CORRELATION OF QUALITY OF LIFE WITH CLINICAL SYMPTOMS AND SIGNS AT THE TIME OF GLAUCOMA DIAGNOSIS*

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ABSTRACT

Purpose: To examine the relationship between clinical measures of visual function and patient-reported measures of symptoms and health status in a large cohort of glaucoma patients at the time of diagnosis.

Subjects and Methods: The 607 patients in the Collaborative Initial Glaucoma Treatment Study (CIGTS) received standardized examinations of visual acuity and visual field at enrollment. In addition, they completed a health-related quality-of-life instrument, which included the Visual Activities Questionnaire (VAQ), Sickness Impact Profile (SIP), a symptom and a comorbidity chart, a question about their degree of worry about becoming blind, and many other items.

Results: The SIP total and dimension scores correlated only weakly, and not significantly, with visual acuity and visual field measures. The VAQ total and subscale scores, particularly the peripheral vision subscale, correlated weakly and significantly with visual acuity and visual field scores, especially those from the better eye. Worry about blindness and symptoms attributed to glaucoma correlated weakly but significantly to visual field scores from the worse eye. Attempts to improve correlations by scoring the visual fields differently, including only paracentral and pericentral test locations in the scores, and simulating binocular visual field scores were largely unsuccessful.

Conclusions: At diagnosis, most patients were relatively free of glaucoma-induced impairments, so clinical measures were poor predictors of a patient's perception of health-related quality of life. The vision-specific VAQ and glaucoma-related symptom score correlated better than the generic SIP with clinical measures at the time of enrollment into CIGTS.

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INTRODUCTION AND LITERATURE REVIEW

At the time of diagnosis of a disease or condition, patients are confronted simultaneously with external information about the problem and proposed treatment options and internal reactions to the illness and the threats the diagnosis brings to the quality of their life. At this time, the patient is expected to make decisions between treatment and no treatment, indeed among various treatment options, during the process of informed consent. For acute illness, the decisions are often clear because of dramatic differences in outcome between options. For subacute or chronic diseases, in which neither death nor cure is a meaningful measure of treatment effect, the decisions are less obvious because they depend on the interactions between knowledge of natural history of disease, treatment effects, and side effects, and the ultimate quality of life expected and desired by the patient. As Cluff[1] points out, "It is time to recognize that the primary objective of medical care is to improve patient function and to reduce the degree of illness...This is what patients have always wanted and what they need."

The medical model presumes that disease is a sequence from etiology to pathology to clinical manifestations over time. In chronic disease states, however, the sequence may be reversed: Functional limitations and perceived health can actually influence physiologic measures. For example, in rheumatoid arthritis, mobility may be impaired so that exercise is avoided, with adverse consequences in cardiovascular and mental health. Thus, studies of chronic disease that measure only physiologic outcomes may miss important factors influencing the process.[2,3]

Glaucoma is a chronic disease that can cause blindness if untreated, but it is asymptomatic in its early stages. Treatment, either medical or surgical, may produce undesirable consequences for a patient's quality of life over long periods. For example, topical beta blockers may lead to impotence and unwanted abandonment of sexual functioning, or a prominent surgical filtration bleb may produce chronic irritation and tearing. In opting for treatment, the patient elects to endure the side effects of treatment as a trade-off for avoidance of later blindness. Unfortunately, we have very little knowledge about how glaucoma affects quality of life and how treatment modifies those effects. Thus, it is difficult to counsel patients to allow them to make decisions regarding their treatment during the informed consent process. Although ophthalmologists have long understood in a compassionate sense the many ways in which glaucoma can affect a patient's life beginning at diagnosis and continuing throughout treatment,[4] it is only recently that quantitative measures that permit valid, reproducible, responsive, and generalizable determinations of functional health status have been available.[5]

The Collaborative Initial Glaucoma Treatment Study (CIGTS), fund-

ed by the National Eye Institute, is a multicenter collaborative clinical trial to determine whether initial surgical or initial medical therapy is best for newly diagnosed glaucoma. The usual clinical measures of visual acuity and visual field will serve as principal outcome variables, but changes in patients' quality of life are an important outcome that will be measured as well. Some clinicians believe that patients prefer medical therapy because they are averse to risk and medical therapy offers relatively low risks, but others argue that the "hassle factor" of using drops that may not be entirely innocuous makes medical therapy less desirable. The observation that glaucoma patients frequently forget to use prescribed medications or omit them because of the side effects they produce[6,7] may imply that patients dislike the negative effect of medications on their quality of life. Contrasting arguments about surgical therapy are also advanced. Patients who have had successful filtering surgery, who no longer need medication, may report they never realized how much the medical therapy bothered them. Other patients may have encountered complications from the surgery that were far worse than those they experienced while they were taking eye drops. Until the CIGTS study was begun, no analysis of the quality-of-life changes produced by medical versus surgical therapy of glaucoma had been attempted.

QUALITY-OF-LIFE MEASUREMENT

As part of a project to design a quality-of-life measurement instrument suitable for worldwide use, the World Health Organization defined quality of life as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns."[8] Quality of life is impacted by many widely valued aspects of human existence that have little or nothing to do with health status, such as a safe environment, adequate housing, guaranteed income, and freedom.[9] As a result, when considering the domains relevant to health or functional status, it is wise to refer to "health-related quality of life." Patrick and Erickson[10,11] outlined 5 broad categories of concepts or domains to be considered: opportunity, health perceptions, functional status, impairments, and death and duration of life. Opportunity is the most difficult to measure, since it covers the loss of options for pleasurable activity an individual might incur because of health status or handicap, and any decreased "reserve capacity" for absorbing stress or negative life events. Health perceptions concern overall satisfaction with health and level of health concerns or worries. Functional status covers any limitations in social, psychological, or physical activity. Impairment includes symptoms, signs, self-reported disease, and conventional physiologic measures. Finally, death and duration of life concern survival and longevity. Attempts to measure health-related quality of life should subsume all 5 of these domains to the

extent that each is relevant and measurable. On the other hand, certain domains will be more relevant for each disease and may require increased attention.[12] Where possible, changes to health-related quality of life in the positive direction, such as might result from health promotion activities, should be identifiable as well.[9]

Because many of the components of quality of life cannot be directly observed, they are typically evaluated according to the principles of item response theory. This theory proposes there is a true quality of life value that cannot be measured directly but can be measured indirectly by asking a series of questions known as "items," each of which measures the same true construct. The answers are converted to numerical scores that are combined to yield "scale scores," further combined to yield "domain scores," and finally to an overall score.[13]

Measurement of health-related quality of life is typically accomplished using a questionnaire administered to a patient by a trained interviewer or self-administered. The least costly way is self-administration, but typically this results in increases in missed responses and missed subjects. In-person interviewing maximizes response rate and decreases omissions but is subject to interviewer bias and requires well-trained interviewers on site. A reasonable compromise is administration by telephone, especially where multiple sites make the availability of in-person interviewers problematic.[14]

The score from a typical questionnaire is equally weighted; that is, each response is counted equally, without regard to the relative importance or utility a patient might assign to each attribute. When making policy decisions based on health status measures, it is well recognized that philosophical and ethical considerations mandate a social metric based on preferences.[15] However, utility weighting of health-related quality of life carries practical and conceptual difficulties. Practically, the sensitivity of utilities to clinical changes is quite variable, and conceptually, utilities often reflect factors other than health status, such as the value placed on life, risk aversion, or attitudes toward certain medical interventions.[16] However, the usual lack of utility weighting in quality-of-life studies led Gill and Feinstein[17] to question the relevance of studies that did not at least include a single global rating of quality of life or health-related quality of life that can reflect the disparate values and preferences of individual patients. Another approach is to use the health-related quality of life results based on unweighted scores in conjunction with a patient's preferences in deciding on an appropriate treatment for an individual.[18]

Once a set of items has been designed to measure one or more domains of health-related quality of life, the instrument must be painstakingly validated. This process involves a test of both the signal-to-noise ratio and various measures of validity. For instruments intended to discriminate between patients with different levels of health-related quality of life, the

way to quantify the signal-to-noise ratio is called reliability or reproducibility. This can be measured within an instrument by comparing responses to items that ask nearly the same question with Cronbach's alpha statistic.[19] Alternatively, the instrument can be readministered to a group of people after an interval, and reproducibility can be calculated using an intraclass correlation coefficient.[20]

For evaluative instruments intended to show change over time, the signal-to-noise ratio is evaluated by a test of responsiveness, such as effect size. This relates changes in mean score over a time interval to the standard deviation of baseline scores or to the standard deviation of score changes in stable subjects. Effect sizes are useful in judging clinical importance; Deyo and Patrick[21] have suggested that effect sizes of 0.20 are small, 0.50 are moderate, and 0.80 or greater are large. Another method of testing responsiveness is to construct a receiver operating characteristic curve against an external standard of change.[20] The area under the curve is a reflection of the accuracy of correctly identifying the changed patient from randomly selected pairs of changed and unchanged patients.

Measurement of validity is more complex. If a gold standard exists, such as a long form of an instrument, and a shorter version is being tested, criterion validity is applicable.[14] Content validity, on the other hand, depends on whether the items of an instrument adequately represent the domain they are supposed to measure. Ordinarily, this cannot be done quantitatively and depends on a commonsense qualitative approach.[14] Most commonly, validity of an instrument is approached through construct validity, or whether the instrument behaves as expected based on a theoretical construct.[22] Construct validity can be evaluated using 3 different approaches: testing for dimensions inherent in the construct (factor analysis), covariation of these dimensions with independent measures of the same phenomenon (convergent validity), and predicted variation of measures according to demographic or health status criteria (discriminant validity).[12,23]

Quality-of-life measurement has become a critical component of controlled clinical trials,[24,25] especially those in which the treatments are very different in therapeutic approach.[26] According to Guyatt and associates,[27] several issues should be addressed before applying a health-related quality-of-life instrument in a clinical trial. First, the purpose of instrument use must be clearly stated. Second, its measurement properties must fit the intended purpose. Third, the general categories of instruments required should be identified, and finally, the appropriate format for the instrument should be selected. These decisions cannot be made parsimoniously unless a clear theoretical model of the associations between the biologic process and the components of health-related quality of life is understood.[28] As such methodologies are applied to trials, it is wise to remember a placebo

effect from participation in a trial, regardless of treatment applied.[29]

Pocock[26] made several cogent statements about the value of quality-of-life measurement in clinical trials. First, as patients abandon their right to choice of treatment in randomization, it seems desirable that "their opinions on their subsequent condition be sought in a rigorously defined manner." Second, the process of eliciting such information may contribute positively to their sense of well-being (see also Greenfield and Nelson[30]). Third, "There is a danger that seemingly sophisticated clinical measures (eg, sphygmomanometry, visual acuity) acquire an undue respectability." For example, "Sloppy measurement of blood pressure may, unjustifiably, be criticized less than a poorly defined health-related quality-of-life technique because the former is still perceived as a 'real measurement'." Finally, "...if the treatments under comparison represent a major difference in therapeutic approach, then health-related quality of life may be of particular importance."

HEALTH-RELATED QUALITY-OF-LIFE INSTRUMENTS: GENERIC VERSUS SPECIFIC

As Bergner[31] has pointed out, health-related quality-of-life assessments should examine factors likely to be affected by an intervention or that have troubled patients in the past, factors that may be affected, and factors that are very unlikely to occur but are possible. Use of a generic instrument that has been validated in a variety of populations with a spectrum of diseases offers several advantages to an assessment. Typically, generic instruments have enough breadth of coverage to reveal important but unexpected quality-of life-effects, such as side effects outside the organ system being treated. They allow comparisons across populations and conditions and can be used in cost-effectiveness analyses. However, they may not have enough responsiveness to detect changes important to a specific disease or condition.[25]

Consequently, a modular approach is often the best strategy, combining a generic instrument with a disease-specific one, both of which have been independently validated.[32] Still, there may be need in a specific study for coverage of additional anticipated factors that require design of new items. While arduous, the process for design of a new instrument is well outlined: item generation from discussions with patients and professionals, item reduction based on frequency and impact, questionnaire formatting, and pilot testing for reliability, responsiveness, and construct validity.[33] Cleary and colleagues[34] designed a new instrument for AIDS patients by using a mixture of items from existing instruments and new items and applied this validation process.

The wisdom of following a modular approach in overall instrument design is illustrated by the work of Parkerson and associates[35] in insulin-

dependent diabetic patients. While the disease-specific Diabetes Quality of Life questionnaire was thought initially to be more responsive than generic measures, it turned out that the generic measures captured as much as or more relevant information than the disease-specific one. On the other hand, in studying elderly elective surgery patients, Mangione and coworkers[36] found that elderly persons have similar global health perception compared with younger individuals. The investigators concluded that since the elderly may have different expectations of health status, use of generic measures alone may not reflect important dimension-specific impairments in health. They may also adapt their leisure activities to suit their functional status, avoiding those that are difficult while not expecting to be able to do them.[37] On the other hand, in a large study of 1,191 elderly Italians, Carabellese and associates[38] found that single sensory impairments (hearing or vision) were significantly and independently associated with increased risk for depression and decreased self-sufficiency in activities of daily living.

Use of disease-specific instruments, especially those that are designed for a specific study, creates difficulties in evaluating the clinical significance of observed changes. How much change in a mean score would translate to meaningful change for a patient? Across several disease-specific instruments using 7-point response scales, validation studies have indicated that a change in mean score of 0.5 units may be considered the minimal important difference.[39]

Health-related quality-of-life studies in nonocular disease

Considerable information on quality-of-life measurement in various diseases can be found in the literature; in fact, a Medline search on quality of life alone yielded 9,176 citations for the period 1990 through 1996. Some of the earlier studies concerned systemic hypertension,[40-43] cardiovascular disease,[44-46] diabetes mellitus,[47] end-stage renal disease,[48] cancer,[49] and various surgical interventions,[50] including organ transplantation.[51]

Many clinicians are suspicious of health-related quality-of-life data, viewing it as soft and subjective and less reliable than clinical examination, laboratory, or radiographic data. As Deyo and colleagues[52] have pointed out, the degree of interobserver variability in lumbar spine radiographs is much greater than that seen in repeated administration of instruments such as the Sickness Impact Profile (SIP). In a now classic multicenter trial of auranofin therapy in rheumatoid arthritis, health-related quality-of-life instruments performed equally as well as clinical measures in documenting the superiority of treatment to placebo.[53] The early Patient Outcome Research Teams (PORTs) supported by the Agency for Health Care Policy and Research (AHCPR) included literature synthesis and analysis of Medicare databases, in an effort to find out "what works" in medicine.

Yet such data do not contain information on dysfunction, discomfort, and patient satisfaction and cannot draw conclusions about relative efficacy of treatment options.[54] Controlled clinical trials with patient-centered outcomes are needed to complement outcomes research.

