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## Neighborhood Disadvantage and Risk of Heart Failure: The Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study

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### Abstract

**Background:** Heart failure (HF) affects >6 million US adults, with recent increases in HF hospitalizations. We aimed to investigate the association between neighborhood disadvantage and incident HF events and potential differences by diabetes status.

**Methods:** We included 23,645 participants from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Study, a prospective cohort of Black and White adults age 45 years living in the continental US. Neighborhood disadvantage was assessed using a z-score of 6 census-tract variables (2000 US Census) and categorized as quartiles. Incident HF hospitalizations or HF related deaths through 2017 were adjudicated. Multivariable adjusted Cox regression was used to examine the association between neighborhood disadvantage and incident HF. Heterogeneity by diabetes was assessed using an interaction term.

**Results:** The mean age was 64.4 years, 39.5% were Black adults, 54.9% females, and 18.8% had diabetes. During a median follow-up of 10.7 years, there were 1125 incident HF events with an incidence rate of 3.3 (quartile 1), 4.7 (quartile 2), 5.2 (quartile 3), and 6.0 (quartile 4) per 1000 person-years. Compared to adults living in the most advantaged neighborhoods (quartile 1), those living in neighborhoods in quartiles 2, 3 and 4 (most disadvantaged) had 1.30 (95%CI=1.06-1.60), 1.36 (95%CI=1.11-1.66) and 1.45 (95%CI=1.18-1.79) times greater hazard of incident HF even after accounting for known confounders. This association did not significantly differ by diabetes status (interaction  $p=0.59$ ). For adults with diabetes, the adjusted incident HF hazards comparing those in quartile 4 vs quartile 1 was 1.34 (95%CI=0.92-1.96) and it was 1.50 (95%CI=1.16-1.94) for adult without diabetes.

**Conclusion:** In this large contemporaneous prospective cohort, neighborhood disadvantage was associated with increased risk of incident HF events. This increase in HF risk did not differ by diabetes status. Addressing social, economic and structural factors at the neighborhood level may impact HF prevention.

### Keywords

Diabetes Mellitus; Heart Failure; Neighborhood Disadvantage

### Introduction

Heart failure (HF) affects more than 6 million US adults, resulting in medical expenditure costs that exceed 20 billion US dollars annually.<sup>1, 2</sup> While HF incidence was relatively stable from the early 1990s to the early 2000s,<sup>3, 4</sup> surveillance data from four US communities showed an increase in HF hospitalizations between 2005 and 2014.<sup>5</sup> As the population burden of HF is projected to increase by 23% in the US by 2030,<sup>2</sup> HF is a growing public health concern.

Neighborhood environments have been shown to affect health outcomes.<sup>6</sup> Living in residential environments characterized by a paucity of resources, high unemployment, high poverty and limited access to healthcare is associated with detrimental health effects, including an increased risk for coronary heart disease, diabetes, hypertension and obesity.<sup>7-9</sup> Recent studies have investigated the impact of neighborhood disadvantage on clinical outcomes like recurrent hospitalizations, symptom burden, and mortality among those with an established HF diagnosis.<sup>10-13</sup> However, studies exploring the association between neighborhood characteristics and incident HF are sparse.<sup>14-17</sup> Two US studies showed that neighborhood environment was associated with HF risk, but they only included low-income population or evaluated community-level poverty in a small geography.<sup>14, 15</sup> Studies from European countries like the UK and Sweden also showed similar results with more challenging living environments associated with greater risk of HF.<sup>16, 17</sup> However, US health inequalities are larger compared to countries like Sweden or the UK.<sup>18</sup> Despite spending a significant amount of money on healthcare, US faces persistent health disparities. Therefore, it is important to understand the influence of various factors, including neighborhood environment, on health outcomes like HF for different populations.

We used data from a contemporaneous community-based prospective cohort, the REasons for Geographic and Racial Differences in Stroke (REGARDS) study to investigate the association between neighborhood disadvantage and incident HF. The REGARDS study included adults across the continental US and oversampled adults from Southeastern states where social disadvantage and poverty levels are higher compared to the rest of the country. Southeastern states also have higher rates and worse outcomes of cardiovascular disease making REGARDS an ideal population for this study. In addition, given the increase in HF hospitalizations among US adults with diabetes<sup>20</sup> and the previously reported findings among Swedish adults with diabetes,<sup>16</sup> we also examined the association separately among adults with and without diabetes

## Methods

Deidentified data can be shared by REGARDS investigators upon request from qualified investigator through formal data use agreements.

### Study population

The REGARDS study is a community-based prospective cohort of 30,239 Black and White adults aged ≥45 years at baseline (2003-2007) from the continental US. A detailed description of the REGARDS cohort study was previously published.<sup>21</sup> Briefly, REGARDS oversampled Black adults and those living in the stroke belt (Tennessee, Louisiana, Mississippi, Arkansas, Alabama, Georgia, North Carolina and South Carolina) and stroke buckle (coastal areas of Georgia, North and South Carolinas) regions. Demographics, health behaviors and medical history were assessed during a telephone interview. Anthropometrics, an electrocardiogram, medication inventory, and blood and urine specimens were collected during an in-home visit. Following the baseline exam, participants or their proxies were contacted twice a year to record any hospitalizations, emergency room visits or deaths. Medical records and death certificates were obtained for possible cardiovascular events and adjudicated by clinical experts. All participants provided informed consent and institutional review boards from all participating institutions approved the study.

