Resource Use and Costs Associated With Diabetic Macular Edema in Elderly Persons

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Objective: To examine trends in resource use and the effect of incident diabetic macular edema (DME) on 1- and 3-year total direct medical costs in elderly patients.

Methods: We used a nationally representative 5% sample of Medicare beneficiaries from 2000 through 2004 to identify patients with incident DME and a control cohort of patients with diabetes mellitus but no history of retinal disease. We summed Medicare reimbursement amounts for all claims and applied generalized linear models to estimate the effect of DME on 1- and 3-year costs. We also examined the use of select imaging techniques and treatments.

Results: After adjusting for demographic characteristics and baseline comorbid conditions, DME was associated with 31% higher 1-year costs and 29% higher 3-year costs. There were significant shifts in the use of testing and treatment modalities. From 2000 to 2004, use of intravitreal injection increased from 1% to 13% of patients; use of optical coherence tomography increased from 2.5% to more than 40%. Use of laser photocoagulation decreased over time.

Conclusions: After adjusting for demographic variables and baseline comorbid conditions, new-onset DME was a significant independent predictor of total medical costs after 1 and 3 years. Diagnostic and treatment modalities used for DME have changed significantly.

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Diabetic retinopathy is the leading cause of vision loss in working-age adults in the United States. Approximately 4.1 million adults aged 40 years and older have diabetic retinopathy, and there are as many as 40,000 new cases of blindness in patients with diabetes mellitus each year. Diabetic macular edema (DME), a form of diabetic retinopathy caused by continued leakage from retinal blood vessels, is the most common cause of vision loss in patients with diabetic retinopathy.

Current understanding of the epidemiology and disease burden of DME is limited. In the Wisconsin Epidemiologic Study of Diabetic Retinopathy, the point prevalence of DME in patients with type 1 or type 2 diabetes mellitus ranged from 2% to 6% and the 10-year incidence ranged from 13% to 25%. An estimated 75,000 patients in the United States develop DME each year. Estimates of costs associated with diabetic eye disease are also sparse. Rein et al used a small single-year sample of Medicare claims data to estimate direct outpatient and physician medical costs for beneficiaries with diabetic retinopathy. Considering only claims with a primary diagnosis of diabetic retinopathy, they estimated total direct medical costs at $595 per person. Using data from the National Long Term Care Survey with matched Medicare claims, Salm et al summed outpatient and physician costs to Medicare for select vision care procedures and estimated that beneficiaries incurred average costs of $1176 per person in the 365 days after diagnosis. Javitt and Aiello analyzed data from population-based epidemiologic studies and clinical trials and found that prevention programs for diabetic eye disease were highly cost-effective. More recently, Vijan et al found that annual retinal screening, as opposed to biennial screening, may not be cost-effective for all patients with type 2 diabetes mellitus.

To our knowledge, there are no published studies of direct medical costs associated with DME. Therefore, we performed a cost-of-illness study in a cohort of elderly patients with diabetes mellitus and new-onset DME and observed the trends in 1-year use of select imaging and treatment modalities.
METHODS

DATA SOURCES

Data are from a 5% national sample of Medicare standard analytic files and corresponding denominator files. Specifically, we used data from the inpatient, outpatient, carrier, home health, hospice, skilled nursing facility, and durable medical equipment files. Inpatient files consist of institutional claims for facility costs covered under Medicare part A, and outpatient files consist of claims from institutional outpatient providers (eg, hospital outpatient departments, ambulatory surgery centers). Carrier files consist of noninstitutional provider claims for services covered under Medicare part B, and durable medical equipment files consist primarily of claims for equipment and supplies. Denominator files contain beneficiary demographic data and information about program eligibility and enrollment.

We obtained research-identifiable files for 1998 through 2005 from the Centers for Medicare & Medicaid Services to allow for a 6-year analysis period (2000-2005) plus 2 years of historical data. We included persons living in the United States who were continuously enrolled in fee-for-service Medicare for at least 2 years before cohort entry and were therefore aged 67 years or older on the date of entry. We restricted the analysis to claims filed during periods of fee-for-service coverage because claims data from Medicare risk plans were unavailable.

