# Factors in Contact Lens Symptoms: Evidence From a Multistudy Database.

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Meng Ching Lin
University of California, Berkeley

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FEATURE ARTICLE ON LINE

# Factors in Contact Lens Symptoms: Evidence from a Multistudy Database

Tan N. Truong*, Andrew D. Graham†, and Meng C. Lin‡

## ABSTRACT

***Purpose.*** This study aimed to examine the effects of demographic, lens performance, and ocular surface response measures on contact lens–related discomfort and dryness, using a large contact lens study database.

***Methods.*** A total of 4164 records were extracted from a database of 220 subjects participating in 46 silicone hydrogel contact lens studies. Subjects discontinued lens wear for 24 hours and were then fit with either comfilcon A or enfilcon A lenses. The fit and performance of the lenses, along with subjective comfort and dryness, were assessed on insertion and after 3 and 6 hours of wear. After 6 hours of wear, ocular surface health was also assessed by fluorescein slitlamp examination.

***Results.*** Decreased comfort at 3 hours after insertion was associated with excessive lens movement ($p < 0.001$), front surface deposits ($p = 0.004$), poor wettability ($p = 0.014$), and Asian ethnicity ($p < 0.001$). After 6 hours of wear, decreased comfort remained associated with greater lens movement ($p = 0.032$) and Asian ethnicity ($p < 0.001$), along with inferior corneal staining ($p < 0.001$). Dryness after 3 hours of wear was associated with greater lens movement ($p < 0.001$), Asian ethnicity ($p < 0.001$), increased deposits ($p < 0.001$), and poor wettability ($p < 0.001$). Dryness after 6 hours of wear remained associated with greater lens movement ($p < 0.001$) and Asian ethnicity ($p < 0.001$), along with inferior corneal staining ($p < 0.001$) and inferior lens decentration ($p = 0.001$).

***Conclusions.*** Excessive lens movement, inferior lens decentration, poor surface wettability and deposits, inferior corneal staining, and Asian ethnicity are associated with discomfort and dryness. Clinicians should consider all these factors to achieve the most comfortable and successful contact lens fit.

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Key Words: silicone hydrogel contact lenses, comfort, lens-induced dryness, lens performance, cornea, conjunctiva, race, ethnicity

Although there have been continual advances in soft contact lens design since the inception of soft lens materials approximately 50 years ago, clinical techniques for evaluating the safety and performance of soft lenses have remained virtually unchanged. Clinical acceptance of soft lens fit is based on the evaluation of both the performance of the lens on the eye and the ocular response to lens wear. For example, fitting characteristics such as lens centration, movement, and tightness are commonly evaluated during a slitlamp examination.[1] Bulbar conjunctival and corneal staining with sodium fluorescein are commonly assessed indicators of the effects of lens wear on the health of the ocular surface.[2]

*OD, MPH
†MA
‡OD, PhD, FAAO
Clinical Research Center, School of Optometry, University of California, Berkeley, Berkeley, California (all authors).

Although these measures are widely used to determine acceptable lens fit and safety, little is known about their relative influences on patient discomfort and dryness sensation during lens wear. Many researchers have investigated subsets of factors thought to be associated with contact lens–induced discomfort or dryness. Often these studies are limited in scope or provide results generalizable only to narrowly defined study populations. It has been shown, for example, that subjective comfort was not strongly associated with tight-fitting lenses but did have some diagnostic utility for identifying loose-fitting lenses, particularly those with high water content.[3] There have also been studies of the relationship between contact lens–induced ocular health changes and symptoms,[4,5] as well as studies of lens designs, materials, and manufacturing methods to determine whether these factors may have any influence on either subjective comfort or ocular health outcomes.[6–9] Recently, there has been a growing interest in how a patient's demographic characteristics, including age, sex, and ethnicity, might influence patient satisfaction and ocular health with lens wear.[10–15]