For the present analyses, we excluded adults with suspected HF at baseline (n=3175) defined as the use of ≥1 HF-related medication (carvedilol; any loop diuretic; angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers plus beta-blockers in the absence of hypertension; or digoxin in the absence of atrial fibrillation).<sup>22</sup> This medication-based method has been previously validated with a high negative predictive value of 95%-99% among this HF-free cohort.<sup>22</sup> We also excluded those whose HF status at baseline could not be determined (n=833);, lost to follow-up (n=374), missing neighborhood characteristics (n=247), informed consent anomalies (n=56) and missing covariate information (n=1909). After exclusions, we included 23,645 adults in the final analysis (Figure S1).

### Neighborhood Disadvantage

Each participant's baseline residential address was geocoded using ESRI ArcMap software and linked to US census tracts. Census tracts are statistical subdivisions of a county with an average population of 4000 (range 1000-8000).<sup>23</sup> To assess the social and economic

context of census tracts, a composite neighborhood measure was calculated as a sum of the z-score of 6 census tract variables from the 2000 US Census (% population with < high school education; % population unemployed; % households with income <\$30,000 per year; % households on public assistance; % population living in poverty; and % households without a car). These variables were identified by the Diabetes LEAD network, a CDC funded collaboration,<sup>24</sup> based on previous work by Xiao et al. (2018).<sup>25</sup> While the study by Xiao et al. (2018)<sup>25</sup> used principal component analysis (PCA), the Diabetes LEAD network used equally-weighted sum of the Z-scores. This measure was highly correlated with the PCA-based measure ( $r>0.9$ ) and was chosen by the network for feasibility across study sites and for reproducibility. Additionally, to be consistent across the network and across the community characteristics examined, Census tract was selected as the geographic unit of analysis. Prior studies have found that Census tract and the smaller Census block groups perform similarly when used to monitor socioeconomic inequalities in health.<sup>26</sup> Finally, per the principles of causal inference, we used the US Census data for the year 2000 to calculate the neighborhood measure such that the exposure precedes the outcome, incident HF that was assessed starting 2005. The neighborhood disadvantage measure ranged between 0-100, with higher values indicating greater disadvantage. Each census tract where at least 1 REGARDS participant lived was assigned a neighborhood score, and the total number of unique census tracts with REGARDS participants was divided into quartiles. Because the quartiles were created based on census tracts, the number of participants in each quartile was unequal. Quartile 4 included participants living in census tracts with greater disadvantage whereas quartile 1 included those living in census tracts with greater advantage. Table S1 and Figure S2 provide distribution of the 6 census variables by the neighborhood disadvantage quartiles. We also calculated the measure using the 2010 Census data to examine if neighborhood disadvantage quartiles changed over time. Between years 2000 and 2010, 69.7% of the participants remained in the same quartile, and 29.3% were reclassified into adjacent quartiles of disadvantage (Table S2).

### HF Hospitalizations and Deaths

Medical records of suspected HF hospitalizations through 12/31/2017 were adjudicated by 2 clinician investigators using structured forms; disagreements were resolved by a committee.<sup>27</sup> Hospitalizations due to HF were identified based on the following: signs and symptoms (orthopnea, exertional dyspnea, paroxysmal nocturnal dyspnea, nocturnal cough, rales on pulmonary exam, cardiomegaly, jugular vein distension, central venous pressure >16 mmHg, peripheral edema, pleural effusion, hepatomegaly, heart rate >120 beats/min, weight loss 4.5 kg within 5 days after diuresis), biomarkers (e.g. B-type natriuretic peptide, troponins, creatinine kinase-MB), and imaging (e.g. chest radiography, ECG, echocardiography, SPECT- Single-photon emission computed tomography).<sup>28</sup> HF deaths were adjudicated by two clinical experts using all available information, including recent hospitalization, baseline medical history, past adjudicated cardiovascular events, death certificates, autopsy reports, the National Death Index, and interviews with next of kin or other proxies.

### Additional baseline variables

Age, education (<high school vs ≥high school), annual household income (≤\$35,000 vs >\$35,000), and health insurance status were self-reported. Geographic region of residence was categorized as stroke belt/buckle (North Carolina, South Carolina, Georgia, Tennessee, Mississippi, Alabama, Louisiana, and Arkansas) or non-stroke belt. Alcohol consumption (none, moderate (≤1 drink/day in women, ≤2 drinks/day in men), or heavy (>1 drink/day in women, >2 drinks/day in men), smoking status (never, current, or past), and physical activity (at least once a week activity enough to work up a sweat vs no such activity) were assessed using standardized questionnaires. Body mass index was calculated from height and weight measured during the in-home visit using a standardized protocol and categorized (<25kg/m<sup>2</sup>, 25-30kg/m<sup>2</sup>, and >30kg/m<sup>2</sup>). Clinical variables included diabetes, hypertension, and dyslipidemia. Diabetes was defined based on glucose levels (fasting ≥126 mg/dL or random ≥200 mg/dL) and/or use of diabetes medications. While REGARDS Study did not collect data on the type of diabetes, given the older age of the participants, majority of them most likely had type 2 diabetes. Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or self-reported use of blood pressure medication. Dyslipidemia was based on self-reported diagnosis or cholesterol levels (total cholesterol ≥240 mg/dL, or LDL cholesterol >160 mg/dL, or HDL cholesterol <40 mg/dL). Information on diabetes medications, blood pressure medications, and statin use was obtained from the medication inventory collected during the in-home visit.