STUDY POPULATION

Based on a previously validated algorithm,13 the DME cohort included patients for whom a diagnosis of cystoid macular edema (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM code 362.53]) or retinal edema (ICD-9-CM code 362.83) was reported on an inpatient, outpatient, and/or carrier claim from 2000 through 2004 and a diagnosis of diabetes mellitus (ICD-9-CM code 250.xx) was reported within the preceding 365 days. The date of cohort entry, or index date, was the date of the earliest claim with a diagnosis of cystoid macular edema or retinal edema. Patients with cystoid macular edema or retinal edema in the 2 years before the index date were not considered incident and were excluded.

By design, patients in the control group did not have a diagnosis from which an index date could be identified. Therefore, we arbitrarily set the index date for controls to July 1, 2002, to allow for a 3-year follow-up period. The control group consisted of a simple random sample of 50,000 Medicare beneficiaries for whom a diagnosis of diabetes mellitus was reported on an inpatient, outpatient, and/or carrier claim within the 365 days before the index date and for whom there was no evidence of a retinal disorder (ICD-9-CM code 362.xx) during the 2 years before the index date. We excluded patients who switched from fee-for-service coverage to managed care before July 1, 2003 (n=347), yielding a final control sample of 49,653 patients. Patients who met the criteria for inclusion in the control group but subsequently developed DME were maintained as controls only.

COSTS

We obtained 1- and 3-year costs billed to Medicare by summing Medicare reimbursement amounts as recorded on each inpatient, outpatient, home health, skilled nursing, hospice, durable medical equipment, and professional service claim. We calculated costs using only information from beneficiaries who had not been censored at the respective time points. In other words, costs included reimbursement for services incurred from the date of cohort entry through the earliest of 365 or 1095 days after cohort entry, death, or the end of fee-for-service coverage. For the control group, we summed costs beginning July 1, 2002. We also calculated prior-year costs for all patients and we included reimbursement for services incurred 365 days before the index date through the day before cohort entry for the DME group or July 1, 2002, for the control group. All costs are expressed in 2002 US dollars. We truncated costs at the 99th percentile to eliminate outliers.

RESOURCE USE

Information about resource use, including use of fluorescein angiography, optical coherence tomography (OCT), intravitreal injection, and laser photocoagulation as well as the number of evaluation and management visits with an ophthalmologist (Current Procedural Terminology codes 902.xx, 993.xx, 994.xx, 92002, 92004, 92012, and 92014) was obtained for the 1-year period following the index date. We mapped unique physician identification numbers as provided on Medicare part B professional claims to American Medical Association physician specialty information to identify ophthalmology visits. Specialty information for optometrists is not available in the American Medical Association data. We considered only 1 procedure (eg, 1 injection, 1 OCT scan) or 1 physician visit per day in the analyses.

STATISTICAL ANALYSIS

We used descriptive statistics to assess differences between patients with and without DME, using χ² tests for categorical variables and Wilcoxon rank sum tests for continuous variables. Categorical variables are presented as percentages and continuous variables are presented as mean (standard deviation). We identified comorbid conditions using coding algorithms described by Birman-Deych et al13 and Quan et al.14 Specifically, we searched all inpatient, outpatient, and carrier claims for 365 days preceding the index date for evidence of cerebrovascular disease, chronic pulmonary disease, coronary heart disease, dementia, hypertension, metastatic cancer, peripheral vascular disease, and renal disease. We also searched for evidence of cataracts (ICD-9-CM code 366.xx), glaucoma (ICD-9-CM code 365.xx), and age-related macular degeneration (ICD-9-CM codes 362.16, 362.42, 362.43, 362.52; cases only) during the same time period.

