Downloaded from http://journals.lww.com/optvissci by vHv0cf9v7TTvBC2tJZK6qEF/ItIc7HTHawt3TNhltv/MxOgMNp0H/LjB0GqM8o2zmptTzntjEbiBgha4cKUBYTab7yGinI4Rzw8Cq/wBV3l4lQ9ZDcRs3I1nzZ98I/VtNOX0mO+85z9gDl8F6WZVoQ== on 06/03/2019

ORIGINAL INVESTIGATION

Impact of Dry Eye on Visual Acuity and Contrast Sensitivity: Dry Eye Assessment and Management Study

Loretta B. Szczotka-Flynn, OD, PhD, FAAO,[1] Maureen G. Maguire, PhD,[2]* Gui-shuang Ying, PhD,[2] Meng C. Lin, OD, PhD, FAAO,[3] Vatinee Y. Bunya, MD,[2] Reza Dana, MD, MPH,[4] and Penny A. Asbell, MD, MBA,[5] for the Dry Eye Assessment and Management (DREAM) Study Research Group

SIGNIFICANCE: Identification of the association of specific signs of dry eye disease with specific visual function deficits may allow for more targeted approaches to treatment.

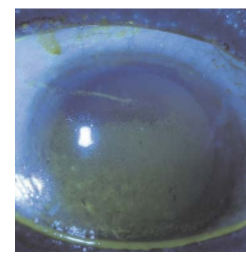
PURPOSE: The purpose of this study was to explore the association of dry eye signs and symptoms with visual acuity (VA) and contrast sensitivity in the Dry Eye Assessment and Management study.

METHODS: Baseline data from participants in the Dry Eye Assessment and Management study were used in this secondary cross-sectional analysis. Standardized procedures were used to obtain results on the Ocular Surface Disease Index (OSDI), high-contrast logMAR VA, contrast sensitivity, tear film debris, tear breakup time (TBUT), corneal fluorescein staining, meibomian gland evaluation, conjunctival lissamine green staining, and Schirmer test scores. Generalized linear models that included age, refractive error status, and cataract status were used to assess the association between VA and contrast sensitivity with OSDI score and each dry eye sign. The Hochberg procedure was used to account for multiple comparisons.

RESULTS: Among 487 participants (974 eyes), worse VA was associated with worse mean score on the OSDI vision subscale (39.4 for VA 20/32 or worse vs. 32.4 for VA 20/16 or better; adjusted linear trend, $P = .02$); scores were not associated with contrast sensitivity. Severe meibomian gland plugging and abnormal secretions were associated with worse mean log contrast sensitivity (1.48 for severe vs. 1.54 for not plugged [$P = .04$] and 1.49 for obstructed vs. 1.57 for clear [$P = .002$], respectively). Longer TBUT was associated with better mean log contrast sensitivity (1.57 for TBUT >5 seconds and 1.51 for TBUT ≤2 seconds, $P < .0001$).

CONCLUSIONS: Worse VA rather than worse contrast sensitivity drives vision-related symptoms in dry eye. Greater tear film instability was associated with worse contrast sensitivity.

Optom Vis Sci 2019;96:387–396. doi:10.1097/OPX.0000000000001387
Copyright © 2019 American Academy of Optometry
Supplemental Digital Content: *Direct URL links are provided within the text.*



Author Affiliations:
[1]Department of Ophthalmology and Visual Sciences, Case Western Reserve University, and University Hospitals of Cleveland Eye Institute, Cleveland, Ohio
[2]Department of Ophthalmology, University of Pennsylvania, Philadelphia, Pennsylvania
[3]School of Optometry, University of California, Berkeley, Berkeley, California
[4]Department of Ophthalmology, Massachusetts Eye and Ear, Harvard Medical School, Cambridge, Massachusetts
[5]Department of Ophthalmology, University of Tennessee Health Science Center, Memphis, Tennessee
*maguirem@pennmedicine.upenn.edu

Dry eye is a highly prevalent condition[1–6] that significantly affects quality of life[2,7] and is additionally a major risk factor for a variety of corneal and ocular surface morbidities such as corneal infection,[8,9] thinning,[10,11] and contact lens intolerance.[12] Disease definitions vary between studies, but studies that define dry eye based on symptoms report a prevalence ranging from 6.5 to 52.4%, with the majority reporting a prevalence of around 20%.[3] The prevalence of disease increases with age, and women are more frequently affected.[3] Dry eye not only results in decreased quality of life but also can affect visual function. In a recent natural history study of dry eye, blurred vision was reported as moderate to very severe in 58% of dry eye patients compared with only 10.5% in healthy controls.[13] Although there are many reports of decreased visual quality of life and symptoms in dry eye patients compared with controls,[2,7,12] there is little information surrounding which specific dry eye signs contribute to diminished visual function.

Previous studies have assessed corneal irregularity from superficial punctate keratitis and tear film instability in their relationship to visual function. Central superficial punctate keratitis in dry eye has been associated with significant deterioration of visual function and optical quality measured by functional visual acuity measurements (time-wise change in continuous visual acuity[14]) and contrast sensitivity.[15–17] Ocular surface damage in the central cornea has also been associated with increased higher-order aberrations and increased corneal backward light scatter.[18] In addition, tear film instability has been associated with an irregular optical surface affecting visual function. For example, temporal changes in higher-order aberrations are associated with the tear film interface in dry eye.[19] However, additional studies are needed to understand the relationship

Copyright © American Academy of Optometry. Unauthorized reproduction of this article is prohibited.

between specific dry eye signs and the corresponding effects on visual function, which in turn will aid clinicians in designing appropriate treatment plans for dry eye patients.

Various methods have been used to subjectively assess visual function in dry eye disease including high- and low-contrast visual acuity, dynamic visual acuity,[14] contrast sensitivity,[20] and disability glare.[15,20–22] Because standard high-contrast visual acuity is not sensitive enough to detect mild ocular disease in other conditions such as cataract and glaucoma and is known to be variable in dry eye disease, other measures of visual function are needed. Contrast sensitivity is a candidate because it is a sensitive indicator of visual function and ocular disease progression.[23–27] However, although previous studies have shown that contrast sensitivity is a sensitive measure of the effects of dry eye on visual function,[15,17] very few have assessed which particular clinical signs impact this measurement. To address this knowledge gap, we obtained data from the Dry Eye Assessment and Management study that has a large, well-characterized cohort with dry eye disease, including information on both the standardized assessment of logMAR visual acuity and contrast sensitivity. In addition, because Sjögren syndrome patients were included in the study, this subset allowed for an assessment of the effect of aqueous deficiency on both measures. Herein, we explore the association of dry eye signs and symptoms at baseline with best-corrected high-contrast logMAR visual acuity and contrast sensitivity.

METHODS

The Dry Eye Assessment and Management study was a multicenter, randomized, double-masked clinical trial to evaluate the effectiveness and safety of supplementation with ω3 fatty acids in relieving the symptoms of moderate to severe dry eye disease.[28] A total of 535 subjects across 27 sites in the United States were enrolled and followed up for 12 months in the primary trial. Eligible participants were randomized to receive either 3 g of fish-derived ω3 eicosapentaenoic and docosahexaenoic acids daily (n = 349) or a placebo containing 5 g of refined olive oil (n = 186). Candidates for the clinical trial were assessed at a screening visit and an eligibility confirmation visit, which together encompass the baseline data used in this secondary cross-sectional analysis. The study protocol was approved by the institutional review board associated with each center, carried out under an Investigational New Drug application for the Food and Drug Administration, conformed with the tenets of the Declaration of Helsinki, and registered on ClinicalTrials.gov (NCT02128763). All subjects provided written informed consent.

