Title
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Journal
Contact Lens and Anterior Eye, 36(6)

ISSN
1367-0484

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Publication Date
2013-12-01

DOI
10.1016/j.clae.2013.06.001

Peer reviewed

Contact Lens & Anterior Eye xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Contact Lens & Anterior Eye

journal homepage: www.elsevier.com/locate/clae

Ethnic differences in dry eye symptoms: Effects of corneal staining and length of contact lens wear☆

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ARTICLE INFO

Article history:
Received 1 August 2012
Received in revised form 15 May 2013
Accepted 7 June 2013

Keywords:
Asians
Ethnicity
Soft contact lenses
Comfort
Contact lens-induced dry eye
Dryness
Race

ABSTRACT

Purpose: To explore the relationships among length of contact lens (CL) wear, degree of corneal staining and severity of dryness symptoms, and to determine whether these relationships differ between Asians and non-Asians.
Methods: Adapted soft CL wearers ($n = 395$; 180 Asian, 215 non-Asian) were required to discontinue CL wear for at least 24 h and report to the University of California, Berkeley Clinical Research Center (UCB-CRC). Fluorescein corneal staining was graded according to Brien Holden Vision Institute scales. Length of CL wear was reported by subjects and subjective dryness ratings were collected using the UCB-CRC Dry Eye Flow Chart (DEFC).
Results: More Asian CL wearers exhibited corneal staining compared to non-Asians, and Asian CL wearers had a higher mean grade of corneal staining ($p < 0.001$), as well as a higher mean DEFC classification ($p < 0.001$). The difference between Asians and non-Asians in grades of corneal staining extent and depth were significant ($p < 0.001$). Among non-Asian CL wearers, dryness symptoms decreased with more years of CL wear and increased in the presence of corneal staining, which was not the case for Asian CL wearers.
Conclusions: Asian soft CL wearers reported more severe dryness symptoms and demonstrated more severe corneal staining overall compared to non-Asians. Among non-Asians, dryness symptoms were less severe on average with increased years of CL wear and more severe in the presence of corneal staining. Dryness severity does not appear to be related to years of CL wear or corneal staining among Asians.

Introduction

Despite advances in contact lens (CL) design and manufacture, patient dissatisfaction with CL wear remains a challenge for practitioners. Evidence from previous studies has contributed to a general consensus that CL-related discomfort is the main reason for discontinuation of wear [1–4], and that the most common type of discomfort is dryness [4]. Approximately 50% of CL wearers experience some dry eye symptoms [5–8]. Although there have been numerous studies of dryness symptoms in CL wearers, little is known about differences that may exist between ethnic groups. Previous data have suggested that differences in subjective and objective evaluation of dry eye exist between Asians and non-Asians. In a study comparing dry eye symptoms after LASIK, symptoms occurred more frequently among Asians than among Caucasians [9]. Schaumberg et al., found that among women, Asians were significantly more likely to report severe dryness symptoms [10]. In a study that examined average and end-of-day dryness in soft CL wearers, Asians reported a higher level of severity in average dryness symptoms compared to non-Asians [11]. These results suggest that ethnicity may need to be factored into subjective measures of symptomatology to maximize sensitivity and specificity in the diagnosis of CL-induced dry eye.

Evidence also suggests that Asians and non-Asians differ not only in subjective reporting of CL-related dryness and discomfort, but also in objective clinical measures of ocular response to CL wear. Lundgrin et al., found that pre-lens non-invasive tear break-up time was significantly shorter for Asians than for non-Asians [12]. Fluorometric studies on apparently healthy corneas (i.e., no corneal staining in the central 3–4 mm zone of measurement) found that changes in corneal epithelial permeability following overnight lens wear with either rigid or soft lenses were more pronounced in Asian than in non-Asian eyes [13,14]. Roseman et al., found that presence of superficial punctate keratitis was more common in Asian soft lens wearers than in non-Asian soft lens wearers [15]. Lin et al., reported that Asian eyes appear to be more susceptible to corneal disruption from the use of biguanide-preserved CL solutions [16]. In total, these results suggest that Asian eyes are at greater risk

☆ Presented at the American Academy of Optometry Annual Meeting, November, 2009.

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http://dx.doi.org/10.1016/j.clae.2013.06.001

for microtrauma during CL wear, which may be explained in part by the higher shear force exerted on the ocular surface due to a thinner post-lens tear film and higher eyelid tension affecting the physical CL-corneal fitting relationship [14]. It is possible that the anatomical and physiological differences that exist between Asian and non-Asian eyes affect their respective ocular responses to contact lenses, thereby contributing to differences in discomfort and dryness symptoms.

