CEBP FOCUS: Geospatial Approaches to Cancer Control and Population Sciences

Measures Matter: The Local Exposure/Isolation (LEx/Is) Metrics and Relationships between Local-Level Segregation and Breast Cancer Survival

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Abstract

Background: The Black-to-White disparity in breast cancer survival is increasing, and racial residential segregation is a potential driver for this trend. However, study findings have been mixed, and no study has comprehensively compared the effectiveness of different local-level segregation metrics in explaining cancer survival.

Methods: We proposed a set of new local segregation metrics named local exposure and isolation (LEx/Is) and compared our new local isolation metric with two related metrics, the location quotient (LQ) and the index of concentration at extremes (ICE), across the 102 largest U.S. metropolitan areas. Then, using case data from the Milwaukee, WI, metropolitan area, we used proportional hazards models to explore associations between segregation and breast cancer survival.

Results: Across the 102 metropolitan areas, the new local isolation metric was less skewed than the LQ or ICE. Across all races, Hispanic isolation was associated with poorer all-cause survival, and Hispanic LQ and Hispanic-White ICE were found to be associated with poorer survival for both breast cancer–specific and all-cause mortality. For Black patients, Black LQ was associated with lower all-cause mortality and Black local isolation was associated with reduced all-cause and breast cancer–specific mortality. ICE was found to suffer from high multicollinearity.

Conclusions: Local segregation is associated with breast cancer survival, but associations varied based on patient race and metric employed.

Impact: We highlight how selection of a segregation measure can alter study findings. These relationships need to be validated in other geographic areas. *Cancer Epidemiol Biomarkers Prev; 26(4); 516–24. ©2017 AACR.*

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Introduction

Segregation and health

Nearly 50 years after the passage of the Fair Housing Act, residential racial segregation still plagues many U.S. cities (1, 2). Black segregation levels declined across the United States from 2000 to 2010 but remain extreme in Northern cities such as Milwaukee, Detroit, Chicago, and New York (3). In addition, Hispanic segregation is increasing nationally (3). Segregation has been linked not only to social and economic inequality (4–7), but also to racial health disparities. Like segregation, racial health disparities persist, including a mortality gap between blacks and whites and lower life expectancy among blacks (8, 9). Previous studies have found that metropolitan areas with higher segregation see worse Black mortality, whereas segregation has a mixed association with White mortality (10, 11). Segregation is thought to contribute to disparities in several ways, including by widening socioeconomic status (SES) gaps across races, concentrating minorities in underserved neighborhoods, and increasing exposure of environmental hazards to minorities (5, 10).

One such health disparity is the widening breast cancer mortality and survival gap between Black and White women (12, 13). Whitman and colleagues (2011) found a positive correlation between Black and White mortality rate ratios and segregation in a sample of 24 cities (14). Mammography utilization has been shown to be decreased in counties with greater Asian and Black segregation but increased in counties with greater Hispanic segregation (15). Pruitt and colleagues (2015) identified Black and Hispanic local segregation to be associated with decreased breast cancer survival (16). In contrast, Warner and Gomez found that residence in a high percent Black neighborhood corresponded to *decreased* Black breast cancer mortality and increased White mortality, but was not associated with survival length (17). Mixed findings among these studies may be partially due to variation among methods used to measure segregation.

Measuring segregation: Metropolitan area metrics

Much research has focused on how to best measure segregation. Massey and Denton outline five major "dimensions" of segregation: evenness, exposure, concentration, centralization, and clustering (18). The majority of the literature on traditional segregation metrics focuses on evenness and exposure/isolation (19–22). Evenness measures how racial/ethnic groups are distributed across the subunits (e.g., census tracts, ZIP codes) within a metropolitan area, with a maximum evenness indicating that proportions for groups are constant across all subunits (18). Dissimilarity is the most common measure of evenness, but the Gini, Atkinson, and entropy indices may be used (19, 23–26). Alternatively, the exposure index measures the geographic potential for two individuals from two different racial/ethnic groups to

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interact (18, 27). Exposure ($E_{m,n}$) has been defined by Lieberson as (27):

$$E_{m,n} = \sum_{i=1}^{N} \frac{x_{im}}{Y_m} \times \frac{x_{in}}{X_i}$$

where i is a specific subunit, N is the total number of subunits in the Metropolitan Statistical Area (MSA), m and n are two racial/ethnic groups, x_{im} is the number of individuals from a specific ethnic group within a specific subunit, Y_m is the total number of individuals from a specific ethnic group in the entire MSA, and X_i is the total population of the subunit. Massey and Denton propose interpreting exposure as the probability that a random individual from group m shares a common subunit with an individual from group n (18). Analogously, the isolation index measures the potential of interaction among members of the same group.