### Statistical Analysis

Crude HF incidence rates, overall and by diabetes status, were estimated for each quartile of neighborhood disadvantage using modified Poisson regression. Kaplan-Meier plots were used to display cumulative incidence of HF hospitalization and deaths by quartile of neighborhood disadvantage. Cox proportional hazards regression models were fit to estimate hazard ratios (HR) for each quartile of neighborhood disadvantage, with quartile 1 (more advantaged) as the reference.<sup>29</sup> Proportional hazards assumptions was tested using the Schoenfeld test. To account for clustering of participants within census tracts, robust standard errors were used to estimate the 95% confidence interval (95% CI). Models were sequentially adjusted for sociodemographic factors (age, sex, education, annual household income, health insurance, region), behavioral factors (alcohol consumption, smoking status, physical activity) and clinical factors (body mass index, dyslipidemia, hypertension, and diabetes status). We also tested for heterogeneity by diabetes status using a statistical interaction term between neighborhood disadvantage and diabetes. A priori, we decided to present analyses stratified by diabetes status regardless of the significance of the interaction term as the risk for HF is generally higher for those with diabetes than those without. In sensitivity analyses, using rms package in R, we investigated neighborhood disadvantage continuously, using restricted cubic splines to assess linearity in the association. Restricted cubic splines may be used to explore nonlinear continuous associations that allow for more flexible curve fitting compared to traditional linear regressions.<sup>30</sup> We fit Fine and Gray sub distribution hazards model to account for death due to non-HF causes as a competing risk. An alpha level of 0.05 was used for statistical significance and all analyses were conducted using SAS 9.4 and R 3.6.3 (<https://www.r-project.org/>).

## Results

Baseline characteristics for all REGARDS participants (n=23,645) in each neighborhood quartile are presented in Table 1. Approximately one-third of the REGARDS participants resided in a census tract characterized as the most disadvantaged (quartile 4). There was a higher proportion of women, Black adults, uninsured adults, and those with less than high school education living in census tracts characterized as the most disadvantaged (quartile 4). The prevalence of obesity, hypertension and diabetes increased as neighborhood disadvantage increased (Table 1). When adults with and without diabetes were examined separately, characteristics across the neighborhood disadvantage quartiles followed a similar pattern (Table S3).

During a median follow-up of 10.7 years, there were 1125 incident HF events (85% hospitalizations and 15% deaths). Adults living in neighborhoods characterized as more disadvantaged had a higher cumulative incidence of HF events compared to those in neighborhoods characterized as less disadvantaged (Figure 1). The incidence rate for HF hospitalizations or deaths was 3.3 (quartile 1), 4.7 (quartile 2), 5.2 (quartile 3), and 6.0 (quartile 4) per 1000 person-years (Table 2). Compared to adults living in the most advantaged neighborhoods (quartile 1), the risk for HF increased as neighborhood advantage decreased (Quartile 2 HR=1.44, 95% CI=1.18-1.77; Quartile 3 HR=1.60, 95% CI=1.32-1.94; and Quartile 4 HR=1.88, 95% CI=1.56-2.27). Adjustment for demographic, behavioral and clinical factors only modestly attenuated the associations (Quartile 2 HR=1.30, 95% CI= 1.06-1.60; Quartile 3 HR=1.36, 95% CI=1.11-1.66; Quartile 4 HR=1.45, 95% CI=1.18-1.79) (Figure 2 and Table S4). In the sensitivity analysis that examined non-HF related death as a competing risk, the magnitude of the hazard ratios was similar to the main analysis (Table S4).

Of the 23,645 participants included in the analysis, 4,435 (18.8%) had diabetes and 19,210 (81.2%) did not have diabetes. There were 423 (9.5%) and 702 (3.7%) incident HF hospitalizations or HF deaths, among adults with and without diabetes, respectively. The crude incidence of HF increased as neighborhood disadvantage increased in both adults with and without diabetes (Table 2). Interaction between neighborhood disadvantage and diabetes was not statistically significant ( $p=0.59$ ). Among adults with diabetes, neighborhood disadvantage was modestly associated with incident HF hospitalizations or deaths in both crude and fully adjusted models, and these associations were not statistically significant (Figure 1 and Table S4). Among adults without diabetes, compared to adults living in the most advantaged neighborhoods (quartile 1), the risk for incident HF progressively increased as neighborhood advantage decreased (Quartile 2 HR = 1.45, 95% CI= 1.14-1.84; Quartile 3 HR= 1.56, 95% CI=1.23-1.97; and Quartile 4 HR=1.65, 95% CI=1.31-2.07) (Figure 2 and Table S4). These associations were attenuated after multivariable adjustment but remained statistically significant (Quartile 2 HR=1.37, 95% CI=1.07-1.75; Quartile 3 HR=1.43, 95% CI=1.12-1.83; and Quartile 4 HR=1.50, 95% CI=1.16-1.94) (Table S4).