Like glaucoma, systemic hypertension is a disease that is usually asymptomatic in its early stages, and its treatment may render the patient symptomatic. Studies of patient quality of life are extremely important in evaluating therapy, since a decreased quality of life with therapy may be the trade-off for decreased cardiovascular complications in the future.[44] Three classes of antihypertensive medication produced similar blood pressure reduction, but 2 of the 3 had adverse effects on health-related quality of life.[40,55] On the other hand, in 902 patients with early stage 1 diastolic hypertension, none of 5 antihypertensive drugs impaired quality of life, and lifestyle changes adopted in treatment had beneficial effects on quality of life.[56]

QUALITY-OF-LIFE STUDIES IN OCULAR DISEASE

Cataract and Corneal Transplantation

Quality of life has been studied as an outcome variable for interventions in several eye diseases, especially cataract. Cataract was the subject of an AHCPR PORT study.[57] The instrument administered for that study included the SIP, 5 items about cataract symptoms, 2 global items about vision, 29 items about medical comorbidity, and a new instrument measuring visual functioning, the VF-14.[58] As might be expected, the VF-14 proved to be three times more responsive to changes in vision than the SIP.[59] A study completed at about the same time, using a more limited coverage of the domains of visual function,[60] led to unrealistically high estimates of the rate of inappropriate surgery.[61]

A Swedish group[62] used a previously unvalidated instrument to explore 37 specific activities of daily life before and after cataract extraction, finding that the correlation with number of problems was best with binocular visual acuity but showed much variation. Similar to the findings of Mangione and associates,[36] elderly patients had a lower expectation of health status. Thus, they had fewer problems before surgery and lower improvement scores after surgery than younger patients.

Using the Activities of Daily Vision Scale (ADVS) and the SF-36 (36-item short form from the Medical Outcomes Study),[63] Mangione and associates[64] found that elderly patients experienced worsening on 7 of 8 SF-36 subscales 12 months after cataract surgery, but the declines were significantly less across all SF-36 dimensions among those patients experiencing improved ADVS scores. They concluded that age-related declines in health (that proceed in spite of treatment) may be attenuated by improvements in visual function, such as after cataract surgery. A British group[65]

used the VF-14, the SIP, and a vision-related SIP to document gains in visual function and quality of life after cataract surgery. They found that even those patients with poor clinical visual outcome showed some gains on the quality-of-life measures. Similar findings were reported by Brenner and coworkers[66] using less-well-validated instruments in a larger series of cataract patients and controls with chronic ocular disease.

Binocular visual function is often casually interpreted as the resultant of the best acuity and field from each eye. Following corneal transplantation, the single most important factor associated with the patient's visual function reported on the VF-14 was their visual acuity in the better eye.[67] If the vision in the better eye were the only important determinant of visual function, one might predict that improvement of vision of one eye would produce enough improvement that the cataract in the other eye should not be operated on. However, Javitt and colleagues[68] showed that improvement in subjective function on a simple 8-question instrument 1 year after cataract surgery was greater after surgery in both eyes than after surgery on 1 eye alone. The finding was confirmed by Desai and associates[65] in the British study referenced above.

Other Nonglaucomatous Eye Disease

Using an investigator-designed instrument, Satterfield and colleagues[69] found that strabismus patients reported difficulties with self-image, securing employment, interpersonal relationships, school, work, and sports. They also had higher levels of distress evidenced on the generic Hopkins Symptom Checklist. Keltner[70] speculated that the observed expanded binocular visual field following surgery for esotropia[71] might contribute to better functional ability and driving performance.

Also using investigator-designed instruments, Battu and coworkers[72] found improvement in vision-related activity following surgical blepharoptosis repair, and Freitas and colleagues[73] demonstrated improved self-reported functional status after photorefractive keratectomy for myopia. Wu and associates[74] designed a 5-minute, 18-item questionnaire to assess visual functioning in AIDS patients with cytomegalovirus retinitis. They found that visual symptoms correlated most strongly with findings in the worse eye and that visual function and global vision scores were moderately correlated with clinical measures. However, the population of cytomegalovirus patients generally had moderately severe visual impairment. Blurred vision, regardless of cause, was found to produce role limitations on the SF-36 greater than the impact of hypertension, history of myocardial infarction, type 2 diabetes mellitus, indigestion, trouble urinating, and headache, when tested on the 1,642 respondents to the Medical Outcomes Study 2-year follow-up.[75]

Glaucoma

Glaucoma in its early manifestations does not produce blurred vision. In fact, in all but the most severe glaucoma, the visual field is damaged more severely than visual acuity. Measures that estimate the degree of binocular field loss were found to correlate with scores of glaucoma patients on a specific instrument designed to be responsive to visual field disability.[76] The same instrument correlated less well but significantly with visual acuity, although different questionnaire items were responsible for the correlation.[77]

The clinical measure of binocular field loss used in the 2 studies was the automated Esterman test [78,79] This test has been recommended by the American Medical Association[80] as a method of evaluating visual field disability, and it has shown remarkable stability and reliability over a 2-year interval in advanced glaucoma patients.[77] The automated Esterman software has had limited distribution and may account for the paucity of literature on its use in various ocular conditions. Buckley and associates[81] reported that 50% of diabetic patients after panretinal photocoagulation failed to achieve an Esterman score sufficient to obtain a British driver's license, but this estimate was revised to 19% in a later study by Mackie and colleagues.[82] Because other visual mechanisms that are mediated binocularly are damaged in early glaucoma, Essock and coworkers[83] recommend that binocular testing be included for routine assessment of glaucoma patients.

Two currently ongoing multicenter collaborative clinical trials funded by the National Eye Institute utilize the Medical Outcomes Study SF-36 in monitoring generic health-related quality of life: the Ocular Hypertension Treatment Study[84] and the Collaborative Logitudinal Evaluation of Keratoconus Study (National Institutes of Health, Bethesda Md). In search of an acceptable vision-specific instrument that would apply to most eye disease, the National Eye Institute (NEI) convened a workshop titled "Measuring the Quality of Life of People With Visual Impairment"[85] and developed an instrument for measurement of visual function—the NEI-VFQ. The full instrument in English and Spanish versions has been published in appendixes to the American Ophthalmological Society thesis of Parrish.[86]

In that study, Parrish correlated visual field impairment scores obtained by binocular Esterman testing and the AMA Guides to Permanent Impairment[80] in glaucoma patients with scores on the SF-36, VF-14, and NEI-VFQ. There was no correlation with SF-36, modest correlation with the VF-14, and modest correlation with VFQ subscales distance activity, vision-specific dependency, and vision-specific social functioning, but no correlation with subscales relating to driving, color vision, general health, or vision-specific expectations.

Gutierrez and associates[87] compared 147 patients with glaucoma ranging in severity from early through end stage to 44 reference-group patients drawn from practices of 5 glaucoma subspecialists. On the SF-36, there was no difference between the groups, but on 7 of 11 subscales of the NEI-VFQ, there was a significant difference, and a trend toward a significant difference was observed in the VF-14 scores. Greater visual field defects in the better eye were significantly associated with poorer NEI-VFQ and VF-14 scores. These findings were most dramatic for patients with the most severe visual field loss in the better eye.

CORRELATIONS: CLINICAL SIGNS VERSUS SYMPTOMS ON HEALTH-RELATED QUALITY OF LIFE

Some investigators are troubled by the mild to moderate correlations between traditional clinical measures of function and scores on health-related quality-of-life instruments. Yet it is well known that a discrepancy between symptoms and clinical signs is common in many different conditions. In patients with benign prostatic hyperplasia, there was so little correlation between the specific symptoms of the disease and outflow obstruction as defined by urodynamic criteria that the investigators suggested there was no need for routine invasive urodynamic investigation of such patients.[88] The size of peptic ulcers is only weakly correlated with symptom reports[89]; cervical arthritic pain cannot be predicted from bone x-rays alone,[90] computed tomographic scanning,[91] or magnetic resonance imaging scanning[92]; clinical response to nonsteroidal anti-inflammatory agents in osteoarthritis shows a low correlation to generic quality-of-life scores[93]; dyspnea in asthmatics corresponds poorly with measures of airway obstruction[94]; and palpitations are more correlated to somatization and hypochondriasis than arrhythmia.[95] In view of this reduced or absent correlation of symptoms and signs in many diseases, Wilson and Cleary[16] observed that research that explores other likely determinants of symptoms, such as psychological factors, patient expectations, social factors, and aspects of the patient-physician relationship, may help clinicians to address better the factors related to reported symptoms.

Differences in symptom reporting between men and women, not attributable to differences in physical morbidity, are consistently found, with women having the higher rates.[96] Advanced age may also be associated with decreased symptom reporting relative to younger patients, even after controlling for severity of illness.[97]

On the proximal to distal continuum proposed by Brenner and associates,[98] signs and symptoms are most proximal, disease-specific functioning lies in the middle, and life satisfaction and affective state are most distal to treatment interventions such as cataract surgery. The more distal an outcome, the less likely that change will be observed following an interven-

tion. Fortunately for ophthalmic outcomes, there is often moderate correlation between objective measures and symptoms or quality of life. Such was the case with cataract surgery and measures of visual acuity and contrast sensitivity.[99]

A similar problem of perception exists that subjective information is too "soft" a basis for drawing definitive conclusions. As pointed out by Deyo and associates,[20] several studies suggest that questionnaire responses can be more reproducible than a physician's examination or interpretations of imaging tests. Combatting this bias among clinicians is one of the major hurdles faced by advocates of outcomes research.

ATTRIBUTION OF SYMPTOMS TO A DIAGNOSIS

It is a common clinical observation that patients who have been newly diagnosed with a medical condition will wonder if all of their symptoms, even those seemingly unrelated, are attributable to the new diagnosis. For example, in untreated mild hypertension, which is unlikely to produce symptoms, complaint attribution rates have been high.[100,101] In a random sample of 60-year-old men with untreated hypertension, 7 symptoms were significantly correlated to blood pressure, yet all were regarded as caused by etiologic factors other than hypertension.[102] Likewise, on initiation of therapy, even with placebos, new symptoms may appear or existing symptoms may exacerbate and be attributed to the therapy.[44]

Considerable data in the literature support the notion that how healthy patients feel and how they score on standardized health status instruments are more closely related to their fears and beliefs about disease and their tendency to somatize distress than to clinical assessments of medical status.[95] A theory to explain this behavior was forwarded by Kirmayer and associates.[103] Until a symptom is attributed, it cannot be said to have a cause. Without cause, there is no possibility of gaining a degree of control over events, nor to apportion moral responsibility and blame. Furthermore, once attribution of 1 symptom occurs, people tend to look for additional symptoms to fit the schema.[104,105] Of course, preexisting psychiatric morbidity,[106] hypochondriasis,[107] and cultural context[103] all play a role in determining the degree to which symptom attribution to a diagnosis tends to occur. Considerations of symptom attribution to a new diagnosis are particularly relevant to the CITGS, in which most patients are relatively healthy apart from glaucoma.

EFFECT OF A NEW DIAGNOSIS ON QUALITY OF LIFE

Not only may a new diagnosis cause symptom attribution, it may also cause psychologic distress and diminished quality of life. In a study of hypertension, Swales[41] found that a patient's expectation of the consequences of disease and its treatment may significantly influence quality of life. Naess and

colleagues[108] showed higher absentee rates at work for hypertensive patients who were aware of their condition that among hypertensive patients not so aware or among normotensive patients, attributing this to a "labeling" effect. One's perspective may also influence expectation. Jachuck and colleagues[109] queried physicians, patients, and family members of hypertensive patients after a period of treatment, finding that the physicians thought the patients were better, the patients had a mixed reaction, and the relatives thought the patients were worse.

In the case of vision problems, a study of participants in the ongoing Life Events and Aging Project at Arizona State University is relevant [110] The investigators identified elderly individuals who developed a new vision problem or diagnosis, having answered "never had" vision problems in 10 prior interviews, compared with a control group from the same population that had vision problems from the onset of the study. They used instruments responsive to psychological distress and mental health status and found that preexisting levels of chronic disease were predictive of distress from new vision problems. In fact, it was the additivity of prior chronic disease rather than the shock of a new problem that caused the greatest psychological concern. Persistent depression from vision loss is not a typical phenomenon,[111] although the diagnosis of glaucoma may induce implicit fears of blindness and immediately alter perceptions of well-being and future health problems.[4]

Patients may show adjustments to chronic illness with time. Among asthmatic patients, those with either chronic airflow obstruction or a history of multiple acute airflow obstructions tend to report less respiratory distress than patients with newly experienced breathlessness.[94] Adjustments with time may be less prominent in patients with visual loss. Among patients with advanced proliferative diabetic retinopathy, scores on the Psychological Adjustment to Illness Scale showed more adjustment difficulty than the normative diabetic sample,[112] but no difference was found between patient with recent partial vision loss and those with chronic stable vision loss. For persons with severe visual loss sufficient to cause registration as a blind person, patients with glaucoma had the poorest adjustment to blindness over time as gauged by the Minnesota Multiphasic Personality Inventory (MMPI) and the Gunzberg Progress Chart of Social Function.[113]

COMORBIDITIES

Data from the Medical Outcomes Study indicate that among chronic conditions, those with the least severe symptoms had the least impact on functioning and well-being, and that multiple conditions showed greater decrements than only one condition.[114] Among angina patients, severity of comorbidity was a better predictor of patients' current health rating and

anticipated gain from relief of angina than was severity of angina.[115]

In patients undergoing cataract surgery, the effect of comorbidity was critically important in evaluating quality of life postoperatively.[64] These patients were administered Activities of Daily Vision Scale (ADVS) and the SF-36 from the Medical Outcomes Study before surgery and at 3 and 12 months postoperatively. Not unexpectedly, the magnitude of postoperative change on the specific ADVS instrument was greater than on the generic SF-36. In fact, several subscales of the SF-36 showed deterioration postoperatively, but this deterioration was much greater for patients without significant improvement in visual function. Thus, it appeared as though an expected age-related deterioration in quality of life was attenuated by improvements in visual function.

CIGTS QUALITY-OF-LIFE INSTRUMENTS

As already indicated, the choice of a quality-of-life measurement instrument for the evaluation of a group of patients with a disease is a complex decision. From the over 50 indices designed to measure one or more aspects of functional health status,[116] and with the lack of a "gold standard,"[117] it was necessary to develop a theoretical construct to guide the choice. It was important to capture all of the relevant domains of health-related quality of life, to use standardized and validated instruments to allow comparison to other diseases and groups of patients, and to use instruments that were sufficiently responsive to changes likely to occur in the study disease and its treatment. Both Janz[118] and Parrish[86] have published excellent discussions of the relative benefits of various generic and vision-specific measures in applications to glaucoma.

For the CIGTS, a modular approach was selected,[119] with a final questionnaire containing 8 sections[120-122] (Table I). The rationale for the selection of items and the psychometric properties of the instrument will be the subject of a future report from the Interviewing Center and the CIGTS full group.

