

**Healthcare Resource Utilization and Costs in Patients with Mantle Cell Lymphoma in the
Third-Line Setting in the US**

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Abstract

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Background: Treatment of mantle cell lymphoma (MCL) is characterized by multiple lines of therapy. Previous studies have described healthcare resource utilization (HCRU) and costs of MCL in the third-line or greater (3L+) setting, but none have estimated outcomes attributable to MCL specifically. Additionally, newer therapies have recently been added to clinical guidelines.

Objective: Identify the attributable HRU and cost of MCL in the year following the initiation of third-line therapy.

Methods: Retrospective cohort study using MarketScan health insurance claims data. The Merative™ MarketScan® Databases are U.S. claims datasets with de-identified medical and pharmacy claims linked to enrollment data for individuals with commercial or Medicare supplemental insurance. Incident third-line mantle cell lymphoma patients (MCL3L) were identified between April 1st, 2016, to December 31st, 2022, and followed up until loss of enrollment or one year after initiation of third-line therapy. Matched cohorts for the commercial and Medicare supplemental populations were selected using propensity scores based on age, sex, cancer-adjusted-CCI, region, commercial vs. Medicare supplemental payer type, and presence of non-heme cancer. Six-month HCRU use was evaluated in patients with at least 6

months of continuous enrollment post-index. Annual costs for all patients were calculated accounting for censoring using Kaplan-Meier Sample Average (KMSA). HRU were compared using a t-test for mean days of utilization and a chi-square test for the presence of utilization or not. Confidence intervals for costs were calculated using the bootstrap method for both cohort-specific outcomes and the difference between the two cohorts.

Results: Third-line or later MCL patients had significantly greater HRU across all care settings compared to matched controls. Within six months post-index, a higher proportion of MCL patients had ≥ 1 inpatient admission (50.5% vs. 11.6%; $p < 0.001$), ≥ 1 emergency department (ED) visit (50.5% vs. 14.7%; $p < 0.001$), and ≥ 1 outpatient visit (100% vs. 50.5%; $p < 0.001$). Among those with ≥ 1 event, MCL patients had significantly higher ED visit counts (1.96 vs. 1.36; mean difference [MD] = 0.60, 95% CI: 0.07 to 1.13; $p = 0.030$) and outpatient visit counts (26.8 vs. 9.4; MD = 17.4, 95% CI: 13.33 to 21.47; $p < 0.001$). Mean number of inpatient admissions (1.81 vs. 1.36; MD = 0.45, 95% CI: -0.06 to 0.96; $p = 0.098$) and mean length of stay per admission (8.72 vs. 5.13 days; MD = 3.59, 95% CI: -0.24 to 7.42; $p = 0.071$) trended higher among MCL patients. Attributable annual costs were \$6,302 (95% confidence interval [CI]: \$4,907–\$7,877) for pharmacy, \$14,410 (95% CI: \$7,482–\$22,885) for inpatient services, \$8,586 (95% CI: \$6,414–\$10,937) for outpatient services, and \$204 (95% CI: \$59–\$353) for ED visits. The total attributable annual cost was \$29,613 (95% CI: \$21,585–\$39,045).

Discussion: We found the one-year attributable costs in third-line plus treatment of mantle cell lymphoma exceeded \$32,000, driven primarily by inpatient and outpatient services. There were significant differences in the % healthcare resource utilization in the 6 months following index, but these results were only in the patients who had at least 6 months of continuous enrollment potentially under-representing sicker patients who disenroll early. As the treatment landscape continues to evolve, understanding these costs is essential for payers and policymakers evaluating the value of emerging therapies.

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1. INTRODUCTION

Mantle Cell Lymphoma (MCL) is an aggressive B-cell neoplasm originating from mature B cells in the mantle zone of lymph nodes, a thin layer surrounding the germinal follicles.¹ MCL accounts for approximately 6% of all newly diagnosed cases of non-Hodgkin lymphoma,¹ with an annual incidence of about one case per 200,000 individuals.² Treatment patterns in MCL are characterized by progressively shorter durations of response: studies report median times to next treatment of 689 days from first- to second-line therapy, 527 days to third-line, and 453 days to fourth-line.³ This pattern reflects a clinical course requiring frequent transitions between lines of therapy, particularly in the third-line or later (3L+) setting.

Patients initiating third-line therapy often receive Bruton tyrosine kinase inhibitors (BTKis) and, in some cases, stem cell transplants, both of which are intensive and high-cost treatment options.³ While prior studies have described healthcare resource utilization (HRU) and costs associated with MCL in both commercial and Medicare populations, these analyses have been descriptive and have not isolated the attributable burden of MCL by comparing outcomes with a matched control population.^{4, 5}

Given the high burden of illness, evolving treatment landscape, and the lack of comparative data, this study aims to quantify the HRU and costs attributable to third-line MCL in a real-world U.S. population using a matched cohort design.

2. METHODS

2.1 Study Design and Data Source

We conducted a retrospective cohort study using data from the IBM® MarketScan® Commercial Claims and Encounters and Medicare Supplemental databases. The Merative™ MarketScan® Databases are U.S. claims datasets with de-identified medical and pharmacy claims linked to enrollment data for individuals with commercial or Medicare supplemental insurance. The study period extended from October 1, 2015, through December 31, 2023, beginning with the nationwide transition from ICD-9 to ICD-10 coding in the United States.

2.2 Study Timeline

We used definitions for diagnosis and lines of therapy (LOT) from Ito, et al⁴, which were refined by expert clinical review of selected data to ensure they were clinically meaningful.

We defined the index date as the date of initiation of third-line therapy for MCL. Patients were required to have continuous enrollment including a six-month washout period prior to their diagnosis date, the time between diagnosis and initiation of third-line treatment, and from the index date through the end of follow-up or 12 months, whichever came first. By default, patients had a minimum of 90 days between diagnosis and the index date to ensure sufficient time to

receive first and second-line therapies, with each line requiring at least 45 days as part of the line of therapy definition below. The follow-up period for costs was up to 12 months after the index date or until censoring due to disenrollment. We studied HRU for 6 months after the index date in the subpopulation that had at least 6 months of continuous enrollment.

Lines of therapy (LOT) were defined as any medication received that is part of National Comprehensive Cancer Network (NCCN) guideline-directed therapy within 45 days of the LOT start date.⁶ The LOT start date was defined as the date of the claim for a unique drug not found in any previous LOT. The index date was defined as the date of the first unique NCCN-directed therapy not present in either the first or second LOT. A full list of medications included in the LOT are described below in section 2.3.1.

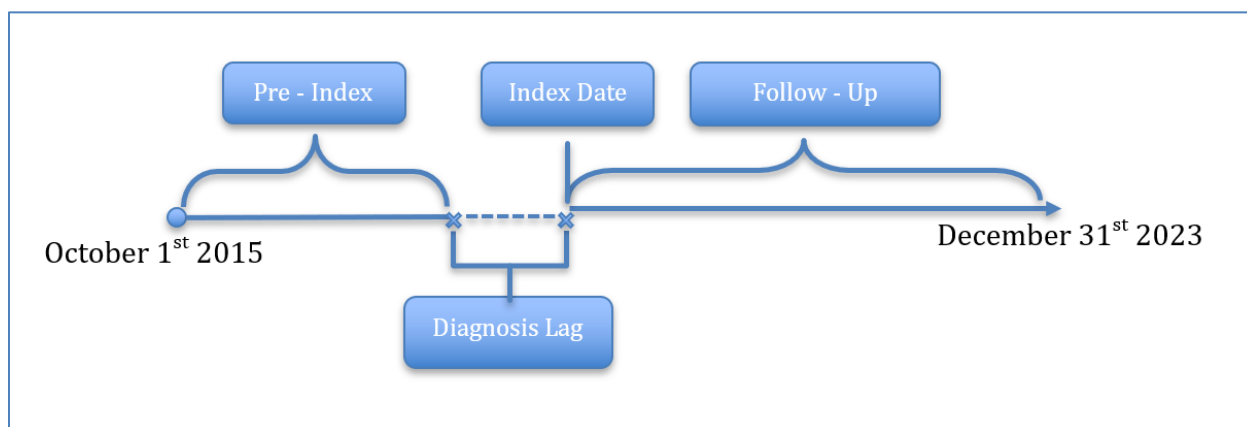


Figure 1. Study Timeline

2.3 Study Population

2.3.1 Inclusion Criteria

Eligible patients were required to be at least 18 years old at the time of diagnosis. Diagnosis of MCL was established using one inpatient claim or two outpatient claims for ICD-10 code C83.1x, spaced at least 30 days apart.⁵ This diagnosis algorithm does not appear to be validated but is based on previous published approaches.^{4,5} Patients must have received at least three different therapies recommended by the National Comprehensive Cancer Network (NCCN), each constituting a distinct line of therapy spaced at least 45 days apart. In addition, patients were required to have used a Bruton's tyrosine kinase inhibitor (BTKi) at any point prior to or during the third line of therapy. BTKi use was defined as the presence of at least one claim for acalabrutinib, ibrutinib, zanubrutinib, or pirtobrutinib.

Therapy lines were identified using either Healthcare Common Procedure Coding System (HCPCS) or National Drug Code (NDC) claims. We were unable to find specific methods of defining LOT within the Market scan database. Given the lack of information we identified MCL

therapies in the following manner. We used claims with MCL in the primary diagnosis position associated with a HCPCS code from the list below from the inpatient or outpatient claims procedure codes, or an NDC from the list below from the pharmacy claims file.

HCPCS-coded drugs included bendamustine (J9034), bortezomib (J9041), brexucabtagene autoleucel (Q2053), carboplatin (J9045), cisplatin (J9060), cyclophosphamide (J9070), cytarabine (J9100), dexamethasone (J1100), doxorubicin (J9000), gemcitabine (J9201), glofitamab-gxbm (J9286), lisocabtagene maraleucel (Q2054), methotrexate (J9260), obinutuzumab (J9301), oxaliplatin (J9263), rituximab (J9312), and vincristine (J9370). NDC-coded drugs, identified using Redbook from 2015 through 2023, included acalabrutinib, dexamethasone, ibrutinib, lenalidomide, pirtobrutinib, prednisone, rituximab, venetoclax, and zanubrutinib. See Appendix 1 for a full list of NDC codes.

2.3.2 Exclusion Criteria

We excluded patients if they had any diagnosis of a hematologic malignancy with similar treatment patterns that could confound outcomes. These conditions included chronic lymphocytic leukemia (C91.1x), diffuse large B-cell lymphoma (C83.3x), follicular lymphoma (C82.x), acute myeloid leukemia (C92.0x), myelodysplastic syndromes (D46.x), marginal zone lymphoma (C88.4 or C83.0x), or granulomatosis with polyangiitis (M31.3). Patients were also excluded if they had missing demographic information that was critical for matching, such as age, sex, or geographic region, during the six-month pre-index baseline period.

