The Relative Burden of Dry Eye in Patients’ Lives: Comparisons to a U.S. Normative Sample

Polyxane Mertzanis, Linda Abetz, Krithika Rajagopalan, Derek Espindle, Robin Chalmers, Christopher Snyder, Barbara Caffery, Timothy Edrington, Trevford Simpson, J. Daniel Nelson, and Carolyn Begley

PURPOSE. To assess the relative burden of dry eye in daily life by comparing Short Form-36 (SF-36) responses from individuals with and without dry eye against U.S. norms.

METHODS. Assessment of 210 people, 130 with non-Sjögren’s keratoconjunctivitis sicca (non-SS KCS), 32 with Sjögren’s Syndrome (SS), and 48 control subjects. The study population data and published normative SF-36 data were compared. Dry eye severity was assessed by recruited severity (control, non-SS KCS, SS), patient self-report (none, very mild/mild, moderate, severe/extremely severe), and clinician-report (none, mild, moderate, severe). Age and gender-matched norms were compared with all defined severity groups.

RESULTS. Compared with the norms, control subjects scored higher on all SF-36 scales. Effect size (ES) ranged from 0.15 to 0.52. Non-SS KCS patients had lower Role-Physical (ES = −0.07), Bodily Pain (ES = −0.08), and Vitality (ES = −0.11) scores, indicating more dry eye impact on those areas versus the norm. All SF-36 scale scores except Mental Health (ES = 0.12) were lower in the SS group than the adjusted norm (ES range: −0.16 to −0.99). Regardless of severity classification, mild patients consistently had lower Role-Physical and Bodily Pain scores than the norm, suggesting impact on daily roles (ES < 0.2). Patients with moderately severe disease also experienced less vitality and poorer general health. The group with severe disease scored lower than the norm across all domains (ES range: −0.14 to −0.91) except Role-Emotional (ES = 0.13) and Mental Health (ES = 0.25).

CONCLUSIONS. These results indicate dry eye’s negative impact on everyday life, particularly in daily activities. Further research using disease-specific measures to examine dry eye’s impact is underway. (Invest Ophthalmol Vis Sci. 2005;46:46–50) DOI:10.1167/iovs.03-0915

Patients’ feelings about the quality of their lives while coping with a chronic illness or disability are important factors to consider when planning and evaluating treatment interventions. Objective clinical measures form part of the assessments that provide insight into a patient’s experience, but do not provide the full scope of the experience. Increasingly, regulatory bodies such as the U.S. Food and Drug Administration (FDA) are also interested in understanding the full scope of a patient’s treatment experience as it applies to day-to-day life. Thus, clinicians, pharmaceutical companies, and the scientific community at large are increasingly involving the patient when assessing the value of treatments. Such results can be used as a surrogate for more traditional methods of assessing the severity of disease or the efficacy of pharmaceutical interventions. This method can be particularly useful when considering disease states for which conventional clinical assessments are unavailable, unreliable, technically challenging, expensive or burdensome to the patient. A case in point is patients who experience dry eye.

Chronic dry eye is a common condition caused by diminished production or increased evaporation of tears (non-Sjögren’s keratoconjunctivitis sicca [non-SS KCS]) or by a systemic immunologic disorder (Sjögren’s Syndrome [SS]) that causes insufficient moisture production in the salivary and tear-producing glands. Typical symptoms reported by patients with dry eye include watery eyes, burning or stinging, ocular grittiness, foreign-body sensation, blurred vision, and photophobia. In general, the dry eye symptoms are treated with artificial tears or tear-conservation techniques, with varying degrees of success. Despite its being an underdiagnosed condition, evidence suggests that dry eye occurs more frequently among the elderly and postmenopausal women. Also, several environmental triggers, such as dry ambient air and nonenvironmental factors, including systemic medications (antihistamines, hormone replacement therapy), are known to exacerbate the condition in a susceptible individual. In such individuals, the environmental conditions cause an increased amount of tear evaporation, or the systemic medications cause a reduction in tear production that may lead to an acute increase in the severity of symptoms. Such an increase can often result in an avoidance of these environments, potentially affecting daily and social life.

