HHS Public Access

Author manuscript

Ann Epidemiol. Author manuscript; available in PMC 2020 September 01.

Published in final edited form as:

Ann Epidemiol. 2019 September ; 37: 10–16. doi:10.1016/j.annepidem.2019.07.012.

The association between perceived discrimination in midlife and peripheral neuropathy in a population-based cohort of women: the Study of Women's Health Across the Nation

Jennifer R. Dusendang,
Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, Michigan

Alexis N. Reeves,
Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, Michigan

Carrie A. Karvonen-Gutierrez,
Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, Michigan

William H. Herman,
Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, Michigan

Department of Internal Medicine, School of Medicine, University of Michigan, Ann Arbor, Michigan

Kelly R. Ylitalo,
Department of Public Health, Baylor University, Waco, Texas

Siobán D. Harlow
Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, Michigan

Abstract

Purpose—Peripheral neuropathy (PN) is highly prevalent condition with serious sequelae. However, many studies of the condition have been restricted to populations with diabetes, limiting evidence of potential contributing risk factors including salient psychosocial risk factors such as discrimination.

Methods—The longitudinal Study of Women's Health Across the Nation was used to assess the relationship between perceived discrimination and prevalent peripheral neuropathy in 1,718 racially/ethnically diverse midlife women. We used multivariable logistic regression to determine

Correspondence to Siobán D. Harlow, 1415 Washington Heights, Ann Arbor, MI 48109.

Conflict of interest: none declared.

the association between perceived discrimination (Detroit Area Study Everyday Discrimination Scale) and PN (symptom questionnaire and monofilament testing) and conducted a formal assessment of the mediating effects of body mass index (BMI).

Results—The overall prevalence of PN was 26.1% in the total sample and 40.9% among women with diabetes. Women who reported perceived discrimination had 29% higher odds of PN as compared to women who did not report perceived discrimination (95% confidence interval (CI): 1.01, 1.66). Approximately 30% of the total effect of discrimination on PN was mediated indirectly by BMI.

Conclusions—More research is needed to determine the contributing factors to non-diabetic PN. Additionally findings re-affirm the impact of financial strain, BMI and diabetes as significant correlates of PN and highlight discrimination as an important risk factor.

Keywords

peripheral neuropathy; discrimination; diabetes; SWAN; midlife; diabetes; women

Peripheral neuropathy (PN) is characterized by damage to various classes of peripheral nerves and is a common comorbidity associated with diabetes. The sensory, autonomic and motor nerve damage that define the condition can cause a multitude of symptoms and signs including pain, numbness, loss of sensation, muscle atrophy, loss of balance, incontinence, and blood pressure irregularities (1). In the United States (US), approximately 20 million people are estimated to have PN (1). According to the American Diabetes Association, about 25% of people over 60 years of age have diabetes (2) and half of these older adults with diabetes are estimated to have PN (1,3).

While PN is more prevalent in populations with diabetes, research suggests that the burden of PN is high even among populations without diabetes. One study of a nationally representative United States sample estimated the prevalence of PN among individuals age 40+ years and without diabetes be 13% (4). Within the Study of Women's Health Across the Nation (SWAN) Michigan site, a subset of non-Hispanic white and African American participants from the larger SWAN cohort, the prevalence of PN among women with an average age of 57.6 years was 27.8% in the total sample and 26.2% among those without diabetes (5). While the pathophysiology of nerve damage is due, in part, to chronic hyperglycemia associated with diabetes, little is known about the pathogenesis of or risk factors for peripheral nerve dysfunction among individuals without diabetes. Emerging evidence suggests that mechanisms associated with obesity and the aging process may be detrimental to peripheral nerves (6–8).

Evidence is conflicting about the prevalence of PN in different racial/ethnic groups. Some studies have found minimal differences by racial/ethnic groups, with a lower prevalence among African Americans and Hispanics compared to Whites, while other studies have found no racial/ethnic difference in PN prevalence (9–11). Diabetes is intricately related to the diagnosis and understanding of PN, and the distribution of diabetes is not uniform across racial/ethnic groups in the United States. The prevalence of diagnosed and undiagnosed diabetes among African Americans is estimated to be nearly twice that in Whites, and

African Americans die of diabetes at a rate 1.3 times higher than Whites (12,13). A higher prevalence of undiagnosed diabetes among African-Americans (12,13) may be also contributing to the lower detected prevalence of diabetes related sequelae such as peripheral neuropathy.

Discrimination has been noted as a salient psychosocial factor linked to several chronic health conditions including hypertension, coronary artery disease, and insomnia among all racial/ethnic groups, with many studies reporting a higher prevalence of perceived discrimination among racial/ethnic minorities compared to Whites (14–20). Additionally, there has been conflicting evidence of moderation of the effect of discrimination among racial/ethnic minorities compared to Whites (16,17,19) particularly for conditions closely linked to diabetes such as metabolic syndrome (17,19). Perceived discrimination, including internalized racism, is also associated with high-risk body size (21–23). A commonly hypothesized model for the association between discrimination and chronic disease is that discrimination causes a chronic stress response that leads-through various biological mechanisms including allostatic load and inflammation - to chronic health conditions, such as diabetes (17,24,25). This work suggests that studies evaluating chronic diseases such as diabetes and cardiovascular disease should account for the potential role of discrimination and obesity. However, the relationship between discrimination, obesity, and PN has not been investigated.

This paper examined whether midlife perceived discrimination is associated prospectively with the prevalence of PN in the multi-ethnic Study of Women's Health Across the Nation (SWAN). Additionally, given the complex relationship between race, socio-economic status, diabetes and PN we investigated whether the relationship between discrimination and PN varied by diabetes status. Lastly, as perceived discrimination is associated with body mass index (BMI) and central obesity (21–23), we also assessed whether this association was mediated by BMI.

