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Age and sex differences in the association between neighborhood socioeconomic environment and incident diabetes: Results from the diabetes location, environmental attributes and disparities (LEAD) network

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A B S T R A C T

Objective: Worse neighborhood socioeconomic environment (NSEE) may contribute to an increased risk of type 2 diabetes (T2D). We examined whether the relationship between NSEE and T2D differs by sex and age in three study populations.

Research design and methods: We conducted a harmonized analysis using data from three independent longitudinal study samples in the US: 1) the Veteran Administration Diabetes Risk (VADR) cohort, 2) the REasons for Geographic and Racial Differences in Stroke (REGARDS) cohort, and 3) a case-control study of Geisinger electronic health records in Pennsylvania. We measured NSEE with a z-score sum of six census tract indicators within strata of community type (higher density urban, lower density urban, suburban/small town, and rural). Community type-stratified models evaluated the likelihood of new diagnoses of T2D in each study sample using restricted cubic splines and quartiles of NSEE.

Results: Across study samples, worse NSEE was associated with higher risk of T2D. We observed significant effect modification by sex and age, though evidence of effect modification varied by site and community type. Largely, stronger associations between worse NSEE and diabetes risk were found among women relative to men and among those less than age 45 in the VADR cohort. Similar modification by age group results were observed in the Geisinger sample in small town/suburban communities only and similar modification by sex was observed in REGARDS in lower density urban communities.

Conclusions: The impact of NSEE on T2D risk may differ for males and females and by age group within different community types.

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1. Introduction

Type 2 diabetes (T2D) is a major cause of morbidity and mortality among adults in the United States. In 2019, the latest year for which data is available, 37.3 million adults had diabetes (Centers for Disease Control and Prevention, 2022; Schwartz et al., 2021). Approximately 90–95% of people with diabetes have T2D, the majority of which can be prevented or delayed through lifestyle changes such as eating healthfully, losing weight, and being physically active (Centers for Disease Control and Prevention, 2022). Although the incidence of diagnosed diabetes has declined in recent years (Benoit, Hora, Albright, & Gregg, 2019), county-level analyses show significant geographic disparities in the risk of T2D (Barker, Kirtland, Gregg, Geiss, & Thompson, 2011) and diabetes-related mortality between rural and urban communities (Callaghan, Ferdinand, Akinlotan, Towne, & Bolin, 2020). Such disparities could be attributed to the combination of area-level socioeconomic conditions, built environment, and other neighborhood factors that differ along the rural-urban spectrum (Dwyer-Lindgren, Mackenbach, Van Lenthe, Flaxman, & Mokdad, 2016; Shrestha et al., 2016).

Evidence suggests that place (i.e., where we live, work, and play) may influence our health and well-being even after accounting for differences in individual-level socioeconomic status (Chamberlain et al., 2022; Ludwig et al., 2011). The association of neighborhood socioeconomic disadvantage with T2D is well-documented (Bilal, Auchincloss, & Diez-Roux, 2018). In the Multi-Ethnic Study of Atherosclerosis, people living in disadvantaged neighborhoods had an increased risk of T2D compared to people in less disadvantaged neighborhoods (Christine et al., 2015). Similarly, in the US Gulf states, higher levels of neighborhood deprivation at the census block-group level were associated with higher levels of diagnosed T2D (Hu et al., 2021). In a previous analysis for the CDC's Diabetes Location, Environmental Attributes, and Disparities (LEAD) Network, we found that a worse neighborhood socioeconomic environment was consistently associated with T2D risk (Thorpe et al., 2022). With the exception of the LEAD study, few studies have explored these associations across the rural-urban spectrum, and documented heterogeneity in the strength of the association that could inform locally relevant T2D prevention strategies.

Community context is an important consideration in the operationalization of neighborhood measures. Many neighborhood factors' meaning, functionality, and composition may differ across various community contexts. For instance, car ownership in a rural area may seem a basic necessity, but this factor may be seen as a luxury item in a highly dense urban area with easy access to public transportation (Jones, 2019; Reading, Raybould, & Jarvis, 1993). Although many neighborhood factors may cluster at the community level, the distribution of many place-based factors, including poverty, housing, education, and racial-ethnic composition, may not necessarily overlap across a range of community types (e.g., urban, small town, rural) (McAlexander, Algur, et al., 2022; Messer et al., 2006). Likewise, due to presence or lack thereof, these place-based factors may differentially shape the mechanisms (e.g., health lifestyles, social cohesion) through which neighborhood disadvantage affect diabetes across community context. For instance, economic deprivation was shown to be more relevant in the counties outside the diabetes belt, and recreational facilities had a more pronounced association with prevalence of diabetes in the Southeastern diabetes belt in the US (Myers et al., 2017). Further, developing neighborhood measures within a range of community types would help offset some methodological challenges in observational studies including structural and random non-positivity biases (Ahern et al., 2013; Oakes, 2004, 2006; Petersen, Porter, Gruber, Wang, & Van Der Laan, 2012) owing to the absence or insufficient variability in individual-level covariates across strata of the neighborhood level exposure and the use of smaller geographic and administrative boundaries (McAlexander, Algur, et al., 2022; Uddin et al., 2022).

Socioeconomic conditions at the neighborhood level may contribute to the development of T2D through impacting collective physical and social resources, health-enhancing behavior, and psychosocial and stress processes (Diez Roux & Mair, 2010; Stafford & Marmot, 2003). In the extant literature, although neighborhood socioeconomic conditions have been consistently associated with the burden of T2D, it is unclear whether neighborhood conditions differentially influence the T2D risk across different sub-populations. Prior studies have shown mixed results regarding whether associations between neighborhood socioeconomic disadvantage and physical health differ by age and sex (Gustafsson et al., 2014; Lei, Berg, Simons, & Beach, 2022; Raleigh & Kiri, 1997; Singh, 2003). Studies have shown that older adults are more sensitive to neighborhood conditions and environmental constraints for walking and physical exercise (Ghani, Rachele, Washington, & Turrell, 2016; Shigematsu et al., 2009), which have the potential to influence the risk of T2D. Further, due to more age-related physical limitations and relatively less travel outside their neighborhood to work, scholars have theorized that older adults may be more vulnerable to neighborhood disadvantages (Robert & Li, 2001). However, no studies to our knowledge have examined whether the previously observed association between neighborhood socioeconomic disadvantage and diabetes risk varies by age and sex.

Additional studies have shown that associations of neighborhood environmental attributes with physical exercise and health outcomes are stronger among women than men (Barber et al., 2016; Humpel, Owen, Iverson, Leslie, & Bauman, 2004; Stafford, Cummins, Macintyre, Ellaway, & Marmot, 2005). Studies also suggest that population subgroups, including women and older adults, are differentially exposed to and become vulnerable to neighborhood, social, and physical conditions (Denton, Prus, & Walters, 2004). These differential processes of exposure and vulnerability have implications for understanding how neighborhood conditions may affect health by differentially influencing psychosocial, behavioral, and physiological mechanisms (Denton et al., 2004). Further, in the health and place literature, there is a general lack of understanding of how community settings (i.e., urban vs. rural) may become salient in shaping mechanisms through which neighborhood conditions yield differential impact for women and older adults. More specifically, previous studies overlook how underlying variables that define neighborhood disadvantage may not uniformly function as markers of disadvantage across a spectrum of community contexts. Understanding population group differences in how community-specific neighborhood disadvantage may confer risk of T2D is important to develop targeted prevention strategies for individuals most at risk.

In this present paper, using a multi-item measure of the neighborhood socioeconomic environment scaled within a spectrum of community types (higher density urban, lower density urban, suburban/small town, and rural) and using a harmonized analytic protocol, we investigated the association between neighborhood socioeconomic environment and incident T2D in three large studies from the Diabetes LEAD Network. Further, we examined whether this association differs by sex and age within each of four community types. Our key hypothesis is that the impact of neighborhood socioeconomic environment (NSEE) would vary across categories of age and sex.

2. Methods

2.1. Diabetes LEAD Network

The CDC-funded Diabetes LEAD Network is a research collaboration targeting the identification of community determinants of T2D and cardiometabolic conditions using a collection of data sources (Hirsch et al., 2020). The Network includes three study sites – Geisinger and Johns Hopkins University (G/JHU), New York University Grossman School of Medicine (NYU), and the University of Alabama at Birmingham (UAB) – and a data coordinating center (DCC) at Drexel University. The G/JHU site used an electronic health record (EHR)-based nested case control cohort. The NYU site used the Veterans Administration Diabetes Risk (VADR) cohort and the UAB team used a population-based

cohort, the REasons for Geographic and Regional Differences in Stroke (REGARDS) study. In order to examine potential effect modification by age and sex in the relationship between neighborhood socioeconomic disadvantage and T2D, the Diabetes LEAD Network collaboratively designed harmonized measures of community features and analytic plans that were implemented across the respective study site cohorts.

2.2. Neighborhood social and economic environment (NSEE)

Based on the work of Xiao and colleagues (Xiao, Berrigan, Powell-Wiley, & Matthews, 2018), the primary exposure of NSEE is an index developed by the LEAD Network (Hirsch et al., 2020; Thorpe et al., 2022) to synthesize various aspects of neighborhood disadvantage at the census tract level. Using six US census variables (% persons with less than a high-school education, % persons unemployed, % of households earning less than $30,000/year, % of households in poverty, % of households on public assistance, and % of households with no cars), NSEE was defined as the summation of z-scores computed using 2000 and 2010 census data. The summed z-scores were scaled from 0 to 100, with higher NSEE values indicating greater socioeconomic disadvantage. The NSEE measure was developed separately within strata of LEAD Network-derived community types (higher density urban, lower density urban, suburban/small town, and rural; described further in the following sub-section) to reflect how its underlying variables may differentially function within urban and rural community contexts (Ahern et al., 2013).

