



Racial disparities of liver cancer mortality in Wisconsin

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Abstract

Purpose To calculate tract-level estimates of liver cancer mortality in Wisconsin and identify relationships with racial and socioeconomic variables.

Methods County-level standardized mortality ratios (SMRs) of liver cancer in Wisconsin were calculated using traditional indirect adjustment methods for cases from 2003 to 2012. Tract-level SMRs were calculated using adaptive spatial filtering (ASF). The tract-level SMRs were checked for correlations to a socioeconomic advantage index (SEA) and percent racial composition. Non-spatial and spatial regression analyses with tract-level SMR as the outcome were conducted.

Results County-level SMR estimates were shown to mask much of the variance within counties across their tracts. Liver cancer mortality was strongly correlated with the percent of Black residents in a census tract and moderately associated with SEA. In the multivariate spatially-adjusted regression analysis, only Percent Black composition remained significantly associated with an increased liver cancer SMR.

Conclusions Using ASF, we developed a high-resolution map of liver cancer mortality in Wisconsin. This map provided details on the distribution of liver cancer that were inaccessible in the county-level map. These tract-level estimates were associated with several racial and socioeconomic variables.

Keywords Liver cancer · Race · Disparities · Cancer mapping · Cancer epidemiology

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Introduction

Liver cancer is a major cause of cancer mortality in the United States. In 2016, there were 39,220 new cases of liver cancer and 27,170 deaths, with a poor 5-year survival rate of 18% [1]. The predominant form of adult liver cancer is hepatocellular carcinoma (HCC), accounting for the vast majority of cases in the United States [2]. HCC is a multifactorial disease which can result due to chronic damage from multiple liver diseases including Hepatitis B, Hepatitis C, alcoholic liver disease, and non-alcoholic fatty liver disease [2, 3]. Liver cancer disproportionately affects minority racial and ethnic groups. The rate per 100,000 is significantly higher in Blacks/African Americans (8.4), Hispanics (9.1), Asian/Pacific Islanders (APIs) (9.5), and American Indians/Alaska Natives (AI/ANs) (10.3) than non-Hispanic Whites (5.7) [4].

Despite these stark racial disparities there have been few studies investigating the relationship between racial composition and liver cancer mortality. In a 2018 systematic review of ethnic density and cancer, only one out of 51 reviewed papers focused on liver cancer outcomes [5]. Neighborhoods with higher percentages of immigrant residents were associated

with 21% higher liver cancer incidence among Hispanic females and 23% higher incidence among API males [6]. A 2018 investigation of HCC incidence in Medical Service Study Areas (MSSAs) of California also found that HCC incidence was elevated among Hispanics and APIs, and incidence was further increased if they lived in predominately ethnic neighborhoods [7]. This study also found that neighborhoods with significantly higher rates of HCC incidence tended to have significantly higher proportions of residents living below the federal poverty line. Previous literature has evaluated differences in rates of liver cancer incidence among foreign-born APIs, US-born APIs, and White individuals [8]. Foreign-born APIs had significantly higher incidence of liver cancer than US-born APIs, and US-born APIs had higher incidence of liver cancer than White individuals. Despite nationally higher rates of liver cancer mortality among Blacks/African Americans relative to Whites, there are few studies which specifically investigate this disparity.

The field of cancer epidemiology has made great strides in mapping mortality in the past decade due to advancements in GIS technology and methods that estimate mortality at much higher resolutions [9–11]. While liver cancer rates have been rising over the past decade, the national mortality rate is fairly low (6.6 per 100,000) [1, 4, 12]. This makes high-resolution (i.e., ZIP code or census tract level) mapping of liver cancer mortality rates challenging, because the rate of cancer in any given small geographic area may be highly unstable from year to year. To the authors' knowledge, the only other study that maps liver cancer incidence or mortality with high resolution is a study of HCC incidence in New York City [13]. In order to overcome this challenge, disease mapping methods such as adaptive spatial filtering (ASF) can be used to estimate spatially detailed but stable disease rates [14]. This approach has been previously used to investigate breast and colorectal cancer rates in Wisconsin and Iowa [15–17].