Although traditional segregation measures have been well studied and validated, they have a major conceptual limitation as summary measures of a larger region (e.g., metropolitan statistical areas, MSAs). They do not provide insight into the racial makeup or lived experiences of smaller subunits within that region. Their equations average the racial compositions of the subunits. On a city scale, the objective of traditional metrics is to determine whether racial groups occupy different spaces within the city. For subunits [tracts and ZIP Code Tabulation Areas (ZCTAs)], we are generally more interested in determining how much a subunit's demographics are manifesting the city's segregation levels, rather than whether groups occupy different spaces within the smaller unit. In order to study segregation at a local level, we require new metrics.

Measuring segregation: small area metrics

Local metrics must describe local experiences of segregation. Existing local segregation indices such as the location quotient (LQ) and the index of concentration at extremes (ICE) have been examined for relationships with cancer outcomes. However, neither of these indices provides an intuitive way to examine coresidence of two races in the same space, which could be useful to measure interactions among individuals of different racial or ethnic groups.

The LQ for a particular ZCTA (or another areal subunit) i and racial/ethnic group m is given as follows (4, 16):

$$\mathrm{LQ}_{im} = \left(\frac{x_{im}}{X_i}\right) \Big/ \left(\frac{Y_m}{Y}\right)$$

where Y is the total population of the MSA. An LQ value of zero indicates that there are no individuals of that particular race/ethnicity within the ZCTA, whereas a value of one indicates that the proportion of that racial/ethnic group within the ZCTA is equal to the proportion of that racial/ethnic group in the larger region (e.g., MSA). In order to correct for potential skew problems, a $\log_{10}(x+1)$ transformation can be applied (16).

The ICE is calculated, per Krieger and colleagues (2016), using a generalized formula (28):

$$\mathrm{ICE}_i = \frac{D_i - P_i}{T_i}$$

where D_i is the population of members of a "deprived" category in ZCTA i, P_i is the population of a "privileged" category in the ZCTA, and T_i is the total population of the ZCTA. The "deprived" and "privileged" categories can be defined by race/ethnicity (i.e., Black as deprived and White as privileged) or by a combination of race/ethnicity and income quintile (e.g., Black/80th percentile or Lower vs. White/20th percentile or higher). The purpose of controlling for income is to reduce multicollinearity between racial composition and SES (28).

An alternative approach to describing local segregation are typology methods that convert numerical indices into categorical classifications (29). These classifications have predefined boundaries to categorize the neighborhoods. Such approaches have been argued as being robust incorporating multiple dimensions of segregation and advantageous by describing neighborhoods in "normative" terms (e.g., "diverse" or "predominately ethnic"; ref. 29). In addition, the proportion of neighborhoods of each type within the metropolitan area can be used as a summary metric for the region (29, 30). This article focuses on comparing numerical metrics, but typological methods provide another potential approach.

Research objectives

In this article, we are interested in the relationship between racial residential segregation and breast cancer survival. First, we propose a new class of local segregation metrics, called local exposure and isolation (LEx/Is), adapting the exposure and isolation metrics into local metrics. Then, we compare LEx/Is with the LQ and ICE across 102 U.S. MSAs. Finally, we examine the relationship between local segregation and breast cancer survival in the Milwaukee, WI, metropolitan area, while comparing LEx/Is, LQ, and ICE. This article thus contributes both a new segregation measurement approach and a comparison of three metrics in the study of an important health disparity.

Methods and Materials

LEx/Is: A new set of local segregation metrics

We propose a novel set of local segregation metrics based on the traditional exposure and isolation indices (18). The purpose of the local exposure and isolation indices is to measure the probability that two individuals living within a specific subunit (i.e., the ZCTA) of either different or the same racial/ethnic group(s) will interact. Using the assumption that individuals within a subunit are randomly mixed, we estimate this probability as randomly and independently selecting two individuals living in that subunit:

$$P_{m,n}(i) = p_{im} \times p_{in} = \frac{x_{im}}{X_i} \times \frac{x_{in}}{X_i}$$

For the case where $m \neq n$, this is the local exposure probability between two groups, while where $m = n$ is the local isolation probability of a single group. We standardize this probability with a logit transformation and center it against the expected case that all races/ethnicities are evenly distributed across the entire MSA. The resulting index is

$$\begin{aligned} E^*_{m,n}(i) &= \mathrm{logit}\left(P_{m,n}(i)\right) - \mathrm{logit}(P_m \times P_n) \\ &= \log\left(\frac{p_{im} \times p_{in}}{1 - p_{im} \times p_{in}}\right) - \log\left(\frac{P_m \times P_n}{1 - P_m \times P_n}\right) \end{aligned}$$

where $E^*_{m,n}(i)$ is the localized exposure/isolation metric (LEx/Is) for ZCTA i, and P_m is the proportion of group m out of the entire MSA. A zero value for local exposure indicates that the estimated probability of the interaction between two people of the given groups within the subunit is equal to the expected probability if the MSA were perfectly mixed. Values greater than zero indicate that the interaction is more likely to occur within the subunit than in the MSA, and values less than zero indicate that it is less likely. Exponentiation of each LEx/Is metric results in the odds ratio of the specific exposure or isolation of interest in the ZCTA relative to the MSA. The resulting local isolation metrics are comparable to LQs (e.g., Black local isolation and Black LQ), and can be used in statistical models in an analogous fashion. The local exposure metrics can additionally be interpreted as meaningful interaction terms of the isolation terms (e.g., Black-Hispanic exposure is a function of Black isolation and Hispanic isolation). Models can be developed including isolation terms only, exposure terms only, or a combination of terms, depending on the research question.