The effects of CL wear on the ocular surface are also known to be dependent on the number of years of CL wear. For example, in short term soft lens extended wear, corneal oxygen uptake is reduced temporarily, whereas the effect is sustained in long term wearers [17]. The literature is sparse with respect to the effects of length of CL wear on corneal staining specifically. In one study comparing daily wear and extended wear of silicone hydrogel lenses over an 18 month period, there was a progressive increase in corneal staining after the first 3 months of CL wear with both lens types, but the severity of staining stabilized thereafter [18]. In a study of factors associated with corneal staining in CL wearers, Nichols and Sinnot found that the total years of CL wear was not correlated with corneal staining [19]. The literature is also sparse with respect to the effects of length of CL wear on dryness symptoms. Although it has been shown that dryness symptoms increase with age for CL wearers and non-wearers alike [20,21], and it may be reasonable to assume that older CL wearers probably have worn CLs longer (see discussion), to our knowledge there has not been a multivariate examination of the changes in dryness symptoms specifically related to the length of CL wearing history. It is also not known whether different ethnic groups change in the same way over time in CL wear with respect to clinical signs or subjective symptoms.

There are mixed results regarding the relationship between corneal staining and dry eye. In a study of solution-induced corneal staining (SICS) in silicone hydrogel CL wearers, overall dryness and dryness at the end of the day were more severe in subjects who experienced SICS versus subjects without SICS [22]. Truong et al., found that inferior corneal staining was significantly associated with an increase in subjective dryness symptoms in silicone hydrogel CL wearers [23]. In another study of objective measures of the severity of dry eye disease, corneal staining was found to be informative only in more severe forms of the disease [24]. In general, most studies have found a lack of association between corneal staining and dryness symptoms in both CL wearers and non-CL wearers [25–27].

In this retrospective study, we examined a large database of corneal staining data and subjective dryness responses from a series of soft CL studies conducted at the University of California Berkeley Clinical Research Center (UCB-CRC) from February 2007 to September 2009, in order to explore the relationships among length of CL wear, corneal staining and dryness symptoms, and to determine whether these relationships differ between Asians and non-Asians.

Methods

Subjects

A total of 2878 records from 395 adapted soft CL wearers (180 Asians and 215 non-Asians) participating in one or more of 84 CL studies at the UCB-CRC were analyzed (Table 1). Subjects between the ages of 18 and 39 years were recruited through campus fliers and direct referrals. All subjects were experienced spherical soft CL wearers who reported having had a comprehensive eye exam within the previous 2 years, who reported wearing contact lenses at least 5 days per week for at least 1 year, and who did not wear rigid lenses or wear their lenses on an overnight basis. Subjects were screened to ensure they were free from any conditions (e.g., allergies, GPC), injuries, behaviors or dependence on any ophthalmic drug that might have adversely affected ocular health or otherwise limited the ability to wear contact lenses on a full-time basis. The Asian group consisted primarily of subjects self-reporting their ethnicities as being Chinese (53.3%), Vietnamese (15.9%), and Korean (13.7%), with the remaining Asian subjects (17.0%) being Pacific Islander, Thai, Japanese, and Taiwanese. All other ethnic groups were classified as non-Asian, and included Caucasians (78.7%), Hispanics (10.9%), Indians (6.2%) and African Americans (4.3%). All studies were carried out at the UCB-CRC under the same study protocol. Informed consent was obtained from all study participants after a full description of the goals, potential risks and benefits, and procedures of the studies. This research project adhered to the tenets of the Declaration of Helsinki, was approved by institutional review board (Committee for Protection of Human Subjects, University of California, Berkeley) and was HIPAA-compliant.

Table 1
Subject age, gender, and ethnicity.

	n	Mean (SD) Age
Asian	180	21.9 (4.1)
Female	130	22.0 (4.1)
Male	50	21.6 (4.2)
Non-Asian	215	22.5 (3.9)
Female	153	22.7 (4.0)
Male	62	21.9 (4.1)

Assessment of clinical signs

After a minimum of 24 h without CL wear and a minimum of 6 h of sleep the previous night, subjects reported to the UCB-CRC within 2 h of awakening wearing their spectacles. We required the subjects to discontinue lens wear for at least 24 h to minimize the immediate and direct effects of different habitual lens types, as well as lens care solutions, which are typically superficial and transient, and in the majority of cases would resolve within 24 h after removing the lenses. As part of our study protocol, reminder calls and email messages were made to all study participants to discontinue lens wear 2 days prior to the study. All reasonable efforts were made to ensure that the majority of subjects removed their lenses before sleep 2 nights prior to the examination (approximately 30–32 h), and donned their spectacles upon awakening the day before the examination.