2.4 Variables and Outcomes

2.4.1 Baseline Characteristics

Baseline demographic and clinical characteristics were assessed during the six-month period prior to the index date. Variables included age, sex, geographic region, health plan type, employment status, and year of index therapy. Two versions of the Charlson Comorbidity Index (CCI) were calculated: the standard version and a cancer-adjusted version (aCCI) that excluded malignancy-related conditions such as cancer and metastatic cancer. This was based on the National Cancer Institute (NCI) CCI which excludes solid tumors, lymphomas, and leukemias.⁷ Additionally, a binary indicator was created to identify whether the patient had a diagnosis of MCL or any of the hematologic cancers from the exclusion criteria.

The aCCI allows for matching between a group which inherently has cancer, and a control group which may or may not have cancer. In order to accurately represent matching between these two groups we created a binary indicator indicating whether patients had a non-heme cancer or not. Patients with a confirmed heme cancer as listed above were excluded as confounders prior to assessment of baseline characteristics. Using the aCCI as well as the binary indicator for matching allows patient non-heme cancer comorbidity to be assessed while still representing a patient's presence of a non-heme cancer in both the MCL and control group.

2.4.2 Healthcare Resource Utilization (HRU)

HRU outcomes were assessed over the first six months following the index date among patients with at least six months of continuous enrollment. Three domains of utilization were analyzed:

Inpatient admissions, including the proportion of patients with at least one admission, the number of admissions per patient, and the length of stay. Emergency department (ED) visits, including the proportion of patients with at least one visit and the number of visits per patient, summarized with the same descriptive metrics. Outpatient services, including the proportion of patients with at least one visit and the number of visits per patient using the same statistical summary.

Please see appendix 2 for the definitions used to identify claims associated with inpatient admissions, emergency visits, and outpatient services in the MarketScan data.

2.4.3 Healthcare Costs

Healthcare costs were assessed over the 12-month follow-up period. These included total healthcare costs as well as component costs for inpatient care, outpatient services, emergency department visits, and pharmacy claims. All costs were reported as raw dollar amounts from the perspective of a U.S. payer.

2.5 Statistical Analysis

2.5.1 Matching Procedure

Matching was conducted separately within the commercial and Medicare populations prior to pooling for analysis. We drew a random sample of 100,000 general population enrollees from each stratum. We assigned an index date selected randomly from one of their observed inpatient or outpatient claims. To be eligible, controls were required to have at least six months of continuous enrollment prior to the assigned index date to ensure availability of baseline demographic and clinical information.

Controls were excluded if they had any diagnosis of the hematologic malignancies used as exclusion criteria for the MCL cohort. Specifically, individuals were excluded if they had any claims for chronic lymphocytic leukemia (C91.1x), diffuse large B-cell lymphoma (C83.3x), follicular lymphoma (C82.x), acute myeloid leukemia (C92.0x), myelodysplastic syndromes (D46.x), marginal zone lymphoma (C88.4 or C83.0x), or granulomatosis with polyangiitis (M31.3). Additionally, all controls were screened using the same MCL diagnosis algorithm used to define the primary cohort, and any individual meeting those criteria was excluded from the matched sample.

Eligible controls were matched 1:1 to MCL patients using nearest neighbor matching without replacement on the propensity score, implemented using the MatchIt package in R. The propensity score was estimated using age (in years), sex, geographic region, the cancer-adjusted Charlson Comorbidity Index, and a binary indicator reflecting presence or absence of any non-MCL hematologic cancer. Covariate balance was assessed using standardized differences, with values less than 0.1 indicating acceptable balance. Once matching was

complete, the commercial and Medicare populations were pooled into a single analytic dataset for outcome comparisons.

For the HRU analysis, we excluded MCL patients with fewer than 6 months of continuous enrollment. We did this in order to obtain an average HRU without relying on a Kaplan-Meier sample average (KMSA) calculation. Among the remaining MCL patients who met the enrollment criterion, we identified those whose original match did not have 6 months of continuous enrollment. These MCL patients were then rematched without replacement. This approach maintains alignment between the cost and HRU analyses by preserving as many original matches as possible and only rematching when necessary.

2.5.2 Descriptive Statistics

Baseline characteristics and outcome variables were summarized using standard descriptive statistics. Continuous variables were reported as means with standard deviations and medians with interquartile ranges. Categorical variables were summarized using frequencies and percentages.

2.5.3 Healthcare Resource Utilization Analysis

We used chi-square tests to compare the proportion of patients with at least one utilization event. We compared the mean number of utilization days for each HRU domain between groups using independent-sample t-tests among patients with at least six months of follow-up. We used these t-tests to generate confidence intervals around the mean differences. We also calculated the mean, standard deviation, median, interquartile range, minimum, and maximum.

2.5.4 Cost Analysis

Cumulative costs over 12 months were estimated using the Kaplan-Meier Sample Average (KMSA) method to account for variable follow-up due to censoring. We used bootstrap confidence intervals to estimate the variability around the annual KMSA average for each independent cohort. Monthly costs were weighted by the probability of remaining enrolled at the start of each month. Attributable costs were calculated as the difference in mean cumulative cost between MCL patients and their matched controls. Confidence intervals for between-group differences were derived using 1,000 bootstrap replications.

2.6 Software

All analyses were conducted using SAS version 9.4 and R version 4.3 or later.

3 RESULTS

3.1 Cohort Selection and Matching

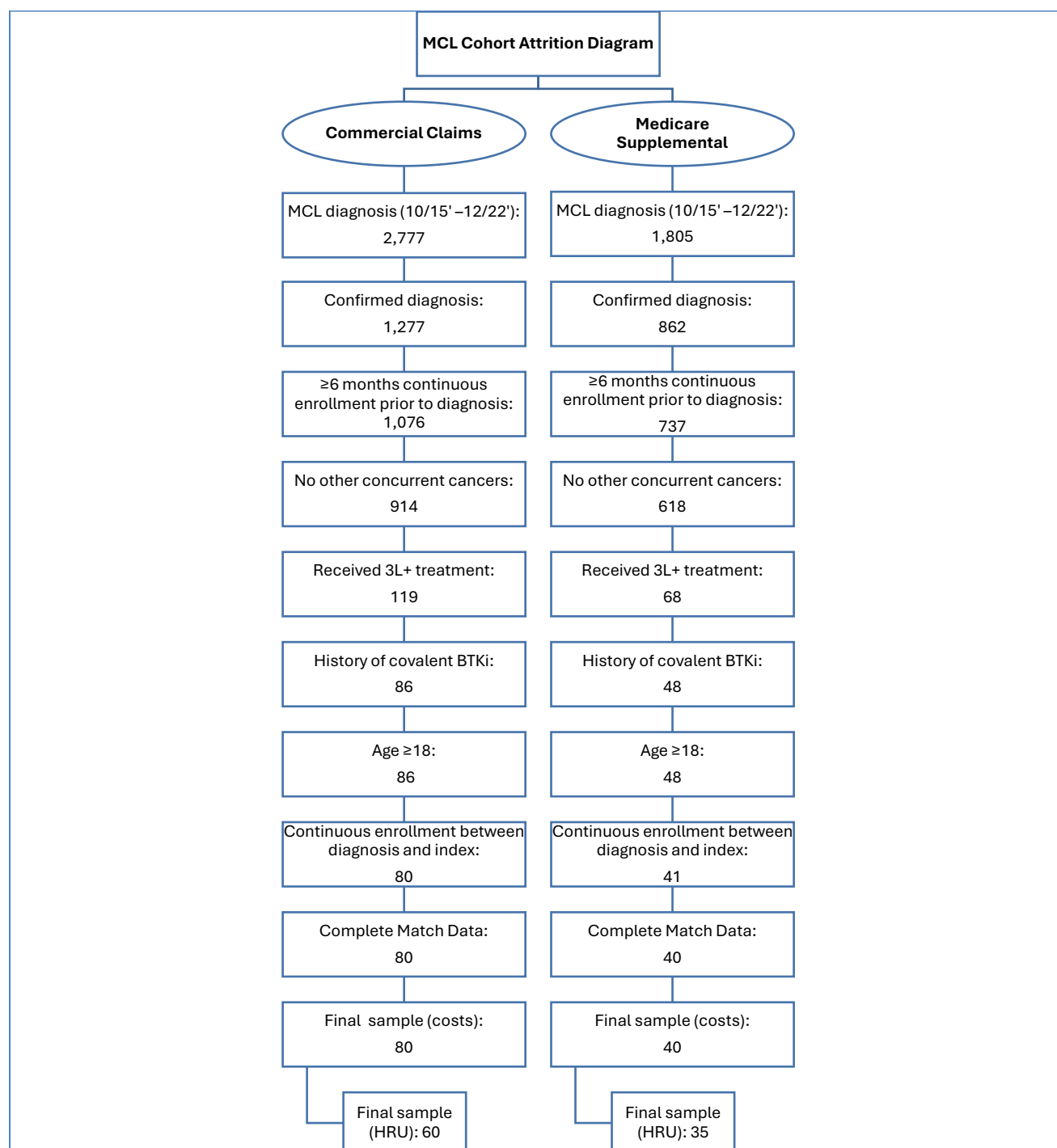
The final analytic cohorts included 80 patients from the commercial population and 40 patients from the Medicare supplemental population who met all of the inclusion criteria. This yielded a final population of 120 patients for analysis (Figure 2).

In the subpopulation that required at least 6 months of continuous enrollment for HRU analysis there were a total of 95 patients out of 120 who met this requirement. This was comprised of 60 commercial and 35 Medicare supplemental patients. Of these, there were 21 commercial and 11 Medicare supplemental patients (32 total out of 95) whose matching control did not have 6 months of continuous enrollment and therefore needed to be rematched.

All covariates were well balanced after propensity score matching, with standardized mean differences (SMDs) less than 0.1. Balance was confirmed using the MatchIt and cobalt packages in R, and visualized with a Love plot provided in appendix 3-6.

The balance amongst the subpopulation that needed to be rematched (n= 36) was not ideal. Among the commercial rematch age, aCCI score = 0, and aCCI score = 1 showed and SMD of >0.1 and <0.2. Among the Medicare population index month (December 2016) and sex were not balanced between >0.1 and <0.2, while age was not balanced above 0.2. Full details of the match characteristics and the associated Love plots can be found in the appendix 7-10. Baseline matching characteristics of this subpopulation can be found in appendix 11-12.