Subjects

The trial was designed to include a broad spectrum of symptomatic patients with moderate or severe dry eye. Eligibility criteria included age ≥18 years, dry eye–related ocular symptoms for at least 6 months, use or desire to use artificial tears on average of two more times a day during the 2 weeks preceding the screening visit, and scores on the Ocular Surface Disease Index between 25 and 80, inclusive, at the screening visit and between 21 and 80, inclusive, at the eligibility confirmation visit. Scores on the 12-item Ocular Surface Disease Index range from 0 to 100, where 0 indicates no ocular discomfort.[29] Three subscales of the Ocular Surface Disease Index (ocular symptoms, vision-related function, and environmental triggers) also provide scores between 0 and 100. In addition to the Ocular Surface Disease Index, participants completed the Medical Outcomes Study 36-Item Short Form Health Survey (scores range from 0 to 100, with higher scores indicating better health-related quality of life), although this was not part of the eligibility assessment. Patients needed to have at least one eye with at least two of the following four signs: conjunctival lissamine green staining score ≥1 on a scale of 0 to 6, corneal fluorescein staining score ≥4 on a scale of 0 to 15, tear film breakup time ≤7 seconds, and Schirmer test with anesthesia measurement ≥1 to ≤7 mm/5 min at each of the screening and eligibility visits. Patients with a history of Sjögren syndrome were included, as were patients with thyroid disease, rheumatoid arthritis, or inflammatory diseases if they were otherwise eligible. Medications for dry eye or regular use of systemic medications including those known to cause ocular dryness was allowed if the patient committed to using them for the next 12 months. However, those who wore contact lens 30 days before the screening visit were ineligible, as were those who had a history of laser-assisted in situ keratomileusis, ocular infection, recent ocular surgery, or contraindications to high-dose ω3 supplementation.

Visual Function Testing

Visual function testing was performed by a Dry Eye Assessment and Management clinician or technician who had completed a

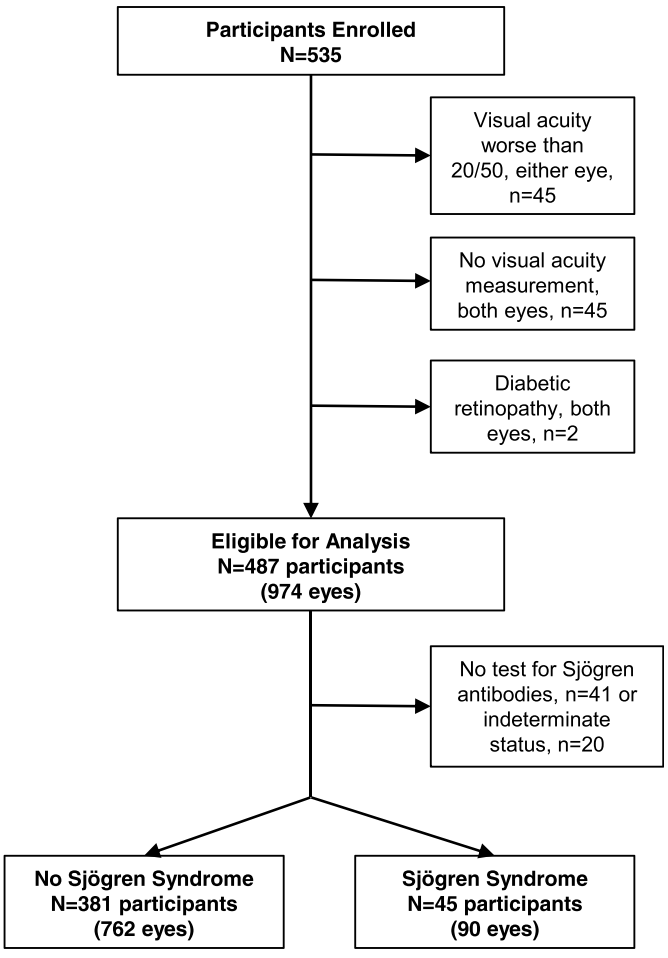


FIGURE 1. Flowchart of participants for the analysis cohorts. Exclusions from the full-study group because of different reasons are shown.

Copyright © American Academy of Optometry. Unauthorized reproduction of this article is prohibited.

TABLE 1. Characteristics of study participants (n = 487 patients, 974 eyes)

Participant characteristics (n = 487 patients)	
Age (y), mean (SD)	57.5 (13.3)
Sex, no. (%)	
Female	394 (80.9)
Male	93 (19.1)
Race, no. (%)	
White	359 (73.7)
Black	61 (12.5)
Other	67 (13.8)
Ethnicity, no. (%)	
Hispanic or Latino	62 (12.7)
Other	425 (87.3)
OSDI score (0–100), mean (SD)	
Total	41.8 (15.5)
Vision-related function subscale	34.6 (19.0)
Short Form-36 score (0–100), mean (SD)	
Physical health	47.5 (9.7)
Mental health	52.4 (9.4)
Ocular characteristics (n = 974 eyes)	
Conjunctival staining score (0–6), mean (SD)	3.0 (1.5)
Corneal staining score (0–15), mean (SD)	3.7 (2.9)
Tear breakup time (s), mean (SD)	3.2 (1.8)
Schirmer test (mm), mean (SD)	9.8 (7.2)
Visual acuity, no. (%)	
20/16 or better	239 (24.5)
20/20	251 (25.8)
20/25	282 (29.0)
20/32	153 (15.7)
20/40	49 (5.0)
Mean (SD), in letters	82.5 (6.1)
Log contrast sensitivity score, no. (%)	
1.72–1.92	300 (30.8)
1.56–1.68	207 (21.3)
1.44–1.52	237 (24.3)
0.84–1.40	230 (23.6)
Mean (SD)	1.6 (0.2)
Refractive error, no. (%)	
Myopia >6 to 11.5 diopters	40 (4.1)
Myopia >3 to ≤6 diopters	88 (9.0)
Myopia >0.5 to ≤3 diopters	277 (28.4)
Emmetropia	325 (33.4)
Hyperopia >0.5 to ≤1.5 diopters	124 (12.7)
Hyperopia >1.5 to 5.5 diopters	120 (12.3)
Mean (SD; diopters)	–0.7 (2.7)

TABLE 1. *Continued*

Ocular characteristics (n = 974 eyes)	
Cataract status, no. (%)	
No cataract	612 (62.8)
Pseudophakic/aphakic	154 (15.8)
Ongoing cataract	208 (21.4)

OSDI = Ocular Surface Disease Index.

certification program. Visual acuity testing and contrast sensitivity testing were performed with correction after manifest refraction during the baseline visit. Monocular visual acuity testing was performed using the Early Treatment of Diabetic Retinopathy Study charts and technique at 3.2 m; different charts were used for the right and left eyes. A light meter was used to ensure that the light hitting the chart was 189 to 377 lux. The sum of the number of letters read correctly on each line was recorded. A letter score of 85 corresponds to an approximate Snellen equivalent of 20/20. Contrast sensitivity was measured with the Mars Letter Contrast Sensitivity Test following the instructions provided from the manufacturer. Briefly, the chart was illuminated uniformly such that a light meter measured 189 to 377 lux on the chart. Participants wore the refractive correction determined by refraction with an add of +2.00 diopters and an occluder or patch on the untested eye. The participants' viewing distance to the chart was 50 cm (20 inches). Different charts were used for the right and left eyes. Each letter read on the chart was marked as correct or incorrect until two consecutive letters were read incorrectly by the patient. The number of letters read on the Mars Contrast Sensitivity Chart was converted to a log contrast sensitivity value where one additional letter was associated with an increase of 0.04 units.

Clinical Examination

A Dry Eye Assessment and Management clinician who completed a certification program for clinical assessment and grading examined each eye and performed an external examination and biomicroscopy with a slit lamp. Tear film debris was graded for each eye as none, mild (present in the inferior tear meniscus), moderate (present in the inferior tear meniscus and in the tear film overlying the cornea), and severe (present in the inferior tear meniscus and in the tear film overlying the cornea or presence of mucus strands in the inferior fornix or on the bulbar conjunctiva). At separate time points, 2% fluorescein dye and 1% lissamine green dye were instilled by placing a small pool of dye into a sterile container using an Eppendorf micropipette and a tip to draw up 5 μL of dye and placing the volume into the inferior cul-de-sac. After instillation of fluorescein dye in the right eye, assessment of tear breakup time was followed sequentially by assessment of corneal fluorescein staining and meibomian gland evaluation, and after instillation of lissamine green, staining evaluation of the interpalpebral conjunctiva was conducted; the sequence of testing was repeated for the left eye. Intraocular pressure was measured for each eye, and Schirmer test was administered to each eye simultaneously.

