Healthcare resource utilization and costs among multiple myeloma patients with double- or triple-class exposure: a retrospective U.S. claims database analysis

Joseph Seungik Yang

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Douglas Barthold

Josh J. Carlson

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Abstract

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Joseph Seungik Yang

Chair of the Supervisory Committee:

Douglas Barthold

School of Pharmacy

Background: Despite recent advancements in the therapeutic landscape, MM remains incurable, and most patients require several lines of therapies (LOTs). The lack of treatment options for these patients has prompted the development of new targeted therapies with novel mechanisms. Currently, there is limited evidence describing the economic burden among MM patients exposed to different drug classes and combinations and across different healthcare settings.

Objective: To describe all-cause and MM-related HCRU and costs among MM patients exposed to different drug classes and combinations (e.g., double- and triple-class exposed) and characterize all-cause and MM-related healthcare costs incurred in different healthcare settings among these MM patients.

Methods: We conducted a retrospective cohort study using administrative claims data from the IBM® MarketScan® Commercial and Medicare Supplemental databases. The study included adult patients (≥18 years) diagnosed with MM between December 1st, 2015 and December 31st, 2019. The study sample comprised double-class exposed (DCE) and triple-class exposed (TCE) cohorts, categorized based on

their earliest exposures to different combinations of immunomodulatory drugs (IMiDs), proteasome inhibitors (PIs), or targeted monoclonal antibody (mAbs). Only patients with ≥ 1 subsequent LOT following the categorization were included, and the start date of the first subsequent LOT was the index date. The primary outcomes of interest were all-cause and MM-related healthcare resource utilization (HCRU) and costs during the follow-up period. We categorized eight different care settings associated with the study sample using the place of service code variable. The total all-cause and MM-related costs incurred by patients in each setting were reported. The Kaplan-Meier sample average (KMSA) technique was used to estimate the cumulative mean outcomes, accounting for differential follow-up periods, and the outcomes were reported as per patient per month (PPPM).

Results: The study included 1,521 MM patients, of which 1,016 (66.8%) patients were DCE and 505 (33.2%) were TCE. Using the estimates from the KMSA, the mean PPPM total all-cause healthcare costs were $20,338 PPPM, and approximately 85% of the total all-cause costs were MM-related. The mean total all-cause and MM-related total costs were driven by overall drug costs, primarily attributed to MM treatment and administration costs. When stratified by the class-exposure status, the TCE cohort was associated with higher HCRU and incurred higher costs than the DCE cohort across all categories. The hospital-based ambulatory setting was the highest cost setting during the follow-up period, with the mean total all-cause and MM-related costs of $7,302 (95% CI: $6,801-$7,784) PPPM and $6,695 (95% CI: $6,239-$7,136) PPPM, respectively.

Conclusion: The findings of this study suggest that the economic burden following exposure to multiple drug classes and combinations is substantial, especially among the TCE cohort compared to the DCE cohort and in the ambulatory setting. Total costs incurred by these patients were primarily MM-related and mainly attributable to MM drug and administration costs. These findings highlight the need for more effective treatments that can mitigate the resource use and economic burden in the management

of MM. Future research on the HCRU and costs incurred after the exposure to recently approved MM treatments with novel mechanisms is warranted.

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1. Introduction

Multiple myeloma (MM) is a rare malignancy of plasma cells, characterized by the proliferation of malignant cells in the bone marrow, which result in immune suppression and end-organ damage.[1] Common complications associated with MM include hypercalcemia, renal dysfunction, anemia, bone loss and fractures.[1] In the United States (US), MM is the third most common hematologic malignancy and accounts for approximately 1.8% of all new cancer cases in the United States (US).[2] MM is most frequently diagnosed among people aged 65 to 74 years and is more common in men than women.[2] In 2022, approximately 34,470 new cases of MM will be diagnosed, and 12,640 patients are expected to die from this disease in the US.[2]

In the last two decades, several classes of drugs have emerged and significantly improved patients' clinical outcomes, such as immunomodulatory drugs (IMiDs; lenalidomide, thalidomide, and pomalidomide), proteasome inhibitors (PIs; bortezomib, carfilzomib, and ixazomib), and targeted monoclonal antibodies (mAbs; daratumumab, elotuzumab, and isatuximab).[3] These drug classes enabled patients to live longer, and the five-year relative survival rate increased from 31.6% in the 1990s to 57.9% in 2012-2018 in the US.[2] Since then, the National Comprehensive Cancer Network Clinical Practice Guidelines in Multiple Myeloma (NCCN Guidelines®) recommend that the initial therapy should involve combinations of an IMiD, a PI, and/or a mAb with a corticosteroid (e.g., dexamethasone).[4] Following the initial treatment, the guideline recommendations for the subsequent therapies vary, and several factors influence the selection, such as the patient's response to previous treatment and tolerance to toxicities.[4] Despite recent advancements in the therapeutic landscape, MM remains incurable, and most patients eventually relapse or become refractory to classes of drugs, requiring several lines of therapies (LOTs).[3]

MM patients who have received multiple prior LOTs have limited treatment options available. Despite previous exposures or refractoriness, these patients are frequently retreated with the same classes of drugs and are more likely to experience poor outcomes.[5] Most MM patients relapse and receive multiple salvage therapies, which decrease patients' response to treatments and the duration of progression-free intervals, while the burden of MM-related symptoms and complications increase.[6] In addition, previous studies have documented that MM is associated with a substantial financial burden, and this burden is more significant among patients with disease progressions and advance through several LOTs.[7-10] The lack of treatment options for these patients has prompted the development of new biologic and targeted therapies with novel mechanisms that can potentially delay disease progression

and improve clinical outcomes. Several therapies with novel mechanisms have been approved by the FDA or are still under investigation, such as antibody-drug conjugates (ADC), chimeric antigen receptor T-cell therapy (CAR-T), and bispecific T-cell engager therapy (BiTE).[11]

It is imperative to have a deeper and more granular understanding of healthcare resource utilization (HCRU) and costs associated with the patient population who can potentially benefit from these novel therapies. It allows the decision-makers to better understand the potential clinical and economic value associated with the new and future innovative MM treatments. While recent studies have described the HCRU and costs among newly diagnosed and heavily pre-treated MM patients, there is limited evidence describing the economic burden among MM patients exposed to different drug classes and combinations and across different healthcare settings.[7-10,12-14] An accurate and current assessment of the economic burden of MM patients would aid in decisions to optimize resource allocations, including access to existing and future therapies.

2. Objectives

The primary objective of this study was to describe all-cause and MM-related HCRU and costs among MM patients exposed to different drug classes and combinations (e.g., double- and triple-class exposed) from a third-party payer perspective in the US. The secondary objective of this study was to describe and characterize all-cause and MM-related healthcare costs incurred in different healthcare settings among these MM patients.

3. Methods

3.1. Study Design and Data Source

This was a retrospective observational cohort study, and the study period was from December 1st, 2015 to December 31st, 2019 (Figure 8.1). We chose December 1st, 2015 as the starting date for this study because it was the earliest date after daratumumab and elotuzumab were approved by the FDA. The data source for this study was de-identified administrative claims from the IBM® MarketScan® Commercial Claims and Encounters (CCAE) and Medicare Supplemental (MDCR) databases. These databases contain fully paid and adjudicated inpatient, outpatient, and pharmacy insurance claims data of active employees, their spouses, and dependents covered by employer-sponsored private health insurance in the US and Medicare-eligible retirees covered by Medicare Advantage and Medicare

Supplemental health insurance plans.[15] One of the advantages of the MarketScan® databases is that it is a compilation of healthcare claims and reflects real-world treatment patterns, resource utilization, and associated direct costs as patients move across the US healthcare system. The MarketScan® databases are fully compliant with the Health Insurance Portability and Accountability Act of 1996 (HIPAA).[15]

3.2. Study Population and Sample

This study included adult patients (≥ 18 years) with ≥ 1 confirmed diagnosis of MM, identified according to the International Classification of Disease (ICD) 9th and 10th Revisions (ICD-9 code 203.0x or ICD-10 code C90.0x), and who have completed ≥ 1 cycle of IMiDs, PIs, or mAb during the study period. At least one inpatient service claim or at least two outpatient service claims within 30 to 365 days apart with a primary or secondary diagnosis of MM defined confirmed diagnosis.