A comparison across MSAs

We first compared three local segregation metrics (LQ, ICE, and LEx/Is) across the 102 largest U.S. MSAs, based on 2010 census data. We also examined the 15 most segregated and 15 least segregated MSAs, according to their 2010 MSA-wide level of Black–White isolation (31). Correlations among the local isolation metric, LQ, and ICE were examined using Kendall's τ. Local exposure was not compared, as it is not conceptually analogous. The statistical distributions of local indices across MSAs were plotted and compared.

The Milwaukee, WI, study area

The Milwaukee-Waukesha-West Allis, WI MSA had a total population of 1,581,159 residents in the 2010 U.S. Census, of whom 69% were non-Hispanic White, 16% were non-Hispanic Black, and 9% were Hispanic/Latino. Milwaukee's metropolitan area is extremely segregated, with the highest level of overall Black-White isolation of the 100 largest MSAs in 2010 (31). The MSA was chosen as the scale for the study in keeping with previous literature examining segregation and cancer outcomes (16, 32–35). In addition, MSAs are recommended over municipal boundaries, as they represent the full extent of the housing market in a given metropolitan setting, and include greater diversity of lived experiences within MSA (36).

Data sources

Patient case data were obtained from the Wisconsin Cancer Reporting System (WCRS) for invasive female breast cancer cases from years 2002 to 2011. WCRS collects reports of newly diagnosed preinvasive and invasive cancer cases from physicians and clinics across Wisconsin, along with demographic information about the patients and tumor characteristics. Only patients who were non-Hispanic White, non-Hispanic Black, or Hispanic were included in the study, as these groups are most affected by segregation and are by far the largest racial and ethnic groups in the region. There was no missing data for ZIP code and only 0.72% of cases were either unstaged or missing stage data. Records missing stage were excluded. Demographic data for ZCTAs was obtained from a combination of the 2000 and 2010 U.S. Decennial Census and the 2008–2012 American Community Survey (ACS; refs. 37–39). Census counts were used to calculate segregation indices for both 2000 and 2010. The percent of households living below the poverty line was obtained from the 2000 Census and the 5-year 2008–2012 ACS. Cases diagnosed in 2005 or earlier were matched to the 2000 Census Variables, whereas cases from 2006 and onward were matched to the ACS and 2010 Census variables.

Statistical analysis

Descriptive analyses were conducted to characterize the study population. Multivariate Cox proportional hazards regressions were used to model survival time for all-cause and breast cancer specific mortality. All models controlled for age, diagnosis stage, race/ethnicity, and ZCTA level shared frailties. Non-Hispanic White patients were categorized as "White," non-Hispanic Black/African American patients were categorized as "Black", and Hispanic/Latino patients, regardless of race, were categorized as "Hispanic." Different models for each local segregation measure were tested with and without controlling for ZCTA SES to investigate collinearity between segregation and SES. SES was measured by the ZCTA's poverty area status (>20% households below poverty line) for models using LEx/Is and LQ, and by controlling for income in the calculation of ICE. Models were stratified on diagnosis stage, age, and ZCTA poverty, due to proportional hazards assumption concerns. All analyses were conducted in the R statistical language (40).

Results

Comparison of local isolation to other local segregation indices across MSAs

Correlations were strongest between local isolation and LQ (Kendall's τ White: 0.729, Black: 0.945, Hispanic: 0.946). ICE, uncontrolled for income, showed moderate to strong correlations with local isolation (Black: 0.624 and Hispanic: 0.428), whereas controlling for income resulted in weaker correlations (Black: 0.326 and Hispanic: 0.265). All correlations were found to be significant at a $P < 0.001$ confidence level. A comparison of Black isolation, Black LQ, and Black ICE (no income) found local isolation to be less skewed than LQ or ICE for the case of all 102 MSAs and the 15 most segregated MSAs, and no worse skewed in the 15 least segregated MSAs, as shown in Fig. 1.

Relationship between racial residential segregation and breast cancer survival

Table 1 presents the characteristics of the study population. Black and Hispanic patients tended to be younger, more likely to live in ZCTAs designated as poverty areas, and more likely to be diagnosed at a later stage. Majorities of Black and White patients lived in ZCTAs where they were the majority race, whereas a plurality of Hispanic patients lived in predominately White ZCTAs. As illustrated in Fig. 2, Black and Hispanic populations are clustered in ZCTAs within Milwaukee County, where there are higher poverty rates. Black isolation ($\tau = 0.447$), Hispanic isolation ($\tau = 0.423$), and Black-Hispanic exposure ($\tau = 0.510$), all were significantly correlated to the poverty level of the ZCTA ($P < 0.001$ for all).

