Dry Eye in the Beaver Dam Offspring Study: Prevalence, Risk Factors, and Health-Related Quality of Life

ADAM J. PAULSEN, KAREN J. CRUICKSHANKS, MARY E. FISCHER, GUAN-HUA HUANG, BARBARA E.K. KLEIN, RONALD KLEIN, AND DAYNA S. DALTON

- PURPOSE: To estimate dry eye prevalence in the Beaver Dam Offspring Study (BOSS), including a young adult population, and investigate associated risk factors and impact on health-related quality of life.
- DESIGN: Cohort study.
- METHODS: The BOSS (2005-2008) is a study of aging in the adult offspring of the population-based Epidemiology of Hearing Loss Study cohort. Questionnaire data on health history, medication use, risk factors, and quality of life were available for 3275 participants. Dry eye was determined by self-report of frequency of symptoms and the intensity of those symptoms. Associations between dry eye and risk factors were analyzed using logistic regression.
- RESULTS: The prevalence of dry eye in the BOSS was 14.5%: 17.9% of women and 10.5% of men. In a multivariate model, statistically significant associations were found with female sex (odds ratio [OR], 1.68; 95% confidence interval [CI], 1.33-2.11), current contact lens use (OR, 2.01; 95% CI, 1.53-2.64), allergies (OR, 1.59; 95% CI, 1.22-2.08), arthritis (OR, 1.44; 95% CI, 1.12-1.85), thyroid disease (OR, 1.43; 95% CI, 1.02-1.99), antihistamine use (OR, 1.54; 95% CI, 1.18-2.02), and steroid use (OR, 1.54; 95% CI, 1.16-2.06). Dry eye was also associated with lower scores on the Medical Outcomes Study Short Form 36 ($\beta = -3.9$, P < .0001) as well as on the National Eye Institute 25-Item Visual Function Questionnaire (NEI VFQ-25) ($\beta = -3.4$, P < .0001) when controlling for age, sex, and comorbid conditions.
- CONCLUSIONS: The prevalence of dry eye and its associated risk factors in the BOSS were similar to previous studies. In this study, dry eye was associated with lower quality of life on a health-related quality-of-life instrument and the vision-specific NEI VFQ-25. (Am J Ophthalmol 2014;157:799–806. © 2014 by Elsevier Inc. All rights reserved.)

RY EYE IS A MULTIFACTORIAL DISEASE OF THE tears and ocular surface, resulting in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. Dry eye can be characterized by a dry, gritty, or burning feeling in the eyes, which may be accompanied by excessive tearing or sensitivity to light, among other symptoms. Prevalence estimates of dry eye disease and severe symptoms have largely varied by study, ranging between 5% and 35%. Dry eye has been shown to affect visual functioning, including visual acuity, as well as to have a negative impact on some health-related quality-of-life measures. It has also been found to be correlated with anxiety and depression.

The known association between dry eye and age has led to thorough study of the disorder in older adult populations, generally focusing on those over 50 years of age. The prevalence and associated risk factors for dry eye have not been widely investigated in younger populations. One of the few investigations that included a wider age range of adults (21-90) was conducted in a very specific group of Veterans Affairs patients. Further, the impact of dry eye on quality of life in younger populations is relatively unknown. In one study including younger adults it was found that both health-related quality-of-life measures and a vision-specific measure were sensitive to severity of dry eye, though this was in a small sample recruited from eye clinics. 14

The aims of this investigation in a large cohort predominately composed of middle-aged adults were to determine the prevalence of dry eye symptoms, identify independent risk factors, and quantify their impact on quality of life.

METHODS

THE BEAVER DAM OFFSPRING STUDY (BOSS) IS AN ONGOING cohort study of aging in the adult children of the population-based Epidemiology of Hearing Loss Study (EHLS). Baseline examinations of BOSS participants (n = 3285), aged 21-84 years, took place between 2005 and 2008. Information on symptoms of dry eye was provided by 3275 participants. The BOSS was approved by the Health Sciences Institutional Review Board of the University of Wisconsin, all participants provided written informed consent, and all study protocols were carried

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From the Departments of Ophthalmology and Visual Sciences (A.J.P., K.J.C., M.E.F., B.E.K.K., R.K., D.S.D.) and Population Health Sciences (K.J.C.), University of Wisconsin, Madison, Wisconsin; and Institute of Statistics, National Chiao Tung University, Hsinchu, Taiwan (G.-H.H.).

