Burden and Health Care Resource Utilization in Neovascular Age-Related Macular Degeneration

Findings of a Multicountry Study

Gisèle Soubrane, MD; Alan Cruess, MD; Andrew Lotery, MD; Daniel Pauleikhoff, MD; Jordi Monès, MD; Xiao Xu, PhD; Gergana Zlateva, PhD; Ronald Buggage, MD; John Conlon, PhD; Thomas F. Goss, PharmD

**Objective:** To describe the burden of bilateral neovascular age-related macular degeneration (NV-AMD) on patient-reported functioning and health resource utilization.

**Methods:** A cross-sectional study of 401 patients with bilateral NV-AMD and 471 elderly control subjects without AMD was conducted in 5 countries. Subjects completed a telephone survey, including the National Eye Institute 25-Item Visual Function Questionnaire, the EuroQol instrument, the Hospital Anxiety and Depression Scale, and history of falls, fractures, and health care resource utilization.

**Results:** The mean age for patients with NV-AMD was 78.1 years, and 65% were women. The patients reported 45% worse vision-related functioning, 13% worse overall well-being, and 30% more anxiety and 42% more depression symptoms than controls after adjusting for covariates (all, \( P < .001 \)). The effect of NV-AMD was also observed as a doubled fall rate (16% vs 8% \([ P < .001]\)) and a quadrupled need for assistance with daily activities (29% vs 7% \([ P < .001]\)) in the patients compared with controls.

**Conclusions:** The evidence of extensive decline in quality of life and increased need of daily living assistance for patients with NV-AMD compared with a control population substantiates the need for new treatments that prevent vision loss and progression to blindness.

*Arch Ophthalmol.* 2007;125(9):1249-1254

Author Affiliations:
Department of Ophthalmology, University Paris XII, Creteil, France (Dr Soubrane); Department of Ophthalmology and Visual Sciences, Dalhousie University, Halifax, Nova Scotia, Canada (Dr Cruess); Division of Clinical Neurosciences, University of Southampton, Southampton, England (Dr Lotery); Department of Ophthalmology, St Franziskus Hospital, Munster, Germany (Dr Pauleikhoff); Instituto de Microcirugía Ocular de Barcelona, Barcelona, Spain (Dr Monès); Covance Market Access Services Inc, Gaithersburg, Maryland (Drs Xu and Goss); Pfizer Ophthalmics, New York, New York (Drs Zlateva and Buggage); and Covance Inc, Princeton, New Jersey (Dr Conlon).

AGE-RELATED MACULAR DEGENERATION (AMD), the leading cause of severe visual loss in people older than 65 years, is a chronic, progressive macular disease that results in loss of central vision and significant functional impairment. Worldwide, 25 million to 30 million people have severe visual loss due to AMD. Neovascular (also termed exudative or wet) AMD (NV-AMD), which represents 10% to 15% of all AMD cases and accounts for 90% of AMD-related severe vision loss, results from abnormal angiogenesis beneath the retina (choroidal neovascularization).

The prevalence of late forms of AMD (defined as the presence of NV-AMD or geographic atrophy) ranges from 1.7% to 1.9% and increases exponentially with age. Choroidal neovascularization may be present before the onset of visual symptoms, and most patients with NV-AMD (hereinafter referred to as NV-AMD patients) experience progression to severe visual loss in the affected eye within 2 years of diagnosis. In addition, patients with choroidal neovascularization in one eye have a 43% probability of progression to NV-AMD in the fellow eye within 5 years. In general, visual impairment has been shown to affect an individual’s independence and physical, emotional, and social health. Patients with AMD-related visual impairment additionally experience restrictions in common activities of daily living such as reading and driving.

For editorial comment see page 1266

Incomplete documentation of the multifaceted consequences of NV-AMD limits our understanding of its effect and fundamentally undermines our ability as a society to make rational policy decisions when considering the value of alternative treatments. Although previous studies have evaluated, to a certain extent, the effect of AMD on quality of life (QOL), there has been no attempt to quantify the total burden of NV-AMD and its burden across countries. Data from such analysis can quantify the economic impact of NV-AMD and intercountry differences in NV-AMD management. The overall objectives of this study were to document the humanistic and economic consequences of NV-AMD in...
patients and to compare these consequences with findings in a similar group of subjects not affected by AMD (control subjects) by means of a simultaneous assessment in 5 countries. This article reports the humanistic burden of NV-AMD and related health care resource utilization (HRU). The economic consequences will be communicated subsequently.