In analyses investigating the association between the neighborhood measure as a continuous measure and HF risk, we observed a non-linear relationship ( $p$  value for non-linearity= $<0.001$ ) (Figure 3). HF risk associated with neighborhood disadvantage increased



steeply between values 0 and 15 of the neighborhood measure, and then plateaued. When stratified by diabetes status, the association was non-linear among adults without diabetes ( $p$  value= $<0.001$ ) but there was no evidence of a non-linear relationship among those with diabetes ( $p$  value=0.28) (Figure 3).

## Discussion

In this prospective cohort study of middle-aged and older US adults, neighborhood disadvantage was associated with an increased risk of incident HF hospitalizations and HF related deaths, even after accounting for demographic and clinical factors. The overall incidence of HF was higher for adults with diabetes than those without diabetes. However, the association between neighborhood disadvantage and HF risk was not statistically different for adults with and without diabetes.

Neighborhood disadvantage has been associated with an increased risk for diabetes,<sup>31, 32</sup> obesity,<sup>33, 34</sup> and coronary heart disease.<sup>35, 36</sup> However, few studies have investigated the relationship between neighborhood environment and HF incidence.<sup>14, 16</sup> In the Southern Community Cohort Study that included a mostly low-income population with Medicaid or Medicare coverage, neighborhood disadvantage was associated with a greater risk for HF hospitalizations.<sup>14</sup> In the REGARDS study, we also found an association between neighborhood disadvantage and HF risk among our middle-age and older study participants who had income levels across a wide range and that association remained even after accounting for individual-level education, income, and clinical factors.

Because neighborhood disadvantage has been shaped by structural factors, including racism, race-based residential segregation, systemic oppression, and neighborhood violence,<sup>36–39</sup> that are associated with the non-uniform access to resources, the risk for cardiovascular disease may be further heightened. These structural determinants may affect neighborhood environments resulting in differences in physical attributes like walkability, physical activity environment, food environment, access to and availability of healthcare facilities, and differences in police brutality and extrajudicial killings<sup>40</sup> that could contribute to adverse health outcomes. For example, an ecological study found that neighborhoods with predominantly Black residents and neighborhoods with greater economic disadvantage had fewer supermarkets compared to neighborhoods with predominantly White residents and neighborhoods with greater economic advantage,<sup>41</sup> which may affect access to healthy food. Neighborhood physical attributes have also been associated with health behaviors (e.g., smoking, physical activity)<sup>42</sup> and cardiovascular risk factors.<sup>7, 31–34, 37</sup> In the REGARDS study, participants living in neighborhoods characterized as more disadvantaged had a higher prevalence of smoking, obesity, hypertension, dyslipidemia and diabetes at baseline than those living in neighborhoods characterized as more advantaged. However, even after accounting for health behaviors and clinical factors, neighborhood disadvantage remained associated with incident HF events, suggesting that additional factors may be at play. Future studies are needed to elucidate the exact mechanism by which this occurs. However, existing knowledge on HF risk factors (e.g., hypertension and diabetes) can provide insights for potential neighborhood level interventions. Community-based initiatives like blood pressure management in Black barbershops or churches have proven effective.<sup>43, 44</sup> Such locally

embedded programs targeting HF risk factors could prove useful for HF prevention in these disadvantaged neighborhoods. Our study findings and the existing evidence, underscore the need for health promotion and HF prevention measures in disadvantaged neighborhoods. Clinicians working in disadvantaged neighborhoods can play a crucial role in HF prevention through comprehensive risk assessment, targeted education for lifestyle modifications and medication adherence, provision of care through neighborhood clinics, remote patient monitoring and telemedicine, and advocacy for better healthcare access generally.

Given the increase in HF hospitalizations among US adults with diabetes,<sup>20</sup> understanding how the neighborhood environment may affect HF risk among adults with and without diabetes is needed. In a Swedish study of adults with diabetes, HF incidence was higher for adults in more disadvantaged neighborhoods compared to those in less disadvantaged neighborhoods.<sup>16</sup> Similar to these findings, we found neighborhood disadvantage to be weakly associated with incident HF events among REGARDS participants with diabetes. However, unlike in the Swedish population, the neighborhood disadvantage-HF association was not statistically significant in our study participants with diabetes. Additionally, we observed that HF incidence was higher among adults with diabetes, and it was similar for those living in neighborhoods with all levels of disadvantage. We also assessed the association among REGARDS participants without diabetes and showed that the risk for incident HF events was progressively greater across quartiles of increasing neighborhood disadvantage even after multivariable adjustment. Compared to adults without diabetes, those with diabetes have an elevated HF risk. This preexisting difference in HF risk for adults with and without diabetes could be the reason for our finding that neighborhood disadvantage is associated with increased HF risk for adults without diabetes but not for those with diabetes. Collectively considered, our study findings highlight the need to evaluate other neighborhood attributes like food and physical activity environment and healthcare access, that may be sensitive to policy change, as potential mediators of increased HF risk in those living in disadvantaged neighborhoods.

