

# Burden of illness of neovascular age-related macular degeneration in Canada

Alan Cruess,\* MD; Gergana Zlateva,† PhD; Xiao Xu,‡ PhD; Sophie Rochon,§ MA

## ABSTRACT • RÉSUMÉ

**Background:** Age-related macular degeneration (AMD) is a retinal disease affecting more than 2 million Canadians over the age of 50. The neovascular form of AMD is responsible for 90% of severe vision loss associated with the disease. This study was conducted to assess the burden of neovascular AMD in the Canadian population.

**Methods:** A cross-sectional, observational study was conducted of self-reported functional health, well-being, and disease burden among elderly subjects in Canada with ( $n = 67$ ) and without ( $n = 99$ ) neovascular AMD. Subjects completed telephone surveys of the National Eye Institute Visual Function Questionnaire (NEI-VFQ-25), the EuroQol questionnaire (EQ-5D), and the Hospital Anxiety and Depression Scale (HADS). Subjects also reported their history of falls and fractures and annual health care resource utilization.

**Results:** Subjects with neovascular AMD reported significantly worse vision-related functioning and overall well-being than controls (adjusted mean scores on the NEI-VFQ-25: 48.0 vs. 87.5;  $p < 0.0001$ ) and significantly more depression symptoms than controls (HADS depression: 5.8 vs. 4.3;  $p = 0.037$ ). Subjects with neovascular AMD also reported more than twice the need for assistance with daily activities compared with controls (19.4% vs. 9.1%;  $p = 0.013$ ) and a nearly 3 times higher fall rate than the control group (22.4% vs. 8.1%;  $p = 0.014$ ). The annual neovascular AMD cost per patient was Can\$11 334, which is over 8 times that of elderly subjects without neovascular AMD (Can\$1412). Over half of the neovascular AMD costs were direct medical costs.

**Interpretation:** Neovascular AMD is associated with significant limitation in functional abilities and quality of life, resulting in increased health care resource utilization and high patient support costs. These findings emphasize the need for new treatments for neovascular AMD that will prevent vision loss and progression to blindness in order to lessen the ensuing economic burden.

**Contexte :** La dégénérescence maculaire liée à l'âge (DMLA) est une maladie rétinienne qui affecte plus de 2 millions de Canadiens de plus de 50 ans. La forme néovasculaire de la DMLA est responsable de 90 % des pertes de vision graves associées à la maladie. Cette étude a donc pour objet d'évaluer le fardeau de la DMLA néovasculaire chez la population canadienne.

**Méthodes :** Une étude transversale basée sur l'observation a été menée sur la santé fonctionnelle, le bien-être et le fardeau de la maladie dont ont fait état des personnes âgées du Canada atteintes ( $n = 67$ ) et non atteintes ( $n = 99$ ) de DMLA néovasculaire. Les sujets ont répondu par sondages téléphoniques au questionnaire du National Eye Institute sur la fonction visuelle (NEI-VFQ-25), à celui d'EuroQol (EQ-5D) et à l'échelle HAD (sur les troubles d'anxiété et de dépression des personnes hospitalisées – HADS). Ils ont aussi fait état de leurs chutes et fractures ainsi que de leur consultation annuelle des centres de soins.

**Résultats :** Les sujets atteints de DMLA néovasculaire ont fait état d'un fonctionnement lié à la vue et d'un bien-être général significativement inférieurs à ceux du groupe témoin (moyenne des résultats du NEI-VFQ-25 après rajustement : 48,0 vs 87,5;  $p < 0,0001$ ) et signalé significativement plus de symptômes de dépression que le groupe témoin (résultats HADS : 5,8 vs 4,3;  $p = 0,037$ ). Les sujets atteints de DMLA ont aussi indiqué qu'ils avaient davantage besoin d'aide pour les activités quotidiennes que ceux du groupe témoin (19,4 % vs 9,1 %;  $p = 0,013$ ) et montré un taux de chute près de 3 fois plus élevé que celui du groupe témoin (22,4 % vs 8,1 %;  $p = 0,014$ ). Les coûts annuels de la DMLA ont été de 11 334 \$ CAN par patient, soit 8 fois plus que chez les sujets âgés sans DMLA (1412 \$ CAN). Plus de la moitié des coûts de la DMLA néovasculaire ont été des frais médicaux directs.

**Interprétation :** La DMLA néovasculaire est associée avec une limitation significative de la capacité de fonctionnement et de la qualité de vie, entraînant un recours accru aux services de santé et des frais élevés de soutien auprès des patients. Ces résultats mettent l'accent sur le besoin de nouveaux traitements pour la DMLA, qui préviendront la perte de vision et la progression vers la cécité afin de réduire le fardeau économique qui s'ensuit.

