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Disparities in Multiple Myeloma Treatment Patterns in the United States: A Systematic Review

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Abstract

We performed a systematic review of the literature investigating the demographic and insurance-related factors linked to disparities in multiple myeloma (MM) care patterns in the United States from 2003 to 2021.

Forty-six observational studies were included. Disparities in MM care patterns were reported based on patient race in 76% of studies (34 out of 45 that captured race as a study variable), ethnicity in 60% (12 out of 20), insurance in 77% (17 out of 22), and distance from treating facility, urbanicity, or geographic region in 62% (13 out of 21). A smaller proportion of studies identified disparities in MM care patterns based on other socio-economic characteristics, with 36% (9 out of 25) identifying disparities based on income estimate or employment status and 43% (6 out of 14) based on language barrier or education-related factors.

Sociodemographic characteristics are frequently associated with disparities in care for individuals diagnosed with MM. There is a need for further research regarding modifiable determinants to accessing care such as insurance plan design, patient out-of-pocket costs, pre-authorization

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criteria, as well as social determinants of health. This information can be used to develop actionable strategies for reducing MM health disparities and enhancing timely and high-quality MM care.

Keywords

Hematologic malignancies; health equity; race; health insurance; social determinants of health

INTRODUCTION

Multiple myeloma (MM) is one of the most common hematologic malignancies in the US with an estimated 34,470 incident cases and 12,640 deaths in 2022.[1] Black individuals have a dramatically higher incidence of MM, as well as a higher rate of MM mortality, compared with White individuals, likely due to several, complex risk factors, which may include genetics and differences in exposure to established MM risk factors.[2] Nevertheless, when the same treatment is provided, Black patients experience similar or better survival after MM diagnosis compared with White patients.[3–6]

Over the past two decades, major advances in the treatment of MM have improved overall survival considerably.[7] However, the benefits have disproportionally been observed among non-Hispanic White individuals, presumably due to under-treatment of minority patients.[8,9] High costs of novel medications and insurance coverage-related factors may have a role in these treatment disparities but data supporting such assertions are conflicting.[10–16]

To our knowledge, there has not been a systematic synthesis of the literature investigating insurance-related factors and social determinants of health (SDOH) linked to disparities in MM care patterns in the United States. This systematic review aimed to examine disparities in MM treatment patterns based on race, ethnicity, and health insurance-related factors among adults in the United States from 2003 to 2021. We have also examined whether geographic factors and SDOH were captured in studies examining disparities in MM care delivery during that time.

METHODS

We followed PRISMA reporting guidelines for this systematic review.[17] The review protocol was registered with the international prospective register of systematic reviews (PROSPERO ID: CRD42022299528) at the onset.

Literature search

Biomedical literature databases were searched using strategies created in collaboration with a medical librarian. The search was limited to the English language and the date range of 2003 to 2021 in PubMed, Ovid Medline, Embase.com, Web of Science, Cochrane Central Register of Controlled Trials, and Clinicaltrials.gov. The search used a combination of standardized terms and keywords including, but not limited to, (multiple myeloma OR plasma-cell myeloma) AND (disparity OR health insurance OR Medicare OR Medicaid OR uninsured OR socioeconomic factors OR minority groups OR African Americans OR

Hispanic OR Latino OR Asian-American). There were a total of 2,393 results imported into EndNote™ reference management software (Clarivate, Philadelphia, US). 1,507 duplicates were identified in Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia), bringing the final total to 886 unique citations. Full search strategies are provided in Appendix Table A.1.

Studies with the following characteristics were eligible for inclusion in our review: original investigations of U.S. adult populations with MM whose primary or secondary aims were to investigate differences in MM treatment patterns by patient race/ethnicity or insurance-related factors. Eligible study types included cross-sectional, cohort, case-control studies, and randomized controlled trials. Preprints, published abstracts, as well as conference proceedings were not included.

Two independent reviewers (H.G. & M.A.F) examined the title and abstract of these identified articles using Covidence; 830 were excluded due to not being relevant to the review question, and 56 met the criteria of relevance. The full texts of the 56 articles were reviewed; three studies were excluded due to their study aims not being within the scope of the review, five for not meeting the study outcome criteria, one for not meeting the study setting criteria, and one for being a conference proceeding; 46 observational studies were included. The flow chart of the selection process is presented in Appendix Figure A.1.

