THE ECONOMIC BURDEN OF DIABETIC MACULAR EDEMA IN A WORKING AGE AND COMMERCIALLY INSURED POPULATION

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Abstract

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INTRODUCTION: Diabetic Macular Edema (DME) is the leading cause of blindness amongst working age adults in most developed countries. Diagnosis and treatment of DME involves many visits to specialists, numerous medications, and great cost. The primary objective of this study was to describe the economic burden of DME in a commercially insured working age population.

METHODS: We conducted a retrospective cohort study using enrollment and health care claims information from a large database of commercially insured, working age adults. We matched a cohort of patients with a claim for DME 1:5 to a diabetic control group without DME and reported health care utilization and cost over a 1, 2 and 3 year period.

RESULTS: The DME cohort had significantly more comorbidities and a higher Charlson Comorbidity Index (CCI) scores than the matched diabetic control cohort. Health care resource utilization rates were significantly higher in DME patients than diabetic control patients for every category. DME patients had claims for significantly higher counts of emergency, outpatient, and inpatient visits than the diabetic control cohort. The total number of days with a visit to any healthcare provider was on average more than 10 days greater in DME cohort patients than in non-DME diabetic patients (27.01 vs. 16.13 days). Among the DME cohort this represents, on average, a visit to a healthcare provider more than once every 2 weeks over the course of a year.

CONCLUSION: We characterized utilization patterns for DME patients and compared them to matched non-DME diabetic patients. We found that DME patients utilized significantly more health care resources and accrued higher costs than the non-DME diabetic patients. DME patients also made more visits to health care professionals. The burden of disease for DME patients is large and may represent a challenge for patients that are trying to attend to family or work. The large and rising cost of treatment only adds burden to patients that are likely already missing work time to visit specialists. DME patients that have nearly 30 days per year with at least one provider visit are likely to have difficult decisions between seeking treatment and taking care of their family or going to work.

INTRODUCTION

Diabetes Mellitus (DM) is an increasingly prevalent disease state with an estimated 8.3% of the US population currently being affected and 1.9 million newly diagnosed cases annually.[1] This disease causes a wide variety of systemic complications, often including ophthalmic conditions such as corneal abnormalities, glaucoma, iris neovascularization, cataracts, neuropathies, and retinopathy.[2] Diabetic retinopathy (DR) is the most common ophthalmic complication of DM and is the leading cause of vision loss for working age adults in the US.[1,3,4] The prevalence of retinopathy among diabetics aged 40 and higher in the US has recently been estimated at 28.5%[5]. DR is clinically diagnosed as either non-proliferative diabetic retinopathy (NPDR), proliferative diabetic retinopathy (PDR) or diabetic macular edema (DME). NPDR is the least severe and usually does not involve any visual impairment. PDR is more severe than NPDR and is usually classified by noticeable vision loss and some involvement of neovascularization protruding through the retina[6]. DME is the most severe and is characterized by swelling or neovascularization of the macula, the part of the retina responsible for detailed central vision. DME is thought to be caused by leaky retinal capillaries that allow fluid to build up on, or under, the macula[7]. DME is the most common reason for vision loss in patients with DR and is the leading cause of blindness among working-age populations in most developed countries. [4,6,8,9]

DME is commonly treated with medications that require intravitreal injection or various forms of eye surgery[10]. The most common medications currently used to treat DME are vascular endothelial growth factor (VEGF) inhibitors or corticosteroids that are

injected into the vitreous fluid of the eye monthly by the ophthalmologist[11,12]. The most common surgical procedure used to treat DME is laser photocoagulation which can involve direct laser treatments of areas of leakage and neovascularization (focal), or grid pattern treatment over a larger part of the retina (grid-pattern)[13]. Laser photocoagulation can have adverse effects that include scarring and possible vision loss. Laser treatment and intravitreal injection both involve visits to the ophthalmologist, local anesthesia of the eye, varying recovery time, and transportation after the procedure.

People living with diabetes experience a high burden of disease comprised of primary care, endocrinology and various other specialist visits, and a multitude of medications to manage their disease. Developing DME is particularly thought to add significantly to this burden[14]. Time spent on doctor visits, hospitalizations, and obtaining or using medications can significantly impact a working age patient's ability to retain employment or attend to family, leading to difficult decisions between seeking health care or attending to family and work. Costs of DME treatments and maintenance medications add greatly to the burden of disease, especially in patients that may be limited in their ability to work due to increased visits.[15] We sought to examine the incremental burden of disease in working age DME patients and to compare the burden to diabetic patients without DME. To our knowledge no published study has characterized the burden of DME in this specific patient population. [16]

METHODS

Study Design

We conducted a retrospective cohort study using enrollment and health care claims information from a large database of commercially insured, working age adults. Individuals were selected based on International Classification of Diseases (ICD-9) codes for diabetes and DME. Diabetic patients with DME were matched at index date in equal proportion to diabetic patients without macular edema. Utilization rates of medical care services and costs for a period of up to 3 years were extracted. The institutional review board of the University of Washington approved this study.