Measurement of fluorescein tear breakup time began approximately 30 seconds after instillation of fluorescein dye. The clinician viewed the cornea through a slit lamp using broad-beam cobalt blue illumination and a yellow barrier filter. The clinician instructed the patient to blink and measured the time to the first

Copyright © American Academy of Optometry. Unauthorized reproduction of this article is prohibited.

discontinuity in the tear film with a stopwatch. The measurement was repeated two more times. The average of the three measurements of tear breakup time per eye was used for analysis. The central five meibomian glands of the lower lid were assessed after application of pressure to the lower eyelid below the lashes using the Meibomian Gland Evaluator (Johnson & Johnson [previously Tear Science], Jacksonville, FL). The number of plugged glands was counted, and secretions were graded as clear liquid oil, mild haze/cloudy liquid, paste (toothpaste consistency), or obstructed (no secretion, including capped orifices). Assessment of corneal staining under the same viewing conditions as those for tear breakup time began approximately 2 to 3 minutes after the fluorescein dye instillation. The staining of the central cornea and four surrounding sectors was each scored from 0 (no staining) to 3 (dense staining). The central cornea was defined as a circular area encompassing approximately one-fifth of the corneal surface with superior, nasal, inferior, and temporal quadrants extending from the central circular zone to the periphery of the cornea, each encompassing another one-fifth of the corneal surface. Grading of conjunctival staining began 1 to 2 minutes after instillation of lissamine green dye. The clinician viewed the temporal and nasal conjunctiva through a slit lamp using white light and graded punctate staining from 0 (no staining) to 3 in each area. The sum of the scores from all sectors per eye was used for corneal and conjunctival staining; in addition, only the central corneal staining score was assessed for association with visual acuity and contrast sensitivity. Approximately 5 minutes after instillation of a topical anesthetic, Schirmer test strips were hung onto the lower conjunctival sac in the temporal one-third of the eyelid. The patient was instructed to close both eyes. After 5 minutes, as measured by a stopwatch, the strips were removed, and the length of wetting of the strip was recorded in millimeters.

Statistical Analysis

Participants were excluded from analysis if their visual acuity scores in at least one eye were worse than 0.44 logMAR (approximate Snellen equivalent of 20/50) or if there was a history of diabetic retinopathy in one or both eyes because ocular pathology other than dry eye would be more likely to be responsible for their decreased vision. We performed descriptive analyses using mean (standard deviation) for continuous measures and percentages for categorical measures. Baseline values for the Ocular Surface Disease Index were the average of the values from the screening and eligibility confirmation visits.

We used the generalized linear model to assess the association between visual acuity and contrast sensitivity with each of the dry eye symptom measurements (Ocular Surface Disease Index total score, vision-related subscale score of the Ocular Surface Disease Index, and Short Form-36 score). In these analyses, visual acuity or contrast sensitivity was modeled as an independent variable, and each dry eye symptom score was modeled as a dependent variable, to determine whether subjects with worse vision reported more symptoms. Because the dry eye symptom measure is person specific, the visual acuity or contrast sensitivity was based on the better eye of this specific measurement. To help with the clinical interpretation and to avoid the strong assumption of linear association, the continuous measures (when modeled as independent variables) were categorized into severity levels, and a linear trend *P* value was used to test the association.

We used the generalized linear models to evaluate the associations between each dry eye sign with visual acuity and with contrast sensitivity. In these models, each dry eye sign was modeled as an independent variable, and visual acuity or contrast sensitivity was modeled as the dependent variable, to determine whether eyes with more severe signs had worse visual acuity scores or contrast sensitivity. Because measures of dry eye signs, visual acuity, and contrast sensitivity are all eye specific, these analyses were performed at the eye level, and their intereye correlation was accounted for by using generalized estimating equations.

Because these associations may differ by the status of Sjögren syndrome, we tested the interaction of Sjögren syndrome status with each independent variable. When a statistically significant interaction was found, analyses stratified by Sjögren syndrome status were performed. Dry Eye Assessment and Management patients

TABLE 2. Adjusted mean scores for the OSDI and SF-36 by visual acuity score and contrast sensitivity in the better eye

	Patients (n)	OSDI (total), mean (SE)*	OSDI vision-related scale, mean (SE)*	SF-36 physical health scale, mean (SE)*	SF-36 mental health scale, mean (SE)*
Visual acuity in the better eye					
20/16 or better	154	41.0 (1.57)	32.4 (1.92)	47.0 (0.98)	52.6 (0.92)
20/20	142	41.7 (1.54)	34.8 (1.89)	46.9 (0.96)	51.7 (0.91)
20/25	139	43.3 (1.54)	36.7 (1.88)	47.0 (0.96)	52.0 (0.91)
20/32 or worse	52	43.2 (2.37)	39.4 (2.91)	47.3 (1.48)	49.6 (1.40)
Linear trend *P* (adjusted *P*†)		.22 (0.44)	**.01 (0.02)**	.93 (0.93)	.14 (0.14)
Contrast sensitivity in the better eye					
1.72–1.92	187	42.5 (1.42)	34.2 (1.74)	46.9 (0.88)	52.7 (0.84)
1.56–1.68	105	40.3 (1.74)	32.9 (2.13)	47.7 (1.08)	51.8 (1.03)
1.44–1.52	120	43.2 (1.65)	38.5 (2.03)	46.4 (1.03)	51.1 (0.98)
0.84–1.40	77	42.1 (1.98)	35.4 (2.43)	47.2 (1.23)	51.1 (1.17)
Linear trend *P* (adjusted *P*†)		.86 (0.86)	.20 (0.20)	.90 (0.93)	.12 (0.14)

Boldface indicates statistical significance. *Adjusted by age (continuous), refractive error status (emmetropia, hyperopia >0.5 to ≤1.5 diopters, hyperopia >1.5 diopters, myopia >0.5 to ≤3 diopters, myopia >3 to ≤6 diopters, myopia >6 diopters), and cataract status. †Adjust for two comparisons for each of outcome measure using the Hochberg procedure. OSDI = Ocular Surface Disease Index; SF-36 = Short Form-36.

Copyright © American Academy of Optometry. Unauthorized reproduction of this article is prohibited.

TABLE 3. Adjusted* mean scores (letters) for visual acuity and log contrast sensitivity by eye-specific signs

Dry eye signs	Eyes	VA score (letters), mean (SE)	Linear trend *P* (adjusted *P*†)	Log contrast sensitivity score, mean (SE)	Linear trend *P* (adjusted *P*†)
TBUT (s)			**<.0001 (<.0001)**		**.003 (.02)**
>5	114	79.7 (0.62)		1.57 (0.02)	
>2 and ≤5	598	82.1 (0.38)		1.58 (0.01)	
≤2	262	82.7 (0.49)		1.51 (0.02)	
Schirmer test score			.98 (.98)		.75 (.96)
≤5	304	81.6 (0.45)		1.55 (0.02)	
6–10	361	82.4 (0.44)		1.56 (0.02)	
11–20	220	82.0 (0.51)		1.57 (0.02)	
21–30	66	80.8 (0.77)		1.51 (0.03)	
>30	23	82.5 (1.26)		1.52 (0.04)	
Tear film debris			**.003 (.02)**		.11 (.55)
None	639	81.5 (0.38)		1.55 (0.01)	
Mild	269	82.9 (0.49)		1.55 (0.02)	
Moderate	66	83.5 (0.94)		1.64 (0.03)	
Corneal staining score			.70 (.98)		.96 (.96)
0–1	266	81.4 (0.47)		1.54 (0.02)	
2–3	210	82.5 (0.52)		1.58 (0.02)	
4–5	278	82.5 (0.49)		1.57 (0.02)	
≥6	218	81.6 (0.55)		1.54 (0.02)	
Central corneal staining score			.07 (.42)		.26 (.78)
0	613	82.0 (0.36)		1.56 (0.01)	
1	271	83.1 (0.47)		1.58 (0.02)	
2	72	79.8 (0.80)		1.53 (0.03)	
3	18	77.3 (1.34)		1.42 (0.06)	
Conjunctival staining			.82 (.98)		.15 (.60)
0–1	136	81.3 (0.56)		1.56 (0.02)	
2–3	511	82.5 (0.40)		1.57 (0.01)	
≥4	327	81.6 (0.45)		1.54 (0.01)	
Meibomian gland			.64 (.98)		**.007 (.04)**
None plugged	144	82.1 (0.56)		1.54 (0.02)	
Mild	295	82.3 (0.47)		1.59 (0.02)	
Moderate	316	81.6 (0.45)		1.57 (0.02)	
Severe	219	82.1 (0.56)		1.48 (0.02)	
Secretions from meibomian glands			.94 (.98)		**.0003 (.002)**
Clear	180	81.9 (0.53)		1.57 (0.02)	
Mild haze/cloudiness	387	82.2 (0.44)		1.58 (0.01)	
Paste	182	81.9 (0.60)		1.56 (0.02)	
Obstructed	225	82.0 (0.55)		1.49 (0.02)	

Boldface indicates statistical significance. Log contrast sensitivity score ranges from 0 (100% contrast required to read letters) to 1.92 (1.2% contrast required to read letters). A score of 1.56 means that 2.8% contrast is required to read letters. A VA (score ranges from 0 to 100) score of 80 is equivalent to 20/25, and a score of 85 is equivalent to 20/20. *Adjusted by age (continuous), refractive error status (emmetropia, hyperopia >0.5 to ≤1.5 diopters, hyperopia >1.5 diopters, myopia >0.5 to ≤3 diopters, myopia >3 to ≤6 diopters, myopia >6 diopters), and ocular status of cataract. †Adjusted for eight comparisons of visual acuity scores and for eight comparisons of contrast sensitivity scores using the Hochberg procedure. TBUT = tear breakup time; VA = visual acuity.