Inquiries to Adam J. Paulsen, Department of Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, 610 North Walnut St, Room 1056 WARF, Madison, WI 53726; e-mail: paulsen@episense.wisc.edu

out in accordance with the tenets of the Declaration of Helsinki.

The BOSS examination consisted of an extensive questionnaire including demographic information, employment history, medical history, risk behaviors, and health-related quality of life. Questionnaires were completed by in-person interviews conducted by technicians trained to a standard protocol or, for those unable to come to the examination sites, by self-administration through a web-based or mailed form (n = 439).

Participants were asked: "How often do you have dry eyes, a dry, gritty, or burning feeling?"; "How much does the dryness in your eyes bother you?"; "Is there a season of the year when the dryness in your eyes is the worst?"; and "Are you currently using eye drops at least once a day for dry eyes?" Objective measures of dry eye, such as the tear break-up time (TBUT) test, Schirmer test, or rose bengal staining, were not administered and information regarding previous doctor diagnosis was not available. Participants who reported that symptoms were present sometimes or more often and that they were moderately bothersome or greater, or those who reported currently using eye drops at least once a day for dry eyes, were considered to be cases.

Health conditions considered in this investigation include history of allergies and doctor-diagnosed systemic diseases including arthritis, osteoporosis, thyroid disease, and diabetes. Hypertension was present if subjects had a measured systolic blood pressure greater than 140 mm Hg or a measured diastolic blood pressure greater than 90 mm Hg (Dynamap Procare 120; GE Medical Systems, Milwaukee, Wisconsin, USA) or had a history of having been told by a doctor that they had high blood pressure and were currently using antihypertensive medications. Information on history of head injury and loss of consciousness was also collected.

Other covariates were considered based on previous findings and biologic plausibility. Medications considered in these analyses included antihistamines, antianxiety medications, acetaminophen, benzodiazepine, anticholinergics, antidepressants, statins, steroids, diuretics, multivitamins, and, among women, hormones used for birth control, infertility, or hormone replacement therapy. Contact lens use (current and past), smoking (current status, pack-years smoked, number of cigarettes per day), alcohol consumption (previous year and grams of ethanol per week), and season at interview were also considered in the analyses.

The Medical Outcomes Study Short Form 36 (SF-36) and the National Eye Institute 25-Item Visual Function Questionnaire (NEI VFQ-25) were administered to assess quality of life. The Physical Component Summary (PCS), Mental Component Summary (MCS), General Health Perception Index (GHPI), and Bodily Pain Index (BPI) were calculated for the SF-36. ^{15,16} The composite and 12 subscale scores were calculated for the NEI VFQ-25. ¹⁷ The self-administered Center for Epidemiologic

Studies Depression Scale (CES-D) was used to assess symptoms of depression.

Risk factor investigation consisted of χ^2 analysis, as well as age- and sex-controlled logistic regression models. Associations were considered statistically significant at or below P value = .05. Additionally, a stepwise procedure was performed to create a final model estimating independent odds of dry eye by risk factor. Risk factors with results suggestive of association (P value <.10) in age- and sexadjusted models were considered for entry into the final model. Age and sex were retained in the model, while retention of all other variables was determined by a 2-tailed P value at or below .05.

Mean score differences were calculated between those with and without dry eye symptoms on both the vision-specific and health-related quality-of-life instruments through ordinary single and multiple linear regression models. Finally, the association between dry eye and depressive symptoms (score of 16 or greater on the CES-D) was estimated using logistic regression. All statistical analyses were conducted using SAS version 9.2 (SAS Institute, Cary, North Carolina, USA).

RESULTS

- PREVALENCE: The mean age of the 3275 participants was 49 years (range 21-84 years), 1789 participants (54.6%) were female, and 2271 (69.3%) had higher than a high school education (Table 1). The prevalence of dry eye symptoms was 14.5% overall (14.1% in those aged 21-49 years, 15.2% in those 50 and older) and was significantly higher in women than in men (17.9% vs 10.5%, P < .0001). Although a slight increase in prevalence of dry eye symptoms was observed by age, this trend for the population overall did not reach statistical significance (P = .06). When stratified by sex, the effect of age on dry eye differed between men and women. In men, estimated prevalence was similar among all age groups and there was no observed effect of age (P = .91), whereas in women prevalence increased with age (P = .02), though this interaction was not significant in multivariable models (Figure 1).
- RISK FACTORS: In separate age- and sex-adjusted models, arthritis, osteoporosis, allergies, thyroid disease, severe headaches or migraine in the previous 3 months, and history of head injury were associated with increased odds of dry eye. Use of a number of medications, including antihistamines, acetaminophen, benzodiazepine, antidepressants, and steroids, also was associated with dry eye in the overall population (Table 2). The association of use of steroids with symptoms of dry eye was only significant with inhaled steroid use (odds ratio [OR] = 2.04, 95% confidence interval [CI] = 1.24, 3.33), as oral steroid use did not exhibit a statistically significantly association

