Article

Validation of the Modified Schein Dry Eye Symptom Questionnaire and Comparison With the Ocular Surface Disease Index

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Purpose: This study evaluated the validity and diagnostic efficacy of a modified Schein dry eye questionnaire and compared it to the Ocular Surface Disease Index (OSDI).

Methods: The original Schein survey was modified to allow numerical scoring on a 0 to 24 scale and evaluated in prospective studies in normal and dry eye subjects. Receiver operating characteristic (ROC) analysis for test efficacy in aqueous deficient dry eye (ADDE) and evaporative dry eye (EDE) related to meibomian gland dysfunction was determined.

Results: Dry eye subtype, age and gender were statistically significant in explaining variation in modified Schein scores (n = 377; general linear model; all P values < 0.006) whereas for Ocular Surface Disease Index (OSDI) only age and gender were significant, but not dry eye subtype. The modified Schein ROC curve had an area under the curve (AUC) of 0.693 (95% confidence interval [CI], 0.635–0.753), with cutpoint of 7.5 (sensitivity of 0.75, specificity of 0.55). Similarly, the OSDI had an AUC of 0.685 (95% CI, 0.610–0.760), at a cutpoint of 10.4 (sensitivity of 0.75, specificity of 0.55). Modified Schein and OSDI correlated well (Pearson $r = 0.81$; $P < 0.001$). Symptom change for the modified Schein with artificial tear treatment was significant in EDE subjects (Dunnet's tests, P value < 0.001).

Conclusions: The modified Schein questionnaire is rapid to administer and score and compares well with the OSDI for test efficacy. Moreover, it differentiates normals from ADDE and EDE subtypes and is responsive to dry eye treatment. These attributes make the modified Schein survey an attractive dry eye symptom characterization instrument.

Translational Relevance: The modified Schein symptom survey, validated against clinical diagnosis and an existing survey, provides a new, efficacious diagnostic and treatment monitoring instrument in dry eye disease.

Introduction

Accurate and reliable measurement of the symptoms of ocular surface disease is important in the diagnosis of dry eye to determine prevalence through epidemiological studies and in monitoring treatment efficacy. Both the Dry Eye Workshop (DEWS) I and II working groups considered dry eye symptom questionnaires in their reports. They suggested that an

appropriate questionnaire should be sensitive enough to monitor disease progression or the effect of treatment over time[1,2] and be able to establish a threshold of disease severity.[1]

As part of the Salisbury Eye Evaluation (SEE) to determine prevalence of dry eye in a population-based sample, Schein and co-workers[3] developed a dry eye symptom questionnaire that would be effective in detecting dry eye symptoms but that was efficient because of the large population to be surveyed. These authors began with a draft version and then refined and validated it using the specific likelihood ratio and latent class analysis in a clinic-based population of defined dry eye subtypes that included aqueous-deficient dry eye (ADDE) and evaporative dry eye (EDE) patients, and normals (n = 90 total subjects). The optimization process left six questions relating to the frequency of the most common dry eye symptoms encountered in their sample.[3] This questionnaire has been labeled the SEE survey or is known informally as the Schein questionnaire.

The Schein instrument is very rapid to administer, ~1 minute, yet it occurred to us that further optimization might be desirable. We added a new response category of "never" to the existing options of rarely, sometimes, often, or all of the time. Moreover, we added numeric values to the responses to allow a semicontinuous reporting paradigm that could establish simple cutpoints to suggest whether respondents were likely to suffer from dry eye and to correlate to severity (Fig. 1).

The purpose of this investigation was to validate the modified Schein dry eye questionnaire against clinical diagnosis and to use a cross-validation method of data-splitting to establish a scale cutpoint and levels of test efficacy. Rasch analysis was used for survey validation by assessing the psychometric properties of the six questionnaire items. Further goals were to evaluate instrument repeatability and sensitivity to treatment change and to provide comparative data using the Ocular Surface Disease Index (OSDI).

Materials and Methods

The modified Schein and OSDI questionnaires were evaluated for test efficacy in five prospective dry eye studies; of which a major aim was questionnaire validation and test efficacy in identifying dry eye disease. All studies used similar inclusion and exclusion criteria (see below) and used the same testing methods and criteria to assign the subjects as normal or dry. The combined data included normals, ADDE, and those with evaporative dry eye related to meibomian gland dysfunction (EDE). No subjects with blepharitis were included.

The total data set represented 377 unique subjects, of which a subset had repeatability data available within one week of the initial administration under conditions matching the initial survey. The use of the questionnaire to track treatment progress stemmed from a study of mid-viscosity artificial tears in dry eye subjects over a six-month treatment period.

