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Medicare costs for neovascular age-related macular degeneration, 1994–2007

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Abstract

Purpose—To assess changes in Medicare payments for neovascular age-related macular degeneration (AMD) since introduction of anti-vascular endothelial growth factor (VEGF) therapies.

Design—Retrospective, longitudinal cohort study

Methods—Using the Medicare 5% sample, beneficiaries with new diagnoses of neovascular AMD in 1994 (N=2,497), 2000 (N=3,927), and 2006 (N=6,041) were identified using International Classification of Diseases (ICD-9-CM). The total first year health and eye care costs were calculated for each beneficiary. Propensity score matching was used to match individuals in the 2000 and 2006 cohorts with the 1994 cohort on age, gender, race, Charlson Comorbidity Index, and low vision/blindness.

Results—The number of beneficiaries newly diagnosed with neovascular AMD more than doubled between the 1994 and 2006 cohorts. Overall yearly Part B payments per beneficiary increased significantly from $3,567 for the 1994 to $5,991 for the 2006 cohort ($p<0.01$) in constant 2008 dollars. Payments for eye care alone doubled from $1,504 for the 1994 cohort to $3,263 for the 2006 cohort ($p<0.01$). Most of the increase in payments for eye care in 2006 reflected payments for anti-VEGF injections, which were $1,609 over 1 year. Mean annual numbers of visits and imaging studies also increased significantly between the 1994 and 2006 cohort. Results were similar in the matched sample.

Conclusions—The introduction of anti-VEGF intravitreal injections has offered remarkable clinical benefits for patients with neovascular AMD, but these benefits have come at the cost of an increased financial burden of providing care for these patients.

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Introduction

The introduction of anti-vascular endothelial growth factor (VEGF) treatments has revolutionized care of age-related macular degeneration (AMD).[1–2] AMD is the leading cause of blindness in elderly individuals in the developed world, and the third-leading cause of blindness worldwide.[3–5] Loss of vision from neovascular AMD in particular results in profound reductions in vision-specific quality of life.[6–7] Three intravitreal anti-VEGF medications are widely used for treatment of the neovascular form of AMD: ranibizumab (Lucentis; Genentech, South San Francisco, CA, USA), bevacizumab (Avastin; Genentech), and pegaptanib (Macugen; OSI-Eyetech, New York, NY, USA).[2, 8–9] Randomized clinical trials and retrospective studies have shown that ranibizumab and bevacizumab dramatically improve the visual prognosis of neovascular AMD, but the cost of treating patients with these medications are high given the price of these treatments and the need for repeated injections.[1, 8–9] The affected population is large; 1.22 million persons are estimated to have neovascular AMD in the United States alone, and the number of people with AMD is expected to increase by 50% by 2020.[3] Hence, one may predict that providing care for the increasing numbers of patients with neovascular AMD is likely to become considerably more expensive. Moreover, with patients returning for as frequent as monthly injections, there are also likely to be associated increases in numbers of office visits, examinations, and in ancillary testing.

Costs and cost-effectiveness of treatments for AMD have been investigated in several studies, most of which have extrapolated data from clinical trials to estimate the costs for each kind of treatment. Smiddy et al. found costs of anti-VEGF treatment per line of vision per year ranging from $84 for as-needed use of bevacizumab to $766 for protocol-style use of ranibizumab.[10] Gower et al. found that ranibizumab was the most effective but also the most costly treatment for neovascular AMD, with estimated 2-year total medical costs of $54,100 for treatment with monthly ranibizumab.[11] Brown et al. estimated that ranibizumab therapy conferred 1.039 quality-adjusted life-years (QALY), or a 15.8% improvement in quality of life over a 12-year period (the mean life expectancy for a patient with neovascular AMD), with a cost of $50,691 per QALY.[12] Coleman et al. evaluated Medicare payments for non-neovascular and neovascular AMD for 1995–9. Their study compared payments on behalf of beneficiaries with AMD to a control group with minimal eye disease, finding a significantly higher median payment of $2,371 over 5 years for patients with neovascular AMD vs. $1,569 for non-neovascular AMD vs. $1,428 for the control group.[13] The time period studied, however, preceded use of photodynamic therapy and anti-VEGF therapies, which have considerably changed the management of AMD over the last decade. Brechner et al. looked specificially at the costs of anti-VEGF injections in the Medicare population in 2008, and they found that the total cost of bevacizumab injections was $20,290,252 and the total cost of ranibizumab injections was $536,642,693, though they did not look at other associated costs of care for neovascular AMD.[14] The overall annual cost of AMD care in the United States was estimated at $575 million in 2004 prior to the widespread use of anti-VEGF intravitreal injections, and was projected to increase to $845 million over the following 15 years simply due to growth in the number of elderly persons even without any change in available treatments.[15]