From the overall study population, the study sample comprised two groups of patients categorized based on their earliest exposures to different combinations of IMiDs, PIs, and mAb. The first group was double-class exposed (DCE), defined by patients exposed to two drug classes of interest through monotherapy or combination regimens. Patients who received the following combination of classes were categorized into the DCE group: IMiD and PI, IMiD and mAb, or PI and mAb. The second group was triple-class exposed (TCE), defined by patients exposed to all three drug classes of interest through monotherapy or combination regimens. The majority of the recommended regimens from the NCCN Guidelines include corticosteroid (i.e., dexamethasone) thus, evidence of receiving corticosteroid did not count as a drug class in the definitions for DCE and TCE.

The patient's exposures to different drug classes and combinations were defined by completing at least one line of therapy (LOT) that contained IMiDs, PIs, or mAb, regardless of sequences or combinations used. The 'pre-index LOT' was defined as the earliest LOT that met the definitions of DCE and TCE and categorized the patients into each group. The 'index LOT' was defined as the new LOT received following the pre-index LOT, and the start date of the 'index LOT' was the index date for each patient (Figure 8.1). To estimate the HCRU and costs following exposures to different drug class combinations, only patients with the index LOT were included.

The baseline period was defined as six months prior to the index date to assess patient demographic and clinical characteristics and baseline HCRU and costs. The study only included patients with continuous enrollment during this period. The study outcomes were assessed during the follow-up period, defined as time from the index date to the end of the study period or the end of continuous enrollment, whichever occurred first (Figure 8.1). Patients with at least one month of follow-up were included.

3.3. Line of Therapy (LOT)

The previously recommended guideline for determining the number of prior LOT in MM was adapted and used in this study to define a LOT.[16] The guideline also described the conditions for a new LOT to identify the 'index LOT' following the 'pre-index LOT'.[16] In general, a LOT was defined as at least one complete cycle of a single drug, a regimen that consists of combinations of different drugs, or planned sequential treatments of various regimens. A treatment was considered a new LOT if one of the following conditions were met:

1. A new MM treatment was added after the initial 28 days after the start of a regimen.
2. Discontinuation of all treatments in a regimen and then restart the regimen with at least one other regimen administered in between.

However, the following scenarios did not meet the conditions for a new LOT:

1. Discontinuation of at least 1 MM treatment in a regimen, but not all treatments in the regimen.
2. Discontinuation and then restart of all MM treatments in a regimen without any new treatments administered in between.
3. Discontinuation of at least 1 MM treatment in a regimen, but not all, and then restart of the discontinued treatment.

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3.4. Study Measures and Outcomes

Baseline demographic and clinical characteristics were assessed for each patient during the baseline period. Information regarding sex, age, Charlson Comorbidity Index (CCI) scores, US region of residence, insurance type (e.g., commercial or Medicare supplemental), and year of the index date were reported.

Age was further stratified into < 65 years and ≥ 65 years.

The primary outcomes of interest were all-cause and MM-related HCRU and costs for each patient during the follow-up period. MM-related HCRU and costs were defined by claims with ICD-9 and ICD-10 codes for MM diagnosis. Total costs were identified using the total payment variable within the MarketScan® database. All costs were adjusted to 2021 US dollars using the medical care component of the Consumer Price Index for urban consumers.[17]

All-cause and MM-related HCRU measures included the number of emergency department (ED) visits, outpatient physician office visits, other outpatient visits (i.e., all outpatient visits excluding ED visits and outpatient physician office visits), outpatient pharmacy prescriptions, hospitalizations, and hospitalization length of stay in days. All-cause healthcare costs included ED costs, outpatient costs, inpatient costs, overall drug costs, and total healthcare costs. MM supportive treatment costs were reported within the overall drug costs, defined as the sum of costs for drug classes commonly used to manage complications experienced by MM patients.[18-19] These included antiresorptive therapy (e.g., bisphosphonates and the receptor activator of nuclear factor-kappa B and its ligand (RANKL) inhibitors) for bone-related events, opioids for pain, selective norepinephrine reuptake inhibitors (SNRI), gabapentinoid, and tricyclic antidepressants (TCA) for chemotherapy-induced neuropathic pain, anticoagulants for venous thromboembolism, and erythropoiesis-stimulating agents (ESA) for anemia. MM-related healthcare costs included MM treatment costs, MM treatment administration costs, ED costs, outpatient costs, inpatient costs, and total MM-related costs. All-cause and MM-related HCRU and costs among patients with ≥ 1 ED, outpatient, or inpatient visits were also reported.

For the secondary objective of this study, different healthcare settings were defined by the place of service code variable available in the MarketScan® database (i.e., MarketScan® variable STDPLAC). This code set represents 50 unique settings used on the claim to specify where services occurred.[20] Based on the place of service codes present in all claims for the study sample, the codes were sorted and categorized into eight different care settings: hospital-based ambulatory, office-based ambulatory, inpatient, emergency/urgent care, institutional stays, laboratory services, behavioral health care, and others (Appendix 1). The categorization of each code was adapted from the previous literature that had classified the place of service code to identify settings for prescriptions.[21] The total all-cause and MM-related costs incurred by patients in each setting during the follow-up period were reported.

Subgroup analyses were conducted based on patient characteristics and healthcare cost types to stratify the study outcomes and make descriptive statistical comparisons. The subgroups were compared by sex, age, years of the index date, exposure to mAb, and insurance type. Age was stratified into under 65 years and 65 years or greater. The healthcare costs were stratified into patient out-of-pocket costs (i.e., the sum of coinsurances, copays, and deductibles) and payer costs (i.e., identified using the net payment variable within the MarketScan® database). All-cause and MM-related total costs incurred by patients in each subgroup and by each cost type during the follow-up period were reported.

3.5. Statistical Analysis

All analyses conducted in this study were descriptive, and no hypothesis testing was conducted. Continuous variables were summarized with mean and standard deviation (SD) or 95% confidence intervals, and categorical variables were summarized with counts and percentages. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

The cumulative HCRU and costs during the follow-up period were estimated using the Kaplan-Meier sample average (KMSA) technique to account for differential follow-up time due to censored patients. Patients were censored at the event of discontinuation in insurance coverage or the end of the study period, whichever occurred first. The KMSA technique estimated the cumulative mean outcomes during the follow-up period by calculating the sum of the products of the monthly probability of patients remaining in the health plan and the monthly mean outcomes (i.e., HCRU and costs) among patients who remain in the health plan.[22-23] The survival weights were calculated with a follow-up time of 48 months. Nonparametric bootstrapping methods with 1,000 independent samples were used to generate the 95% confidence intervals for the KMSA estimates. The costs and HCRU were reported as per patient per month (PPPM), calculated by dividing the mean cumulative HCRU or cost measures per patient during the follow-up period by the mean follow-up duration.

4. Results

4.1. Baseline Patient Characteristics

The study included a total of 1,521 MM patients who met all the inclusion criteria. 1,016 (66.8%) of these patients were DCE, and 505 (33.2%) were TCE (Figure 8.2). Mean age of the overall cohort at the index date was 62.3 years, and 57% were male. The majority of the patients were under 65 years (68.6%) and enrolled in commercial insurance during the study period (67.7%). All patients had a CCI

score of above 2, and the majority had a score over 3 (65.7%). In terms of the region, the largest proportion of the patients was in the South geographical region (38.8%). We observed an increasing trend in the proportions of patients in each index date for the overall cohort. When stratified by class-exposure status, the proportion of the DCE cohort in each index year decreased, while the proportion of the TCE cohort increased across four years of the follow-up period. The majority of the DCE cohort consisted of patients exposed to combinations of an IMiD and a PI (91.7%), which are the most commonly recommended drug combinations (Table 7.1).[4]

4.2. Baseline Healthcare Resource Utilization & Costs

During the baseline period, the overall cohort had 5.20 (95% CI: 5.00-5.40) PPPM all-cause physician office visits and 5.86 (95% CI: 5.67-6.04) PPPM other outpatient visits (Table 7.2). MM-related physician office visits and other outpatient visits were 3.22 (95% CI: 3.11-3.33) PPPM and 4.19 (95% CI: 4.05-4.33) PPPM, respectively. The mean number of all-cause hospitalization was 0.11 (95% CI: 0.10-0.12) PPPM, with the average length of stay of 1.07 (95% CI: 0.96-1.18) PPPM. When we stratified by class-exposure status, healthcare resource utilization were similar in the TCE and the DCE cohorts (Table 7.2).