From \*the Department of Ophthalmology and Visual Sciences, Dalhousie University, Halifax, N.S.; †Pfizer Inc., New York, N.Y.; ‡Covance Market Access Services Inc., Gaithersburg, Md.; and §Pfizer Canada Inc., Montréal, Que.

Correspondence to: Sophie Rochon, MA, 17300 Trans-Canada Highway, Kirkland, QC H9J 2M5; Sophie.Rochon@pfizer.com

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Age-related macular degeneration (AMD) is a retinal disease affecting more than 2 million Canadians over the age of 50 and is the leading cause of blindness in developed countries, and its incidence increases with age.<sup>1</sup> As the Canadian population ages, incidence and prevalence rates are likely to triple over the next 25 years.<sup>2</sup>

AMD can be categorized into atrophic (dry) or neovascular (wet) disease. Neovascular AMD, the most damaging type of AMD, results from abnormal proliferation of blood vessels beneath the retina in a process termed choroidal neovascularization (CNV).<sup>3</sup> These abnormal new blood vessels cause vision loss as the result of disruption of the retinal pigment epithelium, bleeding, or the accumulation of fluid or lipid in the macula. CNV associated with neovascular AMD leads to irreversible loss of central visual acuity (VA). Neovascular AMD is responsible for 90% of severe vision loss associated with AMD,<sup>3</sup> the majority of patients experiencing vision loss in the affected eye within 2 years after diagnosis of the disease.<sup>4,5</sup>

Visual impairment associated with neovascular AMD has deleterious effects on the ability to perform daily activities,<sup>6</sup> compromising a person's independence and quality of life (QOL).<sup>7,8</sup> In addition, loss of income and increased feelings of social isolation for those patients with neovascular AMD who must discontinue employment as a result of their visual impairment may have additive effects.<sup>3</sup>

Although studies estimating the prevalence, emotional distress, and treatment costs associated with neovascular AMD in Canada have been reported,<sup>9–12</sup> comprehensive population-based studies addressing the QOL burden, health care resource utilization, and socio-economic consequences of the disease, relative to similar age groups without AMD, in the Canadian population are not available. The purpose of this study was to assess the impact of neovascular AMD on the QOL and health care resource utilization of an elderly Canadian population affected by the disease compared with a control group without serious vision disorders. Health care resource utilization data collected in the study were used to estimate the cost of neovascular AMD to Canadian society.

## METHODS

### Design and setting

A cross-sectional, observational study of self-reported functional health, well-being, and disease burden among elderly subjects with and without bilateral neovascular AMD was conducted in a multicountry setting: Canada, France, Germany, Spain, and the United Kingdom. The study methods and main results have been described elsewhere.<sup>13</sup> In this report, we present the findings for the Canadian population. Accredited ethics committees and human investigation review boards approved the study protocol in each country and at each study site. No medical interventions or invasive procedures were required by the study protocol. Subject enrollment was conducted from April 2005 to October 2005.

### Subjects

Subjects were required to meet the eligibility criteria, provide written informed consent, and complete a standard telephone survey administered by trained interviewers. Subjects with neovascular AMD had the bilateral subfoveal form of the disease and were categorized into 5 severity levels according to their Snellen VA (feet/feet) in the better-seeing eye: normal, better than 20/40; mild, 20/40 to better than 20/80; moderate, 20/80 to better than 20/200; severe, 20/200 to better than 20/400; near blindness, 20/400 or worse. Control subjects had to have a best-corrected Snellen VA in the better eye of  $\geq 20/40$  and be free of serious potentially confounding ocular pathologies.

### Study assessments

Subjects with neovascular AMD were recruited at 5 retinal clinics. Retinal specialists completed clinical case report forms for each subject. This contained demographic information, VA, diagnostic tests, previous and current treatments for neovascular AMD (within the previous 12 and 24 months), prescribed equipment for eyesight, visual rehabilitation, and concomitant illnesses and comorbidities. Control subjects were recruited in the practices of 6 primary care physicians.

Subject interviews used 3 psychometric, validated QOL instruments and an additional 12 study-specific questions. The National Eye Institute Visual Function Questionnaire (NEI-VFQ-25), designed to assess vision-specific QOL,<sup>14,15</sup> consists of 1 general health and 11 vision-related categories with scores ranging from 0 to 100, where 100 represents the best functioning state. The average scores of the 11 vision-related categories determined the NEI-VFQ-25 summary score for each subject.<sup>14,15</sup> The EuroQol questionnaire (EQ-5D),<sup>16</sup> a general health assessment instrument, has 5 health state questions that measure subjects' mobility, self-care, performance of usual activities, pain or discomfort, and anxiety or depression. Scores are calculated using relative weights for each item; the higher the score the better the QOL. The Hospital Anxiety and Depression Scale (HADS)<sup>17</sup> contains questions that identify the occurrence and level of anxiety and depression symptoms in a subject. Its subscale score ranges from 0 to 21, with higher scores representing poorer mental health.<sup>17</sup> Study-specific questions were posed to determine rate of accidents, falls, fall-related injuries, rate and location of treatment, medications prescribed for depression/anxiety, and nonvision-related medical treatment. Subjects also reported assistance received for activities of daily living (ADL) and social benefits received because of their visual disability.