Data extraction

Two independent reviewers (H.G. & M.A.F) manually extracted the following data items from the 46 manuscripts: bibliographic information, study aims, participants & data source, study design and outcomes, measures of effect size, association between the predictors of interest and disparities in the outcomes of interest, as well as the study funding source and authors' conflicts of interest.

A narrative (descriptive) synthesis of the collected data was conducted. Findings were grouped into categories based on the outcome of interest, including disparities in care patterns pertaining to the receipt of novel agents (as assessed at the time of the study period/by the authors) for induction therapy, stem cell transplant (SCT), and supportive care. Studies that had more than one outcome of interest are represented in each applicable category.

Quality assessment

The study quality assessment tools for Observational Cohort and Cross-Sectional Studies developed by the National Heart, Lung, and Blood Institute of the National Institutes of Health were used to assess the risk of bias in each study.[18]

RESULTS

The quality assessment of the included studies is presented in Appendix Table A.2. The maximum quality assessment score based on the Quality Assessment Tool for Cohort and Cross-Sectional Studies was 14, with a higher score indicating better overall quality.[18] Three studies had a quality score of 12;[19–21] 37 studies scored 11;[4,6,12–14,22–53] and five studies

scored between 9–10.[34,54–57] One study[58] was not evaluated using these criteria due to its mixed-methods research approach. Given that some of the criteria for assessing study quality, such as repeated exposure assessment and study participant follow-up are not typical for cross-sectional studies, we present the list of criteria not met, along with the study type, and the overall quality score, in Appendix Table A.2.

Study characteristics, including the aims relevant to this review's objectives, study participants, the outcome of interest, and key relevant findings are presented in Appendix Table A.3. More studies examining MM treatment pattern disparities were published in recent years, with 36 included studies published from 2017 to 2021, compared to only 10 during 2007–2016 (Appendix Table A.3). Several studies examined SCT (n=17) and novel agents use for induction therapy (n=13); 10 studies focused on timeliness of care, nine on disparities in the use of supportive care. Only five studies focused on maintenance therapy and two on enrollment in clinical trials (Appendix Table A.3).

Overall, 76% of studies identified significant disparities in MM treatment patterns based on patient race (34 out of 45 that captured race as a study variable), 60% (12 out of 20) based on ethnicity, and 77% (17 out of 22) based on insurance characteristics (Table 1); 62% (13 out of 21) found disparities based on distance from treating facility, urbanicity, or geographic region (Table 2). A smaller proportion of studies identified disparities in MM care patterns based on other socio-economic characteristics, with 36% identifying significant disparities based on income estimate or employment status (nine out of 25 that captured those as study variables) and 43% (six out of 14) based on language barrier or education-related factors (Table 2).

Specific to the condition studied, we also evaluated whether each study included patient performance status or comorbidities as study variables (Appendix Table A.3). Out of 46 included studies, 30 adjusted for patient performance status or comorbidities when examining the association between race, ethnicity, or health insurance characteristics and treatment patterns in patients with MM; six studies captured those variables but did not report controlling for them when examining the associations of interest to this review; and 10 studies did not report capturing patient performance status or comorbidities as study variables. Charlson Comorbidity Index and its modifications were most commonly used for comorbidity status adjustment (Appendix Table A.3).

Disparities in novel agents use for induction therapy

Among 13 studies that studied novel agents use for induction therapy, nine reported significant variations by race[6,13,19,22,29,30,51,52,54] (out of 13 that reported race as study variable) two by ethnicity[30,54] (out of three), and two by insurance-related characteristics[21,52] (out of four, Appendix Table A.3). For example, Derman et al, based on an analysis of 639 newly diagnosed MM patients during 2011–2018, reported that Black patients were less likely to receive triplet therapies, compared to White individuals (55% vs. 73%, P<0.001).[19] This included combined proteasome inhibitor (PI) and immunomodulatory drug (IMiD) regimens (35% vs. 46%) and PI and alkylator triplet therapy (20% vs. 27%).[19] Ailawadhi et al., in a study of 4,830 patients with MM diagnosed between 2007 −2013, found an increasing trend of novel therapy use within six months

of MM diagnosis over time in African American (AA), Hispanic, and White patients, however, the uptake increased at a faster rate among White patients compared to AA individuals (P<0.05), while there were no significant differences between Hispanic and White patients.[22]