The mean total all-cause healthcare costs during the baseline period were $29,849 (95% CI: $28,673-$31,026) PPPM and large proportion (81%) of the costs were MM-related, which were $24,177 (95% CI: $23,189-$25,164) PPPM (Table 7.2). Majority (53%) of the all-cause healthcare costs were drug costs of $15,879 (95% CI: $15,205-$16,553) PPPM and most of the costs were related to MM-treatments of $13,030 (95% CI: $12,443-$13,617) PPPM. The mean all-cause outpatient costs were $7,889 (95% CI: $7,277-$8,500) PPPM and the inpatient costs were $5,882 (95% CI: $5,196-$6,568) PPPM. The TCE cohort incurred higher mean total all-cause costs than the DCE cohorts, $39,084 (95% CI: $36,803-$41,364) and $25,260 (95% CI: $24,002-$26,517), respectively (Table 7.2).

4.3. Healthcare Resource Utilization & Costs during the Follow-up Period

After the index date, the mean duration of follow-up was 16.3 months for the overall cohort, 18.4 months for the DCE cohort, and 12.1 months for the TCE cohort. The overall cohort's mean number of all-cause physician office visits and other outpatient visits were 3.03 (95% CI: 2.91-3.13) PPPM and 3.56 (95% CI: 3.42-3.73) PPPM, respectively. MM-related physician office visits and other outpatient visits were 2.21 (95% CI: 2.14-2.29) PPPM and 2.49 (95% CI: 2.42-2.60) PPPM (Table 7.3). The majority of all-cause hospitalization was MM-related, 0.06 (95% CI: 0.06-0.07) PPPM, with the average length of stay of

0.61 days (95% CI: 0.56-0.66) PPPM. When we stratified the HCRU by class-exposure status, the TCE cohort had higher utilization across all categories for all-cause and MM-related than the DCE cohort (Table 7.3).

The mean total all-cause and MM-related total costs were driven by overall drug costs, largely attributed to MM treatment and administration costs, followed by outpatient and inpatient costs (Figure 8.3). The overall cohorts' mean total all-cause healthcare costs were $20,338 (95% CI: $19,384-$20,956) PPPM. Approximately 85% of all-cause total healthcare costs were MM-related (Table 7.3). When we stratified the costs by class-exposure status, the TCE cohort incurred higher costs across all categories compared to the DCE cohort (Table 7.3). The mean total all-cause healthcare costs for the DCE and the TCE cohorts were $17,171 (95% CI: $16,458-$17,599) PPPM and $29,791 (95% CI: $28,804-$30,020) PPPM, respectively.

Among patients with at least one ED, outpatient, or inpatient visit, 22% had MM-related ED visits, 50% had MM-related inpatient admission, and 99% had MM-related outpatient visits. The TCE cohort had higher utilization and incurred higher costs across all-cause and MM-related HCRU, and cost measures compared to the DCE cohort (Table 7.4).

4.4. Costs by Healthcare Settings

Among eight different health care settings defined by the place of service codes, hospital-based ambulatory setting was the highest cost setting during the follow-up period with the mean total all-cause and MM-related costs of $7,302 (95% CI: $6,801-$7,784) PPPM and $6,695 (95% CI: $6,239-$7,136) PPPM, respectively. The next highest cost settings were the inpatient hospital, with total all-cause costs of $6,370 (95% CI: $5,596-$7,219) PPPM and total MM-related costs of $4,862 (95% CI: $4,261-$5,497) PPPM, and office-based ambulatory setting, with total all-cause costs of $2,472 (95% CI: $2,273-$2,679) PPPM and total MM-related costs of $2,115 (95% CI: $1,956-$2,279) PPPM (Figure 8.4).

4.5. Subgroup Analyses

We examined subgroups based on healthcare cost types and patient characteristics (Table 7.5). Majority of the healthcare costs were borne by payers, with total all-cause costs of $16,129 (95% CI: $15,512-$16,771) PPPM and total MM-related costs of $14,054 (95% CI: $13,522-$14,598). The mean total all-cause healthcare costs were similar in males and females, $20,504 (95% CI: $19,915-$21,107) and

$19,118 (95% CI: $18,580-$19,610), respectively. Patients under 65 years incurred higher total all-cause costs compared to patients 65 years or older, $22,484 (95% CI: $21,813-$23,165) and $15,171 (95% CI: $14,728-$15,471), respectively. Similarly, patients with commercial insurance incurred higher total all-cause costs compared to patients with Medicare, $22,693 (95% CI: $22,138-$23,403) and $15,142 (95% CI: $14,732-$15,458), respectively (Table 7.5). We observed the same trend in the mean total MM-related healthcare costs for these subgroups. In addition, we observed an increasing trend in the mean total all-cause and MM-related costs across years of index date. The mean total all-cause healthcare costs were $12,292 (95% CI: $12,131-$12,391) PPPM among patients with index date in 2016, $19,449 (95% CI: $19,117-$19,684) PPPM in 2017, $26,227 (95% CI: $25,878-$26,481) PPPM in 2018, and $32,734 (95% CI: $32,181-$33,054) PPPM in 2019. Patients exposed to mAb had higher mean total all-cause and MM-related costs than patients unexposed to the drug class (Table 7.5).

5. Discussion

This retrospective observational cohort study assessed all-cause and MM-related HCRU and costs among patients exposed to different drug classes and combinations and costs incurred in different healthcare settings. The mean follow-up duration for the overall cohort was 16.3 months. Using the estimates from the KMSA, the mean PPPM total all-cause healthcare costs were $20,338 PPPM, and approximately 85% of the total all-cause costs were MM-related. The overall drug costs were the primary cost driver, followed by outpatient, inpatient, and ED costs. When stratified by the class-exposure status, the TCE cohort was associated with higher HCRU and incurred higher costs compared to the DCE cohort across all categories. The total all-cause healthcare costs for the DCE and TCE cohorts were $17,171 and $29,791 PPPM, respectively. Among different healthcare settings categorized by place of service codes, the mean total all-cause and MM-related healthcare costs for the hospital-based ambulatory setting were the highest, followed by inpatient and office-based ambulatory settings.

The findings from this study provide a deeper and more granular update to the current body of evidence on the economic burden of MM patients following their exposure to IMiD, PI, and/or mAb. To our knowledge, this was the first study to describe the economic burden among double-class exposed MM patients and across different healthcare settings. The results of this study highlighted high monthly costs incurred by MM patients and differences in economic burden across class-exposure status, patient characteristics, and different healthcare settings. These findings emphasize that future therapies with

novel mechanisms that improve health outcomes and reduce economic burden will be valuable to these MM patients.

We assessed the mean total all-cause and MM-related healthcare costs incurred in different healthcare settings for the secondary objective. Patients who received services in hospital-based ambulatory setting incurred the highest mean total all-cause and MM-related healthcare costs. Several reasons may explain this. First, the use of regimens containing more recently approved novel treatments (e.g., carfilzomib, daratumumab, and elotuzumab) have increased in recent years because they have demonstrated improved clinical outcomes when administered in combination with older treatments (e.g., lenalidomide and bortezomib).[25] Most MM treatments are administered as injections, and a hospital-based ambulatory setting is where MM patients most commonly receive treatments. In addition, the previous study has estimated high average monthly costs of receiving triplet regimens containing these newer treatments, ranging from $13,890 to $27,432 per patient.[26] Thus, the high costs incurred in the hospital-based ambulatory setting are primarily attributable to the high costs associated with regimens that contain newer novel treatments.