Figure 2. Cohort Attrition by Payer Type



MCL = Mantle Cell Lymphoma; 3L+ = Third-Line or Later; BTKi = Bruton's Tyrosine Kinase Inhibitor; HRU = Healthcare Resource Utilization

3.2 Baseline Characteristics

Baseline characteristics for the commercial and Medicare populations are summarized in Table 1a and Table 1b, respectively. In the commercial cohort, the mean age was 57.7 (SD 6.3) years for the MCL group and 57.0 (SD 6.6) years for the matched controls. In the Medicare population, the mean age was 77.7 (SD 7.4) years for the MCL group and 77.0 (SD 8.1) years for controls. Sex, region, health plan type, employment status, and comorbidity burden were comparable post-matching across both populations. Cancer-adjusted CCI and non-cancer comorbidity distributions were well balanced. The unadjusted CCI score is inherently unbalanced because each of the patients in the MCL cohort have at least a 2 on the CCI score given their MCL diagnosis.

Table 1a. Baseline Characteristics for Costs – Commercial

Characteristic	Third-Line MCL Cohort (N = 80)	Matched Cohort (N = 80)
Age, mean (SD), years	57.7 (6.3)	57 (6.6)
Year of Index, n (%)		
2016	3 (3.8)	3 (3.8)
2017	5 (6.2)	2 (2.5)
2018	11 (13.8)	12 (15)
2019	27 (33.8)	27 (33.8)
2020	9 (11.2)	7 (8.8)
2021	14 (17.5)	16 (20)
2022	11 (13.8)	13 (16.2)
Region, n (%)		
Northeast	13 (16.2)	11 (13.8)
North Central	24 (30.0)	27 (33.8)
South	31 (38.8)	28 (35)
West	11 (13.8)	11 (13.8)
Unknown	1 (1.2)	3 (3.8)
Charlson Comorbidity Index		
0	0 (0.0)	41 (51.2)
1	0 (0.0)	20 (25.0)
2	42 (52.5)	8 (10.0)
≥3	38 (47.5)	11 (13.8)
Non-Cancer Charlson Comorbidity Index		
0	43 (53.8)	43 (53.8)
1	19 (23.8)	19 (23.8)
2	8 (10)	8 (10)
≥3	10 (12.5)	10 (12.5)
Sex, n (%)		
Female	21 (26.2)	21 (26.2)
Male	59 (73.8)	59 (73.8)
Health Plan Type, n (%)		
Comprehensive	4 (5.0)	2 (2.5)
EPO		2 (2.5)

HMO	11 (13.8)	7 (8.8)
POS	8 (10.0)	13 (16.2)
POS With Capitation	0 (0)	1 (1.2)
PPO	39 (48.8)	36 (45.0)
CDHP	11 (13.8)	9 (11.2)
HDHP	5 (6.2)	9 (11.2)
Missing	2 (2.5)	1 (1.2)
Employment Status, n (%)		
Active Full-Time	41 (51.2)	63 (78.8)
Active Part-Time or Seasonal	1 (1.2)	1 (1.2)
Early Retiree	15 (18.8)	8 (10.0)
COBRA Continuee	1 (1.2)	0 (0)
Long Term Disability	1 (1.2)	0 (0)
Other / Unknown	21 (26.2)	8 (10)
Has non-Heme Cancer		
Yes	18 (22.5)	9 (11.2)
No	62 (77.5)	71 (88.8)

MCL = Mantle Cell Lymphoma; SD = Standard Deviation; n = number; CCI = Charlson Comorbidity Index; CDHP = Consumer-Directed Health Plan; HDHP = High-Deductible Health Plan; EPO = Exclusive Provider Organization; HMO = Health Maintenance Organization; POS = Point of Service; PPO = Preferred Provider Organization; COBRA = Consolidated Omnibus Budget Reconciliation Act; Heme = Hematologic

Table 1b. Baseline Characteristics for Costs – Medicare Supplemental

Characteristic	Third-Line MCL Cohort (N = 40)	Matched Cohort (N = 40)
Age, mean (SD), years	77.7 (7.4)	77 (8.1)
Year of Index, n (%)		
2016	1 (2.5)	1 (2.5)
2017	3 (7.5)	3 (7.5)
2018	9 (22.5)	10 (25.0)
2019	7 (17.5)	9 (22.5)
2020	5 (12.5)	3 (7.5)
2021	7 (17.5)	7 (17.5)
2022	8 (20.0)	7 (17.5)
Region, n (%)		
Northeast	5 (12.5)	3 (7.5)
North Central	20 (50.0)	23 (57.5)
South	11 (27.5)	8 (20.0)
West	4 (10.0)	6 (15.0)
Charlson Comorbidity Index		
0	0 (0.0)	10 (25.0)
1	0 (0.0)	12 (30.0)
2	14 (35.0)	7 (17.5)
≥3	26 (65.0)	11 (27.5)

Non-Cancer Charlson Comorbidity Index		
0	15 (37.5)	16 (40.0)
1	10 (25.0)	8 (20.0)
2	6 (15.0)	9 (22.5)
≥3	9 (22.5)	7 (17.5)
Sex, n (%)		
Female	12 (30.0)	10 (25.0)
Male	28 (70.0)	30 (75.0)
Health Plan Type, n (%)		
Comprehensive	16 (40.0)	6 (15.0)
HMO	4 (10.0)	9 (22.5)
PPO	20 (50.0)	21 (52.5)
CDHP	0 (0)	1 (2.5)
Missing	0 (0.0)	3 (7.5)
Employment Status, n (%)		
Active Full Time	0 (0)	4 (10)
Medicare Eligible Retiree	33 (82.5)	26 (65.0)
Surviving Spouse / Dependent	4 (10.0)	1 (2.5)
Other / Unknown	3 (7.5)	9 (22.5)
Has non-Heme Cancer		
Yes	15 (37.5)	14 (35.0)
No	25 (62.5)	26 (65.0)

MCL = Mantle Cell Lymphoma; SD = Standard Deviation; n = number; CCI = Charlson Comorbidity Index; CDHP = Consumer-Directed Health Plan; PPO = Preferred Provider Organization; HMO = Health Maintenance Organization; Heme = Hematologic

3.3 Healthcare Resource Utilization

A total of 95 third-line MCL patients had at least 6 months of continuous enrollment and were matched 1:1 with a control group. Inpatient admissions occurred in 50.5% of MCL patients compared to 11.6% of controls ($p < 0.001$). Among those admitted, MCL patients had a mean of 1.81 admissions (SD 1.16) versus 1.36 (SD 0.67) in controls, with a mean difference (MD) of 0.45 (95% CI: -0.06 to 0.96; $p = 0.098$). Mean inpatient length of stay was also longer for MCL patients (8.72 vs. 5.13 days), with a mean difference of 3.59 days (95% CI: -0.24 to 7.42; $p = 0.071$). Emergency department (ED) visits occurred in 50.5% of MCL patients versus 14.7% of controls ($p < 0.001$), with higher utilization among MCL patients: 1.96 vs. 1.36 visits, a mean difference of 0.60 (95% CI: 0.07 to 1.13; $p = 0.030$). All MCL patients and 50.5% of controls had at least one outpatient visit ($p < 0.001$), with mean visit counts of 26.8 (SD 15.8) and 9.4 (SD 9.0) respectively, resulting in a mean difference of 17.4 (95% CI: 13.33 to 21.47; $p < 0.001$). Outpatient service breakdown revealed that hospital outpatient encounters and office visits made up the majority of services. Additional details are provided in Appendix 13.

Table 2. Six-Month Healthcare Resource Utilization

Outcome	Third-Line MCL Cohort (N = 95)	Matched Cohort (N = 95)	P-value	MD (95% CI)
Inpatient Admissions				
% with ≥1 admission	50.5% (48/95)	11.6% (11/95)	<0.001*	-
Mean admissions among those with ≥1 admission	1.81 (1.16)	1.36 (0.67)	0.098**	0.45 (-0.06, 0.96)
Min – Max	1 – 5	1 - 3	-	-
Median (IQR)	1 (1.25)	1 (0.5)	-	-
Inpatient LOS				
Mean LOS among those with ≥1 admission	8.72 (12.0)	5.13 (3.0)	0.071**	3.59 (-0.24, 7.42)
Min – Max	1 – 53	1 – 15	–	–
Median (IQR)	4 (8)	4 (2)	–	–
ED Visit				
% with ≥1 visit	50.5% (48/95)	14.7% (14/95)	<0.001*	–
Mean visits (SD)	1.96 (1.5)	1.36 (0.6)	0.030**	0.60 (0.07, 1.13)
Min – Max	1 – 7	1 – 3	–	–
Median (IQR)	1 (2)	1 (0.75)	–	–
Outpatient Visit				
% with ≥1 visit	100% (95/95)	50.5% (48/95)	<0.001*	–
Mean visits (SD)	26.8 (15.8)	9.4 (9.0)	<0.001**	17.4 (13.33, 21.47)
Min – Max	3 – 91	1 – 35	–	–
Median (IQR)	24 (20)	6 (11)	–	–

*P-value from chi-square test. **P-value from t-test. MCL = Mantle Cell Lymphoma; P-value = Probability value; MD = Mean Difference; CI = Confidence Interval; LOS = Length of Stay; ED = Emergency Department; IQR = Interquartile Range.

3.4 Healthcare Costs

Mean total annual healthcare costs were \$32,712 (95% confidence interval [CI]: \$24,972–\$41,428) for MCL patients and \$3,151 (95% CI: \$1,529–\$5,530) for controls with an attributable yearly cost of \$29,613 (95% CI: \$21,585–\$39,045) (Table 3). The largest contributors to cost differences were inpatient services (\$14,410), followed by outpatient (\$8,586), drug (6,302), and ED services (\$204).

