EE499

Health Resource Utilization (HRU) and Costs of Patients with Relapsed/Refractory Multiple Myeloma (RRMM) in the United States (US): A Systematic Literature Review

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INTRODUCTION

- Multiple myeloma (MM) accounts for 18% of hematologic malignancies and 1.8% of new cancer diagnoses in the US.[1,2] It is characterized by recurring disease relapses that increase with each subsequent line of therapy (LOT).[3]
- In the US, 83% of patients with a MM diagnosis receive treatment, with approximately half receiving treatment in the relapsed or refractory (RR) setting.[4] Despite recent prognosis improvements, treatment outcomes worsen with each successive LOT.
- MM remains a significant health burden, emphasizing the importance of understanding the economic impact of RRMM for broader societal and healthcare system implications.
- This systematic literature review aimed to characterize the economic burden of RRMM, focusing on healthcare resource utilization (HRU) and costs in the US.

METHODS

Systematic Literature Review

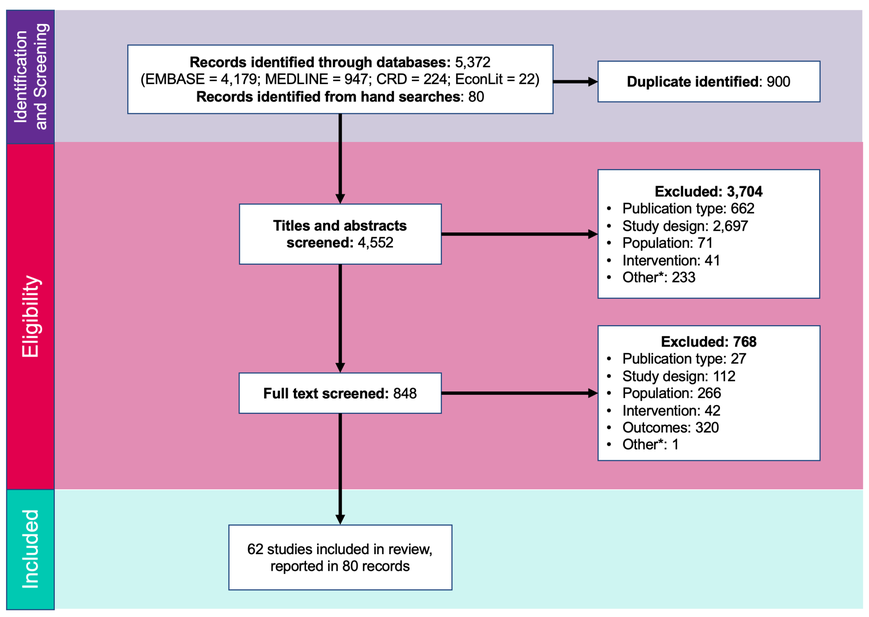
- Searches were conducted using MEDLINE, Embase, EconLit, and NHS-EED (January 2012-March 2024), and publications from key conferences were hand-searched.
- Observational studies involving patients with RRMM, and any pharmacological interventions were eligible for inclusion. Trials reporting hospital HRU outcomes were also eligible.
- Studies that included newly diagnosed, untreated, and/or treatment-naïve patients, reported modeled outcomes and outcomes for non-pharmacological interventions were excluded.
- The systematic literature review protocol was prospectively registered with PROSPERO (CRD42023467098).

Descriptive Summary

- Results were summarized for studies reporting US-based outcomes, with all costs adjusted to 2024 USD.[5]
- Only studies reporting outcomes as per patient per month (PPPM) were included in graphic summaries for cross-study comparison. Evidence was summarized by LOT to better describe cost and HRU trends.
- Among studies that reported overall costs and costs by spending categories, the cost of each component was described as the proportion of overall healthcare costs.