2.3. Community Type

The LEAD Network modified rural-urban commuting area (RUCA) codes from the U.S. Department of Agriculture (Parker, 2013) to create community types. Methods for these modified RUCA codes have been published elsewhere (Hirsch et al., 2020; McAlexander, Algur, et al., 2022). Briefly, we reclassified ten original RUCA categories into four community-type categories (higher density urban, lower density urban, suburban/small town, and rural). For a clearer distinction between densely populated urban areas, census tracts within urbanized areas were divided into high- and low-density urban community types primarily based on land area. RUCA categories micropolitan and small-town core were regrouped into the suburban/small town community type and all remaining RUCA categories were considered rural.

2.4. New onset type 2 diabetes

New onset T2D was measured using previously described approaches (Hirsch et al., 2020). Briefly, G/JHU and VADR identified cases using EHR algorithms that relied on diagnosis codes, laboratory test results (e.g., HbA1c glucose), and diabetes-relevant medication orders. On the other hand, the REGARDS cohort defined T2D based on an elevated fasting or random glucose measure or antihyperglycemic medication use. Full definitions of new onset diabetes can be found in Supplementary Table 1.

2.5. Effect modifiers

Age was categorized into three broad groups: <45, 45–64, and ≥65 years. These categories broadly align with diabetes risk and are consistent with age groups presented in the CDC's 2020national diabetes statistics report. The REGARDS cohort did not have participants aged <45 and so only included the 45–64 and ≥ 65 age groups. Sex was categorized as male and female.

2.6. Community-level covariates

Census tract-level covariates included land use environment and percentages of the populations that were Hispanic and non-Hispanic Black, retrieved from the 2000 and 2010 U.S. Census. The land use environment (LUE) is a continuous factor score calculated from a multiple-group confirmatory factor analysis based on seven components of the built environment. Details on the creation of LUE have been described elsewhere (Meeker et al., 2022).

2.7. Analytic Populations & Statistical Analysis

Geisinger/JHU: G/JHU conducted a nested case control study of 15,888 individuals with new onset of T2D, as previously reported (B. S. Schwartz et al., 2021). Controls (n = 79,435, with 65,084 unique persons)—individuals who never met any of the T2D criteria used for cases—were randomly selected with replacement and frequency-matched to cases (5:1) on age, sex, and year of encounter. At least two encounters were required on different days with a primary care provider prior to ensure that we could detect T2D if present. To ensure T2D was new onset, individuals were required to have at least one encounter with the health system without evidence of T2D at least two years prior to T2D onset date. NSEE 2000 was used for new cases/matched controls in years 2008–2012 and NSEE 2010 for new cases/matched controls in years 2013–2016. Effect modification of the relationship between NSEE and new onset T2D was evaluated using mixed effect logistic regression models, with a random intercept for census tract to account for clustering in place-level NSEE.

UAB/REGARDS: The REGARDS cohort is a population-based, national study of over 30,000 Black and White participants over the age 45 years. REGARDS recruited community-dwelling participants using commercially available contact information. Participants were enrolled between 2003 and 2007 from the contiguous United States, oversampling from the southeastern Stroke Belt (North Carolina, South Carolina, Georgia, Tennessee, Mississippi, Alabama, Louisiana, and Arkansas) and of Black adults (Howard et al., 2005). At enrollment, detailed surveys and clinical measures were collected via telephone and an in-home visit was performed with protocol-trained technicians. A second in-person home visit was conducted approximately 10 years after baseline (2013–2016) to assess the development of stroke risk factors such as T2D. The outcome of incident T2D was assessed among 11,208 study participants without prevalent T2D at baseline and who completed the follow-up exam in 2013–2016. Follow-up time was measured as the time between the two in-home visits. NSEE from 2000 was assigned using participants' baseline geocoded residential addresses. Poisson mixed models with robust variance estimation with NSEE splines were fit to examine the relationship between NSEE and T2D, accounting for possible correlation of participants within census tracts.

NYU/VADR: NYU used the Veterans Administration Diabetes Risk (VADR) cohort—a dynamic retrospective EHR cohort of 4,100,650 US veterans enrolled in the VA for primary care. Patients were included in the cohort if they had at least 2 diabetes-free primary care visits at least 30 days apart within 5 years. T2D was defined as having at least 2 encounters with ICD-9/10 codes for T2D, one encounter with ICD-9/10 codes for T2D, and two elevated hemoglobin A1c lab results (≥6.5%), or any prescription for diabetes medication other than metformin or acarbose alone. Patients were enrolled between 2008 and 2016 and were followed through 2018. Person-year was calculated as the time interval between cohort entry date and date of developing T2D as defined above, date of death, or date of lost to follow up (no VA encounters for at least two years) whichever came first. Median follow up was 5.5 person-years (IQR 2.6–9.8). Patients' baseline addresses were extracted from the VA EHR and geocoded using ArcGIS to identify their census tracts. More information about the cohort is published elsewhere (Avramovic et al., 2020). Frailty survival models with clustering at county level and robust standard error were used to evaluate effect modification separately for each community type.

2.8. Harmonized analysis framework

Analytic variables and statistical approaches were harmonized across the three sites. Because NSEE was defined separately by community type, all analyses are stratified by community type. Although each site's analysis plan reflects the respective study design, as recommended, all primary analyses utilized restricted cubic splines with 5 knots to flexibly describe the relationship between NSEE and new onset T2D. The use of 5 knots in the restricted cubic splines was determined a priori from the LEAD analyst working group using recommendations for 'large' sample sizes ($n > 100$) (Harrell, 2001). This a priori knot specification not only included the knot number but also that the knots were placed using quantiles of NSEE distribution within each site. Results are presented in figures using model predictions, overall and by age and sex. Ratios of predicted risk at each NSEE compared to the predicted risk at median NSEE for the relevant reference category (and corresponding 95% confidence interval) were used to assess the relationships graphically. To assess effect modification by age and sex, interaction terms between each modifier and NSEE were added, separately. The significance of the effect modification was assessed by comparing the full model with interaction and the reduced model without interaction using the likelihood ratio test. Separately by study site, community type-specific quartiles of NSEE were also used to investigate its relationship with T2D. Statistical interactions between NSEE and effect modifiers (e.g., sex and age) were included in separate models, and the interaction terms were tested to formally assess effect modification. Effect modification by age and sex used ≥65 years old and male as the reference groups, respectively. All models were adjusted for individual-level covariates including age, sex, race [non-Hispanic White or non-Hispanic Black], and a site-specific proxy for individual socioeconomic status [Medical Assistance status in the G/JHU cohort (Casey et al., 2018), an income variable in the REGARDS cohort, a low income/disability flag which categorizes veterans as disabled, have low income, or neither in the VADR cohort] and community-level covariates (LUE, % Hispanic and % Non-Hispanic Black population). In main effect models and models evaluating effect modification by sex, continuous age was used as a covariate. In these models, non-linearity of age was evaluated, and quadratic age terms were included where appropriate. Statistical analyses were performed using R (version 4.2.2) (R Core Team & Team, 2022) and SAS 9.3.

2.9. Sensitivity analysis

We further conducted a number of site-specific sensitivity analyses. G/JHU performed three sensitivity analyses. First, the impact of removing cases and controls with NSEE higher than the 97.5th percentile was investigated due to the concern that some primary analysis results might be driven by upper extremes of NSEE. The second sensitivity analysis was limited to samples after dropping cases and controls <20 years old. The third analysis was carried out by replacing NSEE with percent of community living below the federal poverty line (FPL) to check if the observed associations and effect modification findings change with the measure of poverty.

The UAB team also evaluated the associations using a measure of national federal poverty level (FPL) instead of a community-specific NSEE. The UAB team also adjusted for REGARDS sampling regions (Stroke Belt vs non-Stroke Belt) to mitigate potential unmeasured confounding of regional influences on the NSEE-T2D association.

The VADR cohort conducted a three-way NSEE by age by sex interaction analysis for each community type. Given the large sample size of the VADR cohort, NYU was the only site where it was feasible to conduct this three-way interaction analysis within each community type. Further, the VADR cohort ran a sensitivity analysis on the subset of VADR participants residing in census tracts of lower density urban community in the G/JHU cohort. This sensitivity analysis helped us parse out place versus person effect, especially for the inconsistent findings in the lower density urban community across the cohorts.

3. Results

3.1. Study design and participant characteristics

Demographic and neighborhood characteristics and geographic spread of the three study participants stratified by new onset of diabetes cases are summarized in Table 1. The G/JHU case-control study sample included 15,888 new onset of diabetes cases and 79,435 control participants from 785 census tracts in Pennsylvania. Out of 11,208 participants who had no diabetes at baseline (2003–2007) and who took part in the second in-home assessment (2013–2016) of the REGARDS cohort, 1409 had incident diabetes. The REGARDS participants were from 7502 census tracts, approximately half of which are located in the southeastern United States. The VADR cohort included over 4.1 million veterans in 71,835 census tracts across the United States with 539,369 cases of new onset diabetes. The median follow-up time was the longest for the G/JHU cohort (11.2 years), followed by REGARDS (9.5 years) and VADR (5 years).