TABLE 1. Characteristics of Participants With Dry Eye Symptom Data, the Beaver Dam Offspring Study 2005-2008

| Characteristic | N (%) Overall | N (%) <50 Years of Age | N (%) ≥50 Years of Age | P Value |
|---|------------------|---------------------------|---------------------------|---------|
| N | 3275 | 1764 | 1511 | .17 |
| Female | 1789 (54.6) | 983 (55.7) | 806 (53.3) | |
| Male | 1486 (45.4) | 781 (44.3) | 705 (46.7) | |
| Age | , , | , , | , , | |
| 21-34 | 179 (5.5) | 179 (10.1) | NA | NA |
| 35-44 | 931 (28.4) | 931 (52.8) | NA | |
| 45-54 | 1227 (37.5) | 654 (37.1) | 573 (37.9) | |
| 55-64 | 710 (21.7) | NA | 710 (47.0) | |
| 65-84 | 228 (7.0) | NA | 228 (15.1) | |
| Education (y) | | | | |
| <12 | 75 (2.3) | 31 (1.8) | 42 (2.8) | <.0001 |
| 12 | 902 (27.5) | 439 (24.9) | 463 (30.6) | |
| 13-15 | 1088 (33.2) | 597 (33.8) | 491 (32.5) | |
| 16+ | 1183 (36.1) | 688 (39.0) | 495 (32.8) | |
| Smoking history | | | | |
| Never | 1751 (53.5) | 1011 (57.3) | 740 (49.0) | <.0001 |
| Past | 927 (28.3) | 392 (22.2) | 535 (35.4) | |
| Current | 576 (17.6) | 351 (19.9) | 225 (14.9) | |
| Alcohol consumption (grams of ethanol per week) | | | | |
| 0 | 348 (10.6) | 155 (8.8) | 193 (12.8) | <.0001 |
| 1-14 | 1323 (40.4) | 690 (39.1) | 633 (41.9) | |
| 15-74 | 766 (23.4) | 449 (25.5) | 317 (21.0) | |
| 75-140 | 392 (12.0) | 231 (13.1) | 161 (10.7) | |
| >140 | 426 (13.0) | 229 (13.0) | 197 (13.0) | |
| Body mass index | | | | |
| <25 | 607 (18.5) | 418 (23.7) | 189 (12.5) | <.0001 |
| 25-29.9 | 947 (28.9) | 519 (29.4) | 428 (28.3) | |
| 30+ | 1254 (38.3) | 593 (33.6) | 661 (43.7) | |

^aColumn percentages may not add to 100% due to missing data.

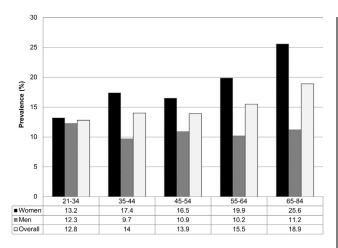


FIGURE 1. Dry eye symptoms by age group (years) and sex, the Beaver Dam Offspring Study 2005-2008.

(OR = 1.47, 95% CI = 0.63, 3.42). Additionally, use of multivitamins was associated with symptoms of dry eye in those under the age of 50.

Among women, those who had used hormones (for birth control, infertility, or menopausal symptoms) were more likely to report dry eye. This effect also differed by age. Among women under the age of 50 years who reported having a period in the past 12 months, use of hormones for contraception, fertility, or hormone replacement therapy was associated with a 71% increase in odds of dry eye symptoms (OR = 1.71, 95% CI = 1.08, 2.73). There was no association between hormone use and dry eye among women 50 years of age and older.