This study extends prior work to apply ASF in estimating liver cancer mortality and uses these estimates to examine potential explanatory factors. Tract-level demographic variables were analyzed in association with liver cancer rates to demonstrate the utility of this mapping method to identify communities at greater risk for liver cancer mortality. In addition, this study investigated whether tracts with higher proportions of racial/ethnic minorities and lower socioeconomic status were associated with higher rates of liver cancer mortality.

Methods

Liver cancer mortality data for residents of the state of Wisconsin were obtained from the Wisconsin Department of Health Services' Vital Record Services. All primary liver

cancer deaths (ICD10 Codes: C22.0–C22.9) from 1 January 2003 to 31 December 2012 were included. These records were linked to their location of residence by ZIP code. Age, sex, race, ethnicity, and cause of death were recorded. A total of 3,204 liver cancer deaths were included in the analysis. A breakdown of the race/ethnicity of these cases has been included in Online Resource 2. Population race counts by census tract were obtained from the 2010 US Census [18]. To calculate the racial composition for each census tract, all Hispanic population counts, regardless of race, were classified as "Hispanic." All other racial/ethnic categories were defined as the non-Hispanic population of that race (i.e., "White" refers to non-Hispanic White). Three markers of socioeconomic status were obtained from the 2008 to 2012 5-year average of the American Community Survey: percent of tract residents who graduated with a bachelor's degree or higher (G), percent of residents who were unemployed (U), and the tract's median household income (I) [19]. These variables were combined to calculate an index of socioeconomic advantage (SEA) using Eq. 1.

$$SEA = Z(\log(I)) + Z(\log(G)) - Z(\log(U)) \quad (1)$$

Equation 1: Calculation of socioeconomic advantage (SEA) based on median household income (I), percent graduated with a bachelor's degree or higher (G), and percent unemployment (U). $Z(x)$ represents a z-score of x to a normal distribution with $\mu=0$, $\sigma=1$.

The SEA index was used to prevent overfitting the statistical model. The construction of this index is based on other measures of deprivation such as the concentrated disadvantage index and the Townsend index [20, 21]. However, car and home ownership were not included since the study area contains a wide variety of urban, suburban, and rural tracts. While other health disparities studies have integrated race and socioeconomic status into a single variable [20, 22], we chose to separate these factors to determine if they had independent effects. Since all non-White racial/ethnic groups experience higher rates of liver cancer relative to Whites on aggregate, it was important to assess if the relationship varied across different non-White groups. Due to the complex historical relationship between race and socioeconomic status, interaction terms were tested to determine if the effects of racial/ethnic composition were moderated by the socioeconomic advantage of the neighborhood. Rurality was calculated as the proportion of rural census blocks within a census tract, according to the 2010 US Census urban/rural designations.

Mortality rates were calculated using ASF [14]. This approach is briefly summarized here. We used a spatial grid of points based on the centroids of census block groups. From each grid point, a spatial filter expanded to include a minimum number of liver cancer deaths in nearby ZIP Code Tabulation Areas (ZCTAs) to create a stable estimate for the

grid point. A threshold of 30 deaths was used based on previous work using ASF for other cancers in Wisconsin [23]. The demographics of the ZCTAs within the filter are used to calculate an age and sex adjusted expected number of deaths. The observed number of deaths within the filter is divided by the expected number of deaths to create a standardized mortality ratio (SMR), which is then assigned to the block group. Census tract SMR estimates were calculated by taking the mean of the block group estimates within the tract. All SMR values are given relative to the state's liver cancer mortality rate. To demonstrate the importance of higher resolution estimates of liver cancer mortality, county-level SMRs were calculated using a similar adjustment method over the same time period.

Tract-level cancer mortality was evaluated first for linear correlation with the demographic and socioeconomic variables. Liver cancer mortality was then modeled as a function of socioeconomic advantage, tract rurality, and the percentage of Black/African American, Hispanic, API, and AI/AN residents. Cancer mortality was log-transformed for regression and correlation analyses due to its right skewed distribution. This was specified as a spatial error regression models with a queen contiguity spatial weights matrix used for the spatial error model [24]. Ordinary linear squares model specification was rejected due to the high level of spatial autocorrelation (Moran's I $p < 0.001$). Due to some instability in the estimates for the socioeconomic variables, tracts were excluded if the standard errors for any of the three ACS variables were outliers (> 1.5 the interquartile range). A total of 74 tracts out of 1,393 total tracts were removed from the regression analysis.