The participants in the REGARDS cohort, on average, were slightly older than participants in the G/JHU and VADR cohorts (63 vs. 54.9 and 59.4 years, respectively). The average age of participants by T2D status was roughly similar in the REGARDS, G/JHU, and VADR cohorts. The REGARDS and G/JHU cohorts included a roughly equal proportion of males and females, whereas VADR participants were predominantly (92.2%) male. In all three cohorts, the proportions of sexes stratified by T2D status were similar to the proportions in the overall cohort. Regarding racial/ethnic composition, the REGARDS cohort had a relatively large proportion of non-Hispanic Black participants compared to VADR and G/JHU (32.8% vs. 14.3% and 1.3%, respectively). Those who developed T2D had a higher proportion of non-Hispanic Black adults across all study sites than those who did not develop diabetes (REGARDS 46.3% vs. 30.8; G/JHU 1.8% vs. 1.1; VADR 18.4% vs. 13.6%).

The distribution of individual-level SES differed across study sites. While definitions of low socioeconomic status (SES) varied across cohorts, the REGARDS and VADR cohorts had higher proportions of participants with low SES. Generally, across sites a slightly higher proportion of participants with diabetes had lower SES compared to those without diabetes. In the G/JHU cohort, 18.6% of participants who had diabetes, compared to 11.3% of those without diabetes, had a history of using Medical Assistance. In the REGARDS cohort, an annual income of <$35,000 was reported by 41% of those who developed diabetes compared to 31.4% among those who did not develop diabetes. Around 40% of VADR participants who had new onset of T2D were considered low income for insurance purposes compared to 37.5% of those who did not develop T2D.

The values for NSEE in neighborhoods of participants differed slightly by T2D status within each community type. Broadly, participants with diabetes compared to participants without diabetes lived in neighborhoods with slightly greater neighborhood disadvantage (higher median value of NSEE), across study sites. For instance, in the REGARDS cohort, participants with diabetes had a median NSEE value of 19.1 compared to a median NSEE value of 13.5 among participants without diabetes in lower density urban communities. In the VADR cohort, the most geographically diverse study sample, the median NSEE value among participants with diabetes was also higher than those without diabetes in lower density urban communities (11.7 vs.10.9).

3.2. Main effect

The main effect of NSEE on T2D risk across community types is presented in Fig. 1. Broadly, the risk of T2D generally increased as NSEE worsened, with the association increasing to the median and then stabilizing in most community types across study sites. However, there were exceptions; one exception was in lower density urban community

Table 1
Baseline characteristics of study population by T2D status.

	Study population								
	G/JHU			REGARDS			VADR		
	No Diabetes	Diabetes	Overall	No Diabetes	Diabetes	Overall	No Diabetes	Diabetes	Overall
	n = 79,435	n = 15,888	n = 95,323	n = 9799	n = 1409	n = 11,208	n = 3,561,281	n = 539,369	n = 4,100,650
Study characteristics									
Study Design		Nested Case-Control			Cohort			Retrospective longitudinal cohort	
Study period		2008–2016			2003–2016			Enrollment 2008–2016, followed through 2018	
Number of counties			37	1294	504	1349	3108	3086	3108
Number of census tracts			785	6831	1285	7502	71,803	68,607	71,835
Follow-up years, median (IQR)	11.2 (7.5, 14.1)	11.2 (7.5, 14.1)	11.2 (7.5, 14.1)	9.5 (8.7, 9.9)	9.55 (8.7, 10.0)	9.47 (8.7, 9.9)	5.4 (2.7, 9.7)	2.6 (0.9, 5.4)	5.0 (2.4, 9.0)
Number of participants	79,435	15,888	95,323	9799	1409	11,208	3,561,281	539,369	4,100,650
Demographics									
Age at enrollment (mean, SD)	54.9 (15.3)	54.9 (15.1)	54.9 (15.2)	63.1 (8.6)	62.2 (7.8)	63.0 (8.5)	58.9 (17.8)	62.5 (12.3)	59.4 (17.2)
Age categories									
<45	19,589 (24.7)	3918 (24.7)	23,507 (24.7)	–	–	–	817,315 (23.0)	41,773 (7.7)	859,088 (21.0)
45-64	39,562 (49.8)	7913 (49.8)	47,475 (49.8)	5657 (57.7)	876 (62.2)	6533 (58.3)	1,320,954 (37.1)	276,753 (51.3)	1,597,707 (39.0)
≥65	20,284 (25.5)	4057 (25.5)	24,341 (25.5)	4142 (42.3)	533 (37.8)	4675 (41.7)	1,422,958 (40.0)	220,839 (40.9)	1,643,797 (40.1)
Sex									
Male, n (%)	40,447 (50.9)	8090 (50.9)	48,537 (50.9)	4297 (43.9)	655 (46.5)	4952 (44.2)	3,266,635 (91.7)	512,920 (95.1)	3,779,555 (92.2)
Female, n (%)	38,988 (49.1)	7798 (49.1)	46,786 (49.1)	5502 (56.2)	754 (53.5)	6256 (55.8)	294,574 (8.3)	26,439 (4.9)	321,013 (7.8)
Race/ethnicity, n (%)									
Non-Hispanic White	76,971 (96.9)	15,112 (95.1)	92,083 (96.6)	6777 (69.2)	757 (53.7)	7534 (67.2)	2,424,107 (68.1)	359,649 (66.7)	2,783,756 (67.9)
Non-Hispanic Black	905 (1.1)	293 (1.8)	1198 (1.3)	3022 (30.8)	652 (46.3)	3674 (32.8)	485,642 (13.6)	99,013 (18.4)	584,655 (14.3)
Hispanic	1094 (1.4)	369 (2.3)	1463 (1.5)	–	–	–	164,941 (4.6)	24,236 (4.5)	189,177 (4.6)
Asian	267 (0.34)	63 (0.40)	330 (0.35)	–	–	–	30,365 (0.9)	4473 (0.8)	34,838 (0.8)
Other/Unknown	198 (0.25)	51 (0.32)	249 (0.26)	–	–	–	456,226 (12.8)	51,998 (9.6)	508,224 (12.4)
Individual SES									
No receipt of Medical Assistance, n (%)	70,444 (88.7)	12,934 (81.4)	83,378 (87.5)						
Annual household income, n (%)									
< $20,000				1032 (10.5)	238 (16.9)	1270 (11.3)			
$20,000 - $34,999				2044 (20.9)	339 (24.1)	2383 (21.3)			
$35,000 - $74,999				3342 (34.1)	474 (33.6)	3816 (34.1)			
≥ $75,000				2316 (23.6)	224 (15.9)	2540 (22.7)			
Refused				1065 (10.9)	134 (9.5)	1199 (10.7)			
NYU income variable/indicator, n (%)									
Disabled							1,211,517 (34.6)	192,341 (36)	1,403,858 (34.8)
Low income							1,312,331 (37.5)	214,927 (40.2)	1,527,258 (37.9)
None of the above							973,825 (27.8)	127,074 (23.8)	1,100,899 (27.3)
Neighborhood Characteristics by LEAD Community Type									
Higher Density Urban (n)	4121	1039	5160	1587	223	1810	410,382	68,286	478,668
NSEE, median (IQR)	23.6 (18.8, 28.3)	23.6 (19.1, 29.3)	23.6 (18.8, 29.3)	24.1 (16.2, 33.6)	27.9 (20.5, 36.4)	24.8 (16.5, 34.0)	20.4 (13.4, 31.1)	21.9 (14.3, 32.9)	20.7 (13.5, 31.4)
NSEE quartiles, n (%)									
NSEE Q1	1082 (26.3)	243 (23.4)	1325 (25.7)	386 (24.3)	29 (13.0)	415 (22.9)	110,775 (27.0)	15,792 (23.1)	126,567 (26.5)
NSEE Q2	1142 (27.7)	310 (29.8)	1452 (28.1)	448 (28.2)	61 (27.4)	509 (28.1)	116,376 (28.4)	18,662 (27.3)	135,038 (28.2)
NSEE Q3	1040 (25.2)	288 (27.7)	1328 (25.7)	410 (25.8)	76 (34.1)	486 (26.9)	98,406 (24.0)	17,372 (25.5)	115,778 (24.2)
NSEE Q4	857 (20.8)	189 (19.1)	1055 (20.4)	343 (21.6)	57 (25.6)	400 (22.1)	84,445 (20.6)	16,423 (24.1)	100,868 (21.1)
% Non-Hispanic Black, mean (SD)	5.1 (5.9)	6.2 (7.8)	5.3 (6.4)	63.4 (33.2)	71.3 (29.4)	64.4 (32.9)	0.3 (0.3)	0.3 (0.3)	0.3 (0.3)

(*continued on next page*)

Table 1 (*continued*)