Boxplots in Fig. 2 reveal Black and White patients had little overlap in their Black local isolation, Black LQ, and Black-White race-only ICE scores, but had more overlap for Hispanic segregation indices. Hispanic patients' segregation scores overlapped with both other races, except for Black patients with high Black local isolation and Black LQ scores. Differences in the scaling of each segregation index are apparent in Fig. 1 as well. ICE scores adjusting for race and income together were in a very tight range and showed heavy overlap across races. Segregation indices were examined for multicollinearity using the variance inflation factor (VIF). ICE was found to have much higher VIFs (Hispanic-White: 5.94, Hispanic-White controlled for income: 10.05) than local isolation (1.22) or LQ (1.32). Correlation between Black-White

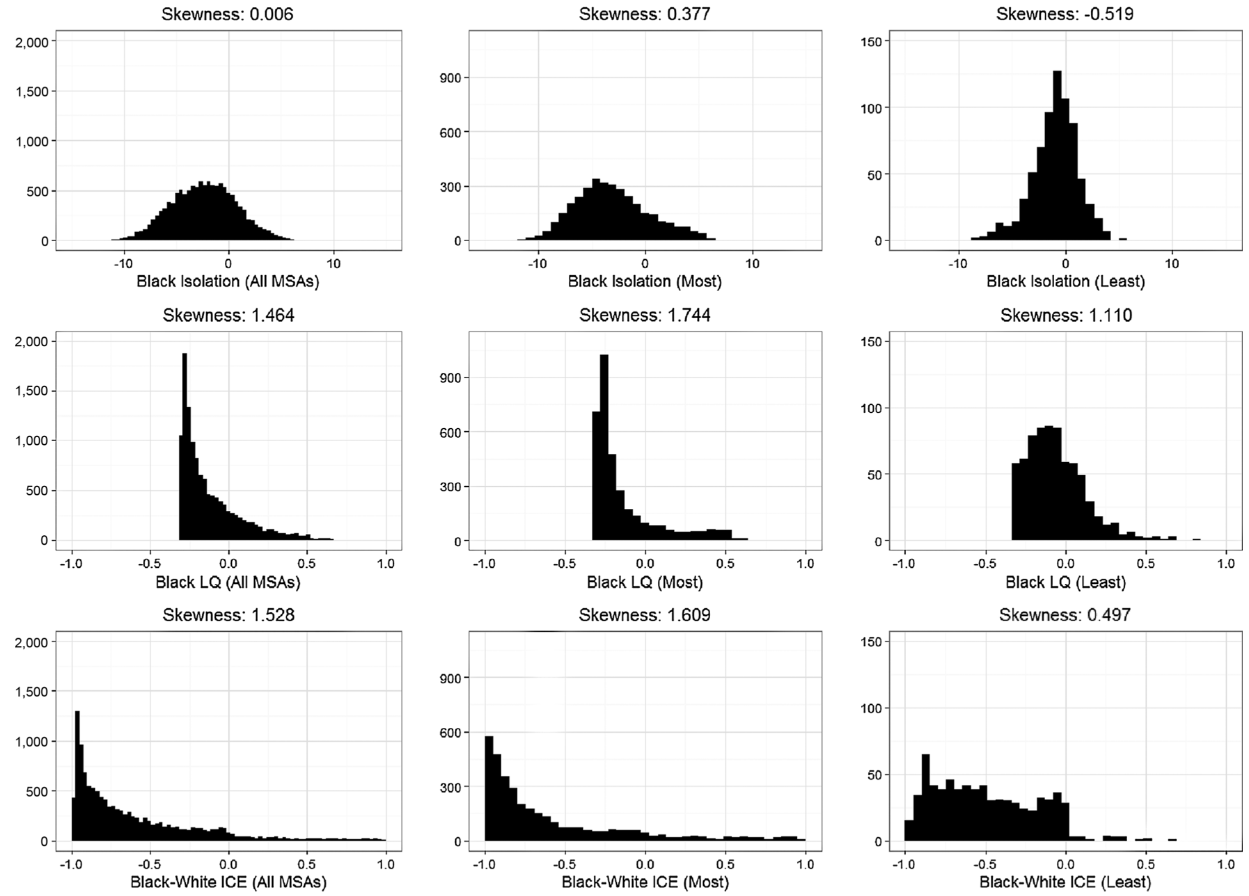

Figure 1.
Comparisons of the distribution of ZCTA-level Black segregation indices in the 102 largest MSAs in the United States (left column), the 15 most Black–White segregated of those MSAs (middle column), and the 15 least segregated (right column).

and Hispanic-White ICE ($\rho = 0.879$) was far higher than the correlation between Black and Hispanic local isolation and LQ ($\rho = 0.230$ and -0.011), likely resulting in the difference in multicollinearity.

