CORRESPONDENCE

Multiple myeloma incidence, transplant utilization, and mortality- impact of social vulnerability

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To the editor:

Multiple myeloma (MM) is a common hematologic malignancy in the United States with various well-documented disparities [1]. The CDC-developed Social Vulnerability index (SVI) contains 16 different social variables at the census tract level and represents a useful geospatial tool with broad applications to help investigate cancer disparities [2]. To understand the role of social vulnerability in MM, we conducted the following research to evaluate the impact of SVI as well as other important variables such as race and ethnicity on transplant utilization and mortality among patients with MM in Wisconsin, considering access to transplant a surrogate to access to tertiary care. Further, to complement our SVI analysis, we utilized geospatial mapping to investigate state-wide patterns in MM incidence, transplant utilization, and mortality.

This study was conducted after Institutional Review Board and WI Division of Public Health Data Governance Board approvals. Patients 18 years and older with newly diagnosed MM from 2009 to 2019 reported to the Wisconsin Cancer Reporting System (WCRS) were identified. Transplant utilization was calculated by year across race and ethnicity groups. Logistic regression models evaluated SVI's impact on transplant utilization and mortality, controlling for age at diagnosis, sex, race/ethnicity, and diagnosis year. Adaptive spatial filtering [3] was used to generate incidence, mortality, and transplant utilization maps. Choropleth maps were created to map the spatial distribution of SVI by 2010 census tract [2]. Detailed methods are described in Supplementary Materials.

Among 4814 patients with newly diagnosed MM, 87% were non-Hispanic White (NHW), 9% non-Hispanic Black (NHB), 2% Hispanic, 2% NH Other/Unknown, with 55% male, and a mean age of 70 years (standard deviation, SD 12) at diagnosis (Table S1), consistent with Wisconsin's 2010 census demographics (6.2% NHB) [4]. Overall, SVI was 0.47: least vulnerable (0–0.25), moderately vulnerable (0.26–0.5), more vulnerable (0.51–0.75), and most vulnerable (0.76–1) represented 28%, 26%, 25%, and 21% of the cohort, respectively. Median follow-up for the entire cohort, non-transplant group, and transplant group was 30.6, 29.1, and 35.1 months, respectively.

In this cohort, 1238 (26%) patients received transplant. Comparing the non-transplant to transplant groups, mean age was 72 (SD 11) versus 61 (SD 9) years, $p < 0.001$ and overall SVI was 0.48 (SD 0.29) versus 0.45 (SD 0.29), $p < 0.001$, respectively (Table S1). Race and ethnicity were significantly associated with transplant use (23% NHB, 21% Hispanic, and 16% NH Other/Unknown compared to 26% NHW patients, $p = 0.033$). Comparing 2009–2014 to 2015–2019, transplant utilization increased from 21% to 30% in all patients ($p < 0.001$), 22% to 31% in NHW patients ($p < 0.001$), 18% to 28% in NHB patients ($p = 0.01$), 13% to 29% in Hispanic patients ($p = 0.064$), and 9% to 28% NH Other/Unknown patients ($p = 0.01$). Logistic regression demonstrated older age at diagnosis, minority race and ethnicity, higher SVI, and earlier year of diagnosis to be independently associated with lower transplant utilization (Table 1).

At a median follow-up of 30.6 months, 2,852 (59%) were deceased; the cause of death was plasma cell disorders in 1837 (64%), cardiovascular disease in 209 (8%), other organ failure in 223 (8%), second malignancy in 209 (7%) of which 162 were solid tumors and 47 were hematological malignancies, and infection/inflammation in 106 (4%). Logistic regression demonstrated older age at diagnosis, higher SVI, lack of transplant utilization, and earlier year of diagnosis, but not race and ethnicity, to be independently associated with mortality (Table 1).