The treatment monitoring study was a prospective, randomized (for artificial tear) masked parallel group investigation involving two mid-viscosity artificial tears. There was no control arm since two treatments for EDE related to meibomian gland dysfunction were investigated. Clinical trial registration number was NCT01207752 (Clinical Trials.gov). The tears were either a propylene glycol 0.6% wt/vol (active) hp-guar-based and mineral oil (inactives) formulation (Systane Balance; Alcon Laboratories, Ft. Worth, TX, USA), or a carboxymethylcellulose (CMC) 0.5% (active) glycerin formulation (Refresh Optive; Allergan Inc., Irvine, CA, USA). Subjects continued their entering dry eye therapy and dosed the artificial tears four times per day every day for six months.

The study population was a clinic-based sample drawn from optometric and ophthalmologic academic centers, the Southern California College of Optometry at Marshall B. Ketchum University and the Gavin Herbert Eye Institute at the University of California at Irvine. The study was approved by the institutional review boards of both institutions and adhered to the tenets of the Declaration of Helsinki. Subjects provided written informed consent and signed Health Insurance Portability and Accountability Act authorizations before study participation.

Major *inclusion* criteria included subjects without dry eye or with either ADDE or EDE, age greater than 18 years, and best-corrected visual acuity of 20/40

Modified Schein Questionnaire*

<u>DURING THE PAST WEEK:</u>

1. Do your eyes ever feel dry?
   ☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ All of the time
2. Do you ever feel a gritty or sandy sensation in your eye?
   ☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ All of the time
3. Do your eyes ever have a burning sensation?
   ☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ All of the time
4. Are your eyes ever red?
   ☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ All of the time
5. Do you notice much crusting on your lashes?
   ☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ All of the time
6. Do your eyes ever get stuck shut in the morning?
   ☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ All of the time

Total: _____ (score of greater than 7.5 indicates dry eye)

* Based on the questions used by Schein OD, Tielsh JM, Munoz MS, Bandeen-Roche K, West S. Relation between the signs and symptoms of dry eye in the elderly. *Ophthalmol.* 1997; 104: 1395-1401.
† Scoring: Never = 0; Rarely = 1' Sometimes = 2; Often = 3; All of the time = 4

Figure 1. The Modified Schein Questionnaire.

or better at distance. Major *exclusion* criteria included blepharitis,[4,5] uncontrolled systemic disease, diabetes, contact lens wear, prior keratorefractive surgery or enhancement within 12 months of assessment, active ocular infection or non-dry eye inflammation, and use of tear-influencing medications such as antihistamines unless the dosing regimen had been consistent for at least 30 days.

All subjects were evaluated using a consistent protocol. However, no symptom scores were used in this classification to qualify the subjects as dry or normal, only the objective measures of corneal and conjunctival staining, tear stability, and the dry eye subtype evaluations. Using the test under consideration to classify study subjects induces selection bias, which potentially overestimates test sensitivity and specificity.[6]

Tear breakup time (TBUT) was assessed using liquid sodium fluorescein (2.0 μL of 1.0% wt/vol, instilled using a micropipette, with a yellow filter to enhance dark spot observation) because noninvasive methods were not available. The subject blinked naturally three times[2] and the mean of three measurements recorded. Subjects were considered to have dry eye disease if the mean TBUT was ≤6.0 seconds[7] or Level 2 severity.

Immediately after TBUT, within four to eight minutes,[8] corneal staining was assessed with use of the yellow barrier filter. Conjunctival staining was assessed using lissamine-impregnated strips, wetted with nonpreserved saline solution that was allowed to soak the strip for at least five seconds[2] to fully elute the dye. Staining was estimated for six zones for each eye; both corneal and conjunctival staining were quantified using the NEI scale.[9] Subjects were considered dry if the corneal and conjunctival total staining score was >6.0 on the 0–33 total NEI scale (Level 2 or greater[10]). ADDE was assigned if the subject was dry by TBUT and staining, and the Schirmer I test without anesthesia was ≤5.0 mm, as recommended by several consensus groups.[8,10,11]

To assign the EDE subtype, assuming a dry condition based on tear stability and staining, subjects had to exhibit greater than or equal to Grade 1.0 secretion quality[12] as an average grade across the entire lower eyelid using a cotton-tipped applicator (Q-tip) to gently express the glands. The EDE subjects had to have a Schirmer I test >5.0 mm wetting in five minutes. Symptoms were assessed with the Schein questionnaire,[13] modified with numerical scores (described below) the OSDI, but the symptom data were not used to characterize the subjects as dry or normal to avoid selection bias.

The Modified Schein Survey

The symptomatology instrument originated from the development work of Schein and co-workers[3] Six questions were selected by Schein et al.,[3] following evaluation of a larger preliminary battery of 12 questions and responses from diagnosed dry eye patients. The final questions were as follows:

- Do your eyes ever feel dry?
- Do you ever feel a gritty or sandy sensation in your eye?
- Do your eyes ever have a burning sensation?
- Are your eyes ever red?
- Do you notice much crusting on your lashes?
- Do your eyes ever get stuck shut in the morning?