A detailed slit-lamp examination of the cornea was performed using fluorescein (BIO GLO™ sterile strips, HUB Pharmaceuticals, LLC, Rancho Cucamonga, CA, USA), cobalt blue light and a Wratten 12 yellow barrier filter. To instill the fluorescein, a drop of Unisol® 4 (Alcon Laboratories, Inc., Fort Worth, TX, USA) was applied to a sterile strip, with excess solution shaken off as in routine clinical practice. The moistened fluorescein strip was applied to a small area (approximately 2 mm^2) on the superior bulbar conjunctiva in each eye, and care was taken not to induce any corneal or conjunctival staining during application. In grading corneal staining, the cornea was divided into 5 areas (central, superior, inferior, nasal, and temporal), and the depth and extent of corneal staining were graded on a scale of 0–4 in 0.50 increments, in accordance with the Brien Holden Vision Institute (formerly CCLRU) grading scales [28]. In order to minimize inter-observer variability, clinicians' assessments of corneal staining were calibrated every 6 months. Observers separately graded corneal staining on 12–40 eyes (depending on subject availability) of real subjects in random order, the results were compared, and any disagreements of >0.5 on the 0–4 grading scale were discussed until a consensus grading standard was reached.

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Assessment of subjective symptoms

Prior to the ocular examination, subjects were asked to rate the dryness they experience with their habitual contact lenses. Subjective ratings of dryness were collected using the UCB-CRC Dry Eye Flow Chart (DEFC) [12] (see Appendix). Each subject self-categorized into 1 of 5 classes of dryness experienced with CL wear: (1 = no dryness; 2 = dryness but without discomfort; 3 = dryness and discomfort but not sufficient to interfere with activities such as reading, computer work, or CL wear; 4 = dryness and discomfort sufficient to sometimes interfere with activities; 5 = dryness and discomfort sufficient to frequently or always interfere with activities. Classes 2 and 3 are considered "functional" dry eye, while Classes 4 and 5 are considered "dysfunctional" dry eye in that symptoms interfere with visual activities including contact lens wear.

Statistical methods and analysis variables

The number of years of CL wear (i.e., full-time wear, at least 5 days per week) was recorded for each subject. The distribution of years of CL wear was close to normal between 0 and 15 years; however, there were 7 subjects who had up to 25 years of wear, whose inclusion exerted excessive leverage in the statistical models and resulted in a relatively poor approximation of normality in the distribution of the residuals. We therefore included these subjects in the group with 15+ years of wearing experience. Consequently, it should be kept in mind when interpreting the modeling results that subjects at the high end of the distribution of CL experience had "15 or more" years of wear.

Corneal staining was quantified in several different ways for the purposes of analysis. The clinical grades (0–4) given in the 5 zones of the cornea were summed to create variables representing total corneal staining ranging from 0 to 20 for each eye (i.e., both eyes were used in the analysis). The total (sum) corneal staining for each eye was calculated separately for extent and depth of staining, and both total corneal staining variables were independently examined as potential explanatory variables in statistical models of DE severity. As with years of CL wear, these total corneal staining variables were relatively normally distributed except for 14 eyes with total corneal staining >6; we therefore also examined a less skewed variable by including these 14 eyes in the highest total corneal staining grade category "6 or higher". Finally, we examined indicator variables for simple presence/absence of corneal staining, and for presence/absence of grade 2 or greater (G2+) staining in any corneal zone. We chose grade 2 as a cut-off criterion because staining severity that is equal to or above this grade is considered clinically significant and may require some intervention (e.g., discontinuation of CL wear) [29]. Along with ethnicity, these constituted the primary independent variables for the purposes of modeling.

Mixed effects analysis of variance models were employed to estimate the effects of our primary independent variables, and to account for within-subject correlations between eyes and across repeated visits. Models were compared by examining *F*-test *p*-values, diagnostic plots, and considering the clinical relevance of effect sizes and clinical interpretability of the models. Nested models were compared by log-likelihood and non-nested models were compared using Akaike's Information Criterion. A thorough exploratory analysis including examination of numerous plots, descriptive statistics and univariate tests was performed as part of the model building process.

Results

The results will be presented in 2 sections. In the first section, an exploratory analysis of the relationships between the outcome variable (DEFC classification) and the primary independent variables is presented. The exploratory analysis is graphically depicted in the directed acyclic graph (DAG) in Fig. 1. The p-values shown in the figure are from individual, piece-wise mixed effects models taking into account repeated measures and within-subject correlations, with the "sink vertex" (the box the arrow points to) as the outcome and the "source vertex" (the box the arrow comes from) as the single explanatory variable. The second section presents the results of the multivariate mixed effects modeling phase of the analysis. The multivariate model section presents parameter estimates and *p*-values that take into account multiple explanatory factors simultaneously, and examines interactions among the explanatory variables.

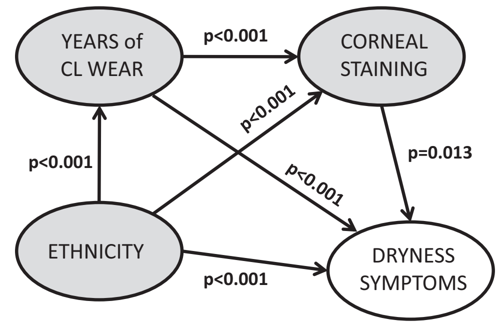

Fig. 1. Directed acyclic graph (DAG) depicting the interrelationships among ethnicity, years of CL wear, presence/absence of corneal staining and Dry Eye Flow Chart (DEFC) classification.