METHODS

The Study of Women's Health Across the Nation is a multi-ethnic longitudinal study of midlife women from seven sites in the United States. Each of the clinical sites selected White women and women of one designated racial/ethnic minority group to participate. African-American women were recruited in Boston, MA, Chicago, IL, Detroit-area, MI, and Pittsburgh, PA; Chinese women in Oakland, CA; Hispanic women in Newark, NJ; and Japanese women in Los Angeles, CA. Women were eligible for the baseline assessment in 1996 if they were between 42 and 52 years of age, had an intact uterus and at least one ovary, had no reported current hormone use, had at least one menstrual period in the past 3 months, and self-identified as one of the site's designated racial/ethnic groups. There have been an additional 15 approximately annual visits following baseline. Visits include both self-reported questionnaires and clinic visits. Further detailed information about SWAN study procedures and methods have been published elsewhere (26). Of the initial 3,302 enrolled women, 2,091 (63%) participated in study visit 15 (2016). The women who participated in visit 15 but were missing data for neuropathy status, diabetes status, body

mass index, or baseline perceived discrimination were excluded from the present analysis, leaving 1,718 women (82%) in the analytic sample.

Perceived discrimination was assessed during the baseline visit using the Detroit Area Study Everyday Discrimination Scale (27,28); responses on this scale have been shown to be consistent over time among women in the SWAN cohort (19). This scale measures ten experiences involving discrimination over the past 12 months such as being treated with less respect or courtesy than other people, receiving poorer service than others, and being ignored. Each question was assessed using a response scale of never, rarely, sometimes, and often. Responses were summed and averaged across the 10 questions to yield final scores between 1 (low perceived discrimination) and 4 (high perceived discrimination) (29). The questions above were not specific to reasons for discrimination, however there was a follow up question that asked participants to attribute their experience of discrimination to one major reason (race/ethnicity, sex, etc.). Previous studies in SWAN show that African-American and Chinese women report slightly higher levels of perceived discrimination than other racial/ethnic groups (29).

PN was assessed during visit 15 using both a symptom questionnaire and monofilament testing. The Michigan Neuropathy Screening Instrument (MNSI) symptom questionnaire acquired information about 15 neuropathy symptoms including burning pain, sensitivity, prickling, lack of hot/cold differentiation, severe dryness of the foot, numbness, open sores, and amputations (30). Participants who identified having 4 or more of these 15 symptoms were categorized as having PN from the screening instrument. This questionnaire and cut-point have been previously validated with clinical diagnoses of PN (31).

The monofilament test was first administered using a 10-gram filament placed on the big toe for less than one second for four repetitions. If the participant correctly identified all 4 repetitions, this procedure was repeated with a 1.4-gram monofilament in order to measure more minute levels of insensitivity. Participants who responded correctly to 2 or fewer of 4 attempts on either the 10-gram or the 1.4-gram test were classified as having PN from the monofilament test. For this analysis, women who screened positive on either the questionnaire or the monofilament test were classified as having PN in order to capture a broad range of neuropathy symptoms and sub-types.

Diabetes status was ascertained using a combined measure that included self-reported use of a diabetes medication including insulin, self-reported doctor-diagnosed diabetes, or a fasting glucose ≥ to 126 mg/dL at any follow-up visit. Race/ethnicity was self-identified at baseline as African-American, Chinese, Hispanic, Japanese, or White. To ensure temporality between perceived discrimination and body mass index (BMI), and because BMI has been hypothesized to change through the menopausal transition independently of discrimination (32–34), BMI was ascertained concurrently (visit 15) with PN when most women in the sample were post-menopausal. BMI was calculated as weight in kilograms divided by measured height in meters squared. Smoking status was based on self-report at visit 15 of smoking regularly since the last study visit. Financial strain at baseline was assessed by self-report of how hard it is for the respondent to pay for basics.

Frequencies, means, and 95% confidence intervals (CI) were calculated to define the characteristics of the eligible study population. Chi-square tests and t-tests were used to test for significant differences in characteristics between women with and without diabetes and with and without PN. Logistic regression adjusted for race/ethnicity, financial strain, smoking status, and diabetes was performed to investigate the relationship between perceived discrimination reported at baseline and PN at visit 15. Additionally, an interaction between race/ethnicity and perceived discrimination was tested. BMI was added to the models in order to assess whether BMI could potentially mediate the relationship between perceived discrimination and PN. A formal mediation analysis to determine whether BMI mediated the effect of discrimination on PN was conducted using the STATA package Paramed (StataCorp LP, College Station, Texas), which decomposes the total effect of discrimination on PN into direct (effect of discrimination alone), indirect (effect of discrimination via BMI) and interactive (discrimination and BMI interaction) effects using the methods outlined by Vanderweele, 2013 (35–37). Because diabetes is a strong risk factor for PN we also tested for interactions between discrimination and diabetes status in all models.

RESULTS

The median baseline age of participants was 46.2 years and the median age at visit 15 was 65.4 years. Approximately one-third of the sample (33.9%) reported financial strain at baseline (Table 1). The average discrimination score was 1.7 (standard deviation (SD) = 0.5) with a range of 1.0 to 3.6, 8.91% of the sample reported no instances of discrimination at baseline. The prevalence of diabetes was 3.6% at baseline and 18.6% by visit 15. At visit 15, 68.6% of the sample was overweight or obese, and the average BMI was 29.2 kg/m^2 (SD = 7.1).

By visit 15, 26.1% of women had PN. The prevalence of PN was higher among women with diabetes (40.9%) compared to women without diabetes (22.8%). Of those with PN, 62.8% were classified as having the condition based on the MNSI questionnaire, 51.7% based on the monofilament test and 14.5% based on both measures (Table 2).

In unadjusted analyses, financial strain and higher perceived discrimination at baseline as well as higher BMI, smoking, and diabetes at visit 15 were positively associated with PN at visit 15 (Table 3). Each unit increase in level of perceived discrimination was associated with 43% higher odds of PN (odds ratio (OR) = 1.43, 95% CI: 1.14, 1.79). Japanese women had 72% lower odds of PN compared to white women (OR = 0.28, 95% CI: 0.16, 0.48), but there were no significant differences in the odds between African-American, Chinese, or Hispanic women and White women.

After adjustment for race/ethnicity, financial strain, current smoking, and diabetes, perceived discrimination remained positively associated with PN (Model 1). Each unit increase in perceived discrimination was associated with 29% higher odds of PN (OR = 1.29, 95% CI: 1.01, 1.66). Next we further adjusted for BMI (Model 2). Doing so attenuated the estimate for perceived discrimination, and it was no longer significantly associated with PN (OR = 1.21, 95% CI: 0.94, 1.56). In the fully adjusted model, Japanese women had 67% lower odds

of PN as compared to White women (OR=0.33, 95% CI: 0.19, 0.58), and financial strain, smoking status, diabetes and BMI were positively associated with PN. There was no significant interaction between discrimination and racial/ethnic group or diabetes.

