Do the characteristics of the site of care influence outcomes?
Associations between community practice-level characteristics and real-world overall survival among patients with multiple myeloma

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OBJECTIVES

- Although use of electronic health record (EHR)-derived real-world data (RWD) for regulatory purposes has increased recently, regulators have raised concern that RWD has limitations because it does not resemble trial data[1].
- Despite controlling for patient-level differences, a common concern in using RWD is the heterogeneity of practices treating patients, and corresponding potential impact on patient outcomes[2].
- This study describes the association of practice-level characteristics and real-world overall survival (rwOS) among patients with multiple myeloma (MM) using nationwide community site data.

METHODS

Study population

- We used the longitudinal US-based Flatiron Health EHR-derived de-identified database, comprising de-identified patient-level structured and unstructured data, curated via technology-enabled abstraction.[3,4]
- In this study, we included patients:
  - diagnosed with MM between 1/1/2017-6/1/2022,
  - had evidence of treatment at a community practice that was established prior to 2017, and
  - had ≥6 months of potential follow-up (for survival analysis).

Practice-level factors

- Case-load factors[5,6] among patients with cancer and ≥1 visit on or after 2017: patient-physician ratio; numbers of visits, physicians, patients with cancer, and with MM (continuous and quintiles)
- Patient diversity: % Black patients, % with Medicaid, % in low socioeconomic status, and % living in rural area (continuous, and binary using US census average[7])
- Practice geographical division (categorical)
- Clinical factors among patients with MM: % received clinical study drugs (CSD), % received genetic testing, % received stem cell transplant and % with R-ISS workup (continuous and quintiles)

Real-world overall survival (rwOS)

- rwOS was defined as months from first-line treatment initiation to date of death, or last confirmed activity.

Statistical analysis

- Descriptive statistics were summarized at the practice-level for each practice-level factor.
- Mixed-effect Cox regression was performed to assess the association between practice-level characteristics and rwOS, adjusting for patient-level demographic and clinical factors (conditional hazard ratio [cHR] and 95% confidence interval [CI]).
- Adjusted patient-level factors included age, gender, race/ethnicity, ECOG status at 1L, insurance, ISS stage, M protein type, risk stratification group, receipt of bone therapy at 1L, creatinine level at 1L, other hematologic diagnosis before 1L, and 1L treatment regimens.
- Exploratory forward selection among practice-level factors were applied with a select-in threshold 0.25.

RESULTS

Patient characteristics

- A total of 4,552 patients with MM from 136 practices were included in the analysis. Patients had a median age of 71, were 55% male, 52% non-Hispanic White, 66% had standard risk disease (under mSMARTguidelines[8]), 24% had other hematologic diagnosis prior to first-line initiation, and 66% received triplets as first-line treatment.

Distribution of practice-level factors

- Across the 136 practices, large heterogeneity was observed for all 15 practice-level characteristics. Practices ranged from 1-163 physicians, 0-58% patients with Medicaid, 0-50% clinical study drug recipients, and 0-85% transplant recipients. (**Table 1**)

Table 1. Distribution of practice-level factors among 136 practices

Variable	Min	Q1	Median	Q3	Max	Mean (SD)
Case load						
# visits among patients with MM	47	2,818	5,938	14,551	96,048	12,264 (15,948)
# patients with cancer	332	2,016	4,851	9,674	89,975	9,313 (12,967)
# patients with MM	3	54	136	294	2,305	262 (349)
# physicians	1	3	7	15	163	15 (23)
Patient-to-physician ratio	110	473	695	963	2,560	820 (506)
Patient Diversity						
% Black patients	0	2%	5%	12%	64%	9% (10%)
% patients with Medicaid ever	0	10%	16%	22%	58%	17% (11%)
% patients in lowest SES index	1%	6%	14%	29%	72%	19% (17%)
% patients in rural area	0	1%	3%	16%	92%	13% (21%)
Clinical factors (among patients with MM)						
% received CSD	0	0	0.6%	3.6%	50%	3.1% (6.5%)
% received genetic testing	20%	66%	74%	80%	100%	72% (12%)
% received stem cell transplant	0	14%	22%	30%	84%	23% (12%)
% with R-ISS workup	0	14%	32%	44%	71%	30% (19%)

Association between practice-level factors and rwOS

- No practice-level factors were associated with rwOS in univariate analyses.
- After adjusting for patient-level factors, 13 out of 15 factors remain unassociated with rwOS, including # visits among patients with MM, # patients with MM, # physicians, patient/physician ratio, % patients living in rural areas, % received genetic testing, % received CSD, % with R-ISS workup, or patient composition by % Black or % in lowest SES index.
- Lower hazard of death was seen among patients from practices with the highest quintile % transplant recipients compared to the lowest quintile (cHR=0.74; 95% CI: 0.55-1.00; **Figure 1**), and unexpectedly, among patients from practices with a higher % patients with Medicaid (cHR=0.76; 95% CI: 0.61-0.95; **Figure 2**).

