# Depression, Visual Acuity, Comorbidity, and Disability Associated with Age-related Macular Degeneration

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***Objective:*** To examine (1) the prevalence of depressive disorders in community-dwelling adults with advanced age-related macular degeneration (AMD) and (2) the relationship in this population between depression, visual acuity, the number of comorbid medical conditions, disability caused by vision loss as measured by the National Eye Institute-Vision Function Questionnaire (NEI-VFQ) and the vision-specific Sickness Impact Profile (SIPV), and disability caused by overall health status as measured by the Sickness Impact Profile-68 (SIP).

***Design:*** Analysis of cross-sectional baseline data from a randomized clinical trial.

***Participants:*** Participants were 151 adults aged 60 and older (mean age, 80 years) with advanced macular degeneration whose vision was 20/60 or worse in their better eye.

***Methods:*** Subjects were interviewed using measures of depression, disability, and chronic medical conditions. Visual acuity was obtained. Nonparametric correlation analyses and linear regression analyses were performed.

***Main Outcome Measures:*** Structured Clinical Interview for DSM-IV (SCID-IV), Geriatric Depression Scale (GDS), NEI-VFQ, SIPV, and SIP.

***Results:*** Of the participants, 32.5% (n = 49) met SCID-IV criteria for depressive disorder, twice the rate observed in previous studies of community-dwelling elderly. Over and above depression (GDS), visual acuity aided in prediction of the level of vision-specific disability (NEI-VFQ and SIPV).

***Conclusions:*** Depressive disorder is a significant problem for the elderly afflicted with advanced macular degeneration. Further research on psychopharmacologic and psychotherapeutic interventions for depressed AMD patients is warranted to improve depression and enhance functioning. Over and above depression, visual acuity aided in predicting vision-specific disability. Treatment strategies that teach patients to cope with vision loss should be developed and evaluated. *Ophthalmology 2001;108:1893–1901 © 2001 by the American Academy of Ophthalmology.*

Age-related macular degeneration (AMD) is the leading cause of vision loss and blindness in people over the age of 65.[1] Recent research[2,3] documents that AMD is associated with significant psychologic distress and reduced function, comparable to that of other serious chronic illnesses. Furthermore, patients with heterogeneous eye diseases referred to a low vision clinic reported high levels of depression,[4–7] and depressed low vision elderly were found to have disability independent of vision-related limitations.[8] Untreated depression has been linked to worsened functioning (disability), immunoendocrine dysregulation, greater likelihood of institutionalization, and increased mortality.[9–14] With the development of successful treatments for depressive disorders,[15,16] increased recognition and treatment of depression among elderly patients with AMD may improve outcomes and contribute to improved quality of life for these patients.[17,18]

The purpose of this article is to examine (1) the prevalence of depressive disorders in older community-dwelling adults with AMD and (2) the relationship in this population between depression, visual acuity, the number of comorbid medical conditions, and disability. In this article, disability is defined in terms of vision-specific and general health-related limitations. Vision-specific disability is defined in terms of the subjects' scores on the National Eye Institute Vision Function Questionnaire (NEI-VFQ) and vision-specific Sickness Impact Profile (SIPV). General health-related disability is defined as measured in terms of the scores on the Sickness Impact Profile-68 (SIP).

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## Material and Methods

### Participants

Participants in this study were community volunteers enrolled between February 1998 and September 1999. This article examines screening and baseline data from a randomized clinical trial to further test the effects of a psychosocial intervention[3] for people with advanced AMD. Individuals were recruited who met the following inclusion and exclusion criteria: (1) diagnosis by an ophthalmologist of AMD confirmed by fundus photographs; (2) visual acuity of 20/60 or worse in the better eye and 20/100 or worse in their other eye with habitual correction (i.e., current glasses); (3) no other unstable eye disease or vision loss caused by another eye disease; (4) age 60 or older; (5) adequate hearing, with a hearing aid if necessary, to complete the interview and to respond in normal conversation; (6) physical ability to come to an interview if wheelchair access transportation were provided; (7) no cognitive impairment as assessed by the Orientation-Memory Concentration Test,[19] and (8) no current alcohol abuse as assessed by the Short Michigan Alcoholism Screening Test.[20]

Overall, 151 of the 204 patients screened met the preceding criteria. Fifty-three (26%) potential subjects were excluded during screening for the one of the following reasons: another eye disease was responsible for vision-loss (n = 6; 2.9%), visual acuity was better than 20/60 (n = 6; 2.9%), cognitive impairment (n = 13; 6.4%), hearing impairment (n = 2; 1%), other health problems limiting mobility (n = 2; 1%), moved out of the area (n = 5; 2.5%). Nineteen otherwise eligible volunteers were not interested after learning the requirements for participation. The 151 study participants and the 19 people who declined participation were similar in demographic and clinical characteristics.