CIGTS BASELINE INFORMATION

The CITGS was designed to study the effect of initial medical versus initial surgical therapy for glaucoma on the primary outcome variable of visual field, and on secondary outcome variables of visual acuity, intraocular pressure, and quality of life. According to Greenfield and Nelson,[30] there are 3 major uses of health-related quality-of-life measures in clinical settings: description of the natural history of a disease, evaluation of treatment, and measurement of quality of care. While the CIGTS instrument was developed with the intent of evaluating treatment effects, its excellent reproducibility makes it likely to be useful in describing the natural history of newly diagnosed glaucoma at baseline.

TABLE I: CIGTS QUALITY-OF-LIFE ASSESSMENT INSTRUMENT

I.	General Health Perceptions 5 items—general health-related quality-of-life perceptions index 9 items—glaucoma perceptions index 2 items—global quality of life and glaucoma effects on quality of life
II.	Adaptations and Social Support All glaucoma-related—4 items with subsidiary questions
III.	Visual Activities Questionnaire (VAQ)—33 items
IV.	Symptoms and Health Problem Chart—43 items, including glaucoma attribution question for all "yes" answers
V.	CES-Depression Questionnaire—8 items
VI.	Sickness Impact Profile—136 items, including glaucoma attribution question for all "yes" answers
VII.	Comorbidities chart—15 items
VIII.	Compliance and Satisfaction With Treatment

CIGTS uses traditional clinical measures as primary outcome variables, because previous national clinical trials[123-128] have developed and used standardized methods for measurement and because clinicians are still skeptical of nontraditional end points. At the onset of the CIGTS, the secondary outcome variables in the study were limited to monocular visual acuity and quality-of-life scores on the CIGTS instrument. However, it was recently decided to add contrast sensitivity testing with the Pelli-Robson chart,[129,130] binocular visual acuity testing,[123] and Esterman binocular visual field testing[78-79,131] to the protocol as secondary variables. These additional tests were available at baseline for only a few CIGTS participants; hence, they are not included in this study of baseline information.

CIGTS is also a community-based study, in that participating community ophthalmologists are allowed to provide the medical and surgical treatment to patients who are followed up at the clinical centers for standardized data collection only. The importance of utilizing community networks of physicians in conduct of prospective cohort studies was underscored by Keller and associates[132] in their description of the Maine Lumbar Spine Study. However, in many if not most cases, the clinical center was the treating ophthalmologist at the patient's request.

SUBJECTS AND METHODS

STUDY ORGANIZATION

Fourteen clinical centers and 1 satellite center participated in the recruitment of patients. At each clinical center, an ophthalmologist functions as the principal investigator, and at some centers, he or she is assisted by other coinvestigator ophthalmologists. A clinic coordinator, usually an experienced ophthalmic technician or nurse, is responsible for ensuring

that the CIGTS protocol is followed, both at the clinical center and in the practices of the participating community ophthalmologists.

The central structure of the project is located at the University of Michigan, Ann Arbor. The Administrative Center provides study direction and is led by the Study Chairman. The Coordinating Center monitors activities of the clinical centers, organizes study meetings, manages quality monitoring, and prepares data for study reports. The Interviewing Center conducts all patient quality-of-life interviews by telephone.

ELIGIBILITY AND EXCLUSION CRITERIA

To be eligible, patients must have:

1. A diagnosis of primary open-angle, pseudoexfoliation, or pigmentary glaucoma in one or both eyes
2. One of 3 combinations of qualifying intraocular pressure (IOP), visual field changes, and optic disc changes, as follows: (a) a qualifying IOP of 21 mm Hg or higher, with a Humphrey 24-2 visual field result that includes at least 3 contiguous points on the total deviation probability plot at the 2.0% level, and a Glaucoma Hemifield Test result that is "outside normal limits," and optic disc changes that are compatible with glaucoma, or (b) a qualifying IOP of 20 to 26 mm Hg, with a Humphrey 24-2 visual field result that includes at least 2 contiguous points in the same hemifield on the total deviation probability plot at the <2.0% level, and glaucomatous optic disc damage, or (c) a qualifying IOP of 27 mm Hg or higher, with glaucomatous optic disc damage (no required visual field changes). All optic disc determinations were made by the clinical center's ophthalmologist.
3. Best-corrected visual acuity score equal to or better than 70 (approximate Snellen equivalent, 20/40) in each eye
4. An age in the range from 25 to 75 years
5. The ability to meet the follow-up requirements for a minimum of 5 years
6. The ability to provide informed consent

Patients were ineligible to participate if they

1. Had a cumulative lifetime use of eye drops for glaucoma that exceeded 14 days
2. Had used eye drops for glaucoma in the 3 weeks prior to baseline 1 visit (washout was permitted)
3. Had optic discs that could not be viewed or photographed with clarity
4. Showed optic disc changes that were considered incompatible with the diagnosis of open-angle glaucoma
5. Were unable to perform accurately on perimetric testing

6. Had a CIGTS visual field score (see below for description) that exceeded 16.0 in either eye
7. Had evidence of ocular disease that might affect the measurement of IOP, the assessment of visual function, visual field testing, and/or the facility of aqueous outflow (eg, keratoconus, conjunctival cicatrization, or uveitis)
8. Had proliferative diabetic retinopathy, diabetic macular edema, or nonproliferative diabetic retinopathy with more than 10 microaneurysms by clinical count noted at the baseline examination
9. Had systemic or localized disease that could cause visual field defects compatible with those caused by glaucomatous optic nerve damage (eg, multiple sclerosis, optic disc drusen)
10. Had undergone ophthalmic laser, refractive, conjunctival, or intraocular surgery in either eye
11. Would likely require cataract surgery within 1 year of randomization
12. Had current or expected long-term use of corticosteroids (ocular, periocular, and systemic—including oral or inhaled administration)
13. Had an extent of hearing impairment that would preclude telephone interviewing
14. Were unable to understand and speak English or Spanish for purposes of completing the telephone interview
15. Were currently incarcerated

ENROLLMENT AND ASSESSMENT METHODS

Newly diagnosed glaucoma patients presenting as they routinely sought eye care were identified either at the clinical center or by participating community ophthalmologists and were offered participation in the study. Upon completion of 2 baseline visits, wherein measures of visual field and IOP were taken at each visit and the eligibility of the patient was verified, informed consent to participate was obtained from eligible patients.

Visual Field

The visual field examination protocol developed for the Advanced Glaucoma Intervention Study (AGIS),[133,134] which makes use of the Humphrey Field Analyzer equipped with Statpac 2 software for the central 24-2 threshold visual field test, is used in CIGTS. The method of scoring the visual field test printouts, however, differs from the method used in AGIS.[135]

Visual Field Scoring. The overall CIGTS visual field score is generated from the total deviation probability plot values on the Humphrey 24-2 printout, in order to account for the extent and depth of visual field loss. For each point, a weight is assigned based on its depth of defect, along with the coexistence of defects with the same or smaller *P* values in at least 2 neighboring defect points ("contiguous points," connected by either a

side or corner). The weight given to the point depends on the depth of the defect at all 3 contiguous points, as follows: If the point has a defect at the $P < .05$ level and at least 2 neighboring points have defects at that level or smaller, then the weight equals 1; if the point is at $P < .02$, and at least 2 neighboring points are at this level or smaller, then the weight equals 2; if the point is at $P < .01$, and at least 2 neighboring points are at this level or smaller, then the weight equals 3; and if the point is at $P < .005$, and at least 2 neighboring points are at this level or smaller, then the weight equals 4. Isolated points that demonstrate a defect, but lack at least 2 neighboring points both depressed to at least $P < .05$, are assigned a weight of 0. Weights are then summed across the 52 points, resulting in a number betweeen 0 and 208. This sum is then scaled to a range from 0 (no defect) to 20 (all points demonstrating a defect at the $P < .005$ level) to yield the overall CIGTS visual field score.

To see the effect on test-retest variability of different scoring criteria, visual fields were also scored using the same system, but by requiring only 1 neighboring point at the same probability level or smaller, and again by requiring no neighbors at the same probability level or smaller. Pointwise scores were retained in the analysis spreadsheet to allow various strategies to be applied for merging information between the patient's 2 eyes (see below).

In addition to scores recorded from the entire visual field, separate scores were calculated considering just the 4 paracentral test locations (scaled to a maximum score of 4) and using only the 12 pericentral points in the ring just peripheral to the 4 paracentral test locations (scaled to a maximum score of 12). These scores were calculated to see whether near and far paracentral defects had a disproportionately large relationship to patient perception of decreased health status.

Global Visual Field Indices. Mean defect (MD) is the mean amount that the patient's threshold values differ from the age-adjusted values in the normative database. Pattern standard deviation (PSD) is a measure of the unevenness of the patient's threshold values relative to the normative values, increasing with focal abnormalities in the visual field. Short-term fluctuation (SF) is an estimate of test-retest reliability derived from double threshold determinations at 10 points. Corrected pattern standard deviation (CPSD) corrects the PSD for unevenness due to test-retest variability (SF), according to the formula $CPSD^2 = PSD^2 - SF^2$.

Baseline Values. A visual field test was performed at each of the 2 baseline patient visits. The scores (pointwise or global) or indices from the 2 visits were averaged to yield a baseline value for the purpose of correlation with health-related quality-of-life indicators.

Glaucoma Hemifield Test. The glaucoma hemifield test is an analysis performed by software resident in the Humphrey perimeter to eval-

uate the extent to which threshold values in 5 clusters of test locations (chosen because glaucoma preferentially affects them) are dissimilar to threshold values in the mirror-image locations in the opposite hemifield above or below the horizontal meridian. It has been found empirically to discriminate well between glaucomatous and nonglaucomatous visual fields.[136] Because an "outside normal limits" result is part of the definition of glaucomatous visual field defects in the CIGTS inclusion criteria, it biases the distribution of glaucoma hemifield test results so that it is inappropriate to correlate this result with the patient-reported variables of quality of life.

Binocular Scoring. The visual field testing was done monocularly, with the fellow eye occluded. A patient's visual functioning in everyday life is, of course, performed binocularly. Three strategies for combining information from the visual field tests of the 2 eyes were applied:

1. At each point, the larger of the scores from the 2 eyes was recorded, the scores summed and scaled as in the calculation of the CIGTS VF score, yielding a global score called Binocular Maximum.
2. At each point, the smaller of the scores from the 2 eyes was recorded, the scores summed and scaled, yielding a global score called Binocular Minimum.
3. At each point, the scores from the 2 eyes were averaged, the scores summed and scaled, yielding a global score called Binocular Average.

After recruitment was nearly complete, it was decided that actual binocular testing should be performed. Visual acuity, contrast sensitivity, and Esterman binocular visual field testing in the course of regularly scheduled follow-up visits was instituted in 1997. The Esterman test covers the visual field out to 60° (rather than the 21° to 27° tested by the Humphrey 24-2 program) and is performed with both eyes open. Even though not contemporaneous with the baseline quality-of-life information, the first Esterman binocular test performed on study patients was included as a visual function measure, to see whether correlations were any stronger than with the baseline scores described above from the monocular 24-2 tests.

Visual Acuity

AGIS visual acuity examination protocol for measuring visual acuity,[133] which is a minor modification of the ETDRS protocol,[125] was used. Patients are tested at a distance of 4 m, prior to any dilating drop administration or IOP testing. Correction is provided according to the results of a standardized refraction protocol. Stand- or wall-mounted Lighthouse light boxes are used under standardized lighting conditions, with the Lighthouse test charts 1 and 2.[137,138]

Health-related Quality of Life

An instrument was developed that incorporates a number of previously developed questionnaires and several components devised specifically for this study. Patients are asked 16 questions on their general health perceptions, 4 questions on adaptations and social support, the 33-item Visual Activities Questionnaire (VAQ),[122] a 43-item symptom and health problem list, the 8-item Center for Epidemiologic Studies—Depression questionnaire,[139] the full 136-item SIP,[121] questions on a number of possible comorbidities, and questions on compliance to and satisfaction with their treatment (Table I). The instrument is administered on the telephone with the patient in his or her home at prearranged times by trained interviewers in the Ann Arbor center.

QUALITY CONTROL MEASURES

Attempts to promote the quality of collected data are ongoing, as follows:

1. A meeting of all clinical center coordinators and ophthalmologists to review protocol requirements and test procedures was held prior to initiation of recruitment.
2. Site visits were conducted to each center before recruitment began and midway through recruitment.
3. At each center, a meeting of participating community ophthalmologists was held to review protocol requirments and test procedures.
4. Monthly interactions of the study Protocol Monitor and the clinical center coordinators review protocol matters.
5. All forms are manually reviewed, and data are double-entered. Data-entry errors are corrected, and all questionable or errant data are returned to the clinical center coordinator for correction or clarification.
6. The study biostatisticians and the database administrator, who are responsible for the integrity and cleanup of the dataset, run analyses as requested by approved investigators according to the investigator's analysis design.
7. Quality monitoring is conducted by an independent CIGTS Data and Safety Monitoring Committee on an annual basis, and ad hoc as necessary.

ANALYSIS STRATEGY

To explore the relationship between the patient-reported variables of quality-of-life measures and symptoms and the visual function indicators, such as visual acuity and visual field scores, Pearson correlation coefficients were calculated on a series of combinations. The working hypothesis was that correlations would be modest between clinical visual function measures and the VAQ total and subscale scores, and weaker with SIP total and dimension scores. It was also hypothesized that pointwise considera-

tion of the better visual field result from the 2 eyes would improve the correlation levels, and that visual field scores derived from the central visual field points would also show stronger correlations.

Two specific items from the quality-of-life instrument were chosen for separate analysis: "Have you been worried or concerned about the possibility of blindness?" from the general health perceptions section, and "During the past 7 days, have you had difficulty seeing when stepping down, such as off curbs, a porch, or stairs?" from the symptoms section. The hypotheses were that patients would derive their worry about blindness from the status of the worse eye, with the "blackest" (most ominous) visual field printout, and that patients with visual field loss would have more difficulty with ambulating through sudden terrain change.

Histograms of the distributions of all variables were prepared for review, though with the large size (expected n = 600) of the sample, even nonnormal distributions would not require that a Spearman nonparametric test be applied. In addition, in this descriptive study, the absolute probability values are not as important as the relative correlations between pairs of relevant variables. If correlations were found that were moderate to strong, linear and logistic multivariate regressions were planned, treating the patient-reported measures as dependent variables, with the clinical visual function measures and demographic characteristics as the independent variables. If correlations were weak, regressions were not planned because so little of the observed variance was likely to be explained by the entered variables.

Test-retest reliability was calculated for all visual field indices and scores, and a correlation matrix was prepared for the subscales of the VAQ to compare with published results on the behavior of the instrument.