These questions were used in the present study to grade symptoms using a slight modification of the scale: "never" was added, and ordinal grades were assigned to the possible answers ("never" = Grade 0, "rarely" = Grade 1, "sometimes" = Grade 2, "often" = Grade 3, and "all of the time" = Grade 4; see Fig. 1). The questionnaire provided a total numerical score (maximum of 24 points if severe symptomatology) that could be used to correlate against signs.

The modified questionnaire was validated against clinical diagnosis, the OSDI validated instrument, and using Rasch analysis. A total of 377 useable charts were available and composed of normals (non-dry eye individuals) and either ADDE or EDE dry eye subtypes.

Statistical Analysis

A univariate general linear model (GLM; Minitab 18) and analysis of variance (ANOVA) were used for each questionnaire (modified Schein and OSDI) to determine factor effects of age, sex, and dry eye subtype. The OSDI data were log-transformed before analysis with the GLM due to non-normal residuals and nonconstant variance. Significant factors for dry eye subtype were compared using Tukey's pairwise comparisons.

Data splitting[14] was used as a cross-validation method to determine a Receiver Operating Characteristic (ROC) curve (R version 3.6.1) and scale cutpoint that optimized sensitivity and specificity, that was subsequently tested for predictive accuracy. Approximately two-thirds of the data were used for model-building, with the remainder available for model-checking.[14]

For the treatment trial using artificial tears over six months, the GLM was used to examine parameter

significance (subject and time in months), followed by Dunnett Simultaneous Tests for level mean, adjusted for multiple comparisons.

Repeatability was assessed using Bland Altman analysis and estimation of the intra-class correlation coefficient; both using R Version 3.6.1.

Rasch analysis was used to evaluate the psychometric properties of the survey items. Rasch analysis is a method of mathematical modelling based on a latent trait, in this case dry eye disease, to determine which items comprising the questionnaire reliably reflect the latent trait. The INFIT and OUTFIT mean square values (MNSQ) with their associated standard deviations (ZSTDs) indicate whether a particular survey item fits the Rasch model. If ZSTDs are beyond ± 3.0, the item is considered to behave in an overly predictive way or to exhibit inconsistent responses relative to the other items.[15] Modified Schein data from normal and dry eye disease subjects were analyzed using Rasch analysis software (Bond and Foxsteps, Version 1.0; Winsteps.com, Chicago, IL, USA). Pearson correlational analysis, modified Schein to OSDI, was undertaken for the questionnaire scores and modified Schein compared to the clinical parameters from the right eye, selected arbitrarily.

Results

General Results: Modified Schein and OSDI

There were a total of 377 subjects who provided modified Schein data; 118 normals (mean age 39.6 years, range 19–85), 36 ADDEs (mean age 59.9 years, range 24–82), and 223 EDEs (mean age 53 years, range 19–89). Age differences were significant (ANOVA; $P < 0.001$). There was a majority of females in all three groups (normals, 39 males, 79 females; ADDEs, nine males, 28 females, EDEs, 61 males, 162 females).

Mean modified Schein score values (±SDs) were 7.2 (5.0), 11.3 (4.8), and 10.4 (4.3) for normals, ADDEs, and EDEs, respectively. The general linear model (these residuals were normally distributed) found significant positive coefficients for age (0.0371), gender (0.797), and dry eye subtype (1.292, ADDE; 0.680, EDE); P values = 0.006, 0.002, and <0.001, respectively. This indicates increasing Schein scores with increasing age and higher scores for females. Tukey pairwise comparisons found significant differences for Schein score between normals and ADDEs (95% CI, −5.353 to −1.176; $P = 0.001$) and normals versus EDEs (95% CI, −3.920 to −1.384; $P < 0.001$). No difference in modified Schein score was found between ADDE and

EDE dry eye subtypes (95% CI, −2.506 to 1.282; $P = 0.73$).

There were a total of 206 subjects who provided OSDI data, from studies wherein copyright permission was granted by Allergan. These included 88 normals, 21 ADDEs, and 97 EDEs. Mean score values (±SDs) were 17.2 (±21.5), 35.7 (±23.3), and 28.1 (±22.6), for normals, ADDEs, and EDEs, respectively. The general linear model was used to analyze the OSDI data after log-transformation. The resulting ANOVA found significant positive coefficients for age and gender (0.014 and 0.43 [female], respectively) and $P < 0.001$, respectively, but not dry eye subtype ($P = 0.232$).

Efficacy in Dry Eye Diagnosis: Modified Schein and OSDI

The modified Schein data were split, with approximately two-thirds randomly selected for model building and the remainder for model checking (predictive accuracy vs. clinical subtype assignment). Thus 85 normals, 26 ADDE and 164 EDE subjects' data were used for model building. The cutpoint data are presented in Table 1. The area under the receiver operating characteristic curve (AUC) was 0.694 (95% CI, 0.626–0.763), demonstrating reasonable discrimination.[16] A best-balance cutpoint of 7.5 (0–24 scale) provided a sensitivity of 0.74 (95% CI, 0.68–0.80) and specificity of 0.54 (95% CI, 0.43–0.65). This specificity is little better than chance, suggesting that healthy patients might be considered as having dry eye using a cutpoint of 7.5. In the model-checking data set, this cutpoint correctly predicted 58% of normals and 79% of the combined dry eye subjects.