	Study population								
	G/JHU			REGARDS			VADR		
	No Diabetes	Diabetes	Overall	No Diabetes	Diabetes	Overall	No Diabetes	Diabetes	Overall
	n = 79,435	n = 15,888	n = 95,323	n = 9799	n = 1409	n = 11,208	n = 3,561,281	n = 539,369	n = 4,100,650
% Hispanic, mean (SD)	5.8 (8.2)	5.8 (7.3)	5.8 (8.1)	8.4 (11.4)	8.1 (11.4)	8.4 (11.4)	0.2 (0.2	0.2 (0.2)	0.2 (0.2)
LUE factor score, median (IQR)	0.24 (−0.38, 0.70)	0.24 (−0.34, 0.66)	0.24 (−0.34, 0.70)	0.12 (−0.50, 0.63)	0.20 (−0.48, 0.69)	0.13 (−0.50, 0.64)	−0.07 (−0.60, 0.49)	−0.04 (−0.56, 0.51)	−0.07 (−0.59, 0.50)
Lower Density Urban (n)	8665	1890	10,555	3937	587	4524	1,311,459	197,583	1,509,042
NSEE, median (IQR)	16.4 (12.8, 21.7)	17.1 (13.4, 22.0)	16.8 (13.0, 22.0)	13.5 (8.2, 24.3)	19.1 (11.1, 30.1)	14.5 (8.4, 25.3)	10.8 (7.1, 16.4)	11.7 (7.7, 18.0)	10.9 (7.2, 16.6)
NSEE quartiles, n (%)									
NSEE Q1	673 (7.8)	84 (4.4)	757 (7.2)	875 (22.2)	73 (12.4)	948 (21.0)	283,454 (21.6)	36,916 (18.7)	320,370 (21.2)
NSEE Q2	2144 (24.7)	410 (21.7)	2554 (24.2)	988 (25.1)	106 (18.1)	1094 (24.2)	360,675 (27.5)	51,285 (26.0)	411,960 (27.3)
NSEE Q3	2486 (28.7)	547 (28.9)	3033 (28.7)	1028 (26.1)	177 (30.2)	1205 (26.6)	373,461 (28.5)	57,129 (28.9)	430,590 (28.5)
NSEE Q4	3362 (38.8)	849 (44.9)	4211 (39.9)	1046 (26.6)	231 (39.4)	1277 (28.2)	293,278 (22.4)	52,166 (26.4)	345,444 (22.9)
% Non-Hispanic Black, mean (SD)	2.5 (2.9)	2.6 (3.3)	2.5 (3.0)	41.6 (35.8)	55.0 (34.3)	43.4 (35.9)	0.1 (0.2)	0.2 (0.3)	0.2 (0.2)
% Hispanic, mean (SD)	2.7 (4.4)	3.0 (5.3)	2.7 (4.6)	5.0 (7.7)	5.0 (8.6)	5.0 (7.9)	0.1 (0.2)	0.1 (0.2)	0.1 (0.2)
LUE factor score, median (IQR)	0.15 (−0.57, 0.93)	0.31 (−0.47, 1.0)	0.17 (−0.52, 1.0)	−0.01 (−0.63, 0.64)	0.03 (−0.60, 0.73)	−0.00 (−0.63, 0.65)	0.09 (−0.59, 0.68)	0.11 (−0.57, 0.70)	0.09 (−0.58, 0.68)
Suburban/Small Town(n)	24,886	5009	29,895	1945	279	2224	803,678	115,603	919,281
NSEE, median (IQR)	15.0 (9.7, 20.4)	16.1 (10.6, 21.7)	15.1 (9.9, 20.4)	11.0 (6.8, 17.3)	13.5 (8.6, 22.2)	11.35 (6.9, 17.8)	11.4 (7.7, 16.7)	11.6 (7.7, 16.8)	11.5 (7.7, 16.7)
NSEE quartiles, n (%)									
NSEE Q1	4817 (19.4)	779 (15.6)	5596 (18.7)	435 (22.4)	47 (16.9)	484 (21.7)	185,289 (23.1)	23,875 (20.7)	209,164 (22.8)
NSEE Q2	5140 (20.7)	906 (18.1)	6046 (20.2)	445 (22.9)	48 (17.2)	493 (22.2)	230,125 (28.6)	32,080 (27.8)	262,205 (28.5)
NSEE Q3	7509 (30.2)	1537 (30.7)	9046 (30.3)	490 (25.2)	70 (25.1)	560 (25.2)	229,738 (28.6)	33,849 (29.3)	263,587 (28.7)
NSEE Q4	7420 (29.8)	1787 (35.7)	9207 (30.8)	575 (29.6)	114 (40.9)	689 (31.0)	158,293 (19.7)	25,778 (22.3)	184,071 (20.0)
% Non-Hispanic Black, mean (SD)	2.2 (4.3)	2.2 (4.4)	2.2 (4.3)	27.0 (30.0)	34.7 (31.7)	28.0 (30.3)	0.1 (0.2)	0.1 (0.2)	0.1 (0.2)
% Hispanic, mean (SD)	2.0 (3.3)	2.2 (3.6)	2.1 (3.4)	3.3 (5.5)	2.9 (4.1)	3.3 (5.3)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)
LUE factor score, median (IQR)	0.26 (−0.68, 1.8)	0.71 (−0.54, 1.9)	0.26 (−0.58, 1.8)	0.02 (−0.62, 0.56)	0.04 (−0.69, 0.64)	0.02 (−0.64, 0.57)	−0.06 (−0.70, 0.54)	−0.05 (−0.69, 0.54)	−0.06 (−0.70, 0.54)
Rural (n)	41,763	7950	49,713	2330	320	2650	1,035,762	157,897	1,193,659
NSEE, median (IQR)	16.0 (13.2, 18.6)	16.2 (13.6, 19.1)	16.0 (13.4, 18.7)	22.4 (16.0, 29.8)	23.7 (17.7, 31.5)	22.6 (16.2, 30.0)	17.8 (13.5, 23.0)	18.2 (13.8, 23.4)	17.9 (13.5, 23.1)
NSEE quartiles, n (%)									
NSEE Q1	13,010 (31.2)	2256 (28.4)	15,266 (30.7)	462 (19.8)	38 (11.9)	500 (18.9)	255,353 (24.7)	35,548 (22.5)	290,901 (24.4)
NSEE Q2	9.744 (23.3)	1802 (22.7)	11,546 (23.2)	464 (19.9)	67 (20.9)	531 (20.0)	279,997 (27.0)	41,376 (26.2)	321,373 (26.9)
NSEE Q3	12,096 (29.0)	2470 (31.1)	14,566 (29.3)	557 (23.9)	81 (25.3)	638 (24.1)	278,508 (26.9)	43,685 (27.7)	322,193 (27.0)
NSEE Q4	6931 (16.6)	1422 (17.9)	8335 (16.8)	847 (36.4)	134 (41.9)	981 (37.0)	221,778 (21.4)	37,271 (23.6)	259,049 (21.7)
% Non-Hispanic Black, mean (SD)	1.8 (4.3)	1.9 (4.4)	1.9 (4.3)	30.9 (27.5)	35.9 (27.5)	31.5 (27.5)	0.1 (0.1)	0.1 (0.1)	0.1 (0.1)
% Hispanic, mean (SD)	1.5 (2.5)	1.5 (2.6)	1.5 (2.5)	2.6 (5.0)	2.8 (5.5)	2.6 (5.1)	0.05 (0.1)	0.05 (0.1)	0.05 (0.1)
LUE factor score, median (IQR)	0.28 (−0.10, 0.67)	0.27 (−0.11, 0.67)	0.28 (−0.10, 0.67)	0.11 (−0.42, 0.79)	0.11 (−0.43, 0.79)	0.11 (−0.42, 0.79)	−0.04 (−0.53, 0.60)	−0.04 (−0.51, 0.59)	−0.04 (−0.53, 0.59)