RESULTS

STUDY SUBJECTS

On February 24, 1997, the CIGTS recruitment goal of 600 patients was reached. The recruitment phase of the study took about 38 months, based on start-up of the 11 original clinical centers by December 31, 1993. Completion of eligibility determination of patients under consideration when the goal was attained led to a final enrollment tally of 607 patients. Center-specific recruitment varied from 35 to 64 patients within the 11 original clinical centers, and from 11 to 18 patients within the 3 centers added in 1995.

Male patients outnumbered female patients by 55% to 45%, and a substantial proportion (231/607, 38%) were black. Age at enrollment showed no male-female difference, but there was a statistically significant difference in mean age at enrollment between blacks and whites (P =.0014), which was consistent for both male and female patients. The median age at entry for black patients is 56 years, 5 years younger than that for white

patients (61 years). Other demographic characteristics of the sample are listed in Table II.

TABLE II: DEMOGRAPHIC CHARACTERISTICS AND OPHTHALMIC STATUS OF ENROLLED CIGTS PATIENTS (N = 607)

CATEGORY	NO.	%	CATEGORY	NO.	%
AGE			**GLAUCOMA TYPE**		
25-49	147	24	POAG	550	90
50-64	269	44	Pseudoexfoliation	29	5
65-75	201	33	Pigmentary	28	5
SEX					
Female	273	45	**ELIGIBILITY**		
Male	334	55	VFD + IOP≥20	439	72
			Disc + IOP≥27	168	28
RACE					
White	337	55	**LENS OPACITY**		
Black	231	38	Post cortical	78	13
Asian	10	2	Ant cortical	98	16
Other	29	5	Post subcapsular	23	4
			Nuclear	288	47
EDUCATION					
≤Grade 6	23	4	**DISC EXAM**		
7-11	105	17	Notching	311	51
Grade 12	167	28	Hemorrhage	20	3
College	146	24			
College graduate	87	14	**OTHER FINDINGS**		
Posgraduate	79	13	Macular degeneration	18	3
			Cataract	167	28
HYPERTENSION			BRVO	0	0
No	382	63	CRVO	0	0
Yes	225	37	Diabetic retinopathy	7	1
			Ant uveitis	0	0
OTHER CARDIO-VASCULAR DX			Post uveitis	0	0
			CRAO/BRAO	0	0
No	516	85	AION	0	0
Yes	91	15	Optic neuritis	0	0
			Prior trauma	0	0
DIABETES					
No	505	83%	Retinal detachment	0	0
Yes	102	17%			
Diet	16	3%			
Oral Meds	64	10%			
Insulin	22	4%			

AION, anterior ischemic optic neuropathy; BRAO, branch retinal artery occlusion; BRVO, branch retinal vein occlusion; CRAO, central retinal artery occlusion; CRVO, central retinal vein occlusion; IOP, intraocular pressure; POAG, primary open-angle glaucoma; VFD, visual field defect.

Over 90% of the subjects had primary open-angle glaucoma, with the remainder evenly distributed between pigmentary and pseudoexfoliative glaucoma. Because of the small numbers of patients in the nonprimary open-angle categories, stratification by glaucoma type in the analysis was not deemed possible. Over 70% of the subjects entered with visual field defects compatible with glaucoma, while the remainder entered with IOP ≥ 27 mm Hg and optic disc findings typical for glaucoma, with normal visual fields. The distribution of CIGTS visual field scores for the worse and better eyes are displayed in Figs 1 and 2. The ophthalmic status of the eye that qualified the subjects for the study ("study eye") is summarized in Table II.

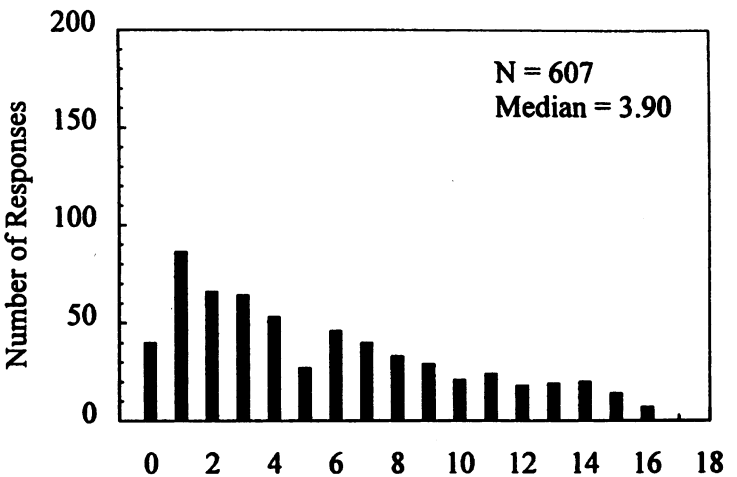

FIGURE 1
Histogram of CIGTS visual field scores from worse eye; possible range is 0 to 20 (increasing visual field abnormality yields higher score).

VAQ CROSS-CORRELATION MATRIX

Cross-correlations of the subscales of the VAQ observed in the CIGTS population at the baseline interview were calculated to see if our population behavior on the instrument was similar to the results published by Sloane and associates.[122] The CIGTS results are summarized in Table III, with the values of Sloane and associates in parentheses. The highest correlations are seen among depth perception, peripheral vision, visual search, and visual processing speed subscales, the subscales most likely to be affected by glaucoma. In general, the cross-correlations are slightly lower than those observed by Sloane and associates, but the relative relationships are consistent. The only subscale that correlated substantially less than reported by Sloane was glare disability, as it related to visual acu-

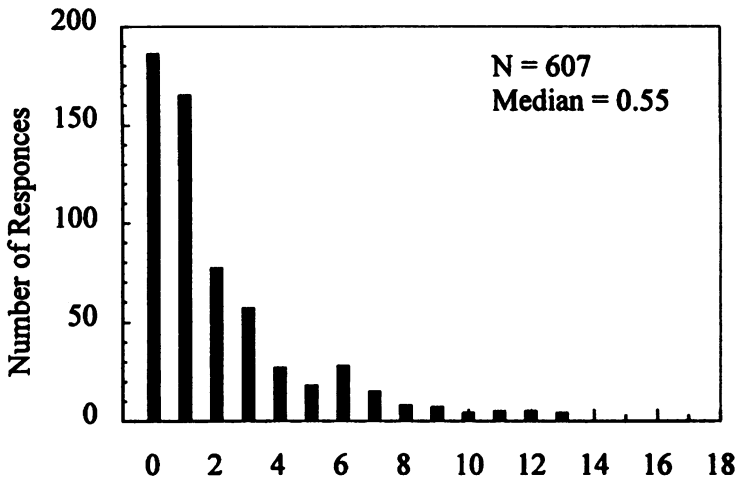

FIGURE 2
Histogram of CIGTS visual field scores from better eye; possible range is 0 to 20 (increasing visual field abnormality yields higher score).

TABLE III: CORRELATION MATRIX FOR THE 8 SUBSCALES OF THE VISUAL ACTIVITIES QUESTIONNAIRE (VAQ) AT THE BASELINE CIGTS INTERVIEW (N = 607)*

VAQ SUBSCALE[†]	GLARE	ADAPT-APTION	ACUITY	DEPTH	PERIPH-ERAL	SEARCH	SPEED
Color	.36(.39)	.40(.46)	.37(.43)	.56(.49)	.53(.57)	.54(.59)	.54(.54)
Glare		.63(.69)	.52(.66)	.49(.57)	.54(.58)	.59(.69)	.55(.65)
Adaptation			.62(.66)	.59(.59)	.60(.58)	.62(.69)	.65(.66)
Acuity				.53(.60)	.55(.49)	.62(.67)	.61(.65)
Depth					.70(.73)	.69(.73)	.73(.74)
Peripheral						.74(.76)	.76(.75)
Search							.80(.82)
Speed							

*Results published by Sloane et al[122] are in parentheses.
[†]Full names of VAQ subscales:

Color discrimination	Depth perception
Glare disability	Peripheral vision
Light/dark adaptation	Visual search
Acuity/spatial vision	Visual processing speed

ity, depth perception, visual search, and visual processing speed. The distribution of VAQ total scores and of VAQ peripheral vision subscale scores is shown in Figs 3 and 4. Cross-correlation was also calculated for item number 15 from the symptom section of the CIGTS instrument about

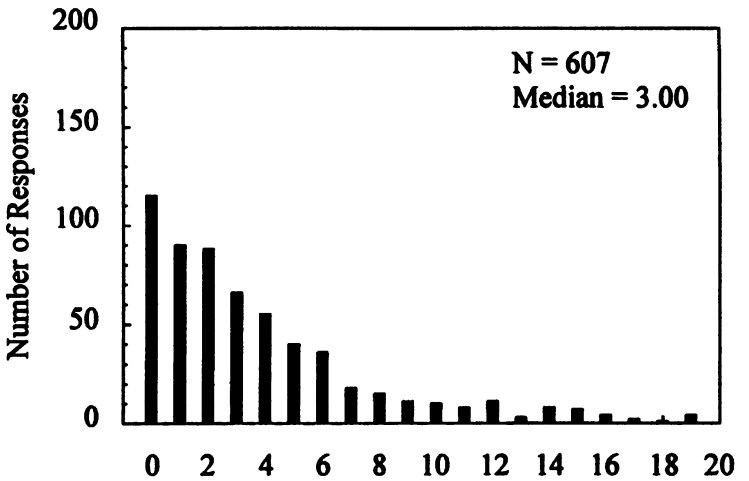

FIGURE 3
Histogram of total score from Visual Activities Questionnaire (VAQ); possible range of frequency of difficulty reported by subject on each item and averaged across all items: 1 (never) to 5 (always).

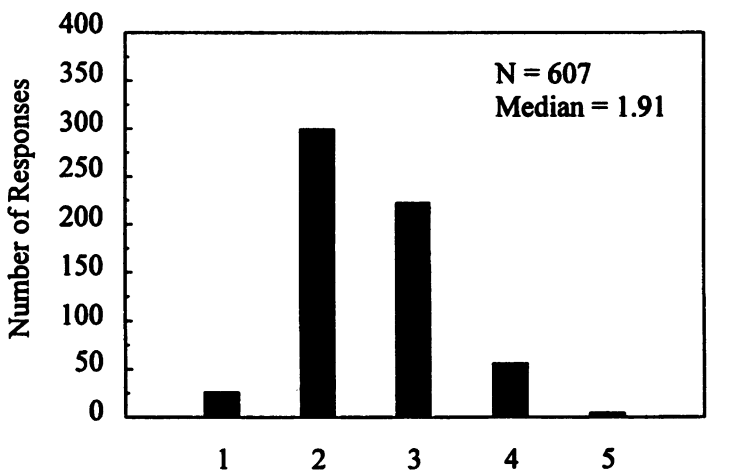

FIGURE 4
Histogram of score from peripheral vision subscale of Visual Activities Questionnaire (VAQ); possible range of average frequency of difficulty: 1 (never) to 5 (always).

trouble seeing steps and curbs (Table IV).

STRATEGIES TO REDUCE VISUAL FIELD SCORE VARIABILITY

Test-retest reliability was calculated for the visual field measures based on

TABLE IV: CORRELATION MATRIX OF TOTAL VAQ AND VAQ SUBSCALE SCORES WITH ITEM ABOUT DIFFICULTY WITH STEPS AND CURBS (N = 607)

VAQ TOTAL AND SUBSCALES	DIFFICULTY WITH STEPS AND CURBS
Total VAQ	0.49
Color discrimination	0.32
Glare disability	0.35
Light/dark adaptation	0.42
Acuity/spatial vision	0.37
Depth perception	0.45
Peripheral vision	0.45
Visual search	0.41
Visual processing speed	0.41

the right eye findings from baseline visits 1 and 2. Individual test location scores were calculated in 3 ways — based on the probability values of the point itself, based on at least 1 neighbor showing a defect as or more severe, and based on at least 2 neighbor points showing a defect as or more severe, as described earlier. The effect of the 3 ways of calculating the score on the mean and standard deviation of the result is shown in Table V. Individual test location mean scores and standard deviations were slightly lower as the cluster size increased, but the effect on the global score was negligible and not statistically significant. This was also true of the scores calculated from the 4 paracentral points and from the 12 points immediately peripheral to the 4 paracentral points. All 3 scoring strategies for the entire field or the 4- and 12-point subsets had standard deviations that were slightly larger than the mean. The global field indices (MD, PSD, SF, and CPSD) also demonstrated standard deviations that exceeded the value of the mean.

CORRELATIONS OF VISUAL FUNCTION AND HEALTH-RELATED QUALITY-OF-LIFE MEASURES

The relationships of various visual function measures and patient-reported health-related quality-of-life variables were explored using Pearson correlation coefficients. Table VI shows the number of such correlations that were examined in 3 major categories: SIP total and dimension scales; VAQ total scale, subscales, and selected comparisons stratified by age and race; and miscellaneous items from symptom scales and general health questionnaire.

SIP Versus Visual Function Measures

The SIP total scores and those of the physical and psychosocial dimension aggregate scores were correlated with various visual function measures and showed correlation coefficients uniformly in a weak range (Table VII).

TABLE V: TEST-RETEST RELIABILITY ON TWO BASELINE VISUAL FIELDS, RIGHT EYES*

		MEAN DIFFERENCE BV1-BV2	STANDARD DEVIATION OF DIFFERENCE
Representative paracentral point (range, 0-4)	cluster size 1	0.46	0.94
	cluster size 2	0.41	0.87
	cluster size 3	0.34	0.77
Representative midperipheral point (range, 0-4)	cluster size 1	0.56	0.97
	cluster size 2	0.50	0.92
	cluster size 3	0.46	0.88
Representative peripheral point (range, 0-4)	cluster size 1	0.71	1.05
	cluster size 2	0.63	1.02
	cluster size 3	0.48	0.96
Global score for full field (range, 0-20)	cluster size 1	1.69	1.94
	cluster size 2	1.64	2.00
	cluster size 3	1.57	2.02
Score for 4 paracentral points (range, 0-4)	cluster size 1	0.39	0.60
	cluster size 2	0.35	0.58
	cluster size 3	0.32	0.56
Score for 12 midperipheral points (range, 0-12)	cluster size 1	1.01	1.24
	cluster size 2	0.96	1.27
	cluster size 3	0.93	1.30
Mean defect (MD)		1.42	1.28
Pattern standard deviation (PSD)		0.91	0.94
Short-term fluctuation (SF)		0.68	0.67
Corrected pattern standard deviation (CPSD)		1.16	1.03

BV1, baseline visit 1; BV2, baseline visit 2.
*Scores calculated using clusters of 1, 2, or 3 neighbor points (N = 607).

The strongest correlation (-0.14) was between the physical dimension aggregate score (higher with greater disability) and the visual acuity in the better eye (lower with greater dysfunction). Visual acuity in the better eye correlated about the same with the SIP total scores (-0.11) as did the CIGTS visual field score in the better eye (higher with greater dysfunction) (0.11). If the SIP scores included only items that the patient attributed to glaucoma, the correlations declined. Visual acuity and CIGTS VF score in the worse eye correlated even more weakly.