We further examined test efficacy, using all available normal and dry eye data, for the entire sample and for the specific ADDE and EDE subtypes. These data are presented in Table 2 and Figure 2 and demonstrate AUCs similar to the model-building data set and the same optimum cutpoint (meaning the best balance of sensitivity and specificity) in the subanaly-

Table 1. Cutpoints for Schein Model-Building Data[*]

Schein Cutpoint (0–24 Scale)	Sensitivity (95% CI)	Specificity (95% CI)
5.5	0.87 (0.82–0.92)	0.42 (0.32–0.52)
6.5	0.82 (0.77–0.87)	0.49 (0.38–0.60)
7.5[†]	0.74 (0.68–0.80)	0.54 (0.43–0.65)
8.5	0.67 (0.60–0.74)	0.55 (0.44–0.66)
9.5	0.56 (0.49–0.63)	0.64 (0.54–0.74)

[*]n = 85 normals and 189 drys (ADDEs and EDEs combined).
[†]Optimum balance of sensitivity and specificity.

Table 2. Total Sample and Subtype Analyses for Modified Test Efficacy

Sample	Normals	Dry Eye Disease	AUC (95% CI)	Cutpoint[*]	Sensitivity (95% CI)	Specificity (95% CI)
All Subjects	118	259	0.693 (0.635–0.753)	7.5	0.75 (0.70–0.80)	0.55 (0.46–0.64)
ADDEs	118	36	0.719 (0.630–0.809)	7.5	0.81 (0.68–0.94)	0.55 (0.46–0.64)
EDEs	118	223	0.689 (0.628–0.750)	7.5	0.74 (0.68–0.80)	0.55 (0.46–0.64)

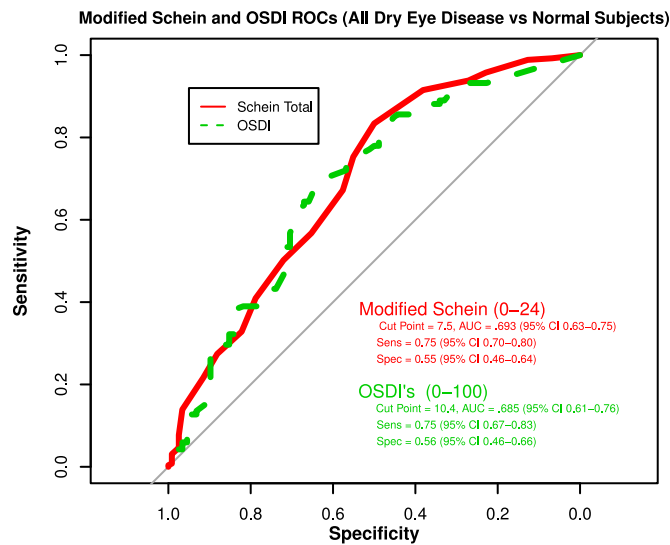[*]Best balance of sensitivity and specificity.

Figure 2. ROC curves for normals (non-dry eye subjects) versus combined ADDE and EDE subtypes.

ses. Taken together, the optimum cutpoint to diagnose dry eye using the modified Schein survey appears to be 7.5 on the 0 to 24 total scale.

OSDI data were analyzed similarly to the modified Schein data, except that data splitting was not undertaken because of the more modest sample size that provided the data. Table 3 provides the AUCs, cutpoints, and test efficacy for OSDI. Figure 2 presents the ROC curve for the combined dry eye subtypes (ADDES and EDEs) versus normals. The cutpoint for the total sample and for EDEs versus normals was 10.3 (0–100 scale) although the ADDE versus normal data suggest the widely recommended cutpoint of approximately 13 to diagnose dry eye.[2,17]

Treatment Efficacy

The modified Schein scores were monitored in a six-month, randomized, subject-masked treatment trial of mid-viscosity artificial tears dosed four times per day in EDE related to meibomian gland dysfunction subjects. Baseline modified Schein scores were within the dry eye range according to the current cutpoint of 7.5, and not different for the two formulations (10.9 ± 4.3 and 10.2 ± 3.2, respectively, for propylene glycol-hp-guar score and CMC 0.5%; $P = 0.398$, 95% CI for difference -1.037 to 2.571; two-sample t-test). The propylene glycol-hp-guar arm enrolled n = 35 subjects to start and completed 33 subjects. The CMC 0.5% arm enrolled n = 34 subjects and completed 26. The modified Schein scores decreased to 6.97 ± 4.2 (n = 33) and 7.92 ± 3.7 (n = 26), respectively, for propylene glycol-hp-guar and CMC 0.5% at six months. The changes from baseline were significant for both artificial tears (propylene glycol-hp-guar, $P < 0.001$; 95% CI, -5.14 to -2.46; CMC 0.5%, $P = 0.001$; 95% CI -3.61 to -0.733, adjusted P values, Dunnett's simultaneous tests). The symptom reductions occurred with improvements in TBUT and ocular surface staining for both artificial tears.