Data Source

We utilized data from the Truven Health MarketScan® Commercial Claims and Encounters Database from 2007 to 2011. The MarketScan database contains pooled health care records for over 52 million people including medical and pharmacy claims for the covered individual, their spouses, and dependents. MarketScan includes information on patient demographics, utilization, diagnoses, and payments for persons using services in indemnity, point-of-service, and PPO plans. The MarketScan database represents a large working age group of Americans and reflects a geographically diverse population.

Study Population and Inclusion Criteria

Patients in the DME cohort were selected using a previously validated algorithm (using ICD-9 code 362.53 or 362.83) in combination with the newer ICD-9 code for DME 362.07. The previously validated algorithm was developed before the

implementation of a specific ICD-9 for DME and was included to capture DME patients that were billed under previous coding mechanisms[17]. For the purposes of this study, working age was considered 18-65 years, however in order to ensure 3-year capture of patients, we limited age eligibility to age 18-62 years. The index date for patients in the DME cohort was coded equal to the first date of a visit with a DME ICD-9 code with a minimum 6-month period of previous continuous enrollment without a DME related claim. The non-DME diabetic cohort was created by selecting for patients with a diabetes ICD-9 (250.xx) and matched to the DME cohort by age (+/- 2 years), gender, region, and calendar years with insurance coverage. In order to select a non-DME cohort that was not biased towards newly diagnosed diabetic patients, the index date for non-DME cohort patients was considered the index date of their matched DME cohort patient. Controls were matched to cases in a 5:1 ratio using the greedy matching algorithm. After matching, only patients with 6 months of continuous insurance coverage before index date and at least one year of continuous coverage after index date were eligible for the study. Separate cohorts with continuous insurance coverage of 1, 2 and 3 years after the index date were created out of the initially identified cohort. These cohorts are referred to as DME 1y, DME 2y, DME 3y, non-DME 1y, non-DME 2y, and non-DME 3y respectively.

Analyses

Demographic variables for all patients were collected and the Deyo-Charlson comorbidity index (CCI) score was constructed.[18] Resource use was examined using current procedural terminology (CPT) codes for various procedures and visits including

use of intravitreal injection, optical coherence tomography (OCT), fluorescein angiography (FA), laser photocoagulation, vitrectomy, mean unique medications, and number of days with a claim for inpatient, outpatient, or emergency room (ER) visits. ER visits were considered as number of visits and not days spent in emergency room, each visit counted as 1 regardless of length of stay. Utilization was tabulated for 1, 2, and 3-year periods for each respective cohort. Mean unique medications used were determined by using the national drug code (NDC) on the prescription claim matched to a generic product identification variable. This was used to determine how many unique drugs were used by a patient, regardless of strength or manufacturer, and represents the total number of different medications a patient had a claim for in the given time period. Costs were examined from a health care system perspective using gross payments to a provider for a service; this is equal to the amount eligible for payment under the medical plan terms after applying rules such as discounts, but before applying coordination of benefits, copayment, or deductible. Health care costs for each outpatient, inpatient and pharmacy claim were tabulated for each patient and reported for each cohort as median cost, mean cost, 1st quartile cost and 3rd quartile cost to illustrate the cost distribution for each cohort.

Statistical Analysis

We generated univariate descriptive statistics to analyze the demographic and utilization differences of DME and Diabetic cohorts, using the Chi-square test for categorical variables and the Wilcoxon rank sum test for continuous variables. Statistical analyses were performed using SAS Version 9.3 (SAS Institute, Cary, NC, USA).

RESULTS

A total of 5,353,000 patients with an ICD-9 code for diabetes were identified between 2007 and 2011, of which 4,346,268 met the age inclusion criteria (Figure 1). Some 70,011 (1.6%) had a DME claim and these were matched 1:5 with diabetic patients with no DME claim - 350,055 patients. Of the DME patients, 45,866 (65.5%) had continuous insurance coverage for the 6 month period before index date. This group was further separated into three cohorts, the 1 year of continuous insurance coverage after index date cohort had 24,326 (34.7%) patients, the 2 year continuous coverage cohort had 11,583 (16.5%) and the 3 year cohort had 4916 (7.0%). The diabetic control group had 221,558 (63.3%) patients with 6 months of continuous insurance coverage before their index date. This group was further separated into three cohorts to match the DME cohorts, the 1 year of continuous insurance coverage after index date cohort had 122,710 (35.1%) patients, the 2 year continuous coverage cohort had 54,467 (15.6%), and the 3 year cohort had 24,844 (7.1%) patients.

The DME and matched diabetic control patients were well matched on age, gender and region (Table 1). The DME patients had significantly more comorbidities and higher CCI scores than the matched diabetic control patients. In all three cohorts of DME patients, the highest percentage of patients had CCI scores of 3+ while in the 3 diabetic control cohorts the highest percentage of patients had a CCI score of 1. In almost every category of specific comorbidity that is part of the CCI score the DME cohorts had significantly higher percentages of people with the disease than their matched diabetic cohorts.