While many studies into these factors have been conducted, little is known about how all of these lens performance measures, ocular health outcomes, and subject characteristics are interrelated and how these relationships may collectively influence subjective comfort. For instance, the ocular surface response and lens behavior on the eye may influence subjective symptoms not only directly but also via a pathway in which lens-fitting characteristics result in an adverse ocular response that, in turn, results in discomfort. Furthermore, any of these relationships may differ depending on the demographic and ocular characteristics of the patient, and these characteristics may themselves directly influence how subjective symptoms are perceived and reported. The directed acyclic graph (DAG) in Fig. 1 depicts the complex interrelated factors that may affect contact lens–associated discomfort and dryness.[16,17] For example, Asians and non-Asians may differ in their perceptions of dryness and/or in their reporting of symptoms; they also differ in ocular anatomy that, in turn, could cause the lens to move differently on the eye; differing lens movement could lead directly to different subjective symptoms or could result in differential keratopathy, which, in turn, could affect symptoms.

To our knowledge, the impact of these many interrelated factors on discomfort and dryness symptoms has not been comprehensively studied in a large-sample size, multivariate analysis. Therefore, in the current study, we used data from a large silicone hydrogel contact lens study database to elucidate the relationships among subjects' ocular and demographic characteristics, contact lens fit and performance measures, clinical grading of ocular surface health outcomes, and subjective ratings of comfort and dryness. The large sample size and multivariate modeling allowed us to overcome some limitations of previous studies that were designed to investigate only specific subsets of these variables and to obtain a better determination of the factors that affect comfort and dryness in silicone hydrogel contact lens wear.

## METHODS

### Study Design

Altogether, 4164 records were extracted from a database of 220 subjects participating in one or more of 46 contact lens studies conducted at a single research site from 2005 to 2007. All studies were randomized, double-masked, contralateral contact lens studies conducted under identical protocols, for the purpose of developing new silicone hydrogel contact lens materials and designs. The lenses used in these studies were made from two investigational silicone hydrogel materials (Table 1). After discontinuing lens wear for a minimum of 24 hours, subjects reported to the research center wearing their spectacles and were screened for eligibility (see below). Subjects were asked to evaluate the comfort of each lens on insertion and after 3 and 6 hours of wear. Dryness sensation was also evaluated at 3 and 6 hours after lens insertion. Contact lens fitting and surface characteristics were evaluated at the same time points as the subjective evaluations. Sodium fluorescein examinations of the ocular surface were conducted at baseline before lens insertion and immediately after lens removal at the 6-hour visit but not at the 3-hour visit to avoid interrupting lens wear, which could bias the subsequent lens performance evaluation and subjective comfort and dryness assessments.

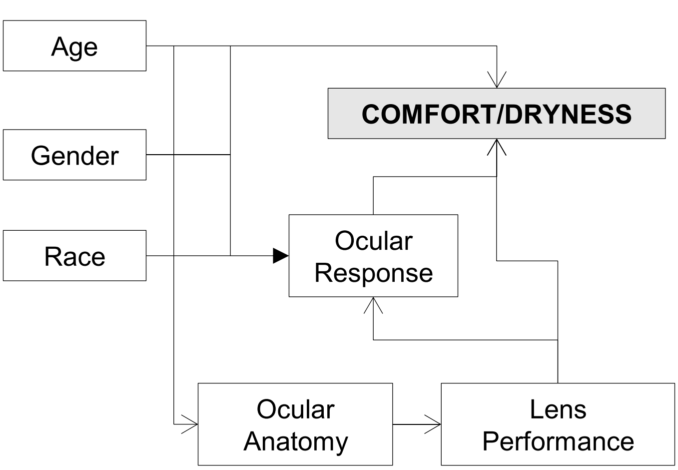


**FIGURE 1.**
Directed acyclic graph (DAG) depicting the possible effects on subjective comfort or dryness of demographics, ocular anatomy, contact lens performance on the eye, the ocular response to contact lens wear, and the interrelationships among these effects.

