Economic Impact of Progression of Age-related Macular Degeneration

Jordana K Schmier[1], Jessica A Levine[2]

1. Senior Managing Scientist, 2. Associate, Exponent, Inc, Virginia, US.

Abstract

While a good deal is known about the economic impact of blindness and low vision worldwide, there is less known about of age-related macular degeneration (AMD), particularly the difference in costs as the condition progresses. This review summarizes what is known about the economic burden of AMD by disease stage. Of particular interest are the types of costs relevant and included for each stage and the methods with which stage is assigned. Across study methods and countries, the cost of drusen and dry AMD appear similar, with the costs of wet AMD many times higher. The distribution of costs varies across disease stage, with greater cost for diagnostic procedures with earlier AMD and more on caregiving and institutional care with wet AMD. Little is known about the incremental impact of bilateral AMD, and the primary reason for that limitation seems to be the wide use of claims databases rather than clinical records or enrolling only patients with bilateral disease.

Keywords

Costs and cost analysis, disease progression, health services research, macular degeneration, visual acuity

Disclosure: The authors have no conflicts of interest to declare.
Received: December 24, 2012 **Accepted:** January 15, 2013 **Citation:** *European Ophthalmic Review,* 2013;6(1):52–7 *DOI: 10.17925/USOR.2013.06.01.52*
Correspondence: Jordana K Schmier, 1800 Diagonal Road, Suite 500; Alexandria, VA 22314 USA. E: jschmier@exponent.com

Introduction

Age-related macular degeneration (AMD) is one of the leading causes of blindness worldwide, exceeded only by cataract and glaucoma.[1] It is estimated that three million people worldwide have a diagnosis of AMD in one or both eyes, and by 2020 that number is expected to double.[1] In earliest stage of AMD, small deposits in the macula called drusen appear but do not impair vision. In people for whom the condition progresses to early or intermediate AMD, these drusen increase in size or quantity and begin to impair central vision. Among patients diagnosed with wet AMD, characterized by neovascular lesions, there is often substantial central vision loss. Patients with wet AMD comprise about 10 % of all AMD patients.[2] While all patients with wet AMD previously had the dry form of the disease, not all progress. Estimates vary, but progression to wet AMD over five years can be as high as 26 % among patients with bilateral large drusen.[3] While the disease may begin in one eye, in as many as 80 % of patients, AMD is bilateral.[4]

Risk factors for AMD include age and smoking; evidence of relationships with other factors is less strong.[5] No treatment is necessary for patients with drusen. There are no current available treatments for dry AMD, however, the landmark Age-Related Eye Disease Study (AREDS) found significant decreases in progression to wet AMD associated with vitamin supplementation, including vitamins A, E, C, copper and zinc.[6,7] Treatment for advanced AMD can include intravitreal injections with vascular endothelial growth factor (VEGF) or various types of laser treatment, depending on the type and location of the lesions.[5] For certain patients, vitrectomy may be appropriate.[5]

Costs associated with AMD and other types of vision impairment range broadly. Direct medical costs, such as office visits, intravitreal injections, and photodynamic therapy can easily identified in claims databases. Other types of costs are more difficult to tease out of existing databases, for many reasons. Some devices and living aids may be covered by insurance, although that can vary by country and insurer. Other non-medical costs, such as home modifications or the use of caregiving, are often borne by the patient and are identified only through self-report. Given the variety of methods used to extract this information about indirect and non-medical costs, aggregating across studies can be challenging.

The purpose of this review is to assemble what is known about the costs throughout the course of AMD, including comparisons across stages of disease as well as consideration of unilateral and bilateral disease. There are many reviews of the economic burden of AMD;[8-11] we have limited the scope of this review to studies that are explicit in describing stage-specific costs.