Our study has several limitations. First, neither a clinical HF diagnosis nor an echocardiogram was available at baseline, so suspected HF cases were excluded using a validated algorithm of relevant baseline medication use. This medication-based algorithm has an excellent negative predictive value of 95%-99%.<sup>22</sup> Second, we identified first-time HF hospitalizations and HF-related deaths but could not capture HF cases diagnosed in an outpatient setting. When considering the entire spectrum of HF, this approach captures the more severe manifestations of HF syndromes and hence, part of the observed associations could be driven by poor access to healthcare in neighborhoods with more disadvantage leading to hospitalizations and death. Third, we used an administrative boundary, census tract, to characterize the neighborhood environment. These units may not necessarily reflect participant's perception of their neighborhood as their interaction with their living environment generally crosses administrative boundaries.<sup>45</sup> Unlike previous studies that have used census block group, we used census tract, a larger spatial unit. Socioeconomic characteristics are not only similar, but they are also highly correlated with surrounding census tracts and relatively stable over the time compared to block groups whose boundaries tend to change more often. Census tracts are also generally recommended over other spatial unit designations like zip-codes.<sup>26</sup> Fourth, study participant's address was collected



only at baseline and was not reassessed during follow up. However, a retrospective study showed that people generally relocate to neighborhoods of similar disadvantage, limiting the implication for this study's conclusion.<sup>46</sup> Individual level socioeconomic factors like income and health insurance were also not reassessed during follow up. Nonetheless, given that 93.3% had health insurance and only 17.3% had income >\$75,000 it is unlikely that there would be significant impact on the final results. Fifth, the REGARDS study only included Non-Hispanic White and Black adults limiting the external validity for other racial and ethnic groups. Lastly, the number of adults with diabetes in our study was comparatively smaller than adults without diabetes. In contrast to existing evidence,<sup>16</sup> we did not find a statistically significant association between neighborhood disadvantage and HF risk among adults with diabetes. However, our study was underpowered to detect an interaction, if it exists, and our limited sample size precluded further investigation. Our study also has several strengths, including a contemporaneous population-based cohort with ongoing follow-up for HF events that are expertly adjudicated. We also included adults from across the continental US with oversampling from the southeastern US states. Hence, the REGARDS cohort is well suited for this current analysis providing a closer look at the southern states which are a part of the "diabetes-belt"<sup>47</sup> as well as the "heart failure belt".<sup>48</sup> Additionally, the REGARDS study population is comparatively more representative of the US population than the research studies supporting clinical practice guidelines that lack real-world diversity.<sup>49, 50</sup>

## Conclusions

This study of a community-based large contemporaneous biracial cohort showed that neighborhood disadvantage was associated with an increased risk of incident HF. Individual-level socioeconomic and clinical factors did not completely explain the increased HF risk among adults living in disadvantaged neighborhoods. Addressing social, economic and structural factors at the neighborhood level may help prevent HF events. Clinicians encountering patients living in socioeconomically disadvantaged neighborhoods should bear in mind their elevated HF risk, independent of more traditional risk factors.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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#### Abbreviations:

<b>HF</b>	Heart Failure
<b>DM</b>	Diabetes
<b>REGARDS</b>	REasons for Geographic and Racial Differences in Stroke

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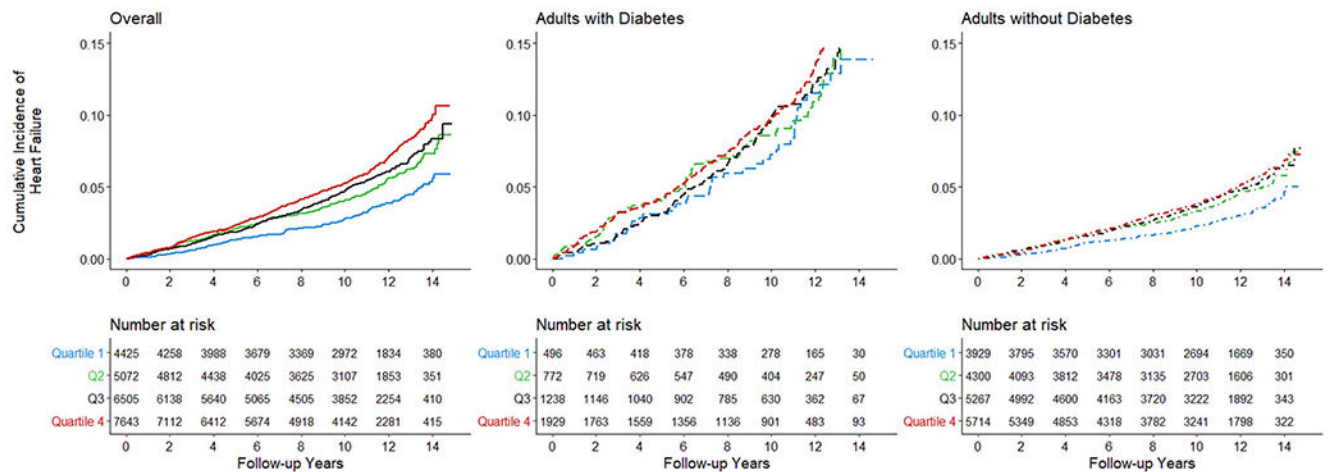
**What is known:**

- Individual socioeconomic factors like income and education predict heart failure risk.
- Recent studies indicate that neighborhood social and economic characteristics also impact heart failure outcomes like recurrent hospitalizations, heart failure symptom burden or mortality.