To estimate the effect of DME on 1- and 3-year costs, we used generalized linear models with a log link and a Poisson-type error. When exponentiated, the coefficients estimate the proportional increase in costs attributable to the variable. We first examined the unadjusted relationship between DME and costs. In multivariable models, we examined the relationship between DME and costs controlling for age, sex, race, geographic region, and comorbid conditions. In sensitivity analyses, we included costs in the prior year as a covariate. We also ran the model including only controls with diabetes-related complications (ICD-9-CM codes 250.4-250.7).

We used SAS version 9.1.3 (SAS Institute Inc, Cary, North Carolina) for all analyses. The study was approved by the institutional review board of the Duke University Health System.

Table 1 shows the baseline characteristics of cases (n=13,115) and controls (n=49,653). The average age in both cohorts was 76 years. Approximately 40% of the patients were men and more than 80% were white. Patients in the DME cohort were twice as likely as controls to have a history of cataracts or glaucoma. Rates of other comorbid conditions were similar between the groups.
with hypertension being the most common. There were slightly more incident cases in 2004 than in the previous 4 years.

**Table 2** shows 1-year resource use for cases and controls. Not surprisingly, patients in the DME group underwent testing and treatment of DME more often than controls. Nearly 60% of patients with incident DME received 1 or more fluorescein angiographic imaging procedures in the year after diagnosis; 38% underwent laser photocoagulation; 18% were evaluated with OCT; and 6% received at least 1 intravitreal injection. Just under half of all intravitreal injection claims for patients with DME were observed in conjunction with a claim for triamcinolone. Compared with controls, nearly 3 times as many patients with DME (92%) were seen by an ophthalmologist in the 365 days after diagnosis, with an average of 3.9 visits per patient. Only 37% of controls were seen by an ophthalmologist in the year beginning July 1, 2002.

When viewed by year of incidence, we observed substantial shifts in the use of DME imaging and treatment procedures.
modalities. In 2000, less than 1% of patients with incident DME received treatment by intravitreal injection and approximately 2.5% underwent OCT. In 2004, 13% of patients with incident DME received at least 1 injection, whereas more than 40% underwent OCT. In contrast, use of laser photocoagulation decreased. In 2000, 43% of patients with DME underwent laser photocoagulation; in 2004, only 30% received this procedure (Figure).

Table 3 shows 1- and 3-year mean direct medical costs. At both time points, costs were more than 30% higher for cases than controls. Inpatient costs contributed most to total Medicare expenditures, accounting for almost half of mean 1- and 3-year payments. Inpatient, outpatient, and professional claims together made up more than 75% of total costs at each time point and were higher for cases than controls. Total costs incurred by patients with DME before incidence were 27% lower than in the incident year ($8897 vs $11 290; data not shown), whereas costs incurred by controls in the year before July 1, 2002 ($8398 vs $7549; data not shown).

Table 4 shows the effects of DME on total direct medical costs. In univariate analyses, DME was associated with 34% higher 1-year costs and 33% higher 3-year costs. After adjustment for age, sex, race/ethnicity, geographic region, and baseline comorbid conditions, DME was a significant independent predictor of total medical costs at 1 and 3 years. In multivariate analyses, DME was associated with 31% higher 1-year costs and 29% higher 3-year costs. At both time points, adjusted effects of DME were most pronounced for Medicare part B professional claims. Diabetic macular edema was associated with 58% higher professional costs at 1 year and 31% higher costs at 3 years (Table 4, model 1). In sensitivity analyses, inclusion of prior-year costs in the model did not appreciably change estimates of the effects of DME on total costs or inpatient costs; however, outpatient and professional costs were moderated by the inclusion of prior-year payments (Table 4, model 2).

When we restricted the control population to patients with diabetic complications (n=8391), the effects of DME on total cost were reduced. In multivariate analyses, DME was associated with 7% higher 1-year costs and 8% higher 3-year costs. Effects on inpatient and outpatient costs were similarly dampened (1% and 12%, respectively, for 1-year costs; 9% and 8%, respectively, for 3-year costs); however, adjusted effects of DME continued to be pronounced for professional costs, with 39% higher 1-year costs and 19% higher 3-year costs (data not shown).