There was no association between a history of smoking or alcohol consumption and dry eye overall or stratified by age. Past and current contact lens use was found to be associated with dry eye symptoms compared to those who had never used contact lenses (OR = 1.34, 95% CI = 1.05, 1.71, and OR = 2.14, 95% CI = 1.65, 2.77, respectively). Current contact lens use displayed a stronger association (OR = 2.39) in those under 50 years of age. The season at interview was not associated with self-report of dry eye symptoms.

In the multivariable model, dry eye symptoms were associated with age, sex, current contact lens use, arthritis,

TABLE 2. Odds Ratios and 95% Confidence Intervals for Dry Eye Symptoms by Risk Factor, the Beaver Dam Offspring Study 2005-2008

| Risk Factor | <50 Years of Age ^a | ≥50 Years of Age ^a | Overall ^a |
|--|-------------------------------|-------------------------------|----------------------|
| Age ^b (per increase in age group) | 1.07 (0.87, 1.33) | 1.23 (1.00, 1.50) | 1.01 (1.00, 1.02) |
| Sex | | | |
| Male | 1.00 [Reference] | 1.00 [Reference] | 1.00 [Reference] |
| Female | 1.60 (1.21, 2.11) | 2.23 (1.65, 3.01) | 1.88 (1.53, 2.30) |
| Contact lens use | | | |
| Never | 1.00 [Reference] | 1.00 [Reference] | 1.00 [Reference] |
| Past | 1.13 (0.79, 1.63) | 1.58 (1.13, 2.21) | 1.34 (1.05, 1.71) |
| Current | 2.39 (1.73, 3.29) | 1.58 (0.98, 2.55) | 2.14 (1.65, 2.77) |
| Chronic conditions | | | |
| Arthritis | 2.07 (1.46, 2.94) | 1.31 (0.97, 1.77) | 1.59 (1.26, 2.00) |
| Osteoporosis | 2.29 (0.70, 7.54) | 1.50 (0.85, 2.65) | 1.70 (1.02, 2.82) |
| Allergies | 1.53 (1.12, 2.10) | 2.19 (1.54, 3.10) | 1.81 (1.43, 2.28) |
| Thyroid disease | 1.45 (0.90, 2.33) | 1.72 (1.17, 2.54) | 1.62 (1.20, 2.18) |
| Migraine headache | 1.57 (1.15, 2.13) | 1.91 (1.31, 2.79) | 1.69 (1.33, 2.15) |
| History of head injury | | | |
| None | 1.00 [Reference] | 1.00 [Reference] | 1.00 [Reference] |
| No loss of consciousness | 0.99 (0.60, 1.64) | 1.06 (0.64, 1.75) | 1.04 (0.73, 1.49) |
| Loss of consciousness | | | |
| <5 minutes | 1.16 (0.78, 1.72) | 1.63 (1.07, 2.47) | 1.34 (1.01, 1.79) |
| ≥5 minutes | 2.38 (0.64, 8.85) | 0.51 (0.07, 3.91) | 1.24 (0.42, 3.62) |
| Medication use | | | |
| Antihistamines | 1.45 (1.01, 2.09) | 1.94 (1.35, 2.79) | 1.65 (1.28, 2.13) |
| Acetaminophen | 1.24 (0.90, 1.70) | 1.34 (0.95, 1.88) | 1.28 (1.02, 1.62) |
| Benzodiazepine | 0.77 (0.32, 1.83) | 2.25 (1.34, 3.78) | 1.59 (1.03, 2.45) |
| Antidepressants | 1.27 (0.87, 1.84) | 1.68 (1.15, 2.45) | 1.44 (1.11, 1.88) |
| Steroids | 1.62 (1.07, 2.45) | 2.06 (1.43, 2.98) | 1.84 (1.40, 2.42) |
| Multivitamin | 1.43 (1.09, 1.88) | 1.03 (0.77, 1.37) | 1.03 (0.77, 1.37) |
| Hormones (women) | 1.85 (1.18, 2.90) | 1.05 (0.53, 2.09) | 1.54 (1.06, 2.24) |

Data presented as OR (95% CI).

allergies, thyroid disease, migraine headache, antihistamine use, and steroid use in the population overall (Table 3). Results were similar when current contact lens wearers were excluded from the analysis (data not shown). In analysis limited to those younger than 50 years, female sex, current contact lens use (compared to those who had never used contact lenses), arthritis, allergies, and multivitamin use were all significantly associated with dry eye symptoms (Table 3). In those 50 years of age or older, age, female sex, allergies, migraine headache, and use of antihistamines and benzodiazepine were associated with dry eye symptoms.