We compared the findings from this study to previously published studies that assessed the economic burden among MM patients following the drug class exposures in the US. Several studies described the economic burden following triple-class exposures. The study by Madduri et al was the first study to describe HCRU and costs among triple-class exposed patients who have received at least one subsequent LOT using the MarketScan® CCAE and MDCR databases. The study identified 154 patients who met the inclusion and exclusion criteria from December 1st, 2015 to September 30th, 2018.[12] The sample size of Madduri et al was smaller than the sample size of the TCE cohort in this study. This may be explained by several reasons. First, the continuous enrollment requirements for the inclusion criteria in this study were different from Madduri et al, where they only included patients with continuous enrollment throughout the study period. Second, while the beginning date for this study was the same as Madduri et al, the study period for Madduri et al ended 15-months earlier than the end of this study period. Lastly, the conditions that define a LOT and a new LOT in Madduri et al differed from this study. Despite differences in sample populations, the findings of the two studies were consistent with similar total all-cause and MM-related healthcare costs, $37,033 PPPM and $35,657 PPPM, respectively.[12] Additionally, both studies reported that most of the total all-cause healthcare costs were MM-related,

and MM therapy medications and therapy administrations represented over 50% of the mean total MM-related healthcare costs.[12]

The study by Jagannath et al also used MarketScan® CCAE and MDCR databases and provided more current cost estimates for the TCE cohorts following their exposures than Madduri et al, where they included adult patients diagnosed with MM between January 1st, 2009 and February 28th, 2021.[13] Jagannath et al included 85 patients in the TCE cohort, which was smaller than the sample sizes of this study and Madduri et al. A potential reason for the small sample size in Jagannath et al might be due to more restrictive patient eligibility requirements. The study required that follow-up LOT to have occurred after January 1st, 2017, and only included patients who have survived at least one year after the index date.[13] The mean all-cause total healthcare costs during the follow-up per patient were $722,992, equivalent to $34,578 PPPM. Consistent with the results from this study and Madduri et al, most of the total all-cause healthcare costs incurred during the follow-up period were MM-related, and MM drugs and administration costs represented the largest proportion of the total MM-related healthcare costs.[13]

In the baseline patient demographic and clinical characteristics of this study sample, we observed an increasing trend in the proportion of patients in each year of index. This trend may be explained by the results of Braunlin et al, where they described the trends in the proportion of patients receiving different drug class combination regimens in 2-year increments across first to fifth LOTs from 2012 to 2019 using the Flatiron Health electronic health records (EHR) database.[24] They identified and described different regimens by the number of agents a regimen consists of (i.e., monotherapy, doublet, triplet, and quad). The triplet regimen in Braunlin et al included all drug class combinations used to define the DCE and TCE groups in this study because dexamethasone was considered as an agent in a regimen, whereas this study did not consider dexamethasone in the definitions of DCE and TCE. Similar to the trend observed in this study, Braunlin et al observed an increasing trend in the use of the triplet regimen across all LOTs over the study period.[24] However, they did not report the changes in the proportions of different drug class combinations within the triplet regimen over the study period. The study results of Braunlin et al and the trend observed in this study indicate that the number of DCE and TCE patients will likely continue to increase in the future. Furthermore, we observed an increasing trend in the mean total all-cause and MM-related healthcare costs across years of index date. Thus, a continuous increase in the number of DCE and TCE patients indicates that the economic burden among MM patients will also

continue to increase, which further highlights the need for future therapies that offer both clinical and economic value.

There are several limitations of this study to consider when interpreting the results of this study. First, administrative claims databases are prone to misclassification bias due to possible errors in the coding of MM diagnosis and measurements of any other variables in the study. Second, the MarketScan® CCAE and MDCR databases are not representative of all patients in the US, and the findings of this study may not be generalizable to MM patients with insurance types not represented within the MarketScan® database. Third, medication use in the claims was assumed as prescribed, and actual consumption or compliance could not be confirmed. Fourth, the end of the study period was December 2019, and the study did not reflect the impact of newer therapies approved after the study period on the study outcomes. Future follow-up studies that assess the HCRU and costs incurred after exposure to CAR-T, ADC, or other newly approved therapies are warranted. Lastly, this study did not consider indirect costs, such as costs associated with absenteeism and presenteeism. Future research on indirect costs is warranted to fully characterize the economic burden associated with MM patients who have been exposed to different drug classes and combinations.

6. Conclusion

This retrospective real-world study assessed and described HCRU and costs among MM patients exposed to different drug classes and combinations. Overall, the study findings suggest that the economic burden following exposure to multiple drug classes and combinations is substantial, especially among the TCE cohort compared to the DCE cohort and in ambulatory and inpatient settings. Total costs incurred by these patients were primarily MM-related and mainly attributable to MM drug and administration costs. These findings highlight the need for more effective treatments that can mitigate the resource use and economic burden in the management of MM. With recent FDA approval for treatments with novel mechanisms, such as ADC and CAR-T therapies, future research on the HCRU and costs incurred after the exposure to these treatments is warranted.

7. Tables

7.1. Baseline patient demographic and clinical characteristics

	Overall (n = 1,521)	**Double-class exposed** (n = 1,016)	**Triple-class exposed** (n = 505)
Sex, N (%)			
Male	867 (57)	576 (56.7)	291 (57.6)
Female	654 (43)	440 (43.3)	214 (42.4)
Age in years*, Mean (SD)	62.3 (10.5)	62.5 (10.8)	62.1 (9.8)
Age group, N (%)			
< 65	1,044 (68.6)	684 (67.3)	360 (71.3)
65+	477 (31.4)	332 (32.7)	145 (28.7)
CCI Group, N (%)			
0	0	0	0
1	0	0	0
2	521 (34.3)	368 (36.2)	153 (30.3)
3+	1,000 (65.7)	648 (63.8)	352 (69.7)
U.S. Region of Residence, N (%)			
North Central	380 (25)	250 (24.6)	130 (25.7)
Northeast	348 (22.9)	243 (23.9)	105 (20.8)
South	590 (38.8)	396 (39)	194 (38.4)
West	202 (13.2)	126 (12.4)	76 (15.1)
Unknown	1 (0.1)	1 (0.1)	0
Insurance Type			
Commercial	1,030 (67.7)	670 (65.9)	360 (71.3)
Medicare	491 (32.3)	346 (34.1)	145 (28.7)
Years at Index LOT Initiation, N (%)			
2016	305 (20)	303 (29.8)	2 (0.4)
2017	406 (26.7)	255 (25.1)	151 (29.9)
2018	401 (26.4)	233 (22.9)	168 (33.3)
2019	409 (26.9)	225 (22.2)	184 (36.4)
Previous class-exposures, N (%)			
Double-class exposed	1,016 (66.8)		
▪ IMiD + PI	932		
▪ IMiD + mAb	44		
▪ PI + mAb	40		
Triple-class exposed	505 (33.2)		

Abbreviations: MM – Multiple myeloma; CCI – Charlson-Deyo Comorbidity Index; LOT – Line of Therapy; IMiD – Immunomodulatory Drug; PI – Proteasome Inhibitors; mAb – Targeted monoclonal antibodies

*Age as of the index date

7.2. All-cause and MM-related HCRU and costs incurred during the baseline period*

	Overall (n = 1,521)	**Double-class exposed** (n = 1,016)	**Triple-class exposed** (n = 505)
	Mean (95% CI)	**Mean (95% CI)**	**Mean (95% CI)**
All-Cause HCRU, PPPM			
ED visits	0.11 (0.09-0.12)	0.11 (0.09-0.12)	0.10 (0.08-0.13)
Outpatient			
▪ Physician office visits	5.20 (5.00-5.40)	4.90 (4.66-5.13)	5.81 (5.45-6.17)
▪ Other outpatient visits	5.86 (5.67-6.04)	5.42 (5.20-5.64)	6.73 (6.39-7.08)
Outpatient prescriptions	4.83 (4.69-4.96)	4.62 (4.46-4.77)	5.24 (4.98-5.50)
Hospitalizations	0.11 (0.10-0.12)	0.10 (0.09-0.11)	0.12 (0.10-0.13)
Inpatient length of stay (days)	1.07 (0.96-1.18)	1.07 (0.93-1.20)	1.06 (0.87-1.26)
MM-related HCRU, PPPM			
ED visits	0.05 (0.04-0.06)	0.05 (0.04-0.06)	0.05 (0.03-0.06)
Outpatient			
▪ Physician office visits	3.22 (3.11-3.33)	3.00 (2.87-3.13)	3.67 (3.48-3.86)
▪ Other outpatient visits	4.19 (4.05-4.33)	3.84 (3.68-4.00)	4.89 (4.63-5.15)
Outpatient prescriptions	0.89 (0.85-0.92)	0.90 (0.85-0.94)	0.87 (0.81-0.92)
Hospitalizations	0.10 (0.09-0.11)	0.10 (0.09-0.11)	0.11 (0.10-0.13)
Inpatient length of stay (days)	1.02 (0.91-1.12)	1.01 (0.88-1.14)	1.04 (0.85-1.23)
All-cause healthcare costs, PPPM**			
ED visits costs	$200 ($147-$254)	$190 ($125-$254)	$221 ($127-$316)
Outpatient costs ‡	$7,889 ($7,277-$8,500)	$7,285 ($6,604-$7,966)	$9,102 ($7,872-10,331)
Inpatient costs	$5,882 ($5,196-$6,568)	$5,722 ($4,923-$6,522)	$6,203 ($4,902-$7,503)
Overall drug costs	$15,879 ($15,205-$16,553)	$12,062 ($11,458-$12,667)	$23,557 ($22,149-$24,967)
▪ MM supportive treatment ‡‡	$489 ($432-$547)	$411 ($345-$477)	$646 ($537-$755)
Total all-cause healthcare costs	$29,849 ($28,673-$31,026)	$25,260 ($24,002-$26,517)	$39,084 ($36,803-$41,364)
MM-related healthcare costs, PPPM**			
MM-related drug costs			
▪ MM treatment costs	$13,030 ($12,443-$13,617)	$9,928 ($9,416-$10,440)	$19,271 ($17,997-$20,546)
▪ MM treatment administration costs	$564 ($481-$646)	$321 ($238-$404)	$1,053 ($876-$1,229)
ED visits costs	$99 ($55-$142)	$96 ($37-$154)	$104 ($46-$162)
Outpatient costs ‡	$6,140 ($5,598-$6,681)	$5,630 ($5,046-$6,215)	$7,164 ($6,037-$8,291)
Inpatient costs	$4,344 ($3,799-$4,889)	$4,170 ($3,590-$4,749)	$4,695 ($3,537-$5,853)
Total MM-related costs	$24,177 ($23,189-$25,164)	$20,145 ($19,162-$21,129)	$32,287 ($30,236-$34,339)