### Design and Procedures

The protocol for this study was approved by the University's institutional review board, and informed consent was obtained. Data used in this study came from interviews conducted by a clinical psychologist and research assistants using the measures described in the following section. Trained personnel measured each patient's visual acuity with habitual correction (i.e., current glasses) using Snellen chart ratings in an examination room with standardized lighting conditions. Subjects were encouraged to use their peripheral sight for this examination. All data were double entered.

### Measures

#### Measures of Depression

*The Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Axis I, Fourth (IV) Edition, Research Version–(SCID-IV).* To identify subjects with depressive disorder, portions of the Mood Episodes section (Module A) and the Global Assessment of Function Scale of the SCID-IV[21] were used to determine the diagnoses of current major depression, minor depression, and subsyndromal symptomatic depression. In accord with the standardized methodology, major depression was diagnosed when five or more of the following depressive symptoms were elicited: depressed mood, loss of interest or pleasure in all or almost all usual activities, weight change, sleep disturbance, psychomotor agitation or retardation, decreased energy, feelings of worthlessness or inappropriate guilt, difficulty with concentration, or suicidal ideation. To meet criteria, one of the five symptoms must be either depressed mood or loss of interest or enjoyment in usual activities, and all symptoms had to be present for most of the day every day for 2 weeks or longer.[22] Minor depression was diagnosed when subjects had at least two of the preceding symptoms of depression but less than five (with one of the symptoms being either depressed mood or loss of interest), and otherwise met the preceding criteria for major depression.[22] Subsyndromal symptomatic depression was identified when subjects had two or more simultaneous symptoms of depression listed previously, other than depressed mood or lack of interest or enjoyment of usual activities, lasting for at least 2 weeks and that interfered with daily life.[23]

*Geriatric Depression Scale (GDS).* To complement the SCID-IV, which is the "gold standard" for the diagnosis of depression, the short version of the GDS[24] was used to assess the severity of depressive symptoms. Scores range from 0 to 15 points, with a score of 5 or more indicating significant depressive symptoms. The GDS has been shown to be a valid and reliable indicator of depressive symptoms.[25–27] In this population the GDS provided similar results to the SCID-IV and allowed us to use a wider range of statistical tests (the SCID-IV being essentially binary). It was not known (a priori) that the SCID-IV and the GDS would behave the same in this population, although this was to be the case.

#### Measures of Disability

*Sickness Impact Profile (SIP).* The SIP (68-item version)[28,29] was administered to measure functional limitations caused by general health status. Scores are calculated by adding the number of items answered affirmatively (i.e., those for which a deficit was identified), with higher scores indicating greater disability. Scores range from 0 to 68. Reliability and validity have been established.[30–32]

*Vision-Specific Sickness Impact Profile (SIPV).* To determine functional limitations caused by vision, the vision-specific SIP[33] was used. The SIPV was derived directly from the SIP. For any question answered affirmatively on the SIP, the subject was asked if he or she believed that the reported deficit was caused by visual dysfunction. As with the SIP, higher SIPV scores mean greater disability as a result of vision loss.

*National Eye Institute Visual Function Questionnaire (NEI-VFQ).* The NEI-VFQ (25 with appendices)[34] also was used to assess impairment in vision-related functioning. The 12 NEI-VFQ subscales are self-rated general health, overall vision, difficulty with near vision activities, difficulty with distance vision activities, limitations in social functioning because of vision, role limitations because of vision, increased dependency because of vision, mental health limitations caused by vision, driving difficulties, limitations with peripheral vision, limitations in color vision, and ocular pain. An overall summary scale (NEI-VFQ) was created using the average of the 12 subscales. As with the subscales, the total score ranges from 0 to 100, where 0 represents the worst possible functioning and 100 the best.