**What the study adds:**

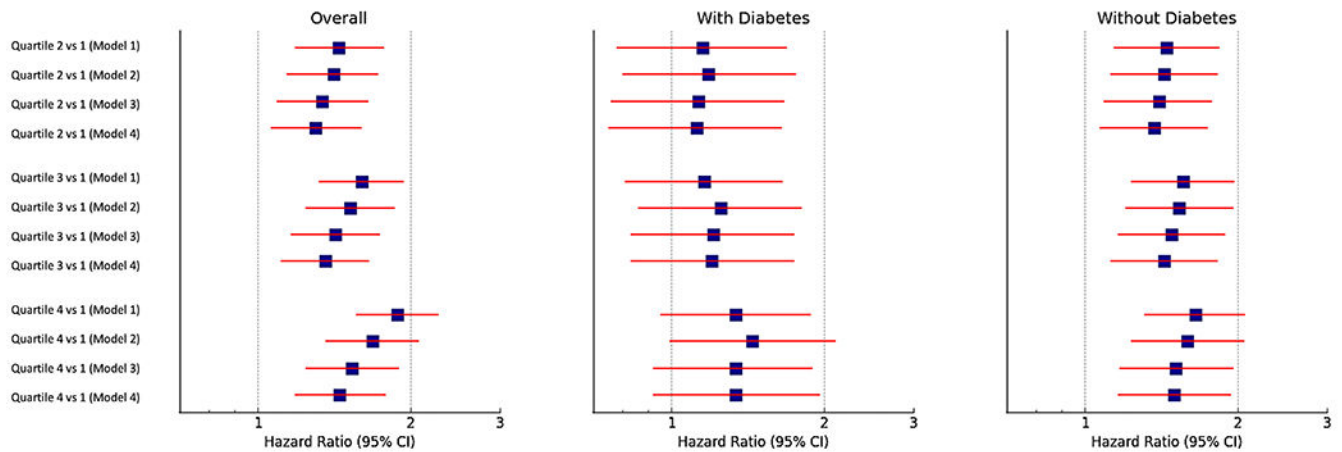
- Individuals in neighborhood with high disadvantage have significantly greater risk of heart failure regardless of individual level socioeconomic factors and established cardiovascular risk factors.
- Clinicians providing care in disadvantaged neighborhoods can play a crucial role in heart failure prevention through comprehensive risk assessment, targeted education for lifestyle modifications and medication adherence.
- These findings provide support for public health measures improving social, economic and structural factors at the neighborhood level that may help prevent heart failure in disadvantaged areas.





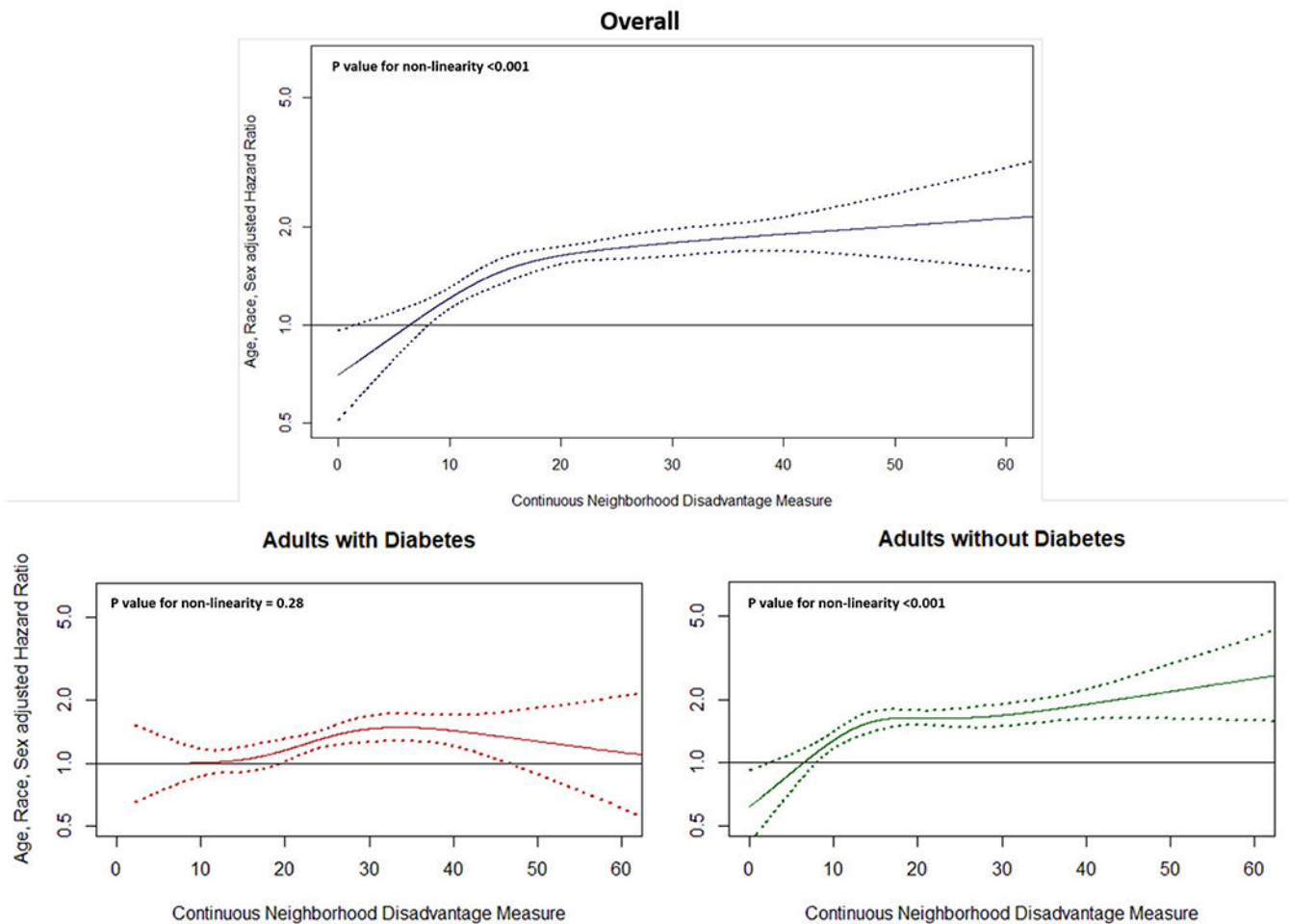
**Figure 1. Kaplan Meier Plots for Cumulative Incidence of Heart Failure by Neighborhood Disadvantage, Overall and by Diabetes Status: The REasons for Geographic and Racial Differences in Stroke (REGARDS) Study**