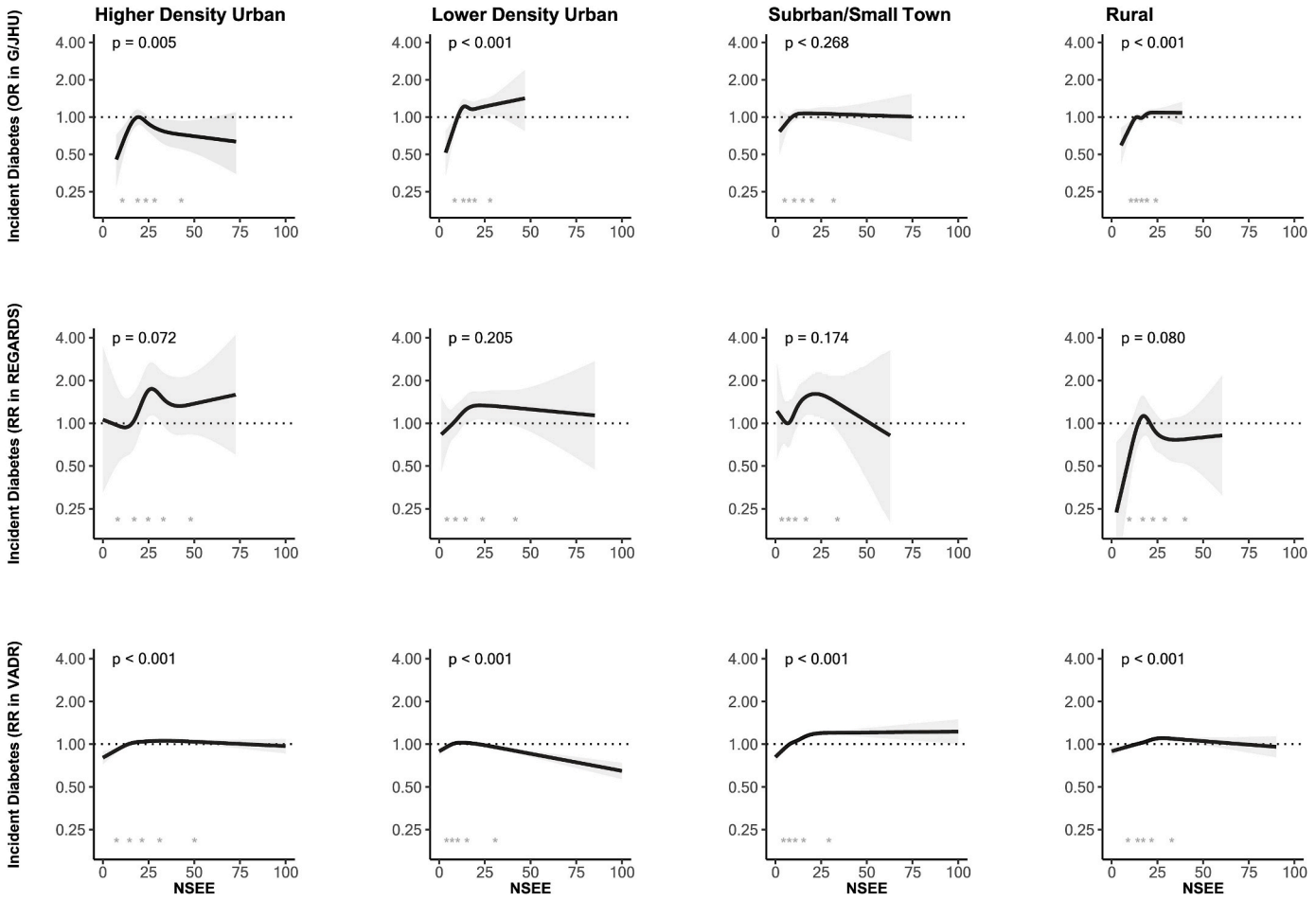

Fig. 1. Main effect of NSEE on T2D using splines within community type across studies. P-values correspond to the overall test for NSEE association and new onset T2D in each spline model.

types, where this association decreased in the VADR cohort. In the G/JHU cohort, the association increased to the median and then declined at higher values of NSEE.

3.3. Effect modification by sex

Results of effect modification by sex are presented by study population and community types using spline figures (Fig. 2) and quartiles (**Table 2**). While results differ by sites and community types, when effect modification was observed there was a stronger association between NSEE and diabetes among females compared to males. There was no significant effect modification by sex observed in higher density urban community types in any of the cohorts. In contrast, we found some evidence of effect modification by sex in other community types. For example, in both spline- and quartile-based analyses in lower density urban communities in the VADR and REGARDS cohorts, we generally observed that risk estimates were higher for females, especially at the higher end of the NSEE score, and risk estimates for females were lower than for males at the lower end of NSEE score.

Consistent with patterns found in lower density urban communities, in suburban/small town communities, the quartile analyses in the G/JHU and VADR cohorts also suggested higher risk for females than males as NSEE worsened. In the G/JHU cohort, the OR for Q4 vs. Q1 among females was: 1.34, 95% CI: 1.12–1.60, whereas among males it was: 0.96, 95% CI: 0.80, 1.15. Similarly, in the VADR cohort, the RR for Q4 vs. Q1 among females was: 1.31, 95% CI: 1.19–1.45, while among males it was: 1.09, 95% CI: 1.05, 1.13. Effect modification by sex was not observed in the REGARDS cohort. Spline analyses showed an increased risk of T2D for females at the higher end of the NSEE spline figure in the G/JHU cohort only.

In rural community types, spline shapes showed an increased risk of diabetes among females at the higher end of NSEE score and a lower risk at the lower end of the NSEE score in the VADR cohort. Similarly, the quartile analysis showed a higher risk among females than males in the VADR cohort (RR for Q4 vs Q1 among females is 1.28, 95% CI: 1.17–1.40, and among males: 1.06, 95% CI: 1.03–1.09). In both spline- and quartile-based analyses, there was no evidence of effect modification by sex in the G/JHU study population and the REGARDS cohort in rural communities.

3.4. Effect modification by age

Results for effect modification by age are also presented by study population and community type using spline figures (Fig. 3) and quartiles (Table 3). While there was some evidence of effect modification by age, results were not consistent across study sites or community types. Overall, evidence of effect modification was more often observed in the VADR cohort than in the other study sites. For example, in the higher density urban communities, spline and quartile analyses showed no significant differences in risk estimates in the G/JHU and REGARDS cohorts by age. However, in the VADR cohort, we observed an increased risk of diabetes for the <45 and 65 years or older groups at the highest levels of NSEE compared to participants in the 45–64 year age group in both spline and quartile analyses.

In lower density urban communities, spline-and quartile-based results also differed by study sites. In the G/JHU study population in all

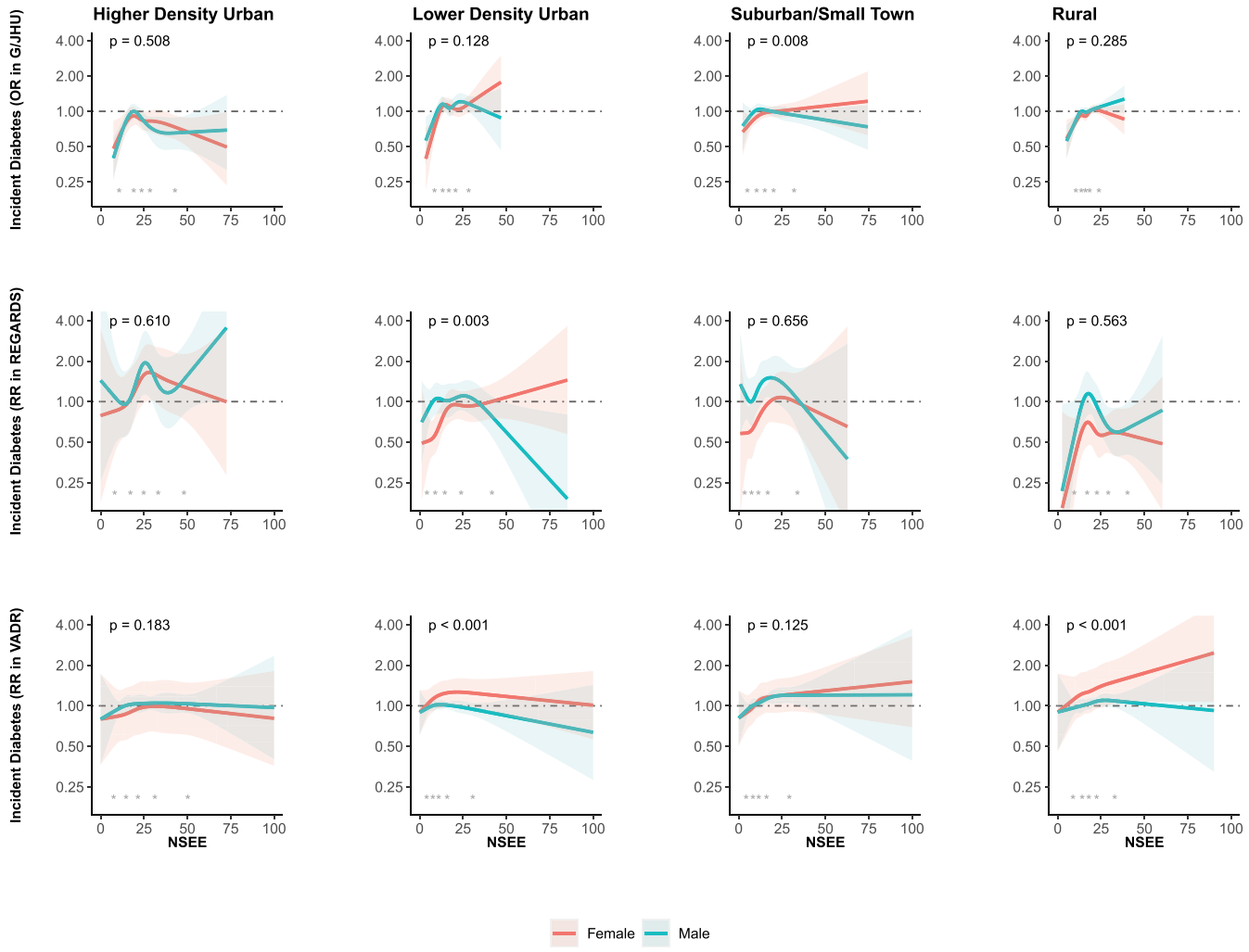

Fig. 2. Effect modification of NSEE-T2D association by sex within community types across studies. P-values correspond to the test for interaction between NSEE splines terms and age group in association with new onset T2D.

age groups, spline shapes showed an increased risk, especially up to knot 2 (27.5th percentile), and then a declining risk that continued up to knot 4 (72.5th percentile). In the upper end of the NSEE distribution, the risk appeared to increase only for individuals 65 years and older, however, the NSEE quartile differences by age groups were not significantly different. In the REGARDS cohort, both spline figures and quartile analysis showed no significant differences. In the VADR cohort, we observed an increased risk for the <45 years group after median NSEE, a declining risk for the 45–64 years old, and a flatter pattern for those 65+ years old. In the VADR cohort, quartile analysis suggested a stronger association among those less than 45 years old (i.e., RR for Q4 vs. Q1: 1.20, 95% CI: 1.12–1.23) and 65 years or older (i.e., RR for Q4 vs. Q1: 1.15, 95% CI: 1.09–1.20). When we ran the VADR analysis by limiting to G/JHU census tracts only, we observed increasing T2D risk with NSEE for the 65+ years old group only, and a declining or flatter patterns for <45 years old and 45–64 years old.