#### Measure of Vision

*Visual Acuity.* Visual acuity of the better eye, worse eye, and weighted acuity of both eyes (0.75 better eye and 0.25 worse eye)[35] were obtained using the Snellen chart. Snellen ratings were then converted to the logarithm of the minimum angle of resolution (LogMAR) scale,[36] which is a logarithmic scale on which an increase of 1 point represents a 10-fold drop in vision on the Snellen scale. Whereas 20/20 refers to normal vision and 20/200 to legal blindness on the Snellen scale, using the LogMAR scale, a measurement of 0.0 represents normal vision and 1.0 legal blindness. Vision levels classified as counting fingers, hand motion, light perception, and no light perception were assigned visual acuity (LogMAR) values of 20/4000 (2.301), 20/8000 (2.602), 20/16000 (2.903), and 20/32000 (3.204), respectively.[35]

#### Measure of Demographic and Health Characteristics and Co-Morbidity

*Health and Impact Questionnaire.* Participants were asked about their general health and the impact of macular degeneration on their lives using the Health and Impact Questionnaire. This is a

Table 1. Demographic Characteristics of Age-related Macular Degeneration Subjects

| | Depressed Group N = 49 | | Nondepressed Group N = 102 | | | Overall N = 151 | |
|---|---|---|---|---|---|---|---|
| | *Mean* | *(Standard Deviation)* | *Mean* | *(Standard Deviation)* | Wilcoxon P Value | *Mean* | *(Standard Deviation)* |
| Age | 80.63 | (5.79) | 79.86 | (6.42) | 0.571 | 80.11 | (6.21) |
| Years of education | 13.71 | (2.99) | 14.17 | (2.86) | 0.648 | 14.02 | (2.9) |
| | *Count* | *(%)* | *Count* | *(%)* | *Fisher exact P value (2-sided)* | *Count* | *(%)* |
| Hollingshead social scale | | | | | | | |
| Level 1 (major business or professional) | 10 | (20.4%) | 21 | (20.6%) | 0.639 | 31 | (20.5%) |
| Level 2 (medium business or professional) | 17 | (34.7%) | 40 | (39.2%) | | 57 | (37.7%) |
| Level 3 (skilled worker) | 12 | (24.5%) | 27 | (26.5%) | | 39 | (25.8%) |
| Level 4 (semiskilled worker) | 9 | (18.4%) | 14 | (13.7%) | | 23 | (15.2%) |
| Level 5 (unskilled) | 1 | (2%) | 0 | (0.00%) | | 1 | (0.07%) |
| Gender | | | | | | | |
| Male (%) | 17 | (34.7%) | 32 | (31.4%) | 0.713 | 49 | (32.5%) |
| Female (%) | 32 | (65.3%) | 70 | (68.6%) | | 102 | (67.5%) |
| Marital status | | | | | | | |
| Currently married | 19 | (38.8%) | 40 | (39.2%) | 1 | 59 | (39.1%) |
| Not currently married | 30 | (61.2%) | 62 | (68.6%) | | 92 | (60.9%) |
| Living arrangement | | | | | | | |
| Lives alone | 20 | (40.8%) | 39 | (38.2%) | 0.859 | 59 | (39.1%) |
| Lives with at least 1 other person | 29 | (59.2%) | 63 | (61.8%) | | 92 | (60.9%) |

medical history including questions on current medical conditions, medications, living arrangements, education, and principal occupation of the subject and of the main wage earner (spouse) if other than the subject. The principal occupation and education of the main wage earner are used in the Hollingshead Two Factor Index of Social Position.[37] To summarize the impact of comorbid medical conditions, a count of reported chronic medical conditions was used.[38] Conditions included in the count were hypertension, diabetes mellitus with current use of insulin or oral medication, previous myocardial infarction, previous stroke, cancer, chronic obstructive pulmonary disease, thyroid condition with use of medication, congestive heart failure, and arthritis with use of medication.

### Statistical Analysis

All statistical analyses were carried out using SPSS (SPSS Inc, Chicago, IL).[39] Descriptive analyses were performed to characterize the demographic and clinical characteristics of the sample as a whole and the depressed and nondepressed subgroups. The Wilcoxon rank-sum test and Fisher's exact test were used to examine demographic and clinical differences between the depressed and the nondepressed groups. To examine the various associations between depression, visual acuity, comorbid medical conditions, and vision-specific and illness-related disability, Spearman correlations were used. A correlation of 0.45 or higher was considered strong, between 0.30 and 0.449 was moderate, and between 0.10 and 0.299 was weak. Along with each Spearman correlation, the corresponding 95% confidence interval (CI) also was reported. The width of the 95% CIs for each correlation backed up the (a priori) qualitative measurements of strong, marginal, and weak (defined previously). The Wilcoxon rank-sum test was used with dichotomous variables (e.g., SCID-IV). To determine whether visual acuity and/or comorbidity added anything (over and above depression) to the prediction of vision-specific and general illness disability, linear regression was used to control for the effect of depression, and Spearman correlation was used to assess the association between disability, number of comorbid conditions, and visual acuity.