Sensitivity analysis indicated no significant interactive effect between discrimination and BMI in association with PN (likelihood ratio chi-squared = 0.29, two-sided *P*-value = 0.59), therefore controlled (non-interactive) direct and indirect effects are presented in the mediation analysis (Table 4). The total effect of discrimination on PN is estimated to be 28.3% (95% CI: 17.1, 36.5%) mediated by BMI (indirect effect); the direct effect of discrimination is non-significant and is slightly higher (OR = 1.21, 95% CI: 0.94, 1.56) than the indirect effect of discrimination via BMI (OR = 1.07, 95% CI: 1.03, 1.12).

DISCUSSION

This is the largest known study of PN in women without and with diabetes. Among women aged 60 to 73 years old, the prevalence of neuropathy was 22.8% in women without diabetes and 40.9% in women with diabetes. Perceived discrimination in midlife was a predictor of having PN 20 years later, and this association was mediated significantly by BMI. We also found that financial strain, higher BMI, current smoking, and diabetes were all associated with an increased odds of PN, confirming prior observations (20–23).

This is the first analysis of the association of discrimination and PN, and we found that each increasing level of perceived discrimination in midlife was associated with 43% higher odds of PN. Discrimination has been found to be a strong indicator for risk of many serious health conditions, including diabetes, obesity and hypertension (10,24–27). Discrimination, along with other types of stressors, increases allostatic load, or the overstimulated or abnormal neurological, immunological, and inflammatory physiological responses induced by chronic stressors (18,19,45–56). Discrimination and other chronic stressors are associated with heightened responsiveness of the cardiovascular system including increased blood pressure reactivity (57,58), red blood cell oxidative stress (59) and increased inflammation (54). Cardiometabolic risk factors including diabetes are associated with PN among individuals with and without diabetes (60) and more recently, diabetic PN was associated with endothelial dysfunction (61). Thus, chronic stressors such as discrimination may be associated with PN through the dysregulation of cardiovascular and metabolic function and pro-inflammatory responses that lead to damage of the peripheral nerves (16, 17). Furthermore, previous work has found an association between discrimination and chronic pain (62,63), potentially through psychological distress (62). Because the symptoms of PN, particularly in the early stages, are characterized by chronic pain it could be that discrimination is at play through the same neurological pathways as chronic pain among both diabetic and non-diabetic PN cases.

While perceived discrimination was a strong predictor for PN in the unadjusted model, this association was attenuated to non-significance when adjusted for BMI – BMI was the most highly significant predicator of PN in the present analysis. Formal mediation results suggest that the association between discrimination and PN is approximately 28.3% (95% CI: 17.1–36.5%) mediated by BMI. In SWAN and elsewhere, discrimination has been shown to be an

independent predictor of BMI (64,65), and discrimination has been found to be a predictor of inflammation with significant moderation by BMI (66). Furthermore, increased body mass index has been shown to contribute to decreased nerve conduction among individuals without diabetes who do not yet have any symptoms of PN (39). Even when no neuropathy symptoms were reported by those participants, they had significantly lower thermal and pain thresholds. This lends support to the mediation results and suggests that the underlying mechanism for discrimination's effect on risk of PN may be related to the physiological effects of obesity and inflammation.

Other factors such as low socioeconomic status and smoking were found to be associated with prevalent PN. Women with lower socioeconomic status have been shown to have higher allostatic load stress markers, which according to the proposed biological mechanism above, could account for some of the increased odds of developing PN for women reporting financial strain (17,68). People of lower socioeconomic status also have poorer nutrition, exercise less, have potentially more exposure to environmental toxins, and have less access to health care than women of higher socioeconomic status (69–71). Even women who seek care for PN symptoms may be less likely to be properly tested and diagnosed based on their socioeconomic status (72). All of these factors may lead to poorer management and greater exacerbations of diseases such as PN among women of lower socioeconomic status. Furthermore, a recent meta-analysis found that smoking was significantly associated with an increased odds of diabetic PN (40). Our results are consistent with these findings. Smoking is hypothesized to contribute to neuropathies by constricting the blood vessels that supply nerves with blood and nutrients (73).

The observed prevalence of PN in our present analysis is higher than reported in previous studies among women with and without diabetes (74,75). In this analysis of the full SWAN cohort, the prevalence of PN is similar to that observed eight years earlier at the Michigan SWAN site (5). Notably, this current analysis found a high prevalence (22.8%) of PN in women without diabetes, suggesting that increased clinical focus on the problem of PN in the general population of women is need, especially given evidence that PN is a significant determinant of multiple dimensions of disability (76,77). Furthermore, the increased prevalence of PN may be due to the method of measurement of PN. Many previous studies have used only monofilament testing to characterize PN, which in the present analysis would lead to a reduction in the number of PN cases by approximately 50% (4,23). Early work describing the use of two instruments (in this case the MNSI and monofilament testing) proved to provide a more sensitive and reliable measure of neuropathies among individuals with diabetes than one instrument alone as each may be capturing differing severities of PN (31).

There are several limitations with this study. First, PN was not measured at baseline or at other early study visits, so we could not separate existing PN from neuropathy that developed over the course of the study period. This may have introduced issues of temporality into our study, however increasing age contributes to neuropathy development, and measures were chosen to establish temporality between perceived discrimination (baseline) and BMI (the mediator, measured concurrently with PN). Perceived discrimination was assessed at baseline, but these experiences can accumulate over time, and

can be a regular and pervasive experience throughout the life course. Perceived discrimination has been shown to be stable over time in the SWAN cohort (19). Because 68 women (10.6%) reported that they experienced discrimination mainly because of their physical appearance, we ran a sensitivity analysis with these women removed in order to reduce the possibility of reverse causation – i.e. that for some, higher BMI (physical appearance) could be leading to discrimination. The estimates of the association of perceived discrimination with PN did not change significantly in this sensitivity analysis (unadjusted OR = 1.39, 95% CI: 1.10, 1.75; adjusted model OR = 1.18, 95% CI: 0.90, 1.53). Despite these limitations, this analysis has many strengths overall. Using two standardized measures of PN gives more robust estimates of disease (19,40). This large, community-based cohort design allowed us to investigate PN among women with and without diabetes, as well as women of diverse racial/ethnic backgrounds.

