

Real-World Disease Burden, Costs and Resource Utilization of Hospital-Based Care Among Mantle Cell Lymphoma, Waldenström Macroglobulinemia, Marginal Zone Lymphoma and Chronic Lymphocytic Leukemia: Disparities and Risk Factors

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Introduction: Mantle cell lymphoma (MCL), Waldenström macroglobulinemia (WM), marginal zone lymphoma (MZL) and chronic lymphocytic leukemia (CLL) are subtypes of non-Hodgkin's lymphoma. Collectively, these subtypes constitute a large proportion of all B-cell malignancies; however, they are typically associated with survival spanning several years with multiple interspersed treatment periods due to frequent relapses. This can predispose patients to repeated hospitalization resulting in significant economic impact. The objectives of this study were to examine real-world treatment patterns, costs and healthcare resource utilization for patients with these lymphomas, as well as identify disparities and risk factors associated with costs incurred in US hospitals.

Methods: A retrospective study was conducted using the Premier Healthcare Database, a geographically diverse all-payer, hospital administrative database containing more than one billion inpatient and hospital-based outpatient encounters. Patients aged ≥ 18 years with at least 1 inpatient or 2 hospital-based outpatient visits with a MCL, WM, CLL, or MZL diagnosis, and who received treatment for these conditions from 1/1/2014 to 10/31/2019 were included in the study. Descriptive analysis was conducted to examine patient sociodemographic and hospital characteristics, all-cause and lymphoma-related healthcare resource utilization and costs. Costs were obtained from patients' discharge files and hospital billing records. Multivariable analysis was performed using generalized linear

models to examine risk factors associated with costs and LOS for each lymphoma type. Treatment evaluated including any use of supportive care (blood transfusion, granulocyte colony stimulating factors [GCSF]), and by regimen (steroids alone, chemotherapy alone, chemo-immunotherapy, rituximab alone, targeted therapy alone, targeted therapy in combination with chemotherapy, other). Statistical significance was determined as a p-value of <0.05.

Results: The study population included 23,952 CLL, 3,387 MCL, 2,655 MZL, and 1,811 WM patients in the US hospital database. Patients with WM were statistically significantly older (77 ± 58.5 years) compared to patients with CLL (74.2 ± 30.2 years), MCL (70.7 ± 37.3 years) or MZL (69.3 ± 33.8 years). More male (71.7%) and white (87.8%) patients were identified in the MCL cohort compared to the general lymphoma cohorts (Males: 58.7%; whites: 86.3). The most common comorbidities included chronic pulmonary disease (27.1%), gastroesophageal reflux disease (17.6%), moderate-severe renal disease (16.6%), congestive heart failure (15.7%) and diabetes without chronic complications (15.2%). Overall, more than two-thirds of patients in each lymphoma group received treatment with steroids alone during hospitalizations. While the use of steroids alone was higher among whites compared to non-white patients (69.5% vs. 60.4%), the use of chemo-immunotherapy was lower in whites compared to non-whites (11.9% vs. 16.2%). The average LOS of inpatient hospitalization ranged from 6.3 days for CLL to 7.4 days for MCL, with the mean costs per hospitalization from \$19,566 (CLL) to \$24,439 (MCL). Non-white patients have significantly longer mean LOS days compared with white patients (CLL: 18.3 vs. 14.8; MCL: 21.7 vs. 18.3; MZL: 21.6 vs. 18.5; WM 19.0 vs. 14.5). Across the 4 lymphoma types, multivariable regression confirmed the descriptive results and demonstrated that higher hospitals costs were associated with patients who were non-white, Hispanic/Latino, treated in hospitals located in the Northeast or West, or had Medicaid; statistically significant increased cost of care was also noted for patients who received targeted therapy or supportive care, such as blood transfusion or GCSF (Table 1).

Conclusions: Real-world data demonstrated the significantly high total hospital costs once patients with MCL, WM, MZL, and CLL patients were hospitalized, with significantly higher impact to minority populations. Given the increased availability of effective oral therapeutics, optimal and timely disease control in the outpatients setting can potentially prevent or decrease hospitalizations and reduce economic burden on healthcare. Future studies are needed to explore the reason for admission, clinical outcomes, and potential preventive

interventions.

Table 1. Multivariable regression analysis of factors associated with total hospital costs

	CLL	MCL	MZL	WM
	% Difference	% Difference	% Difference	% Difference
Age				
Age ≥65 years	Reference	Reference	Reference	Reference
Age < 65 years	11.97*	1.27	8.4	-1.65
Sex				
Male	Reference	Reference	Reference	Reference
Female	-7.44 *	-5.54	-5.99	0.33
Race				
White	Reference	Reference	Reference	Reference
Non-White	12.66 *	14.4 *	14.75 *	11.55
Ethnicity				
Not Hispanic or Latino/Unknown	Reference	Reference	Reference	Reference
Hispanic or Latino	14.86 *	16.12 *	6.93	-10.4
Primary Payor				
Medicare	Reference	Reference	Reference	Reference
Medicaid	4.27	-5.5	13.19	70.86*
Other	-13.1 *	-7.65	-1.58	1.01
Private Insurance	-9.56 *	-7.32	-1.23	11.15
Hospital Characteristics at Index				
South	Reference	Reference	Reference	Reference
Midwest	2.13	6.53	7.51	-0.49
Northeast	38.83 *	55.11 *	41.64 *	7.52
West	21.1 *	12.17 *	14.06 *	10.16
Clinical Conditions at Index (Charlson Comorbidity Index score)				
	2.3 *	1.16	4.47 *	1.24
Supportive Care				
No supportive care	Reference	Reference	Reference	Reference
Any red blood cell or platelet transfusion	76.35 *	48.1 *	65.01 *	59.06 *
Any use of granulocyte colony stimulating factors (GCSF)	57.1 *	60.48 *	40.13 *	81.07 *
Treatment Regimen				
Steroids alone	Reference	Reference	Reference	Reference
Chemotherapy alone	38.77 *	35.15 *	53.17 *	18.09
Chemo-immunotherapy	65.09 *	100.4 *	118.5 *	81.56 *
Other	16.02 *	8.44	31.63	0.74
Rituximab alone	56.97 *	52.63 *	61.13 *	39.86 *
Targeted therapy alone	63.83 *	27.5 *	80.62 *	5.36
Targeted therapy in combination with other	109.9 *	116.3 *	115.9 *	95.05 *
Length of follow up in months	1.32 *	1.22 *	0.87 *	1.17 *

* p<0.001; % differences are calculated using coefficients generated from the multivariable regression model