**TABLE 1.**
Summary of contact lens parameters

| | Investigational Comfilcon A | Investigational Enfilcon A |
|---|---|---|
| Total diameter (mm) | 13.0 to 14.5 | 13.9 to 14.4 |
| Back vertex power (D) | +0.25 to −3.00 | −1.00 to −4.00 |
| Water content (%) | 48 | 46 |
| Modulus (MPa) | 0.8 | 0.5 |
| Oxygen permeability (Dk × $10^{-11}$) | 128 | 100 |

### Subjects

All subjects were recruited from the campus of the University of California, Berkeley, and the surrounding community. Prospective subjects were successful spherical soft contact lens wearers who were free from ocular disease or any ocular abnormality that contraindicated lens wear. The sample group consisted of 44.1% Asian subjects and 55.9% non-Asian subjects. The Asian group included subjects of Taiwanese, Chinese, Japanese, Korean, Vietnamese, and Pacific Islander descent. The non-Asian group consisted of all other ethnicities, with a large majority of Caucasians (78.2%) and Latinos (14.5%), the remainder (7.3%) being African American, East Indian, or multiethnic heritage. The ethnic makeup of our sample closely resembled the demographics of the study population from which our subjects were recruited.[18]

A full explanation of the study goals, procedures, risks, and benefits was given to each prospective subject, and informed consent was obtained. This study observed the tenets of the Declaration of Helsinki, was approved by the University of California, Berkeley, Committee for Protection of Human Subjects, and was HIPAA compliant.

### Ocular Surface Examination

A baseline slitlamp (SL 120; Carl Zeiss Meditec AG, Jena, Germany) examination of the ocular surface was performed initially with white light, followed by instillation of sodium fluorescein (Bio Glo; HUB Pharmaceuticals, LLC, Rancho Cucamonga, CA) and examination of the cornea and conjunctiva under cobalt blue illumination with a Wratten no. 12 yellow barrier filter. All slitlamp findings were graded on a 0 to 4 scale according to the Brien Holden Vision Institute (formerly CCLRU) grading scales.[19] Conjunctival staining was graded separately in the nasal, temporal, superior, and inferior quadrants; peripheral and limbal corneal staining was also graded separately in these four quadrants and in the central 4-mm zone. The examination was repeated after 6 hours of lens wear.

### Lens Performance Evaluation

A slitlamp biomicroscope with a diffuser and eyepiece graticule was used to measure lens conjunctival overlap, postblink lens movement, and primary and upgaze lens lag. The measurements were viewed at 8× magnification and recorded to the nearest 0.1 mm. *In vivo* front surface wettability and deposits were also graded by clinicians using the slitlamp with diffuser. Wettability was graded on a scale of 0 (very poor, immediately displaying nonwetting areas, and rapid drying of the lens surface) to 4 (excellent, lens surface completely wettable, and exhibiting no nonwetting areas during interblink periods). Front surface deposits on the contact lens were graded on a scale of 0 (absent, no deposits) to 4 (severe, deposits covering >75% of surface). Lens tightness was assessed by digital push-up test and rated on a continuous scale from 0% (very loose, falls from cornea without lid manipulation) to 100% (very tight, does not dislodge on lid manipulation). Although this test is highly subjective, it has been shown to be a reproducible and sensitive indicator of lens fit.[3,20]

### Subjective Evaluation

Subjects rated lens comfort on a numerical rating scale from 0 (poor comfort, intolerable) to 100 (excellent comfort, cannot be felt) on lens insertion and after 3 and 6 hours of lens wear. Dryness sensation was also rated on a scale from 0 (no sensation of dryness whatsoever) to 100 (extremely dry, intolerable) after 3 and 6 hours of lens wear.

### Statistical Methods

Linear mixed-effects models were used to account for the nested, multilevel data structure and the correlations between eyes within subjects and between repeat measurements on subjects enrolled in multiple studies. A compound symmetric covariance structure was assumed such that all within-subject repeated measurements have a common covariance, with independence between subjects. In addition, because the test lenses in each study varied slightly in design, the lens type was examined as a potential factor in each model. Because most subjects participated in more than one study, the repeat study visits were also examined in the models. The baseline, 3-hour, and 6-hour visits within each study were modeled separately because it was believed that different sets of factors were likely to influence subjective symptoms at these different time points after lens insertion. The models included fixed effects for the demographic, lens performance, and ocular response variables described above. Initially, each potential fixed explanatory variable was examined in a model with a random effect for eyes-within-subjects. All possible additive combinations of the fixed effects having individual p values <0.15 were then examined in multivariable models, followed by examination of numerous interactions between selected variables. The remaining models with *F* test p values all <0.05 were then examined to select the models whose effect sizes were clinically relevant (e.g., an effect may be statistically significant, but if it estimates a difference in comfort rating of <3 units on the 100-point scale, over the range of that variable observed in our data, that effect would not be considered to be of importance to clinicians). Final models were selected based on consideration of *F* test p values, clinical interpretability and importance of effect sizes, residual and other diagnostic plots, and comparison of the log likelihood between nested models and Akaike Information Criterion for non-nested models.