Health Care Utilization

Utilization rates were significantly higher in DME patients for every category of healthcare utilization. Optical coherence tomography (OCT) was the most commonly utilized procedure with 72.0% of the 1 year DME cohort having a claim but only 3.8% of the diabetic control cohort having a claim for at least one OCT (Table 2). DME patients showed similar percentages receiving any medication in all three years, but received significantly more medications than their matched diabetic cohort. In the 1-year cohorts, diabetic control cohort patients received an average of 6.59 unique medications while the DME cohort received 9.11 ($p<.001$). This pattern of greater numbers of unique medications used for DME patients continued in the 2 year (13.68 vs. 10.05) and 3 year (17.96 vs. 13.38) cohorts as well.

DME patients had claims for significantly higher volumes of ER, outpatient, and inpatient visits than the matched diabetic control patients (Table 3). In the 1-year cohorts, DME patients had a mean of over 10 more days with an outpatient visit than the non-DME diabetic cohort, 25.07 vs. 14.44 days respectively with at least one outpatient claim. The differences in days with an inpatient visit claim were also significantly higher in the DME cohorts every year except the 1y. The total days with a claim for a visit to any healthcare provider was on average more than 10 days greater in DME cohort patients than in non-DME diabetic patients in the 1y, 2y, and 3y year cohorts. Having greater than 27.01 days with a health care provider visit for the 1y DME cohort represents on average a visit to a healthcare provider more than once every 2 weeks over the course of a year.

Health Care Utilization over time

The 3-year DME cohort was used to monitor utilization rates over time by breaking the cohort into specific time periods (Table 4). The 6 month period before and after index date was reported along with the 1st year, 2nd year, and 3rd year after index. DME patients generally utilized more resources in the 6 month period after index date than the 6 months before index date. For example, DME patients had on average 0.39 OCT procedures in the 6 months before index, and 1.71 OCT procedures on average in the 6 months after index date. DME patients also had increased median total cost in each reported time period going from $8,461 to $9,154 in the 6-months before index to 6-months after index, and increasing from $18,121 to $21,536, and then to $26,180 in the 1st, 2nd, and 3rd year after index respectively.

Cost

DME patients incurred considerably higher costs in every category and in every cohort than the matched diabetic controls (Table 5). The total yearly median cost for DME patients of $6517 is more than double what the total yearly median cost for the matched diabetic cohort median cost of $2990. The differences in mean yearly cost, which is more affected by outliers, similarly is more than double in the DME cohorts vs. the non-DME diabetic cohorts, $14,678 and $6801 respectively. The greatest difference in median cost was found in outpatient costs with an average difference of $3870 per patient per year greater median outpatient cost for DME patients. DME patients overall median cost, when combining outpatient, inpatient and pharmacy costs were $3,527 higher per year than the diabetic matched control cohorts.

DISCUSSION

We sought to examine the incremental burden of DME over non-DME diabetic patients in a working age commercially insured population. Consistent with current understanding and data from other patient populations, working age DME patients utilized significantly larger amounts of health care resources and were found to have higher costs than other diabetic patients.[16] DME is a secondary complication of diabetes and represents a progression of the disease, and as reflected in the comorbidity comparison they have greater rates of myocardial infarction, peripheral vascular disease, and renal disease (Table 1). DME patients experienced more than 2 visits per month to a healthcare provider. This represents a significant burden to the healthcare system and to a patient population that must balance seeking healthcare with time spent working and attending to family. Many healthcare specialists have limited times or space in their schedule for patients and may leave patients with difficult decisions between taking available appointment times and attending to work or family obligations.

Shea et. al. examined the burden of DME in elderly patients using a Medicare claims database and found that DME was associated with significantly higher costs and resource use than other elderly diabetic patients[16]. In this analysis of claims from 2000 to 2005, the use of intravitreally injected medications was less common and anti-VEGF agents were just being approved (Macugen 2004, Avastin 2005). They estimated that 5.75% of DME patients utilized any intravitreal medication, where our study found that from 2007 to 2011 over 20% of DME patients in utilized some form of intravitreal

medication. This may represent a trend in treatment patterns for DME. Our study also found increased use of OCT, and laser photocoagulation and decreased use of FA when compared with the prior study. These findings point to a shift in DME treatment patterns but may not accurately estimate usage changes because the study populations are different.

Treatment costs for DME patients were more than double their matched diabetic control patients. Although our analysis looked at cost from an health care system perspective, this represents a large burden to the patients as well, through copays, out of pocket costs and insurance premiums. Furthermore, this claims based analysis does not factor in cost of transportation to the many visits, lost wages for lost time at work, or many other non-insurance based costs. New emerging treatments and medications will continue add to the cost burden of treating DME in the near future.[10,19] Increased costs for treatment and maintenance coupled with lost work time and productivity make the burden of DME an important consideration to patients, employers and the health care system in general.