METHODS

STUDY DESIGN

This cross-sectional, observational study included patients with bilateral subfoveal NV-AMD recruited from 31 retina specialist offices and clinics and non-AMD controls recruited from 30 general practitioner offices and clinics in Canada, France, Germany, Spain, and the United Kingdom. Because previous studies have shown that QOL and functional status impairment are correlated with visual acuity (VA) in the better-seeing eye,14-16 patients were required to have been diagnosed as having bilateral subfoveal NV-AMD. Controls had best-corrected Snellen VA of 20/40 or better and were free of any ocular abnormality that would impair VA. All subjects were at least 50 years of age and were excluded if they had participated in an investigational drug study within 30 days before the survey.

The protocol was approved by central and local accredited ethics committees and human investigation review boards of the participating institutions. No medical interventions or invasive procedures were required by the study protocol.

Site study staff identified potential subjects during routine office visits. Once the subjects provided written informed consent, they were asked to provide telephone contact information and a time when they could complete a standardized telephone survey. Trained interviewers administered the approximately 60-minute survey in the subject’s local language. Site study staff completed a case report form after a review of the subject’s medical record. The recorded data included the subject’s basic demographic information, VA, previous diagnostic test results, treatments for NV-AMD within the previous 24 months, prescribed equipment for eyesight and vision rehabilitation, comitant illnesses, and other ophthalmologic diagnoses or comorbidities. The timing of the interview and case report form completion was not sequenced. Information collected via the subject questionnaire and the case report form was not associated with a subject’s personal identifying information but was associated with a study-specific identifier assigned at enrollment to allow linking of individual subjects’ clinical and survey data in the analysis.

STUDY SURVEY

The survey included 3 validated QOL questionnaires. The National Eye Institute 25-Item Visual Function Questionnaire (NEI VFQ-25), a vision-specific QOL assessment relevant to multiple eye conditions, reflects 11 vision-related constructs plus a single general health rating question.17 Scores on the 12 resulting subscales range from 0 to 100, where 100 represents optimal QOL; the summary score is the average of the 11 vision-related subscale scores. The EuroQol instrument (EQ-5D) describes health-related QOL across the following 5 dimensions: mobility, self-care, performance of usual activities, pain or discomfort, and anxiety or depression.18 Health state valuation scores, calculated using relative weights (scoring coefficients) for each item, range from −0.59 to 1.00, with a higher score indicating better QOL.18 The Hospital Anxiety and Depression Scale (HADS) is designed to detect the presence and severity of anxiety and depression mood disorders and has been used extensively in a variety of patient populations.19 The HADS includes 14 items, of which 7 assess anxiety and 7 assess depression; subscale scores range from 0 to 21, with higher scores representing more symptoms and poorer emotional well-being. In addition, study-specific questions were developed to assess the occurrence of accidents and falls, related injuries and fractures, and HRU.

END POINTS AND STATISTICAL ANALYSIS

The primary end point was the humanistic impact of NV-AMD as measured by the difference between patients and controls in the NEI VFQ-23 summary scores. Other end points included QOL burden using the EQ-5D and HADS and disparity in HRU. We also examined differences in QOL outcomes between different VA levels.

Summary statistics were calculated, including means and standard deviations for continuous variables and frequency distributions for categorical variables. Visual acuity was analyzed as a continuous variable in logMAR (logarithm of the minimum angle of resolution) units. Mean QOL scores (NEI VFQ-25, EQ-5D, and HADS) with 95% confidence intervals (CIs) and continuous HRU variables were compared between patients and controls using analysis of covariance models with outcomes modeled as a function of the study group, controlling for age, sex, race, comorbidities, and country. Multiple logistic regression models that controlled for the same covariates and reported results as odds ratios with 95% CIs evaluated between-group differences in categorical outcomes. Mean QOL scores across the range of VA in the better-seeing eye (normal, >20/40; mild, 20/40 to >20/80; moderate, 20/80 to >20/200; severe, 20/200 to >20/400; and near blindness, ≤20/400) were compared using analysis of covariance models, adjusting for covariates.