In suburban/small town communities, spline and quartile analyses showed slightly divergent patterns of association in the G/JHU and VADR cohorts, especially among the 65 years or older group. For instance, the spline shapes showed a pattern of increased risk for the 65 years or older group and a relatively flatter pattern for the 45–64 years old in both the G/JHU and VADR cohorts. For the <45 years old group in the G/JHU cohort, spline results suggested a lower risk at low NSEE levels. The quartile analysis revealed a notably increased risk of diabetes with increasing NSEE among individuals <45 years old in both the G/JHU and VADR cohorts. Both spline and quartile analyses in the REGARDS cohort did not show significant differences by age.

Finally, in rural communities both spline and quartile analyses showed no significant effect modification by age in both G/JHU study population and the REGARDS cohort. In the VADR cohort, both spline and quartile analyses demonstrated a sharp increasing risk pattern for the <45 years old group, a relatively stable pattern for the 45–64 years old, and a slow increasing pattern for the 65 years or older group.

3.5. *Sensitivity analyses*

Some of G/JHU's primary findings were sensitive to removal of the extreme NSEE values (e.g., cases and controls above 97.5th percentile of NSEE). Specifically, effect modification by age in lower density urban communities was no longer present, although the effect modification by age in suburban/small town communities remained. The effect modification by sex in suburban/small town communities was no longer present. Similarly, removal of persons <20 years old resulted in no significant modification by age in lower density urban communities, but the observed significant effect modification by age and sex in suburban/small town communities remained in both the NSEE spline and quartile models. In FPL analysis, G/JHU found significant effect modification by sex in lower density urban communities only, and effect modification by

Table 2
Adjusted associations of NSEE quartiles with incidence of T2D in sex-stratified models[a].

Higher Density Urban			Men	Women	Interaction p-value
	G/JHU	Q2 vs Q1	1.23 (0.92–1.65)	1.06 (0.83–1.37)	
		Q3 vs Q1	0.97 (0.73–1.30)	1.14 (0.87–1.50)	0.158
		Q4 vs Q1	0.69 (0.46–1.05)	0.89 (0.66–1.20)	
	REGARDS	Q2 vs Q1	1.44 (0.75–2.77)	1.56 (0.90–2.70)	
		Q3 vs Q1	1.59 (0.82–3.08)	1.84 (1.05–3.23)	0.975
		Q4 vs Q1	1.44 (0.71–2.91)	1.45 (0.80–2.62)	
	VADR	Q2 vs Q1	1.06 (1.02–1.11)	1.03 (0.90–1.17)	
		Q3 vs Q1	1.08 (1.03–1.14)	1.13 (0.99–1.28)	0.189
		Q4 vs Q1	1.07 (1.00–1.15)	1.11 (0.97–1.27)	
Lower Density Urban					
	G/JHU	Q2 vs Q1	1.40 (1.08–1.80)	1.72 (1.15–2.57)	
		Q3 vs Q1	1.55 (1.19–2.02)	1.83 (1.23–2.72)	0.710
		Q4 vs Q1	1.49 (1.14–1.94)	1.88 (1.25–2.83)	
	REGARDS	Q2 vs Q1	0.96 (0.66–1.37)	1.44 (0.89–2.31)	
		Q3 vs Q1	1.13 (0.79–1.62)	2.09 (1.33–3.27)	0.027
		Q4 vs Q1	1.04 (0.71–1.54)	2.20 (1.37–3.53)	
	VADR	Q2 vs Q1	1.05 (1.03–1.08)	1.12 (1.04–1.20)	<0.001
		Q3 vs Q1	1.08 (1.04–1.12)	1.21 (1.13–1.31)	
		Q4 vs Q1	1.05 (1.01–1.09)	1.25 (1.15–1.36)	
Suburban/Small Town	G/JHU	Q2 vs Q1	0.96 (0.82–1.14)	1.09 (0.94–1.27)	
		Q3 vs Q1	1.08 (0.92–1.27)	1.20 (1.03–1.40)	0.001
		Q4 vs Q1	0.96 (0.80–1.15)	1.34 (1.12–1.60)	
	REGARDS	Q2 vs Q1	0.78 (0.46–1.32)	1.34 (0.69–2.59)	
		Q3 vs Q1	1.12 (0.73–1.72)	1.34 (0.71–2.51)	0.331
		Q4 vs Q1	1.14 (0.72–1.79)	0.90 (1.01–3.54)	
	VADR	Q2 vs Q1	1.04 (1.-2-1.07)	1.18 (1.07–1.29)	<0.001
		Q3 vs Q1	1.07 (1.04–1.11)	1.24 (1.13–1.37)	
		Q4 vs Q1	1.09 (1.05–1.13)	1.31 (1.19–1.45)	
Rural	G/JHU	Q2 vs Q1	1.03 (0.91–1.18)	1.00 (0.89–1.13)	
		Q3 vs Q1	1.11 (1.01–1.22)	1.15 (1.03–1.28)	0.804
		Q4 vs Q1	1.13 (1.02–1.26)	1.12 (0.99–1.27)	
	REGARDS	Q2 vs Q1	1.97 (1.19–3.28)	1.27 (0.73–2.23)	
		Q3 vs Q1	1.60 (0.94–2.73)	1.27 (0.73–2.22)	0.260
		Q4 vs Q1	1.23 (0.67–2.26)	1.35 (0.75–2.45)	
	VADR	Q2 vs Q1	1.03 (1.01–1.05)	1.09 (0.99–1.19)	<0.001
		Q3 vs Q1	1.06 (1.03–1.08)	1.15 (1.05–1.23)	
		Q4 vs Q1	1.06 (1.03–1.09)	1.28 (1.17–1.40)	

All models were adjusted for age, sex, race/ethnicity, income or its surrogates, land use environment, and % Hispanic and % Non-Hispanic Black at the census-tract level.

[a] The VADR and REGARDS estimated the associations using risk ratios and the Geisinger used odds ratios.

age and sex in suburban/small town communities in the primary analysis were no longer present with FPL. However, the sensitivity analysis using FPL in the REGARDS cohort did not yield different conclusions, nor did adjustment for REGARDS sampling region.

Given the inconsistent effect modification by age findings in lower density urban community, especially between the G/JHU and VADR cohorts, the VADR cohort ran a sensitivity analysis limiting the VADR data in the G/JHU census tracts in the lower density urban community type. This analysis (Supplementary Fig. 1) suggests a higher risk of T2D for both <45 years and 65+ age groups, which roughly corresponds to what we observed in the primary spline analysis in the lower density urban community in the G/JHU cohort, however, these findings were slightly different than what observed in the VADR primary spline analysis.

The VADR cohort also examined whether the associations of NSEE quartiles with T2D risk by different age groups were different for males and females. The effect modification by age and sex together was significant for the lower density urban and rural community types only (in Supplementary Table 2). In suburban/small town, among males, the association was strongest among the <45 years old group (RR for Q4 vs Q1: 1.19, 95% CI: 1.10, 1.28) and among the 65 years of older group (RR for Q4 vs Q1: 1.15, 95% CI: 1.10, 1.20), with increasing risk pattern across higher NSEE quartiles. This pattern was not seen among 45–64 years old males. Among females, NSEE was most strongly associated with T2D for the <45 years old group (RR for Q4 vs Q1: 1.27, 95% CI: 1.11, 1.46) and the 45–64 age group (RR for Q4 vs Q1: 1.25, 95% CI 1.12, 1.39), with increasing risk pattern for both age groups. In rural communities, among males, the association between NSEE quartiles and T2D was most pronounced among the <45 years age group (RR for Q4 vs Q1: 1.29, 95% CI 1.20, 1.39) which revealed an increasing risk of T2D with increased NSEE. Among females, the risk of T2D increased with NSEE for the <45 years age group and for the 45–64 years age group in females.

4. Discussion

In this harmonized analysis of three independent studies, we investigated whether the effects of NSEE on T2D risk differed by sex and age. Overall, we observed that the risk of T2D generally increased with increasing NSEE, that is, with increasing neighborhood disadvantage. By analyzing the association using spline figures, we showed that this association generally increases to the median and stabilizes in most community types across study sites, and quartile-based analyses broadly confirmed similar patterns. We observed more consistent evidence for effect modification by sex than age across study sites. Generally, the risk of T2D associated with higher NSEE was greater for females than males