Repeatability

Fifty-seven subjects (normals, combined with both dry eye subtypes) provided repeatability scores using the modified Schein survey within one week and under similar conditions and time of day as the initial administration. There were nine normals, eight ADDED, and 40 EDED subjects. Mean/Median

Table 3. Total Sample and Subtype Analyses for OSDI Test Efficacy

Sample	Normals	Dry Eye Disease	AUC (95% CI)	Cutpoint[*]	Sensitivity (95% CI)	Specificity (95% CI)
All subjects	88	118	0.685 (0.610–0.760)	10.4	0.75 (0.68–0.83)	0.55 (0.45–0.65)
ADDEs	88	21	0.764 (0.669–0.860)	13.1	0.81 (0.64–0.98)	0.64 (0.54–0.74)
EDEs	88	97	0.668 (0.589–0.746)	10.2	0.74 (0.65–0.83)	0.51 (0.41–0.61)

[*]Best balance of sensitivity and specificity.

95% LoA (scale 0–24)

Upper LoA = 4.32

Mean = −0.4

Lower LoA = −5.12
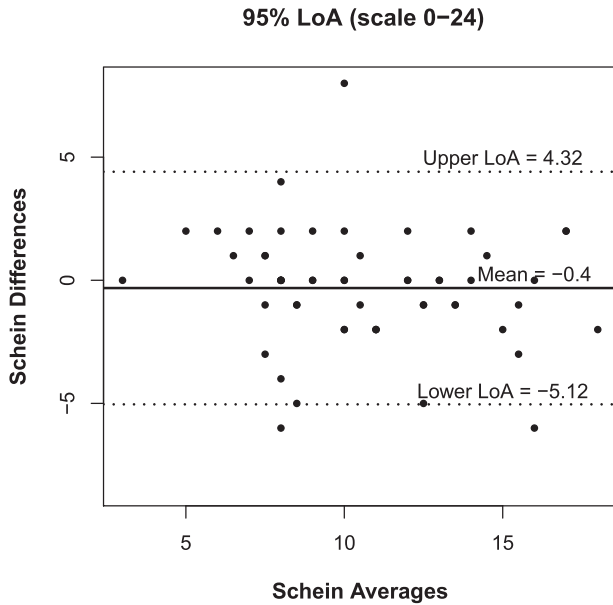
Y-axis: Schein Differences; X-axis: Schein Averages

Figure 3. Bland Altman plot of modified Schein repeatability. The mean difference is very small, demonstrating little bias of repeated scores.

(±SD/interquartile range)–modified Schein values were 11.0/11.0 (3.8/8–13) and 10.3/10.0 (3.4/8–13) for the first and repeat administrations, respectively. These were statistically different ($P = 0.033$; 95% CI, 0.052 to 1.262, paired *t*-test) but not clinically different responses.

The intraclass correlation coefficient was 0.78, considered good reliability[18] (95% CI, 0.65–0.86; R software, model = one-way, type = consistency). The Bland Altman analysis is depicted in Figure 3.

Rasch Analysis

Detailed Schein data (i.e., individual item scores for each subject from each of the six symptom items)

were available for 108 normal and dry eye subjects who all had been evaluated using the standard battery of dry eye tests as above). The Rasch model parameters are summarized in Table 4, and the modified Schein person-item map is presented in Figure 4.

Inspection of the model parameters demonstrates borderline large ZSTDS for the INFIT values for Items 1 (dryness) and 6 (eyelids stuck shut, AM) yet reasonable MNSQ values for these items. The dry symptom may be over-reported as it is common and the sample was under-represented in blepharitis subjects since they were excluded in this investigation, who tend to report their eyes stuck shut in the mornings.[19]

Figure 4 demonstrates a broad range of symptom reporting with the six items but again infrequent reports for item 6 and frequent reports of item 1. Items 2 to 4 (gritty/sandy, burning, redness and lash crusting, respectively) appear to accurately capture the symptoms associated with the dry eye subjects in this sample.

Correlation

In 206 subjects, both normal and dry eye disease, for which both questionnaires were administered concurrently, the Pearson correlation coefficient was 0.81 (95% CI, 0.76–0.86; $P < 0.001$), indicating an excellent relationship.[20] Figure 5 presents the scatterplot.

