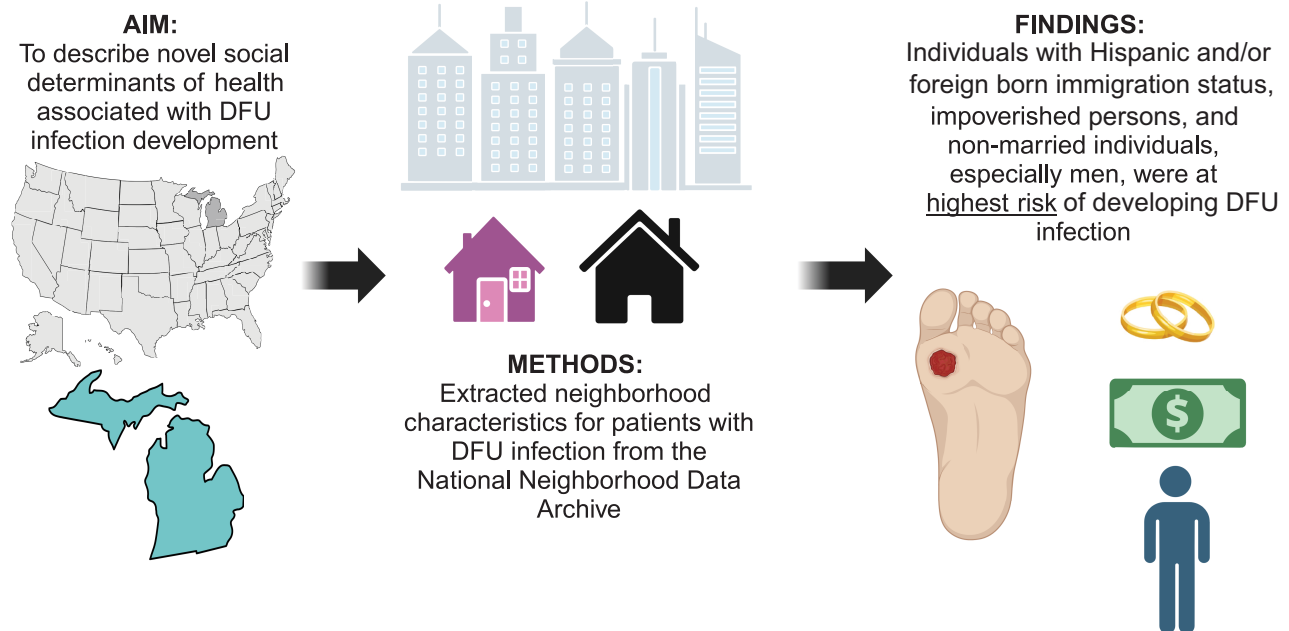


## Residential Address Amplifies Health Disparities and Risk of Infection in Individuals With Diabetic Foot Ulcers

Brian M. Schmidt, Yiyuan Huang, Mousumi Banerjee, Salim S. Hayek, and Rodica Pop-Busui

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### ARTICLE HIGHLIGHTS

- **Why did we undertake this study?**

The study was undertaken to characterize the specific aspects of social determinants of health associated with the development of diabetic foot ulcer (DFU) infection diagnosis.

- **What is the specific question(s) we wanted to answer?**

How do various measures of social determinants of health vary amongst the populations with DFU infection and diabetes?

- **What did we find?**

We found significant differences in neighborhood characteristics driving a higher risk for DFU infection in comparisons with the grouping of individuals with diabetes overall, including increased risk for infection development in individuals with Hispanic and/or foreign-born immigration status.

- **What are the implications of our findings?**

The implications support the use of both social and biological determinants of health to assess risk of advanced complications in managing the at-risk diabetic foot more accurately.



# Residential Address Amplifies Health Disparities and Risk of Infection in Individuals With Diabetic Foot Ulcers

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## OBJECTIVE

To determine the association between social determinants of health (SDOH) and a diagnosis of diabetic foot ulcer (DFU) infection.

