, 1989–2013

	IRR (95% CI)		<i>P</i> value
	Heterosexual	LB	
Crude	Referent group	1.22 (1.01, 1.48)	0.043
Adjusted for confounders ^a	Referent group	1.27 (1.05, 1.54)	0.014
Adjusted for BMI ^b	Referent group	0.85 (0.70, 1.03)	0.091

^aAdjusted for age, family history of type 2 diabetes, race/ethnicity, region of residence, rural status, menopausal status, and visit to health care provider in the past 2 years. ^bAdjusted for confounders and updated BMI as a mediator.

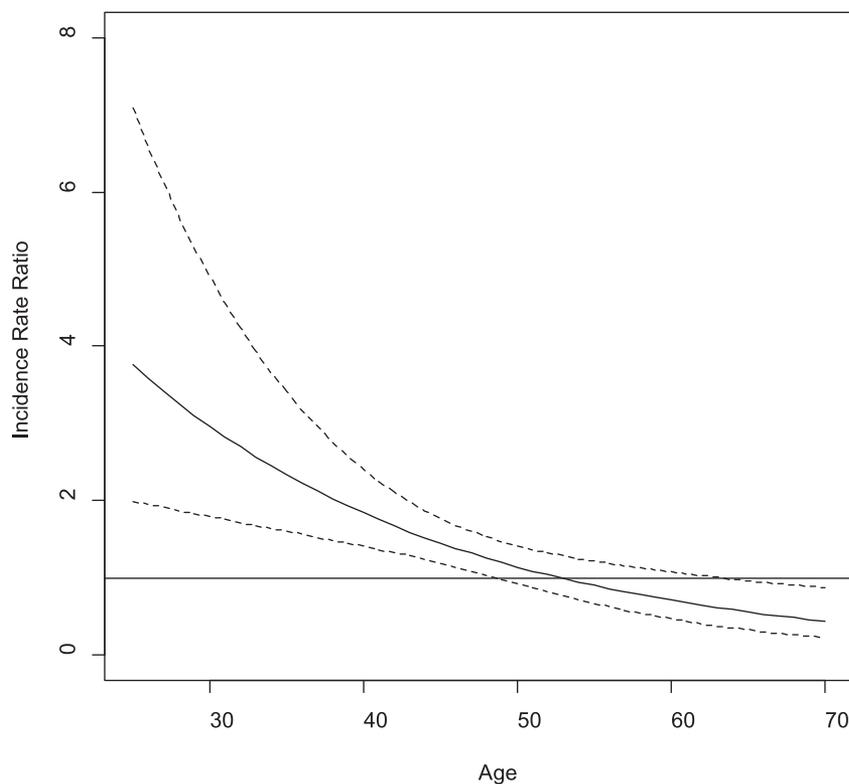


Figure 1—Type 2 diabetes IRR plot for sexual orientation-by-age interaction. The solid line represents the IRR for type 2 diabetes comparing LB women to heterosexual women across age (in years). The dotted lines represents the 95% CI for the IRR.

(41). Most complications related to type 2 diabetes (e.g., retinopathy, neuropathy, and cardiovascular disease) are dependent on the duration of time people live with the disease and poor disease management (42). Given the significantly higher risk of developing type 2 diabetes before age 50 years among LB women, and their potentially longer duration of living with type 2 diabetes, LB women may also be more likely to experience complications compared with heterosexual women. However, research on potential sexual orientation-related differences in disease management is lacking and there exists no information on

the degree that typically prescribed therapies and interventions are effective for LB women. Additional research on the health of LB women after diagnosis is vital to understanding the implications of disease on their subsequent health risks and prognosis. Research is also needed to aid in developing effective clinical practices for treatment of type 2 diabetes in this population.

A related issue that may affect LB women’s detection and management of type 2 diabetes includes concerns around access to care. Research has demonstrated unique challenges related to sexual orientation stigma that hinder LB women

from accessing health care (43), which can adversely impact diabetes diagnosis and management. Compared with general population-based surveys, which had mixed findings with regard to sexual orientation-related differences in type 2 diabetes prevalence, our study found significantly higher incidence among LB women. This discrepancy could be due to high levels of health care access in our study population, which may have resulted in better detection of type 2 diabetes among women in the NHS II compared with women in the general population. Improving health care access may help improve data quality by reducing nondetection bias. Greater access may also improve disease management and prevention of type 2 diabetes complications for LB women.

Findings from this study underscore the importance of developing public health prevention efforts for LB women. Given the large societal and personal costs of type 2 diabetes, and the clinical burden of managing this disease, there is a need to develop and test intervention strategies for LB women to prevent and address risk factors for type 2 diabetes including obesity, stress, and behavioral factors. Similar to studies of women in general, a cross-sectional study found that sexual minority women who exhibited sufficient physical activity and healthy eating habits had lower risk for obesity, chronic conditions, and poor quality of life than those exhibiting less favorable behaviors (44). Although it is important to address behavioral factors such as physical activity, sedentary behavior, and dietary intake, focusing on these factors alone may not be sufficient to eliminate LB women’s disparities in chronic disease. In the NHS II cohort, LB women reported healthier diet quality (38) and greater physical activity (39) than heterosexual women. Although LB women in NHS II also reported greater sedentary behavior (e.g., sitting time) (39), it does not appear that behavioral factors alone explain LB women’s greater BMI and greater incidence of type 2 diabetes. Given the detrimental health impacts of minority stress, it may also be necessary to address societal stigma and psychosocial stress.