The SIP scores were correlated weakly with other measures of the visual field. Mean defect of the better eye (lower with greater dysfunction)

Table VI: Number of correlations examined: Visual function medical history measures versus patient-reported health-related quality-of-life variables

	SIP total + dimension scales	3 SIP scales glaucoma-related	VAQ total and sub-scales	VAQ stratified age/race	Worry about blindness item	Steps/curbs including glaucoma-related	Symptom score including glaucoma
Visual acuity better eye	3	3	9		1	2	2
Visual acuity worse eye	3	3	9		1	2	2
CIGTS VF score better eye	3	3	9	54	1	2	2
CIGTS VF score worse eye	3	3	9		1	2	2
4 paracentral point VF score better eye	3	3	9		1	2	2
4 paracentral point VF score worse eye	3	3	9		1	2	2
12 paracentral point VF score better eye	3	3	9		1	2	2
12 paracentral point VF score worse eye	3	3	9		1	2	2
Mean defect better +worse eye	6	6	18		2	4	4
Pattern standard deviation better +worse eye	6	6	18		2	4	4
Short-term fluctuation better+worse eye	6	6	18		2	4	4
Corrected pattern standard deviation better +worse eye	6	6	18		2	4	4
Pointwise better eye VF score	3	3	9		1	2	2
Pointwise worse eye VF score	3	3	9		1	2	2
Pointwise average VF score	3	3	9		1	2	2
Esterman binocular VF impairment score	3	3	9		1	2	2
Nonocular comorbidity score	3	3	9		1	2	2
Subtotal	63	63	189	54	21	42	42
Total for quality-of-life category	126		243			105	

SIP, Sickness Impact Profile; VAQ, Visual Activities Questionnaire; VF, visual functioning.

TABLE VII: CORRELATION OF SIP SCORES WITH BETTER EYE VISUAL ACUITY AND VARIOUS VISUAL FIELD SCORES (N = 607)

CORRELATION PAIRS	CORRELATION COEFFICIENT	STUDENT'S *t* STATISTIC	*P* VALUE* UNCORRECTED
Total SIP score Better eye visual acuity	-0.11	-2.79	.0054
Physical dimension SIP score Better eye visual acuity	-0.14	-3.42	.0007
Psychosocial dimension SIP score Better eye visual acuity	-0.06	-1.48	.1398
Total SIP score Better eye CIGTS visual field score	0.11	2.77	.0057
Physical dimension SIP score Better eye CIGTS visual field score	0.09	2.34	.0197
Psychosocial dimension SIP score Better eye CIGTS visual field score	0.11	2.83	.0049
Total SIP score—only attributed to glaucoma Better eye visual acuity	-0.08	-2.00	.0460
Physical dimension SIP score—glaucoma attrib Better eye visual acuity	-0.06	-1.51	.1305
Psychosocial dimension SIP score—glauc attrib Better eye visual acuity	-0.05	-1.34	.1808
Total SIP score—only attributed to glaucoma Better eye CIGTS visual field score	0.10	2.41	.0164
Physical dimension SIP score—glauc attrib Better eye CIGTS visual field score	0.07	1.81	.0714
Psychosocial dimension SIP score—glauc attrib Better eye CIGTS visual field score	0.10	2.56	.0108
Total SIP score Better eye mean defect	-0.15	-3.64	.0003
Physical dimension SIP score Better eye mean defect	-0.12	-2.89	.0040
Psychosocial dimension SIP score Better eye mean defect	-0.15	-3.80	.0002
Total SIP score Pointwise worse eye VF score	0.14	3.54	.0004
Physical dimension SIP score Pointwise worse eye VF score	0.13	3.20	.0014
Psychosocial dimension SIP score Pointwise worse eye VF score	0.13	3.28	.0011

Attrib, attribution; SIP, Sickness Impact Profile.

**P* values shown are uncorrected for multiple tests of significance. If a Bonferroni adjustment for 126 correlations on SIP data is applied, only *P* values less than .0004 are significant at the 5% level.

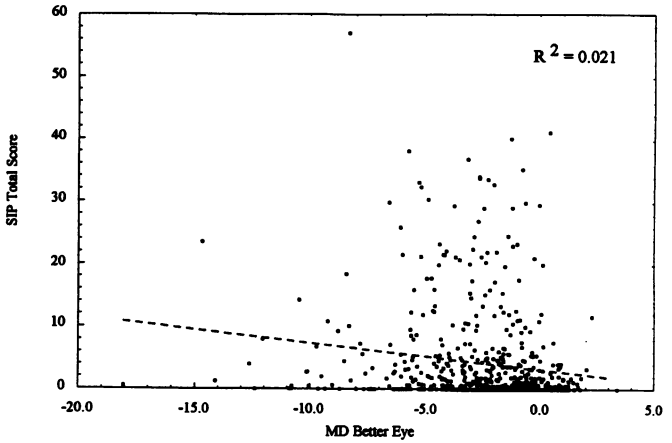

FIGURE 5
Scatterplot of total SIP score versus mean defect (MD) of visual field of better eye. Best-fit linear relationship is plotted.

correlated (-0.15) with total SIP score (Fig 5), this time more strongly in the psychosocial dimension (-0.15) than the physical dimension (-0.12) (Table VII). Correlations with SIP using scores limited to the 4 paracentral points or 12 points immediately peripheral to those were worse than the full field. Other visual field indices (PSD, SF, and CPSD) did not correlate with the SIP scores.

Finally, the visual field score (higher with greater dysfunction) calculated by selecting the worse value from the 2 eyes on a pointwise basis (binocular maximum) correlated weakly (0.14) with the SIP total score and both dimension scores (0.13). Correlation levels declined when using the better eye pointwise score (binocular minimum) or average score (binocular average), and when limiting the scoring to the 4 paracentral points or the 12 points immediately peripheral to those. Correlations also became weaker when the SIP scores considered only items attributed by the patient to glaucoma, probably because of an increased number of zero scores.

Significance levels are displayed prior to correction for multiple tests. If a Bonferroni correction were applied for all 126 correlations considered with the SIP instrument (an extremely conservative statistical position, especially because SIP total and both dimension scores are highly intercorrelated), *P* values displayed should be multiplied by 126, so that only displayed values less than .0004 are statistically significant (reducing the frequency of a type I error to 5%).

VAQ Versus Visual Function Measures

The VAQ total scores and those of the 8 subscale scores were correlated

TABLE VIII: CORRELATION OF VAQ TOTAL SCORES AND SUBSCALE SCORES WITH BETTER EYE VISUAL ACUITY, CIGTS VISUAL FIELD SCORES, AND MEAN DEFECT (N = 607)

CORRELATION PAIRS	CORRELATION COEFFICIENT	STUDENT'S *t* STATISTIC	*P* VALUE* UNCORRECTED
Total VAQ score Better eye visual acuity	-0.18	-4.43	.0000
Adaptation VAQ subscale score Better eye visual acuity	-0.15	-3.78	.0002
Depth perception VAQ subscale score Better eye visual acuity	-0.17	-4.27	.0000
Search VAQ subscale score Better eye visual acuity	-0.15	-3.80	.0002
Speed VAQ subscale score Better eye visual acuity	-0.19	-4.67	.0000
Total VAQ score Better eye CIGTS visual field score	0.15	3.83	.0001
Color VAQ subscale Better eye CIGTS visual field score	0.17	4.32	.0000
Peripheral VAQ subscale Better eye CIGTS visual field score	0.18	4.60	.0000
Search VAQ subscale Better eye CIGTS visual field score	0.14	3.55	.0004
Speed VAQ subscale Better eye CIGTS visual field score	0.15	3.69	.0002
Total VAQ score Mean defect, better eye	-0.19	-4.78	.0000
Color VAQ subscale Mean defect, better eye	-0.17	-4.24	.0000
Peripheral VAQ subscale Mean defect, better eye	-0.21	-5.37	.0000
Search VAQ subscale Mean defect, better eye	-0.17	-4.14	.0000
Speed VAQ subscale Mean defect, better eye	-0.18	-4.59	.0000

VAQ, Visual Activities Questionnaire.

*P values shown are uncorrected for multiple tests of significance. If a Bonferroni adjustment for 243 correlations on VAQ data is applied, only P values less than .0002 are significant at 5% level.

with the same visual function measures and showed correlation coefficients uniformly in a weak range, though somewhat stronger than the SIP (Table VIII). Better-eye visual acuity (lower with greater dysfunction) was correlated (-0.18) with total VAQ (higher with greater disability); and stronger than -0.14 on 4 subscales: light/dark adaptation, depth perception, visual search, and visual processing speed. Better-eye CIGTS visual field score (higher with greater dysfunction) correlated (0.15) with total

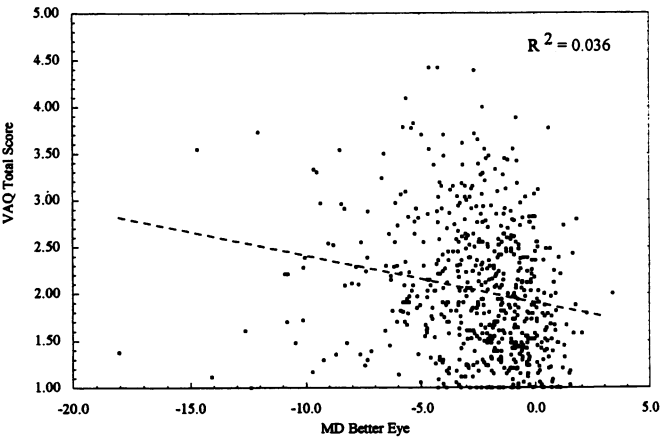

FIGURE 6
Scatterplot of total VAQ score versus mean defect (MD) of visual field of better eye. Best-fit linear relationship is plotted.

VAQ, and above 0.13 on 4 subscales: color discrimination, peripheral vision (0.18), visual search, and visual processing speed. Finally, the better-eye MD (lower with greater dysfunction) correlated -0.19 with total VAQ (Fig 6), and stronger than -0.14 on the same 4 subscales, including peripheral vision at -0.21.

Weaker correlations were encountered when considering the scores from the worse eye. They were also weaker from the 4 paracentral points and 12 points peripheral to those in the better eye, although correlations were consistently better with the 4 paracentral points than the 12-point pericentral ring. PSD, SF, and CPSD in the better eye (higher with greater dysfunction) correlated .11 or .12 with total VAQ score. On the subscales, PSD and CPSD correlated best with color discrimination and peripheral vision, while SF correlated best with color discrimination, acuity/spatial vision, depth perception, and peripheral vision (Table IX).

The average visual field score from the 2 eyes on a pointwise basis (binocular average) correlated about the same with total VAQ (0.18) as either worse eye (binocular maximum) (0.17) or better eye (binocular minimum) (0.18) (Fig 7) (Table X). Subscales correlating best with these simulated binocular measures were color discrimination, visual acuity, peripheral vision (0.22) (Fig 8), visual search, and visual processing speed. As previously, scores derived from the 4 paracentral points correlated less well with VAQ scores than full-field scores, but better than for scores derived from the 12-point pericentral "ring."

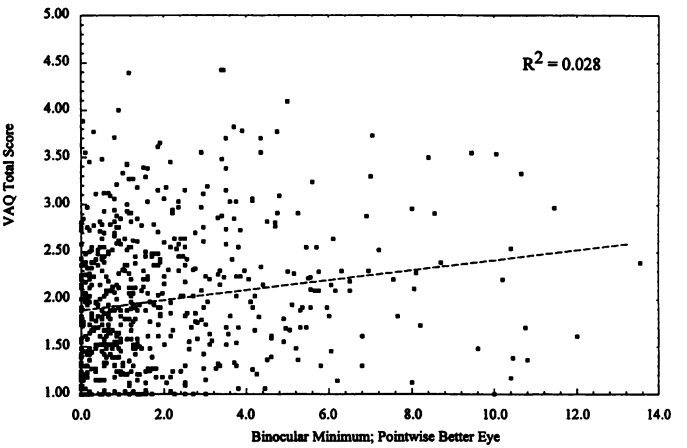

FIGURE 7
Scatterplot of total VAQ score versus simulated minimum binocular score, in which pointwise better eye value is recorded at each point and CIGTS visual field score is calculated. Best-fit linear relationship is plotted.

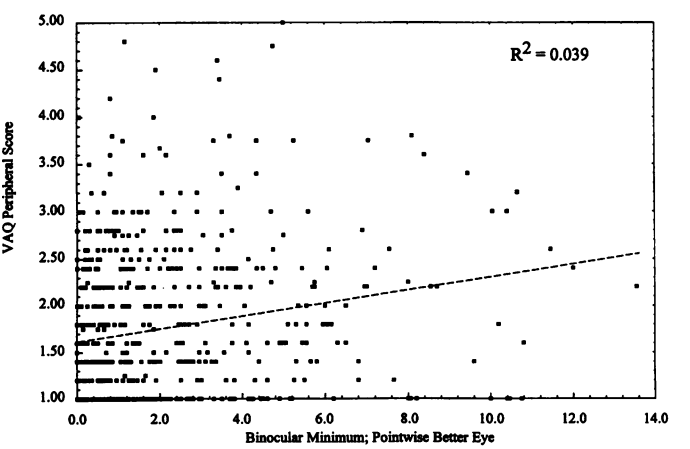

FIGURE 8
Scatterplot of peripheral subscale of VAQ versus simulated minimum binocular score, in which pointwise better eye value is recorded at each point, and CIGTS visual field score is calculated. Best-fit linear relationship is plotted.

TABLE IX: CORRELATION OF VAQ TOTAL SCORES AND SUBSCALE SCORES WITH VARIOUS VISUAL FIELD INDICES (N = 607)

CORRELATION PAIRS	CORRELATION COEFFICIENT	STUDENT'S *t* STATISTIC	*P* VALUE* UNCORRECTED
Total VAQ score Pattern standard deviation, better eye	0.11	2.80	.0052
Color VAQ subscale score Pattern standard deviation, better eye	0.13	3.18	.0015
Acuity VAQ subscale score Pattern standard deviation, better eye	0.08	2.03	.0425
Depth VAQ subscale score Pattern standard deviation, better eye	0.08	2.02	.0439
Peripheral VAQ subscale score Pattern standard deviation, better eye	0.13	3.25	.0012
Total VAQ score Short-term fluctuation, better eye	0.12	3.09	.0020
Color VAQ subscale Short-term fluctuation, better eye	0.17	4.33	.0000
Acuity VAQ subscale score Short-term fluctuation, better eye	0.12	2.89	.0040
Depth VAQ subscale score Short-term fluctuation, better eye	0.11	2.81	.0051
Peripheral VAQ subscale score Short-term fluctuation, better eye	0.12	3.09	.0021
Total VAQ score Corrected pattern standard deviation, better eye	0.11	2.77	.0057
Color VAQ subscale Corrected pattern standard deviation, better eye	0.12	2.95	.0033
Acuity VAQ subscale score Corrected pattern standard deviation, better eye	0.08	1.92	.0557
Depth VAQ subscale score Corrected pattern standard deviation, better eye	0.08	1.92	.0548
Peripheral VAQ subscale score Corrected pattern standard deviation, better eye	0.13	3.16	.0016

VAQ, Visual Activities Questionnaire.