CONCLUSIONS

Nearly all previous PN research has focused primarily on populations with diabetes, however our analysis found that almost one-fourth of women without diabetes have PN. More research is needed to determine the contributing factors to non-diabetic PN. Clinicians should consider this high prevalence when diagnosing and treating both patients with and without diabetes for neuropathy. This study also found that midlife perceived discrimination was a significant predictor of PN and that this association was significantly mediated by BMI. Our findings re-affirm the impact of financial strain, BMI and diabetes as significant correlates of PN measured by symptom questionnaire and monofilament testing and show the impact of discrimination as an important risk factor for PN in women with and without diabetes.

ACKNOWLEDGMENTS

Jennifer R. Dusendang conducted the literature review and had primary responsibility for drafting the manuscript. Jennifer R. Dusendang, Carrie A. Karvonen-Gutierrez, Siobán D. Harlow, William H. Herman, and Alexis N. Reeves and made substantial contributions to conception, design, acquisition, and interpretation of the data as well as to the design of the data analysis. Jennifer R. Dusendang conducted the primary data analysis and Alexis Reeves conducted the mediation analyses. Jennifer R. Dusendang, Carrie A. Karvonen-Gutierrez, Siobán D. Harlow, William H. Herman, Alexis N. Reeves, and Kelly R. Ylitalo contributed to the drafting of the manuscript and the critical revision of the manuscript for important intellectual content. All authors have read and approved the final manuscript.

The Study of Women's Health Across the Nation (SWAN) received grant support from the National Institutes of Health, Department of Health and Human Services, through the National Institute on Aging, the National Institute of Nursing Research, and the National Institutes of Health Office of Research on Women's Health (grants NR004061, AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495, as well as grant AG017719 to the SWAN Repository).

We thank the study staff at each site and all the women who participated in SWAN.

Clinical Centers: University of Michigan, Ann Arbor, Michigan—Siobán Harlow, principal investigator (PI), 2011-present, MaryFran Sowers, PI, 1994–2011; Massachusetts General Hospital, Boston, Massachusetts —Joel Finkelstein, PI, 1999—present; Robert Neer, PI, 1994–1999; Rush University, Rush University Medical Center, Chicago, Illinois—Howard Kravitz, PI, 2009-present; Lynda Powell, PI, 1994–2009; University of California, Davis/Kaiser, California —Ellen Gold, PI; University of California, Los Angeles, Los Angeles, California—Gail Greendale, PI; Albert Einstein College of Medicine, Bronx, New York—Carol Derby, PI, 2011-present, Rachel Wildman, PI, 2010–2011; Nanette Santoro, PI, 2004–2010; University of Medicine and Dentistry-New Jersey Medical School, Newark, New Jersey—Gerson Weiss, PI, 1994–2004; and the University of Pittsburgh, Pittsburgh, Pennsylvania—Karen Matthews, PI.

NIH Program Office: National Institute on Aging, Bethesda, Maryland—Winifred Rossi, 2012-present; Sherry Sherman, 1994–2012; Marcia Ory, 1994–2001; National Institute of Nursing Research, Bethesda, Maryland—Program Officers.

Central Laboratory: University of Michigan, Ann Arbor, Michigan—Daniel McConnell (Central Ligand Assay Satellite Services). SWAN Repository: University of Michigan, Ann Arbor, Michigan—Dan McConnell, 2011-present; MaryFran Sowers, 2000–2011. Coordinating Center: University of Pittsburgh, Pittsburgh, Pennsylvania—Maria Mori Brooks, PI 2012-present; Kim Sutton-Tyrrell, PI 2001–2012; New England Research Institutes, Watertown, Massachusetts— Sonja McKinlay, PI 1995–2001.

Steering Committee: Susan Johnson, Current Chair; Chris Gallagher, Former Chair.

The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute on Aging, National Institute of Nursing Research, Office of Research on Women's Health or the National Institutes of Health.

Glossary

BMI	Body Mass Index
CA	California
CI	Confidence Interval
dL	deciliter
IL	Illinois
Kg	Kilogram
M	Meter
MA	Massachusetts
Mg	Milligrams
MI	Michigan
MNSI	Michigan Neuropathy Screening Instrument
NJ	New Jersey
OR	Odds Ratio
PA	Pennsylvania
SD	Standard Deviation
SWAN	Study of Women's Health Across the Nation

REFERENCES

1. National Institute of Neurological Disorders and Stroke. Peripheral Neuropathy Fact Sheet. 2014;
2. American Diabetes Association. Senior signature series: diabetes 101 2012.
3. van Schie CHM. Neuropathy: mobility and quality of life. Diabetes. Metab. Res. Rev 2008;24(Suppl 1):S45–S51. [PubMed: 18351588]