Segregation was found to be significantly associated with both all-cause survival and breast cancer specific survival, as shown in Table 2. ZCTA poverty area status was significantly associated with decreased all-cause and breast cancer specific

Table 1. Patient demographics for breast cancer cases from the WCRS

	Black (*n*)	%	White (*n*)	%	Hispanic (*n*)	%	All (*n*)	%	*P*
Count	940	11.25%	7,164	85.73%	252	3.02%	8,356	100%	—
Deceased	215	22.87%	1,153	16.09%	33	13.10%	1401	16.77%	<0.001
Breast-specific	148	15.74%	602	8.40%	22	8.73%	772	9.24%	<0.001
Cancer stage									
Localized	468	49.79%	4,658	65.02%	151	59.92%	5,277	63.15%	<0.001
Regional or distant	472	50.21%	2,506	34.98%	101	40.08%	3,079	36.85%	
Age									
18–44	196	20.85%	845	11.80%	73	28.97%	1,114	13.33%	<0.001
45–54	281	29.89%	1,643	22.93%	81	32.14%	2,005	23.99%	
55–64	209	22.23%	1,684	23.51%	48	19.05%	1,941	23.23%	
65–74	136	14.47%	1,390	19.40%	33	13.10%	1,559	18.66%	
75+	118	12.55%	1,602	22.36%	17	6.75%	1,737	20.79%	
ZCTA >20% below poverty	644	68.51%	458	6.39%	106	42.06%	1,208	14.46%	<0.001
ZCTA majority race									
Black	731	77.77%	407	5.68%	26	10.32%	1,164	13.93%	<0.001
White	126	13.40%	6,503	90.77%	124	49.21%	6,753	80.82%	
Hispanic	8	0.85%	92	1.28%	68	26.98%	168	2.01%	
No majority	75	7.97%	162	2.26%	34	13.49%	271	3.24%	

NOTE: First row percentages are percent of race of total number of patients. All other percentages are calculated within race. *P*-value calculated for chi-squared test for differences between races.

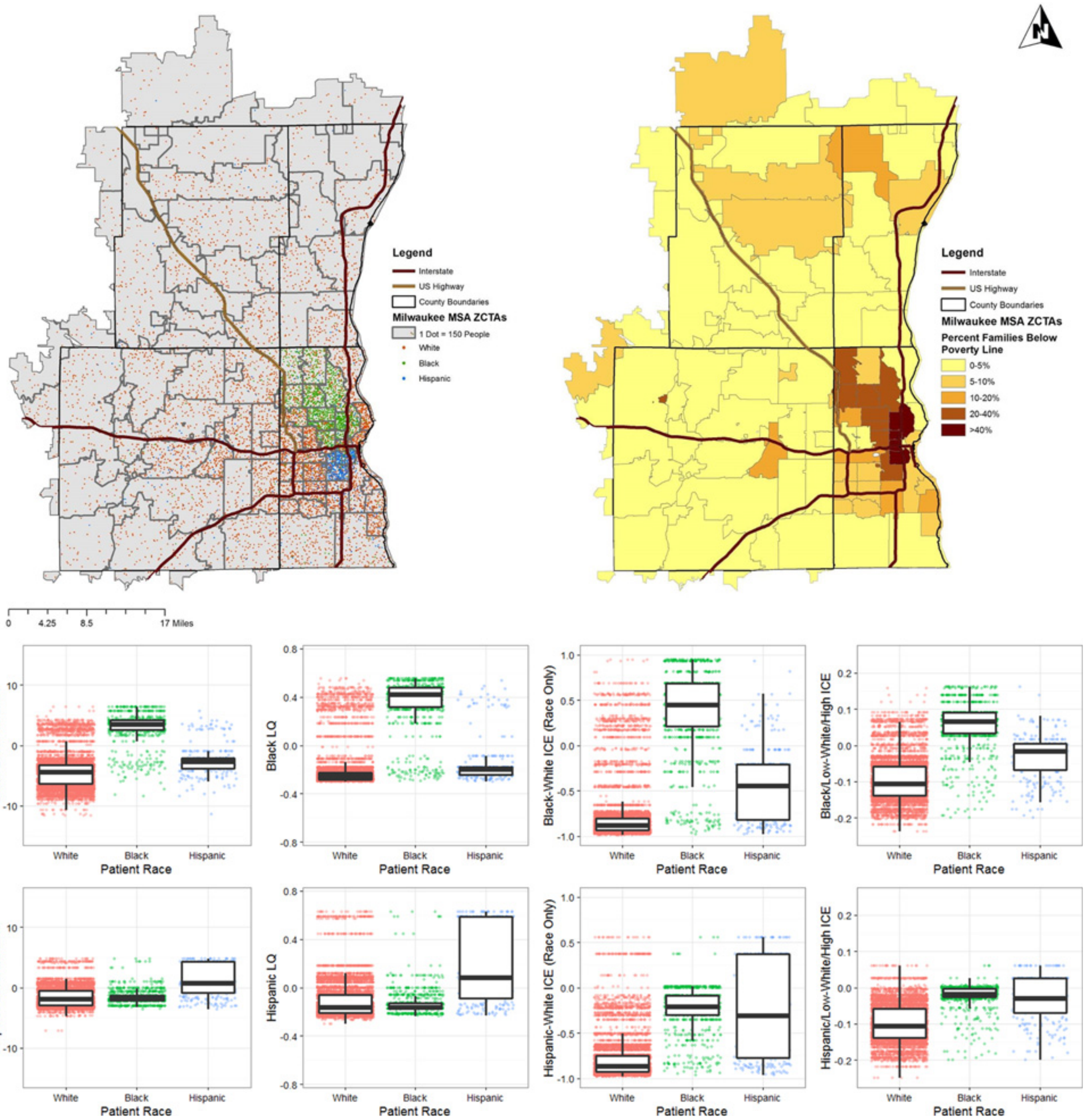

Figure 2.