Reports in the literature are emerging about dry eye and the significant burden caused by it, although empirical evidence regarding the relative burden of dry eye on the patient compared to the normal population is still missing. In this article, we present the relative burden of dry eye on patients’ lives by comparing the general health-related quality of life (QoL) of patients with dry eye of various degrees of severity and the QoL of those without dry eye against the health-related QoL of the general U.S. population.
METHODS

Measures Assessed

This work was part of a much larger validation study for a newly developed questionnaire, the Impact of Dry Eye on Everyday Life (IDEEL). As part of that study, the Medical Outcomes Study Short Form-36 Health Survey (SF-36) was administered as a concurrent validity measure. This article focuses on the results of the SF-36 and compares our study data to published US SF-36 norms. Details of the IDEEL validation study can be found elsewhere (Abetz L, et al. 2003;44:ARVO E-Abstract 2477).

The SF-36 was included as a general measure of health status. It assesses, by means of 36 items, the following areas of health: Physical Functioning, role limitations due to physical problems (Role-Physical), Bodily Pain, General Health Perceptions, Vitality, Social Functioning, role limitations due to emotional problems (Role-Emotional), and Mental Health. A 4-week recall period was used for most of these subscales (except Physical Functioning and General Health, which reflected patients’ health at the time they completed the questionnaire). The SF-36 was scored according to the developer’s instructions, with higher scores indicating better health status. The potential range of scores is from 0 to 100.

Subjects were asked to rate the severity of the condition at the outset of the study, and the clinicians were asked to rate the severity of the patients’ conditions after clinical examinations and discussions of symptoms with the subjects. The results of the clinical examinations and their relation to patient-reported symptoms are reported elsewhere.

Patient Population

To participate in the study, subjects had to be at least 18 years old and must have had an eye examination in the past 18 months with a diagnosis of either non-SS KCS or SS (except for the control subjects). Five optometrists and one ophthalmologist participated as clinical investigators at six study sites. ICD-9CM codes and the San Diego criteria (which include a positive salivary gland biopsy) were used to identify non-SS KCS and SS subjects, respectively, from the investigators’ patient records. Potential study subjects were screened by telephone with a script that ensured the presence of dry eye symptoms in the previous 4 weeks and were excluded if they wore contact lenses, had undergone refractive surgery, had a punctal occlusion within the past 60 days, or had experienced a change in systemic medication regimen within the past 30 days.

Control subjects were recruited from lists of patients who did not have ICD-9CM diagnostic codes for dry eye. During the telephone screening, these subjects had to have responded negatively to the question, “Do you think you have dry eye?” and that they have “never” or “rarely” had dry eye symptoms or used artificial tears. Finally, at least two thirds of the control subjects recruited had to be older than 35 years.

Subjects also had to be literate in English, willing and able to complete a series of questionnaires twice over a 2-week period, and willing to undergo clinical testing for dry eye as part of the study. Subjects signed consent forms before study participation and were compensated for their time. The study was approved by Institutional Review Boards and adhered to the provisions of the Declaration of Helsinki for research in human subjects.

Normative Population

Norms for the general population were taken from the SF-36 Health Survey Manual and Interpretation Guide, which was based on a study in a U.S. population. The 1989 and 1990 General Social Surveys conducted by the National Opinion Research Center assessed 2474 (non-institutionalized) individuals in the U.S. aged between 18 and 94 years, either through mailed questionnaires or telephone surveys. This group comprised the general population. The patients with medical conditions were screened through the practices of 362 medical clinicians and 161 mental health providers in Boston, Chicago, and Los Angeles between February and October 1986.

Analyses

As a precursor to the comparisons to U.S. population norms, tests for differences in SF-36 scale scores among dry eye severity groups were conducted with analysis of covariance (ANCOVA), to adjust for age differences. Dry eye severity was classified by three different methods: recruited severity groups (control subjects, non-SS KCS, and SS) based on previous diagnosis, clinician-reported severity (none, mild, moderate, severe), and patient-reported severity (none/very mild/mild, moderate, severe/extremely severe). In all cases, the sample included control subjects without dry eye. Because cell sizes were unbalanced, the ANCOVAs were implemented using general linear models (GLMs).