RESULTS

Figure 1. PRISMA Diagram



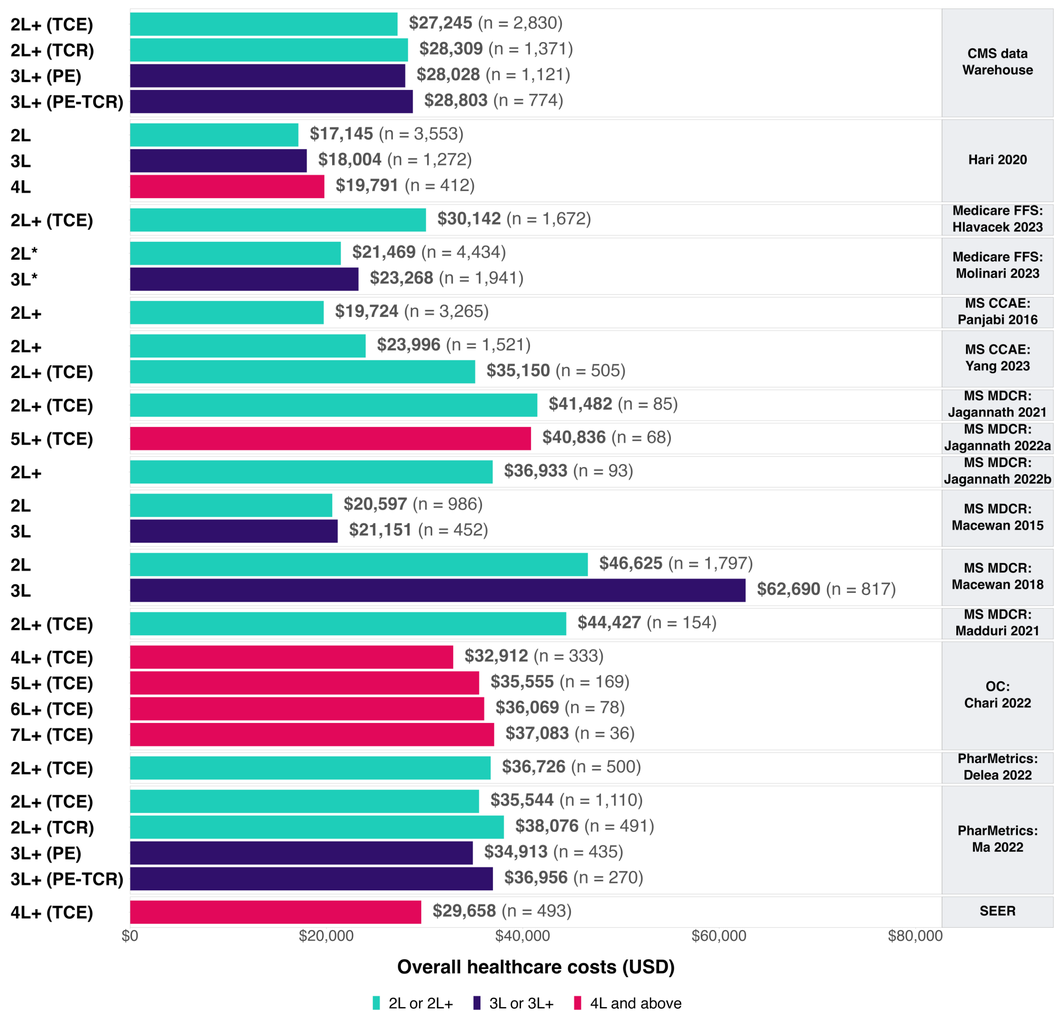
**Records excluded due to language and study period constraints (i.e., Pre-2012).*

- Of the 5,372 records identified (**Figure 1**), 80 records reporting on 62 studies were eligible for inclusion and 46 unique studies were eligible for the descriptive summary.
- Remaining studies were excluded due to unspecified reporting period (n=4), or lack of reported overall healthcare costs, all-cause HRU, or HRU components of interest, with only baseline estimates provided (n=12).
- The descriptive summary included 15 unique studies predominantly reporting outcomes as PPPM and mean.

Overall Healthcare Costs (Per Patient Per Month, 2024 USD)

- Overall healthcare costs varied significantly across studies, likely driven by real-world data informing these estimates. Variability in data sources, methodologies, and analytical approaches further limits reliable cross-study comparisons.
- Within study trends indicate that overall healthcare costs also tended to increase with each subsequent LOT. Patients with refractory status within the same LOT also incurred higher overall healthcare costs (**Figure 2**).

Figure 2. Summary of Overall Healthcare Costs, by LOT (Per Patient Per Month; 2024 USD)



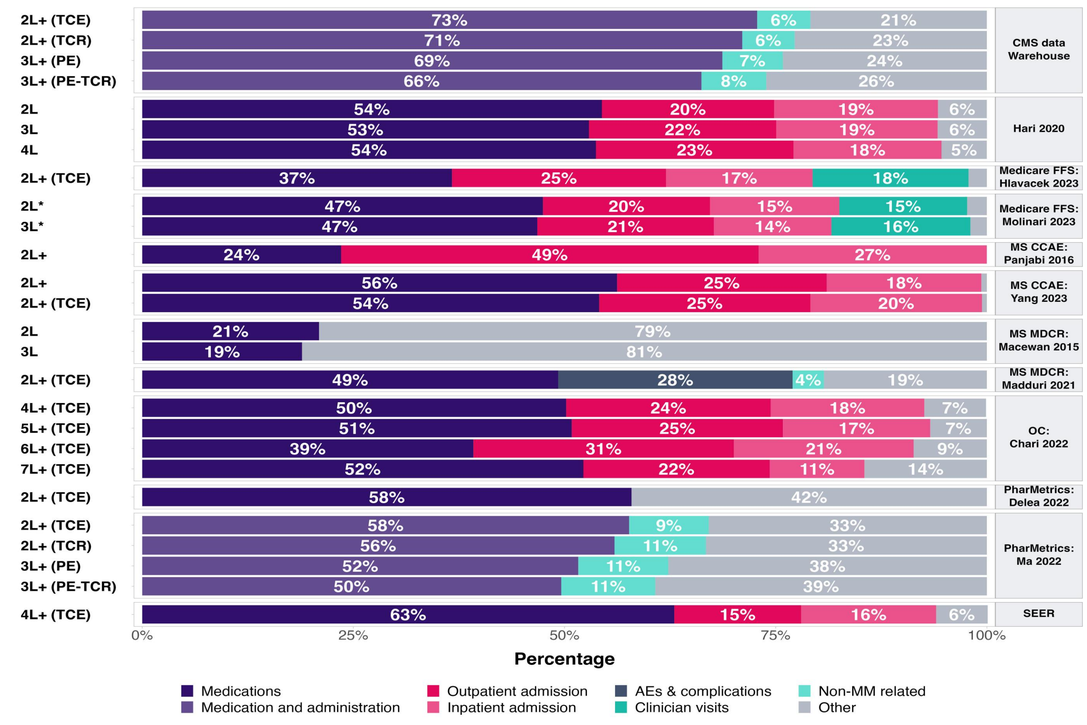
Abbreviations - *LOT: Line of therapy; PE: Penta-exposed; PR: Penta-refractory; TCE: Triple-class exposed; TCR: Triple-class refractory; PE-TCR: Penta-exposed and Triple-class refractory*

