Perceived Stress and Visual Function in Macular Degeneration Patients

THESIS

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By

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Abstract

**Purpose:** Age-related macular degeneration is the leading cause of permanent blindness in developed countries.\(^1\)-\(^3\) Higher levels of depression and disability and lower quality of life has been measured in this population.\(^4\)-\(^7\) The purpose of this study was to measure perceived stress and its relationship to visual function in patients with AMD using the Perceived Stress Scale.

**Methods:** Patients with AMD were enrolled during visits to a retinal specialist for evaluation of the need for treatment with intraocular anti-VEGF injection. Visual acuity was assessed using a backlit ETDRS chart and by-letter scoring. Four surveys were then administered to the patient. They included the Perceived Stress Scale (PSS), Impact of Vision Impairment survey (IVI), and the ENRICHD Social Support Inventory (ESSI), and the Center for Epidemiologic Studies Depression Scale (CES-D). Participants completed a large-print paper version of the surveys when possible, and the survey was read aloud to patients who were unable to complete it for visual reasons. Rasch analysis of PSS responses was performed using Winsteps with the Andrich rating scale model. Item fit to the Rasch model was assessed using infit
mean square statistics. Response category functioning was assessed using category probability curves, and survey targeting for the study population was assessed by comparing Rasch item measures with person measures for all participants.

**Results:** We had a total of 79 participants in this particular part of the study. The mean age was 81.19 with 48.1% being female and 51.9% male. Rasch analysis showed that the PSS was valid to use in this population and measured the desired construct, stress. During our analysis we found that visual acuity in the better and worse eye were correlated with age. Age was also positively correlated with IVI results. Visual acuity in the better eye was correlated to visual acuity in the worse eye. PSS was not correlated with visual acuity in the worse or better eye. IVI results were correlated with PSS results.

**Conclusions:** The PSS is valid for use in patients with AMD. There is an important relationship between the PSS and IVI but not between PSS and visual acuity. Visual acuity is the gold standard for measuring treatment outcomes with AMD, but perhaps self-reported visual function should also be considered when talking about treatment outcomes. Furthermore, since stress is present in these patients and also an inherent part of the anti-VEGF injections, treatment for stress should be considered. Low vision rehabilitation may be one such treatment that addresses quality of life.
This document is dedicated to Ashkhen and Varuzhan Movsisyan
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Field of Study

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Chapter 1:
Introduction and Background

1.1 Prevalence of Age Related Macular Degeneration

Age-related macular degeneration is the leading cause of permanent blindness in developed countries.\textsuperscript{2, 3, 8-10} Approximately 1.75 million people 40 years or older in the United States have either neovascular AMD or geographic atrophy in at least one eye, while 7.3 million are said to have high risk characteristics, including drusen larger than 125 microns in either or both eyes.\textsuperscript{2} Furthermore, it is estimated that the number of people affected by AMD will rise to 3 million by the year 2020.\textsuperscript{2} AMD makes up 46% of severe vision loss (visual acuity 20/200 or worse) in people over the age of 40 in the United States.\textsuperscript{11} The prevalence and severity of AMD varies with age and ethnicity.\textsuperscript{11} For example, in the Beaver Dam Eye Study, the prevalence of AMD was less than 10% in a mainly Caucasian population aged 43 to 54 and more than tripled for people of the same demographic aged 75 to 85.\textsuperscript{3} In one review article of several population based studies of European populations, age-related macular degeneration was the leading cause of blindness in all 6 of them.\textsuperscript{11} AMD has
been shown to lead to a significant decline in a patient’s quality of life, resulting in clinical depression in one third of these patients.⁴⁻⁷

1.2 AMD and Psychological Distress

In one study examining depression in an elderly population with age-related macular degeneration, forty-nine of the 151 subjects (one-third) were said to have a depressive disorder.⁴ The Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Axis I, Fourth (IV) Edition, Research Version- (SCID-IV) was used to identify subjects with depressive disorder. 7.3% percent had major depression, defined as five or more of the following depressive symptoms: 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 be categorized as major depression, one of the five symptoms had to be depressed mood or loss of interest or enjoyment in usual activities, and these symptoms had to have been constant for two weeks or longer. 19.9% had minor depression, defined as having at least two of the symptoms listed above but less than five. 5.3% were shown to have subsyndromal depression, which meant having two or more symptoms of depression other than depressed mood or loss of interest or enjoyment of usual activities.
This combined rate of 32.5% was twice as high as the general population of elderly adults living in the community. This number is also similar to that found in patients with life-threatening conditions such as cancer and heart disease. Results from survey with the Geriatric Depression Scale (GDS) confirmed the SCID-IV findings, showing similar levels of depression among these subjects. Moreover, high levels of disability were found amongst this population. Disability was measured using the Sickness Impact Profile, which measures functional limitations caused by general health status. These patients with AMD showed similar levels of health-related disability to patients with cancer and stroke. To further assess disability directly related to vision, the Vision-Specific Sickness Impact Profile (SIPV) and the National Eye Institute Visual Function Questionnaire (NEI-VFQ) were used. The depressed group showed more disability on 10 of the 12 NEI subscales. This study also found that visual acuity in the better eye was worse in the depressed group.

Another similar study found a 33% rate of depression after 6 weeks of vision loss in the second eye. This longitudinal study also showed a decline in visual function with stable visual acuity in depressed patients. They concluded that as depressive symptoms worsen over time they lead to the deterioration of visual functioning independent of actual visual acuity. This is an important finding when thinking about treatment of AMD in depressed patients. Anti-VGEF injections are available to improve or keep vision stable, yet visual functioning may still decline in patients with depression, despite of measured visual acuity.
The studies listed above and many others examine how vision loss is correlated with depression, but little is currently known about the relationship between a related but distinct construct, perceived stress, and macular degeneration. We are unaware of any studies that have evaluated perceived stress in macular degeneration patients.