Olszewski et al., in their study of 3,038 Medicare beneficiaries diagnosed with MM from 2007 to 2011, found that IMiD use was significantly associated with the receipt of low-income subsidy but this association significantly differed by age group. Low-income subsidy recipients aged 75–84 years had a 32% higher (95% CI, 16%−47%) relative probability of receiving IMiD compared with non-recipients, while the difference was not significant in the younger and older subgroups.[21] Receipt of low-income subsidy was associated with a lower risk of delays between medication refills in all age groups (adjusted relative risk, 0.54; 95% CI, 0.32–0.92).[21]

Other studies did not find disparities in the utilization of upfront novel agents based on race,[4,21,24,31] ethnicity,[22] or insurance-related characteristics[31] (Appendix Table A.3). For example, based on an analysis of 2,837 White and AA adults with newly diagnosed symptomatic MM from September 2009 and April 2016 enrolled in an observational registry, the proportions of AA and White patients who received triplet treatment regimen were not statistically different (44% of non-SCT and 72% of SCT candidate AA patients vs. 48% of non-SCT and 72% of SCT candidate White patients).[24] Furthermore, the types and duration of induction therapy were similar between AA and White individuals.[24]

A study by Dennis et al. of 142 adult patients with a new MM, diagnosed between January 2007 and December 2017 at a single institution, found mixed results.[30] Among the <65 years old subgroup, non-Hispanic White patients were 8 times as likely, and Hispanic individuals were 4 times as likely to receive a triplet regimen compared to non-Hispanic Black patients after adjusting for age, year of diagnosis, and comorbidities (P=0.03 and P=0.05, respectively).[30] However, there were no significant racial/ethnic differences in the use of triplet therapy among patients aged ≥65 years.[30] Fiala and colleagues, based on a study of 6,272 Medicare beneficiaries diagnosed with MM between 2007 and 2013, found that AA patients had 31% lower odds (aOR=0.69; 95% CI, 0.59–0.80), and individuals of other races 21% lower odds (aOR=0.79; 95% CI, 0.63–0.99) of receiving bortezomib, compared to White patients.[13] However, that study did not find a statistically significant difference in lenalidomide use by race.[13] Furthermore, while Medicaid dual enrollment reduced the odds of both bortezomib (aOR=0.69; 95% CI, 0.60–0.78) and lenalidomide (aOR=0.87; 95% CI, 0.75–1.00) utilization, controlling for it did not result in significant changes in the models.[13]

Disparities in SCT utilization

Among 17 studies that studied SCT use, 13 reported significant variations by race[12,14,19,25,29,33,34,34,46,50,52,55,57] (out of 17 that reported race as study variable), five by ethnicity[14,22,25,34,34,50] (out of eight that reported ethnicity as study variable), and four by insurance-related characteristics[25,33,34,52] (out of four, Appendix Table A.3). For example, Al Hadidi et al. examined 913,967 hospitalized adults during 2008–2017, with an occurrence of MM in discharge records, using the Nationwide Inpatient Sample of

Healthcare Cost and Utilization Project.[55] Non-Hispanic Black patients had lower receipt of autologous SCT (OR=0.68; 95% CI, 0.58–0.79) compared to non-Hispanic White patients.[55] Similarly, Al-Hamadani et al. reported that Black (OR=0.59; 95% CI, 0.55–0.62) and Asian (OR=0.77; 95% CI, 0.66–0.89) patients had smaller odds of receiving SCT, compared to White individuals, using the National Cancer Database from 1998 to 2010.[25] In that study, Hispanic patients also had smaller odds of receiving SCT (OR=0.80; 95% CI, 0.73–0.87) compared to Non-Hispanic individuals.[25] Fiala & Wildes found that Medicaid/Medicare dual coverage was associated with smaller odds of SCT use, OR=0.49; 95% CI, 0.35–0.66, compared to traditional Medicare coverage.[33]

Ailawadhi et al. observed an increasing trend in the rate of SCT use within 1 year of MM diagnosis among White and African American patients, but not among Hispanic individuals in their study of 4830 individuals diagnosed with MM between 2007 and 2013 and reported to the SEER-Medicare database.[22] Other studies did not find significant associations of receipt of SCT with race,[6,22,30,58] ethnicity,[12,30,55] or insurance-related facors[52] (Appendix Table A.3).