Correlation analysis was carried out for modified Schein versus the clinical parameters of TBUT, NEI stain (0–33 scale), Schirmer I, tear meniscus height (mm), white-light interferometry (central cornea, Yokoi scale), meibomian gland expression (0–3 scale) and lower eyelid meiboscopy. Several clinical parameters demonstrated significant correlations versus the modified Schein score (i.e., $P < 0.05$), but only fluorescein breakup time (Pearson's $r = −0.303$ [95% CI −0.392 to −0.208]; $P < 0.001$) rose to the level

Table 4. Rasch Model Parameters

Item	INFIT*		OUTFIT	
	MNSQ	ZSTD	MNSQ	ZSTD
1. Do your eyes ever feel dry?	0.59	−3.5	0.58	−3.5
2. Do you ever feel a gritty or sandy sensation in your eye?	1.00	0.1	0.97	−0.1
3. Do your eyes have a burning sensation?	0.84	−1.2	0.82	−1.3
4. Are your eyes ever red?	1.07	0.6	1.02	0.2
5. Do you notice much crusting on your lashes?	1.22	1.4	1.18	1.1
6. Do your eyes get stuck shut in the morning?	1.59	3.1	1.32	1.2

*INFIT and OUTFIT statistics have expectation 1.0 and range from 0 to infinity.[22] MNSQ values of 0.6 to 1.4 are considered reasonable for a rating scale/survey.[22] ZSTD is the standard deviation of the fit parameters.

Modified Schein Person-Item Map

INPUT: 108 Persons 6 Items MEASURED: 108 Persons 6 Items 5 CATS   1.0.0

```
   Persons with  | Items that are less
   more symptoms | frequently reported.
   reported.     |
 3               +
             #   |
                 |
                 |T
                 |
              T  |
 2               +   ItemQ6
                 |
           .#    |
                 |
           .##   |
                 |S
 1         ##    +   ItemQ5
                 |
           ##    |
                 |
          .### S |
                 |
 0         ##  +M
                 |  ItemQ2   ItemQ3
           ##    |
           ##    |
                 |  ItemQ4
          ####   |
-1               +
           ##  |S
                 |
              M  |
          ###    |
-2        ###    +   ItemQ1
                 |
          ###    |
                 |T
                 |
        .####### |
-3               +
                 |
         ##### S |
                 |
                 |
                 |
-4        .####  +
                 |
                 |
                 |
                 |
-5        .###   +
```

```
                          Item 1: Dryness
                          Item 2: Gritty/Sandy
                          Item 3: Burning
                          Item 4: Redness
                          Item 5: Lash crusting
                          Item 6: Stuck shut
```

```
   Persons with | Items that are more
   less symptoms | frequently reported.
   reported. |
```
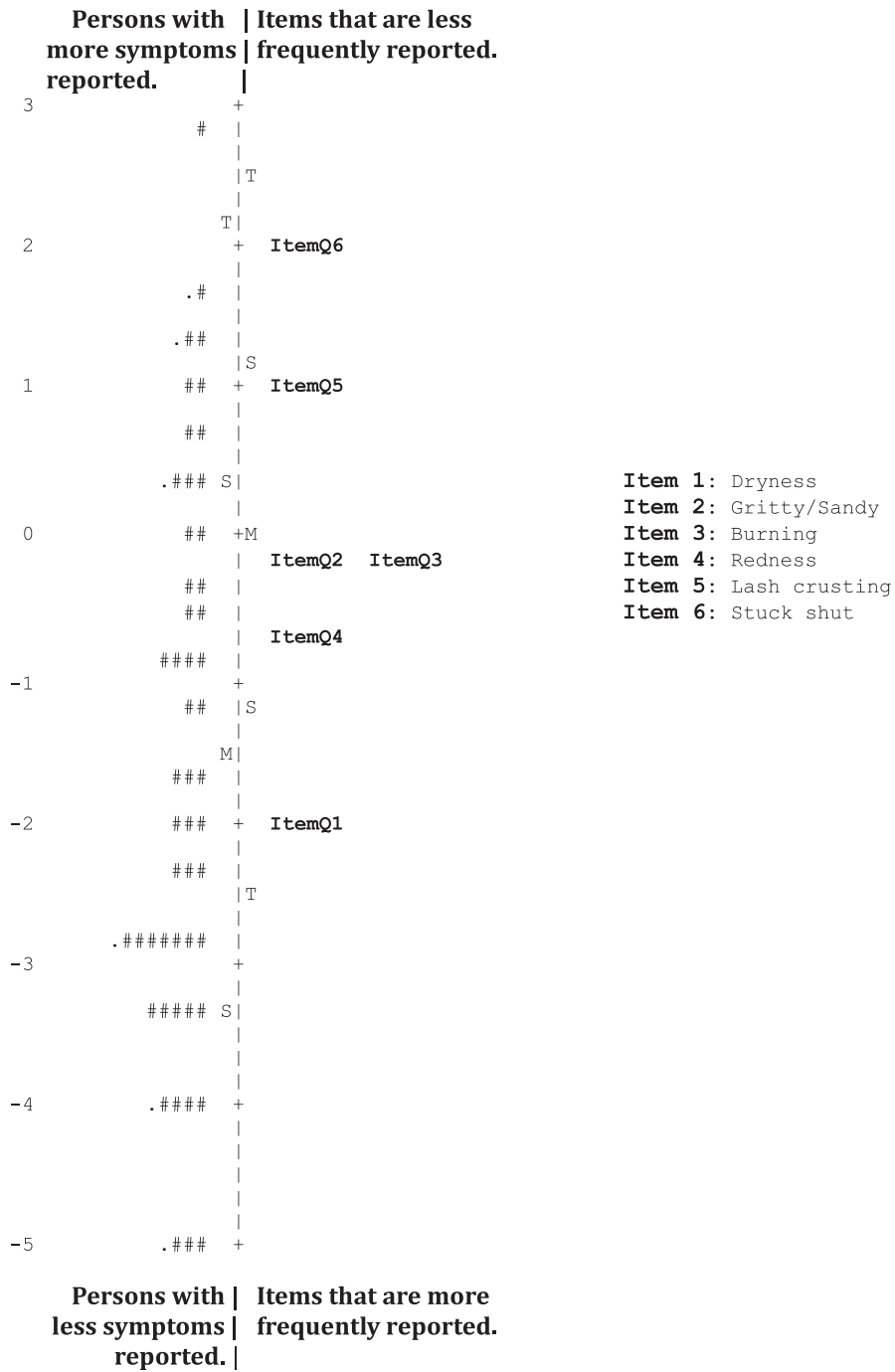
EACH '#' is 2 subjects.