For the main study comparisons, the SF-36 norms in the general U.S. population were adjusted to match the age and gender characteristics of each severity group. These adjusted norms were compared to the mean SF-36 scores of the dry eye severity groups that had been formed using the three aforementioned methods. Control subjects without dry eye were again included in the sample for all comparisons. Effect sizes (ESs) were calculated by computing the difference in SF-36 scores between the study population means and the adjusted norms and dividing the mean difference by the standard deviation of the scales in the overall U.S. population. A minimal clinically important difference was defined as an ES of at least 0.2 or a 5-point difference between groups, as suggested in the literature. Given the differences in sample sizes between the normative sample and the study population, ESs provide more accurate and conservative estimates of differences than statistical significance.

RESULTS

Patient Population

The demographic information of the validation study subjects is presented in Table 1. The population included 210 adult subjects: 130 with non-SS KCS, 32 with SS, and 48 control subjects. There were fewer than statistical significance differences in gender or education among the three groups; however, a one-way ANOVA found statistically significant age differences among the groups (F = 26.52, P < 0.0001). Follow-up pair-wise t-tests showed that the group of control subjects was significantly younger (59 years) than both the non-SS KCS (55 years) and SS groups (58 years), though the latter two groups did not differ in age. A χ² test also indicated statistically significant racial-ethnic differences among the groups (white versus nonwhite, χ² = 8.6130, P = 0.0135). The SS group consisted of fewer nonwhite subjects than expected, whereas the control group had more nonwhites than expected.

Differences in SF-36 Scale Scores by Severity Rating

Significant differences between the various severity levels were noted for all SF-36 scales, with the following exceptions: Role-Emotional scores showed no differences by recruited severity (F = 1.75, P = 0.1765) or patient-reported severity (F = 2.60, P = 0.0553); Physical Functioning scores showed no differences by clinician-reported severity (F = 2.18, P = 0.0916) or patient-reported severity (F = 1.26, P = 0.2907); and Bodily Pain scores showed no differences by clinician-reported severity (F = 2.59, P = 0.0537, Table 2).

Relative Burden of Dry Eye on Health-Related QoL

Age- and gender-matched norms were compared to the recruited severity groups (Fig. 1) based on previous diagnosis and the ESs for the scale scores calculated. Control subjects
had higher SF-36 scores, across all scales, than the normative sample (ES range: 0.15 to 0.52). Non-SS KCS patients had higher Physical Functioning (ES = 0.09), General Health (ES = 0.13), Social Functioning (ES = 0.19), Role-Emotional (ES = 0.07), and Mental Health (ES = 0.06) scores than the norms. However, non-SS KCS patients had lower Role-Physical (ES = −0.07), Bodily Pain (ES = −0.08), and Vitality (ES = −0.11) scores than the norms, indicating that patients with dry eye experience more role limitations, more pain, and less vitality than norms. All SF-36 scale scores were lower for the SS group than the adjusted norms (ES range: −0.16 to −0.99), with the exception of Mental Health (ES = 0.12). Minimal clinically important differences were noted for all scales except Mental Health and Role-Emotional.

Next, norms were compared to clinician-reported severity levels (Fig. 2) on a 4-point scale: none, mild, moderate, and severe. The ESs for the scale scores by clinician-reported severity were calculated. Those who were reported to have no dry eye symptoms had higher SF-36 scores, across all scales, than the age- and gender-matched norms (ES range: 0.18 to 0.60). Subjects with mild symptoms had lower scores for Role-Physical, Bodily Pain, Vitality, and General Health (ES range: −0.01 to −0.17) and higher scores for Physical Functioning, Social Functioning, Role-Emotional, and Mental Health (ES range: 0.03 to 0.13), but not at a clinically meaningful level (ES < 0.2). The subjects with moderate disease had lower scores on Role-Physical (ES = −0.32), Bodily Pain (ES = −0.21), Vitality (ES = −0.42), Role-Emotional (ES = −0.22), and Mental Health (ES = −0.19). The severe group had lower scores than did the normative population across all domains (ES range: −0.38 to −0.91), with the exception of Role-Emotional (ES = 0.13) and Mental Health (ES = 0.23).