### Economic analysis

A societal perspective was used to determine the economic cost of neovascular AMD. The main cost categories focused on direct vision-related medical costs (visual rehabilitation, eyesight equipment, eye doctor visits, eye glasses or contact lenses, retina specialist evaluations, diagnostic tests, and previous treatments for neovascular AMD),

direct nonvision-related medical costs (fall-related injuries, other accident-related injuries, depression/anxiety treatment, and nonvision-related medical treatment), and direct nonmedical-related costs (living in government-sponsored assisted-living facilities, assistance received for daily activities, and social benefit received).

Unit costs were assigned for each type of resource, and rates were inflated from 2004 values to 2005 values (Table 1). Costs were derived from the Canadian Management Information Systems (MIS) database<sup>18</sup> and the Ontario Drug Benefit Formulary/Comparative Drug Index.<sup>19</sup> Annual costs were calculated for each subject by multiplying the number of resource units consumed by the unit cost and then summing the costs for each category of resource utilization.

**Endpoints**

The primary endpoint was the difference in vision-specific QOL between subjects with neovascular AMD and control subjects based on NEI-VFQ-25 summary scores. Secondary endpoints included measuring the QOL burden of neovascular AMD using the EQ-5D questionnaire and HADS, and determining the health care resource utilization and the ensuing annual costs to the group with neovascular AMD and the control group. The association between VA levels in the better-seeing eye of subjects with neovascular AMD and QOL was also investigated.

**Statistical analysis**

Mean and 95% confidence intervals (CIs) of QOL scores from all 3 surveys and continuous health care resource utilization variables were compared between subjects and controls using analysis of covariance (ANCOVA) models with outcomes modeled as a function of the study group controlling for age, sex, race, and comorbidities. All Snellen VA units were converted into their logarithmic Minimum Angle of Resolution (logMAR) for statistical purposes. Multiple logistic regression models evaluated between-group differences in the outcomes of the various categories. Mean QOL scores across the range of VA in the better-seeing eye were compared using ANCOVA models adjusting for covariates. Statistical significance was evaluated at the 0.05 level with no adjustments for multiple comparisons, and analysis was performed by Covance Inc. (Gaithersburg, Md.) using PC-SAS v. 9.1 (SAS Institute, Cary, N.C.).

**RESULTS**

**Demographic and clinical characteristics**

Sixty-seven subjects with neovascular AMD and 99 control subjects took part in the study. The group with neovascular AMD was significantly older than the control group (mean age: 78.8 vs. 61.7, respectively;  $p < 0.0001$ ) and contained more females than the control group (68.7% vs. 54.5%, respectively) (Table 2). The proportion of Caucasians was 98.5% and 88.9% for the group with neovascular AMD and the control group, respectively

(Table 2). The VA of the better-seeing eye, the best corrected VA at diagnosis of neovascular AMD, and comorbid conditions by study sample are listed in Table 2.

**Table 1—Unit costs\* of resources used by subjects with and without neovascular age-related macular degeneration (AMD)**

Health care resource	Year 2005 (Can\$)
<b>Direct vision-related medical costs</b>	
Visual rehabilitation (average cost per visit)	
Ophthalmologist/optometrist	60
Occupational therapist/low-vision rehabilitation	19
Government-sponsored rehabilitation/training/therapy for people with blindness (10–15 sessions)	1 849
Equipment for eyesight (average cost per equipment)	
Eye glasses	128
Contact lenses	10
Hand-held magnifier	18
Stand magnifier	66
Electronic magnifier	103
Filters	18
Telescope	155
Closed-circuit television system	258
Visit to eye doctor (average cost per visit)	
Ophthalmologist	60
Optometrist	41
Change of eye glasses or contact lenses	
Eye glasses	128
Contact lenses	10
Retina specialist evaluation (average cost per visit)	60
Diagnostic test (average cost per test)	
Slit lamp exam/ophthalmoscopy	42
Fundus photography	42
Fluorescein angiography	47
Optical coherence tomography	19
Indocyanine green angiography	43
Previous treatment of neovascular AMD (average cost per treatment)	
Verteporfin (Visudyne) one eye only	2 112
Simultaneous verteporfin treatment both eyes	2 266
Intravitreal corticosteroids per eye	183
Photodynamic therapy with intravitreal steroid injection	308
<b>Direct non-vision-related medical costs</b>	
Falls-related treatment (average cost per visit)	
Hospital emergency room	70
Primary care physician office	56
Specialists	70
Admitted into the hospital	4 038
Medical treatment (average cost per visit)	
Hospital emergency room	70
Primary care physician office	43
Specialists	70
Admitted into the hospital	4 038
Treatment for depression/anxiety	
Prescription medication (average cost per month)	8
Primary care physician/general practitioner (average cost per visit)	43
Specialist/psychiatrist (average cost per visit)	60
Other specialist (average cost per visit)	62
<b>Direct non-medical-related costs</b>	
Living situation (average cost per year)	
Government-sponsored assisted living facility	16 125
Government-sponsored nursing home	21 500
Professional fee for home care	56 600