Statistical significance was evaluated at the .05 level, with no adjustments for multiple comparisons. The data were held and analyzed by Covance Inc under the direction of the statistical consultancy group. All analyses were performed using PC-SAS statistical software, version 9.1 (SAS Institute, Cary, North Carolina).

RESULTS

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS

Data were collected from April 1 through October 28, 2005, for 401 NV-AMD patients and 471 controls. The subject demographic and clinical characteristics are summarized in Table 1. The patient group was older than the control group (mean age, 78.1 vs 63.8 years [P < .001]); had higher percentages of women, white subjects, and subjects living alone; and had a worse mean VA in the better-seeing eye. A higher percentage of patients had vision-related comorbidities (glaucoma and cataract), whereas a higher percentage of controls had other comorbidities, including anxiety disorder and arthritis and rheumatism.

QOL DIFFERENCES BETWEEN STUDY GROUPS

The NV-AMD patients had significantly reduced QOL as measured by the validated questionnaires (Figure 1). The relative difference for the primary end point of NEI VFQ-25 overall scale scores was 49% favoring controls. The adjusted mean score of 48.7 in patients was substantially worse than that of 89.1 in controls (P < .001).

(Reprinted) Arch Ophthalmol. 2007;125(9):1230-1241. ©2007 American Medical Association. All rights reserved.

Downloaded From: by a Non-Human Traffic (NHT) User on 10/23/2018
Neovascular AMD had a negative impact on general QOL as reflected by the 13% relative difference in EQ-5D health state valuation scores (adjusted mean score, 0.65 vs 0.75 \[P < 0.001\]). Patients reported significantly higher anxiety (30% relative difference) and depression (42% relative difference) scores compared with controls (adjusted mean anxiety scores, 6.7 vs 4.7 \[P < 0.001\]; depression scores, 7.1 vs 4.1 \[P < 0.001\]).

Because patients were on average 14 years older than controls and given that the study intended to have a comparably aged control sample, a post hoc analysis on 2 age-matched control subgroups (\( \geq 70 \) years \[n = 128; \text{mean age, 75 years}\] and \( \geq 75 \) years \[n = 54; \text{mean age, 78 years}\]) examined the relationship between age and the 3 QOL measures. Results of subgroup analyses paralleled those reported in the overall analysis (Table 2), indicating that age had no direct impact on study findings. When QOL outcomes between patients (\( n = 136\)) and controls (\( n = 85\)) who had no other comorbidities were compared, results also were similar to those for the overall sample (Table 2).

### IMPACT OF REDUCED VA ON QOL MEASURES

Using the vision-specific NEI VFQ-25, we detected a clear trend of decreasing QOL scores associated with decreasing VA. Vision loss secondary to NV-AMD was significantly associated with reduced NEI VFQ-25 summary and physical functioning scores and with worse HADS depression subscale scores (\( P < .001\) for all). Compared with a mean NEI VFQ-25 summary scale score of 89.1 in controls, patients demonstrated decreasing scores that correlated with the severity of vision loss from 62.4 (normal VA) to 39.4 (near blindness) (Figure 2A). Similar trends were observed in the 3 NEI VFQ-25 physical functioning scales (Figure 2B) and the HADS depression subscale score (Figure 2C). However, no direct relationship was observed between severity of vision loss and HADS anxiety subscale scores or EQ-5D scores (a general QOL measure) (Figure 2C and D).

### AMD-ASSOCIATED COMORBIDITIES

As is common in the low-vision population,20 patients reported more falls and fall-related fractures than did controls. The percentage of patients who had fallen in the past 12 months was twice that reported by controls (16.0% vs 8.3% \[P < 0.001\]). After adjusting for covariates, patients still had a doubled higher fall rate (odds ratio, 2.0 \[P = 0.02\]), with more than half requiring medical treatment. In addition, although a similar percentage of subjects in each group (16.0% in the NV-AMD group, 16.3% in the control group) reported receiving depression or anxiety treatment in the past 12 months, patients reported a significantly longer duration of treatment than did controls (adjusted mean, 9.5 [95% CI, 8.4-10.7] vs 7.8 [95% CI, 6.8-8.8] months \[P = .03\]).

### USE OF HEALTH CARE RESOURCES

The NV-AMD patients frequently required low-vision rehabilitation and received social benefits. One-third reported visits to ophthalmologists and optometrists in addition to their retina specialist. Nearly half of the patients who had no other comorbidities were compared, results also were similar to those for the overall sample (Table 2).