Finally, norms were compared to patient-reported severity levels (Fig. 3) on a 6-point scale: none/very mild/mild, moderate, severe/extremely severe. (These categories were collapsed into mild, moderate, and severe.) The ESs for the scale scores by patient-reported severity are presented. Regardless of severity level, patients with dry eye experienced more limitations in roles due to physical problems (mild ES = −0.08; moderate ES = −0.13; severe ES = −0.67) and more Bodily Pain (mild ES = −0.02; moderate ES = −0.03; severe ES = −0.57). The moderate and severe groups also experienced deficits in General Health Perceptions (moderate ES = −0.05; severe ES = −0.56) and Vitality (moderate ES = −0.20; severe ES = −0.51). The severe group had the worst health-related QoL, reporting lower scores than the norms across all the remaining SF-36 scales: Physical Functioning (ES = −0.22), Social Functioning (ES = −0.35), Role-Emotional (ES = −0.27), and Mental Health (ES = −0.14).
DISCUSSION

These results provide insight into the burden non-SS KCS and SS places on patients. Although definitions of dry eye severity are not standardized within the dry eye field, findings were similar regardless of the methods used to define severity (recruited severity, patient reported, or clinician reported).

Although symptoms are not sight threatening, they become progressively troublesome and exert an increasing burden on the patients as the disease progresses or increases in severity. As discussed in the literature, these types of patients have various degrees of health-related QoL impairment, can become frustrated with their treatment course, repeatedly visit doctors and specialists seeking treatment changes, and may seek alternative treatments leading to significant utilization of medical resources. Furthermore, these patients are reported to have significant lost productivity each year, often losing approximately 5 work days and working an average of 208 days with dry eye symptoms.

Mental health is consistently unaffected by dry eye symptoms, regardless of severity level or diagnosis. However, areas measured by the SF-36 other than mental health are clearly affected. It appears that non-SS KCS most consistently limits daily roles, causes bodily pain or discomfort, and decreases vitality or energy; however, this impact does not reach a clinically meaningful level, as demonstrated by the ESs, until dry eye symptoms become at least moderate in severity. Moreover, as dry eye symptoms become more severe, more aspects of life are affected on a clinically meaningful level, including perceptions of health, physical functioning, social functioning, and role-emotional limitations. In particular, SS has an enormous effect on everyday physical and social functioning.

One possible explanation for these results could be that patients with mild dry eye may be able to make lifestyle changes that allow them to adapt and overcome the adverse impact of the dry eye symptoms. However, as severity increases, adaptive steps taken by patients may be insufficient to overcome the impact of dry eye.

Limitations of this study are threefold. First, the SF-36 questionnaire is a general health measure, which allows for comparisons to norms. Although the SF-36 is generally free from
any biases resulting from leading questions, it contains questions that are not specific to dry eye. Thus, measured impact may have been greater if we had used specific questions for dry eye. This has been illustrated by the IDEEL scale scores that demonstrate impairments in everyday activities, emotional-well being/feelings, and work-related activities, with our control group consistently less affected in these areas than the non-SS KCS and SS groups (Abetz L, et al. *IOVS* 2003;44:ARVO E-Abstract 2477).16 Second, our study population and the normative data presented herein include people with comorbidities for which we have not accounted. When comparing our control group scores with the normative population, it is clear that the control group may have been healthier than the normative population. For this reason, we show the comparisons against both groups, and do not use only our study-specific control group. This leads us to the third caveat, that the normative data were collected in 1989 and therefore may provide dated information. Nevertheless, these results provide a reasonable overview of the burden of dry eye and suggest that daily life, particularly as it relates to daily roles and vitality, is affected by dry eye and that dry eye should be regarded as a serious condition worthy of treatment.

### References