• HEALTH-RELATED QUALITY OF LIFE: Participants with dry eye symptoms scored lower on the SF-36 and on the vision-specific NEI VFQ-25 when controlling for age, sex, and comorbid conditions (Table 4). In the SF-36 the largest differences were in the Bodily Pain and General Health indices. Those with dry eye symptoms scored lower on all 12 of the NEI VFQ-25 subscales, with the largest difference

appearing in the ocular pain score (Figure 2). In analysis controlling for age, sex, education, and a number of comorbid conditions, those who reported dry eye symptoms were also 64% more likely to report depressive symptoms (score ≥16) as measured by the CES-D (Table 4). Stratification by age showed similar results.

DISCUSSION

FEW STUDIES HAVE INVESTIGATED THE PREVALENCE OF and risk factors for dry eye among adults younger than 50 years of age. In the BOSS cohort, which includes young adults, dry eye symptoms were relatively common and had a significant impact on health-related quality of life. Prevalence in the BOSS was 14.1% among those aged 21-49 years, 15.2% among those 50 years of age and older, and 14.5% overall. The overall estimate falls in the range of the prevalence rates reported in previous studies.^{3,9}

^aAdjusted for age and sex.

^bAge groups (y): 21-34, 35-44, 45-54, 55-64, 65-84.

TABLE 3. Odds Ratios and 95% Confidence Intervals for Dry Eye Symptoms by Risk Factor Stratified by Age, the Beaver Dam Offspring Study 2005-2008

| Risk Factor | <50 Years of Age | ≥50 Years of Age | Overall |
|--|-------------------|-------------------|-------------------|
| Age ^a (per increase in age group) | 1.08 (0.85, 1.37) | 1.31 (1.03, 1.65) | 1.12 (1.00, 1.27) |
| Sex | | | |
| Male | 1.00 [Reference] | 1.00 [Reference] | 1.00 [Reference] |
| Female | 1.41 (1.02, 1.95) | 1.76 (1.25, 2.47) | 1.45 (1.14, 1.85) |
| Contact lens use | | | |
| Past | 0.92 (0.61, 1.38) | NA | 1.09 (0.83, 1.43) |
| Current | 2.38 (1.67, 3.37) | NA | 2.09 (1.56, 2.79) |
| Chronic conditions | | | |
| Arthritis | 2.14 (1.46, 3.13) | NA | 1.41 (1.09, 1.82) |
| Allergies | 1.49 (1.05, 2.10) | 2.06 (1.37, 3.10) | 1.54 (1.18, 2.01) |
| Thyroid disease | NA | NA | 1.40 (1.00, 1.97) |
| Migraine headache | NA | 1.71 (1.10, 2.65) | 1.44 (1.10, 1.90) |
| Medication use | | | |
| Antihistamines | NA | 1.80 (1.23, 2.63) | 1.41 (1.07, 1.86) |
| Steroids | NA | NA | 1.47 (1.10, 1.97) |
| Benzodiazepine | NA | 2.08 (1.21, 3.56) | NA |
| Multivitamin use | 1.44 (1.06, 1.94) | NA | NA |

Data presented as OR (95% CI). Multivariable final models generated by stepwise regression. The model for each category includes the risk factors with a listed estimate.

TABLE 4. Dry Eye Symptoms and Health-Related Quality of Life in the Beaver Dam Offspring Study, 2005-2008

| | <50 | <50 Years | | ≥50 Years | | Overall | |
|------------------|----------|------------------|----------|------------------|----------|------------------|--|
| Scale | β | P Value | β | P Value | β | P Value | |
| VFQ composite | -2.79 | <.0001 | -3.82 | <.0001 | -3.27 | <.0001 | |
| SF-36 GHPI | -4.66 | .0001 | -2.98 | .03 | -3.92 | <.0001 | |
| SF-36 MCS | -1.65 | .006 | -1.63 | .01 | -1.67 | .0001 | |
| SF-36 PCS | -1.32 | .01 | -1.73 | .01 | -1.50 | .0005 | |
| CES-D 16+ | | | | | | | |
| No symptoms | 1.00 [Re | 1.00 [Reference] | | 1.00 [Reference] | | 1.00 [Reference] | |
| Dry eye symptoms | 1.53 (1. | 03, 2.29) | 1.81 (1. | 19, 2.77) | 1.64 (1. | 23, 2.19) | |

CES-D = Center for Epidemiologic Studies Depression Scale; GHPI = General Health Perception index; MCS = Mental Component Summary; PCS = Physical Component Summary; VFQ = National Eye Institute Visual Function Questionnaire.