Disparities in the timeliness of care

Among 10 studies that examined timeliness of care, seven reported significant variations by race[4,22,37,41,43,48,51] (out of nine that reported race as a study variable), three by ethnicity[22,41,54] (out of four that reported ethnicity as a study variable), and two by insurance-related characteristics[27,43] (out of three, Appendix Table A.3). Jayakrishnan et al., in a study of 65,723 patients diagnosed with MM between 2004–2016 and who were treated within 120 days of diagnosis, found that compared to non-Hispanic White patients, delayed treatment initiation had greater odds for Hispanic patients during the pre-Affordable Care Act (ACA) era (OR=1.22; 95% CI, 1.07–1.38) but not post-ACA (OR=1.05; 95% CI, 0.94–1.17), while non-Hispanic Black patients had greater odds of having delayed treatment initiation both pre- (OR=1.18; 95% CI, 1.09–1.27) and post-ACA (OR=1.17; 95% CI, 1.09–1.25).[41] Insurance status, was not significantly associated with delayed time to initial treatment.[41]

Bhatnagar et al., in a single-center study of 453 patients that underwent autologous SCT, found that there was a significantly longer time from diagnosis of MM to referral to SCT for Black patients, compared with White patients (median, 1.3 years vs. 0.9 years, P= 0.003).[4] However, Lupak and colleagues, in a single-center study of 194 newly diagnosed MM patients referred for SCT consult between January 1, 2009, and June 30, 2019, found that race (defined as non-Hispanic White, Black, others/unknown) was not significantly associated with time to SCT.[45]

Disparities in the use of supportive care

Among nine studies that examined timeliness of care, six reported significant variations by race[23,32,35,38,53,55] (out of eight that reported race as a study variable), two by ethnicity[53,55] (out of five), and five by insurance-related characteristics[23,32,35,38,42] (out of five, Appendix Table A.3). For example, Zhou and colleagues studies bisphosphonate use among 14,231 patients diagnosed with MM between 2001 and 2011. They found that

non-White individuals were less likely to initiate bisphosphonate therapy in reducing risk for skeletal-related events compared with non-Hispanic White patients.[53]

In a large sample of hospitalized adults during 2008–2017, with an occurrence of MM in discharge records, non-Hispanic Black patients had lower palliative care consultations (OR=0.91; 95% CI, 0.85–0.97), compared to non-Hispanic White patients.[55] Non-White patients were also found to have 23% smaller odds of hospice enrollment (aOR=0.77; 95% CI, 0.61–0.97), compared to White individuals in another study of 2,075 SEER-Medicare registry enrollees diagnosed with MM from 2007 to 2013.[32] In that study, Medicaid-Medicare dual-enrollment was associated with 37% smaller odds of hospice enrollment (aOR=0.63; 95% CI, 0.51–0.77), compared to non-dual Medicare coverage.[32] Other studies have not found a significant association between race (defined as Black, White, other) and bisphosphonate use,[44] or race (defined as White/non-White) and late hospice enrollment.[47]

DISCUSSION

Over the past two decades, a number of studies have examined the association between demographic and insurance-related characteristics and the care patterns among patients with MM. Unfortunately, race-dependent disparities seem to pervade virtually every aspect of MM care from diagnosis to end of life. Most commonly, these have been studied and observed in the utilization of novel agents for induction therapy, SCT, and supportive care (Table 1, Appendix Table A.3).

Patient ethnicity was included as a study variable less often. While disparities have been observed by ethnicity, the findings have been less consistent (Table 1, Appendix Table A.3). Moreover, several studies suggest that Hispanic individuals have better access to MM-related care than their non-Hispanic Black peers.[22,23,25,30,35] Further research is needed to help determine if the difference is just in the degree of disparity or if different mechanisms are at play.

Several studies identified disparities in MM care patterns based on insurance-related factors (Table 1, Appendix Table A.3). However, a very limited set of insurance-related characteristics were examined, such as payer type, dual Medicare/Medicare eligibility, and/or low-income subsidy receipt. This could be due to several of the studies using Surveillance, Epidemiology, and End Results-Medicare linked data and limiting their study samples to traditional (parts A & B) Medicare beneficiaries (Appendix Table A.3). Further research is needed to examine the role of health insurance design on MM care disparities among commercially insured individuals.