Our study identified obesity as a potentially modifiable factor contributing to LB women’s elevated incidence of type 2 diabetes. Because LB women’s greater risk of obesity begins early in the life span (45), efforts to prevent high BMI

Table 3—Results of age-stratified Cox proportional hazards regression models estimating the IRR for type 2 diabetes comparing LB women to heterosexual women in the NHS II, 1989–2013

	IRR (95% CI)		
	Ages 24–39 years	Ages 40–49 years	Ages 50–68 years
Crude	2.52 (1.60, 3.98)	1.32 (0.99, 1.76)	0.91 (0.67, 1.24)
Adjusted for confounders ^a	2.44 (1.54, 3.86)	1.36 (1.02, 1.81)	0.96 (0.70, 1.31)
Adjusted for BMI ^b	1.46 (0.92, 2.33)	0.90 (0.68, 1.20)	0.67 (0.49, 0.92)

Referent group is heterosexual women. ^aAdjusted for age, family history of type 2 diabetes, race/ethnicity, region of residence, rural status, menopausal status, and visit to health care provider in the past 2 years. ^bAdjusted for confounders and updated BMI as a mediator.

beginning in adolescence should be prioritized. In addition, although studies suggest weight loss is difficult to achieve and maintain (46), intensive behavioral interventions containing evidence-based strategies to improve dietary intake and promote physical activity have been found to reduce obesity and improve fitness (47). Nonetheless, the extent to which behavioral interventions developed for the general population are effective for LB women is unknown, and few interventions to promote healthy weight and fitness have been developed specifically for LB women. A notable exception is a multisite collaborative of researchers and community organizations funded by the Office of Women's Health that developed and pilot tested five 12- to 16-week-long interventions tailored for LB women over age 40 years (48). Although the specific components varied by site, each intervention addressed four Institute of Medicine recommendations: increasing physical activity, promoting healthy dietary intake, promoting limited alcohol intake, and reducing consumption of sugar-sweetened beverages. Evaluation of these programs found that 58% of participants achieved at least 3 out of 9 health objectives, and improvements in physical activity and waist-to-height ratio were observed in some program participants relative to those in a comparison group (49). The authors concluded that tailored programs can improve weight-related outcomes among LB women. Results of the current study as well as other studies (31,32) suggest efforts should also focus on LB women younger than age 40 years given their disproportionate burden of experiencing health disparities in multiple domains.

Our study is not without its shortcomings. Because the NHS II comprises professional nurses who are primarily non-Hispanic white, findings may not generalize to ethnic or racial minority women or women in low or high socioeconomic positions. Additional research using longitudinal data from diverse, population-based samples are needed to better understand disease risk among sexual minority women. Research is also needed to identify the influence of other modifiable risk and protective factors, including dietary intake, sedentary behaviors, physical activity, and minority stress factors, in contributing to LB women's differential risk of developing type 2 diabetes. Although the NHS II has collected

information on some of these modifiable factors, the inability to examine their influences in the current study represents a limitation. Another limitation of our study is that measures were based on self-report; therefore, measurement error and misclassification are possible. It is also possible that not all confounders were measured, which could lead to bias in estimates related to uncontrolled confounding. Also, further confirmation of the observation of effect modification by age with other data sources would lend evidence to this study's finding. However, our study has important strengths. One advantage is that women were not recruited based on their sexual orientation, which presumably results in less selection bias than studies sampling participants from lesbian, gay, bisexual, and transgender community settings. In addition, cohort retention is high, as more than 90% of women continue to participate, which likely results in low bias from attrition.

In summary, the elevated incidence of type 2 diabetes among LB women, particularly at younger ages, is alarming and highlights the critical need to expand prevention efforts, screening and detection, and clinical management to this population impacted by health disparities. Additional work is needed to identify appropriate mechanisms for intervention and to continue refining and testing tailored approaches. A better understanding of disease management challenges LB women experience after diagnosis is also needed to help reduce the clinical burden of type 2 diabetes complications. Lastly, expanding efforts by the public health and medical professions to address the detrimental health impacts of social stigma and minority stress may lead to improved health and wellness among LB women.

Acknowledgments. The authors thank the women participating in the NHS II who provided the information about their lives enabling this study to be carried out. The authors also thank Donna Spiegelman, Harvard T.H. Chan School of Public Health, for providing guidance on statistical analysis.

Funding. This study was supported by the National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases through award numbers R01DK099360 and R01DK1129401 and the National Cancer Institute through UM1CA176726.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

Author Contributions. H.L.C. conceived the study and obtained funding. H.L.C. and N.A.V.K. wrote the manuscript. H.-J.J. and B.H. conducted data analysis. M.W. supervised data analysis. H.L.C., N.A.V.K., S.B.A., and F.B.H. edited the manuscript. All authors reviewed and approved the manuscript. H.L.C. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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