Top: Maps of Milwaukee-Waukesha-West Allis, WI, MSA. Top left: Dot map of racial distribution in study area by ZCTA. Top right: Percent households below poverty line in study area by ZCTA. Bottom: Jittered distribution of patients by race for each segregation index. Top row is Black segregation indices, bottom row is Hispanic segregation indices. Columns from left to right are: local isolation, LQ, ICE (uncontrolled for income), ICE (controlled for income). Boxes correspond to the first to third quartiles of each race's distribution. Whiskers extend to 1.5 time the interquartile range.

survival in all models that included it. Local Hispanic isolation was significantly associated with decreased all-cause survival, even after adjustment for poverty area status. Local Black-Hispanic exposure was nearly significant ($P = 0.052$) for poorer all-cause survival when not adjusted for poverty. Hispanic LQ was associated with poorer all-cause and breast cancer specific survival, but these relationships became nonsignificant once adjusted for poverty. Hispanic-White ICE, controlled for income, was found to be significantly associated with poorer all-cause survival, while the unadjusted Hispanic-White ICE was associated with poorer breast cancer specific survival. Unadjusted Black-White ICE was associated with better all-cause and breast cancer specific survival, but this relationship was not significant when ICE was controlled for income. Black patients were found to have significantly poorer survival in all models relative to whites. A model with only individual-level variables found Hispanics to have significantly poorer all-cause survival relative to whites (HR 1.42; 95% CI, 1.00–2.01), but

Table 2. Models for all-cause survival and breast cancer specific survival fitted with (top set) and without (bottom set) inclusion of ZCTA SES data

	Model 1.1a: Local Isolation and poverty HR (95% CI)	Model 1.2a: Local Exposure and poverty HR (95% CI)	Model 1.3a: Full LEx/Is and poverty HR (95% CI)	Model 1.4a: LQ and poverty HR (95% CI)	Model 1.5a: ICE with Race and income HR (95% CI)
All cause survival					
Black segregation	0.99 (0.97–1.01)	—	0.87 (0.71–1.07)	0.77 (0.55–1.09)	0.32 (0.03–3.74)
Hispanic segregation	**1.04 (1.01–1.08)**	—	0.91 (0.73–1.14)	1.40 (0.97–2.14)	**184.9 (1.03.475.9)**
Black-Hispanic exposure (LEx/Is only)	—	1.01 (0.98–1.04)	1.29 (0.85–1.96)	—	—
Breast cancer-specific survival					
Black segregation	0.98 (0.95–1.01)	—	1.01 (0.78–1.29)	0.68 (0.42–1.10)	0.511 (0.02–13.8)
Hispanic segregation	1.03 (0.98–1.08)	—	1.06 (0.80–1.40)	1.32 (0.79–2.19)	9.39 (0.13–640.9)
Black-Hispanic exposure (LEx/Is only)	—	1.01 (0.95–1.04)	0.95 (0.56–1.60)	—	—
	Model 1.1b: Local isolation only HR (95% CI)	**Model 1.2b: Local exposure only HR (95% CI)**	**Model 1.3b: Full LEx/Is only HR (95% CI)**	**Model 1.4b: LQ only HR (95% CI)**	**Model 1.5b: ICE with race (no income) HR (95% CI)**
All cause survival					
Black segregation	1.00 (0.98–1.02)	—	0.97 (0.81–1.17)	0.99 (0.74–1.33)	**0.66 (0.49–0.89)**
Hispanic segregation	**1.05 (1.01–1.09)**	—	1.02 (0.83–1.25)	**1.73 (1.21–2.47)**	**2.29 (1.49–3.48)**
Black-Hispanic exposure (LEx/Is only)	—	1.03[a] (1.00–1.07)	1.07 (0.72–1.57)	—	—
Breast cancer-specific survival					
Black segregation	1.00 (0.97–1.02)	—	1.12 (0.90–1.39)	0.95 (0.64–1.41)	**0.65 (0.44–0.94)**
Hispanic segregation	1.04[a] (0.99–1.09)	—	1.19 (0.92–1.52)	**1.72 (1.08–2.47)**	**2.43 (1.43–4.10)**
Black-Hispanic exposure (LEx/Is only)	—	1.02 (0.98–1.06)	0.77 (0.49–1.24)	—	—

NOTE: Segregation hazard ratio magnitude cannot be directly compared across models with different metrics, due to differences in unit definition.
All models were adjusted for patient race, age, and stage. Models 1.1a, 1.2a, 1.3a, 1.4a controlled for ZCTA poverty level. Bolded indicates significance at 95% confidence ($P < 0.05$).
[a]$P < 0.10$.

this became nonsignificant in models which included local Hispanic segregation.