Results

Tract-level estimates of liver cancer SMRs are shown in Fig. 1. High SMRs were primarily concentrated in Milwaukee and several rural regions in the southwest and northern areas of Wisconsin. Tract-level ASF estimates were compared to county-level estimates in Online Resource 1. Using the tract-level estimates, we tested whether racial and ethnic composition were associated with liver cancer mortality by tract across the entire state. The descriptive statistics of the tract-level variables and bivariate correlation results are included in Online Resource 3. Most census tracts had a small proportion of non-White racial groups, and the average tract was 82.8% White. Out of the non-White groups, Blacks/African Americans had the highest mean percentage followed by Hispanics, APIs, and AI/ANs. However, the percent AI/AN in a tract had the largest variance of any racial group and there were several AI/AN majority tracts.

The spatial patterns of these variables are shown in Fig. 1. Most of the state is comprised of highly rural tracts ($> 80\%$

rural blocks), apart from the major metropolitan statistical areas (MSAs) and several other small micropolitan communities. Areas of high Black/African American and Hispanic composition were confined predominately to the southern metropolitan areas of Milwaukee, Madison, and Racine, while tracts with high AI/AN composition were in rural northern areas, given the distribution of American Indian reservations. The highest degree of variability in SEA was found in and around the large MSAs.

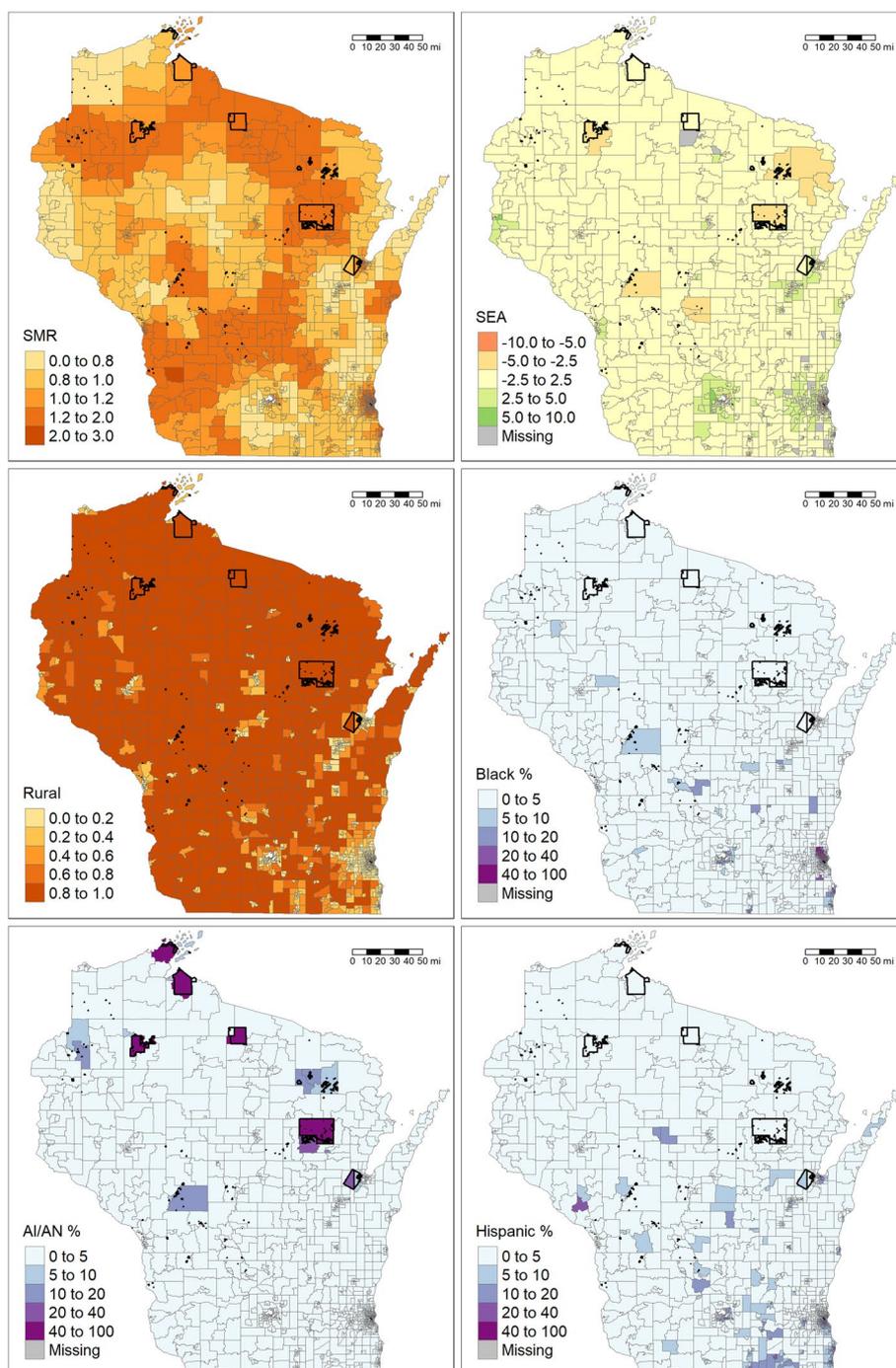
The results of the statewide correlation analysis (reported in Online Resource 3) identified that census tracts with a high percentage of Black/African American residents were strongly associated with increased liver cancer mortality. SEA was moderately associated with lower mortality. Individual socioeconomic measures were all moderately associated with mortality. Of those, unemployment was the most strongly related while percent bachelor's degree attainment had the weakest association. Rurality showed a moderately weak association with decreased liver cancer SMR. Percent Hispanic and percent AI/AN residents were both weakly associated with higher mortality. Percent API was not associated with mortality.