## Results

### Descriptive Analyses

As shown in Table 1, subjects were similar in age, ethnicity, and gender to those most likely to have advanced AMD. Almost 40% of the subjects were married at the time of the interview, and more than half of the subjects (61%) lived with at least one other person.

As shown in Table 2, visual acuity ranged from 20/60 to 20/8000. The median visual acuity was 20/200 (legally blind) in the better eye. Wilcoxon tests were performed to compare the disability scores of subjects with wet and dry AMD. Although there was significant difference between wet and dry AMD in terms of their visual acuity score (Wilcoxon $P = 0.005$), there were no statistically significant differences in terms of their disability scores: SIP (dry mean, 12.12; wet mean, 10.77; Wilcoxon *P*, 0.286), SIPV (dry mean, 7.48; wet mean, 7.32; Wilcoxon *P*, 0.839), NEI-VFQ (dry mean, 58.86; wet mean, 55.58; Wilcoxon *P*, 0.115).

Seventy-eight percent (n = 119) of the subjects reported having at least one comorbid condition in addition to AMD for which he or she was receiving medical care. The mean number of these comorbid medical conditions reported was 1.33 (standard deviation, 1.02). The most frequently reported comorbid conditions were hypertension (32%), heart disease (14%), thyroid disorder with medication (10%), and cancer (8%); together these represented 64% of all reported comorbid conditions.

Almost one third of the subjects (n = 49; 32.5%) met the SCID-IV diagnostic criteria for depression; 11 (7.3%) had major depression, 30 (19.9%) had minor depression; and 8 (5.3%) had subsyndromal depression.

A Wilcoxon test was performed to compare the findings on SCID-IV with the GDS scores. The results showed a significant difference (Wilcoxon $P < 0.001$) between depressed and nondepressed subjects in terms of their GDS scores. The depressed subjects on average had a higher mean GDS score (5.86, representing significant depressive symptoms under GDS criteria) than the nondepressed subjects (1.88, nonsignificant depressive symp-

toms under GDS criteria). This finding supported the claim that GDS and SCID gave similar results.

Table 1 compares the demographic characteristics of depressed and nondepressed subjects based on SCID-IV. No significant differences in demographic characteristics were observed between the depressed and nondepressed subgroups. Table 2 compares the clinical characteristics of depressed and nondepressed subjects based on SCID-IV. The presence of depressive disorder on SCID-IV was highly associated with greater vision-specific and general health-related disability. (Wilcoxon rank-sum statistic for differences in the level of disability between the depressed and nondepressed subgroups revealed a difference on the SIP [$P < 0.001$], SIPV [$P < 0.001$], and NEI-VFQ average [$P < 0.001$].)

Four of 32 subjects (13%) with no comorbid conditions compared with 45 of 119 (38%) with one or more comorbid conditions were depressed. Fisher's exact test of comorbidity (none versus one or more) across the depressed and nondepressed subgroups found a significant difference in comorbidity reported by the two groups ($P < 0.01$).

As shown in Table 2, the depressed group had worse visual acuity in the better eye than did the nondepressed group.

### Correlation Analyses

To examine the relationship between depression, visual acuity, the number of comorbid medical conditions, and vision-specific and health-related disability, a series of Spearman correlations were computed (see Table 3). The findings demonstrated a strong association between the extent of depressive symptoms (GDS) and the level of disability (i.e., subjects reporting more depressive symptoms were also more likely to report that they had more restrictions because of their vision and more limitations because of their general health) (NEI-VFQ, Spearman = −0.514 [95% CI −0.675, −0.353]; SIPV, Spearman = 0.458 [95% CI 0.297, 0.619]; SIP, Spearman = 0.526 [95% CI 0.365, 0.687]).

Visual acuity correlated moderately to weakly with disability specific to vision loss (NEI-VFQ, Spearman = −0.407 [95% CI −0.568, −0.246]; SIPV, Spearman = 0.211 [95% CI 0.05, 0.375]). Analysis showed that visual acuity was only weakly associated with participants' limitations caused by the impact of their overall health status (SIP, Spearman = 0.121 [95% CI −0.04, 0.282]).