## RESEARCH DESIGN AND METHODS

Targeted interrogation of electronic health record data using novel search engines to analyze individuals with a DFU infection during a 5-year period (2013–2017) was performed. We extracted geolocated neighborhood data and SDOH characteristics from the National Neighborhood Data Archive and used univariate and multiple logistic regression to evaluate associations with outcomes in the population with diabetes.

## RESULTS

Among 4.3 million people overall and 144,564 individuals with diabetes seen between 2013 and 2017, 8,351 developed DFU, of which cases 2,252 were complicated by a DFU infection. Sex interactions occurred, as men who experienced a DFU infection more frequently identified as having nonmarried status than their female counterparts. For the population with DFU infection, there were higher rates for other SDOH, including higher neighborhood disadvantaged index score, poverty, nonmarriage, and less access to physician/allied health professionals (all  $P < 0.01$ ). In multiple logistic regression, those individuals who developed DFU infection came from neighborhoods with greater Hispanic and/or foreign-born concentrations (odds ratio 1.11,  $P = 0.015$ ).

## CONCLUSIONS

We found significant differences in neighborhood characteristics driving a higher risk for DFU infection in comparisons with the grouping of individuals with diabetes overall, including increased risk for individuals with Hispanic and/or foreign-born immigration status. These data strongly support the need to incorporate SDOH, particularly ethnic and immigration status, into triage algorithms for DFU risk stratification to prevent severe diabetic foot complications and move beyond biologic-only determinants of health.

Diabetic foot ulcer (DFU) infection is a common problem in outpatient and hospital settings. If unrecognized or undertreated, DFU infections could progress to osteomyelitis when osseous structures are involved. The lifetime risk of a person with diabetes to develop a DFU is estimated to be as high as 35% (1–3). Individuals who develop a DFU infection have a 155-fold increased risk of amputation compared

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with those who do not (4), and in 85% of lower-extremity amputation events the amputations are preceded by the presence of a DFU (5,6). More striking is that an individual's social determinants of health (SDOH), specifically location, play a critical role with regard to amputation: those living in rural areas have a 35% higher odds of amputation compared with their urban counterparts (7–9).

SDOH are intangible factors such as political, socioeconomic, and cultural constructs, as well as place-based conditions including accessible health care and education systems, safe environmental conditions, well-designed neighborhoods, and availability of healthful food, that influence health care outcomes (10). Health care alone is a relatively weak health determinant (11). Despite increased access to multidisciplinary teams (12–14), authoritative consensus practice guidelines (5,15), and multicenter networks dedicated to the study of DFU (16), rates of lower-extremity amputation across the U.S. are increasing for the first time in decades (17,18). This trend persists and may be further exacerbated because access to and control over resources are not appropriately distributed across socioeconomic status or neighborhoods despite increased action to achieve health equity that requires society to address SDOH and health disparities (19). Evaluating patient outcomes within a health care-only construct therefore reinforces risk for vulnerable populations.

Neighborhood disadvantage has been shown to be associated with greater risk of lower-extremity amputation (20,21), poor health care quality and diabetes outcomes (22), and lost productivity among people of marginalized communities afflicted with DFU (9). Evaluating a neighborhood, generally, where a person lives, goes to school, works, plays, and receives care, may provide a nuanced understanding of the interaction between SDOH and disease status at an individual level.

Although racial and neighborhood disadvantage disparities are well established (23), a clear understanding of the specific SDOH that drive more severe outcomes in diabetic foot complications is missing. We hypothesized that individuals who live in a more economically impoverished area have increased risk of DFU infection because of SDOH differences in comparison with risk for the general population with diabetes. The primary objectives of

the current study were to characterize the specific aspects of SDOH that are associated with a DFU infection diagnosis. Secondary objectives were to disaggregate data on sex and race to further identify disparity within the population with DFU infection.