The SVI map showed higher SVI across many rural areas (Fig. S1A) and pockets of high SVI within urban areas such as northern and central Milwaukee (Fig. S1B). The areas with the highest MM incidence and mortality (≥1.91 times the expected rate) overlapped and were found in Milwaukee, Waukesha, Racine, Trempealeau, and Jackson Counties (Fig. S2A, B). The northern, western, and southern regions revealed larger areas of low transplant utilization compared to the eastern region (Fig. S2C). From 2009 to 2019, 26% of all patients with MM in Wisconsin received transplant. Over time, transplant utilization improved for all racial and ethnic groups, aligning with findings from a prior institutional review of MM transplant utilization from 2012 to 2022 by our group [5]. However, despite these improvements, the overall transplant utilization in Wisconsin remains low. This low utilization rate may be even more difficult to increase in the modern era of highly effective novel therapies. Interestingly, despite lower transplant utilization, racial and ethnic minorities did not have higher mortality. Future studies should investigate whether other targets aside from increasing transplant utilization may have a larger effect on improving outcomes for racial and ethnic minorities.

Further, our analysis highlights the effect of social vulnerability and geography on MM epidemiology in Wisconsin. We are the first to investigate the impact of SVI on MM transplant utilization and all-cause mortality. A single-center study by Salafian et al. reported that higher SVI values were associated with lower odds of MM progression-free survival and overall survival post-AHCT [6]. We found that higher SVI was independently associated with lower transplant utilization and higher mortality in MM. SVI appears to be a useful proxy to easily identify high impact areas for MM interventions.

Our state-wide geospatial mapping investigated patterns of MM incidence, transplant utilization and mortality. With the majority of Wisconsin's Black and Hispanic population residing in south and southeastern [4], areas with high incidence, high mortality, and low transplant utilization in those counties (Fig. S2A–C) identify high-impact areas to combat racial and ethnic disparities in MM treatment and outcomes. The high incidence and mortality areas in northern Milwaukee correspond to the geospatial distribution of high SVI (Fig. S1B) and Black individuals in Milwaukee County

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Table 1. Logistic Regression for Transplant Utilization and Mortality.

Characteristic	OR[a]	95% CI[a]	p-value	OR[a]	95% CI[a]	p-value
	Transplant Utilization			Mortality		
SVI – Continuous (No Race Theme)	0.75	0.58, 0.99	**0.041**	1.49	**1.16, 1.92**	**0.002**
Age at Diagnosis - Continuous	0.90	0.90, 0.91	**<0.001**	1.07	1.07, 1.08	**<0.001**
Sex			0.7			0.067
Female	—	—		—	—	
Male	0.97	0.84, 1.12	0.7	1.14	0.99, 1.31	0.067
Race/Ethnicity			**<0.001**			0.7
NH White	—	—		—	—	
NH Black/African American	0.47	0.35, 0.62	**<0.001**	1.04	0.81, 1.34	0.73
Hispanic	0.35	0.19, 0.62	**<0.001**	0.77	0.47, 1.26	0.29
NH Other/Unknown	0.41	0.22, 0.71	**0.0023**	0.99	0.62, 1.60	0.96
Year of Diagnosis			**<0.001**			**<0.001**
2009	—	—		—	—	
2010	0.89	0.59, 1.33	0.57	1.25	0.83, 1.90	0.28
2011	0.89	0.60, 1.32	0.56	0.62	0.43, 0.89	**0.01**
2012	1.44	0.99, 2.10	0.059	0.57	0.40, 0.83	**0.0029**
2013	1.16	0.80, 1.70	0.43	0.48	0.34, 0.68	**<0.001**
2014	1.34	0.93, 1.95	0.12	0.35	0.25, 0.50	**<0.001**
2015	1.97	1.38, 2.83	**<0.001**	0.29	0.14, 0.29	**<0.001**
2016	2.03	1.41, 2.92	**<0.001**	0.21	0.14, 0.29	**<0.001**
2017	2.16	1.50, 3.11	**<0.001**	0.18	0.13, 0.25	**<0.001**
2018	2.21	1.55, 3.17	**<0.001**	0.10	0.07, 0.14	**<0.001**
2019	2.29	1.62, 3.25	**<0.001**	0.06	0.04, 0.09	**<0.001**
Transplant Utilization			—			**<0.001**
No	—	—		—	—	
Yes	—	—	—	0.41	0.34, 0.48	**<0.001**

Statistically significant p-values are bolded.
[a]*OR* Odds Ratio, *CI* Confidence Interval, *SVI* Social Vulnerability Index.