The plots from left to right: overall REGARDS population, adults with diabetes and adults without diabetes. The X axis represents the follow up time in years and Y axis represents the cumulative incidence of heart failure. Within each plot, blue (quartile 1-most advantage), green (quartile 2), black (quartile 3) and red (quartile 4- most disadvantage) lines represent the quartile of neighborhood disadvantage measure.



**Figure 2. Association of Neighborhood Disadvantage and Risk of Incident Heart Failure Events, Overall and by Diabetes Status-The REasons for Geographic and Racial Differences in Stroke (REGARDS) Study**

The plots from left to right: overall REGARDS population, adults with diabetes and adults without diabetes. The X axis represents the magnitude of hazards ratio and on the Y axis we have sets of hazard ratios comparing quartiles 2,3, and 4 (most disadvantage) with quartile 1 (most advantage) of the neighborhood disadvantage measure. Hazard ratios were estimated using Cox regression with sequential adjustment for covariates (model 1 is unadjusted; model 2 adjusted for age, race, sex, education, income, insurance, and geographic region of residence; model 3 additionally adjusted for smoking, alcohol consumption, physical activity and body mass index; model 4 additionally adjusted for dyslipidemia, and hypertension. Model 4 for all REGARDS participants additionally adjusted for diabetes status). The blue color square represents the magnitude of the hazard ratio and the red error bars represent the 95% confidence intervals of the hazard ratio.



**Figure 3. Continuous Association of Neighborhood Disadvantage and Risk of Incident Heart Failure Events, Overall and by Diabetes Status-The REasons for Geographic and Racial Differences in Stroke (REGARDS) Study**

The plot on the top depicts the age, race and sex adjusted non-linear association between neighborhood disadvantage (measure continuously) and incident heart failure risk for all REGARDS population. The bottom left plot depicts the same association but among adults with diabetes and the bottom right for adults without diabetes. While solid lines in all three plots are the age, race and sex adjusted hazard ratio the dashed lines represent the 95% confidence interval bands. Hazard ratios are estimated with reference to the mean of the neighborhood disadvantage measure in quartile 1 for the overall population, among adults with diabetes and adults without diabetes. The X axis represents continuously measured neighborhood disadvantage, and the Y axis represents the magnitude of the hazard ratio.

**Table 1.**

Participant Characteristics by Level of Neighborhood Disadvantage at Baseline, The REasons for Geographic and Racial Differences in Stroke (REGARDS) Study (2003-2007)