This study examines total health and eye-related Medicare payments on behalf of beneficiaries diagnosed with neovascular AMD in a nationally representative cohort of U.S. elderly persons at 3 different time points: 1994, 2000, and 2006.

Methods

We used Medicare 5% Part-B claims and enrollment files to identify a nationally representative sample of Medicare beneficiaries aged 68–95 with a new diagnosis of neovascular AMD (International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM), 362.52, 362.42, and 362.43). The data contained information on demographic characteristics, beneficiaries' zip code of residence, ICD-9-CM diagnosis and procedure codes (Current Procedural Terminology, CPT-4; Healthcare Common Procedure Coding System, HCPCS), physician specialty (U.S. Centers for Medicare and Medicaid Services (CMS), and provider zip codes.

We selected beneficiaries first diagnosed with neovascular AMD in 1994, 2000, and 2006. We utilized a 3–year look-back period (1991–3, 1997–9, 2003–5, respectively) to ensure that they had at least one eye care visit, resided in the United States, had not previously received this diagnosis, and were not in an HMO for more than a year.

For the 3 cohorts, first year eye payments after first diagnosis of wet AMD were calculated for each Medicare beneficiary from Part B claims submitted by an ophthalmologist or optometrist. Total first year payments for eye care retrieved from the claims data for each beneficiary were grouped into anti-VEGF injections, fluorescein angiography (FA) imaging, optical coherence tomography (OCT) imaging, other imaging, laser photocoagulation, photodynamic therapy (PDT), pars plana vitrectomy (PPV), cataract, cornea, glaucoma, visit costs, and other eye-related payments. We also calculated Part-B payments from claims submitted by other providers for comparison. We adjusted the payments to 2008 dollars for general increases in medical prices using the medical component of the Consumer Price Index. Using propensity score matching we accounted for changes in payments attributable to changes in mix of beneficiaries diagnosed with neovascular AMD by matching the 2006 and 2000 cohorts to the 1994 cohort. Variables used in matching were age, race, gender, Charlson Co-Morbidity Index scores (a measure of general health), and low vision/blindness.[16] The propensity score is the probability of having been first diagnosed with neovascular AMD in 1994 conditional on observed covariates. Matching on propensity scores reduces selection bias between individuals in the different cohorts.[17–18] To capture the differences between the cohorts (1994, 2000, and 2006) we modeled the probability Y of cohort 1994 being present in cohort 2000 or 2006 as:

$$Y_{2000}=\beta_1+\beta_2 l_{1994|2000} \text{ and } Y_{2006}=\beta_1+\beta_2 l_{1994|2006}$$

where $l_{x|y}$ is a vector of individual characteristics for the years x and y. Our measures of $l_{x|y}$ were: age, male gender, black race, other race, Charlson Index, and low vision/blindness.

Using the predicted probability of an individual in the 1994 cohort, we paired an individual in the 1994 cohort with his or her nearest match in the 2000 cohort or 2006 cohort. Matching was accomplished using a SAS Greedy 5 to 1 digit match macro (by Lori S. Parsons, accessed April 20, 2009, at http://www2.sas.com/proceedings/sugi26/p214–26.pdf) in which the program attempts to make the best match first by matching the 2000 cohort and the 2006 cohort with the 1994 cohort based on exact matches of 5 digits of their propensity score. Considering all persons not previously matched, the macro then attempted to match individuals based on 4 digits of their propensity score, then 3, then 2, and 1. Individuals unable to be matched on 1 digit were excluded. Standardized differences were calculated for the matched sample and revealed no differences >10%, resulting in a well-matched sample.[19–20]

P-values for the differences in the total health and eye-related costs between the 1994 and 2000 cohort and between the 1994 and 2006 cohort were calculated using independent two sample t-tests for the total sample, and using paired t-tests after matching.