Abbreviations: MM – Multiple myeloma; HCRU – Healthcare resource utilizations; ED – Emergency department; SD – Standard deviation; PPPM – Per-patient per month; CI – Confidence interval.

*Baseline period is defined as from 6 months prior to the index date to the index date

**Total costs were identified using the total payment variable within the MarketScan® database. All costs reported in 2021 U.S. dollars.

7.3. All-cause and MM-related healthcare costs incurred during the follow-up period*

	Overall (n = 1,521)	**Double-class exposed** (n = 1,016)	**Triple-class exposed** (n = 505)
Follow-up duration in months, mean (SD)	16.31 (13.20)	18.40 (13.91)	12.10 (9.51)
	Mean (95% CI)	**Mean (95% CI)**	**Mean (95% CI)**
All-Cause HCRU, PPPM			
ED visits	0.06 (0.05-0.06)	0.05 (0.04-0.05)	0.08 (0.08-0.09)
Outpatient			
▪ Physician office visits	3.03 (2.91-3.13)	2.68 (2.60-2.76)	4.05 (3.98-4.13)
▪ Other outpatient visits	3.56 (3.42-3.73)	3.00 (2.91-3.09)	5.19 (5.09-5.26)
Outpatient prescriptions	3.15 (3.06-3.24)	2.92 (2.83-2.99)	3.84 (3.79-3.89)
Hospitalizations	0.07 (0.06-0.07)	0.05 (0.05-0.05)	0.11 (0.11-0.12)
Inpatient length of stay (days)	0.63 (0.58-0.73)	0.53 (0.49-0.56)	0.96 (0.91-0.99)
MM-related HCRU, PPPM			
ED visits	0.02 (0.02-0.03)	0.02 (0.01-0.02)	0.04 (0.04-0.05)
Outpatient			
▪ Physician office visits	2.21 (2.14-2.29)	1.93 (1.87-1.99)	3.07 (3.01-3.13)
▪ Other outpatient visits	2.49 (2.42-2.60)	2.06 (1.99-2.12)	3.77 (3.72-3.82)
Outpatient prescriptions	0.65 (0.62-0.67)	0.64 (0.62-0.66)	0.68 (0.66-0.69)
Hospitalizations	0.06 (0.06-0.07)	0.05 (0.04-0.05)	0.11 (0.11-0.11)
Inpatient length of stay (days)	0.61 (0.56-0.66)	0.50 (0.47-0.54)	0.93 (0.89-0.97)
All-cause healthcare costs, PPPM			
ED visits costs	$132 ($93-$166)	$119 ($77-$139)	$170 ($136-$178)
Outpatient costs ‡	$5,047 ($4,682-$5,499)	$4,230 ($3,859-$4,511)	$7,452 ($7,004-$7,685)
Inpatient costs	$3,724 ($3,378-$4,040)	$2,968 ($2,773-$3,176)	$6,052 ($5,592-$6,271)
Overall drug costs	$11,435 ($11,057-$11,887)	$9,854 ($9,558-$10,200)	$16,117 ($15,712-$16,357)
▪ MM supportive treatment ‡‡	$362 ($326-$392)	$300 ($271-$332)	$542 ($519-$560)
Total all-cause healthcare costs	$20,338 ($19,384-$20,956)	$17,171 ($16,458-$17,599)	$29,791 ($28,804-$30,020)
MM-related healthcare costs, PPPM			
MM-related drug costs			
▪ MM treatment costs	$10,353 ($10,005-$10,790)	$9,016 ($8,749-$9,331)	$14,308 ($13,922-$14,533)
▪ MM treatment administration costs	$375 ($340-$411)	$268 ($238-$288)	$701 ($669-$717)
ED visits costs	$74 ($36-$104)	$66 ($24-$81)	$103 ($69-$109)
Outpatient costs ‡	$3,945 ($3,619-$4,304)	$3,299 ($3,019-$3,563)	$5,850 ($5,460-$6,050)
Inpatient costs	$2,630 ($2,362-$2,859)	$2,179 ($2,027-$2,354)	$4,061 ($3,857-$4,214)
Total MM-related costs	$17,377 ($16,704-$17,840)	$14,828 ($14,301-$15,326)	$25,022 ($24,395-$25,337)

Abbreviations: MM – Multiple myeloma; ED – Emergency department; HCRU – Healthcare resource utilizations; SD – standard deviation; CI – Confidence interval; PPPM – Per patient per-month.

*The follow-up period is defined as from the index date to the end of the study period

**Total costs were identified using the total payment variable within the MarketScan® database. All costs reported in 2021 U.S. dollars.

‡ Excluding MM treatments, administration, and ED visits costs

‡‡ Include bisphosphonates, RANKL inhibitors, opioid, Tricyclic Antidepressants (TCA), Serotonin-Norepinephrine Reuptake Inhibitor (SNRI), anticoagulant, and erythropoietin agents

7.4. All-cause and MM-related healthcare resource utilization and costs among patients with at least 1 emergency department visit, outpatient visit, or hospitalization during the follow-up period*