1.3 Profiles of Mood States (POMS)

The POMS\textsuperscript{12-14} has been used in patients with Age Related Macular degeneration in a study assessing the effectiveness of an AMD self-management program, including health education and problem-solving skills, to improve quality of life measured in mood and function.\textsuperscript{12} Though it does not measure perceived stress per se, some of the content area (see Appendix A) is similar to the Perceived Stress Scale. The POMS is a 65-item survey designed to measure emotional distress during the previous week.\textsuperscript{12} In this particular study, the POMS was used because it does not inquire about physical symptoms that may confound with physical illness. The responses are on a 5-point scale, ranging from 0= not at all to 4= extremely. Scores range from 0 to 232 with higher scores indicating higher levels of emotional distress.\textsuperscript{12} This survey has been validated for use in older populations.\textsuperscript{15}
1.4 Perceived Stress Scale

1.4.1 History of Perceived Stress Scale

The perceived stress scale (PSS)\textsuperscript{16} measures how much stress people believe exists in their lives. Before the PSS, objective measures such as the number of stressful events that occurred in a given period of time were used in research examining the role of stress as a risk factor in both physical and psychological illness. Such objective measures remove subjective bias and make comparisons between number of stressful events and risk for disease easier to measure. However, using these objective measures implies that the events themselves are risk factors for illness. We know from previous research that people actively assess the situations in their lives and decide whether they are threatening and if they have the resources to deal with these situations or not. Recognizing that a person’s perception of stress, rather than the event itself, dictates that person’s response to the event is important in studying stress as a risk factor for disease.\textsuperscript{16}

The original version of the PSS is a 14-item survey that measures to what degree participants found their lives to be unpredictable, uncontrollable, and overloading.\textsuperscript{16} The authors asserted that these three areas have been shown to be the main aspects of perceived stress. The scale also includes direct questions about how much stress someone is experiencing. It is designed for people with at least a junior high school education. The questions are both easy to understand and generalized and can therefore be used amongst
varying populations. The PSS was found to have good internal and test-retest reliability and correlated expectedly with various self-report and behavioral criteria. It was also shown “to be a better predictor of health and health-related outcomes than either of the two life-event scales.”

1.4.2 Perceived Stress and Self-reported Health

After the development of this subjective scale of stress, Cohen went on to show how the perception of stress was related to self-reported health and illness. Extensive research with the PSS showed that people who were more stressed also reported to be in poorer health. Subjects who had been hospitalized in the previous year had higher PSS scores than those who had not been hospitalized. Moreover, PSS scores were shown to be positively correlated with the Health Services Utilization Scale and the measure of inability to perform routine activities. Higher perceptions of stress also corresponded to increased number of serious illnesses in a person’s life and occurrences of illness in the preceding year. From these findings, Cohen concluded that there is a clear association between self-reported physical illness and higher levels of perceived stress as measured by the PSS.

The PSS and its relationship to health-related behaviors have also been studied. These associations were not as strong as those between the perception of health and PSS but showed statistically significant correlations between "elevated PSS scores and shorter periods of sleep, infrequent
consumption of breakfast, increased quantity of alcohol consumption, usage of licit drugs, and frequency of licit drug usage.” Furthermore, smokers reported higher PSS scores than non-smokers, and those with higher perceived stress reported more dissatisfaction with life than those with lower reported stress. These associations show the importance of perceived stress and its role in leading to poorer health after stressful events.\(^\text{17}\)

\subsection*{1.4.3 PSS and Immunity}

An important aspect of the research in our lab is to look at how stress affects inflammation in the eye. We know from previous research that aging itself has a significant effect on immunity. Specifically, cell-mediated immunity shows a consistent decline with age.\(^\text{18-20}\) We also know that immune function can also be impacted by stress, with effects similar to those of aging. With age, we see a significant decrease in naive T cells and an increase in memory T cells.\(^\text{18}\) In turn, there is a decrease in the production of interleukin-2 (IL-2) and high affinity IL-2 receptors, and less of a response from T cells to novel antigens. This changing response also includes an increase in IL-12, a pro-inflammatory cytokine, which inhibits Th2, an antibody mediated response. Furthermore, an increase in memory T cells of the Th2 response increases interleukin-10, which suppresses the cellular inflammatory response.\(^\text{18}\) All these changes add up to a shift from a Th1 to a Th2 response that may add to a declining cellular immunity in older adults. Moreover, the naive humoral immune
response also deteriorates with age. There is impaired activation and proliferation of B cells and a decrease in antibody production and quality.$^{18}$

Research has shown that psychological stress can exacerbate this decline in immunity in the elderly. The effects of stress vary according to exposure, social support, peoples’ reactivity to stressors, the duration of stress and the efficacy of the restorative processes of the body. An important aspect of stress has been shown to be negative interpersonal events, specifically chronic stress such as caring for a sick spouse, has been shown to have a similar decline in immunity seen with aging, including less Natural Killer cell toxicity, reduced memory T-cell response to Herpes Simplex Virus Type 1, poorer antibody response to influenza virus and shorter response time of the IgG antibody to pneumococcal bacteria vaccine.$^{18}$

Other mechanisms examined in this particular article included buffers of stress, in which social support reduced how stressful people perceived an event to be. Thus, social support is associated with better immune functioning. Most elderly report the same amount of support as younger adults with the exception of older adult caretakers of spouses with dementia or other illnesses. In turn, this loss of an emotional buffer puts these caretakers at higher risk for experiencing stressful events and deteriorating immunity. The exposure to stress, presence of lack of social support, one’s reaction to the stress, along with the duration of the stress impact changes on a physiological and behavioral level. There are changes in the autonomic, neuroendocrine and
immune system, as well as a change in a person’s lifestyle including compliance with medication, likelihood of seeking medical care, decreased sleep and increased alcohol and tobacco use. The health outcomes of these effects include disease susceptibility and psychological disorders, such as stress and anxiety.18

One important focus in our lab is the relationship between stress and C-reactive protein. C-reactive protein levels increase in people under increased levels of stress. Interestingly, higher C-reactive protein levels are a risk factor for developing AMD. So, we believe there may be a connection between stress, C-reactive protein, and AMD visual outcomes.

1.4.4 Who is Stressed?

A paper by Cohen and Janicki-Deverts studied who is stressed and what can happen to the body with stress.21 They concluded that psychological stress has been shown to influence many physiological processes and diseases states. Stress has been found to be a risk factor for depression, cardiovascular disease, HIV/AIDS, delayed wound healing, upper respiratory infections, autoimmune diseases, and total mortality. Stress measured by the PSS has been shown to be associated with elevated markers of biological aging, higher cortisol levels, suppressed immune system, increased susceptibility to infectious disease, and slower wound healing. People with higher PSS scores
also report worse lifestyle choices, such as sleeping fewer hours, skipping breakfast, and consuming more alcohol.