Within-race survival models provided evidence that segregation is related differently to survival across races, as shown in Table 3. Black patients were found to have improved all-cause survival in neighborhoods with higher Black local isolation and LQ, and improved breast cancer specific survival with higher Black local isolation. White patients had significantly poorer survival in ZCTAs with higher Hispanic-White ICE scores adjusted for income (HR 280.9; 95% CI, 1.10–71461.1), but this estimate is highly unstable. Additionally, for whites, the Hispanic LQ ($P = 0.079$) and Hispanic local isolation ($P = 0.056$) were nearly significant predictors of poorer all-cause survival.

Discussion

This article proposes a set of alternative local segregation metrics known as LEx/Is. LEx/Is is conceptually distinct from previous local methods by estimating the relative likelihood of specific racial interactions at the local level. The LQ is the relative percent composition of a specific race/ethnicity, whereas the index of concentrated extremes is an absolute rate difference between "privileged" and "disadvantaged" groups. Comparing these metrics, we found that the local isolation index was most correlated to the LQ. This is expected, as both the LQ and local isolation are only dependent on a single racial proportion within a subunit, whereas ICE is dependent on the percent difference of two races. Although the proposed local isolation metric is similar to the LQ, we consider that the local isolation index may provide a stronger framework for extension and improvement. Future work could incorporate additional data to better estimate the probability of interactions at the local level. In addition, the local exposure index is unique from either LQ or ICE.

A comparison of the distributions of each metric reveals that the local isolation metric tends to be more symmetric and normally distributed, especially in situations of higher overall MSA level segregation. The differences between isolation and LQ are likely due at least in part to selection of the logit term of LEx/Is versus the $\log_{10}(x+1)$ transformation of LQ. For future studies where a normality assumption is necessary, the distributions of different metrics should be considered. Additional transformations can be applied to the LQ and ICE or they can be categorized to make them suitable for these analyses. Proportional hazards models lack such assumptions, allowing us to test all of the metrics for relationships with breast cancer survival in this study.

Survival analyses showed that local segregation had significant relationships with all-cause and breast cancer–specific survival. Notably, models including only patient level covariates identified Hispanic ethnicity as a risk factor for poorer survival, whereas models with a measure of Hispanic segregation associated segregation with poorer mortality but not the patient's Hispanic ethnicity. This difference highlights how using only a patient's race/ethnicity as a variable may mask the areal effect of segregation as an individual-level effect. Local Hispanic isolation and Hispanic-White ICE maintained significant associations even after adjusting for ZCTA SES, indicating that these metrics may be more sensitive than the LQ. The difference between the performance of LQ and local isolation is likely due at least in part to how the logarithmic and logit transformation behave with values very close to 0 or 1. The ICE and LQ are finitely bound by range of proportions. Because of the logistic transformation, LEx/Is will approach $+\infty$ as the proportion product ($p_{im} \times p_{in}$) approaches 1 and will approach $-\infty$ as the product approaches 0. The ICE models, however, violate the assumption of no multicollinearity, making them unsuitable for survival analysis. This high multicollinearity resulted in the unstable confidence intervals shown

Table 3. Patient race-specific survival models controlling for the effects of ZCTA poverty and patient age and stage

	Model 3.1: Local Isolation		Model 3.2: LQ	
	All cause HR (95% CI)	Breast cancer specific HR (95% CI)	All cause HR (95% CI)	Breast cancer specific HR (95% CI)
White patients ($n = 7{,}164$)				
Black segregation	0.99 (0.97–1.02)	0.98 (0.95–1.01)	0.86 (0.59–1.24)	0.69 (0.39–1.20)
Hispanic segregation	1.04[a] (1.00–1.08)	1.04 (0.98–1.09)	1.43[a] (0.96–2.14)	1.47 (0.84–2.57)
Black patients ($n = 940$)				
Black segregation	**0.91 (0.85–0.98)**	**0.91 (0.83–1.00)**	**0.37 (0.14–0.92)**	0.35 (0.11–1.11)
Hispanic segregation	0.98 (0.86–1.11)	0.91 (0.78–1.07)	0.88 (0.21–3.80)	0.49 (0.08–3.07)
Hispanic patients ($n = 252$)				
Black segregation	1.12 (0.92–1.35)	1.16 (0.93–1.44)	3.52 (0.24–52.0)	3.70 (0.21–66.4)
Hispanic segregation	1.02 (0.83–1.25)	1.04 (0.83–1.30)	1.08 (0.16–7.43)	1.20 (0.15–9.58)

NOTE: Segregation hazard ratio magnitude cannot be directly compared across isolation and LQ models, due to differences in unit definition. Bolded indicates significance at 95% confidence.
[a]$P < 0.10$.

in Tables 2 and 3, as multicollinearity results in increased standard error estimates for the effect coefficient (41). It is unclear whether the multicollinearity stems from the extreme segregation seen in the Milwaukee MSA or is a more general concern; additional research is needed to address this question. One possible remedy is to split the models by patient race and only test the effect of the specific ICE which corresponds to the race in question (i.e., Black patients and Black-White ICE).