We examined the effect of incident DME on 1- and 3-year total direct medical costs in patients with diabetes mellitus using longitudinal Medicare claims data. To our knowledge, this is the first study to evaluate the costs of illness associated with DME. Controlling for demographic variables and baseline comorbid conditions, new-onset DME was a significant independent predictor of total medical costs at 1 and 3 years and was associated with 31% and 29% higher costs at these respective time points. However, effects on inpatient and outpatient costs were largely mitigated when the control group included only patients with diabetic complications, suggesting that diabetic complications may drive most of these costs. Professional costs remained high in the sensitivity analysis, suggesting that increases in professional costs are indeed attributable to services for diagnosis and treatment of DME.

Consistent with this increase in professional costs, we observed greater use of resources related to diabetic eye disease in the DME cohort. We also observed significant shifts in practice patterns. In 2000, for example, OCT was used in less than 3% of patients with incident DME. By 2004, use of OCT in patients with incident DME increased 15-fold to more than 40%. After the introduction of OCT for retinal imaging in 1991,15 few studies have examined the utility of the procedure in DME.16-20 In 1998, Hee et al18 found in a pilot study that OCT may be more sensitive than slitlamp examination for detection of reti-
nal thickening in the foveal zone. More recently, Browning et al.16 demonstrated increased sensitivity of OCT for detection of retinal thickening in both the foveal and perifoveal zones and suggested that the procedure become the new standard of care for diagnosis and management of DME. The sharp increase in the use of OCT in our study period may reflect a growing awareness and acceptance of these findings in clinical practice.

Use of intravitreal injection also increased substantially, from less than 1% in 2000 to more than 13% in 2004. Although use of intravitreal triamcinolone for the treatment of DME was first proposed in 1999,21 only 2 studies had been published by early 2004—both nonrandomized interventional case series with a combined total of 42 eyes.22,23 To date, the optimal dose and long-term safety and efficacy of intravitreal triamcinolone remain largely unknown.24 Nonetheless, we observed a considerable increase in the use of this therapy for incident cases, particularly between 2002 and 2004.

Finally, during the same period, use of laser photocoagulation decreased by 30%. The reason for the decrease is unclear, but is perhaps multifactorial. To the extent that intravitreal injection reduced the need for additional laser procedures, the increase in intravitreal injections may be related to the decline in the use of laser photocoagulation. The declining use of laser photocoagulation may also suggest limited specialist use or referral during the incident year, because the procedure is frequently performed by retinal or other specialists. Finally, to the extent that increased use of OCT decreased the type 2 error inherent in subjective clinical examination, potentially inappropriate use of laser photocoagulation may have declined.25 Yet, laser photocoagulation remains the only therapy for DME for which there is strong supporting evidence from large, randomized controlled trials.25,26

Nearly all patients with new-onset DME in this study were seen by an ophthalmologist for evaluation and management during the year following diagnosis (92%); however, only 37% of controls were seen by an ophthalmologist. This finding is particularly striking given that many patients with diabetes mellitus and vision-threatening diseases may be asymptomatic,27 and several large trials have demonstrated the importance of regular ophthalmologic screening and management in all patients with diabetes mellitus to preserve vision and reduce vision loss.25,28-31

Table 4. Effect of Incident Diabetic Macular Edema on 1- and 3-Year Direct Medical Costs