The Duke University Institutional Review Board approved this study.

Results

The number of beneficiaries newly diagnosed with neovascular AMD more than doubled during the study time period, from 2,497 beneficiaries in 1994 to 6,041 beneficiaries in 2006 (Table 1). Compared to the 1994 cohort, beneficiaries in the 2006 cohort were significantly older (81.4 vs. 79.3, $p<0.0001$), less likely to be male (28.2% vs. 32.4%, $p<0.0001$) and more likely to have a higher mean Charlson Index score (2.1 vs. 1.5, $p<0.0001$).

Overall yearly health payments made on behalf of beneficiaries with neovascular AMD increased significantly from $3,567 per beneficiary for the 1994 cohort to $5,991 per beneficiary for the 2006 cohort ($p<0.0001$) in constant 2008 dollars (Table 2). Of the $2,424 increase in payments, $1,759 or 73% represented an increase in payments for eye care. Payments for eye care alone doubled from $1,504 per beneficiary for the 1994 cohort to $3,263 for the 2006 cohort ($p<0.0001$). Most of the increase in such payments in 2006 as compared to 1994 reflected the introduction of anti-VEGF injections; in the 2006 cohort, payments by Medicare Part B for anti-VEGF injections alone were $1,609 over the course of 1 year. Medicare payments per beneficiary for laser photocoagulation fell from $353 in 1994 to $55 in 2006, while payments for photodynamic therapy increased over the three time periods. Payments for FA per beneficiary decreased slightly in the 2006 cohort compared to the 1994 cohort, while payments for OCT increased significantly. Payments for cataract procedures, glaucoma-related eye care, and vitrectomy surgeries decreased significantly for the 2006 compared to the 1994 cohort while payments for office visits increased by 84%.

We then matched Medicare beneficiaries in the 2000 and 2006 cohorts by age, gender, race, Charlson Comorbidity Index, and low vision/blindness to the 1994 cohort. The standardized differences were less than 10% for all variables, indicating well-matched groups.

The total health and eye-related costs in the matched sample were similar to the total sample (Table 3). Again, total Medicare Part B payments per beneficiary increased significantly by 61% from the 1994 cohort to the 2006 cohort. Payments for eye care alone more than doubled in this time period. Much of this increase was related to payments for anti-VEGF therapies which were $1700 in 2006, as well as the increase in payments for photodynamic therapy; partially offsetting this increase was a significant decrease in payments for laser photocoagulation. From 1994 to 2006, payments for fluorescein angiography remained essentially stable, while those for OCT increased significantly. Changes in payments for other eye care services were notable for significant decreases in payments for cataract-related, glaucoma-related, and vitrectomy procedures. Payments for eye care visits increased by 84% from 1994 to 2006.

Several changes in practice patterns were associated with introduction of anti-VEGF therapies (Table 4). There were significant increases in the mean yearly number of visits (2.1 vs. 3.5, $p<0.0001$), OCTs (0 vs. 2.1, <0.0001), and anti-VEGF injections (0 vs. 2.0, $p<0.0001$) between 1994 and 2006.

In addition, between 2006 and 2008 there was a shift in the type of anti-VEGF treatments given for Medicare beneficiaries with neovascular AMD. In 2006, 34.5% of patients received ranibizumab, 40.9% of patients received bevacizumab, and 24.6% of patients

received pegaptanib. By 2008, 44.4% of patients received ranibizumab, 54.5% of patients received bevacizumab, and only 1.1% of patients received pegaptanib.

With 6,041 beneficiaries with a new diagnosis of neovascular AMD in 2006 in the Medicare 5% sample and a yearly total health cost of $5,991 per person, we project that annual Part B payments for beneficiaries newly diagnosed with neovascular AMD in the entire Medicare sample were $724 million in 2006 inflated to 2008 dollars. The annual eye care payments alone were $394 million.

Discussion

The care of patients with neovascular AMD has changed dramatically with the introduction of anti-VEGF medications. Numerous studies have demonstrated the clinical benefits of these medications, but we have only begun to assess the economic impact associated with these new treatments.