Methods

We initially conducted a literature search using PubMed. The search was limited to articles published in English-language journals from 1997 to the present (2012). The initial search terms included 'macular degeneration' and 'costs and cost analysis,' with 'disease progression' or 'severity' added. Articles identified by the search were reviewed for evidence of primary data about the cost of AMD (i.e., not reviews or mentions of costs only in passing). Those describing exclusively the cost of screening programs were excluded. Also excluded were reports on cost-effectiveness of interventions, although baseline data about the costs of treatment have been included if they were relevant to identifying the costs of progression. The remaining papers were reviewed for relevance. In addition, we used a pearl-finding strategy, reviewing reference lists of identified articles, conducting searches of authors who publish in the field, and exploring web

Table 1: Literature Reviewed

Citation	Drusen	Dry	Wet	Method	Data Source	Country/Currency (Year)
Bonastre et al 2003[24]			√	Diagnosis code	Prospective data collection	France € (2000)
Coleman and Yu, 2008[15]		√	√	Diagnosis code	U.S. Medicare 5 % sample	US $ (1995-1999)
Cruess et al 2007[20]			√	Diagnosis code	Prospective data collection	Canada Can$ (2005)
Cruess et al 2008[21]			√	Diagnosis code	Prospective data collection	Canada, France, Germany, Spain, UK € (2005)
Day et al 2011[23]			√	Diagnosis code	U.S. Medicare 5 % sample	US $ (2008)
Garattini et al 2004[13]	√	√	√	Diagnosis code	Prospective data collection	Italy € (1999)
Halpern et al 2006[12]	√	√	√	Diagnosis code	U.S. Medicare 5 % sample	US $ (1999-2001)
Lotery et al 2007[22]			√	Diagnosis code	Prospective data collection	UK £ (2005)
Ruiz-Moreno et al 2008[17]			√	Diagnosis code	Prospective data collection	Spain € (2005)
Schmier et al 2012[16]		√	√	Diagnosis code	U.S. Medicare 5 % sample	US $ (2011)
Soubrane et al 2007[19]			√	Diagnosis code	Prospective data collection	Canada, France, Germany, Spain, UK €
Greiner 2001[18]		√	√	BCVA/proxy estimates	Prospective data collection	Switzerland CHF (1998)
Schmier et al 2006[26]		√	√	BCVA/DLTV	Prospective data collection	US $ (2004)
Schmier et al 2006[25]		√	√	BCVA/DLTV	Prospective data collection	US $ (2004)
Brown et al 2005[11]		√	√	Population level data	Multiple sources	US $ (2003)

sites of relevant organizations (e.g., World Health Organization, American Academy of Ophthalmology, National Eye Institute).

Results

More than 200 publications were identified in the initial literature search. There were fewer than 30 papers found when the search was further limited to terms such as 'disease progression' and 'severity'. Our review of reference lists, Internet searches, and author-specific searches yielded additional papers, with a total of 15 included in this review. A summary of the papers reviewed and the stage(s) of disease on which they report is found in *Table 1*. In describing results in the text, we have converted and inflated values to US dollars to simplify comparing across studies.

General Findings

Many papers were identified in the initial search that presented costs associated with visual impairment that happened to mention that AMD in passing. Although these studies may provide useful information on the costs associated with increasing visual impairment, it is unclear whether the findings are directly applicable to AMD patients. Since the health care resource utilization experience may depend highly on the reason for the visual impairment, we elected not to report on those studies. Patients with different expected disease trajectories, different comorbidities, and different living situations may require a variety of services. Thus, while studies on low vision in general may help fill in gaps associated with our understanding of AMD, we have excluded them from this review.

In identifying papers focusing on progression of disease, we found them grouped into two categories. First, there are papers that have used claims data or other medical records to identify patients by International Classification of Diseases (ICD-9-CM) codes and categorize them by stage of disease. Second, there are papers that assess the burden of illness of AMD by using visual impairment as a proxy for severity or an enhancement of a severity classification. Because of the obvious correlation between stage of disease and visual impairment, we have included both in this review. Existing papers on visual acuity typically use best corrected visual acuity (BCVA) or a threshold of impairment based on a patient-reported questionnaire, such as the Daily Living Tasks Dependent on Vision (DLTV) questionnaire. There is no absolute consensus on a crosswalk between these instruments and visual acuity, so there is likely inconsistency across studies.