## RESEARCH DESIGN AND METHODS

### Data Source

Precision Health at University of Michigan (UM) Health provides a Precision Health Analytics Platform. The platform is a suite of tools, services, and data sets. Of the many available data sets, the geolocation data set featured in DataDirect links National Neighborhood Data Archive (NaNDA) (<https://nanda.isr.umich.edu/about-nanda/>) data to UM Health electronic health records (EHR) through geolocated address coordinates using latitude and longitude (24).

### Study Design

A retrospective case-control analysis was undertaken with use of multiple available cohort systems at the UM Health Precision Health for interrogation of UM's unified EHR from January 2013 to December 2017. The use of EHR data in this study was approved by the University of Michigan Institutional Review Board (HUM00217319) with waiver of consent. A cohort of UM Health patients was constructed and analyzed first through identification of adult patients with diabetes via ICD-9 or -10 codes (Supplementary Appendix A). This same format was applied in stepwise fashion to the collated cohort for identification of individuals with diabetes who developed a DFU and once again to identify a person having an infected DFU with or without peripheral arterial disease, using the supplied ICD-9 and -10 codes. For outcomes in the infected DFU cohort, we queried the same cohort systems for categorization according to major (lower-extremity) amputation as transtibial or transfemoral (CPT codes 27880, 27590, 27882, respectively), minor amputations as toe, ray resection, transmetatarsal, and Chopart amputation (CPT 28820, 28825, 28810, 28805, 28800), and mortality. We then excluded individuals with only a PO Box on record and patients for whom geolocated data were unavailable. For individuals seen multiple times over the study duration for the same diagnosis, only the first encounter meeting eligibility criteria was included. We randomly

chose 100 charts to manually curate to ensure the accuracy of the tools and codes used. Geolocation data were extracted, and all data were fully deidentified.

### Study Variables

Geographic-based SDOH were created from block groups correlating with patient-provided geolocation (address on file). Block groups are contiguous statistical divisions of census tract areas, containing up to 3,000 people and delineated according to participation in the U.S. Census Bureau's Participant Statistical Areas Program. The SDOH and associated deidentified data elements were from two data sets: 1) socioeconomic status and 2) health services (Supplementary Appendix B). All were associated with demographic data. For each covariate compiled, a comparison was made between individuals with diabetes and DFU infection. A data dictionary is included in Supplementary Appendix B and freely accessible from NaNDA at the UM Institute for Social Research.

The constructed data set consisted of four (separate) indices and multiple SDOH based on geolocation. In previous reports investigators identified deleterious effects of residential segregation leading to higher health risks as a result of area deprivation and sociopolitical adversities (25–27). The four indices included neighborhood disadvantaged (NDI), neighborhood affluence (NAI), neighborhood ethnic immigration concentration (NEIC), and the neighborhood education less than high school diploma (NHS). The indices provide a unitless value to describe the relative background of a neighborhood where an individual resided during care.

The NDI was determined according to the proportion (%) of non-Hispanic Black individuals, proportion of female-headed families with children, and the proportion of households with public assistance income or food stamps in a defined area. The NAI included the average of proportion (%) of households with income greater than US\$75,000 (annual), proportion of population age  $\geq 16$  years employed in professional or managerial occupations, and proportion of adults with bachelor's degree or higher. The NEIC includes the average proportion of Hispanic and foreign-born populations, while the NHS includes the proportion of individuals with less than a high school diploma. Higher values indicate that

a greater proportion of the neighborhood identifies with the index's characteristics.

### Statistical Analysis

We analyzed clinical characteristics for the overall cohort and with stratification by two cohorts, DFU infection and diabetes groups, with categorical variables expressed as a number and percentage and continuous variables expressed as mean (SD) and median (interquartile range) for normally and nonnormally distributed continuous data, respectively. The characteristics of individuals in the diabetes and DFU infection groups were compared with  $\chi^2$  tests for categorical variables and unpaired  $t$  tests or Mann-Whitney  $U$  tests for normal and nonnormal continuous variables, respectively. For logistic regression, all SDOH measures were categorized into binary variables with use of the medians of each variable as cutoff points. Then, we demonstrate the clinical characteristics of the patients with DFU infections stratified by sex, following the same principles as described above. Multiple logistic regression was used to assess the

association between the cohorts (diabetes vs. DFU infection) and each SDOH measure at a time, with adjustment for sex, marriage status, race, and smoking status. Data were analyzed with RStudio software (28). All  $P$  values are two sided, and findings were considered statistically significant at  $P < 0.05$ .