Copyright © American Academy of Optometry. Unauthorized reproduction of this article is prohibited.

were classified as having Sjögren syndrome if an antibody profile met the 2012 American College of Rheumatology criteria and had a sum of the Dry Eye Assessment and Management corneal and conjunctival staining scores of ≥3.

All these statistical models included adjustment of pre-selected covariates (age, refractive error, and status of cataract). All statistical analyses were performed in SAS v9.4 (SAS Institute Inc., Cary, NC). To account for the multiple comparisons from analyzing the association of multiple factors with dry eye symptoms and from analyzing multiple dry eyes signs as predictors for visual acuity and contrast sensitivity, we calculated adjusted *P* value using the Hochberg procedure.[30] Adjusted *P* values of <.05 were considered statistically significant.

RESULTS

Characteristics of Analysis Cohort

Among 535 Dry Eye Assessment and Management participants, 487 participants (974 eyes) were eligible for the analysis after excluding participants with visual acuity 20/50 or worse in at least one eye (n = 45 participants), without visual acuity (n = 1 participant), or with diabetic retinopathy (n = 2 participants; Fig. 1). Among these remaining 487 eligible subjects, 61 had no Sjögren syndrome tests or indeterminate Sjögren syndrome status, leaving 45 subjects who had Sjögren syndrome at baseline and 381 subjects without Sjögren syndrome.

The participant and ocular characteristics of the 487 participants are displayed in Table 1. The mean (standard deviation) age was 58 (13) years, 81% were female, 74% were white, 13% were black, and 13% were Hispanic. The mean (standard deviation) Ocular Surface Disease Index scores were 42 (16) for the total and 35 (19) for the vision-related subscale. The mean Medical Outcomes Study 36-Item Short Form Health Survey scores were 48 (9.7) for physical health and 52 (9.4) for mental health. The mean (standard deviation) scores of dry eye signs for the cohort are displayed in Table 1.

Association of Visual Acuity and Contrast Sensitivity with Dry Eye Symptoms

In adjusted analyses (adjusted for age, refractive error, and status of cataract), poorer visual acuity was significantly associated with worse mean Ocular Surface Disease Index vision-related subscale score (adjusted means, 39.4 for visual acuity 20/32 or worse and 32.4 for visual acuity 20/16 or better; adjusted linear trend, *P* = .02). However, visual acuity was not significantly associated with the mean Ocular Surface Disease Index total score or the mean Medical Outcomes Study 36-Item Short Form Health Survey scores (Table 2).

Contrast sensitivity was not significantly associated with mean Ocular Surface Disease Index scores and mean Medical Outcomes Study 36-Item Short Form Health Survey scores (Table 2). There were no significant interactions between Sjögren syndrome and visual acuity or contrast sensitivity on the association with dry eye symptoms (all, *P* ≥ .21).

Association between Dry Eye Signs and Visual Acuity

The results of the adjusted analysis (adjusted for age, refractive error, and status of cataract) for associations between dry eye signs and visual acuity are shown in Table 3. Measures of tear film disruption, including tear film debris and tear breakup time, were not associated with worse mean visual acuity. Counterintuitively, increased tear film debris was significantly associated with better visual acuity score (adjusted mean visual acuity scores, 83.5

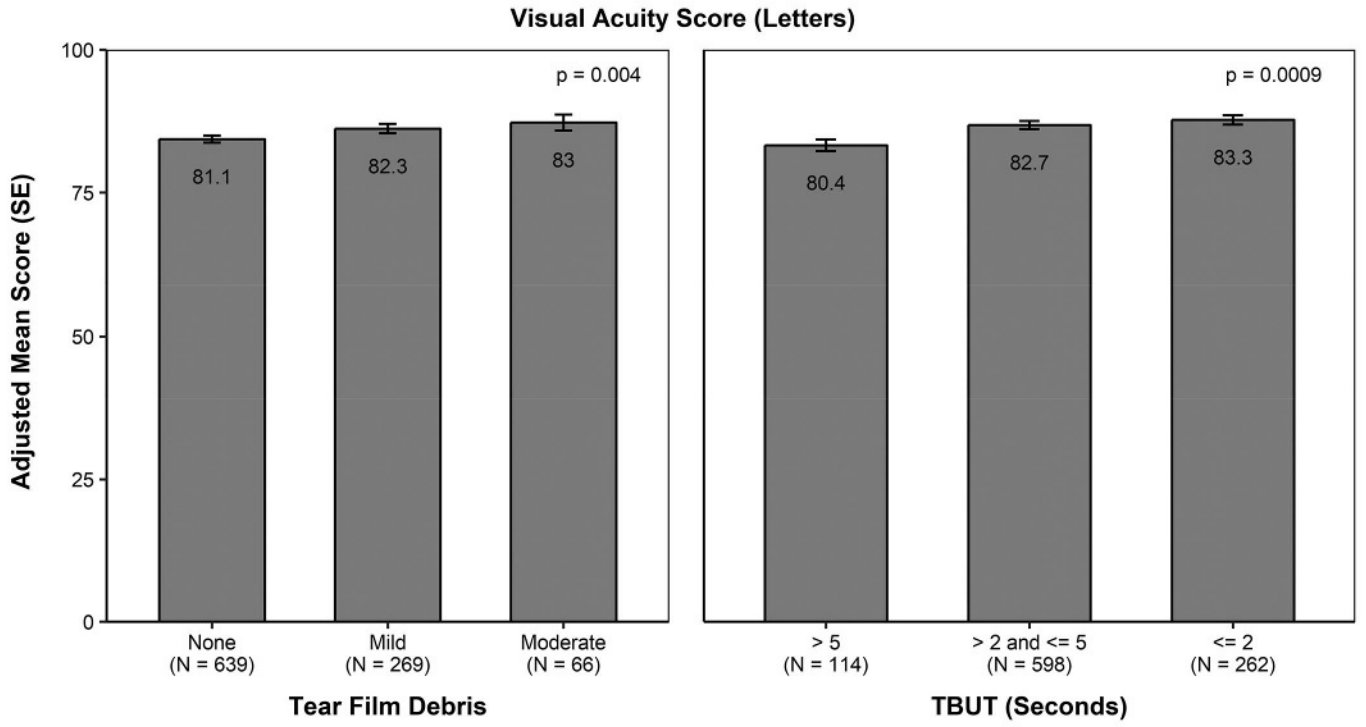


FIGURE 2. Adjusted mean visual acuity score for signs of dry eye disease associated with visual acuity scores. Greater tear film debris (left) and longer tear breakup time (TBUT; right) were associated with better visual acuity. A letter score of 80 is Snellen 20/25.

Copyright © American Academy of Optometry. Unauthorized reproduction of this article is prohibited.