Exploratory analysis

As the DAG shown in Fig. 1 suggests, presence/absence of corneal staining based on extent, years of CL wear and ethnicity all may be associated with severity of dryness symptoms directly. In addition, it is possible that years of CL wear may have some impact on the incidence or severity of corneal staining, if there is a long-term effect of lens wear on the cornea (see Discussion section). It is also possible that Asians and non-Asians differ in either the incidence or severity of corneal staining, or differ in our sample in terms of CL wearing history. Descriptive statistics for DEFC classification and years of CL wear, stratified on ethnicity, are presented in Table 2.

Although our Asian and non-Asian subject groups were well-matched in age, non-Asian subjects had approximately 1.3 years longer wearing time, on average ($p < 0.001$). A greater proportion of subjects in the Asian group exhibited corneal staining compared to the non-Asian group (Table 3a), and among all subjects with corneal staining present, Asian subjects had clinical grades ranging from 0.21 to 0.52 units higher than non-Asians on average. A greater percentage of Asian subjects had corneal staining present, regardless of DEFC classification (Table 3b). A half-step on the 0–4 grading scale can be distinguished by experienced clinicians [30], and therefore, although not of serious clinical concern, the average ethnic difference in corneal staining extent in particular can be considered clinically relevant. The relationships between ethnicity and total corneal staining extent and depth were significant ($p < 0.001$ in both cases).

Table 2
Means and standard deviations (SD) for Dry Eye Flow Chart (DEFC) class and years of contact lens wear (CLW) in Asians and non-Asians.

	Asian			Non-Asian		
	n	Mean	SD	*n*	Mean	SD
DEFC Class	764	3.40	1.19	1336	2.76	1.30
Years CLW	864	6.32	3.42	1464	8.07	3.85

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Table 3a
Corneal staining (CS), graded based on extent and depth, in Asians and non-Asians. The *p*-values shown are from χ^2 tests of homogeneity: the % of subjects with CS is significantly greater among Asians.

	CS Extent			
	n	% No CS	% With CS	*p*-value
Asian	1072	53.35	46.65	<0.001
Non-Asian	1801	65.96	34.04	
	CS Depth			
	n	% No CS	% With CS	*p*-value
Asian	1072	53.35	46.65	<0.001
Non-Asian	1801	66.24	33.76	

Table 3b
Corneal staining (CS), graded based on extent, in Asians and non-Asians, stratified on DEFC class.

	Asian		Non-Asian	
DEFC Class	*n*	% With CS	*n*	% With CS
1	108	47.22	396	31.57
2	54	57.41	130	20.00
3	94	35.11	213	31.46
4	440	42.05	590	37.97
5	68	47.06	6	16.67

Asian subjects averaged approximately 3.4 on the 5-point DEFC scale, whereas non-Asian subjects averaged approximately 2.8. Among Asian subjects, approximately 85.9% reported at least mild dryness symptoms compared to 70.4% among non-Asians (Fig. 2). Taking into account the repeated measures on each subject, the relationship between ethnicity and DEFC classification was significant ($p < 0.001$). History of CL wear in years was also significantly related to DEFC classification ($p < 0.001$), with increased years of wear associated with decreased dryness symptoms. A potential

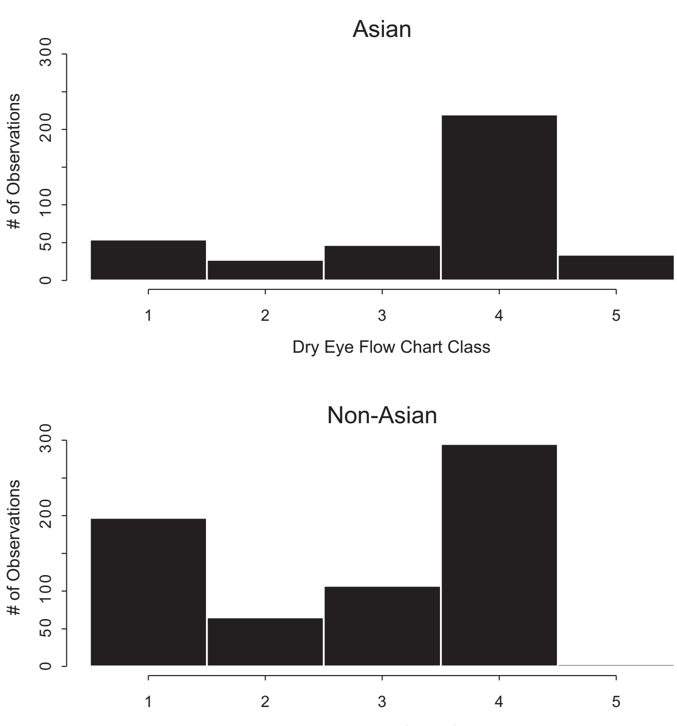

Fig. 2. Distributions of Dry Eye Flow Chart (DEFC) classification in the Asian and non-Asian subject groups.