As might be expected, total Part B Medicare payments for beneficiaries with neovascular AMD increased appreciably from 1994 to 2006. A large proportion of the change in such payments (73%) reflected the substantial increase in payments for eye care, which doubled for beneficiaries with a diagnosis of neovascular AMD between 1994 and 2006.

The largest part of the increase in payments between 1994 and 2006 was due to payments for anti-VEGF injections, with a small increase in the payments for photodynamic therapy. Accompanying the start of payments for such injections, payments for visits and imaging related to neovascular AMD care also rose, while those for laser photocoagulation decreased significantly. The declining payments for laser treatment suggest that anti-VEGF intravitreal injections and photodynamic therapy are often replacing laser photocoagulation as the treatment of choice for neovascular AMD. A recent paper looking at retinal procedures in the Medicare population found a 193-fold increase in the numbers of all types of intravitreal injections between 2001 and 2007 with an 83% decrease in laser treatments for choroidal neovascularization between 1999 and 2007.[21]

In addition to changes in the choice of treatment for neovascular AMD, there was also a shift in practice patterns that occurred in conjunction with the adoption of anti-VEGF intravitreal injections. The mean annual number of visits and OCT’s increased significantly. The changes in the matched and unmatched samples were quite similar, suggesting that the increases were attributable to technological change in treatment of neovascular AMD and in Medicare pricing rather than to changes in the mix of beneficiaries with this diagnosis. Prior to introduction of these anti-VEGF therapies, visits by elderly persons diagnosed with AMD to eye care providers decreased over time, presumably because patients were told that no effective therapy existed.[22] This pattern seems to be changing with the availability of an effective technology. To the extent that this result generalizes to other new eye therapies, it implies higher demand for eye care in the future. Furthermore, the Medicare payments for the additional examinations and diagnostic imaging do not reflect the extra resources that must now be devoted to these patients which include physician and technician time, use of testing equipment, and use of clinic facilities.

Interestingly, payments for care of other eye conditions, such as those for cataracts and cataract surgery, corneal conditions and corneal surgery, glaucoma and glaucoma surgery, and vitrectomy surgery, decreased significantly as the costs associated with care of AMD increased. This could be due to a lower prevalence of these conditions in the later cohorts, or more likely, lower Medicare payment per procedure in the later period. For instance, Medicare payment for cataract surgery was almost cut in half in inflation-adjusted dollars between 1991 and 2000.[23] Another study of Medicare payment for glaucoma procedures

found that the average reimbursement per claim fell by 36% from 1997 to 2006 in nominal dollars.[24]

The estimated payments for annual eye-related care for neovascular AMD in our study for the 1994 cohort are higher than the estimates by the Coleman et al. study for a slightly later time period (1995–9). Part of the difference is attributed to the fact that we inflated our estimates of payments to 2008 dollars which Coleman et al. did not; adjusting Coleman's et al.'s estimates as we did reduced the difference somewhat, but a large discrepancy remains. Furthermore, Coleman et al.'s estimates were reported for any beneficiary with a diagnosis of neovascular AMD irrespective of when the diagnosis was made, while our estimates are for the first year after new diagnosis of neovascular AMD. Diagnostic imaging, treatment, and examinations may all conceivably be more frequent in the initial year after diagnosis than subsequently, particularly in a time period of limited treatment options for AMD. As mentioned above, a 2004 study found that visits to eye care providers tended to decrease over time in patients with AMD.[22]

In addition to the increase in Medicare payments per patient, the number of Medicare beneficiaries being diagnosed with neovascular AMD more than doubled in the 2006 cohort compared to the 1994 cohort, an increase with far-reaching implications for system-wide costs. This increase may be due to a larger number of beneficiaries being diagnosed given the wider range of beneficiaries with neovascular AMD now eligible for treatment, aging of persons at time of first diagnosis of neovascular AMD, and the slightly higher proportion of female beneficiaries with this diagnosis. Physicians may be more likely to code a diagnosis of neovascular AMD if this is a requirement for reimbursement of a newly available procedure. Both older age and female gender have been identified as risk factors for the development of AMD.[25] It is also possible that the advent and widespread use of OCT imaging has allowed earlier and easier diagnosis of neovascular AMD.