TABLE 4. Multivariable* analysis for visual acuity and contrast sensitivity by signs of dry eye

	All patients (n = 974 eyes)			Patients without Sjögren syndrome (n = 762 eyes)		
Dry eye signs	**Eyes (n)**	**Mean (SE)**	**Linear trend *P***	**Eyes (n)**	**Mean (SE)**	**Linear trend *P***
Visual acuity score (letters)						
Tear film debris			**.004**			**.002**
None	639	81.1 (0.40)		498	81.0 (0.43)	
Mild	269	82.3 (0.53)		209	82.6 (0.61)	
Moderate	66	83.0 (0.91)		55	83.3 (1.01)	
TBUT (s)			**.0009**			**.0002**
>5	114	80.4 (0.67)		84	80.4 (0.73)	
>2 and ≤5	598	82.7 (0.47)		478	82.7 (0.53)	
≤2	262	83.3 (0.53)		200	83.9 (0.60)	
Log contrast sensitivity score						
Meibomian gland			**.01**			**.003**
None plugged	144	1.54 (0.02)		109	1.57 (0.02)	
Mild	295	1.58 (0.02)		241	1.59 (0.02)	
Moderate	316	1.57 (0.02)		243	1.57 (0.02)	
Severe	219	1.48 (0.02)		169	1.49 (0.03)	
TBUT (s)			**.009**			.10
>5	114	1.55 (0.02)		200	1.56 (0.03)	
>2 and ≤5	598	1.56 (0.01)		478	1.57 (0.02)	
≤2	262	1.51 (0.02)		84	1.53 (0.02)	

*The model includes age, refractive error status (emmetropia, hyperopia >0.5 to ≤1.5 diopters, hyperopia >1.5 diopters, myopia >0.5 to ≤3 diopters, myopia >3 to ≤6 diopters, myopia >6 diopters), and ocular status of cataract, tear film debris, and TBUT as predictors. Bold numbers are significant.
TBUT = tear breakup time.

letters for moderate tear film debris and 81.5 letters for none; linear trend adjusted, $P = .02$), and longer tear breakup time was significantly associated with worse visual acuity score (adjusted mean visual acuity scores, 79.7 letters for tear breakup time >5 seconds and 82.7 letters for tear breakup time ≤2 seconds; linear trend, $P < .0001$; Fig. 2). When the tear film debris and tear breakup time were considered together in a multivariate model that was adjusted for age, refractive error status, and cataract status, their association with visual acuity remained statistically significant for both tear film debris ($P = .004$) and tear breakup time ($P = .0009$; Table 4). Signs of meibomian gland dysfunction (plugged glands and cloudy secretions), conjunctival staining, and Schirmer test scores were not significantly associated with visual acuity (all linear trends, $P > .64$; Table 3).

There was a statistically significant interaction between the presence of Sjögren syndrome and tear film debris (adjusted, $P = .02$) for the association with visual acuity. In an analysis stratified by Sjögren syndrome status (Appendix Table A1, available at http://links.lww.com/OPX/A404), the mean visual acuity score significantly increased with severity of tear film debris (adjusted linear trend, $P = .001$) in non–Sjögren syndrome patients; however, in Sjögren syndrome patients, the mean visual acuity scores did not show an association with tear film severity (linear trend, $P = .07$).

Associations between Dry Eye Signs with Contrast Sensitivity

The adjusted analyses for associations of dry eye signs with contrast sensitivity are shown in Table 3. Severe meibomian gland plugging was significantly associated with worse mean log contrast sensitivity in both the unadjusted and adjusted analyses (adjusted mean log contrast sensitivity score, 1.48 for severe vs. 1.54 for none plugged; linear trend adjusted, $P = .04$). Similarly, the degree of abnormality in meibomian gland secretions was significantly associated with worse mean log contrast sensitivity (adjusted mean log contrast sensitivity scores, 1.49 for obstructed and 1.57 for clear; linear trend adjusted, $P = .002$). Longer tear breakup time was significantly associated with better mean log contrast sensitivity (adjusted log contrast sensitivity scores, 1.57 for tear breakup time >5 seconds and 1.51 for tear breakup time ≤2 seconds; linear trend adjusted, $P = .02$). When meibomian gland plugging and tear breakup time were considered together in a multivariate model that was adjusted for age, refractive error status, and cataract status, the significant association with contrast sensitivity remained for meibomian gland plugging ($P = .01$) and tear breakup time ($P = .009$; Table 4, Fig. 3). Tear film debris, conjunctival staining, corneal staining, and Schirmer test score were not significantly associated with contrast sensitivity (all linear trend adjusted, $P \geq .55$, Table 4).

DISCUSSION

Dry eye has a deleterious effect on multiple aspects of visual function despite normal visual acuity being documented using standard testing techniques.[31] Our data substantiate the finding that, even among patients with relatively good visual acuity (20/50

Copyright © American Academy of Optometry. Unauthorized reproduction of this article is prohibited.

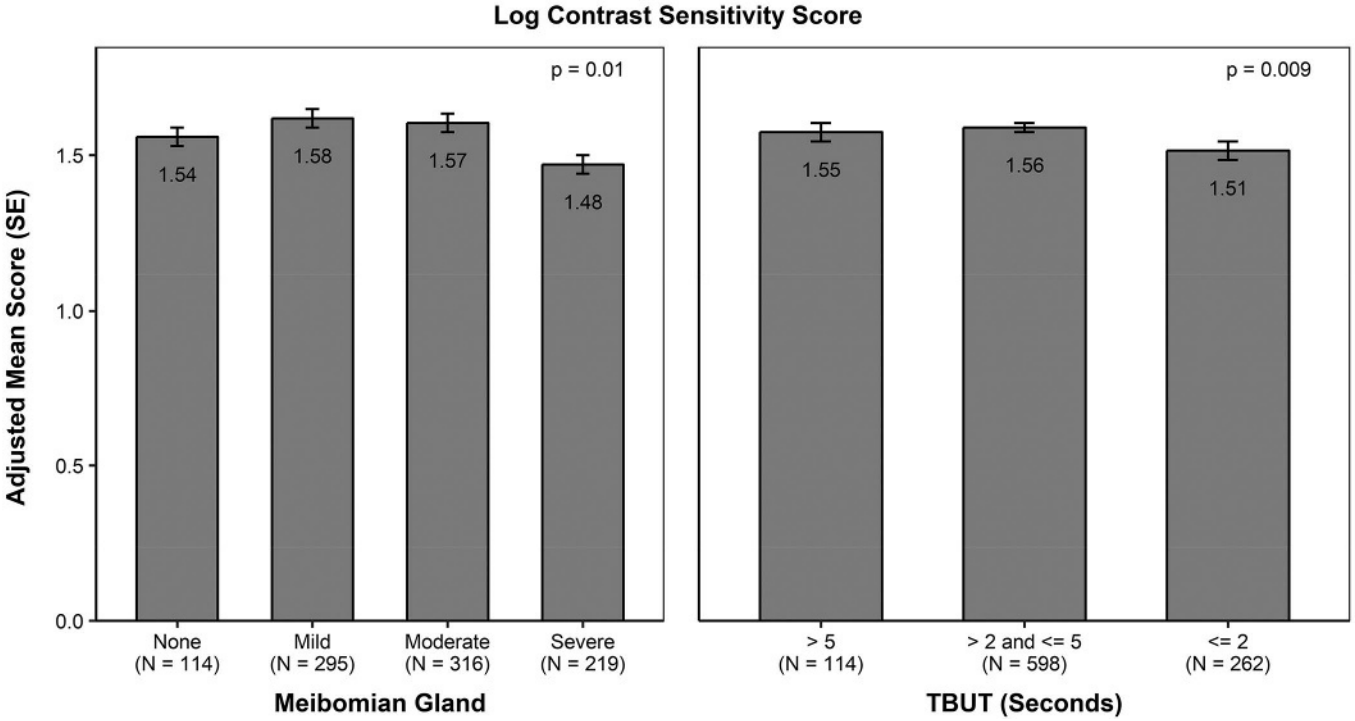


FIGURE 3. Adjusted mean log contrast sensitivity score for signs of dry eye disease associated with contrast sensitivity. Greater meibomian gland plugging (left) and shorter tear breakup time (TBUT; right) were associated with worse contrast sensitivity.

or better), worse visual acuity corresponded to worse scores on the Ocular Surface Disease Index vision-related symptoms subscale in dry eye patients. However, none of the dry eye signs we measured in the study deleteriously impacted visual acuity. Although subtle visual acuity changes could be documented based on differences in tear film debris and tear breakup time, the mean changes were small (approximately two letters) and not in the direction one would expect. Alternatively, we found that contrast sensitivity measurements were more sensitive to differences based on dry eye signs related to tear film stability (tear breakup time and meibomian gland dysfunction) than conventional visual acuity assessments.