<table>
<thead>
<tr>
<th>Costs</th>
<th>Unadjusted</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-y Direct medical costs</td>
<td>1.34 (1.31-1.38)</td>
<td>1.31 (1.28-1.34)</td>
<td>1.29 (1.26-1.32)</td>
</tr>
<tr>
<td>Medicare part A inpatient</td>
<td>1.24 (1.20-1.28)</td>
<td>1.21 (1.17-1.25)</td>
<td>1.22 (1.18-1.27)</td>
</tr>
<tr>
<td>Medicare part A outpatient</td>
<td>1.40 (1.37-1.44)</td>
<td>1.30 (1.27-1.33)</td>
<td>1.19 (1.16-1.22)</td>
</tr>
<tr>
<td>Medicare part B</td>
<td>1.74 (1.71-1.77)</td>
<td>1.58 (1.55-1.60)</td>
<td>1.48 (1.46-1.50)</td>
</tr>
<tr>
<td>3-y Direct medical costs</td>
<td>1.33 (1.30-1.36)</td>
<td>1.29 (1.26-1.32)</td>
<td>1.28 (1.25-1.31)</td>
</tr>
<tr>
<td>Medicare part A inpatient</td>
<td>1.34 (1.29-1.38)</td>
<td>1.30 (1.26-1.34)</td>
<td>1.30 (1.26-1.34)</td>
</tr>
<tr>
<td>Medicare part A outpatient</td>
<td>1.30 (1.26-1.34)</td>
<td>1.22 (1.19-1.26)</td>
<td>1.15 (1.12-1.19)</td>
</tr>
<tr>
<td>Medicare part B</td>
<td>1.43 (1.40-1.45)</td>
<td>1.31 (1.29-1.34)</td>
<td>1.27 (1.25-1.29)</td>
</tr>
</tbody>
</table>

Abbreviation: CI, confidence interval.

a Model 1 adjusted for age, sex, race, geographic region, and comorbid conditions.

b Model 2 adjusted for costs in all prior years, in addition to all covariates in model 1.

Use of existing administrative claims databases offers an alternative approach to estimating disease prevalence and, ultimately, disease burden. The primary advantages of using administrative data are that these data are comprehensive, relatively inexpensive, and free of the usual biases associated with survey methods such as recall bias, nonresponse, and subject attrition. Lee et al.22 used longitudinal Medicare claims data to describe the prevalence of diabetes mellitus, glaucoma, and age-related macular degeneration in a nationally representative cohort of elderly subjects. Javitt et al.33 also used Medicare claims to estimate the incidence of exudative age-related macular degeneration in persons aged 65 and older. Based on the similarity of claims-based estimates to population-based estimates, both teams concluded that Medicare claims are a reliable source of information about the epidemiology of chronic eye disease. Claims data appear particularly well-suited for estimating disease incidence for conditions with well-defined, standardized diagnostic criteria.

Our study has several limitations. First, the analysis includes direct costs to Medicare only and does not account for other important costs such as the effect of decreased functional status secondary to vision loss. Furthermore, because Medicare did not provide reimbursement for most outpatient prescription drugs during the study period, these costs are not included in the analysis. Second, administrative data lack clinical detail regarding severity of illness; therefore, we were unable to determine whether disease was present or procedures were performed in 1 or both eyes. We also were unable to account for factors such as the degree of hyperglycemia or hypertension in the calculation of costs. In sensitivity analyses, however, we compared costs between DME cases and a subgroup of controls with diabetic complications. Although total costs were similar, professional costs were substantially higher in DME cases, suggesting that DME has an important independent effect on costs. To the extent that controls with diabetic complications had more advanced underlying disease than DME cases, our estimate may represent a lower bound. Third, coding of diagnoses and procedures in Medicare claims, as in all administrative data sets, may be inaccurate or incomplete.
Medicare data also do not include claims for beneficiaries during periods of managed care enrollment. Also, it has been estimated that approximately one-third of cases of diabetes mellitus in adults aged 20 years and older is undiagnosed.34 To the extent that this is true in the Medicare population, our findings may underestimate total costs associated with the disease. Finally, the data used in this study represent the experiences of elderly Medicare beneficiaries with incident DME. Therefore, the results may not be generalizable to younger populations or patients with long-standing disease.

In conclusion, after adjustment for demographic variables and baseline comorbidities, new-onset DME was a significant independent predictor of total medical costs at 1 and 3 years. Diagnostic and treatment modalities for DME have changed significantly over time.

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Author Contributions: Ms Shea and Dr Curtis had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Dr Kowalski participated in study conception and design, interpretation of data, and preparation of the manuscript. Ms Shea, Mr Hammill, and Dr Curtis had responsibility for the statistical analysis using the entire raw data set. The authors had full control over the preparation of the manuscript and the decision to submit the manuscript for publication.

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