There was little to suggest a direct association between the number of comorbid conditions and disability in this population, because subjects with more comorbid conditions were only marginally more likely to report greater disability as a result of their overall health (SIP Spearman = 0.299 [95% CI 0.138, 0.460]). The correlation between number of comorbid conditions and vision-related disability was also weak (NEI-VFQ Spearman = −0.215 [95% CI −0.376, −0.054]; SIPV Spearman = 0.201 [95% CI 0.04, 0.362]).

The correlation between visual acuity and depression (Spearman = 0.119 [95% CI −0.042, 0.280]) was weak, and the difference in visual acuity between the depressed and nondepressed subgroups was slight although statistically significant (mean difference = 0.173; $P = 0.047$). This further suggested little in the way of direct association between visual acuity and depression.

### Regression Analyses

To address whether visual acuity or comorbidity aided in predicting the level of disability, over and above depression, a series of linear regressions were performed to remove the effect of depression (GDS) from the disability scores (NEI-VFQ, SIPV, SIP). After each regression was completed, the residuals were examined for association with either visual acuity or comorbidity. In this way, each regression served to remove the effect of depression on the corresponding disability score, and any correlation between what remained (i.e., the residuals) and either visual acuity or comorbidity reflected information about the disability score held by visual acuity or comorbidity over and above the level of depression.

The results showed that visual acuity was at most weakly correlated with the residuals from the regression between SIP and GDS (Spearman = 0.085 [95% CI −0.088,0.228]), weakly correlated with the residuals from the regression between SIPV and GDS (Spearman = 0.210 [95% CI 0.046, 0.365]), and moderately to strongly correlated with the residuals from the regression between NEI-VFQ and GDS (Spearman = −0.442 [95% CI −0.564,-0.315]). Conversely, comorbidity was weakly correlated with the residuals from the regression between SIP and GDS (Spearman = 0.183 [95% CI 0.022,0.340]), weakly correlated with the residuals from the regression between SIPV and GDS (Spearman = 0.094 [95% CI −0.043,0.270]), and also weakly correlated with the residuals between NEI-VFQ and GDS (Spearman = −0.123 [95% CI −0.266,0.038]). These findings demonstrate that over and above depression (GDS), visual acuity aided in predicting the level of vision-specific disability (NEI-VFQ and SIPV) but not general illness-related disability. The number of comorbid medical conditions, however, did not make a significant contribution, beyond depression, in explaining vision-specific or general illness-related disability.

## Discussion

Forty-nine of 151 elderly adults with advanced macular degeneration were found to have a depressive disorder. This rate (32.5%) is approximately twice as high as that found using similar standard diagnostic methods in general populations of older adults living in the community[40–42] and is comparable to that found in outpatients with life-threatening diseases such as cancer and cerebrovascular disease.[43,44] To our knowledge this is the first study of AMD to examine the prevalence of depressive disorders using the SCID-IV, which is the standard diagnostic method for mental disorders. In addition to the presence or absence of depressive disorder diagnosed by the SCID-IV, the GDS was used to characterize the severity of depression along a continuum of symptoms. These two different, yet standard, approaches to assessing depression provided similar results regarding the extent of depression in this population.

Although the prevalence of depression was high in this group, it cannot be certain that these results generalize to all people with advanced AMD in community settings. A related concern is that this study compared the rates of depression in AMD sufferers with previous studies of community samples using comparable, but not identical, methods to assess depression.

In this study population, high levels of disability were found. Scores on the SIP, which is a generic measure of health-related functional status, showed that subjects had similar levels of health-related disability to patients with cancer and stroke. Previous research[2] using the Quality of Well-Being Scale, a comprehensive measure of health-related quality of life, found similar results. General measures of health outcomes have not been sensitive to vision-specific limitations (e.g., the ability to read a variety of every-