\*Costs were obtained from the Canadian Institute for Health Information and the Ontario Ministry of Health and Long-Term Care.<sup>18,19</sup>

### Impact of neovascular AMD on QOL

Subjects with neovascular AMD had significantly reduced QOL as measured by the NEI-VFQ-25 with an adjusted mean summary score of 48.0, as compared with the control subjects' score of 87.5 (45% relative difference;  $p < 0.0001$ ) (Table 3). In the category of general health, the group with neovascular AMD scored significantly lower than the control group (adjusted mean: 39.9 vs. 54.2;  $p = 0.0070$ ) (Table 3). Subjects with neovascular AMD scored significantly lower than controls (all categories,  $p < 0.0001$ ) on all but 1 scale of the NEI-VFQ-25 (ocular pain) (Table 3).

However, EQ-5D health state valuation scores were not significantly lower in subjects with neovascular AMD than in the control group (14% relative difference;  $p = 0.064$ ) (Table 3). Using HADS, the subjects with neovascular AMD reported significantly higher levels of depression than controls (relative difference 28%;  $p = 0.037$ ). The anxiety levels did not differ significantly between the 2 groups (Table 3).

Stratification of VA severity level illustrated that subjects with neovascular AMD showed a significant trend towards a poorer QOL as VA approached blindness ( $p = 0.0044$ )

(Fig. 1A). The NEI-VFQ-25 summary score ranged from 64.7 in those subjects classified as having normal VA to 36.3 in the nearly blind subjects (Fig. 1A). In the categories of near activities, distance activities, and driving, there was a significant deterioration in the NEI-VFQ-25 score as VA decreased (Fig. 1B). EQ-5D and HADS scores were not associated with VA level in subjects with neovascular AMD.

A post-hoc analysis of age-matched controls was conducted to reconfirm comparability and outcomes on QOL given the significant age difference between subjects with neovascular AMD and controls. The following age-matched groups were defined in the control sample: over 70 years of age,  $n = 21$ ; and over 75 years of age,  $n = 9$ . The results of the subgroup analysis paralleled those presented in the overall analysis, indicating that age had no direct impact on the study findings (Table 3). Outcomes were affected by a small sample size.

### Neovascular AMD-associated comorbidities

The group with neovascular AMD had significantly more vision-related comorbid medical conditions than the control group (23.9% vs. 2.0%, respectively;  $p < 0.0001$ ) (Table 2). Furthermore, the proportion of subjects with glaucoma, cataracts, and cancer was significantly higher in the group with neovascular AMD than in the control group ( $p = 0.0024$ , 0.0016, and 0.049, respectively). The control group had a significantly higher proportion of subjects with anxiety disorders and chronic pain ( $p = 0.04$  for both) (Table 2). Twenty-five percent of the subjects with neovascular AMD reported having had an accident in the previous 12 months compared with 17% in the control group, even though the difference did not reach statistical significance because of the small sample ( $p = 0.086$ ). The percentage of subjects with neovascular AMD who had fallen was almost 3 times higher than in the controls (22.4% vs. 8.0%, respectively;  $p = 0.014$ ). Approximately half of the subjects in either group who fell required treatment.

### Health care resource utilization

A higher proportion of control subjects (72.7%) than subjects with neovascular AMD (53.7%) reported living with a spouse or family member ( $p = 0.010$ ), and more subjects with neovascular AMD than control subjects reported living alone (38.8% vs. 27.3%, respectively;  $p = 0.022$ ). Subjects with neovascular AMD were significantly more likely to receive assistance for ADL (19.4% vs. 9.1%, respectively;  $p = 0.013$ ) (Fig. 2). Subjects with neovascular AMD were more likely to visit both ophthalmologists (43.3% vs. 26.3%, respectively;  $p = 0.0046$ ) and optometrists (53.7% vs. 36.4%, respectively;  $p = 0.0048$ ) and to receive nonvision-related medical treatment than control subjects (91.0% vs. 78.8%, respectively;  $p = 0.036$ ). A very small proportion of subjects with neovascular AMD (4.5%) received social benefits, such as disability allowance or pension, housing benefit, and tax benefit. More subjects with severe VA (24%) or near blindness (44%) required assistance with ADL compared with subjects with moderate (19%) or normal/mild VA (0%).