We included evaluation of central corneal fluorescein staining on vision in the Dry Eye Assessment and Management participants, as this has been shown to decrease quality of life in other ocular surface disease patients and central corneal staining directly impacted functional, dynamic visual acuity in a small dry eye study of 22 patients.[15,32] In addition, Huang and colleagues[15] previously found that, in dry eye patients with punctate epithelial keratopathy, contrast sensitivity improved after instillation of artificial tears. However, we were not able to demonstrate an impact on high-contrast visual acuity or contrast sensitivity with increased central corneal staining in our dry eye cohort. The Dry Eye Assessment and Management cohort had relatively low corneal staining scores overall (mean staining score, 3.6 of 15; Table 1), and we used static measures of visual acuity and contrast sensitivity rather than dynamic, which may account for the differences in our findings compared with others.

Using low-contrast optotypes, the measurement of contrast sensitivity can detect subtle vision changes that may not be detected with standard visual acuity testing. In our study, we detected a ~0.07 difference in log contrast sensitivity in eyes with severe meibomian gland dysfunction or obstructed meibomian gland secretions compared with normal eyes and in eyes with short (≤2 seconds) tear breakup time compared with eyes with longer (>5 seconds) times. In other ocular diseases such as glaucoma and age-related macular degeneration, standard high-contrast visual acuity testing did not differentiate between milder ocular disease states when contrast sensitivity did.[23–27] For example, in patients with different stages of glaucoma, mean log contrast sensitivity differed significantly between patients with early and moderate visual field defects (1.76 vs. 1.51, respectively).[33] In another study, the mean log contrast sensitivity was 1.62 for healthy subjects aged 22 to 77 years, with significantly lower values in patients with glaucoma (1.56) or age-related macular degeneration (1.03).[34] In addition, in a study evaluating visual function in recalcitrant neovascular age-related macular degeneration after switching anti–vascular endothelial growth factor treatments, mean log contrast sensitivity improved from 1.32 to 1.40 units, whereas visual acuity remained stable throughout.[35]

The findings of improved visual acuity with worse tear film debris and shorter breakup time were unexpected and counterintuitive. These patients may be compensating by blinking more to distribute the tear film and remove debris that could contribute to improved vision. Evaluating only the Sjögren syndrome group can provide us an indication of the impact of aqueous deficiency on these associations. When we scrutinized only the Sjögren syndrome group, we found no impact of any ocular signs on high-contrast visual acuity. That is, the previous associations and trends of tear film debris and tear breakup time on visual acuity as noted in the entire cohort were not present in the Sjögren syndrome group, suggesting that aqueous deficiency does not contribute to these relationships.

Copyright © American Academy of Optometry. Unauthorized reproduction of this article is prohibited.

Limitations of our study and analyses include having patients with a limited range of symptoms because patients with mild or very severe symptoms as measured by the Ocular Surface Disease Index were excluded. Also, as in most research studies, visual function was measured as a patient read a chart in an examination room where blinking may differ from other everyday activities such as viewing a display screen or reading printed material.

In conclusion, our study found that poorer visual acuity rather than worse contrast sensitivity drives visual symptoms and complaints in dry eye. However, contrast sensitivity measurements are more sensitive to worse tear film stability measures (such as tear breakup time and Meibomian gland plugging) than standard visual acuity assessments. Future studies that examine how specific ocular signs affect various measures of visual function would be helpful in elucidating these relationships and could in turn guide therapies.

ARTICLE INFORMATION

Supplemental Digital Content: Appendix Table A1, Adjusted mean scores for visual acuity (letters) by tear film debris stratified by presence or absence of Sjögren syndrome are available at http://links.lww.com/OPX/A404.

Submitted: August 1, 2018

Accepted: February 17, 2019

Funding/Support: This work was supported by cooperative agreements U10EY022879 and U10EY022881 from the National Eye Institute, National Institutes of Health, Department of Health and Human Services. Additional support was provided by grants from the Office of Dietary Supplements National Institutes of Health, Department of Health and Human Services.

Conflict of Interest Disclosure: None of the authors have reported a financial conflict of interest. The sponsor provided financial support and had a role in the study design and conduct but not the analysis, interpretation, or writing of the report.

Study Registration Information: ClinicalTrials.gov/NCT02128763.

Author Contributions: Conceptualization: LBS-F, MGM, PAA; Data Curation: MGM, MCL; Formal Analysis: MGM, G-sY; Funding Acquisition: MGM, PAA; Investigation: VYB, RD, PAA; Methodology: MGM, G-sY, PAA; Project Administration: LBS-F, MGM, PAA; Writing – Original Draft: LBS-F, MGM, G-sY, MCL; Writing – Review & Editing: LBS-F, MGM, G-sY, MCL, VYB, RD, PAA.

The Dry Eye Assessment and Management (DREAM) Study Research Group

The members of the Dry Eye Assessment and Management (DREAM) Study Research Group who contributed to the research presented in this article are listed below.

Certified roles at clinical centers: clinician (CL), clinic coordinator (CC), data entry staff (DE) principal investigator (PI), technician (T).

Milton M. Hom (Azusa, CA): Milton M. Hom, OD, FAAO (PI); Melissa Quintana (CC/T); Angela Zermeno (CC/T).

Pendleton Eye Center (Oceanside, CA): Robert Pendleton, MD, PhD (PI); Debra McCluskey (CC); Diana Amador (T); Ivette Corona (CC/T); Victor Wechter, MD (CL).

University of California School of Optometry, Berkeley (Berkeley, CA): Meng C. Lin, OD, PhD, FAAO (PI); Carly Childs (CC); Uyen Do (CC); Mariel Lerma (CC); Wing Li, OD (T); Zakia Young (CC); Tiffany Yuen, OD (CC/T).

Clayton Eye Center (Morrow, GA): Harvey Dubiner, MD (PI); Heather Ambrosia, OD (C); Mary Bowser (CC/T); Peter Chen, OD (CL); Helen Dubiner, PharmD, CCRC (CC/T); Cory Fuller (CC/T); Kristen New (DE); Tu Vy Nguyen (C); Ethen Seville (CC/T); Daniel Strait, OD (CL); Christopher Wang (CC/T); Stephen Williams (CC/T); Ron Weber, MD (CL).

University of Kansas (Prairie Village, KS): John Sutphin, MD (PI); Miranda Bishara, MD (CL); Anna Bryan (CC); Asher Ertel (CC/T); Kristie Green (T); Gloria Pantoja, Ashley Small (CC); Casey Williamson (T).

Clinical Eye Research of Boston (Boston, MA): Jack Greiner, MS, OD, DO, PhD (PI); EveMarie DiPronio (CC/T); Michael Lindsay (CC/T); Andrew McPherson (CC/T); Paula Oliver (CC/T); Rina Wu (T).

Mass Eye and Ear Infirmary (Boston, MA): Reza Dana, MD (PI); Tulio Abud (T): Lauren Adams (T); Marissa Arnofsky (T); Jillian Candlish, COA (T); Pranita Chilakamarri (DE); Joseph Ciolino, MD (CL); Naomi Crandall (T); Antonio Di Zazzo (T); Merle Fernandes (T); Mansab Jafri (T); Britta Johnson (T); Ahmed Kheirkhah (T); Sally Kiebdaj (CC/T); Andrew Mullins (CC/T); Milka Nova (T); Vannarut Satitpitakul (T); Chunyi Shao (T); Kunal Suri (T); Vijeeta Tadla (CC); Saboo Ujwala (T); Jia Yin MD, PhD (T); Man Yu (T).

Kellogg Eye Center, University of Michigan (Ann Arbor, MI): Roni Shtein, MD (PI); Christopher Hood, MD (CL); Munira Hussain, MS, COA, CCRP (CC/T); Erin Manno, COT (T); Laura Rozek, COT (T/DE).

Minnesota Eye Consultants (Bloomington, MN): David R. Hardten, MD, FACS (PI); Kimberly Baker (T); Alex Belsaas (T); Erich Berg (CC/T); Alyson Blakstad, OD (CL); Ken DauSchmidt (T); Lindsey Fallenstein (CC/T); Ahmad M. Fahmy, OD (CL); Mona M. Fahmy, OD, FAAO (CL); Ginny Georges (T); Deanna E. Harter (CL); Scott G. Hauswirth, OD (CL); Madalyn Johnson (T); Ella Meshalkin (T); Rylee Pelzer (CC/T); Joshua Tisdale (CC/T); JulieAnn C. Wick (CL).