**P* values shown are uncorrected for multiple tests of significance. If a Bonferroni adjustment for 243 correlations on VAQ data is applied, only *P* values less than .0002 are significant at 5% level.

When the CIGTS study group was stratified by age-groups, the correlation between total VAQ and CIGTS VF score in the better eye was greatest in the 25- to 54-year-old age-group (0.24), and less in the 55- to 64-year-old age-group (0.11) and 65- to 74-year-old age-group (0.15) (Table XI). This trend also held for the VAQ subscales; for example, peripheral vision, ages 25 to 54 (0.25), 55 to 64 (0.11), and 65 to 74 (0.22). When stratified by race, the correlation between total VAQ and CIGTS VF score in

TABLE X: CORRELATION OF VAQ TOTAL SCORES AND SUBSCALE SCORES WITH SIMULATED BINOCULAR VISUAL FIELD SCORES (N = 607)

CORRELATION PAIRS	CORRELATION COEFFICIENT	STUDENT'S *t* STATISTIC	*P* VALUE* UNCORRECTED
Total VAQ score Pointwise better eye VF score	0.17	4.19	.0000
Total VAQ score Pointwise worse eye VF score	0.18	4.41	.0000
Total VAQ score Pointwise average VF score	0.18	4.53	.0000
Color VAQ subscale score Pointwise better eye VF score	0.18	4.57	.0000
Color VAQ subscale score Pointwise worse eye VF score	0.20	4.91	.0000
Color VAQ subscale score Pointwise average VF score	0.20	5.01	.0000
Acuity VAQ subscale score Pointwise better eye VF score	0.12	2.95	.0033
Acuity VAQ subscale score Pointwise worse eye VF score	0.14	3.51	.0005
Acuity VAQ subscale score Pointwise average VF score	0.14	3.47	.0006
Peripheral VAQ subscale score Pointwise better eye VF score	0.20	4.98	.0000
Peripheral VAQ subscale score Pointwise worse eye VF score	0.22	5.62	.0000
Peripheral VAQ subscale score Pointwise average VF score	0.22	5.65	.0000
Search VAQ subscale score Pointwise better eye VF score	0.15	3.80	.0002
Search VAQ subscale score Pointwise worse eye VF score	0.15	3.82	.0001
Search VAQ subscale score Pointwise average VF score	0.16	3.99	.0001
Speed VAQ subscale score Pointwise better eye VF score	0.16	3.87	.0001
Speed VAQ subscale score Pointwise worse eye VF score	0.16	4.03	.0001
Speed VAQ subscale score Pointwise average VF score	0.17	4.15	.0000

VAQ, Visual Activities Questionnaire; VF, visual functioning.
*P values shown are uncorrected for multiple tests of significance. If a Bonferroni adjustment for 243 correlations on VAQ data is applied, only P values less than .0002 are significant at 5% level.

the better eye was greatest in the nonblack patients (0.21) and very low among black patients (0.05). Similar findings were present in the VAQ subscale correlations; for example, peripheral vision, nonblack patients

TABLE XI: CORRELATION OF VAQ SCORES WITH BETTER EYE CIGTS VISUAL FIELD SCORES, STRATIFIED BY AGE AND RACE (N = 607)

CORRELATION PAIRS	CORRELATION COEFFICIENT	STUDENT'S *t* STATISTIC	*P* VALUE* UNCORRECTED
Total VAQ score, ages 25-54 Better eye CIGTS VF score (N = 230)	0.24	3.69	.0003
Total VAQ score, ages 55-64 Better eye CIGTS VF score (N = 186)	0.11	1.55	.1237
Total VAQ score, ages 65-74 Better eye CIGTS VF score (N = 191)	0.15	2.14	.0332
Peripheral VAQ subscale score, ages 25-54 Better eye CIGTS VF score (N = 230)	0.25	3.96	.0001
Peripheral VAQ subscale score, ages 55-64 Better eye CIGTS VF score (N = 186)	0.11	1.55	.1233
Peripheral VAQ subscale score, ages 65-74 Better eye CIGTS VF score (N = 191)	0.22	3.07	.0024
Total VAQ score; nonblack patients Better eye CIGTS VF score (N = 374)	0.22	4.26	.0000
Total VAQ score; black patients Better eye CIGTS VF score (N = 233)	0.05	0.83	.4083
Peripheral VAQ subscale score; nonblack patients Better eye CIGTS VF score (N = 374)	0.26	5.15	.0000
Peripheral VAQ subscale score; black patients Better eye CIGTS VF score (N = 233)	0.08	1.16	.2479

VAQ, Visual Acuities Questionnaire; VF, visual functioning.
**P* values shown are uncorrected for multiple tests of significance. If a Bonferroni adjustment for 243 correlations on VAQ data is applied, only *P* values less than .0002 are significant at 5% level.

(0.26) and black patients (0.08).

Application of a Bonferroni adjustment for 243 correlations performed on VAQ data (a conservative statistical position, since VAQ total and subscale score are highly intercorrelated) requires that P values be multiplied by 243 to estimate the frequency of a type I error. Thus, displayed values less than .0002 are statistically significant at the 5% level.

Miscellaneous Health-Related Quality-of-Life Questionnaire Items and Symptoms Versus Visual Function Measures

Two single items, one from the general health perceptions section on the degree of worry about blindness, and another from the symptom list about difficulty with steps and curbs, were correlated with visual function measures. The distribution of scores of worry about blindness (higher score with increasing worry) is displayed in Fig 9. Worry about blindness (Table XII) correlated better with the worse eye CIGTS VF score (higher with greater disability) (0.12) than with visual acuity (lower with greater disability) (-0.05). Worry about blindness also correlated with the worse eye

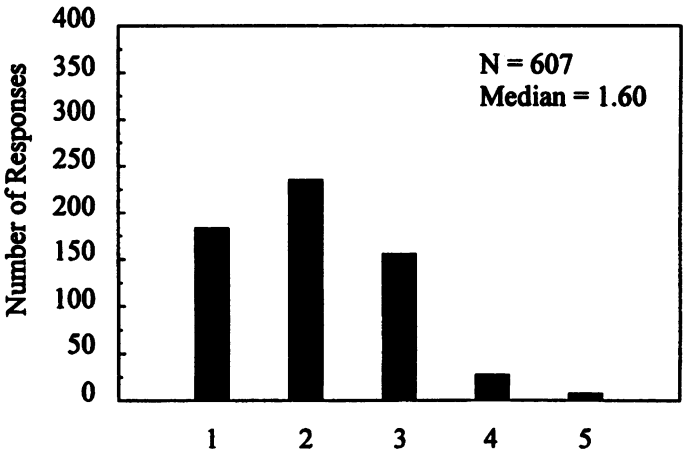

FIGURE 9
Histogram of scores on single item from glaucoma perceptions section of the CIGTS instrument concerning degree of worry about possibility of blindness; range (inverted from original questionnaire) is from 1 (not at all) to 5 (a lot).

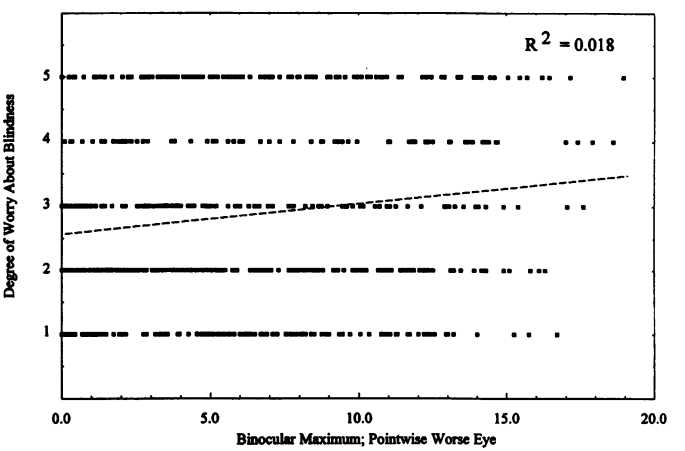

FIGURE 10
Scatterplot of degree of worry about blindness versus simulated maximum binoclar score, in which pointwise worse eye value is recorded at each point and CIGTS visual field score is calculated. Best-fit linear relationship is plotted.

TABLE XII: CORRELATION OF WORRY ABOUT BLINDNESS WITH CLINICAL VISUAL FUNCTION MEASURES (N = 607)

CORRELATION PAIRS	CORRELATION COEFFICIENT	STUDENT'S *t* STATISTIC	*P* VALUE* UNCORRECTED
Worry about blindness Better eye visual acuity	-0.05	-1.32	.1877
Worry about blindness Worse eye visual acuity	-0.05	-1.20	.2313
Worry about blindness Better eye CIGTS visual field score	0.09	2.31	.0210
Worry about blindness Worse eye CIGTS visual field score	0.11	2.81	.0050
Worry about blindness Better eye mean defect	-0.13	-3.28	.0011
Worry about blindness Worse eye mean defect	-0.15	-3.73	.0002
Worry about blindness Better eye pattern standard deviation (PSD)	0.14	3.59	.0004
Worry about blindness Worse eye PSD	0.13	3.11	.0020
Worry about blindness Better eye corrected PSD	0.15	3.69	.0002
Worry about blindness Worse eye corrected PSD	0.12	2.99	.0029
Worry about blindness Better eye pointwise binocular	0.10	2.49	.0129
Worry about blindness Worse eye pointwise binocular	0.13	3.32	.0010
Worry about blindness Pointwise binocular average	0.13	3.18	.0016

*P values shown are uncorrected for multiple tests of significance. If a Bonferroni adjustment for 105 correlations on miscellaneous category of data is applied, only P values less than .0005 are significant at 5% level.

MD (lower with greater disability) (-0.15) better than the better eye MD (-0.13). However, correlations with PSD and CPSD (higher with greater disability) were stronger in the better eye (0.14 and 0.15, respectively) than in the worse eye (0.13 and 0.12, respectively). Finally, on the pointwise worse eye score (binocular maximum), there was correlation with worry about blindness (0.13) (Fig 10), but less with the other simulated binocular scores.

On the steps and curbs question, correlation was low with all visual function measures (Table XIII). When only persons who had a problem with steps and curbs were included in correlations of degree of difficulty with steps and curbs with better-eye CIGTS VF score and better-eye mean defect, correlations increased, but not to significant levels. The correla-

TABLE XIII: CORRELATION OF ITEM ABOUT DIFFICULTY WITH STEPS AND CURBS WITH CLINICAL VISUAL FUNCTION MEASURES (N = 607)

CORRELATION PAIRS	CORRELATION COEFFICIENT	STUDENT'S *t* STATISTIC	*P* VALUE* UNCORRECTED
Difficulty with steps and curbs Better eye visual acuity	-0.06	-1.53	.1265
Difficulty with steps and curbs Worse eye visual acuity	-0.01	-0.14	.9885
Difficulty with steps and curbs Better eye CIGTS visual field score	0.06	1.40	.1623
Difficulty with steps and curbs Worse eye CIGTS visual field score	0.09	2.22	.0266
Difficulty with steps and curbs Better eye mean defect	-0.09	-2.11	.0349
Difficulty with steps and curbs Worse eye mean defect	-0.08	-1.99	.0466
Difficulty with steps and curbs Better eye pointwise binocular	0.07	1.84	.0662
Difficulty with steps and curbs Worse eye pointwise binocular	0.10	2.51	.0124
Difficulty with steps and curbs Pointwise binocular average	0.09	2.38	.0175
Amount of difficulty with steps and curbs Better eye CIGTS score (N = 112)	-0.11	-1.19	.2369
Amount of difficulty with steps and curbs Better eye Mean Defect (N = 112)	0.13	1.38	.1700

**P* values shown are uncorrected for multiple tests of significance. If a Bonferroni adjustment for 105 correlations on miscellaneous category of data is applied, only *P* values less than .0005 are significant at 5% level.

tions of this item with the VAQ is shown in Table IV. Correlations are stronger between these 2 patient-reported variables than between this item and clinical visual function measures.

Ten items from the symptom list dealing with vision (items 1, 2, 3, 4, 6, 10, 12, 14, 15, and 16) (Appendix) were each scored on a scale of 1 to 5, depending on the degree to which the symptom bothered the subject. The scores were summed, yielding a maximum score of 50. The resulting visual symptom score was correlated with the visual function measures. The scores were recalculated, giving points only if subjects indicated they felt the symptom was due to their glaucoma, in whole or in part. The resulting visual symptom (glaucoma) score was also correlated with the visual function measures (Table XIV).

The visual symptom score (higher with increasing symptoms) correlated weakly with the worse-eye CIGTS VF score (higher with increasing dysfunction) (0.12), and improved slightly when considering attribution of

TABLE XIV: CORRELATION OF TOTAL AND GLAUCOMA-RELATED SYMPTOM SCORES WITH VISUAL FUNCTION SCORES (N = 607)

CORRELATION PAIRS	CORRELATION COEFFICIENT	STUDENT'S *t* STATISTIC	*P* VALUE* UNCORRECTED
Total symptom score Worse eye visual acuity	-0.05	-1.13	.2575
Total symptom score Better eye visual acuity	-0.10	-2.48	.0135
Total symptom score Worse eye CIGTS VF score	0.12	3.06	.0023
Total symptom score Better eye CIGTS VF score	0.11	2.68	.0076
Total symptom score Worse eye mean defect	-0.12	-2.99	.0029
Total symptom score Better eye mean defect	-0.15	-3.74	.0002
Total symptom score Pointwise better eye VF score	0.13	3.16	.0016
Total symptom score Pointwise worse eye VF score	0.15	3.83	.0001
Total symptom score Pointwise average VF score	0.15	3.77	.0002
Glaucoma-related symptom score Worse eye visual acuity	-0.03	-0.62	.5370
Glaucoma-related symptom score Better eye visual acuity	-0.08	-1.98	.0477
Glaucoma-related symptom score Worse eye CIGTS VF score	0.14	3.41	.0007
Glaucoma-related symptom score Better eye CIGTS VF score	0.11	2.62	.0090
Glaucoma-related symptom score Worse eye mean defect	-0.14	-3.51	.0005
Glaucoma-related symptom score Better eye mean defect	-0.15	-3.78	.0002
Glaucoma-related symptom score Pointwise better eye VF score	0.13	3.32	.0010
Glaucoma-related symptom score Pointwise worse eye VF score	0.17	4.17	.0000
Glaucoma-related symptom score Pointwise average VF score	0.16	4.06	.0001

VF, visual functioning.