**Table 2—Demographic and clinical characteristics of study sample**

Characteristic	Neovascular AMD ( $n = 67$ )	Control ( $n = 99$ )	$p$ value
<b>Age, years</b>			
Mean (SD)	78.8 (7.6)	61.7 (8.5)	<0.0001
Range	58–90	50–87	
<b>Sex, <math>n</math> (%)</b>			
Male	20 (29.9)	43 (43.4)	0.19
Female	46 (68.7)	54 (54.5)	
Missing	1 (1.5)	2 (2.0)	
<b>Race, <math>n</math> (%)</b>			
Caucasian	66 (98.5)	88 (88.9)	0.18
Other	0 (0.0)	8 (8.0)	
Missing	1 (1.5)	3 (3.0)	
Best corrected VA at diagnosis of neovascular AMD (logMAR), mean (SD)	0.66 (0.64)	NA	NA
Current best corrected VA of better eye (logMAR), mean (SD)	0.62 (0.62)	0.09 (0.70)	NA
<b>Neovascular AMD severity level in better-seeing eye, <math>n</math> (%)</b>			
Normal (>20/40)	10 (14.9)	NA	NA
Mild (20/40 to >20/80)	7 (10.4)	NA	NA
Moderate (20/80 to >20/200)	21 (31.3)	NA	NA
Severe (20/200 to >20/400)	17 (25.4)	NA	NA
Near blind ( $\leq 20/400$ )	9 (13.4)	NA	NA
Missing	3 (4.5)	NA	NA
<b>Comorbid disease,* <math>n</math> (%)</b>			
Glaucoma	6 (9.0)	0 (0.0)	0.0024
Cataract	10 (14.9)	2 (2.0)	0.0016
Anxiety disorder	1 (1.5)	9 (9.1)	0.044
Cancer	7 (10.4)	3 (3.0)	0.049
Other chronic pain	0 (0.0)	6 (6.1)	0.040
Vision-related comorbid disease <sup>†</sup>	16 (23.9)	2 (2.0)	<0.0001

\*Comorbid diseases also investigated: diabetes, diabetic retinopathy, depression, asthma, chronic obstructive pulmonary disease, arthritis and rheumatism, headache, chronic neck or back pain, stroke, sleep disturbance, and substance use disorder. No significant difference was found between groups.

<sup>†</sup>Diabetic retinopathy, glaucoma, and cataract.

Note: AMD, age-related macular degeneration; VA, visual acuity; logMAR, logarithmic Minimum Angle of Resolution; NA, not applicable.

**Annual costs: neovascular AMD and control subjects**

The mean annual cost (2005) associated with bilateral neovascular AMD was Can\$11 334, ranging from Can\$298 to \$96 474, whereas the average cost in the case of control subjects without neovascular AMD was Can\$1412. The allocation of resources for the group with neovascular AMD group varied between the 3 cost categories: direct vision-related medical costs, total nonvision-related medical treatment costs, and total costs for assistance with daily activities received (Table 4).

The mean annual direct vision-related medical cost for subjects with neovascular AMD in Canada was Can\$6314, accounting for 56% of overall subject costs (Table 4). Treatment costs (with verteporfin in particular) were the main cost driver in this category (47%).

Mean direct nonvision-related medical costs were Can\$2383 or approximately 21% of total costs. In comparison, these costs for control subjects amounted to Can\$738. The main cost driver for this category was nonvision-related medical treatment, accounting for up to 20% and 47% of total costs for the group with neovascular AMD and the control group, respectively (Table 4).

Direct nonmedical-related costs made up a relatively small fraction of the total cost for subjects with neovascular AMD (23%), averaging Can\$2636, as compared with Can\$601 for the cost of similar needs by the control group (43% of total cost) (Table 4).

There was no statistically significant difference in the annual cost associated with neovascular AMD across disease severity levels as defined by VA. Subjects with normal vision or mild vision loss had slightly lower costs than those with moderate vision loss or those with severe vision loss or near blindness (Table 5). Differences in these 3 categories of disease severity were driven by escalation of ADL resource use and nonvision-related medical costs with worsening of VA.

**INTERPRETATION**

This is the first multicentre, cross-sectional study to simultaneously assess the clinical, personal, and resource consequences of neovascular AMD in a Canadian population. The findings of this study present quantifiable evidence of significantly impaired QOL, poorer vision-related functioning, higher level of depression symptoms, and increased health care resource utilization in subjects with neovascular AMD compared with elderly controls in Canada.