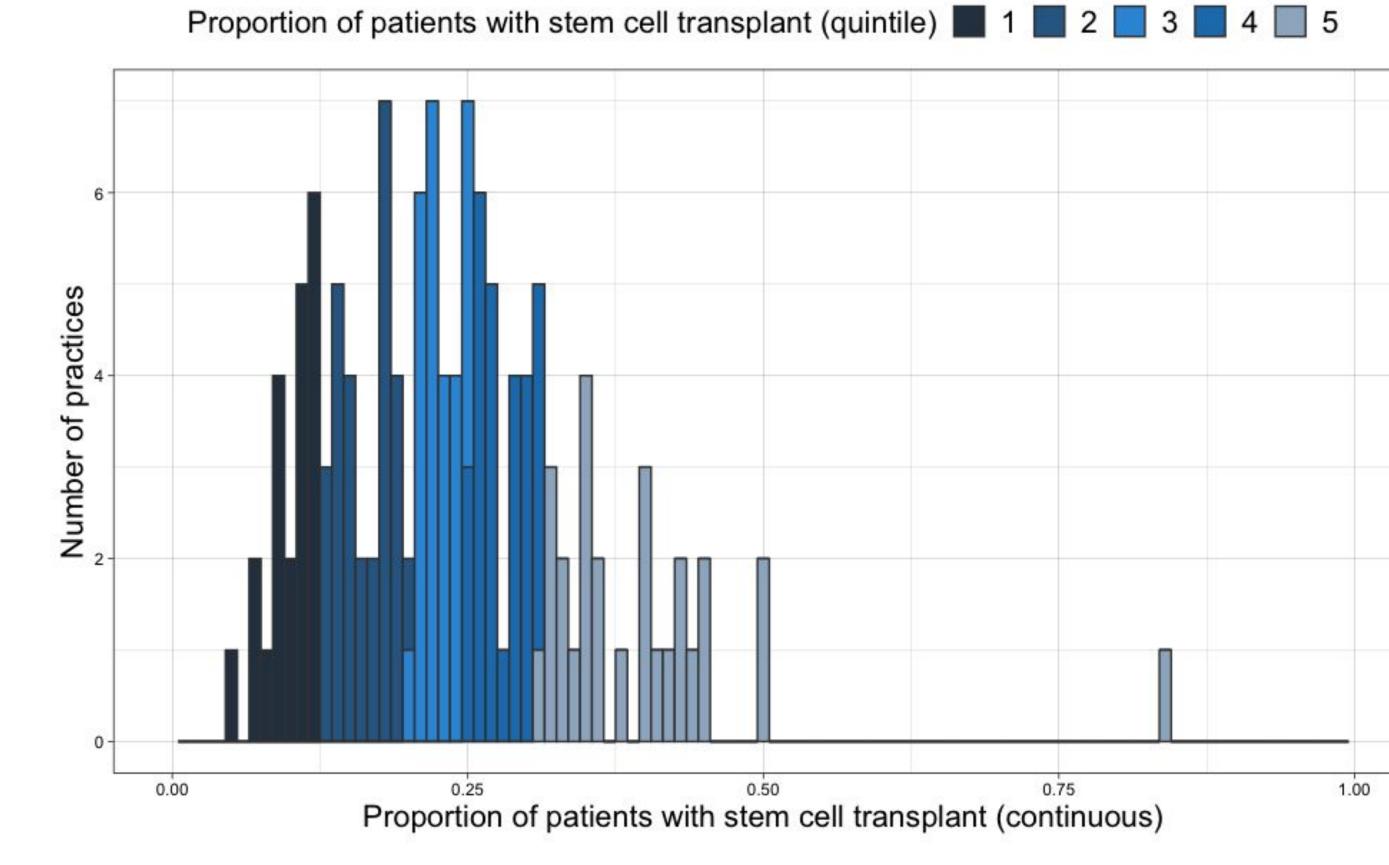### Figure 1. Distribution of % patients with stem cell transplant

Proportion of patients with stem cell transplant (quintile) ■1 ■2 ■3 ■4 ■5

Table 2. Association between % patients with stem cell transplant and real-world overall survival

% transplant	N patients	Mean (sd)	cHR[a] (95% CI)
Q1 (N = 27)	365	7% (3%)	1.00
Q2 (N = 28)	765	16% (3%)	0.97 (0.73 - 1.29)
Q3 (N = 27)	1,145	31% (5%)	0.91 (0.68 - 1.23)
Q4 (N = 27)	1,110	41% (3%)	0.98 (0.73 - 1.33)
Q5 (N = 27)	1,167	57% (6%)	0.74 (0.55 - 1.00)