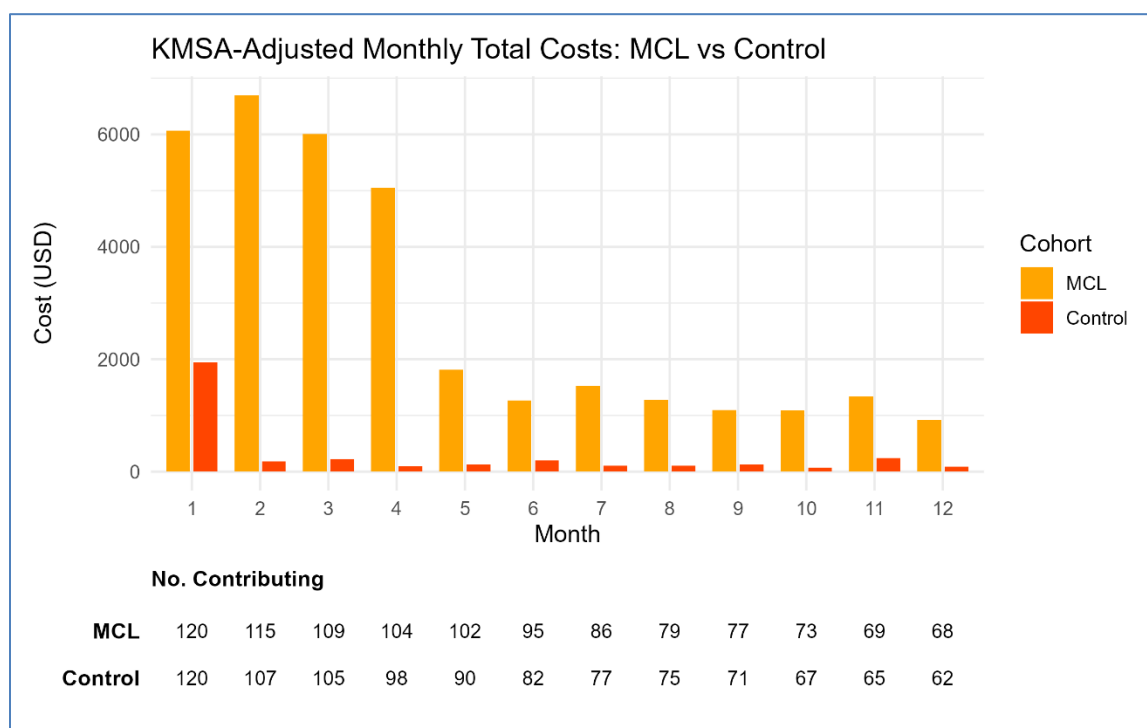
There were persistently higher healthcare costs across all categories for the MCL cohort throughout the 12-month follow-up period (Figure 2). Monthly Costs by pharmacy, ED, Inpatient services, outpatient services are shown in appendix 14-18.

Table 3. Annual Attributable Healthcare Costs

Cost Category	MCL Mean (95% CI)*	Control Mean (95% CI)*	Attributable Cost (95% CI)**
Pharmacy	\$7,079 (5,889–9,504)	\$774 (316–1,365)	\$6,302 (4,907–7,877)
ED	\$318 (191–454)	\$109 (41–226)	\$204 (58.5–353)
Inpatient Svc	\$16,193 (8,554–25,174)	\$1,792 (892–2,936)	\$14,410 (7,482–22,885)
Outpatient	\$8,942 (6,942–11,203)	\$384 (286–486)	\$8,586 (6,414–10,937)
Total	\$32,712 (24,972–41,428)	\$3,151 (1,529–5,530)	\$29,613 (21,585–39,045)

* Bootstrap confidence interval for descriptive means by cohort; **Bootstrap confidence interval for the attributable mean; CI = Confidence Interval; ED = Emergency Department; MCL = Mantle Cell Lymphoma; Svc = Services.

Figure 3. Monthly Total Healthcare Costs



KMSA = Kaplan–Meier Sample Average; MCL = Mantle Cell Lymphoma; USD = United States Dollars; No. = Number.

4 DISCUSSION

We evaluated the attributable healthcare resource utilization and costs among patients with mantle cell lymphoma (MCL) initiating third-line therapy. Using commercial and Medicare supplemental claims data, we identified cohorts of patients with MCL and matched controls without MCL to compare post-index healthcare outcomes. We found that MCL patients had significantly greater healthcare utilization and incurred significantly higher annual costs compared to matched controls. The largest contributors to attributable costs were inpatient services, followed by outpatient care and drug expenditures.

These findings underscore the substantial burden that MCL imposes on patients and the healthcare system, particularly in later lines of therapy. For clinicians, these data highlight the need for early identification of patients who may require resource-intensive care, including those transitioning beyond BTKi therapy. From a payer or policy perspective, the significant cost differences may justify early access to novel, potentially more cost-effective therapies, or the inclusion of care coordination strategies in benefit designs. For researchers and health economists, these results offer benchmarks for modeling economic impact and reinforce the importance of assessing both direct medical costs and resource use when evaluating new treatment options.

To contextualize our findings, we compared them with two recent studies that evaluated healthcare utilization and costs in relapsed or refractory MCL: one using commercial and Medicare claims,⁴ and one using fee-for-service (FFS) Medicare claims.⁵ Each study applied different methods and populations, and when considered together, they contribute to a broader understanding of MCL-related healthcare burden.

Ito et al. used MarketScan data from 2016 to 2020 to describe all-cause healthcare utilization and costs among adults initiating second-line and later treatment for relapsed and refractory (R/R) MCL. The study reported 12-month outcomes stratified by line of therapy but did not include a comparator group or adjust for censoring. In contrast, our analysis focused specifically on third-line or later treatment and applied a matched comparator cohort with Kaplan-Meier Sample Average (KMSA) methods to estimate the attributable burden of MCL. We also extended the study period through 2023 to capture newer therapies such as pirtobrutinib and CAR-T. While Ito et al. characterized the overall burden across treatment lines, our study isolates the burden attributable to MCL in later lines and adds service-level detail, such as outpatient care setting, not included in their report. The two studies together contribute both context on total real-world use and a more specific estimate of MCL-attributable impact.⁴

Squires et al. used 100% Medicare FFS data from 2010 to 2019 to evaluate treatment patterns, survival, and healthcare costs among patients aged ≥66 who had received prior BTKi therapy and initiated third-line treatment. Their analysis described all-cause utilization and costs but did not include a control group or censoring adjustment. Our study complements theirs by estimating the attributable burden of MCL in third-line or later treatment using a matched comparator group and censor-adjusted methods. We also incorporated data through 2023,

capturing more recent therapies, and stratified outpatient care by setting. While Squires et al. focused on an older, post-BTKi population, our study provides estimates of MCL-attributable utilization and costs across a broader real-world cohort. Together, these studies address different but related questions about the burden of MCL care.⁵

Together, these three studies offer a more comprehensive understanding of healthcare burden in relapsed or refractory MCL. Ito et al. describe all-cause costs and utilization across lines of therapy in a broad claims population; Squires et al. focus on older adults with prior BTKi use; and our study quantifies the attributable burden of MCL in the third-line or later setting using a matched comparator and censoring-adjusted cost estimation. These different approaches provide complementary perspectives that help clarify both the total and disease-specific impact of MCL in the real world.

4.1 Limitations

Our study has several important limitations.

First, healthcare resource utilization outcomes were assessed only among patients with at least six months of continuous enrollment following the index date. This excluded individuals who disenrolled early or died shortly after treatment initiation, potentially underestimating true utilization and costs. The restriction reduced the sample size from 120 to 95 patients and required rematching 32 individuals whose original matches lacked sufficient enrollment. In the rematched cohort, covariate balance remained generally acceptable, with no standardized mean differences (SMDs) exceeding 0.2 except for age in the Medicare population. Appendix 6.7 and 6.8 present the full SMDs for the rematched cohorts, while Appendix 6.9 and 6.10 display Love plots illustrating rematch quality. Although the balance appeared less optimal in this subgroup, the small sample size likely magnified minor differences. If covariate balance were evaluated across the full cohort, these discrepancies would likely be less pronounced. This can be seen by visually inspecting similarity of groups shown in Appendices 6.11 and 6.12.

Other limitations include general constraints of claims-based data, such as potential coding errors, lack of clinical detail, and inability to capture care received outside of the insurance system. Second, due to lack of data, censoring could have been the result of either death or disenrollment, which limits interpretation of follow-up time and outcomes. Third, the study includes a relatively small sample of 120 MCL patients, with follow-up time distributed across a six-year period. This may limit the generalizability of findings to more recent treatment patterns and claims data. Fourth, the mean difference results are limited by small sample size, as analyses were restricted to patients with at least one instance of utilization. These comparisons were based on t-tests, which may have been underpowered and contributed to non-significant results for mean inpatient admissions ($p = 0.098$) and mean inpatient length of stay ($p = 0.071$). However, the direction of effect in both outcomes showed higher utilization in the MCL group, suggesting that with a larger sample size, these differences may become statistically significant.

4.2 Conclusion

In summary, we conducted a matched cohort study using real-world commercial and Medicare supplemental data to evaluate the attributable economic burden associated with third-line treatment of MCL. We observed significantly greater healthcare use and higher total annual costs among the MCL cohort compared to matched controls, driven primarily by inpatient and outpatient services. These findings highlight the persistent burden of late-line MCL and may inform future clinical, reimbursement, and policy decisions related to optimizing care pathways for this high-need population.

5 REFERENCES

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6 APPENDIX

6.1 Full NDC list

Drug Name (with salt form)	National Drug Code (NDC) Codes
Acalabrutinib	310051260, 310351260
Bendamustine Hydrochloride	10019007901, 16729025003, 16729025105, 42367052025, 42367052125, 55150039101, 55150039201, 60505609500, 60505609600, 60505622800, 63459034804, 63459039008, 63459039120, 63459039502, 63459039602, 68001057141, 68001057241, 71225012001, 71288010210, 71288010320
Bortezomib	10019099101, 143909801, 25021024410, 409170001, 409170301, 409170401, 43598086560, 50742048401, 55150033701, 60505605004, 63020004901, 63323072110, 63323082110, 68001053436, 68001054036, 68001054136, 70710141101, 70860022510, 71288011810, 72266024401
Carboplatin	10019091201, 10019091202, 10019091203, 10019091501, 10019091601, 10019091701, 10139006005, 10139006015, 10139006045, 15210006112, 15210006312, 15210006612, 15210006712, 15321030, 15321076, 15321130, 15321176, 15321230, 15321276, 15321329, 15321330, 15321429, 15321430, 15321529, 15321530, 15321630, 15323011, 15323111, 15323211, 15323311, 16729029512, 16729029531, 16729029533, 16729029534, 25021020205, 25021020215, 25021020245, 25021020251, 409112910, 409112911, 409112912, 47335015040, 47335015140, 47335028440, 47335030040, 47781060320, 47781060427, 47781060594, 47781060694, 50111096576, 50111096676, 50111096776, 50742044505, 50742044615, 50742044745, 50742044860, 55150033501, 55150038601, 55390015001, 55390015101, 55390015201, 55390015301, 55390015401, 55390015501, 55390015601, 55390022001, 55390022101, 55390022201, 591221911, 591222011, 591333626, 591333712, 591333889, 591345460, 591368711, 61703015005, 61703026205, 61703033918, 61703033922, 61703033950, 61703033956, 61703033961, 61703033962, 61703033963, 61703036018, 61703036022, 61703036050, 61703060005, 63323016610, 63323016720, 63323016721, 63323016800, 63323017205, 63323017215, 63323017245, 63323017260, 66758004701, 66758004702, 66758004703, 66758004704, 67457049154, 67457049215, 67457049346, 67457049461, 67457060820, 67817006112, 67817006312, 67817006612, 67817006712, 69448000512, 69448000531, 69448000533, 69448000534, 69448000538, 703324411, 703324611, 703324811, 703324911, 703326401, 703326601, 703326801, 703326871, 703327401, 703327601, 703327801, 703423901, 703423981, 703424401, 703424481, 703424601, 703424681, 703424801, 703424881, 703424891, 71288010005, 71288010015, 71288010045, 71288010051
Cisplatin	10019091001, 10019091002, 143950401, 143950501, 15307020, 15307097, 15307220, 15307297, 15322022, 15322026, 15322122, 15322126, 16729028811, 16729028838, 25021025350, 25021025351, 44567050901, 44567051001, 44567051101, 44567053001, 47781060925, 47781061023, 49452207801, 49452207802, 49452207803, 51552107609, 55390009901, 55390011250, 55390011299, 55390018701, 55390041450, 55390041499, 60505627700, 62991284901, 62991284902, 63323010351, 63323010364, 63323010365, 63323010391, 63323010395, 65219035950, 67457042410, 67457042551, 68001028324, 68001028327, 68001028332, 68001028333, 69008101, 69008407, 703574711, 703574811, 70860020650, 70860020651
Cyclophosphamide	10019093501, 10019093525, 10019093601, 10019093650, 10019093701, 10019093710, 10019093801, 10019093825, 10019093901, 10019093950, 10019094201, 10019094210, 10019094301, 10019094325, 10019094401, 10019094450, 10019094501, 10019094510, 10019095501, 10019095550, 10019095601, 10019095616, 10019095701, 10019095711,