	Overall	Double-class exposed	Triple-class exposed
All-Cause healthcare resource utilization & costs**			
Emergency Department (ED)			
Number of patients with ≥ 1 ED visits, N	615	392	223
Follow-up duration, mean (SD)	18.23 (13.02)	20.77 (13.90)	13.70 (9.53)
ED visits, mean PPPM (95% CI)	0.12 (0.12-0.13)	0.11 (0.10-0.11)	0.17 (0.17-0.17)
ED costs, mean PPPM (95% CI)	$288 ($233-$306)	$267 ($199-$276)	$340 ($339-$342)
Inpatient			
Number of patients with ≥ 1 hospitalization, N	791	497	294
Follow-up duration, mean (SD)	16.67 (12.6)	18.87 (13.7)	12.97 (9.43)
Hospitalizations, mean PPPM (95% CI)	0.12 (0.12-0.12)	0.10 (0.09-0.10)	0.18 (0.17-0.18)
Length of stay (days), mean PPPM (95% CI)	1.17 (1.13-1.20)	1.03 (1.01-1.05)	1.49 (1.48-1.50)
Inpatient costs, mean PPPM (95% CI)	$6,872 ($6,545-$7,124)	$5,809 ($5,647-$5,953)	$9,439 ($9,263-$9,523)
Outpatient			
Number of patients with ≥ 1 outpatient visits, N	1,511	1,007	504
Follow-up duration, mean (SD)	16.33 (12.9)	18.47 (13.96)	12.13 (9.46)
Physician office visits, mean PPPM (95% CI)	3.03 (2.92-3.14)	2.70 (2.63-2.78)	3.96 (3.89-4.03)
Other outpatient visits, mean PPPM (95% CI)	3.50 (3.39-3.66)	2.98 (2.89-3.08)	5.08 (4.96-5.16)
Outpatient costs, mean PPPM (95% CI) ‡	$5,044 (4,544-5,424)	$4,199 ($3,868-$4,551)	$7,336 ($6,907-$7,571)
MM-related healthcare resource utilization & costs**			
Emergency Department (ED)			
Number of patients with ≥ 1 ED visits, N	336	197	139
Follow-up duration, mean (SD)	18.50 (12.56)	21.43 (13.80)	14.37 (9.16)
ED visits, mean PPPM (95% CI)	0.10 (0.09-0.10)	0.08 (0.08-0.08)	0.13 (0.13-0.13)
ED costs, mean PPPM (95% CI)	$297 ($283-$301)	$286 ($285-$287)	$320 ($319-$321)
Inpatient			
Number of patients with ≥ 1 hospitalization, N	760	473	287
Follow-up duration, mean (SD)	16.67 (12.56)	18.83 (13.71)	13.10 (9.43)
Hospitalizations, mean PPPM (95% CI)	0.12 (0.12-0.12)	0.09 (0.09-0.10)	0.17 (0.16-0.17)
Length of stay (days), mean PPPM (95% CI)	1.17 (1.13-1.21)	1.03 (1.01-1.05)	1.48 (1.46-1.49)
Inpatient costs, mean PPPM (95% CI)	$5,072 ($4,853-$5,267)	$4,481 ($4,322-$4,594)	$6,446 ($6,354-$6,503)
Outpatient			
Number of patients with ≥ 1 outpatient visits, N	1,502	999	503
Follow-up duration, mean (SD)	16.40 (12.96)	18.53 (13.93)	12.13 (9.46)
Physician office visits, mean PPPM (95% CI)	2.22 (2.14-2.31)	1.96 (1.87-2.03)	3.02 (2.97-3.07)
Other outpatient visits, mean PPPM (95% CI)	2.48 (2.41-2.55)	2.07 (2-2.13)	3.69 (3.64-3.76)
Outpatient costs, mean PPPM (95% CI) ‡	$3,907 ($3,527-$4,272)	$3,269 ($2,986-$3,521)	$5,717 ($5276-$5,897)

Abbreviations: MM – Multiple myeloma; CI – Confidence Interval; ED – Emergency Department; PPPM – Per patient per-month.

*The follow-up period is defined as from the index date to the end of the study period

** Total costs were identified using the total payment variable within the MarketScan® database. All costs reported in 2021 U.S. dollars.

‡ Excluding MM treatments, administration, and ED visit costs

7.5. All-cause and MM-related healthcare costs, by subgroups

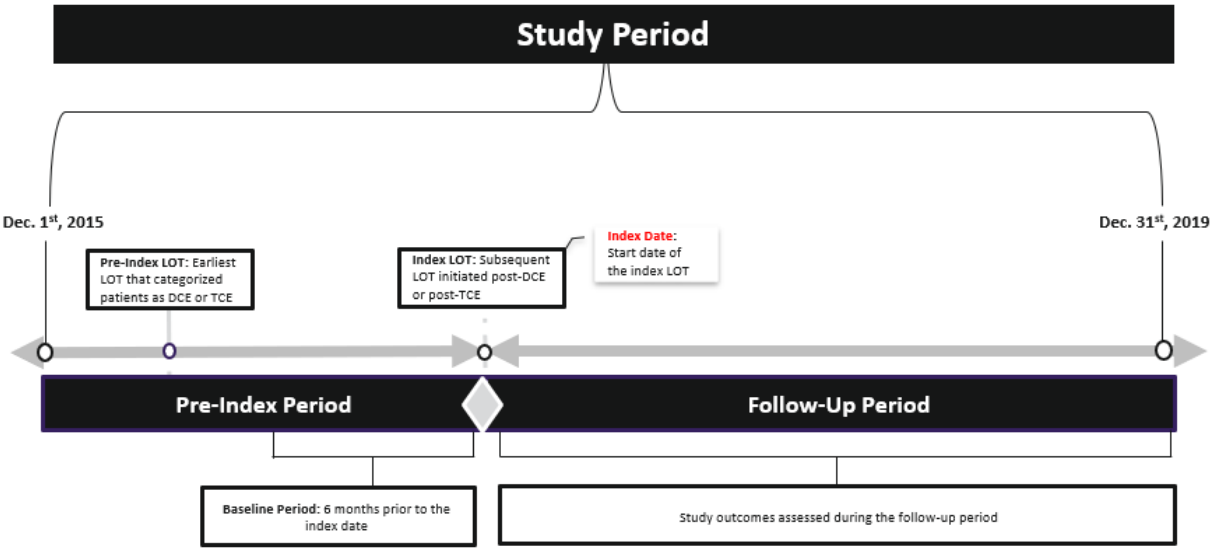
	Follow-up duration (months)	Total all-cause healthcare costs*	Total MM-related healthcare costs*
	Mean (SD)	**Mean (95% CI)**	**Mean (95% CI)**
Healthcare Cost Type, PPPM			
Patient Out-of-Pocket (n = 1,521)	16.31 (13.20)	$187 ($177-$198)	$136 ($127-$145)
Payer (n = 1,521)	16.31 (13.20)	$16,129 ($15,512-$16,771)	$14,054 ($13,522-$14,598)
Gender, PPPM			
Male (n = 838)	15.93 (12.75)	$20,504 ($19,915-$21,107)	$17,393 ($16,837-$17,940)
Female (n = 643)	16.85 (13.32)	$19,118 ($18,580-$19,610)	$15,801 ($15,375-$16,195)
Age Groups, PPPM			
<65 (n =1,015)	15.39 (12.60)	$22,484 ($21,813-$23,165)	$18,949 ($18,420-$19,560)
65+ (n = 466)	18.36 (13.64)	$15,171 ($14,728-$15,471)	$12,590 ($12,247-$12,838)
Year of Index, PPPM			
2016 (n = 298)	26.78 (16.99)	$12,292 ($12,131-$12,391)	$10,334 ($10,194-$10,421)
2017 (n = 397)	21.99 (11.40)	$19,449 ($19,117-$19,684)	$16,209 ($15,912-$16,409)
2018 (n = 388)	13.60 (6.29)	$26,227 ($25,878-$26,481)	$21,813 ($21,547-$22,024)
2019 (n = 398)	5.58 (3.22)	$32,734 ($32,181-$33,054)	$28,285 ($27,733-$28,534)
Exposure to targeted mAb, PPPM			
Unexposed (n = 907)	18.86 (14.14)	$16,416 ($15,936-$16,915)	$14,075 ($13,641-$14,510)
Exposed (n = 574)	12.31 (9.71)	$28,123 ($27,434-$28,741)	$22,921 ($22,343-$23,388)
Insurance Type, PPPM			
Commercial (n = 1,001)	15.08 (12.44)	$22,693 ($22,138-$23,403)	$19,177 ($18,679-$19,712)
Medicare (n = 480)	18.93 (13.77)	$15,142 ($14,732-$15,458)	$12,492 ($12,127-$12,763)

Abbreviations: MM – Multiple myeloma; PPPM – Per patient per month; SD – Standard deviation; CI – Confidence interval; mAb – monoclonal antibodies (e.g., daratumumab, elotuzumab)

*Total costs were identified using the total payment variable within the MarketScan® database. All costs reported in 2021 U.S. dollars.