Table 2. Clinical Characteristics of Age-related Macular Degeneration Subjects

| | Depressed Group n = 49 | | Nondepressed Group n = 102 | | Fisher Exact P Value | Overall n = 151 | |
|---|---|---|---|---|---|---|---|
| | *Count* | *(%)* | *Count* | *(%)* | | *Count* | *(%)* |
| Self-rated health | | | | | | | |
| Good to excellent | 36 | (73.5%) | 89 | (87.3%) | 0.041 | 125 | (82.8%) |
| Poor to fair | 13 | (26.5%) | 13 | (12.7%) | | 26 | (17.2%) |
| LogMAR of best eye (frequencies) | | | | | | | |
| 0.477–0.999 | 7 | (14.3%) | 28 | (27.5%) | >0.09 | 35 | (23.2%) |
| 1.000–1.499 | 31 | (63.3%) | 63 | (61.8%) | | 94 | (55.6%) |
| 1.500–1.999 | 2 | (4.1%) | 3 | (2.9%) | | 5 | (3.3%) |
| 2.000–2.602 | 9 | (18.4%) | 8 | (7.8%) | | 17 | (11.3%) |
| | Mean | (SD) | Mean | (SD) | *P* value | Median | Range |
| Log of best eye | 1.27 | (0.49) | 1.1 | (0.44) | 0.047 | 1 | 40.477–2.602 |
| Log of worst eye | 1.75 | (0.59) | 1.61 | (0.6) | 0.157 | 1.4 | 0.699–2.903 |
| Log of weighted eye | 1.39 | (0.47) | 1.23 | (0.43) | 0.067 | 1.25 | 0.533–2.602 |
| Visual acuity (Snellen) | 20/372 | | 20/252 | | 0.047 | 20/200 | 20/60–20/8000 |
| | | | | | | Mean | (SD) |
| Number of comorbidities | 1.67 | (1.07) | 1.17 | (0.97) | 0.007* | 1.33 | (1.02) |
| General illness disability (SIP) | 15.76 | (9.51) | 8.91 | (7.48) | <0.001* | 11.13 | (8.77) |
| Vision-related disability (SIPV) | 10.1 | (6.61) | 5.96 | (5.14) | <0.001* | 7.3 | (5.96) |
| NEI-VFQ average | 49.44 | (13.38) | 60.6 | (12.6) | <0.001* | 56.98 | (13.85) |
| NEI-VFQ 12 Subscales | n Mean | (SD) | n Mean | (SD) | *P* value | n Mean | (SD) |
| General health | 49 59.08 | (19.83) | 102 73.33 | (18.24) | <0.001* | 151 68.71 | (19.87) |
| General vision | 49 36.33 | (17.66) | 102 40.49 | (14.60) | 0.101 | 151 39.14 | (15.72) |
| Ocular pain | 49 79.59 | (20.99) | 102 90.56 | (15.97) | <0.001* | 151 87.01 | (18.42) |
| Near vision | 49 23.52 | (11.45) | 102 31.9 | (20.36) | 0.029 | 151 29.18 | (18.36) |
| Distant vision | 44 32.56 | (18.66) | 98 41.26 | (20.30) | 0.014 | 142 38.56 | (20.15) |
| Driving | 3 63.89 | (31.55) | 15 47.78 | (24.08) | 0.403 | 18 50.46 | (25.16) |
| Color vision | 49 68.37 | (30.52) | 100 75.75 | (27.63) | 0.149 | 149 73.32 | (28.72) |
| Peripheral vision | 48 61.98 | (28.71) | 102 69.85 | (27.80) | 0.109 | 150 67.33 | (28.37) |
| Social functioning | 49 54.34 | (26.83) | 102 69.16 | (23.17) | 0.002* | 151 64.35 | (25.3) |
| Mental health | 48 46.07 | (20.58) | 102 63.65 | (19.41) | <0.001* | 150 58.03 | (21.37) |
| Role difficulties | 49 34.06 | (15.58) | 102 48.28 | (22.20) | <0.001* | 151 43.67 | (21.31) |
| Dependency | 49 45.66 | (25.2) | 101 65.16 | (25.65) | <0.001* | 150 58.79 | (27.03) |

* $P = <.01$

SD = standard deviation.

day items, including newspapers and medicine labels, the ability to recognize people, see traffic lights, the amount of worry about vision, etc.).[38] This study used the SIPV and the NEI-VFQ, which are newer, vision-specific measures. When the 12 NEI subscales were analyzed, the depressed group showed more disability on 10 of the 12 subscales with significantly poorer general health, poorer mental health, more role difficulties, greater dependency, poorer social functioning, and more problems with near and distant vision. Few subjects still drive, and there was no difference in problems of driving expressed by the depressed and nondepressed groups. That the nondepressed subjects have significantly higher ratings on the ocular pain subscale is curious, because AMD is not known to cause pain. This subscale also captures reports of eyestrain, and it is possible that the nondepressed group attempted more tasks requiring vision and, as a consequence, experienced greater eye fatigue and discomfort.