Further, none of these classification systems are without flaws. For example, the ICD-10 includes categories to identify mild, moderate, or severe visual impairment and whether the impairment is monocular or binocular. The vast majority of patients may still be placed in the same category as previous systems, but the recognition that bilaterality of disease is potentially important should be kept in mind; the use of the ICD-10 system may represent a substantial improvement over existing classification systems. Thus, we have tried to be explicit about how visual impairment was described in each study and whether there was mention of bilateral disease.

Cost of Drusen

Direct medical costs associated with drusen are generally limited to outpatient monitoring of progression. Table 2 presents a brief summary of the types of costs associated with AMD. Claims-based analyses may exclude patients with other comorbidities, and routine ophthalmic evaluations may occur at the same frequency among patients with drusen as among patients without any evidence of drusen. Among the few studies that have identified costs for patients with drusen only, they have found substantially lower costs than patients with wet AMD.

Table 2: Types of Costs

Disease Stage	Direct Medical Costs	Direct Non-Medical Costs	Indirect Costs
Drusen	Outpatient monitoring	None	None
Dry	Outpatient monitoring Vitamins/ supplements	Living aids (limited) Home modifications (limited)	Caregiving (limited) Lost productivity (limited)
Wet	Outpatient monitoring Treatment	Living aids Home modifications	Caregiving Lost productivity

We identified two papers presenting the cost of drusen, one using U.S. data[12] and the other using data from Italy.[13]

In the study based on U.S. data, the U.S. Medicare 5 % sample was used to identify patients with AMD, stratify them into a number of categories, and compare annual costs from 1999-2001.[12] Patients were classified as having drusen, dry AMD, wet AMD, and both dry and wet AMD based on diagnosis codes in the claims data. Medicare expenditures for beneficiaries with drusen, based on diagnosis codes, comprised 28–40 % of expenditures for patients with wet AMD and ranged from $204 to $334 ($338 to $508 in US $ 2012).[12] Medicare expenditures for patients with drusen were very close (within 5 %) of those of patients with dry AMD. Patients with drusen had much lower use of diagnostic procedures and physician visits compared with patients with wet age-macular degeneration. For example, in 2001, patients with drusen had an annual average of 0.15 fluorescein angiographies, compared with 2.3 for patients with diagnoses of both wet and dry AMD during the year. Similarly, patients with drusen tended to have about one less ophthalmologist visit per year, with an average of 1.4 to 2.0, compared to patients with both dry and wet disease.[12]

A study that captured data from patients 50 years and older treated in Italian ophthalmology departments in 1998 and 1999 presents costs for patients with drusen, geographic atrophy, and choroidal neovascularization, based on a physician-confirmed diagnosis.[13] Almost one-quarter of the participants (113/476) were diagnosed with drusen and all but one had drusen in both eyes. For patients with drusen, mean annual INHS costs were €158.1 ($279 in US $ 2012) for patients and mean private costs, not covered by the INHS were €50.3 ($89 in US $ 2012).[13] For patients with drusen, diagnostic procedures were the single largest cost (40 % of total costs) and consultations were second highest (22 % of costs). Of note is that although the distribution of type of costs varied by stage of disease, the mean INHS costs were nominally higher for patients with drusen than for those with dry age-related macular degeneration. Private expenditures were significantly lower (€50.3 compared to €68.8 for patients with dry AMD).[13]

Cost of Dry AMD Identified by Diagnosis Code

Dry AMD, typically characterized by multiple drusen or irregularities of the retinal pigment epithelium,[5] is currently untreatable. Routine monitoring, including dilation, is generally conducted annually but may be recommended at shorter intervals among patients with a high risk profile.[5] The AREDS Study Group has produced multiple reports of the value of supplementation to delay progression to wet AMD.[6,7] These supplements and/or dietary modifications are frequently out-of-pocket costs for patients; thus their costs are often not counted in claims-based analyses. Alternatively, researchers make assumptions about the use of these vitamins and their typical costs and use those assumptions in their estimates of the economic burden of AMD.[14]

Four studies were identified that estimated the cost of dry AMD as identified by diagnosis codes. Three of the studies were conducted in the U.S.;[12,15,16] one was conducted in Italy.[13] Overall, direct medical costs related to dry AMD typically appear to be similar to costs among patients with drusen.