To determine how stress was related to demographics across the United States, the PSS was administered nationally at three different times in the course of 26 years, in 1983, 2006 and 2009. The distribution of stress remained generally the same across the three surveys over the 26 years. In all three instances, women reported more stress than men, stress decreased with increasing age, also with increased education and income. Furthermore, minorities reported more stress than whites. Those who were unemployed reported more stress than the employed in 1983 and 2006 but not in 2009, compared to the retired who reported the least amount of stress across the three surveys.

An interesting and important finding in this nationwide survey across two decades was that reported stress tended to decrease with increasing age. The authors explained that this could be because people tend to perceive life events as less stressful and have better coping skills. They used another study as an example which showed that as people age, they focus more on the positive aspects of life rather than stressing about negative events. This is important with regard to our own research, as the population we are studying is older and possibly inherently less stressed when compared to younger individuals.
1.5 Treatment of AMD with Anti-VEGF Injections

1.5.1 Mechanism of Anti-VEGF Injections

The most severe vision loss associated with macular degeneration comes from choroidal neovascularization. Anti-vascular endothelial growth factor (anti-VEGF) intravitreal injections work to stop the growth of leaky blood vessels in the eye to prevent further vision loss and possibly improve vision. A review of several trials on macular degeneration and anti-VEGF injections showed that those who received anti-VEGF injections, pegaptanib, renibizumab, or bevacizumab, “gained 15 or more letters of visual acuity, lost fewer than 15 letter of visual acuity, and had vision 20/200 or better after one year of follow-up.” Also, despite the much lower cost of bevacizumab, it had similar results to ranibizumab. When compared to controls, both ranibizumab and bevacizumab had better visual outcomes than pegaptanib.22

1.5.2 Anti-VEGF for the Treatment of Predominantly Classic Choroidal Neovascularization (CNV) in Age-related Macular Degeneration (ANCHOR)

A two year clinical trial called Anti-vascular endothelial growth factor (VEGF) Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization (CNV) in Age-related Macular Degeneration (ANCHOR) looked at treatment with an anti-VEGF agent, ranibizumab and with verteporfin photodynamic therapy (PDT) for classic CNV.23 This study was conducted as a randomized, double masked trial across multiple centers in various countries.
Patients were either assigned to verteporfin PDT with a monthly sham injection or sham verteporfin PDT with a monthly intraocular injection of ranibizumab. The outcomes were measured at 12 and 24 months. The measures included percentage of patients losing less than 15 letter from baseline visual acuity score, percentage gaining 15 letters or more from baseline, and the mean change in VA score over time.\textsuperscript{23}

The study concluded that the improvement in visual acuity was both statistically significant and clinically meaningful at month 12 and 24. Ninety percent of patients treated with ranibizumab had lost less than 15 letters from baseline, compared to 65.7% of PDT patients. Up to 41% had gained 15 or more letters, while only 6.3% of the PDT group had gained 15 or more letters. On average, visual acuity improved from baseline by 8 to 10 letters, whereas declining by 9.8 letters in the PDT group. This extensive two year clinical trial showed the clinical benefit of ranibizumab over PDT in patients with classic CNV.\textsuperscript{23}

\textbf{1.5.3 MARINA study}

Yet another study by the MARINA study group looked at ranibizumab for the treatment of wet age-related macular degeneration.\textsuperscript{24} This was also a two-year, multicenter, double blind study. Participants were randomly assigned to the study group, receiving 24 monthly injections of ranibizumab, or the control group, receiving 24 monthly sham injections. Their main measure was the
percentage of patients losing less than 15 letters from baseline visual acuity at month 12. Similar to ANCHOR, 94.5% of the patients given 0.3mg of ranibizumab and 94.6% of patients given 0.5mg ranibizumab lost fewer than 15 letters, compared to 62.2% of patients in the sham injection group. Thirty-three percent of the 0.5mg group and 24.8% of the 0.3mg group showed an improvement of visual acuity by 15 or more letters, while only 5.0% of the sham injection group showed this same improvement. Mean increase in acuity was 7.2 letters in the 0.5mg group and 6.5 letters in the 0.3mg group. The sham injection group lost an average of 10.4 letters in acuity. These improvements in VA in the ranibizumab treatment groups were maintained at 24 months.\textsuperscript{24}

### 1.5.4 ANCHOR, MARINA, and HORIZON Conclusions

Another publication looking at the seven year outcomes of clinical trials such as ANCHOR, MARINA and HORIZON showed that 37% of eyes reached a goal acuity of 20/70 or better, with 23% achieving acuity 20/40 or better.\textsuperscript{25} On the other hand, 37% of eyes ended with 20/200 acuity or worse. Compared to baseline findings of ANCHOR or MARINA, 43% of eyes had stable or improved letter score 7 years later, while 34% of eyes decreased in acuity by 15 letters or more. After the HORIZON study was concluded, participants were shown to have a mean of 6.8 anti-VEGF injections in a span of 3-4 years. Those with 11 or more injections had a better gain in letters since the end of the trial. Active wet AMD was diagnosed with spectral-domain OCT in 68% of study eyes, and
46% were receiving injections at that time. Ninety-eight percent showed macular atrophy, detected with fluorescein angiography. This analysis of patients 7 years after treatment with ranibizumab in the ANCHOR or MARINA trials demonstrated that one third of patients improved in visual acuity, while one third had poorer outcomes. Looking at baseline, half of the eyes were stable, one third had worsened by 15 or more letters. Even years later, these patients are at significant risk for continued vision loss.25

1.5.5 Stress Associated with Anti-VEGF injections

The monumental trials above show why anti-VEGF injection is the standard of care for wet AMD. However, few studies have looked at how this treatment course affects patients psychologically. One review of ten trials examined this very question and yielded important answers.26 One of these answers, corroborated by two studies, was that patients’ expected pain level during injection was much higher than the actual pain experienced. 51% of participants in one trial and 64% in another reported the injection was less painful than they had thought. The review went on to list what exactly patients are most anxious about in the process of receiving an injection. Again citing two studies, the article stated that patients were most anxious about the injection itself, but also the insertion of eye drops and the speculum, and the application of the drape. Furthermore, there was no statistically significant difference in the pain experienced between different modes of anesthesia (topical anesthetic
drops, topical gel, topical pledget anesthesia, subconjunctival and peribulbar injection).