In this study visual acuity in the better eye was found to be worse in the depressed group. Differences between the depressed and nondepressed patients were nonsignificant using the visual acuity of the worse eye ($P = 0.157$) and the weighted LogMAR ($P = 0.067$). In addition, when those who retained what is considered useful vision (i.e., LogMAR $< 1.0$) were compared with those who were legally blind (LogMAR $\geq 1.0$), differences between the depressed and nondepressed patients were nonsignificant. These analyses defined depression on the basis of SCID-IV diagnosis or significant depressive symptoms (i.e., GDS $\geq 5$). When the visual acuity in the better eye was analyzed across those who had major, minor, subsyndromal depression and no depression, differences in visual acuity remained nonsignificant. Because the differences between the NEI-VFQ quality-of-life scores of the depressed and nondepressed groups were statistically significant, these findings may suggest visual acuity does affect depression.

It is possible that the correlation between visual acuity and depression was artificially low in this study, because the range of acuity was restricted. For example, patients with acuities better than 20/60 in the better eye were excluded.

It also should be noted that subjects in this study were relatively healthy, mobile, and cognitively intact and, as such, may underrepresent both the depression and disability associated with advanced AMD.

In this population no matter how depression or disability was measured, the correlation between depression and dis-

Table 3. Correlation between Measures of Depressive Symptoms, Visual Acuity, Comorbidity, and Disability: Spearman Correlation Matrix (95% Confidence Intervals in Parentheses)

| Spearman's rho | Unweighted Average of the 12 National Eye Institute Visual Function Questionnaire Subscales | Vision-specific Sickness Impact Profile Total Score | Sickness Impact Profile Total Score |
|---|---|---|---|
| GDS | −0.514 (−0.675, −0.353) | 0.458 (0.297, 0.619) | 0.526 (0.365, 0.687) |
| LogMAR | −0.407 (−0.568, −0.246) | 0.211 (0.05, 0.372) | 0.121 (−0.04, 0.282) |
| Comorbidity | −0.215 (−0.376, −0.054) | 0.201 (0.04, 0.362) | 0.299 (0.138, 0.460) |

| Spearman's rho | Geriatric Depression Scale |
|---|---|
| LogMAR | 0.119 (−0.042, 0.280) |
| Comorbidity | 0.224 (0.063, 0.385) |

Comorbidity = number of comorbid conditions; GDS = Geriatric Depression Scale; LogMAR = LogMAR of the better eye.

ability was very strong. Subjects with a diagnosis of depression on the SCID-IV and with severe depressive symptoms on GDS had significantly higher disability scores on SIP, as well as SIPV and NEI-VFQ. Positive links between disability and depression have been reported in a heterogeneous low-vision clinic population,[4,7,8] as well as other studies not involving diseases of the eye.[9,45–48]

One possible contribution to the strong relationship between depression and disability is that depression and disability are related constructs. The depression measures may have asked similar questions to the disability measures. The SCID-IV, for example, uses decreased energy in the diagnosis of depression; disability measures may also pick up on inactivity. The NEI-VFQ includes mental health items. However, the greater disability of the depressed subgroup on most of the NEI-VFQ subscales suggests that the depressed group has lesser ability to function in a variety of domains and thus, this presents a fairly clear picture of greater overall vision-specific disability among the group of depressed AMD subjects.

The protocol for this study was based on Snellen visual acuity converted to LogMAR. It is possible that other measures of visual acuity may have yielded different results. In this study, weaker association was found between visual acuity and disability than between depression and disability. As would be anticipated, the correlation between visual acuity and vision-specific disability was better than with the general health-related disability.

In this population visual acuity had little correlation with the severity of depressive symptoms. This demonstrates that the depression associated with AMD may commonly occur even at vision levels that could be considered useful and not only in those with very poor vision. This suggests that depression may occur earlier in the course of AMD.

The possibility that comorbidity or visual acuity added to the prediction of disability, beyond what could be explained by the strong correlation between depression and disability, was examined by removing the effect of depression (GDS) from the disability scores (NEI-VFQ, SIPV, SIP). This analysis showed that the number of comorbid conditions added little to the prediction of vision-specific disability (NEI-VFQ and SIPV) or general health-related disability (SIP) beyond what could be explained by depression. Visual acuity, however, did add to the prediction of vision-specific disability in this population.

This study indicates that a large number of people with AMD are depressed and disabled. Primary care physicians who deal with the elderly, and certainly ophthalmologists, should consider using the brief and accurate SCID-IV diagnostic criteria for depression in taking histories. Because recent treatments for depression are often effective and have few side effects,[49–52] ophthalmologists should consider referral for treatment of depression in AMD patients. Further research should evaluate the impact of treatment for depression on the disability experienced by people with AMD. Furthermore, this study indicates that reduced vision is responsible for vision-related disability independent of depression. For this reason low-vision rehabilitation, including cognitive behavioral therapy,[3] should be more readily available and recommended.