### RESULTS

A total of 4.3 million people were available for evaluation within the UM Health system and 1.2 million during the 5-year study period. Among these, 144,564 had a diagnosis of diabetes, of whom 8,351 (5.8%) experienced a sentinel DFU event during the study period, and 2,677 (32.1%) of those with a DFU developed at least one DFU infection during the time period. After application of eligibility criteria, 2,522 individuals with DFU infection were included (Fig. 1) and 155 were excluded. We randomly chose 100 charts to manually curate to ensure the accuracy of the tools and codes used. A neighborhood location was constructed from this final cohort, and it represented a

geolocation rate of 94.2% for this study for those charts randomly reviewed.

### Demographics

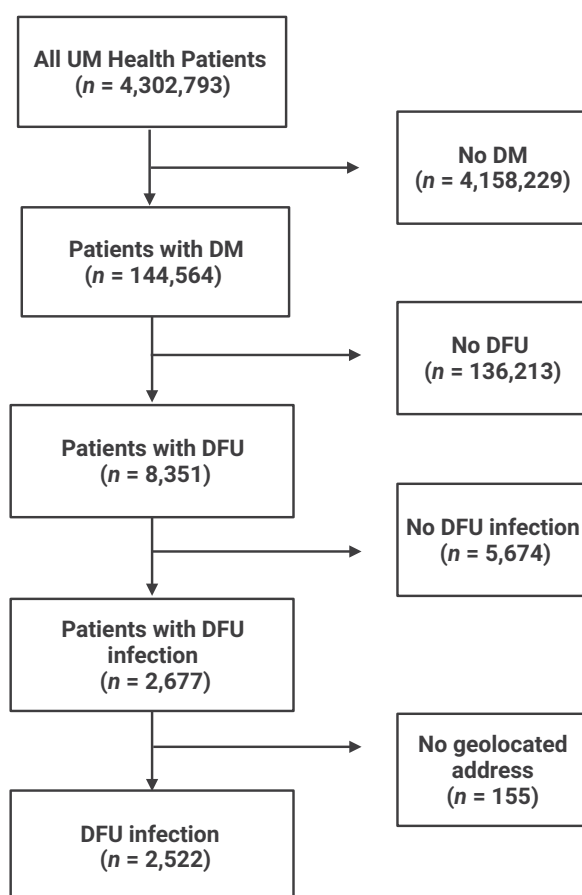
As compared with individuals with diabetes without a DFU infection, the population with DFU infection was older and more likely to be White and male (all  $P < 0.01$ ) in aggregate (Table 1). On disaggregation of data by sex, there was no apparent sex effect on infected DFU compared with the rest of diabetes population (Supplementary Appendix C).

However, as shown in Table 2, the percentage of men who experienced a DFU infection and who were not married was higher as compared with females who experienced DFU infection and were not married ( $P = 0.028$ ). There were no differences between men and women who experienced a DFU infection with an income below federal poverty level ( $P = 0.195$ ). All neighborhood level indices were similar between men and women (all  $P > 0.05$ ). Additionally, the no. of physicians/allied health professionals per 1,000 people and no. of hospitals and outpatient care clinics per square mile among men and women were similar ( $P > 0.05$ ).

### Geolocated SDOH

According to the most recent U.S. census, 12.4% of Washtenaw County residents live below the federal poverty level—contrasting with ~13.7% of people with diabetes living below the federal poverty level, which is 10.5% greater than for the Washtenaw County population (Supplementary Appendix C).