This study has several important limitations. First, MarketScan is a large dataset, but due to being based on submitted commercial insurance claims has several limitations. Claims data relies on accurate entry of codes for billing, diagnosis, and procedures however, provider knowledge or ability to correctly code claims is known to vary.[20] It is likely that some procedures don't get coded for in the claim and are instead done under claims for other visits/procedures limiting the accuracy of the results. Second, we matched diabetic control cohorts to the DME patients on age, sex, region and insurance coverage, but not on comorbidities. The DME and non-DME diabetic groups are very

different in many ways, including progression of diabetes and likely time with diabetes, which is shown in the comorbidity differences. The intention of our study was to examine the real world burden associated with the average working age DME and diabetic patient, not necessarily the equivalently comorbid diabetic patient. Our approach limits the conclusions about the specific incremental burden that DME adds to an equivalently sick patient in order to describe the average burden between these populations. Third, we were able to estimate total days with a health care related visit by tabulating the total days with any outpatient or inpatient billed claim, however there are several limitations to this method. No distinction was made between level of service or estimated time the service would take. There is also the possibility of visits that weren't billed or had no claims filed, as well as the possibility of claims being sent in on the wrong day. If procedures were billed to the wrong day it's possible that a day with multiple procedures would show up as multiple days with a visit. Fourth, treatment of DME is rapidly changing as new medications and procedures are being developed or changing in popularity, and even in our study period the usage patterns between 2007 and 2011 are likely to have changed. Specifically, the use of intravitreal medications such as corticosteroids and anti-VEGF medications were likely to vary as new medications were brought to market during our study period.[21]

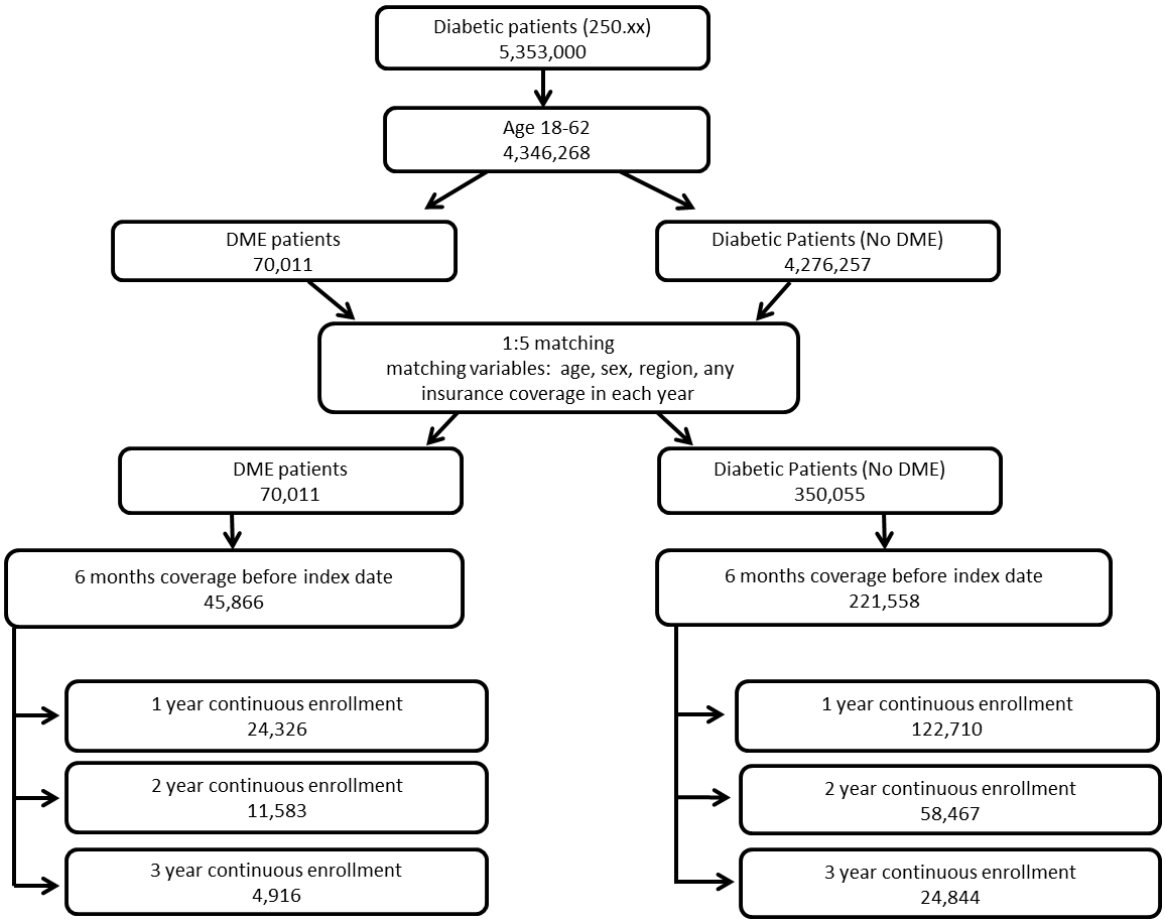
Future study may provide insight into the specific burden that DME adds to a comparatively progressed diabetic patient. For example, a similar claims based retrospective study could match patients on various key comorbidities and compare utilization rates to better model what incremental burden DME specifically adds to a comparable diabetic patient. Further study should also investigate utilization rates of

individual DME medications. Characterizing adherence and persistence could help identify differential burden on patients being treated with specific procedures or medications. This would help to identify real-world utilization patterns and provide insights for comparison with the strict utilization required in rigorously controlled clinical trials. Finally, costs were described in our study by looking at mean, median and quartile costs for cohort patients. Future analysis that included a multivariate regression cost analysis would be useful to more accurately model the incremental cost burden of DME.