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Discussion
by
Barbara S. Hawkins, PhD

## Methodology and Implications for Interpretation of Findings

The first objective of the study by Brody et al was to "examine the prevalence of depressive disorder in community-dwelling adults with advanced age-related macular degeneration." I am not qualified to discuss the methods that Ms. Brody and her coinvestigators used to diagnose depression in these patients. However, the good correlation they found between the "gold standard" and the Geriatric Depression Scale suggests that the diagnoses of depression in the patient population was reliable.

As an epidemiologist, I can comment on estimates of prevalence. These investigators have reported that the percentage of patients who had depression, which they termed "prevalence," was twice as great as has been reported by other investigators. Estimates of prevalence should be derived from well-defined samples of the population so that an estimate is applicable beyond the subset of individuals studied. Thus, to accept the estimated high rate of depression found in this study as applicable to other patients with advanced age-related macular degeneration (AMD) and vision loss, one must be convinced that the patients studied are representative of this subset of the elderly population. Subjects for this study were selected from patients who were examined at a university ophthalmology clinic. One must ask whether patients seen at this particular ophthalmology clinic are representative of those seen elsewhere. Typically, population-based studies have identified too few such patients to provide reliable estimates of distributions of patient characteristics. In Table 1, mean age and the percentage of the patients who were women have been summarized for this study and for three other ophthalmology clinic-based studies of patients with advanced AMD and vision loss, ordered by numbers of patients studied. The Natural History Study of Geographic Atrophy was another single-center observational study. Two of the studies, the Macular Photocoagulation Study (MPS) clinical trials of laser photocoagulation for neovascular AMD and the clinical trials of verteporfin for subfoveal AMD (TAP Study), were multicenter; indeed, the TAP Study was international. The mean ages of patients and the percentages of women were lower for the larger studies than for the smaller studies. This observation suggests that the patients in these four studies may differ on other relevant characteristics. Typically, patients who volunteer for or who are selected for clinical studies differ from other eligible individuals in the population. For example, study participants may have better access to health care, greater mobility, heightened perception of the need for medical care, or more motivation based on altruism or hope of personal gain. In addition to these considerations, the size of the confidence interval around the estimated prevalence of depression (not reported by the authors) must be considered. Thus, the prevalence of depression estimated in this study should be interpreted and extrapolated with caution.

A third methodologic issue is that this analysis is cross-sectional. The investigators are restricted to analyzing associations among various health states at one point in time. Thus, it is not possible to ascertain whether depression occurred soon after the diagnosis of AMD or after significant loss of visual acuity or whether patients already were depressed for other reasons. The temporal relationship of these states can be determined only from prospective longitudinal studies.

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Table 1. Characteristics of Patients in Selected Clinical Studies of Advanced Age-related Macular Degeneration

| | No. of Patients | Mean Age, Yrs | Women, % |
|---|---|---|---|
| Brody et al. | 151 | 80 | 68 |
| GA Natural History[1] | 156 | 78 | 65 |
| TAP Study[2] | 609 | 75 | 56 |
| MPS Trials[3–6] | 1,319 | 72 | 53 |

GA Natural History Study, single-center natural history study of geographic atrophy.[1] TAP, Treatment of Age-related Macular Degeneration With Photodynamic Therapy.[2] MPS, Macular Photocoagulation Study, limited to clinical trials of laser photocoagulation for choroidal neovascularization associated with age-related macular degeneration.[3–6]

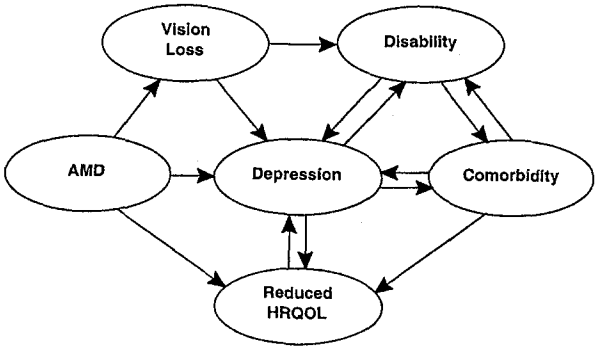


Figure 1. One possible simple model of health-related consequences of age-related macular degeneration. HRQOL = Health-related quality of life.