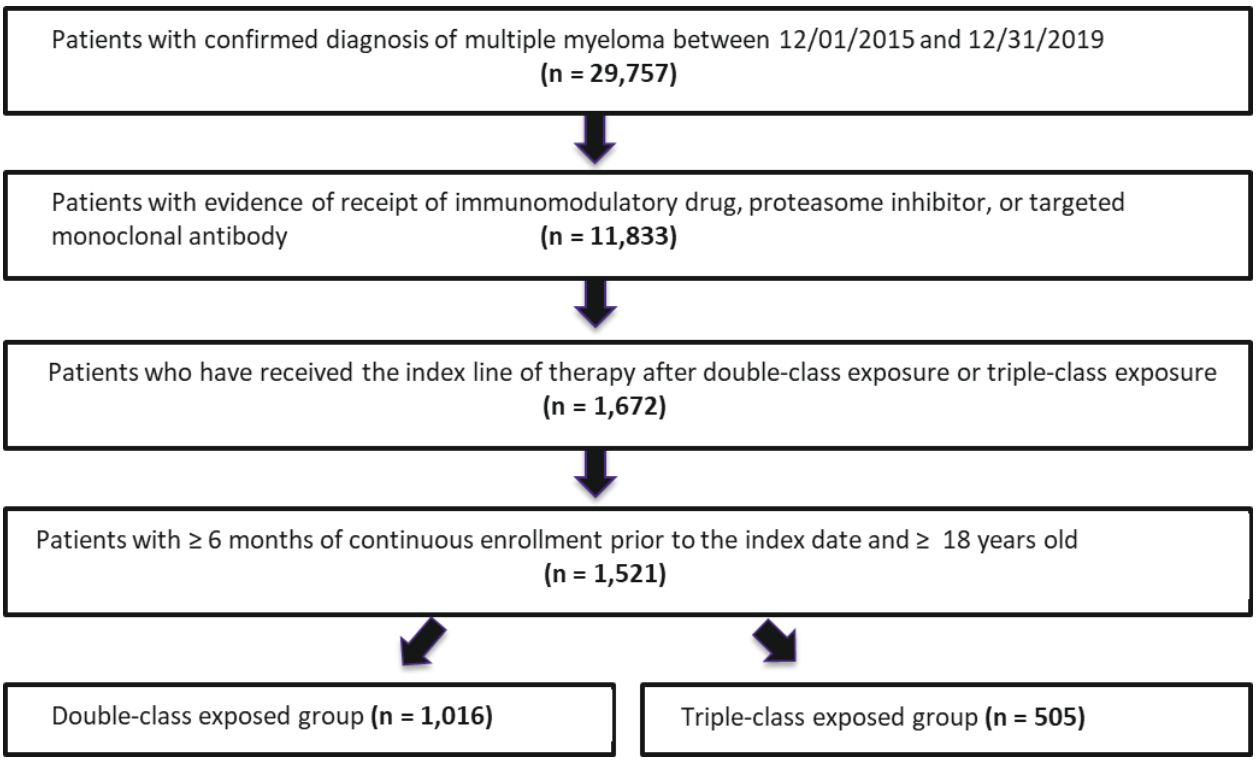
8. Figures

8.1. Study Schematic

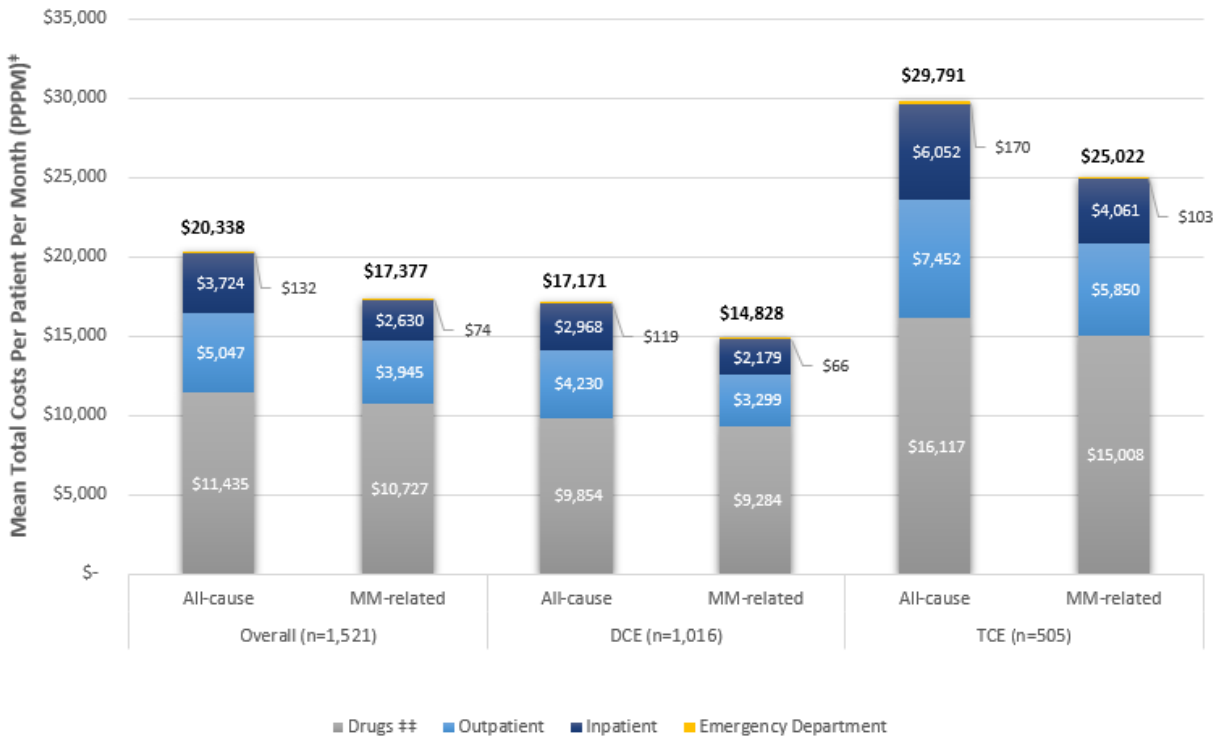


Abbreviations: LOT – Line of therapy; DCE – double-class exposed; TCE – triple-class exposed

8.2. Sample Selection and Attrition Flow Chart

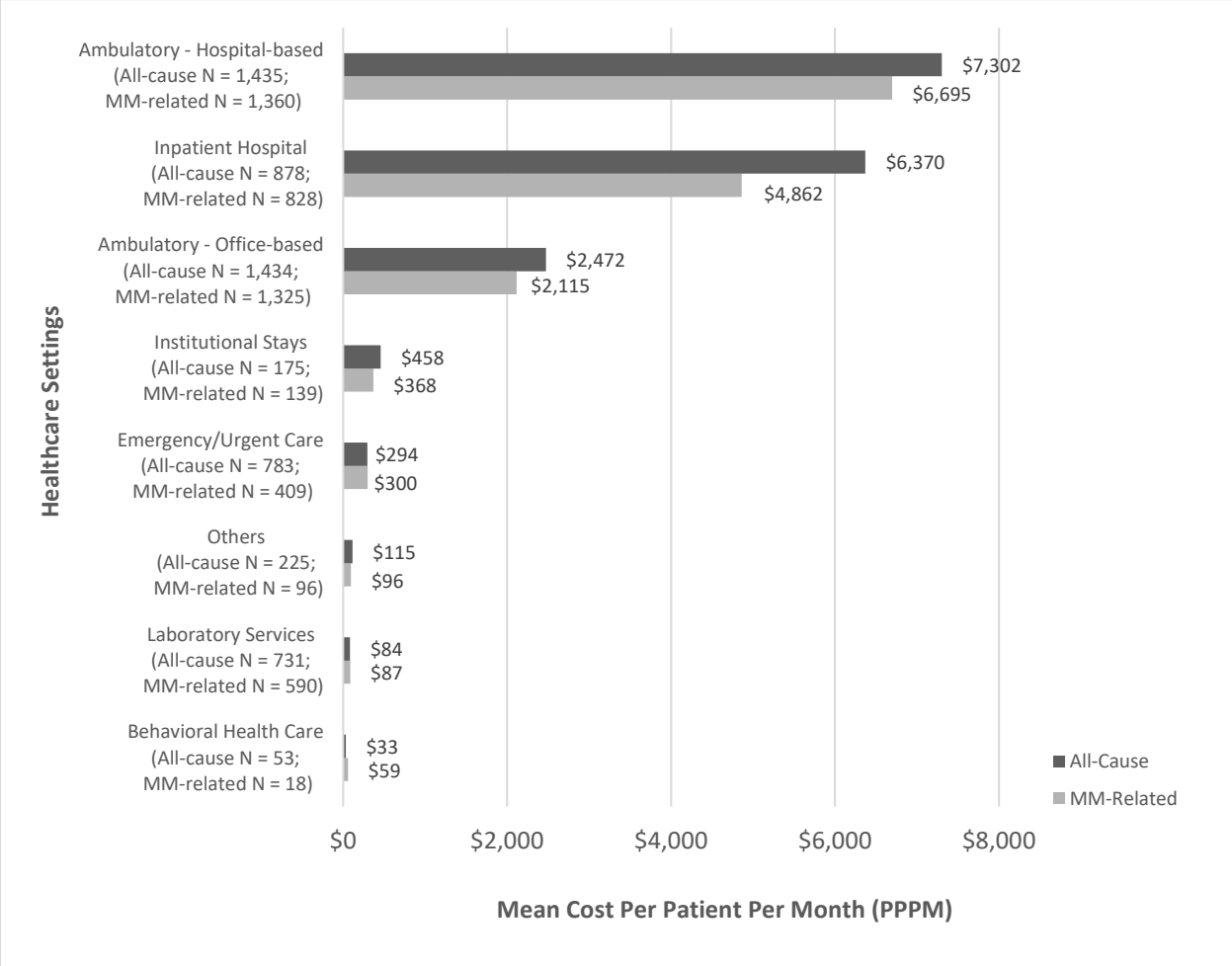


8.3. Components of the total all-cause and MM-related costs for the overall, double-class exposed (DCE), and triple-class exposed (TCE) cohorts during the follow-up period*



Abbreviations: DCE – Double-class exposed; TCE – Triple-class exposed; MM – Multiple myeloma; PPPM – Per patient per-month;
*The follow-up period is defined as from the index date to the end of the study period
‡ Total costs were identified using the total payment variable. All costs reported in 2021 U.S. dollars.
‡‡ Drug costs include drug administration costs.