Table 4
Multivariate model of dry eye classification. Asian ethnicity and absence of corneal staining serve as arbitrary baselines. The colon (:) indicates a multiplicative interaction term. CLW = contact lens wear; CS = corneal staining, graded based on extent.

Explanatory variable	Estimate	*F*-test *p*-value
Intercept	3.358	<0.001
Ethnicity (non-Asian)	−0.427	<0.001
Asian: years of CLW	−0.0003	0.0171
Non-Asian: years of CLW	0.026	
Asian: CS present	−0.046	0.0100
Non-Asian: CS present	0.239	

interaction between ethnicity and years of CL wear is suggested by the fact that DEFC classification was not significantly different depending on years of CL wear among Asians ($p = 0.951$), whereas DEFC classification appears to be lower with more years of wear among non-Asians ($p = 0.005$).

Total clinical grade of corneal staining extent ($p = 0.042$) and its presence/absence ($p = 0.013$) were significantly related to DEFC classification. Presence/absence of corneal staining depth was also significantly related to DEFC classification ($p = 0.012$). In all cases, the presence of corneal staining, or more severe corneal staining, was associated with an increase in dryness symptoms. Fig. 3 reveals a potential interaction between ethnicity and the presence or absence of corneal staining. Among non-Asians, a significantly higher DEFC score is found in subjects with corneal staining present ($p = 0.001$), whereas among Asians, DEFC score was not significantly different in subjects with and without corneal staining ($p = 0.082$).

Multivariate models

We compared a number of multivariate mixed effects models of DEFC classification that took into account the repeated measures on each subject and included additive effects for ethnicity, years of CL wear and corneal staining, as well as their interactions. The best fitting model with a clear clinical interpretation shows significantly higher DEFC classification for Asians overall ($p < 0.001$), a decrease in dryness symptoms with more years of CL wear for non-Asians ($p = 0.008$) but not for Asians ($p = 0.983$), and increased dryness symptoms in the presence of corneal staining (extent) for non-Asians ($p = 0.002$) but not for Asians ($p = 0.484$). Table 4 shows the model parameter estimates and p-values. To summarize the modeling results: (a) Asians overall, regardless of years of wear or corneal staining status, have higher DEFC scores on average than do non-Asians; (b) the DEFC scores of Asians, on average, do not appear to be affected by years of CL wear or presence of corneal staining; (c) in contrast, non-Asian subjects have higher average DEFC scores in the presence of corneal staining, and have lower average DEFC scores with more years of CL wear.

In models employing the clinical grade of corneal staining, rather than an indicator of presence/absence, there was also an estimated increase in DEFC classification with increasing severity of corneal staining extent for non-Asians only, but it was not significant at the $\alpha = 0.05$ level ($p = 0.088$). This shows that models using a simple indicator for presence or absence of corneal staining provide a better fit than do models that distinguish the finer grades on the 0–4 scale. There was not a significant increase in DEFC classification with increased severity of staining extent for Asians ($p = 0.208$). Nearly identical results were found for corneal staining depth.

Discussion

The purpose of this retrospective database study was to explore the relationships among length of CL wear, corneal staining and severity of dryness symptoms, and to determine whether these relationships differ between Asians and non-Asians. The