The adjusted mean NEI-VFQ-25 summary scores for subjects with neovascular AMD in our study were similar to those in the NEI-VFQ-25 development study<sup>15</sup> and the Submacular Surgery Trials (SST) report.<sup>20</sup> The severity level of neovascular AMD was significantly associated with QOL as measured by the NEI-VFQ-25, the QOL decreasing as VA progressed towards blindness, particularly in the cate-

**Table 3—Quality of life (QOL) outcomes in subjects with neovascular age-related macular degeneration (AMD) and control subjects**

QOL outcome	Neovascular AMD		Control		p value
	n	Adjusted* mean (95% CI)	n	Adjusted* mean (95% CI)	
<b>NEI-VFQ-25</b>					
General health	67	39.9 (27.6, 52.1)	99	54.2 (43.2, 65.2)	0.0070
General vision	66	45.0 (37.1, 53.0)	99	82.5 (75.3, 89.6)	<0.0001
Ocular pain	66	84.3 (75.3, 93.2)	99	80.2 (72.2, 88.2)	0.29
Near activities	66	33.5 (24.9, 42.1)	99	85.8 (78.2, 93.5)	<0.0001
Distance activities	66	37.7 (28.1, 47.3)	99	86.2 (77.5, 94.8)	<0.0001
Vision specific					
Social function	66	49.4 (38.7, 60.0)	99	93.0 (83.5, 102.5)	<0.0001
Mental health	66	37.0 (26.9, 47.0)	99	83.6 (74.5, 92.6)	<0.0001
Role difficulties	65	41.8 (31.7, 51.9)	99	83.3 (74.2, 92.3)	<0.0001
Dependency	65	50.2 (40.4, 60.1)	99	95.2 (86.4, 104.1)	<0.0001
Driving	51	13.2 (−0.8, 27.2)	67	90.1 (77.9, 102.2)	<0.0001
Colour vision	66	73.5 (63.7, 83.3)	99	96.5 (87.7, 105.3)	<0.0001
Peripheral vision	66	57.8 (49.0, 66.6)	99	88.5 (80.6, 96.4)	<0.0001
<b>Composite score</b>	<b>66</b>	<b>48.0 (41.2, 54.8)</b>	<b>99</b>	<b>87.5 (81.4, 93.6)</b>	<b>&lt;0.0001</b>
<b>EQ-5D</b>					
Health state valuation	63	0.64 (0.52, 0.76)	99	0.74 (0.63, 0.84)	0.064
<b>HADS</b>					
Depression	63	5.8 (4.0, 7.6)	99	4.2 (2.6, 5.8)	0.037
Anxiety	63	6.4 (4.6, 8.3)	99	5.4 (3.7, 7.0)	0.19
<b>Subjects over 70 years of age</b>					
NEI-VFQ-25 composite score	66	46.6 (35.1, 58.0)	21	89.2 (77.5, 101.0)	<0.0001
EQ-5D health state valuation	63	0.59 (0.45, 0.73)	21	0.77 (0.63, 0.92)	0.0012
HADS depression	63	6.0 (3.3, 8.6)	21	3.7 (1.0, 6.5)	0.0295
HADS anxiety	63	7.2 (4.8, 9.7)	21	6.3 (3.8, 8.9)	0.33
<b>Subjects over 75 years of age</b>					
NEI-VFQ-25 composite score	66	53.6 (47.1, 60.2)	9	95.2 (81.6, 108.8)	<0.0001
EQ-5D health state valuation	63	0.63 (0.55, 0.72)	9	0.76 (0.60, 0.93)	0.085
HADS depression	63	5.4 (3.8, 6.9)	9	3.6 (0.5, 6.7)	0.20
HADS anxiety	63	6.3 (5.0, 7.7)	9	5.5 (2.7, 8.3)	0.49

\*Adjusted for age, sex, race, vision-related comorbidities (yes/no), and other comorbid diseases.  
 Note: CI, confidence interval; NEI-VFQ-25, National Eye Institute Visual Function Questionnaire; EQ-5D, EuroQuol questionnaire; HADS, Hospital Anxiety and Depression Scale.

gories of near activities, distance activities, and driving. The SST also reported decreasing NEI-VFQ scale scores across diminishing VA levels.<sup>20</sup> The assessment of subjects with neovascular AMD conducted with a general health QOL instrument, the EQ-5D, showed a lack of association between EQ-5D scores and different VA levels. A previous study also found no association between the survey and VA levels, and the authors concluded that the EQ-5D is not sensitive enough to evaluate health states across VA levels.<sup>21</sup> Subjects with neovascular AMD reported significantly more depression symptoms than control subjects, most likely a consequence of their decreased QOL. The utilization of the HADS instrument is a novel means by which to assess the psychological well-being of subjects with neovascular AMD.