CONCLUSION

We characterized the healthcare utilization patterns for DME patients and compared them to matched non-DME diabetic patients. We found that DME patients utilized significantly more health care resources and accrued larger costs than the non-DME diabetic patients. The burden of disease for DME patients is large and may represent a challenge for patients that are trying to attend to family or work. With nearly 30 days per year with at least one provider visit there are likely to be difficult decisions for patients between seeking treatment or attending to family and work. Employers are also likely to feel the burden of lost productivity, work days or even by having to hire more staff. The large and rising cost of treatment only adds burden to patients that are likely already missing work time to visit specialists. DME is a heavily burdensome disease to patients, employers and the health care system in general.

Figure 1. Selection criteria for Diabetic Macular Edema and Diabetic cohorts



*DME=Diabetic Macular Edema

Table 1. Demographic and Comorbidities of DME and non-DME Diabetic cohorts

	DME 1y	non-DME 1y	p-value	DME 2y	non-DME 2y	p-value	DME 3y	non-DME 3y	p-value
	n = 24,326	n = 122,710		n = 11,583	n = 58,467		n = 4,916	n = 24,844	
Age									
mean	50.73 (SD=7.34)	50.76 (SD=7.32)	0.5111	50.70 (SD=7.01)	50.69 (sd=7.03)	0.9442	50.79 (SD=6.64)	50.82 (SD=6.65)	0.648
18-29	395 (1.62%)	1,935 (1.58%)		160 (1.38%)	808 (1.38%)		52 (1.06%)	247 (0.99%)	
30-44	3,933 (16.17%)	19,777 (16.12%)		1,767 (15.26%)	9,104 (15.57%)		727 (14.79%)	3,677 (14.80%)	
45-54	10,817 (44.47%)	54,648 (44.53%)		5,467 (47.20%)	27,350 (46.78%)		2,387 (48.56%)	11,983 (48.23%)	
55-62	9,181 (37.74%)	46,350 (37.77%)		4,189 (36.17%)	21,205 (36.27%)		1,750 (35.60%)	8,937 (35.97%)	
Gender									
male	12,955 (53.26%)	65,422 (53.31%)	0.8672	6,132 (52.94%)	30,983 (52.99%)	0.9174	2,550 (51.87%)	12,970 (52.21%)	0.6681
female	11,371 (46.74%)	57,288 (46.69%)		5,451 (47.06%)	27,484 (47.01%)		2,366 (48.13%)	11,874 (47.79%)	
Region	**DME 1y**	**non-DME 1y**	**p-value**	**DME 2y**	**non-DME 2y**	**p-value**	**DME 3y**	**non-DME 3y**	**p-value**
Northeast	3,200 (13.15%)	16,163 (13.17%)		1,406 (12.14%)	7,100 (12.14%)		619 (12.59%)	3,098 (12.47%)	
North Central	5,703 (23.44%)	28,672 (23.37%)		2,723 (23.51%)	13,695 (23.42%)		1,133 (23.05%)	5,876 (23.65%)	
South	11,939 (49.08%)	60,269 (49.11%)		5,794 (50.02%)	29,183 (49.91%)		2,439 (49.61%)	12,233 (49.24%)	
West	3,378 (13.89%)	17,070 (13.91%)		1,637 (14.13%)	8,365 (14.31%)		717 (14.59%)	3,597 (14.48%)	
Other	106 (0.44%)	536 (0.44%)		23 (0.20%)	124 (0.21%)		8 (0.16%)	40 (0.16%)	