Black-Hispanic exposure was not significantly related to survival in any model. Nevertheless, the local exposure component of LEx/Is presents a new opportunity to investigate how different racial and ethnic groups co-occupying and interacting socially in the same space could affect health outcomes. While a term looking at the interaction between two LQs is possible, it would not be as easy to interpret as local exposure. Similarly, the ICE focuses on the difference between groups and cannot measure coresidence or diversity directly. Furthermore, local exposure provides a value-agnostic framework to look at racial interactions, whereas ICE requires prior judgment regarding which group is privileged and which is deprived, especially when income-adjusted.

Splitting the models by patient race revealed that the relationship between segregation and survival varied significantly by patient race. Notably, Black patients tended to fare better in communities with high Black isolation for both all-cause and breast cancer specific survival. This finding echoes prior work by Warner and Gomez, who found that Black women living in predominantly Black neighborhoods in highly segregated cities in California experienced improved survival (17). It is very important to note that these results do not necessarily mean that residential racial segregation confers a survival benefit for Black women. Whitman and colleagues found that metropolitan area segregation was associated with larger disparities in Black-White breast cancer mortality (14). Beyond breast cancer, Gibbons and Yang's analysis of Philadelphia neighborhoods found Black individuals living in predominately White neighborhoods were nearly twice as likely to report poor or fair health relative to their counterparts (42). In combination, these findings may suggest that while metropolitan area segregation is associated with poorer survival, within the existing reality of segregation, racial and ethnic enclaves may protect the health of minority residents. Black patients in Black neighborhoods may benefit, for instance, from a combination of increased social support, better access to health care, more willingness to access care, or less exposure to stress due to racism. This "ethnic density effect" has also been documented in the United Kingdom, where minority individuals experienced less interpersonal racism in areas with higher ethnic density and suffer from less disease when economic deprivation is controlled (43). More research is necessary to examine the health effects of living in diverse neighborhoods. There was a limited ability to investigate the effects of diversity in this study given the extreme segregation of Milwaukee, but the local exposure index would be well suited for such an approach.

There are several study limitations. First, data on individual-level SES was not available, and thus our findings rely on ZCTA level socioeconomic measures. It is important not to assume that all patients living in poverty areas were impoverished or the converse. Additionally, this study had very few Hispanic patients ($n = 252$), making any sort of interaction between Hispanic ethnicity and segregation difficult to identify. This study is limited to a single metropolitan area, which is one of the most segregated cities in the country. Thus, these findings are not universally generalizable. In particular, Southern and Western cities have a different history of residential segregation and often have different racial distributions than those in the Midwest and Northeast (44). Studies comparing findings across multiple MSAs are necessary to determine whether these relationships depend on geographic region or overall segregation levels. By pooling multiple MSAs, larger sample sizes would enable the investigation of the interaction of patient race and specific segregation experiences.

Finally, the LEx/Is metrics—like the LQ and ICE—do not account for spatial information about the local areas, such as their location, adjacency, or physical area. Spatial approaches to traditional, non-local segregation metrics exist—such as centrality, spatially adjusted dissimilarity, and measures of spatial heterogeneity (18, 22, 23, 45). These approaches, however, are unsuitable for our goal of describing segregation on a local scale. There are proposals for a combined spatial and local segregation metric, but such approaches are technically challenging and have yet to be applied to health questions (46). A major future direction for the field will be to integrate spatial knowledge into studies of segregation and health outcomes.

In conclusion, this study reveals the critical importance of measurement in research examining relationships between segregation and health outcomes. Findings varied widely depending on the metric used. These metrics have different interpretations and meanings. Future studies would benefit from incorporating multiple segregation measures. More work is necessary to identify relationships between local level segregation and other cancer outcomes, and to determine whether the relationships described here exist in other metropolitan areas. Finally, qualitative studies should complement this work to investigate how segregation is perceived by cancer patients and survivors and to identify potential mechanisms linking segregation to survival. Measures of racial residential segregation are important tools for better understanding cancer survival disparities, and this article highlights the need for a cautious and systematic approach when investigating these relationships.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: A. Bemanian, K.M.M. Beyer
Development of methodology: A. Bemanian, K.M.M. Beyer
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): K.M.M. Beyer
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): A. Bemanian, K.M.M. Beyer
Writing, review, and/or revision of the manuscript: A. Bemanian, K.M.M. Beyer
Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): K.M.M. Beyer
Study supervision: K.M.M. Beyer
Other (I serve as a research mentor for the first author, Mr. Bemanian.): K.M.M. Beyer

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