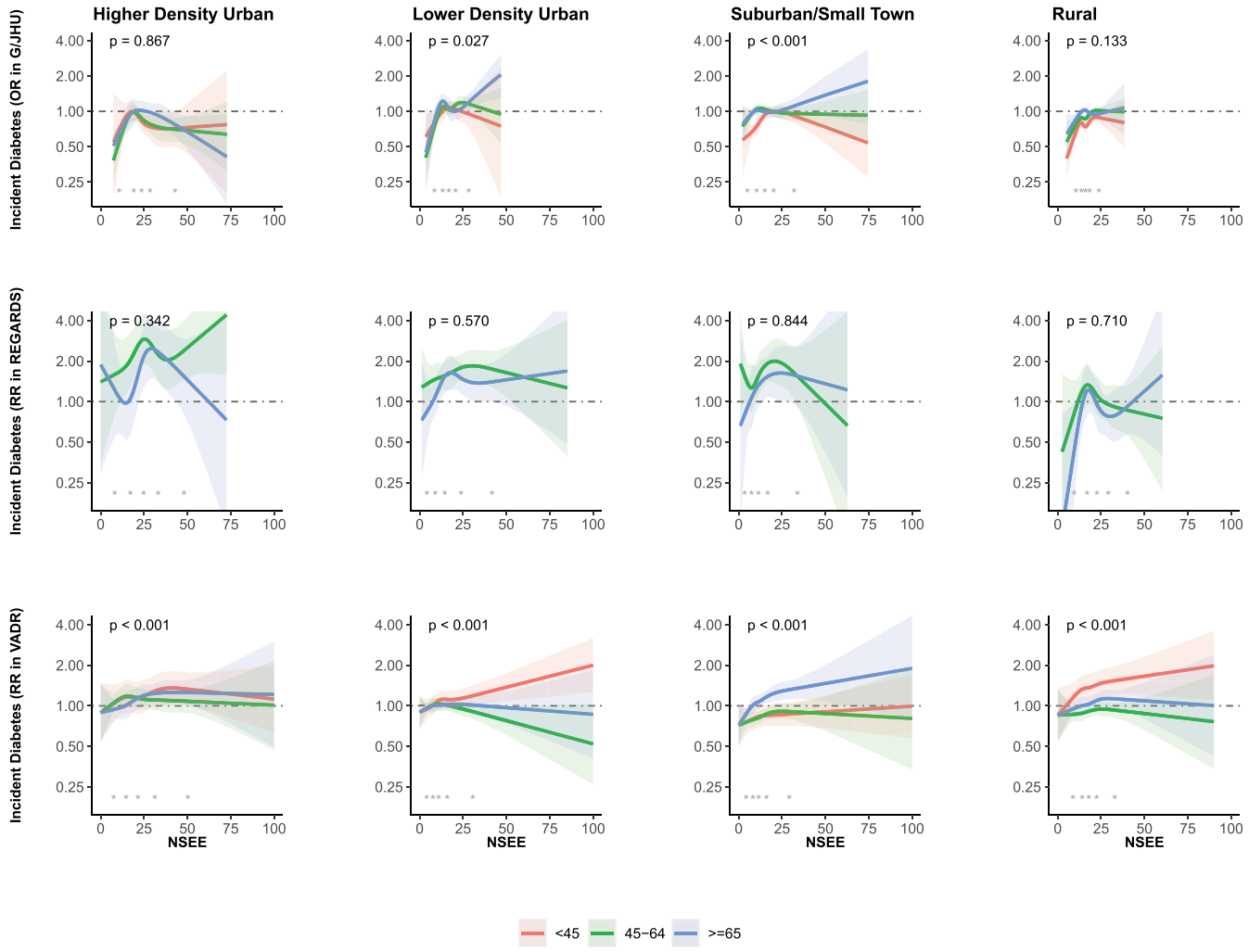

Fig. 3. Effect modification of NSEE-T2D association by age within community types across studies. P-values correspond to the test for interaction between NSEE splines terms and age group in association with new onset T2D.

in most community types. However, the risk associated with NSEE among females was lower (vs. men) at lower levels of NSEE. We observed that the impact of NSEE on T2D risk generally differed by age, yet there was considerable heterogeneity in these results across study sites and community types. This study does not explicitly compare NSEE-T2D associations across community types but shows the nuances of the differential relationships across study sites.

Consistent with previous studies (Christine et al., 2015, 2017; Hu et al., 2020; Thorpe et al., 2022), our analyses found that individuals living in socioeconomically disadvantaged neighborhoods generally had an increased risk of T2D, although associations differed in magnitude across study sites and by community type. This association was least apparent in higher density urban settings, however, findings were broadly consistent in other community types. Most prior studies of the association between neighborhood disadvantage and health outcomes do not include community types across the urban-rural spectrum, limiting the generalizability of their findings to other community types, or fail to examine associations by community type (Christine et al., 2015, 2017; Hu et al., 2020; Ludwig et al., 2011). The LEAD Network's diverse mix of community types allowed the Network to evaluate associations between neighborhood disadvantage and T2D and modifiers of these associations in each of four community types. Especially given the nuanced impact of community types (McAlexander, Algur, et al., 2022; McAlexander, Malla, et al., 2022) and how neighborhood disadvantages are intricately linked to community types, this work is critical to informing targeted local T2D prevention strategies. In some communities with greater access barriers, stronger social communities and organizations, such as senior citizen's clubs, may be utilized for targeted interventions.

With some exceptions, we observed that the NSEE-T2D association was stronger among females than males in most communities. Although a stronger effect of neighborhood disadvantage among women is often reported in the health disparities literature, only a few studies exclusively focus on the incidence of diabetes as an outcome measure, and our findings are consistent with those studies. For instance, using a large EHR database, researchers in Madrid, Spain reported a stronger association of neighborhood SES with the hazard of incidence of diabetes for women than men (Bilal, Hill-Briggs, Sanchez-Perruca, Del Cura-Gonzalez, & Franco, 2018). Similarly, another EHR-based study using data from 7 counties in Southern Minnesota observed a stronger association between the area deprivation index (measured at the census block group) and the prevalence of several cardiometabolic conditions, including diabetes among women (Chamberlain et al., 2022). In the Jackson Heart Study, Barber and colleagues found that neighborhood disadvantage was significantly associated with the risk of cardiovascular events among African-American women but not among men (Barber et al., 2016). However, these studies did not stratify by community type. Unlike these studies, using a community type-specific measure of

Table 3
Adjusted associations of NSEE quartiles with incidence of T2D in age-stratified models.[a]

			<45	45–64	65+	Interaction p-value
Higher Density Urban	G/JHU	Q2 vs Q1	1.01 (0.72–1.43)	1.15 (0.85–1.56)	1.41 (0.92–2.16)	0.538
		Q3 vs Q1	0.97 (0.64–1.46)	0.99 (0.75–1.30)	1.45 (0.91–2.32)	
		Q4 vs Q1	0.65 (0.42–1.01)	0.75 (0.52–1.10)	1.16 (0.73–1.85)	
	REGARDS	Q2 vs Q1	–	1.44 (0.87–2.41)	1.66 (0.81–3.38)	0.436
		Q3 vs Q1	–	1.39 (0.82–2.38)	2.50 (1.23–5.05)	
		Q4 vs Q1	–	1.31 (0.75–2.30)	1.71 (0.81–3.61)	
	VADR	Q2 vs Q1	1.05 (0.94–1.18)	1.02 (0.98–1.07)	1.09 (1.02–1.15)	<0.001
		Q3 vs Q1	1.14 (1.02–1.28)	0.99 (0.94–1.06)	1.19 (1.12–1.27)	
		Q4 vs Q1	1.23 (1.09–1.39)	0.96 (0.89–1.03)	1.26 (1.15–1.37)	
Lower Density Urban	G/JHU	Q2 vs Q1	1.43 (0.94–2.19)	1.58 (1.10–2.27)	1.58 (1.00–2.50)	0.834
		Q3 vs Q1	1.51 (0.99–2.30)	1.79 (1.28–2.50)	1.67 (1.03–2.70)	
		Q4 vs Q1	1.52 (0.99–2.31)	1.87 (1.33–2.64)	1.49 (0.94–2.34)	
	REGARDS	Q2 vs Q1	–	1.01 (0.70–1.44)	1.26 (0.79–2.03)	0.670
		Q3 vs Q1	–	1.27 (0.90–1.80)	1.74 (1.12–2.72)	
		Q4 vs Q1	–	1.29 (0.88–1.89)	1.70 (1.06–2.71)	
	VADR	Q2 vs Q1	1.06 (1.00–1.13)	1.06 (1.02–1.09)	1.05 (1.02–1.08)	<0.001
		Q3 vs Q1	1.15 (1.08–1.22)	1.06 (1.02–1.10)	1.09 (1.05–1.13)	
		Q4 vs Q1	1.20 (1.12–1.23)	0.98 (0.94–1.03)	1.15 (1.09–1.20)	
Suburban/Small Town	G/JHU	Q2 vs Q1	1.15 (0.89–1.48)	0.98 (0.83–1.17)	0.98 (0.83–1.15)	0.001
		Q3 vs Q1	1.45 (1.19–1.76)	1.06 (0.90–1.27)	1.04 (0.86–1.24)	
		Q4 vs Q1	1.56 (1.27–1.92)	1.03 (0.85–1.25)	1.04 (0.86–1.24)	
	REGARDS	Q2 vs Q1	–	0.78 (0.48–1.28)	1.40 (0.70–2.80)	0.498
		Q3 vs Q1	–	1.02 (0.67–1.56)	1.54 (0.81–2.96)	
		Q4 vs Q1	–	1.17 (0.74–1.85)	1.91 (1.00–3.65)	
	VADR	Q2 vs Q1	1.08 (1.00–1.15)	1.04 (1.01–1.08)	1.06 (1.02–1.09)	0.005
		Q3 vs Q1	1.12 (1.04–1.20)	1.09 (1.05–1.13)	1.07 (1.03–1.10)	
		Q4 vs Q1	1.21 (1.12–1.32)	1.08 (1.03–1.13)	1.09 (1.04–1.14)	
Rural	G/JHU	Q2 vs Q1	1.02 (0.84–1.25)	1.03 (0.91–1.17)	1.00 (0.86–1.17)	0.255
		Q3 vs Q1	1.10 (0.95–1.28)	1.18 (1.07–1.31)	1.05 (0.92–1.21)	
		Q4 vs Q1	1.22 (1.04–1.43)	1.19 (1.06–1.34)	0.94 (0.79–1.12)	
	REGARDS	Q2 vs Q1	–	1.39 (0.87–2.23)	2.06 (1.08–3.94)	0.799
		Q3 vs Q1	–	1.31 (0.82–2.08)	1.73 (0.89–3.39)	
		Q4 vs Q1	–	1.19 (0.69–2.05)	1.63 (0.80–3.33)	
	VADR	Q2 vs Q1	1.11 (1.04–1.19)	1.03 (1.00–1.06)	1.02 (0.99–1.04)	<0.001
		Q3 vs Q1	1.16 (1.08–1.24)	1.05 (1.02–1.08)	1.05 (1.02–1.09)	
		Q4 vs Q1	1.30 (1.21–1.39)	1.05 (1.01–1.08)	1.06 (1.03–1.09)	

All models were adjusted for age, sex, race/ethnicity, income or its surrogates, land use environment, and % Hispanic and % Non-Hispanic Black at the census-tract level.- REGARDS cohort does have participants <45.