4. Gregg EW, Gu Q, Williams D, et al. Prevalence of lower extremity diseases associated with normal glucose levels, impaired fasting glucose, and diabetes among U.S. adults aged 40 or older. Diabetes Res. Clin. Pract 2007;77:485–488. [PubMed: 17306411]
5. Ylitalo KR, Herman WH, Harlow SD. Performance-based physical functioning and peripheral neuropathy in a population-based cohort of women at midlife. Am. J. Epidemiol 2013;177(8):810–817. [PubMed: 23524038]
6. Miscio G, Guastamacchia G, Brunani A, et al. Obesity and peripheral neuropathy risk: a dangerous liaison. J. Peripher. Nerv. Syst. [electronic article]. 2005;10:1085–9489. (http://hdl.handle.net/2318/89831). (Accessed June 27, 2018)
7. Sing J, Volckmann E, Graham, et al. Neuropathy Associated with Nondiabetic Obesity. Neurology [electronic article]. 2014;82(10 Supplement):S36.006 (http://n.neurology.org/content/82/10_Supplement/S36.006.short). (Accessed July 3, 2018)
8. Ylitalo KR, Herman WH, Harlow SD. Serial anthropometry predicts peripheral nerve dysfunction in a community cohort. Diabetes. Metab. Res. Rev. [electronic article]. 2013;29(2):145–51. (http://www.ncbi.nlm.nih.gov/pubmed/23161607). (Accessed July 3, 2018)
9. Eichholz M, Alexander AH, Cappelleri JC, et al. Perspectives on the impact of painful diabetic peripheral neuropathy in a multicultural population. Clin. Diabetes Endocrinol. [electronic article]. 2017;3(1):12 (https://clindiabetesendo.biomedcentral.com/articles/10.1186/s40842-017-0051-2). (Accessed June 27, 2018)
10. Lanting LC, Joung IMA, Mackenbach JP, et al. Ethnic differences in mortality, end-stage complications, and quality of care among diabetic patients: a review. Diabetes Care [electronic article]. 2005;28(9):2280–8. (http://www.ncbi.nlm.nih.gov/pubmed/16123507). (Accessed June 27, 2018)
11. Herman WH, Kennedy L. Underdiagnosis of Peripheral Neuropathy in Type 2 Diabetes. 2005; (http://care.diabetesjournals.org/content/diacare/28/6/1480.full.pdf). (Accessed July 24, 2018)
12. Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying cause of death 1999–2015 on CDC WONDER online database, released December 2017. Data are from the Multiple Cause of Death Files, 1999–2016, as compiled from data provided by the 57 vital statstics jurisdictions through the Vital Statistics Coop. 2016;
13. Centers for Disease Control and Prevention. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011 2011;1–12.
14. McDonald JA, Terry MB, Tehranifar P. Racial and gender discrimination, early life factors, and chronic physical health conditions in midlife. Women's Heal. Issues 2014;24(1):e53–e59.
15. Taylor SE, Repetti RL, Seeman T. Health psychology: what is an unhealthy environment and how does it get under the skin? Annu. Rev. Psychol 1997;48:411–447. [PubMed: 9046565]
16. Lewis TT, Matthews KA, Hall M. Chronic Exposure to Everyday Discrimination and Sleep in a Multi-Ethnic Sample of Middle-Aged Women. 2014;32(7):810–819.
17. Upchurch DM, Stein J, Greendale GA, et al. A longitudinal investigation of race, socioeconomic status, and psychosocial mediators of allostatic load in midlife women: Findings from the study of women's health across the nation. Psychosom. Med 2015;77(4):402–412. [PubMed: 25886828]
18. Beatty Moody DL, Chang Y-F, Pantesco EJ, et al. Everyday Discrimination Prospectively Predicts Blood Pressure Across 10 Years in Racially/Ethnically Diverse Midlife Women: Study of Women's Health Across the Nation. (https://academic.oup.com/abm/advance-article-abstract/doi/10.1093/abm/kay069/5105795). (Accessed September 25, 2018)
19. Beatty Moody DL, Chang Y, Brown C, et al. Everyday Discrimination and Metabolic Syndrome Incidence in a Racially/Ethnically Diverse Sample: Study of Women's Health Across the Nation. Psychosom. Med 2018;80(1):114–121. [PubMed: 28787363]
20. Lewis TT, Yang FM, Jacobs EA, et al. Racial/ethnic differences in responses to the everyday discrimination scale: A differential item functioning analysis. Am. J. Epidemiol 2012;175(5):391–401. [PubMed: 22306556]
21. Hunte HER, Williams DR. The association between perceived discrimination and obesity in a population-based multiracial and multiethnic adult sample. Am. J. Public Health [electronic article]. 2009;99(7):1285–92. (http://www.ncbi.nlm.nih.gov/pubmed/18923119). (Accessed July 3, 2018)

22. Cozier YC, Yu J, Coogan PF, et al. Racism, Segregation, and Risk of Obesity in the Black Women's Health Study. Am. J. Epidemiol. [electronic article]. 2014;179(7):875–883. (https://academic.oup.com/aje/article-lookup/doi/10.1093/aje/kwu004). (Accessed July 3, 2018)
23. Tull ES, Wickramasuriya T, Taylor J, et al. Relationship of Internalized Racism to Abdominal Obesity and Blood Pressure in Afro-Caribbean Women. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2608441/pdf/jnma00353-0025.pdf). (Accessed July 3, 2018)
24. Fleming I, Baum A, Davidson LM, et al. Chronic stress as a factor in physiologic reactivity to challenge. Heal. Psychol 1987;6(3):221–237.
25. Pop-Busui R, Ang L, Holmes C, et al. Inflammation as a therapeutic target for diabetic neuropathies. Curr. Diab. Rep 2016;16(29):1–10. [PubMed: 26699764]
26. Sowers MF, Crawford S, Sternfeld B, et al. SWAN: A Multicenter, Multiethnic, Community-Based Cohort Study of Women and the Menopausal Transition. Women's Heal. Res. Fac. Publ. [electronic article]. 2000;(https://escholarship.umassmed.edu/wfc_pp/505). (Accessed July 4, 2018)
27. Williams DR, Spencer MS, Jackson JS. Race, stress, and physical health: The role of group identity. Rutgers Ser. self Soc. identity [electronic article]. 1999;2(Self, social identity, and physical health: Interdisciplinary explorations):71–100. (http://psycnet.apa.org/record/1999-02710-004). (Accessed August 6, 2018)
28. Williams DR, Yan Y, Jackson JS. Racial Differences in Physical and Mental Health Socio-economic Status, Stress and Discrimination. J. Health Psychol. [electronic article]. 1997;2(3):335–351. (http://journals.sagepub.com/doi/pdf/10.1177/135910539700200305). (Accessed August 6, 2018)
29. Lewis TT, Yang FM, Jacobs EA, et al. Racial/ethnic differences in responses to the everyday discrimination scale: a differential item functioning analysis. Am. J. Epidemiol 2012;175(5):391–401. [PubMed: 22306556]
30. Moghtaderi A, Bakhshipour A, Rashidi H. Validation of Michigan neuropathy screening instrument for diabetic peripheral neuropathy. Clin. Neurol. Neurosurg. [electronic article]. 2006;108(5):477–481. (https://www.sciencedirect.com/science/article/pii/S0303846705001459). (Accessed June 27, 2018)
31. Herman WH, Pop-Busui R, Braffett BH, et al. Use of the Michigan Neuropathy Screening Instrument as a measure of distal symmetrical peripheral neuropathy in Type 1 diabetes: results from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications. Diabet. Med 2012;937–944. [PubMed: 22417277]
32. Wildman RP, Sowers MR. Adiposity and the menopausal transition. Obstet. Gynecol. Clin. North Am. [electronic article]. 2011;38(3):441–54. (http://www.ncbi.nlm.nih.gov/pubmed/21961712). (Accessed May 28, 2019)
33. Polotsky H, Polotsky A. Metabolic Implications of Menopause. Semin. Reprod. Med. [electronic article]. 2010;28(05):426–434. (http://www.thieme-connect.de/DOI/DOI?10.1055/s-0030-1262902). (Accessed May 28, 2019)
34. Davis SR, Castelo-Branco C, Chedraui P, et al. Understanding weight gain at menopause. Climacteric [electronic article]. 2012;15(5):419–429. (http://www.tandfonline.com/doi/full/10.3109/13697137.2012.707385). (Accessed May 28, 2019)
35. VanderWeele TJ. A three-way decomposition of a total effect into direct, indirect, and interactive effects. Epidemiology [electronic article]. 2013;24(2):224–32. (http://www.ncbi.nlm.nih.gov/pubmed/23354283). (Accessed June 27, 2018)
36. Valeri L, VanderWeele TJ. Mediation analysis allowing for exposure–mediator interactions and causal interpretation: Theoretical assumptions and implementation with SAS and SPSS macros. Psychol. Methods [electronic article]. 2013;18(2):137–150.(http://doi.apa.org/getdoi.cfm?doi=10.1037/a0031034). (Accessed June 27, 2018)
37. Emsley R, Liu H, Dunn G, et al. Paramed: A command to perform causal mediation analysis using parametric models. Stata J. 2014;
38. Anderson SG, Narayanan RP, Malipatil NS, et al. Socioeconomic deprivation independently predicts painful diabetic neuropathy in type 2 diabetes. Exp. Clin. Endocrinol. diabetes 2015;123:423–427. [PubMed: 26069072]