Another important conclusion of the review was that other factors, such as the number of injections and change in visual acuity influenced pain perception by patients. In two studies, pain reported by patients tended to be higher if it was their first injection. Also, improved vision from a previous injection led to lower pain scores after injection. Finally, female gender and age over 65 also yielded lower pain scores in this particular study by Rifkin and Schaal in 2012.\textsuperscript{27} What exactly is causing patients to be apprehensive towards anti-VEGF treatment? Thetford et al. (2013) concluded it was the fear of having an injection in the eye, fear of losing vision, and not knowing exactly what the treatment process involves.\textsuperscript{28}

\textbf{1.5.6 Anti-VEGF Treatment and Quality of Life}

Another important question is how anti-VEGF treatment affects the quality of life of patients. One study used the Impact of Vision Impairment Questionnaire (IVI) to assess the quality of life of patients undergoing intravitreal injections. The IVI is a 28 item questionnaire with 3 to 4 responses ranging from “not at all” to “a lot”. The questionnaire can be examined in three sub-scales, including: Reading and Accessing Information, Mobility and Independence, and Emotional Well-being. In this particular study, the IVI was administered at baseline, 6 months, and 12 months to patients newly diagnosed
with wet macular degeneration about to start receiving anti-VEGF injection. A comprehensive examination was performed at each visit, including visual acuity measured with a back-illuminated logarithm of minimum angle of resolution VA chart.

This study concluded that a change in acuity in the eye being treated with anti-VEGF injections for wet AMD influences a person’s reported quality of life. This result was shown to be the same whether the better or worse eye was receiving treatment. A gain of two lines of visual acuity improved reported ability to read and assess information, and also improved emotional wellbeing. A loss of two or more lines of visual acuity led to a worse ability to read and access information, along with poorer mobility. These results demonstrated that even the worse eye should receive treatment and injections should aim to improve VA or at least maintain stable VA to preserve the patient’s quality of life.26

1.6 Impact of Vision Impairment Questionnaire (IVI)

1.6.1 Validity of IVI

The above study showed how the IVI could be used to assess a patient’s quality of life as he/she undergoes intravitreal anti-VEGF injection. Another study further examined the validity of the IVI.29 The IVI Profile was developed to look at limitations in a person’s life that stem from his or her vision loss. It is a 28 item questionnaire that asks about participation or lack of participation in daily events due to visual restraints. This study confirmed the internal and
construct validity and reliability of the IVI. The study said that face validity was ensured in the use of focus groups in the construction of the questionnaire to assure that the questions were relevant to people with visual impairment.

To evaluate the construct validity of the IVI, they looked at how it correlated with actual function-based measurements of vision. They found that in general, reported difficulty with tasks did correspond with reduced levels of vision. “IVI scores correlated most strongly with vision-specific global measures of restriction of participation.” The IVI was also shown to not differ with other health conditions and did not correlate with age, which also helps its construct validity. The study concluded that the IVI also has acceptable reliability over a short period of time and gives similar outcomes, regardless of administration. For example, similar results are seen when patients fill out the survey themselves and if it is administered to them by a healthcare professional.

1.7 Rasch Analysis

1.7.1 The Rasch Model

The Rasch model\textsuperscript{30} is a model for scoring and evaluating tests and surveys. It was originally developed for use in educational testing, but its use has been extended to a range of other purposes including health-related quality of life.\textsuperscript{31} Rasch model allows for interval-level scoring from the ordinal-level responses that subjects give on surveys.\textsuperscript{30} It allows for survey questions (or “items”) to be used to create a linear scale that subjects can be placed on
based on their responses to the questions.\textsuperscript{30} This interval scale provides validity for the use of common statistical procedures, like t-tests which are not valid for ordinal-level data. In addition to these scoring features, Rasch analysis also allows researchers to develop and evaluate questionnaires.\textsuperscript{30}

1.8 Purpose of Study

The purpose of this study was to examine perceived stress in patients with AMD using the PSS. We examined whether visual acuity or self-reported visual functioning (IVI scores) are related to perceived stress in these patients, and how stress varies with demographic factors. Additionally, we used Rasch analysis to examine the validity of using the PSS in people with AMD. The PSS has been used in various populations to assess how perceived stress is related to perceived health and inflammation, but it has never been used in macular degeneration patients. Results from this study will be of use in future studies of the relationships among stress, inflammation, and AMD treatment outcomes.
Chapter 2:

Methods

2.1 Description of Study

This prospective study involved identifying patients with age-related macular degeneration and administering surveys to evaluate how stress affects visual acuity and visual functioning. Subjects completed a total of 4 surveys, including perceived stress, depression, social support, and self-reported visual functioning. Some of those participating also had their blood drawn at the study visit for a related study of the relationship between stress and inflammation. All study participants were patients at the Ohio State University Department of Ophthalmology’s Havener Eye Institute. The study was approved by the Biomedical Institutional Review Board of the Ohio State University.

2.2 Research Subjects

Patients with age-related macular degeneration receiving care at Ohio State’s Havener Eye Institute were eligible to participate in this study. All of the patients recruited were under the care of the same retina specialist. Potential participants were identified by reviewing daily schedules for this retinal specialist. There were two types of patients in our study; those with active disease receiving intravitreal injections and those who did not need current
treatment. At each study visit, our research team would arrive before the start of the day to review charts and take note of any patients with AMD. After these patients were identified, the retina specialist and study staff would educate the patient on the general goal of the study and ask if the patient might be interested in participating. Once the patient agreed to participate, the study staff would more thoroughly explain the process of the project, obtain written consent, and educate patients on their privacy rights and have them sign HIPAA forms. All study visits occurred during regularly-scheduled clinic appointments.

2.3 Visual Acuity

Visual acuity of each eye was measured using a back-illuminated Early Treatment Diabetic Retinopathy Study (ETDRS) chart\textsuperscript{32} at 2 meters. If the patient could not read the letters at 2 meters, the chart was moved up to 1 meter. The patient was encouraged to guess throughout the process and the stopping point was missing 3 out of the 5 letters in a row. Letter by letter scoring was utilized to yield the most accurate acuity for each eye, as several studies have shown that scoring acuity letter by letter is better than scoring by whole line increments in terms of repeatability of the visual acuity measurement.\textsuperscript{33} Subjects were tested with their habitual distance correction in place.
2.4 Survey Administration

After visual acuity, four surveys were administered to the patient. They included the Perceived Stress Scale (PSS), Impact of Vision Impairment survey (IVI), and the ENRICHD Social Support Inventory (ESSI), and the Center for Epidemiologic Studies Depression Scale (CES-D) (See Appendices B,C,D, and E). The questionnaires were printed in large print; the stem was 32 point print while the answer choices were 22 point print, with one question per page to make them accessible to our patient population (see Appendix A for an example page). Participants could fill out the surveys themselves, or if the patient’s vision was severely reduced, or if they did not feel comfortable reading the surveys, research staff read each question and its answer choices aloud and marked the patient’s responses.