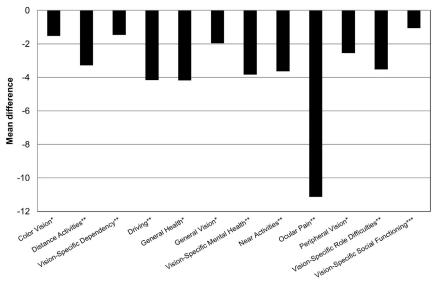
Data presented as mean difference in score (dry eye symptom positive-dry eye symptom negative) and *P* value, except for CES-D, presented as odds of a score greater than or equal to 16 (indicating depression) for those with dry eye symptoms vs those without (95% confidence interval). All estimates controlling for age, sex, education, cardiovascular disease, diabetes, severe headaches or migraines, arthritis, cancer, hypertension, asthma, thyroid disease, diabetic retinopathy, age-related macular degeneration, retinal detachment, cataract, and glaucoma.

The small difference in prevalence by age goes against some of the previous findings that age is a strong risk factor for dry eye. In this population, a few notable differences in risk factors may help to explain the similarity in prevalence. First, among the younger age group, current contact lens use is more strongly associated with dry eye. As a larger proportion of the younger group uses contact lenses to correct vision, the prevalence of dry eye may become more similar to the older group. The observed effect of multivitamins may be explained in the same way. A final risk factor

that showed an increased risk in the younger population was arthritis, potentially indicating that common chronic inflammatory processes may begin to occur at younger ages or that earlier onset of arthritis may also increase comorbidity.

Even in this population including those under 50, dry eye symptoms were associated significantly with lower scores on health-related quality of life as measured by the SF-36 and the NEI VFQ-25. This association remained even when controlling for factors and diseases more commonly

^aAge groups (y): 21-34, 35-44, 45-54, 55-64, 65-84.



Mean difference in subscale score between those reporting dry eye symptoms and those without.

FIGURE 2. Dry eye symptoms and the National Eye Institute Visual Functioning Questionnaire-25 subscales, the Beaver Dam Offspring Study 2005-2008.

thought to impact these scores. In previous studies the relationship between dry eye symptoms and health-related quality of life has varied, with some showing no correlation¹⁸ while others have shown an association between general health-related quality of life, 10 vision-specific quality of life, 12 and activities of daily living. 19 In the BOSS, dry eye was inversely associated with the physical and mental component score of the SF-36. Similarly, dry eye was inversely associated with multiple subscales in the NEI VFQ-25 in this cohort. In a previous study focusing on vision-specific quality of life, only 2 subscales, ocular pain and mental health, were related to dry eye symptoms. 12 However, in the current study associations were found between dry eye and all of the 12 NEI VFQ-25 subscales, though the effect was greatest with ocular pain. The lower scores on other subscales, such as the near vision scale, show that dry eye may be associated with disruptions in daily function in addition to discomfort or pain. Additionally, the impact of dry eye on health-related quality of life in this population was similar across age groups. In the case of the SF-36 General Health Perception Index, those under 50 years of age with dry eye symptoms scored lower than those over 50 respective to the participants without dry eye in their age group. However, it is unclear if this is attributable to a lower frequency of other major health conditions at younger ages or is a reflection of the intensity of dryness symptoms experienced by younger participants. The effect of dry eye at all ages in this study suggests that the impact of dry eye on an individual's perception of his or her health is substantial and of importance as a public health problem.

Despite the quality-of-life impact shown in the BOSS, only a few participants reported a history of being diagnosed by their doctor as having Sjögren syndrome, a common cause of dry eye symptoms, and 157 of the 477 participants with dry eye symptoms (33%) reported using eye drops daily for dry eye specifically. The impact of treatment on quality of life could not be investigated, as information on type of eye drops and frequency of administration was not available. Similarly, information on cost of eye drops or loss of productivity could not be quantified and may also have an impact on quality-of-life estimates. Even so, among young to middle-aged adults, most people with dry eye symptoms had not been diagnosed and many had not been treated in the BOSS. Although this lack of treatment may indicate that knowledge of dry eye is low in the population or that the symptoms of dryness among the BOSS participants were not severe enough to seek care, it is important to note that the impact on the health-related quality-of-life measures remains. In either case, knowledge about the risk factors of dry eye would benefit care-seeking behavior in similar populations.