39. Ylitalo KR, Sowers M, Heeringa S. Peripheral vascular disease and peripheral neuropathy in individuals with cardiometabolic clustering and obesity: National health and nutrition examination survey: National Health and Nutrition Examination Survey 2001–2004. Diabetes Care. 2011;34:1642–1647. [PubMed: 21593304]
40. Clair C, Cohen MJ, Eichler F, et al. The effect of cigarette smoking on diabetic peripheral neuropathy: a systematic review and meta-analysis. J. Gen. Intern. Med 2015;30(8):1193–1203. [PubMed: 25947882]
41. Katon JG, Reiber GE, Nelson KM. Peripheral neuropathy defined by monofilament insensitivity and diabetes status: NHANES 1999–2004. Diabetes Care. 2013;36:1604–1606. [PubMed: 23275365]
42. Sutin AR, Stephan Y, Terracciano A. Weight discrimination and risk of mortality. Psychol. Sci 2015;26(11):1803–1811. [PubMed: 26420442]
43. Lewis TT, Everson-Rose SA, Powell LH, et al. Chronic exposure to everyday discrimination and coronary artery calcification in African-American women: The SWAN heart study. Psychosom. Med 2006;68(3):362–368. [PubMed: 16738065]
44. Troxel WM, Matthews KA, Bromberger JT, et al. Chronic stress burden, discrimination, and subclinical carotid artery disease in African American and Caucasian women. Heal. Psychol 2003;22(3):300–309.
45. Lewis TT, Williams DR, Tamene M, et al. Self-Reported Experiences of Discrimination and Cardiovascular Disease. Curr. Cardiovasc. Risk Rep. [electronic article]. 2014;8(1):365 (http://link.springer.com/10.1007/s12170-013-0365-2). (Accessed July 24, 2018)
46. Paradies Y A systematic review of empirical research on self-reported racism and health. Int. Epidemiol. Assoc. Int. J. Epidemiol. [electronic article]. 2006;35:888–901. (https://academic.oup.com/ije/article-abstract/35/4/888/686369). (Accessed November 1, 2018)
47. Williams DR, Mohammed SA. Discrimination and racial disparities in health: evidence and needed research. J. Behav. Med. [electronic article]. 2009;32(1):20–47. (http://link.springer.com/10.1007/s10865-008-9185-0). (Accessed November 1, 2018)
48. Clark R, Anderson N, Clark V, et al. Racism as a stressor for african american: A Biopsychosocial Model. Am. Psychol 1999;
49. Juster R-P, McEwen BS, Lupien SJ, et al. Allostatic load biomarkers of chronic stress and impact on health and cognition. 2009;(https://ac.els-cdn.com/S0149763409001481/1-s2.0-S0149763409001481-main.pdf?_tid=b70435aa-8449-4be9-8f57-554b82cd996e&acdnat=1540559969_9e557ddcd6de0d60d2a47eb936052df3). (Accessed October 26, 2018)
50. Guyll M, Matthews KA, Bromberger JT. Discrimination and Unfair Treatment: Relationship to Cardiovascular Reactivity among African-American and European Women. Heal. Psychol 2001;20(5):315–325.
51. Wagner J, Lampert R, Tennen H, et al. Exposure to discrimination and heart rate variability reactivity to acute stress among women with diabetes. Stress Heal. 2015;31(3).
52. Beatty Moody DL, Waldstein SR, Tobin JN, et al. Lifetime racial/ethnic discrimination and ambulatory blood pressure: The moderating effect of age. Heal. Psychol 2016;35(4).
53. Pantesco EJ, Leibel DK, Ashe JJ, et al. Multiple forms of discrimination, social status, and telomere length: Interactions within race. Psychoneuroendocrinology. 2018;98. [PubMed: 30409385]
54. Beatty DL, Matthews KA, Bromberger JT, et al. Everyday Discrimination Prospectively Predicts Inflammation Across 7-Years in Racially Diverse Midlife Women: Study of Women's Health Across the Nation. 2010;14(4):384–399.
55. Brondolo E, Rieppi R, Kelly KP, et al. Perceived racism and blood pressure: A review of the literature and conceptual and methodological critique. Ann. Behav. Med. [electronic article]. 2003;25(1):55–65. (https://academic.oup.com/abm/article/25/1/55-65/4631549). (Accessed May 30, 2019)
56. Lockwood KG, Marsland AL, Matthews KA, et al. Perceived discrimination and cardiovascular health disparities: a multisystem review and health neuroscience perspective. Ann. N. Y. Acad. Sci. [electronic article]. 2018;(http://doi.wiley.com/10.1111/nyas.13939). (Accessed August 13, 2018)