Spatial regression analysis results are shown in Table 1. For the racial composition variables, all effects are given per 20% absolute increase in of the composition (e.g., the effect for percent Black corresponds to the relative change in SMR of a 60% Black tract versus a 40% Black tract). The only significant predictor was Black racial composition. The relative change in mortality for each 20% change percent Black was 4.5% (95% CI 2.7–6.4%). Therefore, a tract with 90% Black population would be predicted to have a 19.9% higher rate of liver cancer mortality (95% CI 11.6–29.1%) relative to the mean tract (Percent Black: 7.7%) in Wisconsin. Interactions between SEA and racial percentages were not statistically significant except for the interaction between SEA and Percent API. However, while this effect was statistically significant ($p = 0.017$), the effect size yielded a rate ratio (RR) of 0.9998 (95% CI 0.9996–0.9996) suggesting it is likely not clinically significant. These interaction terms were removed, and Table 1 represents the final regression model.

Discussion

This study demonstrates the benefits of adaptive spatial filtering in mapping a less common disease such as liver cancer. Using traditional disease mapping scales such as counties can hide variance. This is especially problematic in counties which have heterogeneous populations, such as Milwaukee County. Online Resource 1 shows that calculating county-level SMRs suggests that Milwaukee County has an elevated rate of liver cancer, but the ASF SMRs show there are both extreme hotspots and coldspots within the

Fig. 1 Maps of liver cancer mortality and covariates in Wisconsin. Black borders represent American Indian reservations and lands. Upper Left: Liver Cancer Standardized Mortality Ratio, Upper Right: Socioeconomic Advantage (NA values either due to no residents or survey standard error is too large), Center Left: Tract Rurality, Center Right: Percent Black/African American Residents, Bottom Left: Percent American Indian/Alaska Native Residents, Bottom Right: Percent Hispanic Residents



county. ASF rates have the benefit of being stabilized and do not need as many cases to estimate rates. There has been one previous ZCTA level analysis of liver cancer, which used crude rates in New York City [13]. While that approach was appropriate for the highly populous study area of New York, crude rates are not sufficient for estimating rates in lower population areas such as rural Wisconsin. This study demonstrated how ASF can be used across a large and heterogeneous study scope.