At the neighborhood level, several disparities between cohorts with DFU infection and cohorts with diabetes were identified, as highlighted in Table 1. For instance, individuals with DFU infection were 34% more impoverished than the Washtenaw County residents (16.6% v. 12.4%) and 21% more lived in poverty compared with individuals with diabetes without DFU infection (13.7% vs. 16.6%). Additionally, the percentage of individuals who identified as not married was higher for the cohort with DFU infection compared with the overall cohort with diabetes (60.9% vs. 47.6%,  $P < 0.001$ ), while access to available health care such as access to “physicians” (1.50 vs. 1.73) and “health practitioners” such as a podiatrist (0.62 vs. 0.66) per 1,000 people was



**Figure 1**—Study population flowchart. DM, diabetes mellitus.

**Table 1—Demographic and neighborhood SDOH characteristics of the cohorts with diabetes and with DFU infection**

	Diabetes ( <i>n</i> = 19,841)	DFU infection ( <i>n</i> = 2,522)	<i>P</i>
Population density (people per sq. mile)	2,179.84	2,205.91	0.592
Age (years)			
18–29	15.7	18.1	<0.001
30–39	11.9	12.9	<0.001
40–49	12.9	15.0	<0.001
50–69	26.8	27.1	0.007
≥70	10.6	11.1	<0.001
Sex, <i>n</i> (% male)	10,637 (53.6)	1,553 (61.6)	<0.001
Race, <i>n</i> (%)			<0.001
White	15,398 (77.7)	2,051 (81.5)	
Black	2,892 (14.6)	363 (14.4)	
Asian	615 (3.1)	28 (1.1)	
Mixed	229 (1.2)	63 (2.5)	
Other	690 (3.5)	11 (0.4)	
Never smoker, <i>n</i> (%)	8,360 (42.1)	959 (38.0)	<0.001
Not married, <i>n</i> (%)	9,447 (47.6)	41,536 (60.9)	<0.001
Income below poverty	13.7 (11.6)	16.6 (14.5)	<0.001
Neighborhood high school index	0.086 (0.065)	0.090 (0.078)	0.003
Median (Q1, Q3)	0.074 (0.040, 0.116)	0.074 (0.041, 0.117)	
Population above median, <i>n</i> (%)	10,798 (54.4)	1,385 (54.9)	0.639
Neighborhood disadvantage index	0.106 (0.095)	0.111 (0.104)	0.026
Median (Q1, Q3)	0.075 (0.044, 0.130)	0.073 (0.046, 0.131)	
Population above median, <i>n</i> (%)	10,624 (53.5)	1,327 (52.6)	0.378
Neighborhood affluence index	0.393 (0.180)	0.390 (0.174)	0.517
Median (Q1, Q3)	0.360 (0.248, 0.517)	0.362 (0.254, 0.505)	
Population above median, <i>n</i> (%)	8,969 (45.2)	1,151 (45.6)	0.680
Neighborhood ethnic/immigration concentration	0.058 (0.054)	0.056 (0.059)	0.130
Median (Q1, Q3)	0.038 (0.023, 0.075)	0.037 (0.021, 0.071)	
Population above median, <i>n</i> (%)	1,150 (45.6)	9,599 (48.4)	0.008
No. of physicians/1,000 people	1.73 (2.99)	1.50 (2.66)	<0.001
No. of other health practitioners/1,000 people	0.66 (0.80)	0.62 (0.71)	<0.01
No. of hospitals/square mile	0.43 (1.19)	0.40 (1.18)	NS
No. of physicians/1,000 people	1.73 (2.99)	1.50 (2.66)	<0.001
No. of outpatient care clinics/square mile	0.850 (2.097)	0.888 (2.089)	0.388

Data are percentages or mean (SD) unless otherwise indicated. Q, quartile.

lower (for both  $P < 0.01$ ). However, there were no differences in the number of hospitals per square mile (0.43 vs. 0.40,  $P > 0.1$ ) for the cohorts. As expected, current smokers were more prevalent in the cohort with DFU infection compared with those with diabetes without DFU (20.9% vs. 8.3%,  $P < 0.001$ ).