Information about patients' socioeconomic status was not captured and analyzed consistently (Table 2). Furthermore, little is known about the patient cost burden related to transportation, delays in the receipt of care, and management of treatment-related side effects. This limits the current understanding of the mechanisms for race- and ethnicity-based disparities in care plans. A better understanding of more granular and modifiable determinants of access to care such as patient out-of-pocket costs, pre-authorization criteria,

as well as social determinants of health, could potentially help in developing specific and actionable strategies toward the goal of reducing MM health disparities.

The Inflation Reduction Act of 2022 mandates that the U.S. Secretary of Health and Human Services negotiate prices of certain expensive drugs each year (starting with 10 drugs covered by Medicare in 2026 and increasing to 20 drugs in 2029), requires drug companies to pay a rebate to the government if drug prices rise faster than inflation for Medicare (starting 2023), expand eligibility for Medicare Part D low-income subsidy full benefits up to 150% of the federal poverty level (starting 2023), and cap out-of-pocket spending on prescription drugs for Medicare beneficiaries to $2,000, effective in 2025.[59] This will likely reduce the cost-related access barriers for the majority of individuals with MM who are Medicare beneficiaries but future studies are needed to confirm this.

Whereas policy solutions aimed at addressing cost-related access barriers to MM care are vital, actions aimed at advancing health equity should encompass all aspects of MM care and begin with ensuring people from diverse backgrounds are enrolled in clinical trials. In a review of 12,055 patients enrolled in therapeutic MM trials identified from ClinicalTrials.gov, Duma and colleagues found that non-Hispanic White patients were more likely to be enrolled in clinical trials (enrollment fraction [EF]=0.18%, calculated by dividing the number of trial participants by the 2014 SEER MM prevalence), compared to non-Hispanic Black (EF=0.06%; P<0.0001) and Hispanic individuals (EF=0.04%; P<0.0001).[56] The FDA's newest guidance on diversity is an important step forward toward the inclusion of underrepresented racial and ethnic populations in clinical trials.[60] Addressing these disparities requires multidisciplinary efforts that fully engage all stakeholders, including the historically underrepresented communities.

While this systematic review contributes new knowledge to the field, this review is not without limitations. Following our review protocol, we included only studies that examined associations between patient race, ethnicity, or insurance-related factors and treatment patterns of MM. This may have limited the scope of the review. Furthermore, we may have missed studies that were published after January 28, 2022, or were not available through the data resources searched; this is particularly true of "grey literature", which does not appear in peer-reviewed journals. Finally, we did not attempt to conduct a meta-analysis given the heterogeneity in the study outcomes and the measures of effect.

CONCLUSION

Significant disparities in the MM care patterns were found based on patient race, ethnicity, and insurance-related characteristics. A better understanding of granular and modifiable determinants of access to care such as insurance plan design, patient out-of-pocket costs, pre-authorization criteria, as well as social determinants of health, could potentially help in advancing specific and actionable strategies to address MM health care disparities.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1:

Summary of results on race, ethnicity & health insurance characteristics, systematic review of disparities in multiple myeloma treatment patterns in the U.S., 2003–2021