In their comparison of U.S. Medicare beneficiaries that relied on diagnosis codes in claims data from 1999 to 2001, Halpern et al found that the costs for patients with dry AMD, based on diagnosis codes, were within 5 % of those with drusen and ranged from $205 to $347 annually ($339 to $528 in US $ 2012).[12] The annual rate of use of each type of service (diagnostic procedures, therapeutic procedures, and physician interactions) was almost identical, and in some cases slightly less than among patients with drusen.

Coleman and Yu used the U.S. Medicare 5 % sample to estimate costs for dry and wet AMD from 1995 to 1999.[15] Median eye-related medical costs over the five-year period were $832 for patients with dry AMD compared with $658 for controls ($1378 and $1090 in US $ 2012, respectively). This should be considered a lower bound for the difference in Medicare expenditures, as other studies have found that the difference in ophthalmic costs does not account for the total difference between costs of AMD patients and controls.

A recent study using US Medicare data explored the changes in costs associated with progressing from dry to wet AMD from 1998 to 2009.[16] The study followed 1,184 patients for 11 years after diagnosis with dry AMD in 1998. One-fifth of patients progressed to wet AMD. Among patients who did not progress to wet AMD, annual total Medicare expenditures ranged from $11,678 to $25,392 ($11,678 to $25,589 in US $ 2012). Costs associated with ophthalmic care ranged from $287 to $682 ($298 to $707 in US $ 2012) for patients who did not progress from dry AMD.

In the study conducted in Italy, 95 % of patients with geographic atrophy had bilateral disease (73 of 78 participants).[13] A study that captured data from patients treated in Italian ophthalmology departments presents costs for patients with drusen, geographic atrophy, and choroidal neovascularization, based on a physician-confirmed diagnosis.[13] Mean annual INHS costs were €147.9 ($261 in US $ 2012) for patients with geographic atrophy and private costs were €68.8 ($121 in US $ 2012). Rates of resource use were similar to those by patients with drusen, however, use of over-the-counter products, including supplements and eye drops, were almost twice as high for dry AMD patients compared with patients with drusen.

Costs of Wet AMD Identified by Diagnosis Code

There is consistent evidence, particularly since the approval of VEGF inhibitors, that patients with wet AMD have costs many times greater than those with early stages of the disease. Patients with wet AMD likely exhibit costs in a number of categories, including direct medical costs (related to vision as well as falls, evidence that all costs increase for those with visual impairment), direct non-medical costs (vision aids, home modifications, additional transportation), indirect costs (caregiving, housekeeping), and

intangible (pain, suffering, measurable by patient-reported questionnaires or utility assessment tools).

This review identified 12 publications covering eight studies reporting on the costs of wet AMD that required a diagnosis code, either from claims data or otherwise physician-confirmed as support.[12,13,15-24] Four of the studies used the U.S. Medicare 5% sample.[12,15,16,23] Five report on the same multinational study conducted in Europe and Canada.[17,19-22]

One of the studies using US Medicare data found that the direct medical costs associated with AMD vary greatly by whether the patient undergoes photodynamic therapy (PDT) in a given year. Those who had PDT had average annual costs approximately four times greater than those who did not.[12] Accordingly, the use of individual resources was higher for patients with wet AMD than those with dry or drusen. Among patients who had PDT, the average number of procedures during the year ranged from 1.8 to 2.6, suggesting that there were either multiple procedures and/or bilateral disease.

The study using Medicare data to evaluate costs of progression over more than a decade found that patients who progress to wet AMD have total costs approximately twice that of controls and about 30 % higher than patients with dry AMD.[16] There were more dramatic differences in ophthalmic medical costs for wet AMD patients compared with dry, with health care expenditures 4.5–9 times higher for patients with wet AMD compared with dry.

Another study using the Medicare 5 % sample estimated average annual costs for patients diagnosed with wet AMD in 1994, 2000, and 2006.[23] Day and colleagues found that costs increased from $3567 to $5991 (in US$ 2008, $4065 to $6828 in US $ 2012) over the time period, with most of the cost in the final year of analysis associated with anti-VEGF treatment. There was a significant decrease in costs for laser therapy over the years, from $353 to $55 annually ($402 to $63 in US $ 2012).