This study evaluated whether there was a general relationship between liver cancer mortality and racial composition, rurality, and socioeconomic status in the state of Wisconsin. The results of these analyses strongly suggest that liver cancer mortality was higher in predominately Black census tracts. There was a weak correlation between AI/AN composition and liver cancer mortality, but this association was not significant in the spatially-adjusted multivariate analysis. This study found no evidence that liver cancer mortality is

Table 1 Results of regression analyses

	Rate ratio (95% CI)	<i>p</i>
Multivariate spatial error model		
SEA	1.000 (0.996–1.003)	0.914
Percent Black	1.045 (1.027–1.064)	< 0.001
Percent Hispanic	0.987 (0.963–1.012)	0.301
Percent API	1.011 (0.974–1.048)	0.567
Percent AI/AN	1.010 (0.991–1.030)	0.302
Rurality	1.009 (0.988–1.031)	0.392
AIC	–4,726.9	

The rate ratios are exponentiated coefficients of the log-linear model. Rate ratios for racial percentages expressed per 20% (absolute) change

AIC Akaike information criterion

related to the percent API residents and only a very weak correlation between percent Hispanic and liver cancer mortality, despite the elevated liver cancer rates in the API and Hispanic populations nationally and prior studies identifying API and Hispanic ethnic enclaves having higher rates of HCC incidence [4, 6, 7]. This relationship may not have been replicated in Wisconsin due to the low number of API and Hispanic majority tracts. SEA was associated with lower liver cancer mortality in the correlation analysis, but this relationship was not significant in the multivariate analysis. Rurality did not have a clear relationship with liver cancer mortality. It was weakly correlated with lower tract mortality, and no relationship was found in the multivariate analyses. This was surprising, given previous studies that show rural counties tend to have higher rates of risk factors associated with liver cancer, such as obesity and smoking, and overall higher rates of chronic health problems [3, 25, 26].

Consistent with other public health problems, “place matters” for liver cancer mortality. Due to the issue of spatially correlated residuals, a spatial error model (SEM) was required instead of a traditional linear regression. Conceptually, the SEM defines the error term as consisting of two separate portions: a normally distributed independent term and a spatially autocorrelated term. This spatial term represents other place-based phenomena that are not captured by the model’s specifications that are associated with increased risk for liver cancer. Such phenomena could include local differences in healthcare quality and access, neighborhoods with higher rates of viral hepatitis infections, or rates of alcohol use. Clusters of low SEA likely indicate areas where these hazards agglomerate. This could explain why SEA was not significant in the spatial error model. By adjusting for the effect of clustering, the relationship between SEA and liver cancer mortality diminishes. This suggests the relationship between SEA and mortality is not uniform across the entire state.

This study is limited by a cross-sectional, ecological design, which prevents any sort of inference on causality. The outcome and determinants of health under study were defined at the census tract level, while liver cancer occurs on the individual level. Additionally, these models only examined the relationship between social determinants and liver cancer at the point of death. However, causes of liver cancer (e.g., viral hepatitis, alcohol use) frequently require years to decades of chronic hepatic damage before resulting in cancer [27]. Given the long latency from initial development of liver disease to liver cancer and death, this is an incomplete assessment of the role social determinants may play in determining liver cancer disparities. Repeating this study in the context of other states may be useful, given the differences in the history of racial migration and discrimination across the many regions of the United States [28, 29].

Conclusion

The results of this study demonstrate the importance of a place-based approach when assessing cancer disparities. The resulting maps demonstrate a more detailed view of the distribution of liver cancer in Wisconsin; these maps provided detailed information on the racial and socioeconomic disparities in liver cancer mortality. The findings of this study indicate that Black/African American communities in Wisconsin are at the highest risk of increased liver cancer mortality. This study’s findings can be used to guide future public health efforts in the state and these methods can be applied to other public health problems. Future work is necessary to assess the spatial patterns of specific risk factors for liver cancer to inform interventions to reduce the burden of liver cancer.

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