Poor VA has been shown to significantly increase an individual's risk of a fall.<sup>22,23</sup> Similar findings were documented in this study, in which 22.4% of subjects with neovascular AMD reported having fallen in the previous 12 months. Low vision was also associated in subjects with neovascular AMD with greater use of assistance for ADL, such as trans-

portation for health care and assistance with self-care, than in the control group. As expected, subjects with neovascular AMD were more likely to visit ophthalmologists and optometrists; they also received more nonvision-related medical treatment than the control group. This study documents that a large amount of resources are required to support individuals progressing toward blindness due to neovascular AMD.

To date, there has not been a published Canadian study that comprehensively documents the different aspects of costs related to health care resource utilization in the bilateral neovascular AMD patient population. In a 2004 study by Sharma et al.,<sup>11</sup> economic resources consumed by patients with all types of AMD were examined. The average annual total cost per AMD patient was estimated to be approximately Can\$3865 (2004), with a range of approximately Can\$201 to \$13 318. Direct medical costs were the main cost driver, accounting for 93% of the total cost (the main contributor to the cost in this category being previous treatment with photodynamic therapy). It was also determined that the VA in the better-seeing eye was inversely proportional to direct nonmedical costs. It was concluded that patients with AMD consumed a high level of economic resources.<sup>11</sup> In our study, which focused solely on patients with neovascular AMD and included a control group, the mean annual cost for a Canadian with bilateral neovascular AMD was calculated to be Can\$11 334, which is more than 8 times that of an elderly person without neovascular AMD (Can\$1412). As was seen in the study by Sharma et al.,<sup>11</sup> direct vision-related costs constituted the majority of all neovascular AMD costs, of which previous treatment of neovascular AMD was the key driver (Can\$5307).

A 2003 European study conducted by Bonastre et al.<sup>4</sup> found that costs associated with a patient with neovascular AMD were €3360 (Can\$5571), of which direct medical costs also accounted for half of the costs. This finding is lower than the one calculated here for Canada, but the former accounted only for laser photocoagulation as a treatment option for neovascular AMD. In this study, data for more costly treatments, such as photodynamic therapy with verteporfin, were included, which increased the overall total of direct medical costs. Further, the assessment

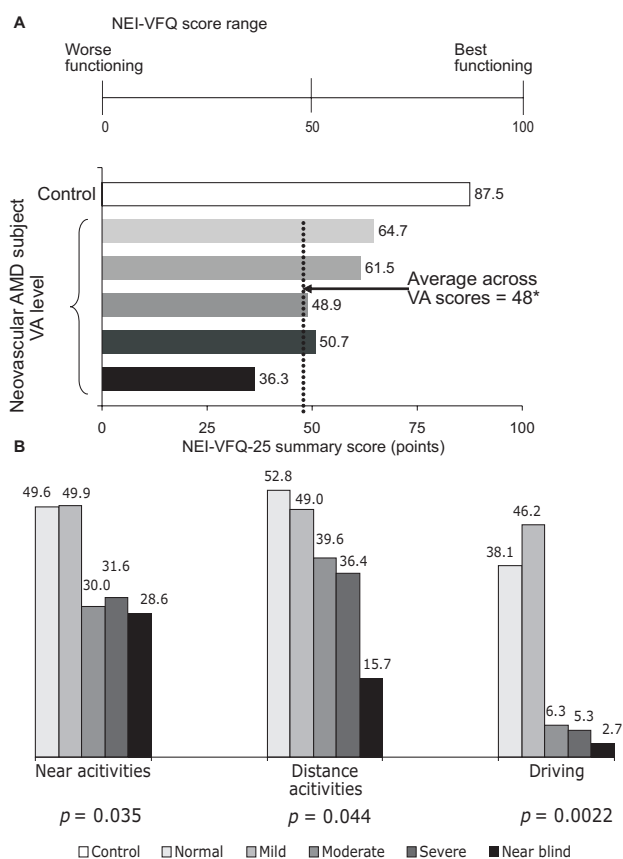


Fig. 1—Adjusted National Eye Institute Visual Function Questionnaire (NEI-VFQ-25) score (adjusted for age, sex, race, and comorbidities) of (A) summary scale by visual acuity (VA) of the better-seeing eye in neovascular age-related macular degeneration (AMD) subjects compared to controls and (B) different activities across neovascular AMD VA levels in better-seeing eye. (Normal, VA [ $>20/40$ ]; mild, VA [ $20/40$  to  $>20/80$ ]; moderate, VA [ $20/80$  to  $>20/200$ ]; severe, VA [ $20/200$  to  $>20/400$ ]; near blind, VA [ $\leq 20/400$ ]; \* $p = 0.0044$  across VA levels.)