Tauber Eye Center (Kansas City, MO): Joseph Tauber, MD, PhD (PI); Megan Hefter (CC/T).

Silverstein Eye Centers (Kansas City, MO): Steven Silverstein, MD (PI); Cindy Bentley (CC/T); Eddie Dominguez (CC/T); Kelsey Kleinsasser, OD (CL).

Icahn School of Medicine at Mt. Sinai (New York, NY): Penny Asbell, MD, MBA, FACS (PI); Brendan Barry (CC/T); Eric Kuklinski (CC/T); Afsana Amir (CC/T); Neil Chen (CC/T); Marko Oydanich (CC/T); Viola Spahiu (CC/T); An Vo, MD (T); Matthew Weinstein, DO (T).

University of Rochester Flaum Eye Institute (Rochester, NY): Tara Vaz, OD (PI); Holly Hindman, MD (PI); Rachel Aleese (CC/T); Andrea Czubinski (CC/T); Gary Gagarinas, COMT, CCRA (CC/T); Peter McDowell (CC); George O'Gara (DE); Kari Steinmetz (CC/T).

University of Pennsylvania Scheie Eye Institute (Philadelphia, PA): Vatinee Bunya, MD (PI); Michael Bezzerides (CC/T); Dominique Caggiano (CC/T); Sheri Drossner (T); Joan Dupont (CC); Marybeth Keiser (CC/T); Mina Massaro, MD (CL); Stephen Orlin, MD (CL); Ryan O'Sullivan (CC/T).

Southern College of Optometry (Memphis, TN): Michael Christensen, OD, PhD (PI); Havilah Adkins (CC); Randy Brafford (CC/T); Cheryl Ervin (CL); Rachel Grant, OD (CL); Christina Newman (CL).

Shettle Eye Research (Largo, FL): Lee Shettle, DO (PI); Debbie Shettle (CC).

Stephen Cohen, OD, PC (Scottsdale, AZ): Stephen Cohen, OD (PI); Diane Rodman (CC/T).

Case Western Reserve University (Cleveland, OH): Loretta Szczotka-Flynn, OD, PhD (PI); Tracy Caster (T); Pankaj Gupta MD MS (CL); Sangeetha Raghupathy (CC/T); Rony Sayegh, MD (CL).

Mayo Clinic Arizona (Scottsdale, AZ): Joanne Shen, MD (PI); Nora Drutz, CCRC (CC); Lauren Joyner, COA (T); Mary Mathis, COA (T); Michaele Menghini, CCRP (CC); Charlene Robinson, CCRP (CC).

Wolston & Goldberg Eye Associates (Torrance, CA): Damien Goldberg, MD (PI); Lydia Jenkins (T); Brittney Rodriguez (CC/T); Jennifer Picone Jones (CC/T); Nicole Thompson (T); Barry Wolstan, MD (CL).

Northeast Ohio Eye Surgeons (Stow, OH): Marc Jones, MD (PI); April Lemaster (CC/T); Julie Ransom-Chaney (T); William Rudy, OD (CL).

Tufts Medical Center (Boston, MA): Pedram Hamrah, MD (PI); Mildred Commodore (CC); Christian Iyore (T); Lioubov Lazarev (T): Leah Mullen (T); Nicholas Pondelis (T); Carly Satsuma (CC).

University of Illinois at Chicago (Chicago, IL): Sandeep Jain, MD (PI); Peter Cowen (CC/T); Joelle Hallak (CC); Christine Mun (CC/T); Roxana Toh (CC).

The Eye Centers of Racine & Kenosha (Racine, WI): Inder Singh, MD (PI); Pamela Lightfield (CC/T); Eunice Lowery (T); Sarita Ornelas (T); R. Krishna Sanka, MD (CL); Beth Saunders (T).

Mulqueeny Eye Centers (St. Louis, MO): Sean P. Mulqueeny, OD (PI); Maggie Pohlmeier (CC/T).

Oculus Research at Garner Eyecare Center (Raleigh, NC): Carol Aune, OD (PI); Hoda Gabriel (CC); Kim Major Walker, MS, RN (CC/T); Jennifer Newsome (CC/T).

Resource Centers

Chairman's Office (Icahn School of Medicine at Mount Sinai, New York, NY): Penny Asbell, MD, MBA, FACS (Study Chair); Brendan Barry (Clinical Research Coordinator); Eric Kuklinski (Clinical Research Coordinator); Shir Levanon (Clinical Research Coordinator); Michael Farkouh, MD, FRCPC, FACC, FAHA (Medical Safety Monitor); Seunghee Kim-Schulze, PhD (Consultant); Robert Chapkin, PhD, MSc (Consultant); Giampaolo Greco, PhD (Consultant); Artemis Simopoulos, MD (Consultant); Ines Lashley (Administrative Assistant); Peter Dentone, MD (Clinical Research Coordinator); Neha Gadaria-Rathod, MD (Clinical Research Coordinator); Morgan Massingale, MS (Clinical Research Coordinator); Nataliya Antonova (Clinical Research Coordinator).

Coordinating Center (University of Pennsylvania Perelman School of Medicine, Philadelphia, PA): Maureen G. Maguire, PhD (PI); Mary Brightwell-Arnold, SCP (Systems Analyst); John Farrar, MD, PhD (Consultant); Sandra Harkins (Staff Assistant); Jiayan Huang, MS (Biostatistician); Kathy McWilliams, CCRP (Protocol Monitor); Ellen Peskin, MA, CCRP (Director); Maxwell Pistilli, MS, MEd (Biostatistician); Susan Ryan (Financial Administrator); Hilary Smolen (Research Fellow); Claressa Whearry (Administrative

Copyright © American Academy of Optometry. Unauthorized reproduction of this article is prohibited.

Coordinator); Gui-Shuang Ying, PhD (Senior Biostatistician); Yinxi Yu (Biostatistician).

Biomarker Laboratory (Icahn School of Medicine at Mount Sinai, New York, NY): Yi Wei, PhD, DVM (Co-Director, Biomarker Laboratory); Neeta Roy, PhD (Co-Director, Biomarker Laboratory); Seth Epstein, MD (Former Co-Director; Biomarker Laboratory); Penny A. Asbell, MD, MBA, FACS (Director and Study Chair).

Investigational Drug Service (University of Pennsylvania Perelman School of Medicine, Philadelphia, PA): Kenneth Rockwell, Jr., PharmD, MS (Director).

Peroxisomal Diseases Laboratory at the Kennedy Krieger Institute, Johns Hopkins University, Baltimore, MD: Ann Moser (Co-Director/Consultant); Richard O. Jones, PhD (Co-Director/Consultant).

Meibomian Gland Reading Center (University of Pennsylvania Perelman School of Medicine, Philadelphia, PA): Ebenezer Daniel, PhD, MBBS, MPH (PI); E. Revell Martin (Image Grader); Candace Parker Ostroff (Image Grader); Eli Smith (Image Grader); Pooja Axay Kadakia (Student Researcher).

National Eye Institute, National Institutes of Health, Department of Health and Human Services: Maryann Redford, DDS, MPH (Program Officer).

Office of Dietary Supplements/National Institutes of Health, Department of Health and Human Services.

Committees

Executive Committee: (members from all terms of appointment): Penny Asbell, MD, MBA, FACS (Chair); Brendan Barry, MS; Munira Hussain, MS, COA, CCRP; Jack Greiner, OD, PhD, MS; Milton Hom, OD, FAAO; Holly Hindman, MD, MPH; Eric Kuklinski, BA; Meng C. Lin OD, PhD. FAAO; Maureen G. Maguire, PhD; Kathy McWilliams, CCRP; Ellen Peskin, MA, CCRP; Maryann Redford, DDS, MPH; Roni Shtein, MD, MS; Steven Silverstein, MD; John Sutphin, MD.

Operations Committee: Penny Asbell, MD, MBA, FACS (Chair); Brendan Barry, MS; Eric Kuklinski, BA; Maureen G. Maguire, PhD; Kathleen McWilliams, CCRP, Ellen Peskin, MA, CCRP; Maryann Redford, DDS, MPH.