The NDI and NHS mean values were higher for the cohort with DFU infection (both  $P < 0.05$ ), while the NAI and NEIC were not different between cohorts. The percentage of individuals from neighborhoods with an NEIC above the median was higher in the population with DFU infection ( $P = 0.008$ ). In addition, there was strong collinearity between NDI and NAI indices ( $r = -0.70$ ,

$P < 0.001$ ); however, the proportion of individuals above the median disadvantaged index value was not significantly different among cohorts.

In logistic regression, after adjustment for sex, race, smoking status, and marriage status, there were several notable neighborhood disadvantages for individuals with DFU infection (Table 3). First, of the indices evaluated, NEIC, when an individual with DFU infection was from a neighborhood with higher concentration of Hispanic origin and/or foreign-born individuals, was the only index to predict DFU infection development (odds ratio [OR] 1.11 [95% CI 1.02, 1.21];  $P = 0.015$ ). No other index or covariate was significant in logistic regression analysis.

Additional SDOH measures that associated with the development of DFU infection included decreased access to physicians per 1,000 people (1.14 [1.04, 1.24];  $P = 0.003$ ) and hospitals per square mile (1.22 [1.11, 1.34];  $P < 0.001$ ) in the patient's census tract associated with their geolocated address. More outpatient care clinics per square mile were associated with protection from DFU infection development (0.90 [0.82, 0.98];  $P = 0.012$ ).

## Outcomes

Overall, 555 individuals had lower-extremity amputations (22%) and 304 individuals died (12.1%) during the study

**Table 2—Summary statistics for individuals with DFU infection with stratification by sex**

	DFU infection, male	DFU infection, female	DFU infection, total	P
n	1,553	969	2,522	
Population density (SD)	2,140.8 (2,305.1)	2,310.2 (2,575.3)	2,205.9 (2,413.4)	0.087
Age (years)				
18–29 (SD)	0.179 (0.119)	0.185 (0.129)	0.181 (0.123)	0.234
30–39 (SD)	0.128 (0.071)	0.130 (0.077)	0.129 (0.073)	0.469
40–49 (SD)	0.153 (0.095)	0.145 (0.085)	0.150 (0.091)	0.028
50–69 (SD)	0.272 (0.061)	0.269 (0.066)	0.271 (0.063)	0.250
≥70 (SD)	0.113 (0.074)	0.109 (0.065)	0.111 (0.071)	0.131
Race, n (%)				0.587
White	1,276 (82.4)	775 (80.1)	2,051 (81.5)	
Black	210 (13.6)	153 (15.8)	363 (14.4)	
Asian	16 (1.0)	12 (1.2)	28 (1.1)	
Mixed	40 (2.6)	23 (2.4)	63 (2.5)	
Other	7 (0.5)	4 (0.4)	11 (0.4)	
Not married status, n (%)	972 (62.6)	564 (58.2)	1,536 (60.9)	0.028
Never smoker, n (%)	591 (38.1)	368 (38.0)	959 (38.0)	0.841
Income below poverty (SD)	0.163 (0.143)	0.171 (0.148)	0.166 (0.145)	0.195
Neighborhood high school index (SD)	0.091 (0.079)	0.090 (0.075)	0.090 (0.078)	0.631
Neighborhood disadvantage index (SD)	0.110 (0.103)	0.113 (0.105)	0.111 (0.104)	0.450
Neighborhood affluence index (SD)	0.390 (0.174)	0.391 (0.174)	0.390 (0.174)	0.860
Neighborhood ethnic immigration concentration (SD)	0.057 (0.061)	0.055 (0.056)	0.056 (0.059)	0.383
No. of physicians/1,000 people (SD)	1.534 (2.855)	1.434 (2.335)	1.495 (2.667)	0.360
No. of other health practitioners/1,000 people (SD)	0.605 (0.729)	0.637 (0.688)	0.618 (0.714)	0.272
No. of hospitals/square mile (SD)	0.405 (1.174)	0.400 (1.183)	0.403 (1.177)	0.928
No. of outpatient care clinics/square mile (SD)	0.844 (1.963)	0.959 (2.277)	0.888 (2.089)	0.178

period in the cohort with DFU infection. Of the 555 amputations, 253 (45.6%) and 302 (54.4%) were minor and major amputations, respectively. Higher NAI was

protective against major amputation (OR 0.76 [95% CI 0.59, 0.97];  $P = 0.027$ ) with adjustment for sex, race, marriage, and smoking status. No other index or covariate

was significant in logistic regression analysis for amputation or death.