Charlson Comorbidity Index									
0	15 (.06%)	445 (0.36%)		9 (0.08%)	203 (0.35%)		5 (0.1%)	88 (0.35%)	
1	3,598 (14.79%)	60,285 (49.13%)		1,606 (13.87%)	27,541 (47.11%)		673 (13.69%)	11,504 (46.30%)	
2	1,790 (7.36%)	22,293 (18.17%)		844 (7.29%)	10,984 (18.79%)		375 (7.63%)	4,692 (18.89%)	
3+	18,923 (77.79%)	39,687 (32.34%)		9,124 (78.77%)	19,739 (33.76%)		3,863 (78.58%)	8,560 (34.45%)	
Specific Charlson Comorbidities	**DME 1y**	**non-DME 1y**	**p-value**	**DME 2y**	**non-DME 2y**	**p-value**	**DME 3y**	**non-DME 3y**	**p-value**
Myocardial Infarction	1,843 (7.58%)	4,477 (3.65%)	<.0001	876 (7.56%)	2,251 (3.85%)	<.0001	357 (7.26%)	999 (4.02%)	<.0001
Congestive Heart Failure	3,484 (14.32%)	6,567 (5.35%)	<.0001	1,710 (14.76%)	3,218 (5.50%)	<.0001	733 (14.91%)	1,404 (5.65%)	<.0001
Peripheral Vascular Disease	3,406 (14.0%)	6,708 (5.47%)	<.0001	1,744 (15.06%)	3,430 (5.87%)	<.0001	770 (15.66%)	1,492 (6.01%)	<.0001
Cerebrovascular Disease	4,538 (18.65%)	11,640 (9.49%)	<.0001	2,284 (19.72%)	5,921 (10.13%)	<.0001	963 (19.59%)	2,550 (10.26%)	<.0001
Dementia	86 (0.36%)	228 (0.19%)	<.0001	48 (0.41%)	107 (0.18%)	<.0001	24 (0.49%)	47 (0.19%)	<.0001
Chronic Pulmonary Disease	5,264 (21.64%)	26,255 (21.40%)	0.398	2,729 (23.56%)	13,371 (22.87%)	0.1063	1,181 (24.02%)	5,819 (23.42%)	0.3637
Rheumatologic Disease	889 (3.65%)	3,810 (3.10%)	<.0001	470 (4.06%)	1,926 (3.29%)	<.0001	221 (4.50%)	865 (3.48%)	<.0001
Peptic Ulcer Disease	611 (2.51%)	2,434 (1.98%)	<.0001	324 (2.80%)	1,265 (2.16%)	<.0001	150 (3.05%)	543 (2.19%)	<.0001
Mild Liver Disease	406 (1.67%)	1,664 (1.36%)	0.0002	192 (1.66%)	785 (1.34%)	0.0083	72 (1.46%)	341 (1.37%)	0.6142
Diabetes	23,948 (98.45%)	121,032 (98.63%)	0.0237	11,411 (98.52%)	57,668 (98.63%)	0.3196	4,853 (98.72%)	24,530 (98.74%)	0.9195
Diabetes with Chronic Complications	17,266 (70.98%)	21,234 (17.30%)	<.0001	8,285 (71.53%)	10,464 (17.90%)	<.0001	3,487 (70.93%)	4,397 (17.70%)	<.0001
Hemiplegia or Paraplegia	335 (1.38%)	776 (0.62%)	<.0001	174 (1.50%)	380 (0.65%)	<.0001	80 (1.63%)	164 (0.66%)	<.0001
Renal Disease	5,791 (23.81%)	7314 (5.96%)	<.0001	2,863 (24.72%)	3,545 (6.06%)	<.0001	1,241 (25.24%)	1,530 (6.16%)	<.0001
Cancer	2,023 (8.32%)	9,834 (8.01%)	0.1138	1,008 (8.70%)	4,866 (8.32%)	0.1779	455 (9.26%)	2,122 (8.54%)	0.1038
Moderate or Severe Liver Disease	214 (0.88%)	767 (0.63%)	<.0001	104 (0.90%	351 (0.60%)	<.0001	34 (0.69%)	150 (0.60%)	0.4728
Metastatic Cancer	325 (1.34%)	1,649 (1.34%)	0.9231	166 (1.43%)	734 (1.26%)	0.1207	75 (1.53%)	311 (1.25%)	0.1211
AIDS	103 (0.42%)	483 (0.39%)	0.5003	51 (0.44%)	236 (0.40%)	0.5726	18 (0.37%)	96 (0.39%)	0.8336