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Dexamethasone Acetate, Micronized	38779190501, 38779190503, 38779190504, 38779190508, 38779190509, 49452246004, 51927223100, 51927374700, 62991153502, 62991153504, 62991153505, 63370006015, 63370006020, 63370006025, 63370006035, 63370006050
Dexamethasone Isonicotinate	5.19E+10
Dexamethasone Isonicotinate, Micronized	5.19E+10
Dexamethasone Sodium Phosphate	10039006201, 10039006202, 10039006203, 10039020401, 102329001, 10719008611, 10719013810, 10974007205, 12071050678, 12071051578, 12072030005, 12671001501, 12671001507, 131123005, 144316213, 150090505, 150090510, 157015775, 16590006805, 168024703, 17022129501, 17137186308, 17236004893, 17236004895, 17337000900, 17478026451, 17478027835, 17478027910, 182072062, 182300762, 182300766, 182301466, 182507131, 182702262, 191009321, 191009352, 21695084705, 21695084830, 223648505, 223648508, 223648815, 223740125, 223740230, 223740301, 223740405, 223740505, 223740625, 223740701, 223740810, 23490541101, 23490541300, 24208064055, 24208072002, 25332001005, 25332011302, 259029705, 259029710, 298587967, 302141275, 302141475, 303993005, 303993438, 304054055, 304080555, 314089630, 314089670, 314089675, 33261078501, 351045170, 35470547901, 35470936501, 364236054, 364255170, 364668132, 364668146, 364668153, 364668154, 364668156, 364671153, 364723753, 385100375, 38779007101, 38779007102, 38779007103, 38779007104, 38779007105, 38779007106, 38779007108, 38779007109, 38779007115, 38779007125, 38779010301, 38779010303, 38779010304, 38779287601, 38779287602, 395814119, 395814162, 402058701, 402058781, 402066110, 402074805, 402080705, 402080710, 402080730, 403073918, 403074018, 403074218, 403118018, 405093508, 405605005, 41764073805, 418192105, 418192130, 418192131, 418192161, 42254008805, 43797010910, 44437080705, 454058705, 456107405, 45861003880, 463109005, 463111305, 469061001, 469165000, 469165020, 469165050, 469908087, 47202363808, 47202364405, 47202400901, 47202400905, 47202401005, 47471055705, 47649010401, 47649010405, 47679025320, 47679031030, 47679038100, 47679038120, 485158705, 49072015705, 494110405, 49452247001, 49452247002, 49452247003, 49452247004, 49452247005, 49452247006, 496010801, 49727072855, 49999043425, 50090041400, 50090062703, 50090192200, 50090231302, 50090231303, 50090236300, 50090330000, 50090354100, 50090456700, 50272058705, 50930058705, 50930074805, 51079053693, 51309040502, 51309040505, 51309040530, 51309040610, 51309040705, 51309040805, 51309040810, 51432086135, 51432086205, 51552002501, 51552002502, 51552002503, 51552002504, 51552002505, 51552002510, 51552002525, 51728067713, 51728070378, 517490125, 517490525, 517493025, 51927143000, 51944339000, 51944339030, 51944445005, 51944445035, 52079605, 52079625, 52079626, 52079627, 52079710, 52079726, 52079906, 52079907, 522093270, 52349010330, 52349011730, 52372067901, 52372067902, 52372067903, 52372067904, 52372067905, 52372067906, 524008015, 52406022205, 52406058705, 52406058710, 52406058730, 52406058781, 525033470, 52604058705, 527018265, 52765074805, 52959028803, 52959135203, 53014020113, 53014020313, 53225366001, 53268010675, 53268034110, 53268064055, 536080065, 536414065, 536415165, 536415170, 536415175, 536647591, 537235331, 537235375, 54274071609, 54569119000, 54569122400, 54569149400, 54569157500, 54569222300, 54569232800, 54569301800, 54569302700,

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Doxorubicin Hydrochloride	10019092001, 10019092102, 13100691, 13101679, 13107694, 13108691, 13109691, 13109694, 13110679, 13111683, 13113691, 13114691, 13114694, 13115679, 13116683, 13117687, 13123691, 13124691, 13125679, 13126683, 13128683, 143908401, 143908501, 143908601, 143908701, 143908801, 143908901, 143909001, 143909101, 143909201, 143909301, 143927501, 143927701, 143936901, 143937001, 143937101, 143937201, 143954601, 143954701, 143954801, 143954810, 143954901, 143954910, 15335122, 15335222, 15335322, 16714000101, 186153013, 186153101, 186153231, 186153241, 186153261, 186153281, 186157512, 25021020705, 25021020725, 25021020751, 38779065206, 38779065209, 45963073355, 45963073357, 45963073360, 45963073368, 469100161, 469883020, 469883130, 469883250, 49452243701, 53150031410, 53150031501, 53150031701, 53150032010, 53905023206, 53905023606, 54868313100, 55390023110, 55390023210, 55390023301, 55390023510, 55390023610, 55390023701, 55390023801, 55390024110, 55390024210, 55390024301, 55390024510, 55390024610, 55390024701,

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Rituximab-pvvr	69023801, 69024901
Venetoclax	74056111, 74056114, 74056607, 74056611, 74057611, 74057622, 74057630, 74057634
Vincristine Sulfate	13744686, 13745686, 13746686, 2719401, 2719501, 2719601, 2719801, 2719809, 2719901, 2719909, 364244851, 364244852, 402102801, 402102802, 469163000, 469163010, 469163030, 469352000, 469352010, 469352020, 49452811401, 49452811402, 49452811403, 49452811404, 51309020002, 51309020003, 51309020005, 51309020102, 51309020105,

	53258035200, 53258035201, 53258035202, 53443000740, 53443000741, 53443000743, 54868319600, 61703030906, 61703030916, 61703030925, 61703030926, 703440211, 703441211, 94534101, 94534201, 94534501
Vincristine Sulfate Liposome	2.05E+10
Zanubrutinib	7.26E+10
riTUXimab-abbs	63459010310, 63459010450
riTUXimab-arrx	55513022401, 55513032601
riTUXimab-pvvr	69023801, 69024901
vinCRISStine sulfate liposome	20536032201, 72893000803

6.2 Service Definitions

Cost Category	Definition
Inpatient Services	Claims from claims_s with STDPLAC == 21 (inpatient hospital) and SVCSCAT matching:– Facility or physical inpatient care: codes beginning with "A10"– Mental health inpatient care: "A301", "A302", "A303"– Substance abuse inpatient care: "A311", "A312", "A313"– Inpatient professional services: "A221" followed by 305–307, 401, 402, 406, 411, 451–456, 459, 461–469, or 499 - Excludes ED-designated claims (SVCSCAT ending in "20")
Outpatient Services	Claims from claims_o where STDPLAC is in:11, 15, 17, 18, 19, 22, 24, 41, 42, 49, 50, 53, 62, 65, 71, 72, 75, or 99
Emergency Department	Claims from either claims_o or claims_s where:– STDPLAC == 23 (emergency department) or – SVCSCAT ends in "20"
Pharmacy (Drug) Services	Claims with a Mantle Cell Lymphoma (MCL) ICD code in the primary diagnosis position and a National Drug Code (NDCNUM) that appears in the Appendix 1 drug list
Total Costs	All costs across inpatient, outpatient, emergency, and pharmacy categories

MCL = Mantle Cell Lymphoma; ICD = International Classification of Diseases; NDC = National Drug Code; NDCNUM = National Drug Code Number; SVCSCAT = Service Category; STDPLAC = Place of Service Code

6.3 Balancing – Commercial

Category	Covariate	Type	Unadjusted SMD	Adjusted SMD	Balance Status
Propensity Score	Distance	Continuous	0.5661	0.3568	Balanced, <0.1
Demographics	Age	Continuous	1.3930	0.0139	Balanced, <0.1
	Sex (Male)	Binary	0.2819	0.0000	Balanced, <0.1
Geographic Region	Region – North Central	Binary	0.1088	0.0750	Balanced, <0.1
	Region – Northeast	Binary	−0.0188	0.0125	Balanced, <0.1
	Region – South	Binary	−0.0679	−0.1000	Balanced, <0.1
	Region – Unknown	Binary	0.0094	−0.0125	Balanced, <0.1
	Region – West	Binary	−0.0364	0.0250	Balanced, <0.1
Index Month	Index Month (Oct 2015–Dec 2022)	99 Binary Vars	Range: −0.0422 to 0.0302	All ≤ 0.0250	All Balanced, <0.1
Non-Cancer Comorbidity (aCCI)	aCCI Score = 0	Binary	0.2579	−0.0625	Balanced, <0.1
	aCCI Score = 1	Binary	0.2819	0.0000	Balanced, <0.1
	aCCI Score = 2	Binary	0.0704	0.0500	Balanced, <0.1
	aCCI Score ≥ 3	Binary	0.0788	0.0250	Balanced, <0.1
Cancer History	Presence of Non-	Binary	0.2248	0.0875	Balanced, <0.1

	Hematologic Cancer				
Matching Summary	<i>Matched 80 MCL to 80 controls (1:1) from original pool of 80 MCL and 87,474 controls; all 99 covariates balanced (<0.1 SMD).</i>				