8.4. All-cause and MM-related costs incurred by a patient in each healthcare setting during the follow-up period*



Abbreviations: MM – Multiple myeloma; PPPM – Per patient per-month.

*The follow-up period is defined as from the index date to the end of the study period.

‡ Total costs were identified using the total payment variable. All costs reported in 2021 U.S. dollars..

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10. Appendices

Appendix 1. The components and descriptions of each place of service values for eight different healthcare settings

`Place of Service` Code Value	`Place of Service` Name	`Place of Service` Description
Hospital-based Ambulatory Setting		
19	Off Campus - Outpatient Hospital	A portion of an off-campus hospital provider-based department which provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization
22	On Campus - Outpatient Hospital	A portion of a hospital's main campus which provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services to sick or injured persons who do not require hospitalization or institutionalization.
24	Ambulatory Surgical Center	A freestanding facility, other than a physician's office, where surgical and diagnostic services are provided on an ambulatory basis.
95	Outpatient – NEC	Outpatient setting, not elsewhere classified (NEC)
Office-based Ambulatory Setting		
11	Office	Location, other than a hospital, skilled nursing facility (SNF), military treatment facility, community health center, State or local public health clinic, or intermediate care facility (ICF), where the health professional routinely provides health examinations, diagnosis, and treatment of illness or injury on an ambulatory basis.
12	Home	Location, other than a hospital or other facility, where the patient receives care in a private residence.
15	Mobile Unit	A facility/unit that moves from place-to-place equipped to provide preventive, screening, diagnostic, and/or treatment services.
17	Walk-in Retail Health Clinic	A walk-in health clinic, other than an office, urgent care facility, pharmacy or independent clinic and not described by any other Place of Service code, that is located within a retail operation and provides, on an ambulatory basis, preventive and primary care services.
49	Independent Clinic	A location, not part of a hospital and not described by any other Place of Service code, that is organized and operated to provide preventive, diagnostic, therapeutic, rehabilitative, or palliative services to outpatients only.
50	Federally Qualified Health Center	A facility located in a medically underserved area that provides Medicare beneficiaries preventive primary medical care under the general direction of a physician.
65	End-Stage Renal Disease Treatment Facility	A facility other than a hospital, which provides dialysis treatment, maintenance, and/or training to patients or caregivers on an ambulatory or home-care basis.
71	Public Health Clinic	A facility maintained by either State or local health departments that provides ambulatory primary medical care under the general direction of a physician.
72	Rural Health Clinic	A certified facility which is located in a rural medically underserved area that provides ambulatory primary medical care under the general direction of a physician.
Inpatient Setting		
21	Inpatient Hospital	A facility, other than psychiatric, which primarily provides diagnostic, therapeutic (both surgical and nonsurgical), and rehabilitation services by, or under, the supervision of physicians to patients admitted for a variety of medical conditions.
Emergency / Urgent Care Setting		
20	Urgent Care Facility	Location, distinct from a hospital emergency room, an office, or a clinic, whose purpose is to diagnose and treat illness or injury for unscheduled, ambulatory patients seeking immediate medical attention.
23	Emergency Room– Hospital	A portion of a hospital where emergency diagnosis and treatment of illness or injury is provided.

41	Ambulance – Land	A land vehicle specifically designed, equipped and staffed for lifesaving and transporting the sick or injured.
42	Ambulance – Air or Water	An air or water vehicle specifically designed, equipped and staffed for lifesaving and transporting the sick or injured.
Institutional Stays		
13	Assisted Living Facility	Congregate residential facility with self- contained living units providing assessment of each resident's needs and on-site support 24 hours a day, 7 days a week, with the capacity to deliver or arrange for services including some health care and other services.
31	Skilled Nursing Facility	A facility which primarily provides inpatient skilled nursing care and related services to patients who require medical, nursing, or rehabilitative services but does not provide the level of care or treatment available in a hospital.
32	Nursing Facility	A facility which primarily provides to residents skilled nursing care and related services for the rehabilitation of injured, disabled, or sick persons, or, on a regular basis, health-related care services above the level of custodial care to other than individuals with intellectual disabilities.
34	Hospice	A facility, other than a patient's home, in which palliative and supportive care for terminally ill patients and their families are provided.
Laboratory Services		
81	Independent Laboratory	A laboratory certified to perform diagnostic and/or clinical tests independent of an institution or a physician's office.
Behavioral Health Care		
51	Inpatient Psychiatric Facility	A facility that provides inpatient psychiatric services for the diagnosis and treatment of mental illness on a 24-hour basis, by or under the supervision of a physician.
53	Community Mental Health Center	**A facility that provides the following services:** outpatient services, including specialized outpatient services for children, the elderly, individuals who are chronically ill, and residents of the CMHC's mental health services area who have been discharged from inpatient treatment at a mental health facility; 24 hour a day emergency care services; day treatment, other partial hospitalization services, or psychosocial rehabilitation services; screening for patients being considered for admission to State mental health facilities to determine the appropriateness of such admission; and consultation and education services.
55	Residential Substance Abuse Treatment Facility	A facility which provides treatment for substance (alcohol and drug) abuse to live-in residents who do not require acute medical care. Services include individual and group therapy and counseling, family counseling, laboratory tests, drugs and supplies, psychological testing, and room and board.
56	Psychiatric Residential Treatment Center	A facility or distinct part of a facility for psychiatric care which provides a total 24-hour therapeutically planned and professionally staffed group living and learning environment.
57	Non-residential Substance Abuse Treatment Facility	A location that provides treatment for substance (alcohol and drug) abuse on an ambulatory basis. Services include individual and group therapy and counseling, family counseling, laboratory tests, drugs and supplies, and psychological testing.
61	Comprehensive Inpatient Rehabilitation Facility	A facility that provides comprehensive rehabilitation services under the supervision of a physician to inpatients with physical disabilities. Services include physical therapy, occupational therapy, speech pathology, social or psychological services, and orthotics and prosthetics services.
62	Comprehensive Outpatient Rehabilitation Facility	A facility that provides comprehensive rehabilitation services under the supervision of a physician to outpatients with physical disabilities. Services include physical therapy, occupational therapy, and speech pathology.
Others		
1	Pharmacy**	A facility or location where drugs and other medically related items and services are sold, dispensed, or otherwise provided directly to patients.
2	Telehealth Provided Other than in Patient's Home	The location where health services and health related services are provided or received, through telecommunication technology. Patient is not located in their home when receiving health services or health related services through telecommunication technology.
3	School	A facility whose primary purpose is education.
4	Homeless Shelter	A facility or location whose primary purpose is to provide temporary housing to homeless individuals (e.g., emergency shelters, individual or family shelters).

25	Birthing Center	A facility, other than a hospital's maternity facilities or a physician's office, which provides a setting for labor, delivery, and immediate post-partum care as well as immediate care of new born infants.
60	Mass Immunization Center	A location where providers administer pneumococcal pneumonia and influenza virus vaccinations and submit these claims as electronic medical claims, paper claims, or using the roster billing method. This generally takes place in a mass immunization setting, such as a public health center, pharmacy, or mall but may include a physician office setting.
99	Other Place of Service	Other place of service not identified above.