### Table 1. Demographic and Clinical Characteristics of Study Sample

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>NV-AMD Patients (n = 401)</th>
<th>Control Subjects (n = 471)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>Mean (SD)</td>
<td>78.1 (6.9) vs 63.8 (8.4)</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>79 vs 63</td>
</tr>
<tr>
<td></td>
<td>Range</td>
<td>53-95 vs 50-88</td>
</tr>
</tbody>
</table>
| Sex, No. (%)
| Male                                  | 140 (34.9) vs 202 (42.9) |
| Female                                | 260 (64.8) vs 267 (56.7)  |
| Race, No. (%)
| White                                 | 397 (99.0) vs 422 (89.6) |
| Black                                 | 0 vs 5 (1.1)              |
| Asian                                 | 0 vs 6 (1.3)              |
| Other                                 | 2 (0.5) vs 25 (5.3)       |
| Country                               |                          |                           |
| Canada                                | 67 (16.7) vs 99 (21.0)   |
| France                                | 87 (21.7) vs 92 (19.5)   |
| Germany                               | 83 (20.7) vs 93 (19.7)   |
| Spain                                 | 89 (22.2) vs 96 (20.4)   |
| United Kingdom                        | 75 (18.7) vs 91 (19.3)   |
| Living situation in the past
| 12 mo, No. (%)
| Living with spouse or family member  | 269 (67.1) vs 376 (79.8) |
| Living alone                          | 118 (29.4) vs 94 (20.0)  |
| Living in assisted living facility or nursing home | 15 (3.7) vs 5 (1.1) |
| Current best corrected VA in better seeing eye, logMAR U
| Mean (SD)                             | 0.6 (0.7) vs 0.1 (0.7)   |
| Median                                | 0.7 vs 0                   |
| Range                                 | 0-2 vs -0.2-0.4           |
| Comorbid diseases, No. (%)\(^b\)
| Cataract                              | 92 (22.9) vs 25 (5.3)    |
| Glaucoma                              | 32 (8.0) vs 5 (1.1)      |
| Cancer                                | 33 (8.2) vs 22 (4.7)     |
| Stroke                                | 14 (3.5) vs 5 (1.1)      |
| Substance use disorder                | 8 (2.0) vs 1 (0.2)       |
| Diabetes                              | 40 (10.0) vs 74 (15.7)   |
| Low vision due to other reasons       | 2 (0.5) vs 53 (11.3)     |
| Anxiety disorder                      | 15 (3.7) vs 51 (10.8)    |
| Asthma                                | 11 (2.7) vs 26 (5.5)     |
| Arthritis and rheumatism              | 44 (11.0) vs 87 (18.5)   |

Abbreviations: logMAR, logarithm of the minimum angle of resolution; NV-AMD, neovascular age-related macular degeneration; VA, visual acuity.
\(^a\) Column percentages may not add up to 100% because of missing data.
\(^b\) Categories are not mutually exclusive. Not all comorbid diseases assessed are listed. Differences between study groups are statistically significant (\( P < .05\) for all listed comorbidities. Other comorbid diseases assessed included depression, chronic obstructive pulmonary disease, headache, chronic neck or back pain, heart disease, and sleep disturbance.

(45.1%) were referred for low-vision rehabilitation; 34.7% attended rehabilitation; 42.6% were prescribed vision-enhancing equipment; and 9.7% received social benefits, including disability and pension, housing and tax benefit, and transportation subsidies.

A significantly higher percentage of patients reported receiving assistance with activities of daily living than did controls (28.9% vs 6.6% \[P < .001\]), and 3.6 times more patients received assistance with activities of daily living in general. The odds of needing help with administrative tasks (eg, paying bills and scheduling appointments) was almost 17 times higher in patients (odds
Outcomes for the primary end point did not differ significantly across countries. The adjusted mean NEI VFQ–25 overall scale score for patients and controls were 48.0 vs 87.5 for Canada, 44.4 vs 91.8 for France, 51.3 vs 96.3 for Germany, 56.5 vs 92.6 for Spain, and 52.7 vs 96.7 for the United Kingdom (P < .001 for each). Results on the EQ-5D and HADS were similar across the countries.