A total of 409 individuals had peripheral arterial disease and therefore had an

**Table 3—Multiple logistic regression model for individuals with DFU infection**

SDOH measure	OR (DFU infection)	P	95% CI lower bound	95% CI higher bound
Population density	1.063	0.157	0.977	1.157
Age (years)				
18–29	0.989	0.793	0.908	1.076
30–39	1.021	0.631	0.938	1.111
40–49	1.004	0.927	0.922	1.093
50–69	0.938	0.142	0.862	1.021
≥70	1.081	0.074	0.993	1.176
Income below poverty	1.024	0.579	0.941	1.115
Neighborhood high school index	0.987	0.765	0.906	1.075
Neighborhood disadvantage index	1.048	0.277	0.963	1.141
Neighborhood affluence index	0.982	0.679	0.902	1.070
Neighborhood ethnic immigration concentration	1.112	0.015	1.021	1.210
No. of physicians/1,000 people	1.137	0.003	1.044	1.238
No. of other health practitioners/1,000 people	1.054	0.227	0.968	1.147
No. of hospitals/square mile	1.219	<0.001	1.113	1.337
No. of outpatient care clinics/square mile	0.897	0.012	0.824	0.976

ischemic component to the DFU infection. In individuals with a neuroischemic DFU infection, 25 of 46 (54.3%) who underwent major amputation died, while 20 of 61 (32.8%) who underwent minor amputations died. There was significant association between amputation status and death. Minor amputation was protective against death for those with an ischemic component to their DFU infection (OR 0.41 [95% CI 0.17, 0.97];  $P = 0.03$ ).

## CONCLUSIONS

To the best of our knowledge, this is the first report to demonstrate an association between neighborhood-level SDOH and the development of DFU infection. In this cohort, managed according to current standards of care in a tertiary center, the DFU prevalence was ~6% and the proportion of DFU that became infected was ~32%. These contemporary data add insight to the reported prevalence rates of 6.3% (29) and 25–60% (4,30,31) for DFU and DFU infection, respectively, in various prior cohorts, and thus provide valid inference for clinical, epidemiologic, and health services research.

This study also identified several notable disparities among individuals with DFU infection as compared with the rest of the individuals with diabetes including novel associations between sex interactions and nonmarriage status, as the percentage of men who were not married suffered DFU infection more frequently than women who were not married. Furthermore, the analysis demonstrated the impact of immigration status and ethnicity on outcomes. These findings are important as, to date, there are limited data about neighborhood-level SDOH and the role it plays in health care disparities in the population with diabetic foot.

As it would be expected, the aggregated demographics for this large sample size revealed people with DFU infection to be older and more often men, and of White race (all  $P < 0.001$ ). However, the latter is likely reflective of the region that UM Health serves. While in general these data are consistent with prior reports (32), they highlight a critical need to further investigate SDOH on a neighborhood level in underserved communities where disparities are commonly present (7–9,33,34). On disaggregation of demographic data by sex and racial categories, disparities in DFU infection became

dissimilar in comparison with the population with diabetes.

First, we used several indices to evaluate broad socioeconomic factors within a neighborhood. The indices provide a rapid method to assess the neighborhoods where people live. Mean values of NDI and NHS indices were higher, indicating more disadvantaged status and less high school education, respectively, for the population with DFU infection. Research has shown that people with lower income and less education are two to four times more likely to develop diabetes and more likely to be affected by complications of diabetes (35–37). Meanwhile, mean NAI and NEIC indices were lower (all  $P < 0.001$ ) for the population with DFU infection. Despite lower mean NAI and NEIC values for the cohort with DFU infection, the median NEIC value of Hispanic and/or foreign-born status for the population with DFU infection was significantly higher than the median value for the population with diabetes (48.4 vs. 45.6, respectively;  $P = 0.008$ ).