**P* values shown are uncorrected for multiple tests of significance. If a Bonferroni adjustment for 105 correlations on miscellaneous category of data is applied, only *P* values less than .0005 are significant at 5% level.

the symptom to glaucoma (0.14). The MD of the better eye (lower with increasing dysfunction) correlated (-0.15) just as well whether or not attribution to glaucoma was considered. There was no correlation with PSD,

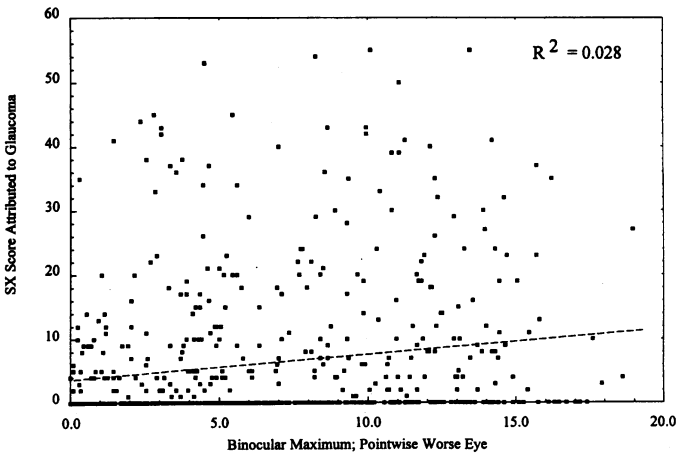

FIGURE 11
Scatterplot of score generated from 10 items from symptom list that deal with vision, which were attributed by patient in some degree to glaucoma, versus simulated maximum binocular score, in which pointwise worse eye value is recorded at each point and CIGTS visual field score is calculated. Best-fit linear relationship is plotted.

CPSD, or SF. Finally, the binocular pointwise score from the worse eye correlated to visual symptom scores (0.15), improving to 0.17 when symptom attribution to glaucoma was considered (Fig 11).

Application of a Bonferroni adjustment for 105 correlations performed on miscellaneous data (a conservative statistical position) requires that *P* values be multiplied by 105 to estimate the frequency of a type I error. Thus, displayed values less than .0005 are statistically significant at the 5% level.

Binocular Esterman Visual Field Scores

The binocular Esterman test scores obtained to date in the study (n = 701), including some patients with 2, 1, or no Esterman tests, were compared to binocular pointwise scores (binocular maximum, minimum, and average) calculated from the Humphrey 24-2 test done on the same day. The lack of independence of observations because of duplicate measures for some subjects was recognized, and no probability values were calculated. The correlation between Esterman results and the pointwise better-eye score (binocular minimum) was moderately good (0.45), as contrasted to the pointwise average (binocular average) (0.40) and the pointwise worse-eye score (0.35).

The first binocular Esterman score for each patient in the study (n = 472) was correlated with the baseline patient-reported variables of health-

TABLE XV: CORRELATION OF PATIENT-REPORTED VARIABLES AT BASELINE WITH BINOCULAR ESTERMAN SCORES ON FIRST TEST (N = 472)

CORRELATION PAIRS	CORRELATION COEFFICIENT	STUDENT'S *T* STATISTIC	*P* VALUE* UNCORRECTED
Total SIP score Binocular Esterman score	-0.01	-0.30	.7642
SIP physical dimension score Binocular Esterman score	-0.04	-0.90	.3685
SIP psychosocial dimension score Binocular Esterman score	0.02	0.43	.6683
Total SIP score—attributed to glaucoma Binocular Esterman score	0.02	0.36	.7212
SIP physical dimension score—glaucoma attrib Binocular Esterman score	-0.02	-0.35	.7236
SIP psychosocial dimension score— glaucoma attrib Binocular Esterman score	0.03	0.57	.5687
Total VAQ score Binocular Esterman score	-0.11	-2.41	.0163
VAQ color subscale score Binocular Esterman score	-0.10	-2.10	.0363
VAQ glare subscale score Binocular Esterman score	-0.11	-2.32	.0206
VAQ adaptation subscale score Binocular Esterman score	-0.09	-1.93	.0545
VAQ acuity subscale score Binocular Esterman score	-0.06	-1.22	.2228
VAQ depth subscale score Binocular Esterman score	-0.06	-1.32	.1862
VAQ peripheral subscale score Binocular Esterman score	-0.10	-2.23	.0238
VAQ search subscale score Binocular Esterman score	-0.09	-1.88	.0605
VAQ speed subscale score Binocular Esterman score	-0.12	-2.52	.0122
Worry about blindness Binocular Esterman score	-0.03	-0.64	.5222
Trouble with steps and curbs Binocular Esterman score	-0.04	-0.83	.4096
Degree of trouble with steps and curbs (n=85) Binocular Esterman score	0.25	2.33	.0221
Total symptom score Binocular Esterman score	0.01	0.32	.7476
Glaucoma-related symptom score Binocular Esterman score	0.05	1.19	.2364

Attrib, attribution; SIP, Sickness Impact Profile; VAQ, Visual Activities Questionnaire.
**P* values shown are uncorrected for multiple tests of significance.

related quality of life and symptoms (Table XV). With the SIP total score and both of the dimension aggregate scores, there was no correlation. With the total VAQ score, correlation was very weak (.11) and above .10 on only 3 subscales—glare senstivity, peripheral vision, and visual processing speed. There was no correlation of the first binocular Esterman score with the item concerning worry about blindness, or the item concerning steps and curbs. However, when considering only people who had trouble with steps and curbs, there was modest correlation (0.25) between the Esterman score and the degree of difficulty with steps and curbs. The visual symptom score, with or without considering attribution to glaucoma, showed no correlation.

Comorbidity Correlations

A nonocular comorbidity score was calculated from the 14 nonocular conditions on the comorbidities questionnaire. Each item was assigned a score of 0 to 4 depending on the degree to which the problem interfered with the subject's daily activities. The 14 scores were summed, yielding the nonocular comorbidity score, which was correlated with the patient-reported variables. See Fig 12 for the distribution of scores. Excellent correlation was observed with the total SIP (0.71) and both physical dimension (0.66) and psychosocial dimension (0.61) scores (Table XVI). If one

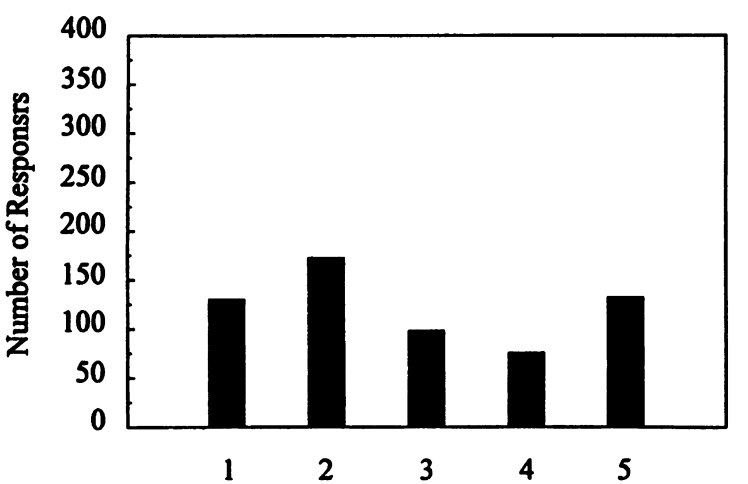

FIGURE 12

Histogram of scores on nonocular comorbidity index, calculated as sum of responses on 14 nonocular items from section 7 of CIGTS instrument, inverted from original questionnaire, from 0 (no problem or no interference of problem in daily activities) to 4 (a lot of interference of problem in daily activities); possible range is 0 to 56, divided into 5 score bins.

TABLE XVI: CORRELATION OF PATIENT-REPORTED VARIABLES AT BASELINE WITH NONOCULAR COMORBIDITY SCORES (N = 607)

CORRELATION PAIRS	CORRELATION COEFFICIENT	STUDENT'S *t* STATISTIC	*P* VALUE* UNCORRECTED
Total SIP score Nonocular comorbidity score	0.71	24.99	.0000
SIP physical dimension score Nonocular comorbidity score	0.66	21.86	.0000
SIP psychosocial dimension score Nonocular comorbidity score	0.61	18.74	.0000
Total SIP score—attributed to glaucoma Nonocular comorbidity score	0.23	5.69	.0000
SIP physical dimension score—glaucoma attrib Nonocular comorbidity score	0.23	5.75	.0000
SIP psychosocial dimension score —glaucoma attrib Nonocular comorbidity score	0.20	4.92	.0000
Total VAQ score Nonocular comorbidity score	0.41	10.89	.0000
VAQ color subscale score Nonocular comorbidity score	0.24	6.15	.0000
VAQ glare subscale score Nonocular comorbidity score	0.20	4.99	.0000
VAQ adaptation subscale score Nonocular comorbidity score	0.33	8.58	.0000
VAQ acuity subscale score Nonocular comorbidity score	0.37	9.69	.0000
VAQ depth subscale score Nonocular comorbidity score	0.33	8.60	.0000
VAQ peripheral subscale score Nonocular comorbidity score	0.37	9.70	.0000
VAQ search subscale score Nonocular comorbidity score	0.33	8.48	.0000
VAQ speed subscale score Nonocular comorbidity score	0.37	9.64	.0000
Worry about blindness Nonocular comorbidity score	0.21	5.19	.0000
Trouble with steps and curbs Nonocular comorbidity score	0.37	9.80	.0000
Degree of trouble with steps and curbs (n=112) Nonocular comorbidity score	0.37	4.23	.0000
Total symptom score Nonocular comorbidity score	0.44	11.96	.0000
Glaucoma-related symptom score Nonocular comorbidity score	0.42	11.34	.0000

Attrib, attribution; SIP, Sickness Impact Profile; VAQ, Visual Activities Questionnaire.
**P* values shown are uncorrected for multiple tests of significance.

considers only the SIP score derived by limiting scores only to items attributed to glaucoma, the correlations are greatly reduced: total SIP (0.23), physical dimension (0.23), and psychosocial dimension (0.20).

Correlations of the nonocular comorbidity score with the total VAQ were moderate (0.41) and between 0.20 and 0.37 on each of the subscales. The nonocular comorbidity score correlated equally well with the item involving steps and curbs (0.37) and less well with worry about blindness (0.21). The visual symptom score correlated with the nonocular comorbidity score (0.44), and not much less well when the symptom score considered only those symptoms related to glaucoma (0.42).

DISCUSSION

CIGTS POPULATION COMPARED WITH PREVIOUS STUDIES

The 607 individuals recruited into CIGTS represent a unique population with newly diagnosed glaucoma. Because they are newly diagnosed, and because people over 75 years of age were excluded, this is a younger population than a cross-section of glaucoma patients under treatment would be. For example, the glaucoma sample studied by Parrish[86] in a quality-of-life study had only 9% under age 50 and 22% in the 50- to 65-year-old bracket, while CIGTS had 24% and 44%, respectively.

Because CIGTS wished to study a group of people that did not have confounding nonglaucomatous ocular disease, a best-corrected visual acuity of at least 20/40 Snellen equivalent on the Lighthouse charts in each eye was required. In addition, excluded were patients with significant diabetic retinopathy, patients with any disease that could cause visual field defects that could be confused with glaucoma, patients who had undergone ocular surgery including laser, and patients who would likely require cataract surgery within 1 year of entry. Even so, 28% of patients had some degree of cataract, and even more had early lens opacities. None, of course, had previous glaucoma surgery, in contrast to 80% of the group studied by Parrish[86] who had from 1 to 7 surgeries for glaucoma.

Thirty-eight percent of the CIGTS study group were black, and they had a median age fully 5 years younger than white patients. The distribution of educational level attained by the patients was almost identical to that of Parrish, so it is not likely that this national multicenter collaborative study selected significantly for more highly educated patients. Thirty-seven percent of the CIGTS patients were hypertensive, 15% had other cardiovascular disease, and 17% were diabetic with few other serious illnesses reported, so there was not a heavy load of systemic comorbidity in the sample enrolled. Four hundred fourteen of our 607 patients had a comorbidity score of 4 or less on a scale of 56 (Fig 6).

Seventy percent of the patients entered the study with glaucomatous

field defects, while 30% entered with normal 24-2 threshold fields but unequivocal ocular hypertension and glaucomatous disc changes. The mean CIGTS VF score in the worse eye was 5.1 ± 4.3 (on a scale of 1 to 16, since patients were excluded if their score was >16 to 20), and the mean score in the better eye was 1.8 ± 2.6. Severe visual field loss in both eyes was not common, but 16 patients had a VF score of 10 or greater in their better eye (and the worse eye having an even higher score) at the time of diagnosis (Fig 1).

In summary, the CIGTS study group, contrasted to the group studied by Parrish,[86] is younger, consists of more African Americans, and has much less advanced glaucoma, better visual acuity and visual field results, and a lighter load of ocular and systemic comorbidity. A priori, one might expect less interference with health-related quality of life than Parrish observed, whether generic instruments or vision-specific ones are used to measure it.

BEHAVIOR OF STANDARDIZED HEALTH-RELATED QUALITY-OF-LIFE INSTRUMENTS

Whenever standard, validated quality-of-life instruments are used in a different population than was previously studied, it is useful to examine known characteristics such as the correlations among subscales to see if the instrument is behaving similarly in the new population. The VAQ has known properties of subscale correlation.[122] When these are compared with those observed in the baseline CIGTS interview (Table III), they are remarkably similar, though the CIGTS cross-correlations are a little weaker. The subscale that showed substantially less correlation with other subscales was glare disability, which is one of the least important factors from the standpoint of glaucoma-related impairments. On balance, the VAQ behaved as predicted in the CIGTS population. The SIP has been validated in so many different populations that it can safely be assumed to be valid in the CIGTS study group.

VISUAL FIELD VARIABILITY

Visual field data are known to be highly variable, especially in areas of the field showing partial defects, and most of the patients in CIGTS had a partial field defect in at least 1 eye. This variability affects single thresholds, clusters, and global visual field indices. In an effort to find a global objective measure of an individual visual field that showed reduced test-retest variability, several strategies were employed. Individual test locations were scored in 3 ways — based on the probability values on the total deviation plot of the point itself, based on at least 1 neighbor showing a defect as severe or more severe, and based on at least 2 neighbor points showing a defect as severe or more severe. Individual test location mean scores and

standard deviations were slightly lower as cluster size increased, but the effect on the global score was negligible. This was also true for summed scores of the 4 central points or the pericentral ring of 12 points peripheral to the 4 central points. Consequently, the strategies used in this study to lessen variability to a significant degree were not successful. Threshold visual field data are inherently noisy, and ex post facto attempts to lessen variability have often been tried but with little success.

CORRELATIONS WITH SICKNESS IMPACT PROFILE

The SIP did not correlate well with clinical measures of visual function at baseline in the CIGTS study group. Visual acuity in the better eye correlated best with the physical dimension aggregate score (r = -0.14), the correlation declining when the SIP scores included only items the patient attributed to glaucoma. The visual field scores all correlated weakly with the SIP scores. The strongest correlation (r = -0.15) was between mean defect in the better eye and the psychosocial dimension aggregate score.