Clinic Monitoring Committee: Ellen Peskin, MA, CCRP (Chair); Mary Brightwell-Arnold, SCP, Maureen G. Maguire, PhD; Kathleen McWilliams, CCRP.

Data and Safety Monitoring Committee: Stephen Wisniewski, PhD (Chair); Tom Brenna, PhD; William G. Christen, Jr., SCD, OD, PhD; Jin-Feng Huang, PhD; Cynthia S. McCarthy, DHCE, MA; Susan T. Mayne, PhD; Mari Palta, PhD; Oliver D. Schein, MD, MPH, MBA.

Industry Contributors of Products and Services

Access Business Group, LLC (Ada, MI): Jennifer Chuang, PhD, CCRP; Maydee Marchan, MChE; Tian Hao, PhD; Christine Heisler; Charles Hu, PhD; Clint Throop; Vikas Moolchandani, PhD.

Compounded Solutions in Pharmacy (Monroe, CT)

Leiter's (San Jose, CA)

Immco Diagnostics Inc. (Buffalo, NY)

OCULUS Inc. (Arlington, WA)

RPS Diagnostics, Inc. (Sarasota, FL)

TearLab Corporation (San Diego, CA)

TearScience Inc. (Morrisville, NC)

REFERENCES

1. Jie Y, Xu L, Wu YY, et al. Prevalence of Dry Eye Among Adult Chinese in the Beijing Eye Study. Eye (Lond) 2009;23:688–93.

2. Paulsen AJ, Cruickshanks KJ, Fischer ME, et al. Dry Eye in the Beaver Dam Offspring Study: Prevalence, Risk Factors, and Health-related Quality of Life. Am J Ophthalmol 2014;157:799–806.

3. Stapleton F, Alves M, Bunya VY, et al. TFOS DEWS II Epidemiology Report. Ocul Surf 2017;15:334–65.

4. Tian YJ, Liu Y, Zou HD, et al. Epidemiologic Study of Dry Eye in Populations Equal or Over 20 Years Old in Jiangning District of Shanghai. Zhonghua Yan Ke Za Zhi 2009;45:486–91.

5. Tong L, Saw SM, Lamoureux EL, et al. A Questionnaire-based Assessment of Symptoms Associated with Tear Film Dysfunction and Lid Margin Disease in an Asian Population. Ophthalmic Epidemiol 2009;16:31–7.

6. Viso E, Rodriguez-Ares MT, Gude F. Prevalence of and Associated Factors for Dry Eye in a Spanish Adult Population (the Salnes Eye Study). Ophthalmic Epidemiol 2009;16:15–21.

7. Le Q, Zhou X, Ge L, et al. Impact of Dry Eye Syndrome on Vision-related Quality of Life in a Non-clinic-based General Population. BMC Ophthalmol 2012;12:22.

8. Cowell BA, Wu C, Fleiszig SM. Use of an Animal Model in Studies of Bacterial Corneal Infection. ILAR J 1999;40:43–50.

9. Moss SE, Klein R, Klein BE. Long-term Incidence of Dry Eye in an Older Population. Optom Vis Sci 2008;85:668–74.

10. Ali NM, Hamied FM, Farhood QK. Corneal Thickness in Dry Eyes in an Iraqi Population. Clin Ophthalmol 2017;11:435–40.

11. Liu Z, Pflugfelder SC. Corneal Thickness Is Reduced in Dry Eye. Cornea 1999;18:403–7.

12. Foulks GN. What Is Dry Eye and What Does It Mean to the Contact Lens Wearer? Eye Contact Lens 2003;29:S96–100.

13. McDonnell PJ, Pflugfelder SC, Stern ME, et al. Study Design and Baseline Findings from the Progression of Ocular Findings (PROOF) Natural History Study of Dry Eye. BMC Ophthalmol 2017;17:265.

14. Kaido M, Matsumoto Y, Shigeno Y, et al. Corneal Fluorescein Staining Correlates with Visual Function in Dry Eye Patients. Invest Ophthalmol Vis Sci 2011;52:9516–22.

15. Huang FC, Tseng SH, Shih MH, et al. Effect of Artificial Tears on Corneal Surface Regularity, Contrast Sensitivity, and Glare Disability in Dry Eyes. Ophthalmology 2002;109:1934–40.

16. Koh S, Maeda N, Hirohara Y, et al. Serial Measurements of Higher-order Aberrations After Blinking in Patients with Dry Eye. Invest Ophthalmol Vis Sci 2008;49:133–8.

17. Koh S, Maeda N, Ikeda C, et al. The Effect of Ocular Surface Regularity on Contrast Sensitivity and Straylight in Dry Eye. Invest Ophthalmol Vis Sci 2017;58:2647–51.

18. Koh S. Mechanisms of Visual Disturbance in Dry Eye. Cornea 2016;35(Suppl. 1):S83–8.

19. Ferrer-Blasco T, Garcia-Lazaro S, Montes-Mico R, et al. Dynamic Changes in the Air-tear Film Interface Modulation Transfer Function. Graefes Arch Clin Exp Ophthalmol 2010;248:127–32.

20. Puell MC, Benitez-del-Castillo JM, Martinez-de-la-Casa J, et al. Contrast Sensitivity and Disability Glare in Patients with Dry Eye. Acta Ophthalmol Scand 2006;84:527–31.

21. Ridder WH, 3rd, LaMotte J, Hall JQ, Jr., et al. Contrast Sensitivity and Tear Layer Aberrometry in Dry Eye Patients. Optom Vis Sci 2009;86:E1059–68.

22. Rolando M, Iester M, Macri A, et al. Low Spatial-contrast Sensitivity in Dry Eyes. Cornea 1998;17:376–9.

23. Elliott DB, Hurst MA. Simple Clinical Techniques to Evaluate Visual Function in Patients with Early Cataract. Optom Vis Sci 1990;67:822–5.

24. Essock EA, Fechtner RD, Zimmerman TJ, et al. Binocular Function in Early Glaucoma. J Glaucoma 1996;5:395–405.

25. Ghaith AA, Daniel J, Stulting RD, et al. Contrast Sensitivity and Glare Disability After Radial Keratotomy and Photorefractive Keratectomy. Arch Ophthalmol 1998;116:12–8.

26. Hawkins AS, Szlyk JP, Ardickas Z, et al. Comparison of Contrast Sensitivity, Visual Acuity, and Humphrey Visual Field Testing in Patients with Glaucoma. J Glaucoma 2003;12:134–8.

27. Wood JM, Lovie-Kitchin JE. Evaluation of the Efficacy of Contrast Sensitivity Measures for the Detection of Early Primary Open-angle Glaucoma. Optom Vis Sci 1992;69:175–81.

28. Asbell PA, Maguire MG, Pistilli M, et al. n-3 Fatty Acid Supplementation for the Treatment of Dry Eye Disease. N Engl J Med 2018;378:1681–90.

29. Allergan. 12-Item Ocular Surface Disease Index (OSDI) Administration and Scoring Manual. Madison, NJ: Allergan, Inc; 2004.

30. Hochberg Y, Benjamini Y. More Powerful Procedures for Multiple Significance Testing. Stat Med 1990;9:811–8.

31. Uchino M, Schaumberg DA. Dry Eye Disease: Impact on Quality of Life and Vision. Curr Ophthalmol Rep 2013;1:51–7.

32. Saboo US, Amparo F, Abud TB, et al. Vision-related Quality of Life in Patients with Ocular Graft-versus-host Disease. Ophthalmology 2015;122:1669–74.

33. Bambo MP, Ferrandez B, Guerri N, et al. Evaluation of Contrast Sensitivity, Chromatic Vision, and Reading Ability in Patients with Primary Open Angle Glaucoma. J Ophthalmol 2016;2016:7074016.

34. Haymes SA, Roberts KF, Cruess AF, et al. The Letter Contrast Sensitivity Test: Clinical Evaluation of a New Design. Invest Ophthalmol Vis Sci 2006;47:2739–45.

35. Nixon DR, Flinn NA. Evaluation of Contrast Sensitivity and Other Visual Function Outcomes in Neovascular Age-related Macular Degeneration Patients After Treatment Switch to Aflibercept from Ranibizumab. Clin Ophthalmol 2017;11:715–21.

Copyright © American Academy of Optometry. Unauthorized reproduction of this article is prohibited.