SMD = Standardized Mean Difference; aCCI = Cancer-Adjusted Charlson Comorbidity Index; MCL = Mantle Cell Lymphoma

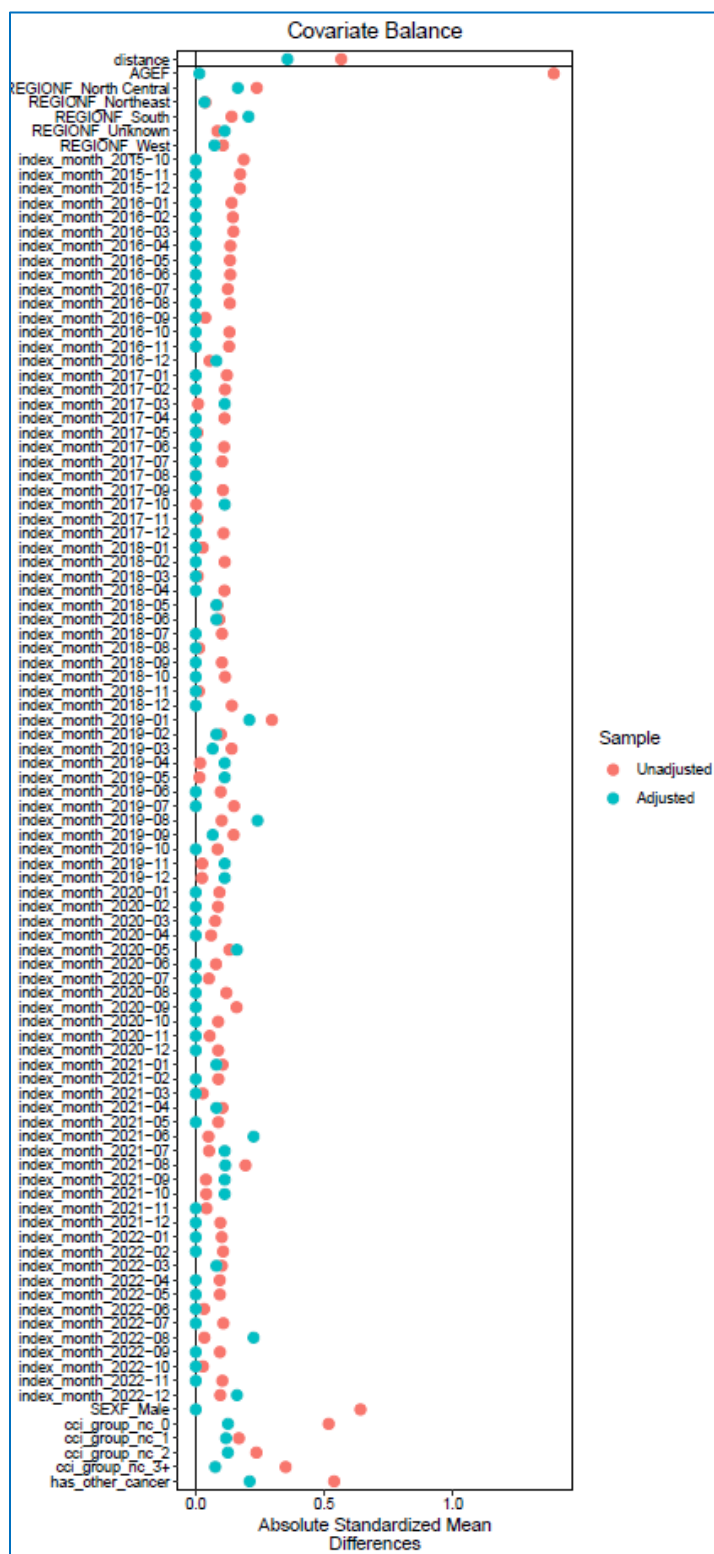
6.4 Balancing – Medicare Supplemental.

Category	Covariate	Type	Unadjusted SMD	Adjusted SMD	Balance Status
Propensity Score	Distance	Continuous	0.6865	−0.0038	Balanced, <0.1
Demographics	Age	Continuous	0.4049	0.0942	Balanced, <0.1
	Sex (Male)	Binary	0.2577	−0.0500	Balanced, <0.1
Geographic Region	Region – North Central	Binary	0.1388	−0.0750	Balanced, <0.1
	Region – Northeast	Binary	−0.1073	0.0500	Balanced, <0.1
	Region – South	Binary	−0.0169	−0.0750	Balanced, <0.1
	Region – Unknown	Binary	−0.0021	0.0000	Balanced, <0.1
	Region – West	Binary	−0.0125	0.0000	Balanced, <0.1
Index Month	Index Month (Jan 2015–Feb 2024)	123 Binary Vars	Range: −0.0193 to 0.0880	All ≤ 0.0250	All Balanced, <0.1
Non-Cancer Comorbidity (aCCI)	aCCI Score = 0	Binary	−0.1575	−0.0250	Balanced, <0.1
	aCCI Score = 1	Binary	−0.0025	0.0500	Balanced, <0.1

	aCCI Score = 2	Binary	0.0287	−0.0750	Balanced, <0.1
	aCCI Score ≥ 3	Binary	0.1313	0.0500	Balanced, <0.1
Cancer History	Presence of Non- Hematologic Cancer	Binary	0.2838	0.0250	Balanced, <0.1
Matching Summary	<i>Matched 40 MCL to 40 controls (1:1) from original pool of 40 MCL and 89,405 controls; all 123 covariates balanced (<0.1 SMD).</i>				

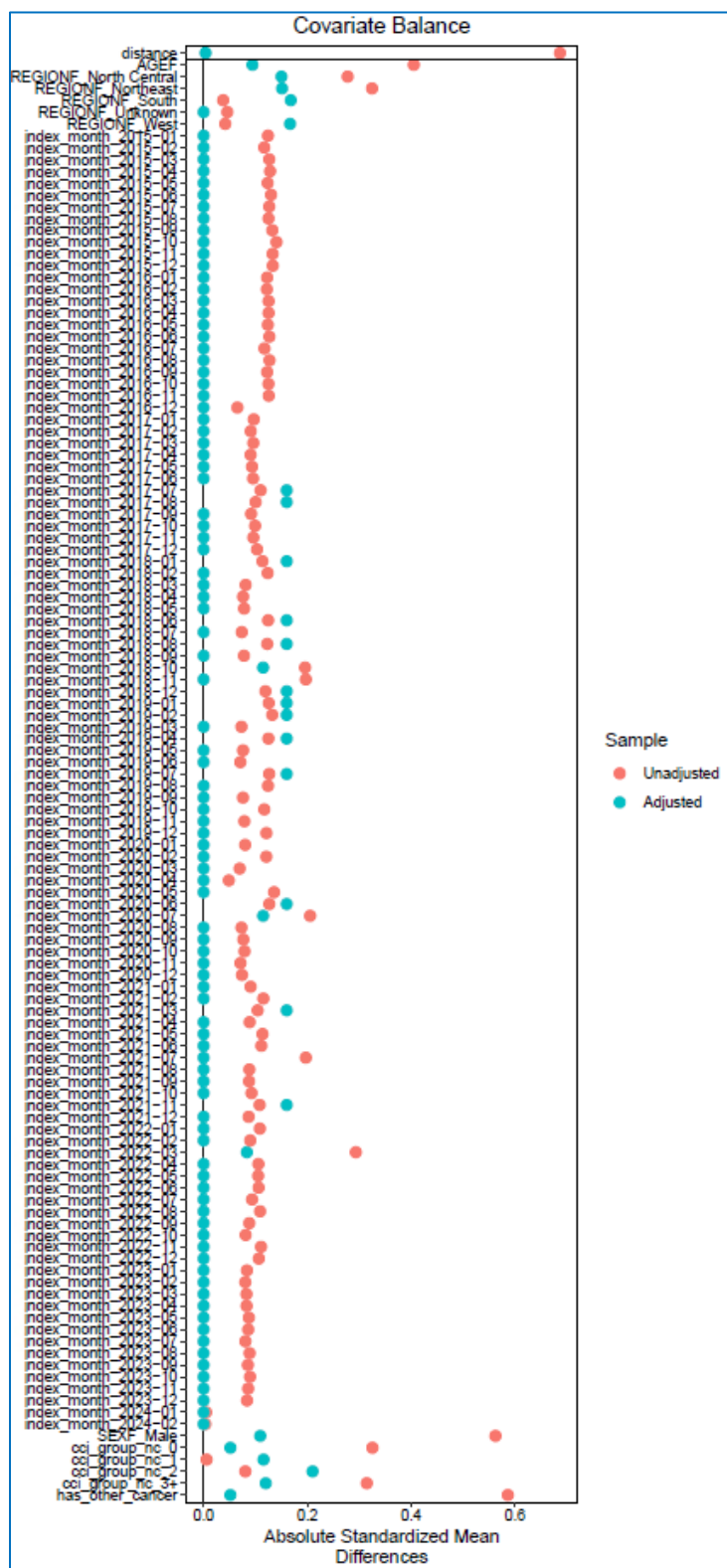
SMD = Standardized Mean Difference; aCCI = Cancer-Adjusted Charlson Comorbidity Index;
MCL = Mantle Cell Lymphoma

6.5 Love Plot – Commercial



cci_group_nc = aCCI = Cancer-Adjusted Charlson Comorbidity

6.6 Love Plot – Medicare Supplemental



cci_group_nc = aCCI = Cancer-Adjusted Charlson Comorbidity

6.7 Rematch Balance – Commercial

Category	Covariate	Type	Unadjusted SMD	Adjusted SMD	Balance Status
Propensity Score	Distance	Continuous	0.3856	0.2670	Balanced, <0.1
Demographics	Age	Continuous	0.7788	−0.1638	Not Balanced
	Sex (Male)	Binary	0.3515	0.0476	Balanced, <0.1
Geographic Region	Region – North Central	Binary	0.1384	0.0000	Balanced, <0.1
	Region – Northeast	Binary	0.0612	0.0476	Balanced, <0.1
	Region – South	Binary	0.1220	−0.0476	Balanced, <0.1
	Region – Unknown	Binary	−0.0029	0.0000	Balanced, <0.1
	Region – West	Binary	0.0747	0.0000	Balanced, <0.1
Index Month	Index Month (Oct 2015–May 2022)	96 Binary Vars	Range: −0.0235 to 0.0885	All ≤ 0.0476	All Balanced, <0.1
Non-Cancer Comorbidity (aCCI)	aCCI Score = 0	Binary	−0.4629	−0.1905	Not Balanced
	aCCI Score = 1	Binary	0.1919	0.1905	Not Balanced
	aCCI Score = 2	Binary	0.1620	0.0000	Balanced, <0.1
	aCCI Score ≥ 3	Binary	0.1819	0.0000	Balanced, <0.1
Cancer History	Presence of Non-	Binary	0.0950	0.0476	Balanced, <0.1