57. Guyll M, Matthews KA, Bromberger JT. Discrimination and unfair treatment: Relationship to cardiovascular reactivity among African American and European American women. Heal. Psychol. [electronic article]. 2001;20(5):315–325. (http://doi.apa.org/getdoi.cfm?doi=10.1037/0278-6133.20.5.315). (Accessed July 3, 2018)
58. Richman LS, Bennett GG, Pek J, et al. Discrimination, Dispositions, and Cardiovascular Responses to Stress. (https://pdfs.semanticscholar.org/c434/4e6868d20a826a809e7a300940ce8f495fe8.pdf). (Accessed July 3, 2018)
59. Szanton SL, Rifkind JM, Mohanty JG, et al. Racial Discrimination Is Associated with a Measure of Red Blood Cell Oxidative Stress: A Potential Pathway for Racial Health Disparities. Int. J. Behav. Med. [electronic article]. 2012;19(4):489–495. (http://link.springer.com/10.1007/s12529-011-9188-z). (Accessed July 3, 2018)
60. Ylitalo KR, Sowers M, Heeringa S. Peripheral vascular disease and peripheral neuropathy in individuals with cardiometabolic clustering and obesity: National Health and Nutrition Examination Survey 2001–2004. Diabetes Care [electronic article]. 2011;34(7):1642–7.(http://www.ncbi.nlm.nih.gov/pubmed/21593304). (Accessed June 27, 2018)
61. Roustit M, Loader J, Deusenbery C, et al. Endothelial Dysfunction as a Link Between Cardiovascular Risk Factors and Peripheral Neuropathy in Diabetes. J. Clin. Endocrinol. Metab. [electronic article]. 2016;101(9):3401–3408. (https://academic.oup.com/jcem/article-lookup/doi/10.1210/jc.2016-2030). (Accessed July 3, 2018)
62. Brown TT, Partanen J, Chuong L, et al. Discrimination hurts: The effect of discrimination on the development of chronic pain. Natl. Institutes Heal. [electronic article]. 2018;(10.1016/j.socscimed.2018.03.015). (Accessed May 30, 2019)
63. Dugan SA, Lewis TT, Everson-Rose SA, et al. Chronic discrimination and bodily pain in a multiethnic cohort of midlife women in the Study of Women's Health Across the Nation. Pain [electronic article]. 2017;158(9):1656–1665. (http://www.ncbi.nlm.nih.gov/pubmed/28753588). (Accessed May 30, 2019)
64. Lewis TT, Kravitz HM, Janssen I, et al. Self-reported experiences of discrimination and visceral fat in middle-aged African-American and caucasian women. Am. J. Epidemiol 2011;173(11):1223–1231. [PubMed: 21354991]
65. Marniemi J, Kronholm E, Aunola S, et al. Visceral fat and psychosocial stress in identical twins discordant for obesity. J. Intern. Med 2002;251:35–43. [PubMed: 11851863]
66. Beatty DL, Matthews KA, Bromberger JT, et al. Everyday Discrimination Prospectively Predicts Inflammation Across 7-Years in Racially Diverse Midlife Women: Study of Women's Health Across the Nation. J. Soc. Issues [electronic article]. 2014;70(2):298–314. (http://www.ncbi.nlm.nih.gov/pubmed/25342861). (Accessed June 27, 2018)
67. Miscio G, Guastamacchia G, Brunani A, et al. Obesity and peripheral neuropathy risk: a dangerous liaison. J. Peripher. Nerv. Syst 2005;10:354–358. [PubMed: 16279984]
68. Seeman M, Merkin S, Karlamangla A, et al. Social status and biological dysregulation: the "status syndrome" and allostatic load. Soc. Sci. Med 2014;118:143–151. [PubMed: 25112569]
69. Novakovi R, Cavelaars A, Geelen A, et al. Socio-economic determinants of micronutrient intake and status in Europe: a systematic review. Public Health Nutr. [electronic article]. 17(5):1031–1045. (https://www.cambridge.org/core/services/aop-cambridge-core/content/view/5F78BE1AAC8A2B51A078BFA5961E0466/S1368980013001341a.pdf/review_article_socioeconomic_determinants_of_micronutrient_intake_and_status_in_europe_a_systematic_review.pdf). (Accessed June 27, 2018)
70. Murray TC, Rodgers WM, Fraser SN. Exploring the relationship between socioeconomic status, control beliefs and exercise behavior: a multiple mediator model. J. Behav. Med 2012;35:63–73. [PubMed: 21442246]
71. Adler NE, Newman K. Socioeconomic disparities in health: pathways And policies inequality. Health Aff. 2002;21(2):60–76.
72. McKinlay J, Piccolo R, Marceau L. An additional cause of health care disparities - the variable clinical decisions of primary care doctors. J. Eval. Clin. Pract 2013;19(4):664–673. [PubMed: 23216876]

73. U.S. Department of Healthand Human Services. A report of the Surgeon General: how tobacco smoke causes disease: what it means to you. 2010;1–16.

74. Gregg EW, Gu Q, Williams D, et al. Prevalence of lower extremity diseases associated with normal glucose levels, impaired fasting glucose, and diabetes among U.S. adults aged 40 or older. Diabetes Res. Clin. Pract. [electronic article]. 2007;77(3):485–488. (https://www.sciencedirect.com/science/article/pii/S016882270700040X). (Accessed June 27, 2018)

75. Katon JG, Reiber GE, Nelson KM. Peripheral Neuropathy Defined by Monofilament Insensitivity and Diabetes Status. 1999;(http://care.diabetesjournals.org/content/diacare/early/2012/12/19/dc12-1102.full.pdf). (Accessed June 27, 2018)

76. Ylitalo KR, Herman WH, Harlow SD. Performance-based Physical Functioning and Peripheral Neuropathy in a Population-based Cohort of Women at Midlife. Am. J. Epidemiol. [electronic article]. 2013;177(8):810–817. (https://academic.oup.com/aje/article-lookup/doi/10.1093/aje/kws327). (Accessed June 27, 2018)

77. Karvonen-Gutierrez CA, Ylitalo KR, Karvonen-Gutierrez C. Prevalence and Correlates of Disability in a Late Middle-Aged Population of Women. J. Aging Health [electronic article]. 25(254):701–717. (http://journals.sagepub.com/doi/pdf/10.1177/0898264313488165). (Accessed July 4, 2018)

78. Dyck P, Karnes J, Daube J, et al. Clinical and neuropathological criteria for the diagnosis and staging of diabetic polyneuropathy. Brain. 1985;108(4):861–880. [PubMed: 4075076]

79. Moghtaderi A, Bakhshipour A, Rashidi H. Validation of Michigan neuropathy screening instrument for diabetic peripheral neuropathy. Clin. Neurol. Neurosurg 2006;108:477–481. [PubMed: 16150538]

Table 1.