Coleman and Yu's analysis of the Medicare 5% sample was limited to eye-related costs.[15] Median eye-related costs from 1995-1999 were $1607 ($2661 in US $ 2012) for patients with wet AMD, which was almost twice that for patients with dry AMD and 2.4 times greater than costs f or controls.

Soubrane and colleagues and Cruess and colleagues report on a cross-sectional study of 401 patients with bilateral subfoveal neovascular AMD and 471 controls (50 years and older with BCVA of 20/40 or better and no ophthalmic conditions) recruited in Canada, France, Germany, Spain, and the United Kingdom.[19,21] Diagnosis was confirmed by a retina specialist and patients completed a number of questionnaires by telephone.[19,21] The Canadian data are presented separately[20] as are data from the UK[22] and data from Spain.[17] Soubrane and colleagues focus on the patient burden and health care resource use[19] while Cruess et al,[20] Lotery et al,[22] and Ruiz-Moreno[17] report on the costs specifically.

The study of patient burden study found significant differences between patients and controls on each of the patient-reported questionnaires.[19] It also found that the use of health care resources was higher among patients than controls.[19] In particular, significantly more patients required assistance with activities of daily living (29 % of patients vs 7 % of controls). The multinational study of economic burden found that the average annual total cost for patients with bilateral neovascular AMD varied from €5300 ($8459 in US $ 2012) in the United Kingdom to €12,445 ($19,863 in US $ 2012) in Germany.[21] There are many possible explanations for the wide variation. Unit costs were derived from various sources in each country in the local currency and then converted to Euros. Services that are not provided or covered in some countries are included in the total cost rather than limiting the total cost estimates to services provided in each country. The studies categorized patients by VA levels (normal or better than 20/40; mild or 20/40 to > 20/80; moderate or 20/80 to > 20/200; severe, or 20/200 to >20/400; near blindness or ≤ 400). The study presents cost (direct vision-related medical, direct non-vision-related medical, direct non-medical, and overall) by country and VA level, aggregated to three VA categories. Across the 20 comparisons (five countries, four cost comparisons), only two were significant, and one approached significance. In the UK, direct non-medical-related costs and overall costs were significantly higher as VA decreased, and in Germany, there was a trend towards higher direct non-vision-related medical costs as VA decreased.

Cruess and colleagues report more specifically on the costs (presented in Can$ 2005) of the Canadian patients.[20] Mean annual costs associated with bilateral neovascular AMD was $11,334 ($12,014 in US $ 2012) compared with $1412 ($1497 in US $ 2012) for controls. Interestingly, there were nominal but not significant differences in costs across VA categories, which were collapsed to normal/mild, moderate, and severe/near blindness to compensate for the smaller sample size. The distribution of type of costs (direct vision-related medical, direct non-vision-related medical, and direct non-medical) varied by VA but, again, not significantly. Lotery and colleagues present data on the 75 patients who participated in the study in the UK. 22 Again, costs were many times higher for patients compared to controls (£3824 vs £517, p<0.0001; $8927 vs $1207 in US $ 2012). As one might expect, there were significant differences in direct vision-related medical costs and direct non-medical related costs but not in the non-vision-related medical costs between patients and controls. One-fourth of patients received some sort of assistance with daily activities compared with just 7 % of controls receiving assistance. Among patients, the two largest drivers of total costs were assistance with activities of daily living (29 % of total costs), and diagnostic testing (19.0% of total costs).[22] The UK results did not explore the impact of increasing visual impairment on costs. In Spain, the total costs for patients with wet AMD were more than five times greater than controls (€5733 vs. €1070, p<0.0001; $9150 vs $1708 in US $ 2012).[17]