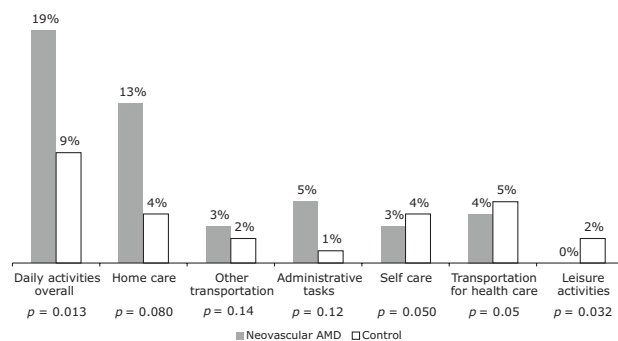


Fig. 2—Comparison of assistance with activities of daily living between study groups. (AMD, age-related macular degeneration.)

**Table 4—Mean annual health utilization cost\* per subject with neovascular age-related macular degeneration (AMD) compared with control subjects**

	Neovascular AMD, n = 67		Control, n = 99	
	Year 2005 (Can\$)	% of total cost	Year 2005 (Can\$)	% of total cost
Health care utilization cost				
Direct vision-related medical cost	6 314.47	55.71	72.62	5.1
Total visual rehabilitation-related costs	74.80	0.66	NA	NA
Total eyesight equipment-related costs	32.52	0.29	NA	NA
Total costs for eye doctor visits	104.71	0.92	36.22	2.6
Total eye glasses-related or contact lenses-related costs	40.24	0.36	36.41	2.6
Total retina specialist evaluation costs	272.31	2.40	NA	NA
Total diagnostic test-related costs	482.58	4.26	NA	NA
Total previous treatment of neovascular AMD-related costs	5 307.30	46.83	NA	NA
Direct non-vision-related medical cost	2 383.02	21.03	737.98	52.3
Total fall-related costs	138.14	1.22	44.33	3.1
Total other accidents-related costs	3.87	0.03	0.71	0.1
Total non-vision-related medical treatment costs	2 214.70	19.54	659.34	46.7
Total depression/anxiety-related treatment costs	26.31	0.23	33.60	2.4
Direct non-medical-related cost	2 636.24	23.26	601.02	42.6
Total living situation-related costs	240.68	2.12	0.00	0.0
Total costs of assistance for daily activities received	2 312.57	20.40	601.02	42.6
Total amount of social benefits received for visual disability	82.99	0.73	NA	NA
<b>Total cost per subject</b>	<b>11 333.72</b>	<b>100.00</b>	<b>1411.62</b>	<b>100.0</b>

\*Based on Canadian dollars in 2004 values indexed to Canadian dollars in 2005 values.  
Note: NA, not applicable.

**Table 5—Annual costs according to disease severity level (defined by visual acuity) of neovascular age-related macular degeneration**

Visual acuity	Mean direct vision-related medical cost (Can\$)	Mean direct non-vision-related medical cost (Can\$)	Mean direct non-medical-related cost (Can\$)	Mean overall cost (Can\$)
Normal/mild vision loss (n = 17)	9205.17	1450.32	0.00	10 655.49
Moderate vision loss (n = 21)	6903.42	2301.51	1465.14	10 670.07
Severe vision loss/nearly blind (n = 26)	4240.44	2843.02	4823.85	11 907.31
p value	0.43	0.44	0.11	0.95

of nonmedical costs by Bonastre et al.<sup>4</sup> was based on patient estimates of expenditures in contrast to our study, which collected cost data directly from the source. Our findings have implications for estimating total expenditures for prevention or treatment of neovascular AMD.

There are several limitations to this study. It included only clinics and subjects that were willing to participate, thus inducing a representation bias. Furthermore, the neovascular AMD population living in nursing homes was not included in the study, which may have led to an underestimation of the full burden and impact of neovascular AMD on the population.<sup>24</sup> Another limitation was the relatively small size of the neovascular AMD cohort, which may have affected some of the subgroup analysis.

We have documented that, in Canada, neovascular AMD is associated with a significant functional, emotional, and economic burden, highlighting the importance of early management of this disease. Subjects with neovascular AMD have significantly lower quality of life, poorer vision-related performance, more falls and fractures, greater reliance on caregivers, and higher health care resource utilization compared with a control group of subjects without the disease. Moreover, poorer vision was associated with increased use of assistance for ADL, higher levels of treatment for other

comorbidities, and greater total costs. Neovascular AMD constitutes a major public health priority for health care programs, thus it is vital to raise awareness of the humanistic aspects of neovascular AMD, as the burden of illness will only increase as the population ages. Early detection and treatment of neovascular AMD could significantly reduce the decline of VA, which would help to maintain a person's well-being and reduce health care-related costs over the lifetime.

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**Key words:** quality of life, health care resource utilization, visual acuity