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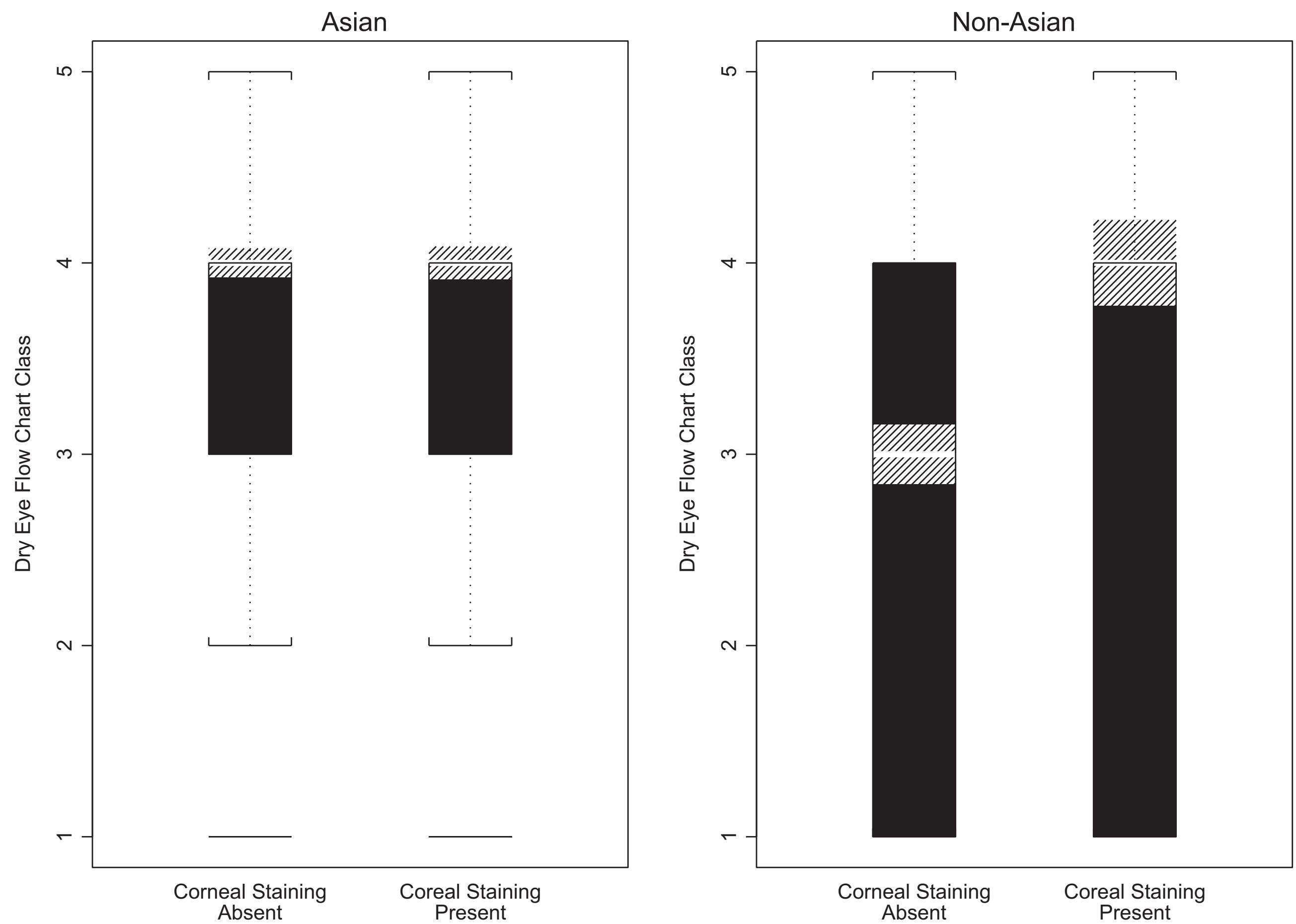


Fig. 3. Dry Eye Flow Chart (DEFC) classification as a function of presence/absence of corneal staining, in the Asian and non-Asian subject groups. The boxes depict the inter-quartile range (IQR), the whiskers encompass all data not exceeding a standard span (1.5 * IQR), and outliers are shown individually. The hashed regions of the boxplots represent approximate 95% confidence intervals for the medians.

motivation for exploring these relationships came from our observations of a large group of seasoned CL wearers over many years that revealed both a substantial number who exhibited a range of non-transient corneal staining (present at least 24 h after cessation of lens wear) and a wide range of dryness symptoms. Except for cases in which there is deep epithelial cell loss, recovery from corneal staining is quite rapid after cessation of CL wear. Grade 2 or less staining can resolve overnight, if not within a few hours [31]. Because these signs were visible after at least a 24-h washout period, we strongly suspected that this was not the result of transient insult to the corneal surface from having worn and just removed lenses or from temporary solution toxicity, and could represent new evidence of a changing ocular surface *observable by clinicians* from long-term contact lens wear.

The results of this study suggest that Asian and non-Asian eyes differ in both corneal staining and in subjective symptoms of dryness. As in previous studies, we observed a greater proportion of subjects in the Asian group with corneal staining, and among all subjects with corneal staining present, Asians had a higher average clinical grade of staining [15]. In addition, Asians had more severe dryness symptoms compared to Non-Asians, which is also in agreement with previous studies [9–11]. Although the magnitude of these ethnic differences would be considered small in terms of routine clinical practice, they are nevertheless statistically significant and thus could provide valuable knowledge in a clinical trial environment. It must also be kept in mind that these differences were observed after a minimum of 24 h without CL wear, and the differences between ethnic groups immediately after lens removal could be more pronounced, as suggested by Roseman et al. [15].