Per our calculations, the total first year healthcare payments for Medicare beneficiaries with newly diagnosed neovascular AMD would be $724 million in 2008 dollars. In comparison, the annual direct medical cost of all types of AMD in 2004 was estimated to be only $575 million.[15] This is without taking into consideration the anticipated increases in the numbers of patients with AMD in an aging population; the number of patients with AMD overall is anticipated to grow from 1.75 million in 2000 to 2.95 million in 2020.[3]

One factor which may ameliorate the cost of neovascular AMD care is the shift from the use of pegaptanib and ranibizumab to bevacizumab. Among Medicare beneficiaries receiving anti-VEGF injections for neovascular AMD, we found a marked difference from 2006 to 2008 in the proportion of patients receiving ranibizumab, bevacizumab, and pegaptanib, with a shift towards bevacizumab use in the majority of patients in 2008. Brechner et al. also found that 58% of Medicare beneficiaries received bevacizumab intravitreal injections for neovascular AMD in 2008.[14] Smiddy's et al.'s analysis estimated that the biggest improvement in cost per benefit would be yielded by switching from ranibizumab to bevacizumab, which would reduce costs by approximately 80%.[10] The recent publication of the one-year results of the Comparison of Age-Related Macular Degeneration Treatment Trials (CATT) showing equivalent effects on visual acuity of bevacizumab and ranibizumab when used at the same dosing schedule will likely further shift treatment patterns towards the use of bevacizumab.[26]

Strengths of this study include the use of a nationally representative sample of elderly American patients with neovascular AMD in a variety of practice settings and the analysis of actual rather than projected payment data. Our study is limited by the fact that we only included Medicare beneficiaries in their first year after a new diagnosis of neovascular AMD

in our analysis. Thus, we only examined payment data and practice patterns for newly diagnosed individuals rather than all individuals in the population with neovascular AMD. Medicare claims data also does not include information on the laterality of the eye with neovascular AMD, or whether one or both eyes were treated. In addition, we did not specifically measure payments for care of complications of treatment for neovascular AMD (such as endophthalmitis and retinal tear or detachment), or the indirect costs associated with neovascular AMD (such as productivity losses from decreased vision), nor the potential cost offset of vision saved by anti-VEGF treatments for AMD.

The economic burden of treatment of neovascular AMD must be weighed against the impact of vision loss from neovascular AMD. AMD is the leading cause of blindness in elderly individuals in developed countries, with the most severe vision loss typically due to the neovascular form of the disease.[5] While bevacizumab and ranibizumab injections were responsible for the majority of the increased cost per beneficiary in 2006, these are also the interventions which confer the most value for patients. Ranibizumab therapy was found to confer a 15.8% improvement in quality of life over 12 years for the average person with a subfoveal choroidal neovascular membrane, which was considerably higher than for any other therapy.[12] Even with the high cost of ranibizumab injections, the cost-utility was $50,691/QALY for the second-eye model, which is within the conventional $100,000/QALY upper limit for cost-effectiveness. [12] With the CATT trial showing equivalent effects on visual acuity of the two medications when given at the same dosing regimen, bevacizumab is presumably highly cost-effective. [26]

In summary, the development of anti-VEGF intravitreal injections has offered remarkable clinical benefits for patients with neovascular AMD, but these benefits must be weighed against the considerable increased economic burden of providing care for these patients.

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Table 1

Demographic characteristics of Medicare beneficiaries with new diagnoses of neovascular age-related macular degeneration

	1994 cohort (N= 2,497)	2000 cohort (N= 3,927)	p-value	2006 cohort (N= 6,041)	p-value
Age (yrs)	79.3	80.3**	<.0001	81.4**	<.0001
Male (%)	32.4%	33.8%	0.2521	28.2%**	0.0001
Black (%)	1.9%	1.2%*	0.0205	1.5%	0.2075
White (%)	97.0%	97.1%	0.7262	96.1%*	0.0271
Charlson Index	1.5	1.7**	<.0001	2.1**	<.0001
Low vision/blindness (%)	4.4%	4.5%	0.9068	4.1%	0.5051