	Hematologic Cancer				
Matching Summary	<i>Matched 21 MCL to 21 controls (1:1) from original pool of 21 MCL and 60,384 controls; 96 of 99 covariates balanced (<0.1 SMD). Not balanced: Age, aCCI score = 0, aCCI score = 1.</i>				

SMD = Standardized Mean Difference; aCCI = Cancer-Adjusted Charlson Comorbidity Index; MCL = Mantle Cell Lymphoma

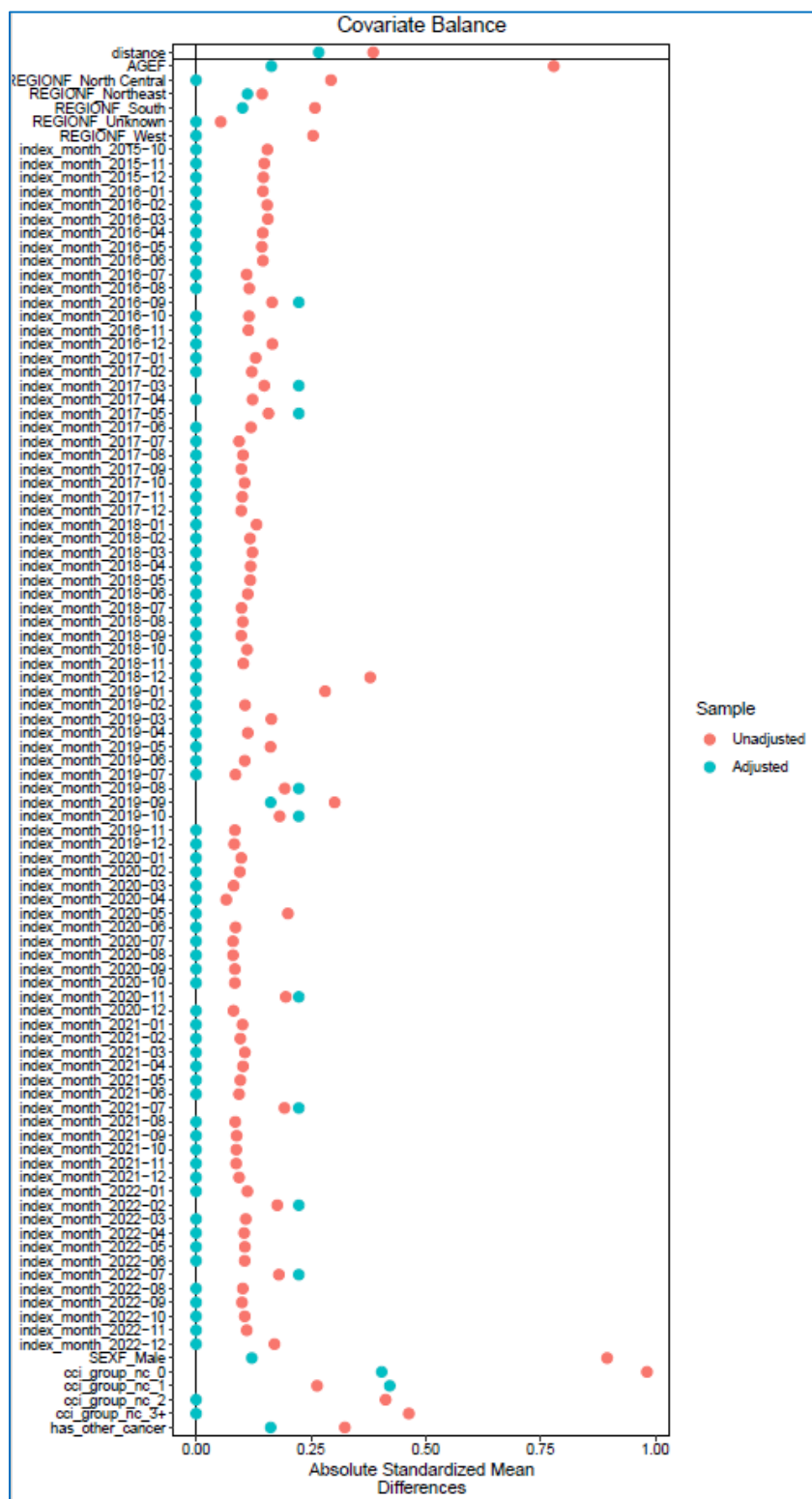
6.8 Rematch Balance – Medicare Supplemental

1. Category	Covariate	Type	Unadjusted SMD	Adjusted SMD	Balance Status
Propensity Score	Distance	Continuous	0.7779	-0.0002	Balanced, <0.1
Demographics	Age	Continuous	0.1400	0.2079	Not Balanced
	Sex (Male)	Binary	0.1977	0.1818	Not Balanced
Geographic Region	Region – North Central	Binary	0.0891	0.0909	Balanced, <0.1
	Region – Northeast	Binary	0.2350	0.0000	Balanced, <0.1
	Region – South	Binary	-0.0160	0.0909	Balanced, <0.1
	Region – Unknown	Binary	0.0109	0.0000	Balanced, <0.1
	Region – West	Binary	0.1638	0.0000	Balanced, <0.1
Index Month	Index Month (Jan 2015–Mar 2023)	99 Binary Vars	Range: – 0.0225 to 0.0878	All ≤ 0.0909	All Balanced, <0.1
Non-Cancer Comorbidity (aCCI)	aCCI Score = 0	Binary	-0.3838	0.0909	Balanced, <0.1
	aCCI Score = 1	Binary	0.1977	0.1181	Not Balanced
	aCCI Score = 2	Binary	0.0704	-0.0909	Balanced, <0.1
	aCCI Score ≥ 3	Binary	0.0723	-0.0909	Balanced, <0.1
Cancer History	Presence of Non-Hematologic Cancer	Binary	0.3729	0.0000	Balanced, <0.1

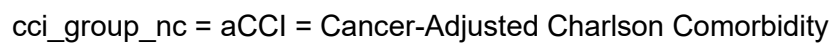
Matching Summary	Matched 11 MCL to 11 controls (1:1) from original pool of 11 MCL and 63,507 controls; 113 of 116 covariates balanced (<0.1 SMD). Not balanced: Age, Sex (Male), aCCI score = 1.
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SMD = Standardized Mean Difference; aCCI = Cancer-Adjusted Charlson Comorbidity Index;
MCL = Mantle Cell Lymphoma

6.9 Rematch Love Plot – Commercial



cci_group_nc = aCCI = Cancer-Adjusted Charlson Comorbidity



6.11 Rematch Characteristics – Commercial

Characteristic	MCL (n = 21)	Control (n = 21)
Age, mean (SD)	55.14 (8.14)	56.48 (5.61)
Sex		
Male, n (%)	17 (81.0%)	18 (85.7%)
Female, n (%)	4 (19.0%)	3 (14.3%)
Region, n (%)		
North Central	7 (33.3%)	7 (33.3%)
Northeast	5 (23.8%)	4 (19.0%)
South	7 (33.3%)	8 (38.1%)
West	2 (9.5%)	2 (9.5%)
Index Year, n (%)		
2016	2 (9.5%)	3 (14.3%)
2017	2 (9.5%)	0 (0.0%)
2018	3 (14.3%)	3 (14.3%)
2019	8 (38.1%)	9 (42.9%)
2020	2 (9.5%)	2 (9.5%)
2021	1 (4.8%)	0 (0.0%)
2022	3 (14.3%)	3 (14.3%)
aCCI Group, n (%)		
Score = 0	7 (33.3%)	11 (52.4%)
Score = 1	6 (28.6%)	2 (9.5%)
Score = 2	4 (19.0%)	4 (19.0%)
Score ≥ 3	4 (19.0%)	4 (19.0%)
Non-Hematologic Cancer		
Yes	2 (9.5%)	1 (4.8%)
No	19 (90.5%)	20 (95.2%)

SD = Standard Deviation; MCL = Mantle Cell Lymphoma; aCCI = Adapted Charlson Comorbidity Index.

6.12 Rematch Characteristics – Medicare Supplemental

Characteristic	MCL (n = 11)	Control (n = 11)
AGEF, mean (SD)	75.64 (7.43)	74.09 (7.19)
Sex = Male, n (%)		
Male, n (%)	7 (63.6%)	5 (45.5%)
Female, n (%)	4 (36.4%)	6 (54.5%)
Region, n (%)		
North Central	5 (45.5%)	6 (54.5%)
Northeast	0 (0%)	0 (0%)
South	3 (27.3%)	2 (18.2%)
West	3 (27.3%)	3 (27.3%)
Index Year, n (%)		
2016	1 (9.1%)	3 (27.3%)
2017	1 (9.1%)	0 (0.0%)
2018	3 (27.3%)	4 (36.4%)
2019	1 (9.1%)	1 (9.1%)
2020	3 (27.3%)	3 (27.3%)
2021	0 (0%)	0 (0%)
2022	2 (18.2%)	0 (0.0%)
aCCI Group, n (%)		
Score = 0	2 (18.2%)	1 (9.1%)
Score = 1	4 (36.4%)	4 (36.4%)
Score = 2	2 (18.2%)	3 (27.3%)
Score ≥ 3	3 (27.3%)	3 (27.3%)
Non-Hematologic Cancer		

Yes	5 (45.5%)	5 (45.5%)
No	6 (54.5%)	6 (54.5%)

SD = Standard Deviation; MCL = Mantle Cell Lymphoma; aCCI = Adapted Charlson Comorbidity Index.