Patients with wet AMD in Italy had bilateral disease 91 % of the time.[13] Costs for patients with wet AMD were two to three times higher and significantly greater than for patients with drusen or dry AMD. Covered annual average medical expenditures totaled €540.1 for wet AMD patients; their private costs averaged €46.5 annually ($953 and $82 in US $ 2012, respectively). Interestingly, the proportion of private costs was very different by AMD stage. For those with wet AMD, private costs totaled 8 % of the total (private plus INHS costs), while for dry AMD privately-paid costs comprised 32 % of total costs.[13]

Greiner estimated the cost of care for wet AMD patients in Switzerland and also distinguished by visual acuity.[18] Costs were derived from expert panels and interviews. While the goal of the study was to develop a cost-effectiveness model of verteporfin therapy, the baseline costs are useful. As

vision deteriorated, costs increased, from 4683 CHF per patient per year to 15,231 CHF per patient per year ($5539 to $18,013 in US $ 2012). Cost drivers varied by severity, with diagnostic procedures responsible for the plurality (37 %) of costs for patients with the best vision and institutional care the largest cost driver (57 % of costs) for patients with highly impaired vision.

Costs of AMD Across Visual Acuity Levels

We identified two publications describing one study that evaluated the costs of AMD across levels of visual acuity but did not necessarily compare costs by dry vs wet AMD.

Two related studies present data on use of services and devices[25] and with caregiving[26] among patients with AMD. These studies were conducted with the assistance of ophthalmologists, who identified patients with AMD and provided information on their BCVA but did not report whether they had dry or wet AMD.[25,26] These studies categorized patients not by dry or wet AMD but by their scores on the Daily Living Tasks Dependent on Vision questionnaire (DLTV), a patient-reported survey.[27] Developers of the DLTV have estimated visual acuity for average DLTV item scores.[28] Costs included in the study were self-reported and included vision rehabilitation and counseling, supplements, use of devices and caregiver time. These studies found a stair-step pattern between DLTV scores and costs associated with age-related macular degeneration. The annual average total cost across all levels of DLTV/VA was $5833 ($7804 in US $ 2012); among patients with only mild visual impairment, it ranged from $506 (patients with VA better than 20/32) to $1843 (patients with VA 20/32 to < 20/50) ($677 to $2466 in US $ 2012, respectively).[25] These AMD patients reported an average weekly need for caregiving of 5.8 and 6.6 hours, respectively.[26] Among patients with moderate visual impairment (VA 20/50 to better than 20/80), total annual costs were estimated to be $4807 ($6431 in US $ 2012); among those with VA 20/250 or worse, it was $48,676 ($65,122 in US $ 2012). The driver of these costs was an increase in the need for caregiving.[25] Among those with moderate visual impairment, patients reported needing 8.8 hours of help per week, while those in the lowest VA category reported an average of 94.1 hours of caregiving required per week.[26] These studies valued caregiving regardless of whether it was formal (paid) or informal (unpaid), but 63 % of patients with the worst VA reported paid caregiving.

Related Health Care Resource Utilization

There were also studies that identified resource use likely associated with macular degeneration, although costs were not presented. For example, the public health impact associated with a diagnosis of wet AMD, including comorbidities such as depression, new hip fractures, and institutionalization, were evaluated by Bandello and colleagues.[29] The study estimated outcomes associated with risk of AMD developing in the second eye and premature mortality. In contrast, Tournier et al suggest that these findings might require careful adjustment; they found wet AMD to be associated with an increased risk of depression and fracture but no relationship with institutionalization once they adjusted for incident or prevalent status of AMD.[30]

Societal Burden of Age-related Macular Degeneration

One study estimating the macroeconomic impact of AMD considered both loss of employment and loss of salary associated with AMD.[11] Brown and colleagues estimated that the total loss in gross domestic profit in the US due to dry AMD was $24.4 billion ($34.1 billion in US $ 2012).[11] In addition to presenting the loss to GDP from dry AMD, Brown and colleagues also estimated the GDP loss from wet AMD.[11] The macroeconomic costs of wet AMD, again considering both salary loss and unemployment and expressed as total GDP loss, was estimated to be $5.4 billion ($7.5 billion in US $ 2012).[11] Just more than half of these costs ($2.9 billion, $4.0 billion in US $ 2012) were associated with patients 65 years of age and older and the remainder with younger patients. The increased prevalence but lower employment rate in the older population accounts for the difference.