The PSS questionnaire used in this study contained 10 items and has previously been suggested to be valid. The answer choices 0 to 4, 0 being never, 4 being very often. The IVI reading and accessing information subscale, a 9 item survey that assesses difficulties with simple visual tasks such as reading and watching television, was used. The ESSI is a 7-item instrument looking at social support and how it relates to outcomes in patients dealing with serious health condition. The CES-D is a 20 item survey asking people about symptoms related to depression. Along with the four surveys, there was also a comorbidity questionnaire that assessed the patient’s overall health.
2.5 Comorbidity Questionnaire

Along with the four surveys, there was also a study staff administered comorbidity questionnaire (The Charlson Comorbidity Index\textsuperscript{36, 37}) that assessed the patient’s overall health.

2.6 Blood Draw

Though not a part of the study described in this thesis, many of the participants also had blood drawn during the study visit. Blood was drawn after the surveys by study staff or staff from the Department of Ophthalmology. This occurred for all patients who were receiving anti-VEGF injections as part of a larger study of inflammation.

2.7 Payment and Follow-Up

Participants were paid for their participation at the end of the study visit. All participants were provided with a list of Columbus counseling resources as well. Patients in the inflammation study repeated all procedures at approximately 3 months and one year from baseline.

2.8 Data Analysis

After each study visit, data was entered into a Microsoft Access database and stored on secure College of Optometry servers. Responses were coded from 0 to 4, 0 being the least amount of the measured construct. The
polarity of positively worded items were switched for analysis. For example, if a PSS question was asking about feeling positive about dealing with a stressful situation, saying you felt this way all the time would be coded as a 0, indicative of a low amount of the measured construct “perceived stress”. Winsteps software version 3.69\textsuperscript{38} was used to conduct Rasch analysis on survey items. IBM SPSS version 21 was used for all other statistical analyses.

2.8.1 Rasch Analysis

2.8.1.1 Overview and Scoring of Questionnaires

Rasch analysis\textsuperscript{39} takes ordinal level raw score data and converts it into interval measures that are consistent with the fundamental aspects of measurement. These features of measurement include unidimensionality, hierarchical order, and equal interval scaling. Unidimensionality means that the measurement obtained is of a single dimension or construct. For example, the Perceived Stress Scale should measure “stress” and not some combination of “stress” and, say, “general health” or some other construct.

Rasch analysis takes raw survey scores and yields measures of the “item measure” (amount of the construct required to answer a question a certain way) and “person measure” (amount of the construct measured for each individual person). Using this model, the probability of a response to any given survey question can be represented as the difference between person measure and item measure.
Questionnaires that measure visual function (or any other construct) can then be conceptualized as rulers with items arranged from easy to hard and a distributions of participants from less to more able. This allows for inference about what a person can/cannot do based on where he or she falls on the scale. For example, if one is in the middle of the visual function range, we can infer that he/she can do things on the easier end and not things on the more difficult end of the ruler (see Figure 2.1 from Mallinson, 2008).

Another feature of measurement that the Rasch analysis exhibits is hierarchical order. This means the ordering of items from least to most challenging, which is also the operational definition of the construct being measured. Rasch requires that the definition of visual function or quality of life remain the same across all patients being compared to one another. Hierarchical order ensures that only patients whose operational definition of the construct is the same are compared. The third aspect of measurement required by Rasch analysis is equal interval. A linear scale allows for comparisons of differences in patient function over time, for example, before and after a given intervention, or between patients from different clinics. In order to make conclusions about how visual function has changed over time, there must be an origin point.
2.8.1.2 Questionnaire Validation

In addition to scoring questionnaires, Rasch analysis can be used as a form of validation. This has become very common in the health sciences.\textsuperscript{40, 41} We used published guidelines for Rasch parameters\textsuperscript{41} to determine whether there was evidence that the Perceived Stress Scale provides useful measurements in patients with AMD. Person separation is one important measure examined by Rasch analysis. It is testing how reliable the items being used are. In other words, are the items or questions separating the participants into different groups adequately along the scale. If separation is too narrow this means there is redundancy in the test items and not enough separation among participants’ abilities to distinguish between them. On the contrary, separation that is too wide usually means there are gaps among item difficulties and person abilities. To be used for meaningful measurements, selected items must separate relevant persons by their performance.\textsuperscript{42} The infit mean square statistic was used to determine whether individual questions fit the Rasch model, category response probability curves to determine whether the survey response options were appropriate, and principal component analysis of the residuals to determine whether the survey was unidimensional. Table 2.1 provides a summary of the guidelines for each of these parameters.
2.8.1.3 Relationships among Stress and Visual and Demographic Factors

In order to examine the relationships among perceived stress as measured by the PSS and visual acuity, self-reported visual function, and other participant characteristics, we used Pearson correlation coefficients when both variables were continuous. We used ANOVA to determine relationships between categorical predictors and PSS scores. P values less than 0.05 were considered statistically significant.
Table 2.1. Rasch Parameter Guidelines, Adapted from Pesudovs et al.\textsuperscript{41, 42}

<table>
<thead>
<tr>
<th>Rasch Parameter</th>
<th>Description</th>
<th>Ideal Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category Functioning</td>
<td>Do the response categories appropriately reflect the peoples’ answers to survey items?</td>
<td>All curves ordered and categories used frequently enough</td>
</tr>
<tr>
<td>Item Infit Mean Square</td>
<td>Do the individual survey items fit the Rasch model?</td>
<td>Between 0.7 and 1.3</td>
</tr>
<tr>
<td>Person Separation</td>
<td>Does the survey adequately separate between people with different levels of the measured construct?</td>
<td>At least 2.0</td>
</tr>
<tr>
<td>PCA of model residuals</td>
<td>Is the survey unidimensional?</td>
<td>&lt;2.0</td>
</tr>
</tbody>
</table>
Chapter 3:

Results

3.1: Descriptive Statistics

3.1.1 Age and Visual Acuity

We had a total of 79 participants in this particular part of the study. As seen in table 3.1, the mean age was 81.19, with a minimum age of 58 and a maximum age of 97 and a standard deviation of 8.966. Table 3.1 also shows the acuities in LogMAR letter score for the better and worse eye. The mean acuity in the better eye was 60.86 logMAR letter score (equivalent to 20/63) with a standard deviation of 20.484. The lowest better eye acuity was 4 (20/800), while the best was 90 (20/15). The mean acuity in the worse eye was 35.29 logMAR letter score (equivalent to 20/200) with a standard deviation of 26.348. The lowest worse eye acuity was 0 (worse than 20/800), while the best was 84 (20/20).