6.13 Outpatient Service Categories

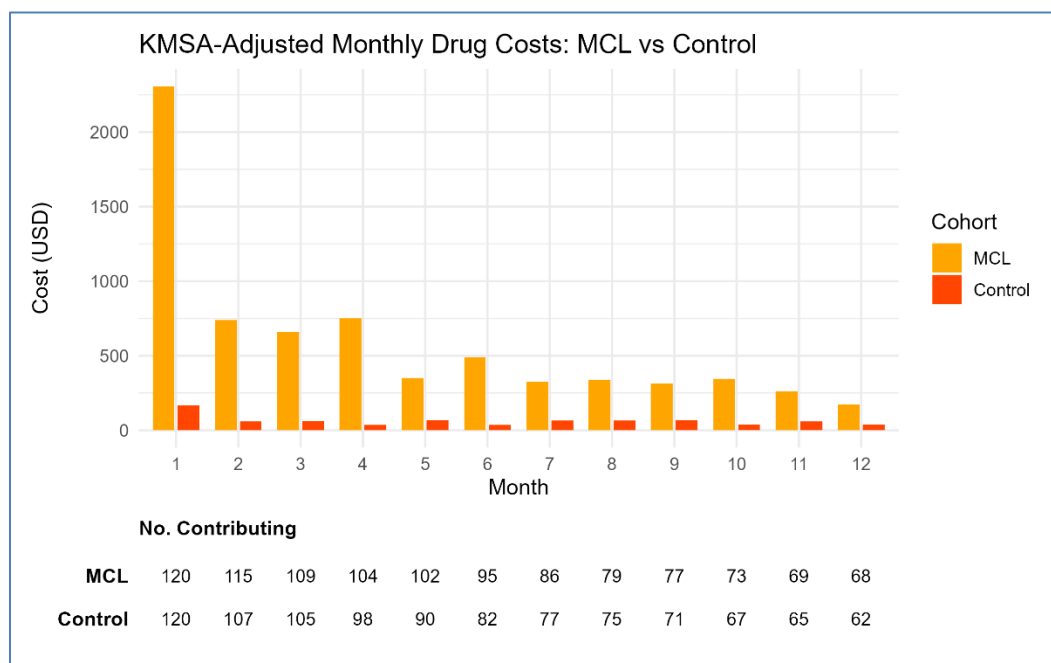
Subcategory	MCL, n (%)	Control, n (%)
Hospital Outpatient	11,920 (74.9%)	1,112 (37.1%)
Office Visit	3,826 (24.0%)	1,817 (60.6%)
Outpatient Surgery	126 (0.79%)	53 (1.77%)
Urgent Care / Ambulance	35 (0.22%)	12 (0.4%)
Retail Clinic	6 (0.038%)	2 (0.067%)
Mobile Unit	4 (0.025%)	1 (0.033%)
Behavioral Health	1 (0.006%)	0 (0%)

6.14 Monthly Costs by Category and Cohort

Annual Costs		Costs by Month											
Cost Type		1	2	3	4	5	6	7	8	9	10	11	12
Drug - MCL	7054	2308	739	659	750	352	490	325	338	312	345	7054	2308
Drug - Control	771	167	60	62	37	69	36	65	67	69	40	771	167
ED - MCL	318	56	87	29	38	35	20	13	18	10	3	318	56
ED - Control	109	89	5	2	1	4	1	4	1	1	1	109	89
Inpt Svc - MCL	16142	1581	4451	2914	3331	819	255	404	283	310	64	16142	1581
Inpt Svc - Control	1830	148	43	51	0	11	93	0	1	11	0	1830	148
Outpt Svc - MCL	8942	2153	920	1015	870	500	405	660	563	402	577	8942	2153
Outpt Svc - Control	384	174	36	29	26	24	20	13	11	11	12	384	174
Total - MCL	34121	6066	6700	6006	5047	1811	1263	1520	1273	1097	1087	34121	6066
Total - Control	3517	1941	179	221	96	134	197	104	107	133	73	3517	1941

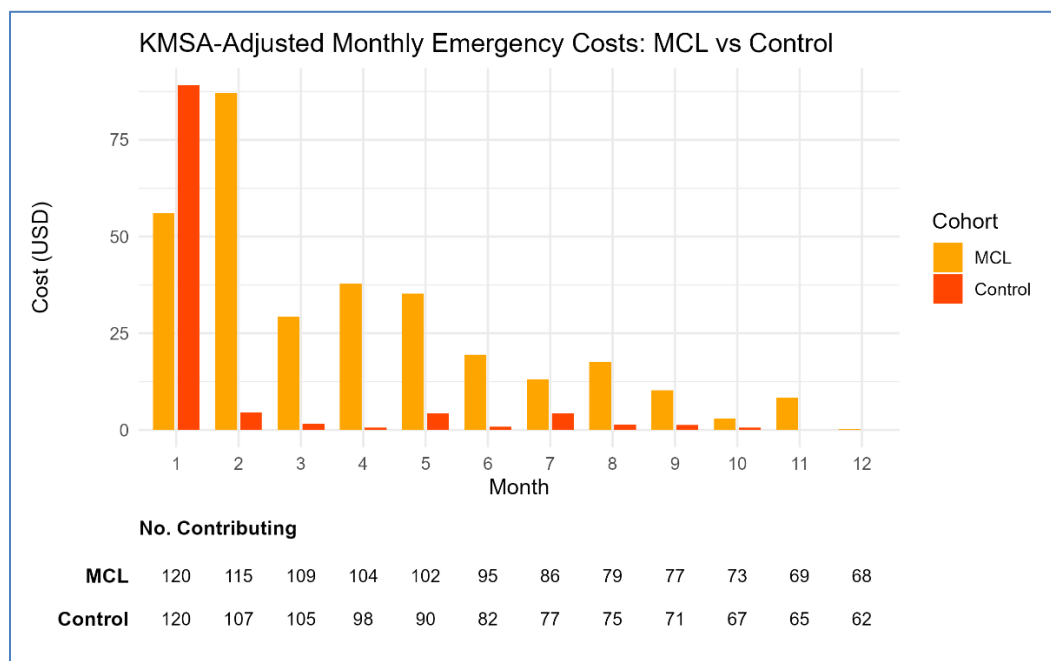
MCL = Mantle Cell Lymphoma; ED = Emergency Department; Inpt = Inpatient; Svc = Services; Outpt = Outpatient; Co = Control.

6.15 KMSA-Adjusted Monthly Costs by Cohort: Drug



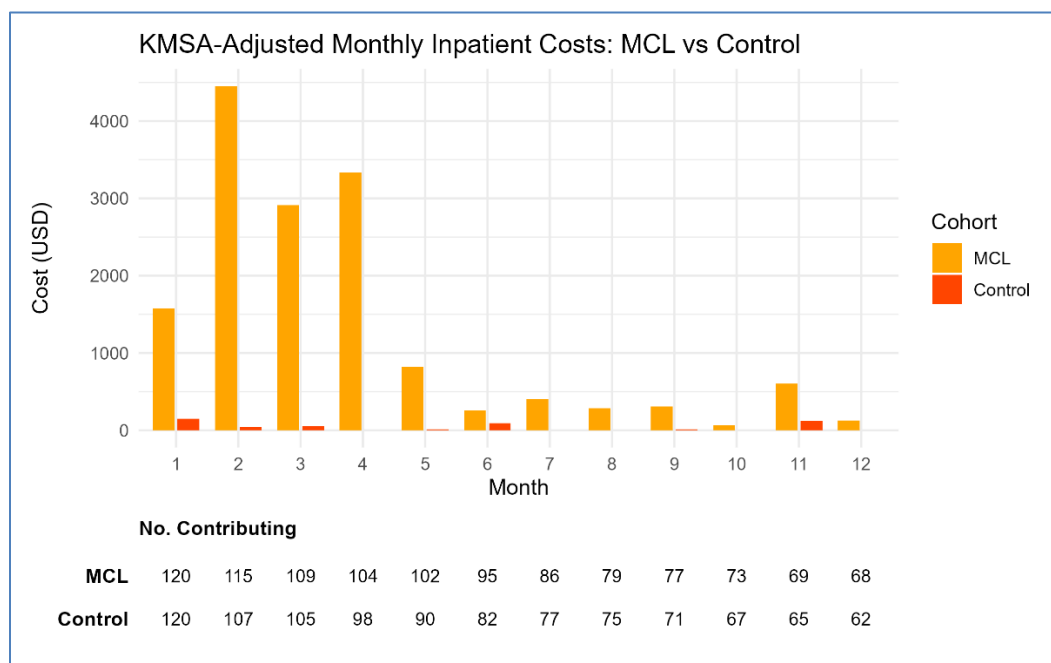
KMSA = Kaplan–Meier Sample Average; MCL = Mantle Cell Lymphoma; USD = United States Dollars; No. = Number

6.16 KMSA-Adjusted Monthly Costs by Cohort: Emergency



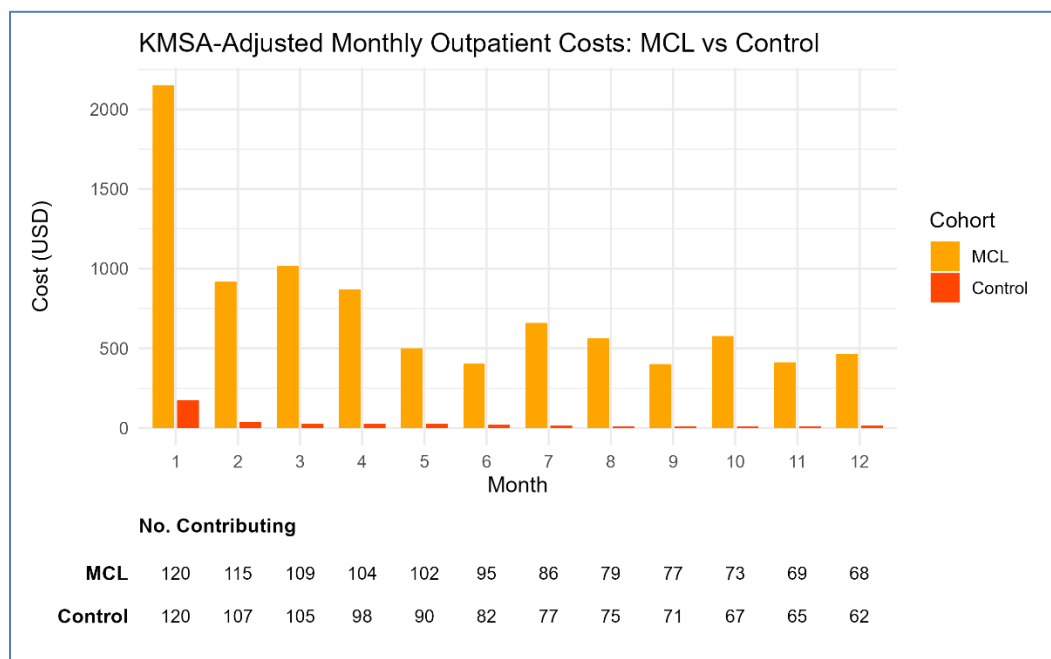
KMSA = Kaplan–Meier Sample Average; MCL = Mantle Cell Lymphoma; USD = United States Dollars; No. = Number

6.17 KMSA-Adjusted Monthly Costs by Cohort: Inpatient



KMSA = Kaplan–Meier Sample Average; MCL = Mantle Cell Lymphoma; USD = United States Dollars; No. = Number

6.18 KMSA-Adjusted Monthly Costs by Cohort: Outpatient



KMSA = Kaplan–Meier Sample Average; MCL = Mantle Cell Lymphoma; USD = United States Dollars; No. = Number