Figure 4.   The Person–Item map demonstrates a broad spread for the six symptom items, frequent reports of dryness, and infrequent reports of eyes stuck shut.
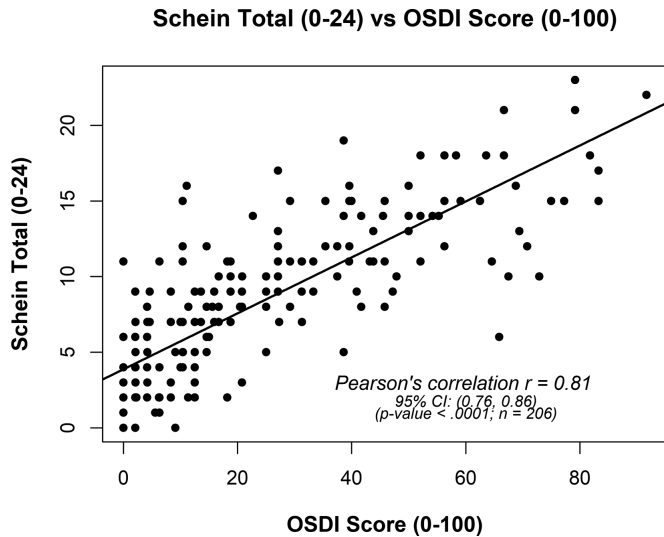
Schein Total (0-24) vs OSDI Score (0-100)

Pearson's correlation r = 0.81
95% CI: (0.76, 0.86)
(p-value <.0001; n = 206)

Figure 5. Modified Schein and OSDI correlation for all subjects, normal, and both dry eye subtypes.

of a fair level of association (*r* value 0.25–0.50; Dawson and Trapp[20]).

Discussion

This investigation involved further development of a previously validated dry eye symptomatology questionnaire, and validation in the absence of selection bias. Changes were made to the original Schein instrument in an effort to provide quantitation (using an ordinal scale) for individual questions and a total score (a semi-continuous scale, 0–24) to allow diagnosis of both dry eye subtypes compared to non-dry eye individuals, as well as provide the opportunity for use as a quantitative monitoring tool.

Rasch analysis can be used for survey development to analyze individual items for optimization by eliminating those that do not well-reflect the underlying trait.[15,21] In the present study, the Schein questionnaire was previously validated in the major dry eye subtype groups[3] so in this case Rasch analysis provides a snapshot of the psychometric behavior of the modified questionnaire. The Rasch results suggest (Fig. 4 and Table 4) that all six symptom queries well-reflect the symptoms of dry eye disease. MNSQ values of 0.6 to 1.4 are considered reasonable for a survey instrument[22] and all six items fall within that range. Furthermore, the ZSTDs, while borderline for "dryness" and "stuck shut in the morning," suggest that the dryness symptom is overly predictive and perhaps underrepresented for stuck shut due to the exclusion of blepharitis subjects from this sample. The

symptom capture for dryness is part of nearly all major dry questionnaires and should be retained.

We validated the modified Schein survey against clinical diagnosis and found that it well-separates non-dry eye persons from both dry eye subtypes (general linear model and Tukey comparisons). Moreover, it provides reasonable repeatability under consistent conditions; combined normal and dry eye subject score means for two visits of 11.0 and 10.3, respectively (n = 57), which was statistically, but not clinically significant. Modified Schein scores diminished with artificial tear treatment in EDE subjects, mirroring other clinical sign reductions, demonstrating usefulness in dry eye treatment trials. The modified Schein instrument also demonstrates concurrent validity when compared to the OSDI (Fig. 5).