*DME=Diabetic Macular Edema

Table 2. Resource Utilization amongst DME and non-DME Diabetic Cohorts

	DME 1y	non-DME 1y	p-value	DME 2y	non-DME 2y	p-value	DME 3y	non-DME 3y	p-value
	n = 24,326	n = 122,710		n = 11,583	n = 58,467		n = 4,916	n = 24,844	
Intravitreal injection									
n patients utilizing (%)	4,856 (20.0%)	98 (0.1%)		2,588 (22.3%)	73 (0.1%)		1,218 (24.8%)	39 (0.2%)	
mean yearly usage per cohort patient	0.60	0.00	<.0001	0.41	0.00	<.0001	0.35	0.00	<.0001
mean per utilizing patient	2.99	2.49	0.0165	3.69	3.25	0.0533	4.3	4.56	0.4419
Fluorescein Angiography (FA)									
n patients utilizing (%)	11,692 (48.1%)	510 (0.4%)		6,158 (53.2%)	383 (0.7%)		2,736 (55.77%)	210 (0.8%)	
mean yearly usage per cohort patient	1.21	0.01	<.0001	0.86	0.01	<.0001	0.72	0.01	<.0001
mean per utilizing patient	2.51	2.06	<.0001	3.24	2.24	<.0001	3.86	2.41	<.0001
Optical Coherence Tomography (OCT)	**DME 1y**	**non-DME 1y**	**p-value**	**DME 2y**	**non-DME 2y**	**p-value**	**DME 3y**	**non-DME 3y**	**p-value**
n patients utilizing (%)	17,517 (72.0%)	4,620 (3.8%)		8,759 (75.6%)	3,443 (5.9%)		3,815 (77.6%)	1,866 (7.5%)	
mean yearly usage per cohort patient	2.77	0.07	<.0001	2.10	0.07	<.0001	1.80	0.07	<.0001
mean per utilizing patient	3.85	1.89	<.0001	5.55	2.43	<.0001	6.96	2.79	<.0001
Laser photocoagulation									
n patients utilizing (%)	11,965 (49.2%)	417 (0.3%)		6,252 (54.0%)	314 (0.5%)		2,780 (56.6%)	176 (0.7%)	
mean yearly usage per cohort patient	1.28	0.01	<.0001	0.91	0.01	<.0001	0.74	0.00	<.0001
mean per utilizing patient	2.6	1.78	<.0001	3.36	2.06	<.0001	3.9	2.03	<.0001
Vitrectomy	**DME 1y**	**non-DME 1y**	**p-value**	**DME 2y**	**non-DME 2y**	**p-value**	**DME 3y**	**non-DME 3y**	**p-value**
n patients utilizing (%)	1,159 (4.8%)	58 (0.0%)		822 (7.1%)	50 (0.1%)		437 (8.9%)	27 (0.1%)	
mean yearly usage per cohort patient	0.10	0.00	<.0001	0.08	0.00	<.0001	0.07	0.00	<.0001
mean per utilizing patient	2.11	2.01	0.4131	2.23	1.88	0.3608	2.24	1.96	0.4868
Unique RX's									
n patients utilizing (%)	18,259 (75.1%)	90,104 (73.4%)		9,408 (81.2%)	47,025 (80.4%)		4,206 (85.6%)	21,222 (85.4%)	
mean yearly usage per cohort patient	9.11	6.59	<.0001	6.84	5.03	<.0001	5.99	4.46	<.0001
mean per utilizing patient	12.14	8.98	<.0001	16.847	12.497	<.0001	20.988	15.66	<.0001

*DME=Diabetic Macular Edema

Table 3. Resource Utilization amongst DME and non-DME Diabetic Cohorts

	DME 1y	non-DME 1y	p-value	DME 2y	non-DME 2y	p-value	DME 3y	non-DME 3y	p-value
	n = 24,326	n = 122,710		n = 11,583	n = 58,467		n = 4,916	n = 24,844	
Emergency Room Visits									
n patients utilizing (%)	6,861 (28.2%)	24,550 (20.0%)		5,065 (43.7%)	19,197 (32.8%)		2,558 (52.0%)	10,306 (41.5%)	
mean yearly usage per cohort patient	0.59	0.35	<.0001	0.59	0.34	<.0001	0.53	0.33	<.0001
mean per utilizing patient	2.105	1.735	<.0001	2.68	2.09	<.0001	3.078	2.35	<.0001
Outpatient Visit									
n patients utilizing (%)	24,326 (100%)	122,442 (100%)		11,583 (100%)	58,467 (100%)		4,916 (100%)	24,844 (100%)	
mean yearly usage per cohort patient	25.07	14.44	<.0001	23.84	13.79	<.0001	23.44	13.47	<.0001
mean per utilizing patient	25.07	14.47	<.0001	47.69	27.57	<.0001	70.32	40.4	<.0001
Inpatient Visit	**DME 1y**	**non-DME 1y**	**p-value**	**DME 2y**	**non-DME 2y**	**p-value**	**DME 3y**	**non-DME 3y**	**p-value**
n patients utilizing (%)	24,237 (100%)	122,701 (100%)		11,583 (100%)	58,467 (100%)		4,916 (100%)	24,844 (100%)	
mean yearly usage per cohort patient	1.94	1.69	0.0960	2.05	1.10	<.0001	1.83	0.87	<.0001
mean per utilizing patient	1.95	1.69	0.0008	4.11	2.19	<.0001	5.48	2.62	<.0001
Total Days With A Visit									
n patients utilizing (%)	24,326 (100%)	122,710 (100%)		11,583 (100%)	58,467 (100%)		4,916 (100%)	24,844 (100%)	
mean yearly usage per cohort patient	27.01	16.13	<.0001	25.90	14.88	<.0001	25.27	14.34	<.0001
mean per utilizing patient	27.01	16.13	<.0001	51.79	29.77	<.0001	75.80	43.02	<.0001