In women in the BOSS, prevalence of dry eye symptoms increased with age, whereas in men the prevalence was relatively stable across all age groups. Previous studies of older adults showed an increased prevalence of dry eye for men and women as age increased.^{3,9} One possible explanation for this difference may deal with patterns of hormone use among women.

As in some previous studies, hormone use in the BOSS was found to increase odds of dry eye symptoms among women. Previous findings deal almost exclusively with

^{*} p-value<0.001 **p-value<0.0001

^{***}p-value=0.00

hormone replacement therapy, however.²⁰ In this population any use of hormones for contraception or infertility was found to be significantly associated with dry eye, even among premenopausal women younger than 50, suggesting that these hormones may also contribute to dry eye symptoms. This relationship remains unclear and warrants further investigation, including incidence of dry eye symptoms with use of specific hormones and mode of administration.

Also in the BOSS, a number of medications such as antihistamines and steroids, some commonly used, were found to be associated with dry eye. The associations between many of these medications and dry eye symptoms have been found in previous studies.^{3,4} Although causal inferences cannot be determined owing to the cross-sectional nature of this study, use of alternative medications, when possible, should be considered for patients who complain of dry eye symptoms.

Many of the systemic diseases found previously to be associated with dry eye in older adults also showed significantly increased odds of comorbidity in this younger population. As previously noted, arthritis was associated with dry eye. Similarly, thyroid disease was associated with increased odds of dry eye, indicating that hormone dysfunction may play a role in early onset of symptoms.

Also, an association was found between report of migraine headaches and dry eye symptoms. A previous study also found this relationship, though the causal direction of the relationship is unclear.²¹ It is possible that dry eye may trigger or cause migraines, though it is also possible that dry eye and migraines stem from a common inflammatory process. This association should be investigated further.

In previous studies, behavioral risk factors such as smoking and alcohol consumption were found to be associated with dry eye signs and symptoms. These did not prove to be significant factors in the BOSS population overall or by age group. The data on alcohol consumption in this study deal with previous-year use only; and as suggested by a previous study, past heavy drinking may be associated with dry eye. This relationship warrants further investigation. Different smoking patterns or current number of cigarettes smoked per day did not display an association with dry eye. Whether this is attributable to changes in social norms or settings where smoking takes place is unknown. The season at interview was also not found to be a significant factor

in reporting dry eye, which lowers concern that examinations conducted during heating season could show increased reporting of symptoms.

The strengths of this investigation include the large sample size, including young adults—something that has been missing in previous studies of dry eye. The large amount of data collected in the BOSS allows for adequate control of possible confounders. Also, the BOSS cohort is not clinic based, which limits the potential biases that come from access to care and care-seeking behavior, which can be found in previous dry eye studies.

A limitation of this study is that dry eye symptom data were collected by self-report and no objective measurements were conducted. Symptom-based assessment of dry eye has been used and validated in numerous studies and is commonly used in diagnoses of dry eye clinically, often in conjunction with objective measures. 23-26 Further, the Schimer test, rose bengal staining, and TBUT test have been shown to have poor correlation with dry eye symptoms and to have poor repeatability.^{27–29} Clinician assessment has also been shown to underestimate severity of dry eye when compared to patients' self-reported symptoms.³⁰ However, it is possible that symptoms in the young may not be caused by meibomian gland and corneal surface problems that are commonly found in the old. Physical examination to better characterize the cause of the symptoms is needed. One further limitation of this study is the crosssectional design; as such, causal inferences cannot be made.

In conclusion, prevalence of dry eye symptoms was relatively high in this study of a US population including young adults. Few studies have investigated dry eye in this younger age range. Dry eye symptoms also proved to have a significant impact on health-related quality of life and symptoms of depression, independent of other chronic diseases. The high prevalence of dry eye and its impact on quality of life in young and middle-aged adults make this an important public health problem. Many of the chronic diseases, medications, and other risk factors previously found to be associated with dry eye were also found in this study and some, such as hormone use, warrant further investigation. Further longitudinal study of dry eye is necessary to measure incidence, to establish the temporal relationship between exposures and onset of symptoms, and to measure the impact of long-term symptoms on quality of life.

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