**INTERCOUNTRY DIFFERENCES**

Outcomes for the primary end point did not differ significantly across countries. The adjusted mean NEI VFQ–25 overall scale scores for patients and controls were 48.0 vs 87.5 for Canada, 44.4 vs 91.8 for France, 51.3 vs 96.3 for Germany, 56.5 vs 92.6 for Spain, and 52.7 vs 96.7 for the United Kingdom (P < .001 for each). Results on the EQ-5D and HADS were similar across the countries.

**COMMENT**

To our knowledge, this AMD burden-of-illness study is the first major multinational study to simultaneously assess the consequences of NV-AMD through clinical assessments and patient-reported QOL and HRU measures. We found that patients with bilateral NV-AMD reported substantially worse QOL, poorer vision-related functioning, and more anxiety and depression symptoms compared with controls without AMD. These results were consistent across all 5 countries.

The NEI VFQ–25 scale scores reported by controls in this study were similar to those of reference groups with comparable eye conditions reported in the NEI VFQ–25 development study and the Submacular Surgery Trials report. In the present study, patients had an unadjusted mean NEI VFQ–25 overall score of 46 (95% CI, 44–48), which was significantly worse than that of the controls and slightly lower than that of patients with bilateral NV-AMD reported in other studies (score range, 50–82). Because the only prior study reporting the mean NEI VFQ overall scale score by VA grouped patients by different acuity ranges, it is difficult to determine whether differences in VA explain the lower score observed herein relative to other published studies.

Among patients, those with lower VA levels reported significantly worse NEI VFQ–25 scores, particularly in the functional areas of general vision, physical function-
ing, near activities, distance activities, driving, and peripheral vision. The Submacular Surgery Trials also documented declining NEI VFQ scale scores across VA levels of 20/20 to 20/40, 20/50 to 20/160, and 20/200 to 20/800, except for the peripheral vision subscale. 21 At one time it was believed that NV-AMD patients function well as long as they have a good VA in 1 eye. To further explore the effect of NV-AMD on vision-related functioning, we matched patients with normal VA in the better-seeing eye to a subgroup of controls by VA and conducted a post hoc analysis. Even with normal VA in the better-seeing eye, patients reported substantially worse vision-related functioning than did controls (mean NEI VFQ-25 overall scale scores, 62.5 vs 91.8 \[P<.001\]).

Hayshow that NV-AMD has severe negative consequences for patient functioning, even in patients with good VA in 1 eye. These data dispute an earlier recommendation 24 of initiating NV-AMD therapy only at the onset of choroidal neovascularization in the second eye and instead support a strong clinical rationale for detecting and treating NV-AMD early.

In addition to worse vision-related functioning, patients reported significantly more anxiety and depression symptoms than did controls. The HADS has not previously been used in AMD patients. Compared with those with cataract, 25 NV-AMD patients in our study reported slightly fewer anxiety symptoms (HADS anxiety observed score, 6.4 vs 6.9-7.2) and more depression symptoms (HADS depression observed score, 6.6 vs 4.5-4.6). Further, with increasingly more severe vision loss, NV-AMD patients reported more depression symptoms in the present study.

Although patients reported significantly worse EQ-5D health state valuation scores than controls, there was no association between health state valuation scores and VA level. This finding is consistent with another AMD study, 20 in which the EQ-5D, a general measure of QOL, was assessed by VA level with no discernible trend reported and may suggest that the EQ-5D is insensitive for measuring difference across VA levels. At the time of the study design, we believed the EQ-5D would be a suitable measure, given its length (5 items only) and established psychometric properties in other chronic diseases. The information suggesting the inadequacy of EQ-5D as a utility measure in the population of patients with AMD was not known at the time of study design; however, we recognize the limitation of this utility measure now. Although there are alternative measurement methods for assessing patient utility, they would have been difficult to implement in this study, given likely resource limitations in the physician practices selected and other limits based on the overall study design and implementation strategy, including telephone interview of study subjects.

Besides worse functioning and well-being, the NV-AMD patients also reported more falls and needed more assistance related to activities of daily living than controls. Poor VA has been shown to approximately double an individual's risk of falling, and poor vision may be responsible for 25% to 50% of all falls. 20,27 In the present study, twice as many patients as controls reported a fall in the preceding 12 months, and the percentage of patients receiving assistance with daily activities was 4 times higher. Together, these findings suggest that preserving vision in NV-AMD patients through earlier intervention will help preserve their independence and functioning.