	Race		Ethnicity		Insurance status	
Study	**Included as a study variable**	**Identified significant differences**	**Included as a study variable**	**Identified significant differences**	**Included as a study variable**	**Identified significant differences**
Ailawadhi et al., 2021	Yes	**Yes**	Yes	No	Yes	**Yes**
Ailawadhi et al., 2020	Yes	No	No	—[a]	No	—[a]
Ailawadhi et al., 2019	Yes	**Yes**	Yes	**Yes**	No	—[a]
Ailawadhi, et al., 2018	Yes	**Yes**	Yes	**Yes**	No	—[a]
Ailawadhi et al., 2017	Yes	**Yes**	Yes	**Yes**	No	—[a]
Al Hadidi et al., 2021	Yes	**Yes**	Yes	**Yes**	Yes	NR
Al-Hamadani et al., 2014	Yes	**Yes**	Yes	**Yes**	Yes	**Yes**
Aung et al., 2021	Yes	No	Yes	No	No	—[a]
Bhatnagar et al., 2015	Yes	**Yes**	No	—[a]	No	—[a]
Bhatt et al., 2016	No	—[a]	No	—[a]	Yes	**Yes**
Chen et al., 2017	Yes	No	No	—[a]	No	—[a]
Costa et al., 2015	Yes	**Yes**	Yes	**Yes**	No	—[a]
Covut et al., 2021	Yes	**Yes**	No	—[a]	No	—[a]
Dennis et al., 2020	Yes	**Yes**	Yes	**Yes**	Yes	NR
Derman et al., 2020	Yes	**Yes**	No	—[a]	No	—[a]
Duma et al., 2018	Yes	**Yes**	Yes	**Yes**	No	—[a]
Fakhri et al., 2018	Yes	**Yes**	No	—[a]	Yes	**Yes**
Fiala et al., 2020	Yes	**Yes**	No	—[a]	Yes	**Yes**
Fiala, Wildes & Vij, 2020	Yes	**Yes**	No	—[a]	Yes	**Yes**
Fiala, Vij & Wildes, 2019	Yes	No	No	—[a]	No	—[a]
Fiala & Wildes, 2017	Yes	**Yes**	No	—[a]	Yes	**Yes**
Fiala et al., 2015	Yes	**Yes**	No	—[a]	Yes	**Yes**
Fillmore et al., 2019	Yes	**Yes**	No	—[a]	No	—[a]
Fossum et al., 2021	Yes	**Yes**	Yes	No	Yes	**Yes**
Freeman et al., 2019	Yes	No	No	—[a]	Yes	**Yes**
Friese et al., 2009	Yes	**Yes**	No	—[a]	No	—[a]
Olszewski et al., 2018	Yes	**Yes**	No	—[a]	Yes	**Yes**
Giri et al., 2019	Yes	**Yes**	Yes	No	Yes	**Yes**
Goto et al., 2020	Yes	No	No	—[a]	Yes	No
Jayakrishnan et al., 2021	Yes	**Yes**	Yes	No	Yes	No

	Race		Ethnicity		Insurance status	
Study	**Included as a study variable**	**Identified significant differences**	**Included as a study variable**	**Identified significant differences**	**Included as a study variable**	**Identified significant differences**
Jayakrishnan et al., 2020	Yes	**Yes**	Yes	**Yes**	Yes	No
Joshi et al., 2021	Yes	**Yes**	Yes	**Yes**	Yes	**Yes**
Joshua et al., 2010	Yes	**Yes**	No	—[a]	No	—[a]
Keating et al., 2011	Yes	NR	Yes	NR	Yes	**Yes**
Kumar et al., 2020	Yes	**Yes**	Yes	No	Yes	**Yes**
Leng et al., 2019	Yes	No	No	—[a]	No	—[a]
Lupak et al., 2021	Yes	No	No	—[a]	No	—[a]
Munshi et al., 2021	Yes	**Yes**	No	—[a]	No	—[a]
Odejide et al., 2018	Yes	No	No	—[a]	No	—[a]
Olszewski et al., 2017	Yes	No	No	—[a]	Yes	**Yes**
Pan et al., 2021	Yes	**Yes** [b]	No	—[a]	No	—[a]
Rohatgi et al., 2007	Yes	**Yes**	No	—[a]	No	—[a]
Schriber et al., 2017	Yes	**Yes**	Yes	**Yes**	No	—[a]
Sweiss et al., 2019	Yes	**Yes**	No	—[a]	No	—[a]
Warren et al., 2013	Yes	**Yes**	Yes	NR	Yes	**Yes**
Zhou et al., 2021	Yes	**Yes**	Yes	**Yes**	No	—[a]
Total Yes	45	34	20	12	22	17

Source: Authors' analysis of peer-reviewed published studies, as described in the text. Notes: Study characteristics and main results are available in appendix exhibit 4.

[a] Not applicable;

[b] Based on univariate analysis; NR – not reported.

Table 2:

Summary of results on socio-economic and geographic characteristics, systematic review of disparities in multiple myeloma treatment patterns in the U.S., 2003–2021