ROC analysis suggests that the modified Schein questionnaire demonstrates acceptable discrimination, with AUCs ranging to 0.719 from 0.689 (Table 2 and Fig. 2).[16] The cutpoints for normals versus combined dry eye subtypes and for normals versus individual subtypes were consistent at 7.5 on the 0 to 24 scale. This cutpoint resulted in test sensitivity of 0.74 or greater (Table 2), which is considered effective for dry eye diagnosis.[10]

ROC analysis was also investigated for the OSDI, for normals vs. both dry eye subtypes and individually for the subtypes (Table 3). AUCs were similar to those for the modified Schein (0.668 to 0.764), with the greater AUC and cutpoint of ~13 occurring for the ADDE subtype. This may be a result of the generally greater severity of the ADDE dry eye subtype, although we did not quantify severity herein. The AUCs found in our study for OSDI are slightly greater, but similar to those reported by Yazdani et al.[23] in a large study of normals and dry eye subjects analyzed using varying clinical cutoffs. Wang et al.[24] also found a modest AUC for the OSDI and test sensitivity and specificity, similar to our results. Taken together, the evidence from these several studies suggests that symptoms alone are insufficient to accurately diagnose dry eye, and that additional clinical tests are necessary.

The TFOS DEWS II reports reviewed the currently available dry eye symptom questionnaires for domains sampled and utility (e.g., whether useful for epidemiological or clinical studies, Table 6; TFOS DEWS II Epidemiology report[25]), and for screening criteria and validation methods (Table 2; TFOS DEWS II Diagnostic methodology report[2]). Modification of the Schein questionnaire (labeled "SEE" as used in the Salisbury Eye Evaluation study[3]) has allowed the instrument to become practical for clinical studies through dry eye discrimination and sensitivity to treatment. Similar

surveys include the Ocular Comfort Index, SPEED, OSDI, and DEQ-5 instruments, with these latter two recommended for use by the DEWS II diagnostic methodology report.[2]

The Ocular Comfort Index was psychometrically developed and validated using Rasch analysis[15] but is not referenced frequently in the literature. Wang et al.[24] have recently assessed diagnostic efficacy for the SPEED, OSDI and DEQ-5 surveys in normal and dry eye subjects (unspecified with regard to dry eye subtype). Of these, only OSDI approached the test sensitivity level of 0.70, considered adequate for a dry eye diagnostic test.[10] Not reaching diagnostic AUC or sensitivity levels were DEQ-5 and SPEED.[24]

In contradistinction, Ngo et al.[26] validated the SPEED survey with Rasch analysis and in an efficacy study found high AUCs for SPEED (0.928) and OSDI (0.970). Several studies, including the present investigation, have found lesser efficacy for OSDI in diagnosing dry eye.[23,24] The contrasting efficacy results may be due to study sample size or entry criteria differences. The modified Schein questionnaire offers several advantages over existing questionnaires and has several limitations.

The instrument is extremely efficient, taking approximately one to two minutes to answer and to score. It has the major advantage that it is not protected by copyright, which can inhibit the use of questionnaires such as the DEQ-5 and the OSDI. The copyright inhibition can entail outright refusal for use of the OSDI in studies of competitor dry eye product companies or can entail a sizeable fee requirement annually for use of the questionnaire. To achieve universal acceptance and adoption, tests are needed for dry eye diagnosis and monitoring that are not only valid and efficacious but widely available without restriction.

The modified Schein instrument only surveys frequency of dry eye symptoms, and not their intensity, occurrence relative to time of day, nor vision-, or etiological components. These aspects of dry eye symptomatology may be important to dry eye sufferers' quality of life and should be incorporated into patient reported outcomes. Future research should examine the inter-laboratory reproducibility of the modified instrument and be examined in a treatment trial with a placebo control because our study did not include this. Additional investigation is needed to determine the meaningful clinical important difference in a large treatment trial,[17,27] and to determine whether the modified Schein scale can be used to classify subjects as having mild, moderate or severe dry eye severity beyond the 7.5 scale cutpoint.

In summary, the modified Schein instrument is valid and differentiates normal from dry eye persons. It is clinically repeatable under stable conditions and has the ability to monitor dry eye treatment in concert with other clinical indicators. The consistent diagnostic cutpoint is 7.5 on the 0 to 24 scale. The modified Schein survey demonstrates similar test efficacy in dry eye diagnosis yet is more rapid to administer and score compared to the OSDI. It has promise for an effective screening questionnaire and in the symptom assessment as part of the larger battery of dry eye tests.

Acknowledgments

Disclosure: **J.R. Paugh,** None; **E. Chen,** None; **J. Kwan,** Coopervision Inc. (E); **T. Nguyen,** None; **A. Sasai,** None; **M. Thomas De Jesus,** LensGen (E); **A.L. Nguyen,** None; **M.T. Christensen,** None; **D. Meadows,** None

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