Dryness symptoms decreased with increased years of CL wear for non-Asians, but did not change for Asians. In addition, dryness symptoms were more severe on average in the presence of corneal staining for non-Asians, but not for Asians. One possible explanation for these differences is that Asian eyes may have an inherently lower corneal sensitivity compared to Non-Asians. In a study comparing corneal sensitivity between subjects with differently pigmented irides, Millodot found that subjects with blue irides had significantly more sensitive corneas than subjects with brown irides, and that sensitivity is lower in non-Caucasian subjects with darker pigmented eyes compared to Caucasians with darker pigmented eyes [32]. In a more recent study comparing LASIK-induced dry eye symptoms between Asians and Caucasians, corneal sensation at 3 and 6 months post-LASIK was decreased in Asians compared to Caucasians [9]. If Asians truly have less sensitive corneas and are already desensitized, this may help explain why the increased corneal staining in our Asian subjects did not lead to an increase in subjective dryness and discomfort. Additional controlled studies with larger sample sizes are needed to confirm whether inherent corneal sensitivity differences exist between ethnicities. If the corneal staining observed in this study is indeed related to symptoms of dryness in non-Asians but not in Asians, our results would suggest that a clinical measure such as corneal staining may not be a good indicator for dry eye status in a racially/ethnically diverse study population. In other words, inconsistent findings in the literature with respect to the relationship between ocular surface signs and subjective symptoms may be due, in part, to the different ethnic profiles of the subject groups under investigation. In addition, it is not known how much cultural differences contributed to the differences in subjective ratings between Asian and non-Asian subjects. Future investigation regarding this issue is warranted to advance our understanding and interpretation of subjective ratings for different ethnic/racial groups.

The decrease in dryness symptoms with more years of lens wear for non-Asians may be explained by a decrease in corneal sensitivity with CL wear. Millodot observed a reduction in corneal sensitivity with both hard and soft CL wear, and a more pronounced reduction in sensitivity with hard CL wear [33,34]. With hard CL wear, a significant recovery of corneal sensitivity was observed within the first hour after lenses were removed, however, complete recovery took longer and was also related to length of CL wear [35,36]. In a more recent study involving silicone hydrogel lenses, Situ et al. found that a decrease in corneal sensitivity occurred after only 2 weeks of wear, suggesting that hypoxia is not the sole explanation for decreased corneal sensation [37]. On the contrary, it has also been shown that corneal sensitivity in long-term extended wearers of low Dk/t soft contact lenses was similar to those of non-lens-wearing subjects. In fact, another recent study found that corneal sensitivity was reduced after subjects ceased low Dk/t lens wear for 1 week and did not change when transferred into high Dk/t silicone hydrogel lenses, although this study used a different mode of corneal stimulation than the Millidot and Situ studies [38]. Unfortunately, there was no mention of the ethnic make-up of these subjects in any of these studies.

In a post hoc analysis, we were able to investigate whether habitual contact lens type (hydrogel or silicone hydrogel) had any significant effect in our models for a subgroup of 344 subjects for whom this information was available. Although there did not appear to be a significant effect of lens type when added to the model as a main effect or as an interaction with ethnicity, when included as an interaction with years of lens wear, dry eye score appeared to be reduced (i.e., comfort improved) over time for silicone hydrogel lens wearers, but not for hydrogel lens wearers ($p < 0.001$). This result must be viewed with caution, however, as the characteristics of the subgroups that did and did not provide detailed habitual lens information may or may not be the same, making it difficult to determine to what target population such a result can be generalized. It does, nevertheless, provide some suggestion that lens-wearing comfort could improve over time in successful silicone hydrogel wearers. An alternative interpretation is that perhaps the cornea becomes desensitized with long term wear of silicone hydrogel lenses, thus leading to reduced perception of dryness. However, Golebiowski et al., recently reported that corneal sensitivity did not change over 12 months of silicone hydrogel extended wear, suggesting that long term corneal desensitization is not the cause of our result [38]. A properly designed study with a large sample size is needed to answer this question definitively.

It is possible that the corneal staining observed in our subjects was “normal”, idiopathic corneal staining and unrelated to long-term contact lens wear. Estimates of the prevalence of idiopathic staining in non-contact lens wearers vary widely due to differences in subject selection, study methodology and observer training and criteria [39], yet there is some evidence to suggest that the staining we observed more than 24 h after discontinuation may not be simply “normal” staining unrelated to long-term lens wear. Although some estimates of the prevalence of idiopathic staining in non-CL wearers are as high as 79% [40], other studies have reported prevalences ranging from 0% to 19% [41–43], compared with the approximately 39% of subjects with corneal staining in the current study. Due to the large size of our database, we can speculate that this excess prevalence of corneal staining, over and above the prevalence of idiopathic staining seen in non-contact lens wearers, and which was not the result of transient insult to the corneal surface due to lens wear within 24 h, is due to a changing ocular surface observable by clinicians from long-term contact lens wear.