Stronger correlations of clinical visual function and generic measures of perceived health status have been found in patients with cataract[58] and retinal vascular disease.[121] However, in patients with cataract who had surgery, SIP scores improved in two thirds, but to a clinically significant degree in only 21%, and the mean change was not statistically significant.[57] Apparently, in this group of newly diagnosed glaucoma patients, the degree of visual impairment as judged by traditional clinical visual function measures was not sufficient to produce stronger correlation with generic perceived health status as measured by the SIP. Even in more advanced glaucoma patients, as studied by Parrish[86,140] and Gutierrez,[87] clinical measures were not well correlated with generic health status measures.

In this study group, the pointwise binocular score in the worse eye (binocular maximum) correlated better with total SIP score than did the better-eye score (binocular minimum) or averaged score (binocular average). Since the better eye should be the driver of functional visual impairment, it may be that concern over the diagnosis and severity of damage in 1 eye influenced responses in the psychosocial dimension to a greater degree than actual functional impairment influenced responses in the physical dimension. Overall, the weak correlations with this generic instrument imply that glaucoma at the time of diagnosis has not materially influenced patients' perceptions of their overall health-related quality of life.

The significance levels of the correlations between SIP scores and the visual function scores were weak enough so most of the statistical significance disappeared when corrections for multiple tests were applied. However, when viewed on a relative basis, the correlation levels are still meaningful and interesting. One might incorrectly conclude from the cor-

relation levels that the SIP instrument is not of much value in a glaucoma study. While that may be true at baseline, it is possible that inclusion of this generic instrument will detect nonocular side effects of treatment that appear over time. Without the presence of the SIP in the CIGTS battery, there would be no way of capturing such data that might be of substantial relevance to the desirability of medical versus surgical glaucoma management.

As a final check to ensure that the SIP instrument is associated in the expected way with nonocular disease, a nonocular comorbidity score was calculated. Excellent correlation was observed ($r = 0.71$) with the total SIP score and both physical dimension ($r = 0.66$) and psychosocial dimension ($r = 0.61$) aggregate scores (Table XVI). When SIP item scores were included only if patients attributed the problem to their glaucoma, the correlations reduced greatly: total SIP ($r = 0.23$), physical dimension ($r = 0.23$), and psychosocial dimension ($r = 0.19$). Thus, the SIP retained its association with nonocular comorbid conditions but showed less association with newly diagnosed glaucoma. Moreover, the results demonstrate that patients are able to distinguish the causes of their impairments and may attribute some, but definitely not all, of their problems to a new diagnosis, however frightening that diagnosis may be.

CORRELATIONS WITH THE VISUAL ACTIVITIES QUESTIONNAIRE

The VAQ has not been used in other studies of ocular disease, but the VF-14 and the NEI-VFQ have. Prior to cataract surgery, VF-14 scores correlated with logMAR visual acuity in the eye to be operated on at 0.03, and with the visual acuity in the better eye at 0.27.[58] Following cataract surgery, the change in VF-14 scores correlated with the change in logMAR visual acuity in the eye operated on at -0.07, and with the change in visual acuity of the better eye at -0.22.[57]

In Parrish's study[86,140] of glaucoma patients from a subspecialty practice, VF-14 scores correlated with binocular visual acuity at -0.59, and with Esterman visual field impairment after correcting for visual acuity at -0.38. The NEI-VFQ subscales correlated with visual acuity in the range of -0.09 to -0.61 and with Esterman visual field impairment at -0.12 to -0.56.

In this study, the VAQ also correlated weakly with the visual function measures, although more strongly than did the SIP. Better eye visual acuity correlated with total VAQ ($r = -0.18$), and most strongly with the following subscales: light/dark adaptation, depth perception, visual search, and visual processing speed. In view of the fact that the worst visual acuity of any eye in the CIGTS was 20/40 Snellen equivalent, it is not surprising that acuity/spatial vision was not one of the better correlated subscales or that correlation with the total VAQ was not as strong as the VF-14 or NEI-VFQ correlations found by Parrish, whose patients

had binocular visual acuity impariments ranging from 0 to 99%. The distribution of visual acuities in the better eye in this study was reasonably normally distributed within the narrow range of acuity scores from 70 to 100. In fact, subtle loss of visual acuity might be expected to influence activities subsumed by the 4 subscales that were most strongly correlated.

Better-eye CIGTS VF score correlated (r = 0.15) with the total VAQ, and best on the following subscales: color discrimination, peripheral vision, visual search, and visual processing speed. Better-eye mean defect showed even better correlations (r = -0.19), with the same subscales correlating better than the rest. The peripheral vision subscale correlated with better eye MD at r = -0.21. Though correlations were weak, the pattern of those correlations is true to what one might expect to find among persons with a disease that preferentially affects the peripheral vision. It is also reassuring to note that worse-eye visual field scores correlated less well with total and subscale VAQ scores. This is true because, with both eyes open, the better eye will usually determine the degree of functional impairment. Correlations were considerably weaker than those observed by Parrish,[86,140] in part because only a few of the CIGTS patients had substantial impariment of visual field in both eyes at baseline. In Parrish's group, the mean binocular visual field impairment was 25%, with a range of 0 to 100%.

Correlations were weaker when considering the scores from the 4 paracentral points, and weaker still considering the scores from the 12 pericentral points immediately peripheral to the paracentral ones. This result is interesting because conventional wisdom dictates that only visual field defects close to fixation are symptomatic. Apparently, field loss outside the central points, though not specifically symptomatic, may affect patients' perceptions of visual well-being. Among the global visual field indices, MD is clearly the most correlated with the VAQ, though SF, PSD, and CPSD did correlate with total VAQ score and the same 4 subscales as did MD.

Interestingly, the average from the 2 eyes on a pointwise basis (binocular average) correlated better with total VAQ (r = 0.18) than did binocular minimum, the pointwise better-eye score, but the differences in correlation coefficients were negligible. This may simply relate to better reproducibility of the average compared with minimum or maximum pointwise values. Once again, the peripheral vision subscale correlated best with the binocular average score (r = 0.22). Stratification of the CIGTS study group by age category and race disclosed that most of the VAQ correlation with the better-eye CIGTS score was greatest within the 25- to 54-year-old agegroup, and among nonblack patients. Presumably, younger patients have little else wrong with them except glaucoma, so visual difficulties correlate

better with visual field scores (due to glaucomatous damage). No explanation of the racial difference is immediately apparent, but this is worthy of study over time as the CIGTS progresses.

With the number of subjects in this trial, probability values for correlation coefficients between VAQ scores and clinical visual function scores above .15 are significant at levels below $P = .0002$, so even after application of a Bonferroni correction for the correlations performed with VAQ total and subscale scores, statistical significance still persists at the 5% level. More important than statistical significance in a descriptive study of baseline data such as this are the size of the correlation coefficients (uniformly weak) and the relative correlation values among the pairs of variables.

CORRELATIONS WITH OTHER ITEMS AND SYMPTOMS

Two single items were chosen for special consideration because of their direct relevance to glaucoma patients. The first, worry about blindness, is a common feeling voiced by patients and may even be a concern about which the patient remains silent. While correlations were weak, they showed an interesting pattern. Better correlations occurred with worse-eye visual field scores (from all scoring methods) than with better-eye visual field scores or with visual acuity in either eye. An explanation for this might be that patients' worry about blindness is driven by the amount of damage they have been told they already have, perhaps in an emphatic way to encourage treatment compliance. They would focus attention on the worse eye (blacker visual field printout) in making that determination. But since most patients did not have advanced visual field loss, the correlation level remained weak.

Another item of special interest to glaucoma patients is the difficulty with the steps and curbs question. It is certainly one of the commonest visual disabilities voiced by patients with ocular disease, and it seems to the author to be commoner still among glaucoma patients. Mills and Drance[76] found it to be a common complaint of patients with advanced glaucoma. Correlation of "steps and curbs" was poor with all clinical visual function measures. When only patients who admitted difficulty with steps and curbs were considered, correlation of degree of difficulty with steps and curbs and visual field scores improved, but not to significant levels. The probable explanation is that CIGTS patients have not sufficiently advanced visual field loss to have much difficulty with steps and curbs.

Ten items from the symptom list that deal with vision were selected for correlation with the visual function measures. As expected, since symptoms and signs are often poorly correlated, the visual symptom score correlated weakly with each visual field measure, but most strongly to MD of the better eye ($r = -0.15$) and to the pointwise worse eye

(binocular maximum) score (r = 0.15). The binocular maximum correlation improved (r = -0.16) when only symptoms thought to be caused in whole or part from glaucoma were scored. This was the only time that improved correlation resulted from limiting symptoms scored to those perceived to be glaucoma-related. That may provide an explanation why the pointwise worse eye, rather than better eye, correlated more strongly: Symptoms may be more frequently manifested by patients who are more worried about blindness.

ESTERMAN BINOCULAR VERSUS SIMULATED BINOCULAR SCORES

A recent addition to the CIGTS protocol is Esterman binocular fields. The Esterman test is performed with both eyes open, and test locations extend more than twice as far peripherally as on the 24-2 test. Attempts to simulate a binocular test by using pointwise better eye values did produce moderately good correlation with Esterman scores (r = 0.45) obtained on the same day. Correlations were better than observed with either binocular average or binocular maximum scores. The correlations would probably have been better if the extent of tested field were more similar between the Esterman (60 degrees eccentricity) and the 24-2 (21-27° eccentricity) examinations.

The first binocular Esterman score for each patient, on which such testing had been performed during 1997 when the Esterman test was added to the protocol, was correlated with the baseline patient-reported variables. Even though the Esterman testing was not contemporaneous to baseline, glaucoma is a slowly progressive disease, and it was unlikely that the later Esterman test would be markedly different from one that could have been performed at baseline. Somewhat surprisingly, correlations were very weak, even weaker than with the monocular or binocular visual field scores from the Humphrey 24-2 examinations. The only item that showed modest correlation to the Esterman result was the degree of difficulty with steps and curbs (r = 0.25) when limited to persons who admitted trouble with steps and curbs. However, as visual field loss becomes more advanced, the ability of the Esterman test to predict self-reported functional visual impairment may improve. With very advanced loss, Mills and Drance[76] showed that Esterman scores correlated moderately well with scores on a specific instrument designed to be responsive to visual field disability.

CONCLUSIONS AND RECOMMENDATIONS

In a study of quality of life in glaucoma patients, Parrish[86,140] used different quality-of-life instruments than were used in CIGTS, including the generic SF-36 and the vision-specific VF-14 and NEI-VFQ, and different meth-

ods of measuring the clinical vision variables of visual acuity and visual field. Nonetheless, the difference in severity of glaucoma was almost certainly the reason why the correlation levels were so different in this study and the one reported by Parrish. In a sense, the 3 studies dealing with quality of life in glaucoma seem to run on a continuum, with CIGTS patients having the mildest disease and the lowest correlations with patient-reported impairments, the Parrish study[86,140] patients having intermediate to advanced disease and intermediate correlations, and Mills and Drance[76] patients having only end-stage disease with moderately good correlations.

The most important findings of this study of baseline clinical measures and quality of life are that, at least at diagnosis, patients are relatively free of glaucoma-induced impairments and that clinical measures are poor predictors of a patient's perception of health status. Physicians cannot and should not rely on traditional measures such as visual field to assess the impact of glaucoma on a patient, especially in its early stages. Careful discussion with a patient about his or her concerns, symptoms, and feelings can bring a closer understanding of how glaucoma is affecting that patient's health-related quality of life, even without administering a standardized instrument. That, in turn, may help to guide rational choice of therapy, estimate the likelihood of compliance, and suggest avenues of appropriate counseling.

However, even at the early stage of glaucoma impairment experienced by the majority of patients in this study at baseline, the choice of instruments for following patients in the CIGTS over time appears sound. Future glaucoma studies could use the SIP or SF-36 as a generic measure, and the VAQ or NEI-VFQ as glaucoma-specific instruments, using results from Parrish[86,140] Gutierrez and associates,[87] and this study as referent populations.

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TABLE XVII: COLLABORATIVE INITIAL GLAUCOMA TREATMENT STUDY: PRINCIPAL PERSONNEL

RESOURCE CENTERS

Administrative Center, University of Michigan, Ann Arbor: Paul R. Lichter, MD (study chairman).

Coordinating Center, University of Michigan, Ann Arbor: David C. Musch, PhD, MPH (director); Kenneth E. Guire, MS (deputy director), Mary L. Harper, BA (database administrator), Carol L. Standardi, RN, CRNO (protocol monitor).

Interviewing Center, University of Michigan, Ann Arbor: Nancy K. Janz, PhD (director), Patricia A. Wren, MPH, MS (deputy director).

PROJECT OFFICE

National Eye Institute, Bethesda, Maryland: Donald F. Everett, MA (NEI representative).

STUDY GROUPS

Data and Safety Monitoring Committee: Sheryl F. Kelsey, PhD (chair).

Steering Committee: Paul R. Lichter, MD (chair), Richard P. Mills, MD (associate chair).

CLINICAL CENTERS

Cullen Eye Institute, Baylor College of Medicine, Houston, Texas: Ronald L. Gross, MD (Principal Investigator).

Dean A. McGee Eye Institute, University of Oklahoma, Oklahoma City: Gregory L. Skuta, MD (principal investigator).

Department of Ophthalmology, University of Florida, Gainesville: Mark B. Sherwood, MD (principal investigator).

Department of Ophthalmology, University of Minnesota, Minneapolis: Martha M. Wright, MD (principal investigator).

Department of Ophthalmology, University of Washington, Seattle: Richard P. Mills, MD (principal investigator), Howard S. Barnebey, MD (satellite coinvestigator).

Divison of Ophthalmology, The Cleveland Clinic Foundation, Cleveland, Ohio: Edward J. Rockwood, MD (principal investigator).

Doheny Eye Institute, University of Southern California, Los Angeles: Dale K Heuer, MD (principal investigator to 1997), Rohit Varma, MD (principal investigator 1997-).

Long Island Ophthalmic Surgery Consultants, PC, Lynbrook, New York: Stanley J. Berke, MD (principal investigator).

New York Eye and Ear Infirmary, New York City: Robert Ritch, MD (principal investigator).

Scheie Eye Institute, University of Pennsylvania, Philadelphia: Jody R. Piltz, MD (principal investigator).

The Center for Sight, Albany, New York: Steven T. Simmons, MD (principal investigator).

Wake Forest University Eye Center, Winston-Salem, North Carolina: L. Frank Cashwell, MD (principal investigator).

Wills Eye Hospital, Philadelphia, Pennsylvania: George L. Spaeth, MD (principal investigator).

Wilmer Ophthalmological Institute, Johns Hopkins University, Baltimore, Maryland: Henry D. Jampel, MD (principal investigator).

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