	Income estimate or employment status		Language barrier or education-related factors		Distance from treating facility, urbanicity, or geographic region	
Study	**Included as a study variable**	**Identified significant differences**	**Included as a study variable**	**Identified significant differences**	**Included as a study variable**	**Identified significant differences**
Ailawadhi et al., 2021	Yes	**Yes**	Yes	**Yes**	Yes	**Yes**
Ailawadhi et al., 2020	No	__*a*	No	__*a*	No	__*a*
Ailawadhi et al., 2019	Yes	NR	No	__*a*	Yes	NR
Ailawadhi, et al., 2018	Yes	NR	Yes	NR	Yes	NR
Ailawadhi et al., 2017	No	__*a*	No	__*a*	No	__*a*
Al Hadidi et al., 2021	Yes	NR	No	__*a*	No	__*a*
Al-Hamadani et al., 2014	Yes	**Yes**	Yes	**Yes**	Yes	**Yes**
Aung et al., 2021	No	__*a*	No	__*a*	No	__*a*
Bhatnagar et al., 2015	No	__*a*	No	__*a*	No	__*a*
Bhatt et al., 2016	Yes	NR	No	__*a*	Yes	No
Chen et al., 2017	Yes	No	No	__*a*	Yes	No
Costa et al., 2015	No	__*a*	No	__*a*	No	__*a*
Covut et al., 2021	Yes	NR	Yes	NR	Yes	NR
Dennis et al., 2020	Yes	NR	Yes	NR	No	__*a*
Derman et al., 2020	No	__*a*	No	__*a*	No	__*a*
Duma et al., 2018	No	__*a*	No	__*a*	No	__*a*
Fakhri et al., 2018	Yes	**Yes** *b*	No	__*a*	No	__*a*
Fiala et al., 2020	No	__*a*	No	__*a*	No	__*a*
Fiala, Wildes & Vij, 2020	No	__*a*	No	__*a*	No	__*a*
Fiala, Vij & Wildes, 2019	No	__*a*	No	__*a*	No	__*a*
Fiala & Wildes, 2017	Yes	**Yes**	No	__*a*	Yes	No
Fiala et al., 2015	Yes	**Yes**	No	__*a*	No	__*a*
Fillmore et al., 2019	No	__*a*	No	__*a*	No	__*a*
Fossum et al., 2021	Yes	**Yes**	Yes	**Yes**	Yes	**Yes**
Freeman et al., 2019	Yes	No	Yes	**Yes**	Yes	**Yes**
Friese et al., 2009	No	__*a*	No	__*a*	Yes	No
Olszewski et al.,2018	No	__*a*	No	__*a*	No	__*a*
Giri et al., 2019	Yes	No	Yes	**Yes**	Yes	**Yes**
Goto et al., 2020	No	__*a*	No	__*a*	Yes	**Yes**

	Income estimate or employment status		Language barrier or education-related factors		Distance from treating facility, urbanicity, or geographic region	
Study	**Included as a study variable**	**Identified significant differences**	**Included as a study variable**	**Identified significant differences**	**Included as a study variable**	**Identified significant differences**
Jayakrishnan et al., 2021	Yes	No	Yes	**Yes**	Yes	**Yes**
Jayakrishnan et al., 2020	Yes	No	Yes	No	Yes	**Yes**
Joshi et al., 2021	No	__[a]	No	__[a]	No	__[a]
Joshua et al., 2010	No	__[a]	No	__[a]	No	__[a]
Keating et al., 2011	Yes	NR	Yes	NR	Yes	NR
Kumar et al., 2020	Yes	No	Yes	No	Yes	**Yes**
Leng et al., 2019	Yes[c]	No	Yes[c]	No	Yes	**Yes**
Lupak et al., 2021	Yes	No	No	__[a]	No	__[a]
Munshi et al., 2021	No	__[a]	No	__[a]	No	__[a]
Odejide et al., 2018	Yes	No	Yes	No	Yes	**Yes**
Olszewski et al., 2017	Yes	**Yes**	No	__[a]	Yes	**Yes**
Pan et al., 2021	Yes	**Yes**	No	__[a]	No	__[a]
Rohatgi et al., 2007	Yes	**Yes**	No	__[a]	Yes	**Yes**
Schriber et al., 2017	No	__[a]	No	__[a]	No	__[a]
Sweiss et al., 2019	No	__[a]	No	__[a]	No	__[a]
Warren et al., 2013	No	__[a]	No	__[a]	No	__[a]
Zhou et al., 2021	No	__[a]	No	__[a]	No	__[a]
Total Yes	25	9	14	6	21	13

Source: Authors' analysis of peer-reviewed published studies, as described in the text. Notes: Study characteristics and main results are available in appendix exhibit 4.

[a] Not applicable;

[b] Based on univariate analysis;

[c] Combined socioeconomic status was calculated from education, poverty level, and income data from the 2000 census. NR – not reported.