3.1.2 Sex, High school Education and Injection Status

Table 3.2 shows that 48.1% of our sample were female and 51.9% male. Education was rated on a 0-4 scale; 0 being less than high school, 1: high school, 2: some college, 3: college, and 4: advanced degree. Table 3.3 shows
that 11.4% had lower than a high school education, 29.1% had a high school educated, 15.2 had some college, 20.3 had a college education, and 22.8 had an advanced degree. Moreover, table 3.4 displays that 53.2 % of the participants were received injections the day of their study visit, while 46.8% of the patients did not need an injection at their study visit.
Figure 3.1 Age Distribution of Subjects
Table 3.1. Demographics: Age and ETDRS Visual Acuity Better and Worse Eye

<table>
<thead>
<tr>
<th></th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>58</td>
<td>97</td>
<td>81.2</td>
<td>9.0</td>
</tr>
<tr>
<td>Better Eye ETDRS Visual Acuity</td>
<td>4</td>
<td>90</td>
<td>60.9</td>
<td>20.5</td>
</tr>
<tr>
<td>Worse Eye ETDRS Visual Acuity</td>
<td>0</td>
<td>84</td>
<td>35.3</td>
<td>26.3</td>
</tr>
</tbody>
</table>
Figure 3.2. Percentage of Male and Female Participants
Table 3.2 Education Level by Percent of Total

<table>
<thead>
<tr>
<th>Education Level</th>
<th>Percent of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (Less than high school)</td>
<td>11.4</td>
</tr>
<tr>
<td>1 (high school)</td>
<td>29.1</td>
</tr>
<tr>
<td>2 (Some college)</td>
<td>15.2</td>
</tr>
<tr>
<td>3 (College)</td>
<td>20.3</td>
</tr>
<tr>
<td>4 (Advanced degree)</td>
<td>22.8</td>
</tr>
</tbody>
</table>
Table 3.3. Percentage of Subjects Receiving Anti-VEGF Injections

<table>
<thead>
<tr>
<th>Injection Status</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (No injection)</td>
<td>46.8</td>
</tr>
<tr>
<td>1 (Injection)</td>
<td>53.2</td>
</tr>
</tbody>
</table>
3.2: Rasch Analysis

3.2.1 Infit Analysis

First, using the Rasch model we examined fit statistics by looking at the “infit mean square” analyses for each question on the PSS survey. This is a chi-square like statistic that tests the fit of each question to the Rasch model. A good value is considered to be between 0.70 to 1.3, anything significantly greater than 1.3 means that there is large variability in the way participants answered a certain question and therefore it may not useful in further analysis.

Initially this analysis was run on the 10 items in the PSS. All items fell within the 0.70 to 1.3 range except for the question regarding if a participant felt “confident”, which had a MNSQ value of 1.74. Therefore, this question was excluded from the proceeding analyses.

After this, another Rasch analysis was run and again all but one of the items fell within the accepted range. The item that asked about “things going your way” had a MNSQ value of 1.43 and fell out of that 0.7 to 1.3 range.

Finally, when the analysis was performed, all of the questions fit into the desired 0.7 to 1.3 range, thus we were left with 8 items to further analyze. Table 3.4 shows each item with its infit mean square fit statistic. Figures 3.5, 3.7, and 3.9 show the person-item maps for each of the three versions tested. These maps show the relationships between the amount of stress measured for each individual participant (labeled as an “X”) and the amount of stress required by each question.
3.2.2 Category Function

Figures 3.4, 3.6, and 3.8 show the category response probabilities for both the 10, 9, and 8 question versions of the PSS that we tested. Response category functioning is shown by the category probability plotted against the person measure relative to item difficulty graph. This graph shows the probabilities of a response in each category as a function of a person’s stress level. Ideally, for low stress levels there should be a high probability of answers in the low categories (like “never or almost never”), and for high stress levels there should be a high probability of responses in the high categories (like “all the time”). Each category should also have some point along the stress continuum at which it is the most likely response option. We found that the PSS’s five category response structure met all of these criteria for all three versions and therefore did not make any changes.

3.2.3 Person Separation

A separation value greater than 2.0 signifies adequate differentiation between items. Using the eight items that we included in the analysis, a separation value of 2.37 was calculated. This gave us confidence that our items were properly distinguishing between differing levels of stress and separating our participants on the scale adequately.
3.2.4 Unidimensionality

We used principal component analysis of the Rasch residuals to determine if the PSS was unidimensional. If there is no significant structure present in the data after the Rasch model is fit, it indicates that there are not other factors being measured. Eigenvalues for the PCA of less than two are consistent with unidimensionality. We found that the eigenvalue for the first contrast of the principal component analysis of the eight item scale was 2.0. This is on the borderline of acceptable, indicating minimal multidimensionality.

Table 3.4 Rasch Fit Statistics for the PSS.

<table>
<thead>
<tr>
<th>ITEM</th>
<th>MEASURE</th>
<th>S.E.</th>
<th>Infit MNSQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulties Piling Up</td>
<td>0.5</td>
<td>.17</td>
<td>0.83</td>
</tr>
<tr>
<td>Control Irritation</td>
<td>0.43</td>
<td>.16</td>
<td>1.11</td>
</tr>
<tr>
<td>Unable to Control</td>
<td>0.26</td>
<td>.16</td>
<td>1.04</td>
</tr>
<tr>
<td>On Top of Things</td>
<td>0.22</td>
<td>.16</td>
<td>1.09</td>
</tr>
<tr>
<td>Could not Cope</td>
<td>0.03</td>
<td>.16</td>
<td>1.11</td>
</tr>
<tr>
<td>Upset</td>
<td>-0.36</td>
<td>.15</td>
<td>1.25</td>
</tr>
<tr>
<td>Angered</td>
<td>-0.38</td>
<td>.15</td>
<td>0.85</td>
</tr>
<tr>
<td>Nervous/Stressed</td>
<td>-0.7</td>
<td>.15</td>
<td>0.69</td>
</tr>
</tbody>
</table>
Figure 3.3. Category Probability Curve for 8 Item PSS
Figure 3.4. Map for 8-Item PSS
Figure 3.5. Category Probability Curve for 9-Item PSS (Minus Item 4)
Figure 3.6. Map for 9-Item PSS (Minus item 4)
Figure 3.7. Category Probability Curve for Full PSS
Figure 3.8. Map for Full PSS
3.3 Visual Acuity, Self-reported Visual Functioning, and Perceived Stress

Visual acuity in both the better and worse eye were inversely correlated with age, such that those participants who were older had poorer visual acuity (Pearson correlation coefficients = -0.509 and -0.497 respectively, P < 0.001) (see Figures 3.10). Age was also inversely correlated with self-reported visual functioning (IVI) results (-0.463, P<0.001) (see Figure 3.11). Visual acuity in the better eye was correlated to visual acuity in the worse eye (0.644, P<0.001). Better eye visual acuity was also significantly correlated with self-reported visual functioning (0.573, P<0.001) as expected.