Figure 2. Distribution of % patients with Medicaid

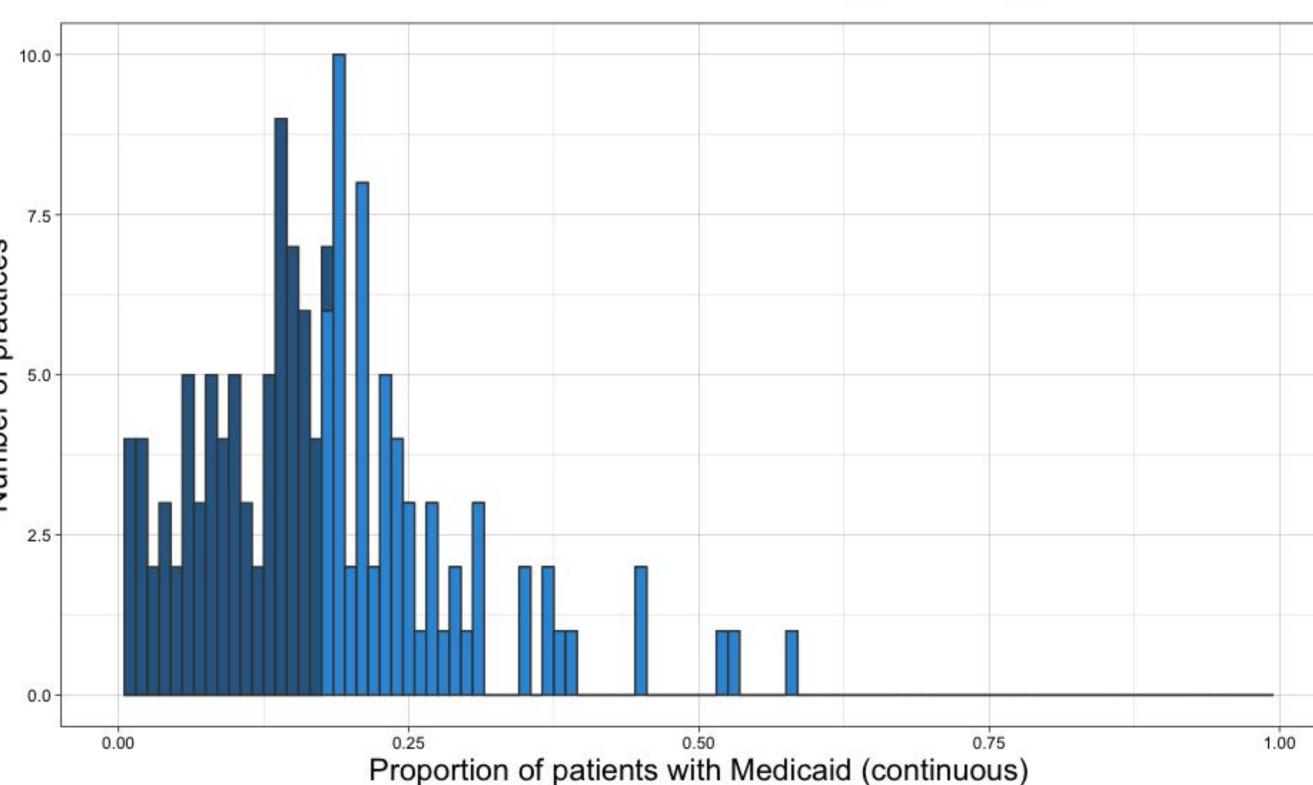Proportion of patients with Medicaid (binary) ■<17.8% ■≥17.8%

Table 3. Association between % patients with Medicaid and real-world overall survival

% Medicaid	N patients	Mean (sd)	cHR[a] (95% CI)
<17.8% (N = 74)	2,838	10% (5%)	1.00
≥17.8% (N = 62)	1,714	26% (9%)	0.76 (0.61 - 0.95)

[a] Conditional hazard ratios were estimated using mixed-level Cox regression model with practice as random intercept, adjusted for all patient- and practice-level factors.

RESULTS (continued.)

Exploratory analyses

- In the exploratory forward selection for a parsimonious model, three factors, including % patients with Medicaid, % patients with R-ISS workup, and practice location, were included with a select-in threshold at 0.25, adjusting for all patient-level factors.
- Full model with both practice- and patient-level factors was not statistically significantly better than the patient-level only model (ANOVA test for partial log-likelihood: df= 45; p = 0.108). In contrast, the parsimonious model was statistically significantly better than the patient-level only model (df = 14; p = 0.01).

DISCUSSION

Strengths

- This study systematically assessed the distribution of practice- level factors among patients treated in community settings.
- We demonstrated the wide variability of practice-level factors and multitude aspects captured in contemporary EHR-derived RWD.
- We found no association with practice-level factors on rwOS among multiple myeloma patients. These results provided insights to the association between practice setting and patient outcomes.

Limitations

- This study was limited to a single cancer type.
- There is potential unmeasured confounding due to missingness and loss to follow-up.
- We did not explore multi-level interactions due to sample size.

CONCLUSIONS

- In this hypothesis-generating study of patients with MM, we observed a wide variability in practice-level factors across community sites, yet rwOS was not strongly associated with most practice-level characteristics.
- Future studies in other care and oncological settings are needed.

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