Conclusions and Considerations for Future Research

Limits of Current Knowledge

The widespread of the U.S. Medicare database makes sense, given that the Medicare program is likely the single largest payer for AMD services in the country. However, although selection criteria are not identical, many of the published studies of the costs to Medicare almost certainly include the same patients and thus bring into question the independence of their findings. Similarly, while the methods are sound, much of what is known about the cost of AMD in Europe is based on a single study.[17,19-22] What is known outside of Europe and North America does not appear to have made its way to English-language publications at this time. Further, some of the studies described in this review considered sex, race, age, and comorbidities in identifying controls and/or selecting patients for analysis; others did not.

Unilateral vs Bilateral Disease

An important difference exists between the claims database studies that identified patients from diagnosis codes and the studies that included a physician diagnosis: the claims databases cannot be used to separate or compare patients with unilateral vs. bilateral disease. While it is understandable that laterality is not usually recorded since physician payment is unrelated to which eye is involved, it hampers analysis of costs as it is uncertain whether progression or fellow eye involvement is reflected. The only claims-based study that attempted to do so was Halpern and colleagues, with its attempt to consider either progression or bilateral disease, indicated by both a single patient having diagnosis codes for both dry and wet AMD during a single calendar year.[12]

General Conclusions

Together, these studies seem to suggest that the diagnosis of wet AMD, rather than deterioration of VA within disease stage, is the primary driver of costs. Treatment is expensive, yet so are caregiving or institutional living, as several studies have demonstrated. While many studies have not fully captured the costs associated with dry AMD because they were limited to direct medical costs, which typically excludes supplements, the cost of dry AMD is consistently no more than half the cost of wet AMD. Delaying progression of dry AMD, or better yet, minimizing or eliminating risk factors, could lead to a substantial reduction in costs borne by health care payers, individuals, and society. ■

1. World Health Organization, Vision 2020, The right to sight: global initiative for the elimination of avoidable blindness action plan 2006–11, Geneva, Switzerland 2007.
2. Macular Degeneration Partnership, What is AMD?, http://www.amd.org/what-is-amd.html, Accessed April 11, 2012.
3. Chew EY, Sperduto RD, Milton RC, et al., Risk of advanced age-related macular degeneration after cataract surgery in the age-related eye disease study: AREDS report 25, *Ophthalmology*, Feb 2009;116(2):297–303.
4. Wang JJ, Mitchell P, Smith W, Cumming RG, Bilateral involvement by age related maculopathy lesions in a population, *Br J Ophthalmol*, Jul 1998;82(7):743–7.
5. American Academy of Ophthalmology, Preferred Practice Pattern: Age-Related Macular Degeneration, 2008.
6. AREDS Research Group, A randomized, placebo-controlled,

clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss: AREDS report no. 8, *Arch Ophthalmol*, Oct 2001;119(10):1417–36.
7. AREDS Research Group, The effect of five-year zinc supplementation on serum zinc, serum cholesterol and hematocrit in persons randomly assigned to treatment group in the age-related eye disease study: AREDS Report No. 7, *J Nutr*, Apr 2002;132(4):697–702.
8. Gupta OP, Brown GC, Brown MM, Age-related macular degeneration: the costs to society and the patient, *Curr Opin Ophthalmol*, May 2007;18(3):201–5.
9. Bonastre J, Le Pen C, Anderson P, et al., The epidemiology, economics and quality of life burden of age-related macular degeneration in france, germany, italy and the united kingdom, *The European Journal of Health Economics*, June 2002;3(2):94–102.
10. Schmier JK, Jones ML, Halpern MT, The burden of age-related macular degeneration, *Pharmacoeconomics*, 2006;24(4):319–34.
11. Brown GC, Brown MM, Sharma S, et al., The burden of age-related macular degeneration: a value-based medicine analysis, *Trans Am Ophthalmol Soc*, 2005;103:173–84; discussion 184–76.
12. Halpern MT, Schmier JK, Covert D, Venkataraman K, Resource utilization and costs of age-related macular degeneration, *Health Care Financ Rev*, Spring 2006;27(3):37–47.
13. Garattini L, Castelnuovo E, Lanzetta P, et al., Direct medical costs of age-related macular degeneration in Italian hospital ophthalmology departments A multicenter, prospective 1-year study, *Eur J Health Econ*, 2004;5(1):22–7.
14. Rein DB, Zhang P, Wirth KE, et al., The economic burden of major adult visual disorders in the United States, *Arch Ophthalmol*, Dec 2006;124(12):1754–60.
15. Coleman AL, Yu F, Eye-related medicare costs for patients with age-related macular degeneration from 1995 to 1999, *Ophthalmology*, Jan 2008;115(1):18–25.
16. Schmier JK, Covert DW, Lau EC., Patterns and costs associated with progression of age-related macular degeneration, *Am J Ophthalmol*, Oct 2012;154(4):675–81 e671.
17. Ruiz-Moreno JM, Coco RM, Garcia-Arumi J, et al., Burden of illness of bilateral neovascular age-related macular degeneration in Spain, *Curr Med Res Opin*, Jul 2008;24(7):2103–11.
18. Greiner RA, Cost of care for patients with age-related macular degeneration in Switzerland and cost-effectiveness of treatment with verteporfin therapy, *Semin Ophthalmol*, Dec 2001;16(4):218–22.
19. Soubrane G, Cruess A, Lotery A, et al., Burden and health care resource utilization in neovascular age-related macular degeneration: findings of a multicountry study, *Arch Ophthalmol*, Sep 2007;125(9):1249–54.
20. Cruess A, Zlateva G, Xu X, Rochon S, Burden of illness of neovascular age-related macular degeneration in Canada, *Can J Ophthalmol*, Dec 2007;42(6):836–43.
21. Cruess AF, Zlateva G, Xu X, et al., Economic burden of bilateral neovascular age-related macular degeneration: multi-country observational study. Pharmacoeconomics. 2008;26(1):57–73.
22. Lotery A, Xu X, Zlatava G, Loftus J., Burden of illness, visual impairment and health resource utilisation of patients with neovascular age-related macular degeneration: results from the UK cohort of a five-country cross-sectional study, *Br J Ophthalmol*, Oct 2007;91(10):1303–7.
23. Day S, Acquah K, Lee PP, et al., Medicare costs for neovascular age-related macular degeneration, 1994–2007, *Am J Ophthalmol*, Dec 2011;152(6):1014–20.
24. Bonastre J, Le Pen C, Soubrane G, Quentel G, The burden of age-related macular degeneration: results of a cohort study in two French referral centres, *Pharmacoeconomics*, 2003;21(3):181–90.
25. Schmier JK, Halpern MT, Covert DW, et al., Impact of visual impairment on service and device use by individuals with age-related macular degeneration (AMD), *Disabil Rehabil*, Nov 15 2006;28(21):1331–7.
26. Schmier JK, Halpern MT, Covert D, et al., Impact of visual impairment on use of caregiving by individuals with age-related macular degeneration, *Retina*, Nov-Dec 2006;26(9):1056–62.
27. Hart PM, Chakravarthy U, Stevenson MR, Jamison JQ, A vision specific functional index for use in patients with age related macular degeneration, *Br J Ophthalmol*, Oct 1999;83(10):1115–20.
28. McClure ME, Hart PM, Jackson AJ, Stevenson MR, Chakravarthy U. Macular degeneration: do conventional measurements of impaired visual function equate with visual disability?, *Br J Ophthalmol*, Mar 2000;84(3):244–50.
29. Bandello F, Lafuma A, Berdeaux G, Public health impact of neovascular age-related macular degeneration treatments extrapolated from visual acuity, *Invest Ophthalmol Vis Sci*, Jan 2007;48(1):96–103.
30. Tournier M, Moride Y, Lesk M, et al., The depletion of susceptibles effect in the assessment of burden-of-illness: the example of age-related macular degeneration in the community-dwelling elderly population of Quebec, *Can J Clin Pharmacol*, Winter 2008;15(1):e22–35.