Perceived stress as measured by the PSS was not correlated with visual acuity in the worse (-0.005, P=0.968) or better eye (0.030, P=0.793) (Figures 3.13 and 3.14). These results indicate that there was not a significant relationship between visual acuity and perceived stress in the participants with AMD in this study. The relationships between stress and age and education level, respectively, are shown in Figures 3.15 and 3.16.

Interestingly, IVI results were correlated with PSS results (-0.231, P=0.04), indicating that there is a significant relationship between self-reported visual functioning and perceived stress. Participants with lower levels of self-reported visual functioning had generally higher levels of perceived stress (Figure 3.17). We also found that social support levels were predictive of stress (-0.475, P<0.001), indicating that patients with higher levels of social support as measured by the ESSI had generally lower levels of stress.
Figure 3.9 Visual Acuity by Age
Figure 3.10 IVI Score by Age
Figure 3.11 IVI Score by Better-eye Visual Acuity
Figure 3.12 PSS by Worse-Eye Visual Acuity
Figure 3.13 PSS by Better-Eye Visual Acuity
Figure 3.14 PSS by Age
Figure 3.15 PSS by Education Level
Figure 3.16 PSS vs. IVI
Chapter 4: Discussion

4.1 Public Health Concern

Age related macular degeneration is a major public health concern being that it is the leading cause of permanent vision loss in developed countries.\(^2,9-11\) Along with increased difficulty with activities of daily living, including reading and cooking, macular degeneration also contributes to one’s psychological well-being. Multiple studies have shown that those with vision loss tend to be more depressed than their control counterparts.\(^4, 6, 7, 43\) One study looking at one third of their subjects with macular degeneration had depressive disorder.\(^4\) Though there are numerous studies examining the issue of depression amongst patients with macular degeneration, the issue of stress has not been thoroughly studied. Currently there is no research on stress and its relationship to macular degeneration. This is important because macular degeneration and its subsequent treatment may cause a patient to experience stress which in turn has been shown to have negative effects on one’s health and immunity. Knowing how all these integral pieces fit into the larger puzzle can change the way we care for these patients.
4.2 PSS and AMD

The perceived stress scale is a commonly used survey to assess how much stress one believes exists in his or her life.\textsuperscript{16} This survey is widely used in different scenarios, specifically to study how stress affects self-reported health and health outcomes. Due to its popularity in research and use in diverse populations, we thought it would be worthwhile to investigate its use in patients with AMD. Moreover, none of the studies using the PSS have run the questionnaire through a Rasch analysis to see if the survey is accurately measuring the question of interest. Therefore, we did just that to show that the PSS can be effectively used in people with AMD.

4.3 Rasch Analysis

The Rasch model was used to analyze validity, including category function, person separation and unidimensionality. The category function results showed that based on the difficulty of the questions and stress level, we could predict how a subject would answer to each particular question. Person separation confirmed that the PSS was able to separate our subjects into distinct groups along a scale based on their reported stress. Finally, the PSS was found to be unidimensional (or have only minor evidence of multidimensionality) in that it only measures stress and no other factors. These were all good indicators that the PSS survey studied what we wanted it to, stress, and was valid for use in our patient population. This is important
because it lays the groundwork for this survey to be used more in AMD patients to assess how stress from the disease and treatment is affecting their lives and their vision and health outcomes.

Knowing that the survey could successfully be used in patients with AMD, we analyzed the relationships among stress and a number of visual and demographic factors. Importantly, we found that visual acuity did not predict perceived stress. There was a general trend for those with worse acuity to report more stress but this was not statistically significant.

Self-reported visual functioning, on the other hand, did predict stress score. More subjective measures of vision, such as the IVI more directly address how someone feels they are functioning on a day to day basis, which seems to more closely correspond with stress level. For example, if a person does not read to begin with, he or she will not be as psychologically affected by losing the ability to read due to vision loss. However, someone who is an avid reader and suddenly cannot do so due to AMD will experience and report more stress.

4.4 Stress and Inflammation in AMD

Furthermore, with the PSS shown to be effective for measuring stress in AMD patients, we are working on a study that looks at stress (using the PSS to measure perceived stress) and its effects on inflammation and C-reactive protein levels in patients receiving injections for wet macular degeneration. C-
reactive protein is a risk factor for AMD. The use of this survey allows for future work in studying the potential causes of stress with vision loss and treatment.

If stress is present in patients with macular degeneration and stress is also part of the treatment process (getting an injection in the eye), and then stress negatively impacts one’s immune system, this becomes a vicious cycle that is not in favor of the patient’s well-being. For this reason, it is worth considering treatment options for the stress in these patients. For example, low vision rehabilitation addresses loss of valued activities and seeks to improve the patient’s quality of life might be beneficial for stress reduction. With the aging population and increase in the number of people with macular degeneration, vision rehabilitation is becoming a crucial part of patient care. Studies in this area could show its importance and make rehabilitation part of the treatment plan, along with injections to slow disease progression.

4.5 Treatment Outcome Measures

Thus far, visual acuity is by far the most common tool used to describe treatment success. However, in our study, visual acuity was not found to be significantly correlated with stress. Therefore, perhaps self-reported visual function should also be considered when talking about treatment outcomes, since it is shown to predict perceived stress. Self-reported functioning questionnaires, like the IVI, may be a better indicator of one’s ability to complete
valued activities such as reading or recognizing faces, and this may be related to psychology.