Characteristics	Quartile 1 <sup>†</sup> (Most advantaged) (n=4425)	Quartile 2 (n=5072)	Quartile 3 (n=6505)	Quartile 4 (Most disadvantaged) (n=7643)
Neighborhood disadvantage measure, mean (SD)*	6.4 (1.9)	12.3 (1.8)	19.7 (2.7)	33.8 (7.9)
Neighborhood disadvantage measure, range	(0.0, 9.4)	(9.4, 15.5)	(15.5, 24.6)	(24.6, 84.9)
Age (years), mean (SD)	64.5 (9.1)	64.3 (9.3)	64.4 (9.3)	64.5 (9.5)
Black Participants, n (%)	451 (10.2%)	1079 (21.3%)	2548 (39.2%)	5268 (68.9%)
Women, n (%)	2120 (47.9%)	2630 (51.9%)	3651 (56.1%)	4574 (59.8%)
Less than high school education, n (%)	93 (2.1%)	341 (6.7%)	713 (11.0%)	1491 (19.5%)
Annual household income, n (%)				
< \$20,000	183 (4.1%)	497 (9.8%)	1033 (15.9%)	2167 (28.4%)
\$20,000 - \$35,000	661 (14.9%)	1207 (23.8%)	1659 (25.5%)	2113 (27.6%)
\$35,000 - \$75,000	1551 (35.1%)	1815 (35.8%)	2122 (32.6%)	1796 (23.5%)
> \$75,000	1495 (33.8%)	1021 (20.1%)	928 (14.3%)	658 (8.6%)
Declined to report	535 (12.1%)	532 (10.5%)	763 (11.7%)	909 (11.9%)
Health insurance, n (%)	4324 (97.7%)	4818 (95.0%)	6075 (93.4%)	6843 (89.5%)
Geographic region of residence, n (%)				
Stroke buckle	1214 (27.4%)	1774 (35.0%)	2279 (35.0%)	2875 (37.6%)
Stroke belt	632 (14.3%)	1050 (20.7%)	1686 (25.9%)	1555 (20.3%)
Non-belt	2579 (58.3%)	2248 (44.3%)	2540 (39.0%)	3213 (42.0%)
Heavy alcohol consumption, n (%)	1528 (34.5%)	1245 (24.5%)	1210 (18.6%)	1178 (15.4%)
Current smoking, n (%)	395 (8.9%)	662 (13.1%)	967 (14.9%)	1431 (18.7%)
No regular physical activity, n (%)	3241 (73.2%)	3495 (68.9%)	4379 (67.3%)	4910 (64.2%)
Body mass index >=30kg/m <sup>2</sup> , n (%)	1188 (26.8%)	1641 (32.4%)	2424 (37.3%)	3256 (42.6%)
Dyslipidemia, n (%)	2486 (56.2%)	2877 (56.7%)	3666 (56.4%)	4216 (55.2%)
Hypertension, n (%)	2017 (45.6%)	2683 (52.9%)	3791 (58.3%)	4968 (65.0%)
Diabetes, n (%)	496 (11.2%)	772 (15.2%)	1238 (19.0%)	1929 (25.2%)

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Characteristics	Quartile 1 <sup>†</sup> (Most advantaged)	Quartile 2	Quartile 3	Quartile 4 (Most disadvantaged)
Insulin use, n (%)	96 (19.4%) (n=4425)	135 (17.5%) (n=5072)	249 (20.1%) (n=6505)	473 (24.5%) (n=7643)

\* Neighborhood disadvantage measure calculated as sum of the z-score of 6 US Census variables: % population with < high school education; % population unemployed; % households with income <\$30,000 per year; % households on public assistance; % population living in poverty; and % households without a car, scaled to range between 0 and 100. Higher value indicates more disadvantage.

<sup>†</sup> Quartiles were created based on the number of unique census tracts where REGARDS participants lived (not participants). Quartile 1 is most advantaged and quartile 4 most disadvantaged.

Table 2.

Incidence of Heart Failure Hospitalizations or Deaths by Neighborhood Disadvantage, Overall and by Diabetes Status-The REasons for Geographic and Racial Differences in Stroke (REGARDS) Study

Neighborhood Disadvantage <sup>*†</sup>	Number of HF events/Total of people	Total person years	Crude Incidence Rate/ 1000 person-years (95% CI)	Crude Incidence Rate Ratio (95% CI)
Overall (n = 23645)				
Quartile 1 (most advantaged)	108/4425	45207	3.32 (2.83-3.89)	Ref
Quartile 2	161/5072	49319	4.72 (4.16-5.37)	1.42 (1.16-1.75)
Quartile 3	208/6505	62114	5.20 (4.67-5.80)	1.57 (1.29-1.90)
Quartile 4 (most disadvantaged)	225/7643	69344	6.04 (5.49-6.65)	1.82 (1.51-2.19)
Adults with diabetes (n = 4435)				
Quartile 1 (most advantaged)	42/496	4616	9.10 (6.75-12.26)	Ref
Quartile 2	72/772	6921	10.40 (8.27-13.08)	1.14 (0.79-1.67)
Quartile 3	115/1238	11060	10.40 (8.69-12.45)	1.14 (0.81-1.62)
Quartile 4 (most disadvantaged)	194/1929	16434	11.80 (10.28-13.56)	1.30 (0.93-1.80)
Adults without diabetes (n = 19210)				
Quartile 1 (most advantaged)	108/3929	40591	2.66 (2.21-3.21)	Ref
Quartile 2	161/4300	42399	3.80 (3.26-4.43)	1.43 (1.12-1.82)
Quartile 3	208/5267	51054	4.07 (3.56-4.66)	1.53 (1.21-1.93)
Quartile 4 (most disadvantaged)	225/5714	52909	4.25 (3.73-4.84)	1.60 (1.27-2.01)

\* Quartiles were created based on the number of unique census tracts where REGARDS participants lived and not the number of participants.

† Neighborhood disadvantage measure calculated as sum of the z-score of 6 US Census variables: % population with < high school education; % population unemployed; % households with income <\$30,000 per year; % households on public assistance; % population living in poverty; and % households without a car