This was confirmed in multivariable analysis, where the NEIC value was the only neighborhood index characteristic predictive of DFU infection development. This supports that the location where a person lives may influence disease outcome. Specifically, it supports the need to determine care algorithms specific to these populations for people from neighborhoods with higher percentages of Hispanic individuals and/or locations with higher percentages of foreign-born individuals.

Further, on evaluation of neighborhood-specific SDOH, a sex bias was revealed with respect to nonmarried status. Specifically, the proportion of the population with DFU infection who identified as not married was highest for men as compared with their female counterparts. This disparity was not observed in the general diabetes cohort, has not been reported in the population with DFU, and highlights the multifactorial role marriage and/or social support may play in clinical outcomes.

Other neighborhood SDOH including access to health care varied between DFU infection and diabetes cohorts. The population with diabetes was better served in terms of physicians and health professionals per 1,000 people. The number of hospitals per 1,000 people was similar ( $P > 0.05$ ), and other SDOH such as population density did not contribute to DFU infection development.

Multiple reports indicate that physician shortages are linked to poor diabetes outcomes (38–40), which is aligned with our data for the population with DFU infection. It is also known that having access to a multidisciplinary team involved in limb salvage can mitigate possible effects of social disadvantage. However, not having timely and appropriate access to providers or hospitals because of where one lives results in an unmitigated structural barrier that needs to be addressed to reduce diabetic foot complications. This is best demonstrated by the outcomes from our study that demonstrate that individuals with a higher affluence index (NAI) are less likely to undergo major amputation as compared with those with lower affluence index. In addition, the performance of minor amputations in individuals with neuroischemic ulcer was protective against death.

There are several important strengths to this study including the use of a large contemporary population managed according to current standards, the use of innovative precision tools to access and evaluate individuals impacted by DFU, and the longitudinal assessment of adverse outcomes (e.g., infection) in populations with DFU. Additionally, this study identified several novel associations between sex and marital status, since men presenting with a DFU infection were less likely to be married compared with women with DFU infection, and demonstrated the impact of immigration status and ethnicity on outcomes. There are also limitations to this study. First, the study was performed at a large tertiary medical center, which represents a barrier to generalizability. To increase generalizability, we used publicly available data sets. Geocoding was successful for 94% of the UM Health patient population. Only 2.5% of all patient addresses were a PO Box, and strict exclusion criteria were implemented on data cleaning to remove these. Second, data were assessed retrospectively and metrics like hemoglobin A<sub>1c</sub> were not recorded. Inherent to a retrospective analysis is the risk of bias and an inability to confirm causation. However, the risk of bias was mitigated with use of authoritative guidelines for infection assessment on established ICD-9 and -10 coding terminologies consistent with those used by usual care practices in the U.S. (5). We did not perform subgroup analysis based on diabetes type. Strong association



between neighborhood SDOH and DFU infection, different from the association for the general diabetes population, is reported. Finally, longitudinal trends over the 5-year study period were not reported. To date, there are limited data about neighborhood-level SDOH and the role it plays in health care disparities in the population with diabetic foot. We acknowledge that further efforts are needed to determine causal and temporal relationships for SDOH on an individual level.

In summary, SDOH neighborhood-level data may be useful in identifying individuals who are at risk of developing DFU infection. The data strongly support the following as SDOH that independently associate with DFU infection: being below the federal poverty limit, not married status, and less access to health care providers. Further prospective implementation science research is urgently needed for implementation at the point of care of effective novel risk stratification systems that include tailored SDOH to promote optimized care for populations at risk beyond biology-only determinants. In additional research, investigators should measure population mobility and its impact on disease outcomes. Thus, these geolocated SDOH provide actionable targets to reduce the high morbidity associated with DFU infection and provide targets to deconstruct existing health disparities in communities of need.

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