4.6 Role of Vision Rehabilitation

Another area of future research is whether time since first vision loss is related to the amount of perceived stress. We did not measure that in our study and therefore do not know how long each person has been dealing with AMD. As stated previously, this can potentially have an impact on how stressed one feels about their vision loss. Someone with severely reduced vision for the past ten years may be acclimated to life and not be bothered that they cannot read the small print on medicine bottles. On the other hand, someone who has always had 20/20 vision and now has 20/60 vision due early dry macular degeneration will probably experience more stress as they slowly lose the ability to complete tasks that were once second nature. In future studies this may give insight into why people with poorer acuity may not necessarily be more stressed.

One study by Rovner\textsuperscript{44} found that vision rehabilitation along with mental health intervention reduced the percentage of depressed patients by half when compared to standard outpatient low vision rehabilitation. The mental health aspect was behavioral activation, or teaching adaptive behaviors to achieve valued goals. They concluded that with the increasing number of older patients with AMD, integrated care between ophthalmology, optometry, rehabilitation
and psychology could prevent depression in this population. Similar studies can be conducted looking at perceived stress and low vision rehabilitation.

Another review article looking at improving depression in patients with AMD noted that depression in these patients stems from loss in ability to complete tasks that were at one point second nature, such as reading. Since low vision rehabilitation focuses on “activity re-engagement”, it may have an antidepressant effect. The paper notes that although there is research to show that low vision rehab improved depression, they do not believe there is current research looking at its effects on anxiety. The author goes on to state that behavioral interventions can also be used to treat depression AMD patients.

4.7 Contributing Factors to Coping with AMD

Moreover, there are other life factor that are in play when studying stress. For example, one of the surveys administered to our patients was the ESSI, which looked at social support. In fact, another member of our lab reported that social support was in fact a predictor of lower levels of stress. This goes to show that it is not a simple correlation where a person has vision loss from AMD and thus they are stressed. The psychological response to any life stressor is multidimensional and probably includes how long someone has had the disease, how much help does he or she have with daily activities, does he or she have someone to talk to about his or her worries and more. We found
important correlations that open the door for further investigation and insight into how to best treat these patients and not just their disease.

4.8 Limitations and Future Work

There were limitations to our study. It was often difficult or impossible for the subjects to read the surveys. Despite the large print and one question per page printing, if our subjects could not read the surveys we read it to them and recorded their answers. This could cause patients to reply differently than if they were reading the surveys themselves and no one knew what they were answering. Also, many patients had family members with them in the exam room, which could also alter how questions were answered. However, because we were administering surveys mostly before an injection visit, we did not ask the family members to leave the room in an attempt to provide for as much patient comfort as possible. In the future we could analyze our results based on if the surveys were read to patients or not and if they were accompanied by a family member or not to see if there would be differences in the results.

An area for future research is whether time since first vision loss is related to the amount of perceived stress. We did not measure that in our study and therefore do not know how long each person has been dealing with AMD. As stated previously, this can potentially have an impact on how stressed one feels about their vision loss. Someone with severely reduced vision for the past ten years may be acclimated to life and not be bothered that they cannot read
the small print on medicine bottles. On the other hand, someone who has always had 20/20 vision and now has 20/60 vision due early dry macular degeneration will probably experience more stress as they slowly lose the ability to complete tasks that were once second nature. Future studies may give insight into why people with poorer acuity may not necessarily be more stressed.

With the PSS shown to be effective for measuring stress in AMD patients, we are currently working on a study that looks at stress (using the PSS to measure perceived stress) and its effects on inflammation and C-reactive protein levels in patients receiving injections for wet macular degeneration. The use of this survey allows for future work in studying the potential causes of stress with vision loss and treatment and the potential role of stress in affecting visual treatment outcomes.
Bibliography


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15. Janet M. Kaye PhD MPLP, Laura N. Gitlin PhD, Morton H., Kleban PhD LAWBDKM. Older People’s Performance on the Profile of Mood States (POMS). Clinical Gerontologist 2010;7:35-56.


Appendix A: POMS

Below is a list of words that describe feelings people have. Please circle the number that best describes how you feel right now.

Tense
Angry
Worn Out
Unhappy
Proud
Lively
Confused
Sad
Active
On-edge
Grouchy
Ashamed
Energetic
Hopeless
Uneasy
Restless
Unable to concentrate
Fatigued
Competent
Annoyed
Discouraged
Resentful
Nervous
Miserable
Confident
Bitter
Exhausted
Anxious
Helpless
Weary
Satisfied

Responses:
Not At All
A Little
Moderately
Quite a lot
Extremely
Bewildered
Furious
Full of Pep
Worthless
Forgetful
Vigorous
Uncertain about things
Bushed
Embarrassed
Appendix B: Perceived Stress Scale

In the last month how often have you:

Been upset because of something that happened unexpectedly?
Felt that you were unable to control the important things in your life?
Felt nervous and “stressed”?  
Felt confident about your ability to handle your personal problems?
Felt that things were going your way?
Found that you could not cope with all things that you had to do?
Been able to control irritations in your life?
Felt that you were on top of things?
Been angered because of things that were outside of your control?
Felt difficulties were piling up so high that you could not overcome them?

Responses:
Never
Almost never
Sometimes
Fairly often
Very often
Appendix C: CES-D

During the past week:

I was bothered by things that usually don’t bother me.

I felt that I could not shake off the blues even with help from my family and friends.

I felt I was just as good as other people.

I had trouble keeping my mind on what I was doing.

I felt that everything I did was an effort.

I felt hopeful about the future.

I thought my life had been a failure.

I felt fearful.

I felt lonely.

People were unfriendly.

Responses:

- Rarely or none of the time
- Some or a little of the time
- Occasionally or a moderate amount of the time
- Most or all of the time
Appendix D: ESSI

Is there someone available to you whom you can count on to listen to you when you need to talk?

Is there someone available to give you good advice about a problem?

Is there someone available to you who shows you love and affection?

Is there someone available to help you with daily chores?

Can you count on anyone to provide you with emotional support (talking over problems or helping you make a difficult decision)?

Do you have as much contact as you would like with someone you feel close to, someone in whom you can trust and confide?

Responses:

None of the time
A little of the time
Some of the time
Most of the time
All of the time
Appendix E: IVI

In the past month, how much has your eyesight interfered with:

Your ability to see and enjoy T.V.?

Shopping? (finding what you want and paying for it)

Generally looking after your appearance? (face, hair, clothing etc.)

Opening packaging? (for example, around food, medicines)

Reading labels or instructions on medicines?

Operating household appliances and the telephone?

Reading ordinary size print? (for example newspapers)

Getting the information that you need?

Recognizing or meeting people?

Responses:
- Not at all
- A little
- A fair amount
- A lot
- Don’t do this for other reasons