There are several limitations to this study. First, only practices that wanted to participate were included, and it is possible that these sites may differ in unknown ways.

**Figure 2.** Adjusted mean differences in quality-of-life outcomes across neovascular age-related macular degeneration (NV-AMD) severity levels in the better-seeing eye. Quality of life is measured by the National Eye Institute 25-Item Visual Function Questionnaire (NEI VFQ-25) summary scores (A) and NEI VFQ-25 physical functioning scores (B), the Hospital Anxiety and Depression Scale (HADS) scores (C), and the EuroQol health state valuation scores (D). Differences are adjusted for age, sex, race, comorbidities, and country.

©2007 American Medical Association. All rights reserved.
This study provides evidence that bilateral, subfoveal NV-AMD has a significant emotional and functional impact on patients, providers, and society overall. Patients with bilateral NV-AMD reported substantially worse QOL, poorer vision-related functioning, more anxiety and depression, more falls and fractures, greater dependency on caregivers, and higher HRU compared with controls. Given the humanistic and HRU burden, we expect the economic consequences of NV-AMD to be considerable; to test this hypothesis, our empirical data concerning HRU and NV-AMD management across countries is being used to model the economic consequences of NV-AMD. The strong association between deteriorating VA and continuous decline in QOL speaks to the need for early detection and treatment of NV-AMD to arrest VA loss and preserve the patient’s independent functioning and well-being. Effective therapies for the management of NV-AMD are in development, and it is essential to raise awareness of the burden of NV-AMD to ensure that the consequences of the disease are given full consideration when decisions that affect patient access to therapy are made.

Submitted for Publication: August 4, 2006; final revision received December 13, 2006; accepted December 16, 2006.

Correspondence: Gisèle Soubrane, MD, Department of Ophthalmology, University Paris XII, Centre Hospitalier Intercommunal de Créteil, 40 Avenue de Verdun, Créteil, France (gisèle.soubrane@chicreteil.fr).

Financial Disclosure: Drs Soubrane, Crueu, Lotery, Pauleikhoff, and Mones were investigators in the present study and received compensation from Pfizer Inc for their work. Drs Xu, Goss, and Conlon are employees of Covance Inc, the company that held the contract for conducting the study funded by Pfizer Inc. Drs Zlateva and Buggage are employees of Pfizer Inc and own Pfizer Inc stock and stock options.

Funding/Support: This study was supported by Pfizer Inc.

CONCLUSIONS

This study provides evidence that bilateral, subfoveal NV-AMD has a significant emotional and functional impact on patients, providers, and society overall. Patients with bilateral NV-AMD reported substantially worse QOL, poorer vision-related functioning, more anxiety and depression, more falls and fractures, greater dependency on caregivers, and higher HRU compared with controls. Given the humanistic and HRU burden, we expect the economic consequences of NV-AMD to be considerable; to test this hypothesis, our empirical data concerning HRU and NV-AMD management across countries is being used to model the economic consequences of NV-AMD. The strong association between deteriorating VA and continuous decline in QOL speaks to the need for early detection and treatment of NV-AMD to arrest VA loss and preserve the patient’s independent functioning and well-being. Effective therapies for the management of NV-AMD are in development, and it is essential to raise awareness of the burden of NV-AMD to ensure that the consequences of the disease are given full consideration when decisions that affect patient access to therapy are made.

Submitted for Publication: August 4, 2006; final revision received December 13, 2006; accepted December 16, 2006.

Correspondence: Gisèle Soubrane, MD, Department of Ophthalmology, University Paris XII, Centre Hospitalier Intercommunal de Créteil, 40 Avenue de Verdun, Créteil, France (gisèle.soubrane@chicreteil.fr).

FINANCIAL DISCLOSURE: Drs Soubrane, Crueu, Lotery, Pauleikhoff, and Mones were investigators in the present study and received compensation from Pfizer Inc for their work. Drs Xu, Goss, and Conlon are employees of Covance Inc, the company that held the contract for conducting the study funded by Pfizer Inc. Drs Zlateva and Buggage are employees of Pfizer Inc and own Pfizer Inc stock and stock options.

FUNDING/SUPPORT: This study was supported by Pfizer Inc.

REFERENCES