*DME=Diabetic Macular Edema

Table 4. Resource utilization amongst DME patients over time from first claim

total patients (n) = 4916	DME 6 months prior to index	DME 6 months after index	DME 1st Year after index	DME 2nd Year after index	DME 3rd Year after index
Optical Coherence Tomography (OCT)					
n patients utilizing (mean per utilizer)	913 (2.11)	3,056 (2.75)	3,318 (3.71)	2,056 (3.66)	1,939 (3.47)
total number (cohort mean)	1,923 (0.39)	8,405 (1.71)	12,298 (2.50)	7,528 (1.53)	6,729 (1.37)
Fluorescein Angiography (FA)					
n patients utilizing (mean per utilizer)	780 (1.82)	2,066 (2.07)	2,305 (2.51)	1,080 (2.45)	866 (2.45)
total number (cohort mean)	1,417 (0.29)	4,283 (0.87)	5,791 (1.18)	2,642 (0.54)	2,120 (0.43)
Intravitreal Injection					
n patients utilizing (mean per utilizer)	154 (1.64)	654 (1.84)	797 (2.34)	518 (2.69)	590 (3.35)
total number (cohort mean)	252 (0.05)	1,201 (0.24)	1,865 (0.38)	1,393 (0.28)	1,974 (0.40)
Laser Procedure					
n patients utilizing (mean per utilizer)	512 (1.68)	2,277 (2.12)	2,474 (2.58)	1,196 (2.15)	920 (2.04)
total number (cohort mean)	860 (0.17)	4,835 (0.98)	6,386 (1.30)	2,574 (0.52)	1,880 (0.38)
Vitrectomy procedure					
n patients utilizing (mean per utilizer)	125 (1.78)	164 (2.01)	240 (2.20)	145 (1.86)	98 (1.81)
total number (cohort mean)	223 (0.05)	330 (0.07)	529 (0.11)	272 (0.06)	117 (0.04)
Mean Unique Medications Used					
n patients utilizing (mean per utilizer)	3,752 (8.64)	3,922 (8.84)	4,042 (11.81)	4,093 (11.94)	4,091 (12.17)
total number (cohort mean)	32,417 (6.59)	34,677 (7.05)	47,747 (9.71)	48,864 (9.94)	49,801 (10.13)
Emergency Room Visits					
n patients utilizing (mean per utilizer)	718 (4.59)	752 (5.39)	1,271 (6.76)	1,351 (7.56)	1,389 (8.10)
total number (cohort mean)	3,280 (0.67)	4,051 (0.82)	8,594 (1.75)	10,212 (2.08)	11,248 (2.29)
Outpatient Visit Days					
n patients utilizing (mean per utilizer)	4,916 (10.82)	4,916 (11.97)	4,916 (22.69)	4,850 (23.14)	4,832 (25.23)
total number (cohort mean)	53,232 (10.83)	58,856 (11.97)	111,524 (22.69)	112,251 (22.83)	121,925 (24.80)
Inpatient Days					
n patients utilizing (mean per utilizer)	4,909 (1.62)	4,899 (1.55)	4,913 (2.19)	791 (9.20)	864 (10.27)
total number (cohort mean)	7,938 (1.61)	7,610 (1.55)	10,779 (2.19)	7,281 (1.48)	8,872 (1.80)
Total Days With a Visit					
total number (cohort mean)	61,170 (12.44)	66,466 (13.52)	122,303 (24.88)	119,532 (24.31)	130,797 (26.61)
Total Cost					
mean cost (median cost)	$3,934 ($8,461)	$4,690 ($9,154)	$9,409 ($18,121)	$8,929 ($21,536)	$9,216 ($26,180)
Quartile 1 -- Quartile 3	$1,925 -- $8,491	$2,503 -- $9,205	$4,858 -- $18,870	$4,094 -- $19,365	$4,224 -- $21,414

*DME=Diabetic Macular Edema

Table 5. Cost associated with DME and non-DME Diabetic patients

	DME 1y	non-DME 1y	DME 2y	non-DME 2y	DME 3y	non-DME 3y
Outpatient Cost						
Mean (Median)	$14,010 ($6,256)	$5,427 ($2,012)	$25,567 ($12,183)	$10,377 ($4,637)	$37,210 ($18,266)	$14,939 ($7,489)
Quartile 1 -- Quartile 3	$2,923 -- $13,080	$747 -- $5,330	$5,981 -- $24,141	$1,881 -- $10,719	$9,212 -- $34,566	$3,295 -- $16,007
Inpatient Cost						
Mean (Median)	$3,558 ($16,351)	$3,236 ($15,279)	$12,645 ($21,878)	$5,553 ($16,413)	$17,470 ($24,568)	$7,540 ($17,199)
Quartile 1 -- Quartile 3	$8,168 -- $36,066	$7,676-- $32,189	$10,011 -- $50,546	$8,172 -- $35,522	$11,070 -- $57,988	$8,526 -- $37,237
Pharmacy Cost	**DME 1y**	**non-DME 1y**	**DME 2y**	**non-DME 2y**	**DME 3y**	**non-DME 3y**
Mean (Median)	$3,258 ($3,026)	$2,054 ($1,478)	$6,993 ($6,147)	$4,243 ($2,775)	$11,277 ($9,517)	$6,722 ($4,229)
Quartile 1 -- Quartile 3	$1,108 -- $5,772	$373 -- $3,580	$2,269 -- $11,533	$693 -- $6,845	$3,879 -- $17,374	$1,135 -- $10,097
Total Cost						
Mean (Median)	$15,308 ($6,556)	$7,577 ($2,905)	$31,442 ($13,506)	$13,338 ($6,011)	$39,016 ($18,730)	$18,461 ($9,183)
Quartile 1 -- Quartile 3	$3,155 -- $13,314	$1,106 -- $6,623	$6,636 -- $27,208	$2,462 -- $12,766	$9,560 -- $35,491	$4,075 -- $18,614

*DME=Diabetic Macular Edema

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