RWD53

A Statistical Modeling Framework for Process-Mined Real-World Data Supporting HTA of Multiple Myeloma Technologies in a Brazilian Health Maintenance Organization

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BACKGROUND

Real-world data (RWD) from administrative claims are essential for health technology assessment (HTA), but issues related to data quality and structural inconsistencies challenge valid inference. Process mining (PM) enables deterministic reconstruction of care pathways, while statistical modeling provides the inferential robustness required for evaluating the value, efficiency, and budgetary impact of oncology technologies.[1-4]

Multiple myeloma (MM) is a complex hematologic malignancy that often requires sequential, multi-drug regimens across several lines of therapy, generating substantial healthcare resource utilization and costs.[5,6] In Latin America, and particularly in Brazil, real-world evidence describing longitudinal treatment pathways and cost accumulation is limited.[7]

Process mining applied to administrative claims can reconstruct complex patient care trajectories such as those observed for MM and provide a structured view of treatment patterns and direct medical costs from a payer perspective, as demonstrated in the present work.

OBJECTIVES

- To describe real-world MM treatment pathways and transitions across lines of therapy using process mining.
- To quantify direct medical costs and identify cost drivers by treatment phase/line and by treatment complexity (therapeutic class exposure).
- To compare annual costs between patients initiating therapy in 2014–2019 versus 2020–2024 within a Brazilian private payer setting.

METHODS

Design and data source:

A retrospective cohort (2014–2024) of MM patients from a Brazilian managed-care organization (Unimed Paraná, Brazil), was analyzed. Eligible patients had > 9 claims associated with the ICD-10 code for MM (C90.0) or recurrent use of MM-specific therapies.

Population:

Patients with ≥9 claims coded with ICD-10 C90.0 and/or recurrent (≥3 months) use of MM-specific therapies (proteasome inhibitors, immunomodulatory agents, monoclonal antibodies, bispecific antibodies, CAR-T). Patients without MM-specific antineoplastic treatment and/or ASCT were excluded.

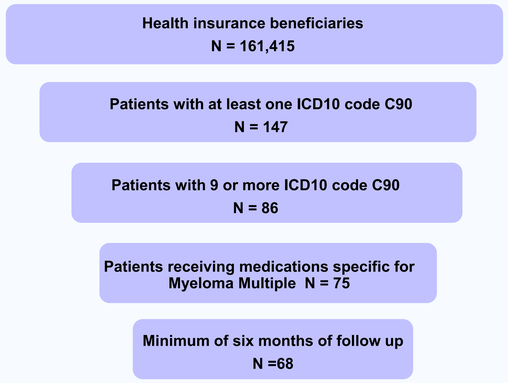
Analytic approach:

1. **Data transformation** encompassed (i) coding harmonization, (ii) rule-based derivation of treatment episodes, and (iii) PM extraction of event logs with standardized timestamps.
2. **Process mining** was performed with UpFlux AI™ to reconstruct care pathways and transitions between treatment lines and maintenance.
3. **Statistical modeling** included distributional diagnostics, descriptive and simple parametric and non-parametric inference testing.
4. Analyzed outcomes included (i) treatment regimens/lines and transitions, (ii) healthcare resource utilization, and (iii) direct medical costs from the private payer perspective.
5. **Costing methods:**

   Claims-paid amounts; costs adjusted to 2024 and converted to USD using annual average exchange rates.

RESULTS

The restructuring of the PM database yielded a coherent longitudinal dataset covering **68 patients (62% male; mean age 65.8 ± 11.1 years)** and **26 therapeutic regimens**, among which the majority employing **bortezomib, daratumumab, and lenalidomide (Figure 1)**.



• **Progression through lines**:

28% reached second-line therapy and 7% reached third-line therapy; >70% had first-line therapy as their last recorded treatment.

• **Total and per-patient costs:**

Total cost USD 12,671,857; mean total cost per patient USD 186,350.83 (SD 164,645.73); mean annual cost USD 78,425.81.

Cohort comparison:

Patients initiating treatment in 2020–2024 incurred higher expenditures (USD 144,823 ± 19,244) than the 2014–2019 group (USD 78,346 ± 78,742; t-test p=0.001), consistent with the incorporation of advanced therapies.

• **Cost distribution by phase:**

First-line therapy represented ~50% of total costs, followed by first-line maintenance (~25%) (**Table 1**).

• **Costs by treatment complexity:**

Mean monthly costs increased with broader class exposure (single-exposed USD 3,491.26; double-exposed USD 9,504.87; triple-exposed USD 12,796.55; p<0.001) (**Table 2**).

Table 1. Total costs according to treatment lines (2024 USD).

Treatment line	N	Total cost (USD)	% cost
Diagnostic stage	62	645,057.28	5%
1st line	68	6,350,272.78	50%
Maintenance-1st line	25	3,205,476.78	25%
2nd line	19	1,123,846.39	9%
Maintenance-2nd line	3	762,136.96	6%
3rd line	5	561,695.04	4%
4th line	1	23,371.38	0%

Table 2. Monthly costs based on type of exposure (2024 USD).

Monthly cost / patient	Exposed (N=43)	Double-exposed (N=48)	Triple-exposed (N=9)	p
Mean	3,491.26	9,504.87	12,796.55	<0.001
Standard deviation	3,403.18	6,612.93	4,624.81	
Median	2,830.05	7,803.07	10,511.70	
1st quartile	1,616.20	5,339.42	9,189.20	
3rd quartile	4,211.63	12,450.34	16,292.97	
Minimum	271.51	731.79	7,576.10	
Maximum	20,117.78	34,667.04	20,016.42	

DISCUSSION

- This real-world analysis demonstrates **substantial heterogeneity in MM care pathways** within a Brazilian supplementary (private) healthcare context, consistent with evolving therapeutic options and individualized sequencing.
- Costs were concentrated in early phases because most patients remained in first-line therapy and/or maintenance for long periods; therefore, **interpretation of line-specific costs should consider both the number of patients and time spent in each phase**.
- **Higher annual costs in 2020–2024 likely reflect greater uptake of newer, higher-cost agents** (e.g., daratumumab and lenalidomide) and more complex combinations.
- **Process mining proved useful to transparently reconstruct treatment trajectories from claims**, offering a complementary, descriptive approach that can inform hypotheses and support pathway-centric discussions in HTA and managed care.
- **Limitations**: The lack of **clinical variables** (e.g., stage, response) inherent to claims data, may under-capture therapies obtained outside the payer system, and **eligibility based on repeated claims may introduce selection and immortal time/survivor bias**.

CONCLUSION

- Process mining of administrative claims enabled a structured depiction of MM treatment pathways and transitions across lines of therapy in Brazil.
- Direct medical costs were high and increased markedly with treatment complexity (greater therapeutic class exposure).
- These findings can support payer and policy discussions on pathway management, budgeting, and the impact of adopting newer combination regimens, acknowledging claims-based limitations.

DISCLOSURES

Ethical Approval: The study analyzed de-identified administrative data in compliance with the Brazilian General Data Protection Law (Lei Geral de Proteção de Dados number 13.709/2018). Ethical review was waived as no identifiable patient information was accessed. Certificate of Presentation for Ethical Assessment (CAAE): 84828624.2.0000.0020.

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