[a] The VADR and REGARDS estimated the associations using risk ratios and the Geisinger used odds ratios.

neighborhood disadvantage, our analysis provides a nuanced insight into the differential impact of neighborhood disadvantages on T2D by sex and age.

Our findings regarding the differential effect of NSEE for women and men can be attributed to several potential mechanisms through which neighborhood disadvantages potentially lead to variations in diabetes burden by sex. For example, sex differences in access to health-enhancing resources (e.g., access to the park and recreational facilities and physical activity) (Cohen, Williamson, & Han, 2021) and in psychosocial stress and perceived vulnerability associated with deteriorated neighborhoods (Bassett & Moore, 2013; Stafford et al., 2005) may underlie the stronger effect of NSEE for women than men. It is also plausible that observed patterns reflect unmodeled effect modification of the association between individual socioeconomic status and diabetes risk by sex. Studies suggest that, compared to men, women are more likely to perceive personal security concerns and ambient threats (e.g., crime, violence) in some aspects of the neighborhood conditions, including serious crime and physical and social disorder in the neighborhood (Snedker, 2015). Exposure to such chronic neighborhood stressors has implications for physiological dysregulations and constraining healthy behaviors (e.g., physical exercise) that have the potential to lead to diabetes onset (Hackett & Steptoe, 2017; McEwen & Gianaros, 2010).

While the differential effect of neighborhood disadvantage for women and men is often reported, how geographic location and community settings (e.g., urban vs. rural) become salient in shaping divergent pathways for women and men is not yet well understood and may vary by study population. For example, in the early 1990s, community-based outreach clinics (CBOCs) were mounted to reduce geographic disparities in access to healthcare among rural veterans. However, studies suggest that women veterans living in rural settings are less likely to use CBOCs than men veterans (Chapko, Hedeen, Maciejewski, Fortney, & Borowsky, 2000). If differential by NSEE, the lower use of CBOCs may impact testing for diabetes (through lab access), and thus, testing may differ by sex. Future studies may investigate how neighborhood conditions within urban-rural community contexts mitigate or augment the role of NSEE in health.

Within community types, we observed that the association between NSEE and T2D risk might differ by age. Still, there was heterogeneity in associations observed across both study sites and community types, and no consistent pattern emerged. In the Pennsylvania-based G/JHU cohort, the effect of NSEE on T2D was consistently slightly higher among ≥65 years old and lower among <45 years old in lower density urban and suburban/small town community types. In the national VADR cohort, we observed a consistently higher risk of T2D among those living in a worse NSEE environment among individuals <45 years old compared to those ≥65 years old in lower density urban and rural

communities. However, the association flipped in the suburban/small town community, where the risk estimates were larger among those aged ≥65 years, similar to G/JHU findings. These differences across community types are complex. Broadly, neighborhood disadvantage is shown to be associated with a lower likelihood of chronic disease management among the elderly population (Durfey, Kind, Buckingham, DuGoff, & Trivedi, 2019) and rural veterans experience a higher prevalence of physical health problems (Weeks, Wallace, Wang, Lee, & Kazis, 2006). However, what community features or individual-level characteristics account for differences in associations across community types remains unclear. One plausible explanation regarding the higher impact of NSEE could relate to lower engagement with medical care among younger versus older veterans in LDU and rural areas, potentially due to a lack of trust or some other unmeasured factor that differentially shapes norms and behaviors (e.g., social connectivity). Such ad-hoc explanations, however, warrant further exploration of how differential norms and access factors may help explain neighborhood disparities in chronic disease. We further note that while the three sites in this study used harmonized approaches to the measurement of NSEE and potential confounders of the NSEE-T2D population, differences in the composition of the sites' populations and study geography may explain, in part, these inconsistent findings.

Neighborhood disadvantage is often theorized to be most consequential for older adults as they may have more prolonged exposure to neighborhood conditions and are more likely to experience declines in functional ability, making them more vulnerable to neighborhood adversity (Robert & Li, 2001). Consistent with prior studies, however, in our VADR site, the impact of NSEE on T2D risk was greater in the younger age group. However, such theorizing inadequately addresses how age differences in the NSEE-chronic disease risk may manifest differentially depending on urban-rural community contexts. A study using EHR data from seven counties (mostly metropolitan or micropolitan counties) in southern Minnesota reported a stronger association of various chronic conditions, including prevalent diabetes, with census block group-level area deprivation index among the younger age group, similar to what was observed in the VADR cohort in low density urban and rural communities. That study observed more than a two-fold increased odds for diabetes among young adults (20–49 years) and no increased odds for individuals 70 years and older (Chamberlain et al., 2022). Similarly, another study using data from a smaller area of 64 census tracts in the south Texas coastal city (Corpus Christi) found some evidence to suggest that neighborhood advantage is more protective against stroke among younger and male participants in models with limited adjustment for individual-level SES factors (Lisabeth, Diez Roux, Escobar, Smith, & Morgenstern, 2007). From a life course perspective, one possible explanation is that living in disadvantaged areas during the critical period of emerging adulthood may program the body to start an early onset of stress-related physiological dysregulations that potentially lead to chronic diseases (Kim, Evans, Chen, Miller, & Seeman, 2018; Martin, Kane, Miles, Aiello, & Harris, 2019).

5. Limitations

Because data for these analyses come from three distinct studies, it is challenging to tease out how differences in study populations, study designs, data collection, measures of association, or length of follow-up may have influenced observed variation in results. Each study adjusted for individual-level SES differently, and individual-level measures of socioeconomic status or other social determinants of health were particularly limited in the EHR-based cohorts (VADR and G/JHU). Despite these differences and except for a few inconsistent results in the lower density urban community type across G/JHU and VADR cohorts, we obtained consistent results. The inconsistent results remind us not to rely too heavily on a single finding to draw generalizable conclusions. We stratified our analyses by community types due to concerns for contextual heterogeneity and the importance of taking differences in spatial scales into account (Hirsch et al., 2020), and we developed our NSEE measures separately for each community setting. While valuable to understand NSEE-T2D associations across vastly different geographic settings, the community type-specific NSEE measures reduced our ability to directly compare results across community types. However, we emphasize the importance of locally tailoring the implementation of policies and evidence-based programs, thus warranting an understanding of the interrelationships between neighborhood-level determinants and T2D risk separately for each community type. For example, in communities where older adults face the worst impact of NSEE, intervention programs run through social and cultural organizations that senior citizens most trust may help reduce community-specific disparities in diabetes risk. Some have argued that composite measures of socioeconomic status, such as NSEE, violate the consistency assumption because changing each component may not equally affect the outcome, however, we saw that our FPL analyses seemed to temper such concerns. One neighborhood's NSEE value could be affected by that of a neighboring community (i.e., spillover effects), which could violate the stable unit treatment value assumption.

Each study population differed substantially, and each measured and adjusted for individual-level SES differently. Completeness of race/ethnicity data and measurements of social determinants of health were limited in the EHR-based cohorts (VADR and G/JHU). While ideally, we would also examine for effect modification by race/ethnicity and individual SES, we opted to focus on the more consistent measures of sex and age. Despite differences in study populations, we obtained consistent results except for a few inconsistent results in the lower density urban community type across G/JHU and VADR cohorts.

Regarding limitations within specific cohorts, the VADR cohort was large and included veterans across racial and ethnic groups, yet most patients in the cohort were white male veterans, limiting generalizability and comparability to the other sites. Nonetheless, the absolute number of women and non-white race/ethnic groups in this cohort was still large relative to the other two datasets. In the REGARDS, there is a potential risk of survivorship bias, as participants had to remain in the cohort long enough to attend the follow-up exam when incident T2D was assessed. REGARDS also included non-Hispanic Black and White participants only. The G/JHU cohort was limited to a predominantly non-Hispanic White population, but the study sample was representative of the general population in the study region.

6. Conclusions

Despite the above limitations, our findings support that neighborhood socioeconomic context significantly influences the risk of diabetes across community type and geography. Further, the influence of neighborhood context is not homogenous across populations with different demographic characteristics. As we observed across study sites, there are differential impacts of NSEE for males and females and younger and older adults. Policy interventions should consider the differential role of neighborhood-level conditions in efforts to reduce the burden of diabetes across population groups.

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Ethical Statements

This study went through institutional review of the following study sites: Drexel University, Geisinger-Johns Hopkins University, New York University School of Medicine, and University of Alabama at Birmingham.

Data availability

The authors do not have permission to share data.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ssmph.2023.101541.

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