[4], reflecting the fact the Milwaukee is one of the most segregated cities in the United States [7]. Outside of south and southeastern Wisconsin, the areas with high incidence and mortality around Brown County align with a significant concentration of Wisconsin's Hispanic population [8]. Beyond geographical concentrations of racial and ethnic minorities, around a fourth of Wisconsin's population lives in rural areas [9]. Rural cancer patients face many challenges and disparities in cancer care delivery and outcomes [10]. Previous studies in MM have also shown that rural patients have higher incidence and mortality [1]. Three of the four MM transplant centers in the state are in south and southeastern Wisconsin, which may partially explain the large areas of low transplant utilization in the northern and western parts of the state. Regions of low transplant utilization exist even within southeastern Wisconsin, which suggests that aside from proximity to transplant center, other factors are driving low transplant utilization. Limitations of our study are detailed extensively in the Supplementary Materials.

In conclusion, this state-wide analysis reveals overlapping areas of higher-than-expected MM incidence and mortality. Stem cell transplantation is underutilized in Wisconsin, but utilization has improved over time, with racial and ethnic gaps decreasing. Considering access to transplantation as a surrogate to access to novel MM therapies (e.g., bispecific antibodies, CAR-T) and clinical trials, which have severe underutilization by similar racial/ethnic and demographic groups [11], these findings have implications beyond transplant utilization and highlight key areas and vulnerable populations that should be a priority for further investigation and interventions. The correlation of SVI to transplantation access is mirrored in novel therapies, as demonstrated by a recently published study finding that patients with hematologic malignancies residing in areas with higher SVI were less likely to receive CAR-T therapy [12]. Solutions to improving outcomes for vulnerable populations are systemic in nature, interventions to address issues including but not limited to poverty, unemployment, financial toxicity, education, and housing and food insecurity. Community engagement, including partnerships with local organizations, mobile health units, and federally qualified health centers, will be essential to reach vulnerable populations and tailor interventions to local needs. Drivers of higher incidence, worse mortality, and lower transplant utilization in these priority groups need to be studied in future efforts. Importantly, while some countries around the world have adopted metrics similar to the SVI that are regional-specific [13] and conducted geospatial mapping [14] to access cancer epidemiology, we believe that these methods can be more broadly adopted and applied beyond the United States context. We believe that our methodology of utilizing both SVI and geospatial mapping can be widely adopted to identify vulnerable populations and geographical opportunities for interventions in local contexts globally.

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DATA AVAILABILITY

Data is available through request and approval from the WI Cancer Reporting System. Social Vulnerability Index data is publicly available from the Centers for Disease Control and Prevention and the Agency for Toxic Substances and Disease Registry.

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AUTHOR CONTRIBUTIONS

JFW and AD contributed to the study conception and design. Material preparation and data collection were performed by NE. Analysis were performed by NE and YZ. The first draft of the manuscript was written by JFW, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

COMPETING INTERESTS

JFW, NS, YZ, BC, and TWFY declare no conflicts of interest. AD reports clinical trial funding to institution - Abbvie, Alexion, Prothena, Janssen, Novartis, and Regeneron; IRC, DMC, or Steering Committee role with Abbvie, BMS, Janssen, and Prothena; Advisory Board role with Abbvie, BMS, Janssen, Prothena, and Pfizer.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Approval was granted by the Institutional Review Board of the Medical College of Wisconsin and the Wisconsin Division of Public Health Data Governance Board. All methods were performed in accordance with the relevant guidelines and regulations. A limited data set was utilized from the WI Cancer Reporting System where the only HIPAA identifiers utilized are dates or certain allowable geographic subdivisions. Thus, informed consent was not applicable for this study.

ADDITIONAL INFORMATION

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41409-025-02733-9.

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