Characteristics of All Participants, Participants with Diabetes and Participants with Peripheral Neuropathy, Study of Women's Health Across the Nation, 1996–2016

	Total (n= 1718)		Diabetes (n = 320)		*P*-value[a]	Peripheral Neuropathy (n = 449)		*P*-value[b]
Visit 15 age in years, mean (SD)	65.6	(2.7)	65.6	(2.7)	0.88	65.6	(2.7)	0.73
Race / ethnicity, N (%)					<0.01			<0.01
African-American	454	(26.4)	134	(41.9)		141	(31.4)	
Chinese	174	(10.1)	26	(8.1)		40	(8.9)	
Hispanic	97	(5.7)	35	(10.9)		31	(6.9)	
Japanese	171	(10.0)	18	(5.6)		16	(3.6)	
White	822	(47.9)	107	(33.4)		221	(49.2)	
Financial strain, N (%)					<0.01			<0.01
Very or somewhat hard	570	(33.9)	144	(45.1)		185	(42.0)	
Not hard	1111	(66.1)	175	(54.9)		256	(58.0)	
Smoking, N (%)					<0.01			<0.01
Current	111	(6.5)	49	(12.3)		43	(9.7)	
Former or never	1590	(93.5)	277	(87.7)		401	(90.3)	
BMI in kg/m^2, mean (SD)	29.2	(7.1)	33.1	(7.4)	<0.01	31.4	(7.6)	<0.01
Perceived discrimination, mean (SD)	1.7	(0.5)	1.8	(0.5)	<0.01	1.8	(0.5)	<0.01

Abbreviations: SD, standard deviation; BMI, body mass index

[a]Two-sided *P*-value comparing women with and without diabetes; chi-square test for categorical variables; t-test for continuous variables

[b]Two-sided *P*-value comparing women with and without peripheral neuropathy; chi-square test for categorical variables; t-test for continuous variables

Table 2.

Prevalence of Peripheral Neuropathy by Diabetes Status, Study of Women's Health Across the Nation, 1996–2016

	Total (n = 1718)		With Diabetes (n = 320)		Without Diabetes (n = 1398)		
	n	%	n	%	n	%	*P*-value[a]
Peripheral Neuropathy	449	26.1	131	40.9	318	22.8	<0.01
MNSI, ≥ 4 symptoms	282	16.4	106	33.1	176	12.6	<0.01
Monofilament insensitivity, < 3 correct responses	232	13.7	58	18.8	174	12.5	<0.01
Both MNSI and Monofilament	65	3.8	33	10.7	32	2.3	<0.01

Abbreviations: MNSI, Michigan Neuropathy Screening Instrument

[a]Two-sided chi-square test comparing women with and without diabetes

Table 3.

Unadjusted and Adjusted Logistic Regression Models Predicting Peripheral Neuropathy by Perceived Discrimination and Body Mass Index, Study of Women's Health Across the Nation (n=1665), 1996–2016

	Unadjusted			Model 1[b]			Model 2[c]		
	OR	**95% CI**	***P*-value[d]**	**OR**	**95% CI**	***P*-value[d]**	**OR**	**95% CI**	***P*-value[d]**
Perceived Discrimination	1.43	1.14, 1.79	<0.01	1.29	1.01, 1.66	0.04	1.21	0.94, 1.56	0.14
BMI	1.06	1.04, 1.07	<0.01	--			1.04	1.03, 1.06	<0.01
Diabetes[a]	2.35	1.82, 3.04	<0.01	2.05	1.57, 2.69	<0.01	1.78	1.35, 2.34	<0.01
Race / Ethnicity									
African-American	1.23	0.95, 1.58	0.11	0.91	0.69, 1.20	0.55	0.8	0.60, 1.06	0.11
Chinese	0.81	0.55, 1.19	0.29	0.75	0.50, 1.12	0.16	0.95	0.63, 1.44	0.82
Hispanic	1.28	0.81, 2.01	0.29	1.01	0.61, 1.67	0.97	0.99	0.54, 1.50	0.68
Japanese	0.28	0.16, 0.48	<0.01	0.26	0.15, 0.46	<0.01	0.33	0.19, 0.58	<0.01
White	REF			REF			REF		
Financial strain[a]	1.66	1.28, 2.01	<0.01	1.45	1.14, 1.84	<0.01	1.46	1.14, 1.86	<0.01
Current smoker[a]	1.88	1.26, 2.79	<0.01	1.45	0.95, 2.2	0.09	1.64	1.07, 2.52	0.02

Abbreviations: OR, odds ratio; CI, confidence interval; BMI, body mass index

[a] Referent groups: no diabetes, "not very hard" to pay for basics, never smoked regularly

[b] Model 1 adjusted for diabetes, race/ethnicity, financial strain, and current smoking

[c] Model 2 additionally adjusted for BMI

[d] All *P*-values are two-sided

Table 4.

Controlled Direct and Indirect Effects (Odds Ratio Scale) of Perceived Discrimination on Peripheral Neuropathy via Body Mass Index (BMI), Study of Women's Health Across the Nation, 1996–2016

	OR[a]	95% CI	*P*-value[c]	% Mediated	95% CI
Total Effect[b]	1.30	1.01, 1.68	0.04		
Direct Effect[b]	1.21	0.94, 1.56	0.14	28.34	17.1, 36.5
Indirect Effect[b]	1.07	1.03, 1.12	<0.01		

Abbreviations: OR, odds ratio; CI, confidence interval

[a]Odds ratios (95% confidence intervals) for peripheral neuropathy are per 1-unit increase in perceived discrimination

[b]Mediation models adjusted for race/ethnicity, financial strain, current smoking, and diabetes.

[c]All *P*-values are two-sided