* Significantly different from the 1994 cohort at the 5% level

** Significantly different from the 1994 cohort at the 1% level

Table 2

Distribution of mean Medicare payments in year following diagnosis of neovascular age-related macular degeneration (AMD) (in 2008 constant dollars)[1]

	1994 cohort (n=2,497)	2000 cohort (n=3,927)	p-value	2006 cohort (n=6,041)	p-value
Total health and eye care related payments					
Total health	3567	4314**	<0.0001	5991**	<0.0001
Eye-related	1504	1924**	<0.0001	3263**	<0.0001
AMD treatment payments					
Anti-vascular endothelial growth factor injections	0	0	N/A	1609**	< 0.0001
Laser	353	231**	<0.0001	55**	<0.0001
Photodynamic therapy	0	50**	<0.0001	153**	<0.0001
Imaging payments					
Fluorescein angiography	303	291	0.2162	281**	0.0014
Optical coherence tomography	0	3**	<0.0001	102**	<0.0001
Other imaging	59	120**	<0.0001	106**	<0.0001
Other payments for eye-related care					
Cataract	141	91**	<0.0001	66**	<0.0001
Cornea	5	2	0.1844	1	0.0784
Glaucoma	24	8**	0.0003	12**	0.0048
Vitrectomy	109	137	0.0953	32**	<0.0001
Visits	116	136**	<0.0001	213**	<0.0001
Other	392	855**	<0.0001	633**	<0.0001

*Significantly different from the 1994 cohort at the 5% level

**Significantly different from the 1994 cohort at the 1% level

[1]The Medical Care Price Index from 1991 to 2008 was obtained from the Bureau of Labor Statistics website and used to calculate the adjusted price in 2008 dollars.

Table 3

Distribution of mean Medicare payments in year following diagnosis of neovascular age-related macular degeneration (AMD) in matched sample (in 2008 constant dollars)[1]

	1994 cohort (n=2,488)	2000 cohort (n=2,488)	p-value	2006 cohort (n=2,488)	p-value
Total health and eye care related payments					
Total health	3572	4088**	<0.0001	5742**	<0.0001
Eye-related	1504	1924**	<0.0001	3390**	<0.0001
AMD treatment payments					
Anti-vascular endothelial growth factor injections	0	0	N/A	1700**	<0.0001
Laser	353	228**	<0.0001	50**	<0.0001
Photodynamic therapy	0	50**	<0.0001	165**	<0.0001
Imaging payments					
Fluorescein angiography	303	287	0.1396	289	0.1961
Optical coherence tomography	0	4**	<0.0001	106**	<0.0001
Other imaging	59	115**	<0.0001	110**	<0.0001
Other payments for eye-related care					
Cataract	142	91**	<0.0001	68**	<0.0001
Cornea	5	2	0.1113	1*	0.0438
Glaucoma	24	8**	0.0002	13*	0.0162
Vitrectomy	109	144*	0.0422	32**	<0.0001
Visits	116	133**	<0.0001	214**	<0.0001
Other	392	863**	<0.0001	643**	<0.0001

*Significantly different from the 1994 cohort at the 5% level

**Significantly different from the 1994 cohort at the 1% level

[1]The Medical Care Price Index from 1991 to 2008 was obtained from the Bureau of Labor Statistics website and used to calculate the adjusted price in 2008 dollars.

Table 4

Mean number of services for neovascular age-related macular degeneration provided per year in matched sample

	1994 cohort (N= 2,488) Mean (Min, Max, Median)	2000 cohort (N=2,488) Mean (Min, Max, Median)	p-value	2006 cohort (N= 2,488) Mean (Min, Max, Median)	p-value
Visits	2.1 (0,21,2)	2.0* (0,15,2)	0.0302	3.5** (0,27,3)	<0.0001
Fluorescein angiography	1.6 (0,16,1)	1.7**(0,22,1)	0.0002	1.6 (0,21,1)	0.4008
Optical coherence tomography	0 (0,0,0)	0.03**(0,2,0)	<0.0001	2.1** (0,17,1)	<0.0001
Anti-vascular endothelial growth factor (VEGF) injections	0 (0,0,0)	0 (0,0,0)	N/A	2.0 (0,19,0)	N/A (anti-VEGF injections not available in 1994 and 2000)