There is evidence of other long-term effects on the cornea with CL wear. Contact lenses in the long run can significantly inhibit the normal homeostatic turnover rate of the corneal epithelium [44–47]. In short-term soft lens extended wear, corneal oxygen uptake is reduced temporarily, whereas the effect is sustained in long term wearers [17]. Holden et al., found that extended wear of hydrogel lenses induced significant changes in the epithelial, stromal and endothelial layers of the cornea. Although the changes to the epithelium were reversible after cessation of CL wear, the effects on the stroma and endothelium were longer lasting [48]. The reduction in oxygen supply to the eye with CL wear can lead to hypoxia, which ultimately can affect epithelial metabolism and lead to reduced corneal sensation [17]. The decrease in corneal sensitivity may be an adaptation to chronic hypoxia, decreased corneal pH, or mechanical stimulation [49], although corneal sensitivity seems to be less affected with high-Dk CL wear [50]. To our knowledge, there is no published work that has examined how these corneal effects differ in various ethnic groups.

There is disagreement in the literature as to whether age could also be a factor in the decrease of dryness symptoms among non-Asian wearers. It has been reported that the prevalence of dryness symptoms declines with advancing age among CL wearers and non-CL wearers alike [51]. It has also been observed that although central corneal sensitivity was found to remain unchanged until middle age [52], peripheral corneal sensitivity decreased throughout life [53]. If age is a surrogate for length of CL wear, then our findings of decreased dryness symptoms with increased years of CL wear may be explained by the change in corneal sensitivity with age.

In contrast, other studies suggest that dryness symptoms increase with age for both CL wearers and non-CL wearers. For example, the prevalence of dry eye increased with age in both the Beaver Dam Eye Study ($n = 3722$) and the Physicians' Health Studies ($n = 25{,}444$), both of which included primarily Caucasian subjects [20,54]. The age range of the Beaver Dam Eye Study cohort was broader (48–91 years) and included older subjects than in the present study; similarly, the Physicians' Health Studies included only subjects 50 years and older. Length of CL wear for the subjects was not reported. The younger age of our study cohort may explain why our results differ from these studies of primarily older adults. Another possible explanation as to why our findings are in contrast to theirs is that a decrease in corneal sensitivity that occurs with prolonged CL wear could override the increase in dryness symptoms with age in our younger study cohort. If this is the case, it supports the notion that there may be an effect of long-term CL wear on dryness symptoms that is not simply a proxy for natural change with age.

One limitation of this study that should be kept in mind is that our studies had a strong preponderance of female subjects. The U.C. Berkeley campus student enrollment, from which the majority of our subjects were recruited, is approximately 53% female and 47% male. This difference is not enough to explain the predominance of females in our studies. It could be that there is a greater gender difference in the population among contact lens wearers than among people in general. It may also be the case that females are more likely than males to participate in a contact lens research study. Although we do not have concrete evidence for either of these possible explanations, it should be noted that the gender makeup of our subject group is somewhat different than the study population from which they were sampled.

A second limitation of this study is that, while it shows significant associations between DE severity and the explanatory variables race, corneal staining, and years of CL wear, it should not be construed as a predictive model due to a moderately large amount of unexplained variance. With our associative multivariate models, simply knowing a patient's race, years of wear and corneal staining status is not sufficient to make a precise prediction of dry eye score. The unexplained variance not accounted for by our models highlights the fact that there are many other factors that would need to be incorporated in any attempt to develop an accurate predictive model of DE status.

In conclusion, this study has shown that Asian CL wearers experience more severe dryness symptoms and more severe corneal staining overall compared to non-Asians. Furthermore, dryness symptoms are less severe on average with increased years of CL wear, and more severe in the presence of corneal staining, in non-Asians but not in Asians. Recognizing these differences between Asian and non-Asian CL wearers may help us to better understand dryness symptoms associated with CL wear in different ethnic groups, and thereby improve the ways in which we evaluate and treat dry eye in a diverse CL-wearing population.

Conflict of interest

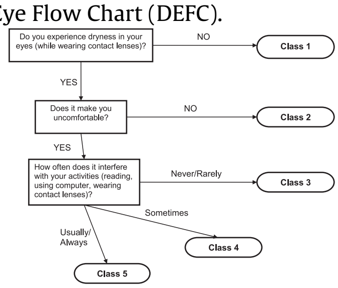
No conflicting relationship exists for any author.

Acknowledgements

This research project was supported in part by the University of California at Berkeley Clinical Research Center with unrestricted funds from Carl Zeiss Vision, Cooper Vision, Roberta J. Smith research fund and the Morton Sarver Foundation. Sponsors had no role in the design or conduct of this research.

Appendix A. APPENDIX

The University of California Berkeley-Clinical Research Center (UCB-CRC) Dry Eye Flow Chart (DEFC).



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Please cite this article in press as: Tran N, et al. Ethnic differences in dry eye symptoms: Effects of corneal staining and length of contact lens wear. Contact Lens Anterior Eye (2013), http://dx.doi.org/10.1016/j.clae.2013.06.001

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