RESULTS *(CONTINUED)*

Cost Drivers

- Medications, along with inpatient and outpatient services, were consistently the top three spending categories, collectively accounting for over 80% of overall healthcare costs in six studies (Figure 3), with medications being the most frequently reported spending category (n=12), followed by inpatient and outpatient services (n=7).
- Medications accounted for approximately half of the overall healthcare costs in 8 studies.
- Three studies reported non-MM related costs, which ranged between 4% and 11% of the overall costs.

Figure 3. Distribution of Costs by Spending Category (Per Patient Per Month)



Abbreviations *- AE: Adverse events; LOT: Line of therapy; MM: Multiple myeloma; PE: Penta-exposed; PR: Penta-refractory; TCE: Triple-class exposed; TCR: Triple-class refractory; PE-TCR: Penta-exposed and Triple-class refractory.*
"Other" *refers to drug administration costs, emergency room visits, stem cell transplants, and any other cost categories not specified. Note that these categories were not consistently reported in all studies featuring the "other" category in this figure.*

Heavily Pre-treated Groups

- Based on a within study comparison among heavily pretreated patients in a single study (OC: Chari 2022), PPPM costs and HRU increased by therapy lines 4L+ to 7L+ (**Figure 2**). Overall healthcare costs increased with each consecutive therapy line. Medications accounted for approximately 50% of total costs, dropping to 39% in 6L+, where reduced medication costs were offset by increased hospitalization costs (**Figure 3**)**.**
- Two studies detailed total all-cause costs: $826,882 (2024 USD) over 20.9 months for patients since their first LOT post triple-class exposure (n=85; 91% MM-related)[6], and $893,628 (2024 USD) over 21.9 months for patients with at least four prior LOTs, including post triple-class exposure (n=68; 89% MM-related).[7]

Healthcare Resource Use (Per Patient Per Month)

- HRU estimates reported across different studies varied, consistent with the variability the reported cost estimates.
- HRU data on medications, inpatient, and outpatient admissions were less consistently reported, but several studies (n=10) did report inpatient and outpatient admissions and hospital length of stay (LOS).
  - The mean number of outpatient admissions was reported in 8 studies; showing an increase with more therapy lines. Rates ranged between 4.82 and 6.70 per month in advanced lines, with refractory patients experiencing slightly higher admission rates.
  - Fewer studies (n=4) reported monthly inpatient admissions, ranging from 0.10 to 0.62. Advanced therapy lines showed rates ranging from of 0.20 to 0.62. There were mixed results regarding the association of increasing inpatient admissions with advancing therapy lines.
  - The mean hospital LOS was reported in 9 studies, ranging from 0.63 to 3.00 days per month. Longer stays were observed in advanced therapy lines and among refractory patients (1.80 to 3.00 days), particularly in studies focusing on the 4L+.

Limitations

- Most of the studies were retrospective in design, using claims databases as their sources of patient data, which introduced heterogeneity in the evidence base due to differences in study methodologies, including analytical techniques, data collection approaches, sources, and outcome definitions.
- In most studies, LOT subgroups included patients under broader LOT labels (e.g., 2L+, 3L+). This grouping may impact trends related to LOT and its association with HRU and costs, as it was not possible to gauge the extent to which each LOT (e.g., the proportion of costs and HRU incurred by 3L patients grouped under 2L+) within these broad categories contributes to the observed estimates presented by LOT designation.
- The heterogeneity in the evidence limits the ability to compare results across studies or draw conclusions regarding trends between different studies.
- Most summary measures of costing data used means as opposed to medians, which are generally preferred given they are more resistant to outliers.

CONCLUSIONS

- This study offers a comprehensive and up-to-date summary of published cost and HRU estimates for RRMM in the US.
- This review highlights the substantial economic burden of RRMM in the US, with costs and HRU increasing with each additional LOT. This mirrors the clinical challenge where treatment outcomes decline as therapy progresses despite recent patient prognosis improvements.
- Medication costs were the main component of the overall healthcare costs, accounting for approximately half of the total costs incurred. Hospital visits (inpatient and outpatient) were also key drivers.
- The findings of this study highlight the unmet need for novel and effective treatments that can reduce prolonged HRU and associated costs, especially in the more expensive later-line settings.

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