## RESULTS

The primary outcomes for this analysis are the subjective ratings of comfort and dryness. Comfort ratings were given by the subjects at 10 minutes after lens insertion and after 3 and 6 hours of lens wear; dryness ratings were given after 3 and 6 hours of lens wear but not immediately after lens insertion. In the following sections, we will first describe the demographic and ocular characteristics of our subjects and then present the modeling results showing how subject characteristics, ocular response variables, and lens performance measures are related first to comfort and then to dryness ratings. Descriptive statistics are provided in Tables 2 and 3. Both direct effects of significant explanatory variables on the outcomes, as well as significant interactions among the explanatory variables will be identified.

**TABLE 2.**
Descriptive statistics for subjective outcomes and potential lens performance explanatory variables

| | Min | Max | Median | Mean | SD |
|---|---|---|---|---|---|
| Comfort rating | 10 | 100 | 95 | 91.37 | 10.26 |
| Dryness rating | 0 | 90.91 | 5 | 9.62 | 14.92 |
| Wettability | 0.5 | 4.0 | 3.5 | 3.19 | 0.69 |
| Deposits | 0.0 | 2.5 | 0.0 | 0.23 | 0.38 |
| Horizontal Decentration (mm) | 1.0-nasal | 0.5-temporal | centered | 0.06-nasal | 0.14 |
| Vertical Decentration (mm) | 0.9-inferior | 0.6-superior | 0.1-inferior | 0.11-inferior | 0.22 |
| Movement (mm) | 0.0 | 1.2 | 0.2 | 0.21 | 0.15 |
| Tightness (%) | 25 | 90 | 50 | 48.44 | 7.87 |
| 1° gaze lag (mm) | 0 | 2 | 0 | 0.05 | 0.16 |
| Upgaze lag (mm) | 0 | 3 | 0 | 0.10 | 0.28 |

**TABLE 3.**

Mean ± SD age and ocular characteristics by race and sex

| | Asian | | Non-Asian | |
|---|---|---|---|---|
| | Male | Female | Male | Female |
| No. subjects | 26 | 71 | 36 | 87 |
| Age (y) | 23.3 ± 5.4 | 21.9 ± 3.4 | 23.9 ± 5.5 | 23.0 ± 3.9 |
| Keratometry horizontal (D) | 42.85 ± 1.24 | 43.38 ± 1.54 | 43.49 ± 1.30 | 43.92 ± 1.18 |
| Keratometry vertical (D) | 43.71 ± 1.30 | 44.40 ± 1.55 | 44.34 ± 1.38 | 44.63 ± 1.15 |
| PAS (mm) | 9.7 ± 1.7 | 10.5 ± 1.2 | 10.6 ± 1.5 | 10.3 ± 1.4 |
| HVID (mm) | 11.6 ± 0.6 | 11.5 ± 0.4 | 12.0 ± 0.5 | 11.8 ± 0.5 |

Non-Asians had significantly steeper corneas in both meridians, although the difference was of minimal clinical importance. Non-Asians also had significantly wider HVID.

HVID, horizontal visible iris diameter; PAS, palpebral aperture size (vertical).

## Subject Characteristics

Of our 220 subjects, 44.1% were Asian and 55.9% non-Asian. The majority of our subjects were female (72%), with 28% being male. Ages ranged from 18 to 44 years, with a mean ± SD of 23.0 ± 4.6 years. Mean ± SD horizontal and vertical corneal curvatures were 43.41 ± 1.32D and 44.27 ± 1.35D, respectively, and ranged from 39.12 to 48.25D in the horizontal meridian and from 40.25 to 48.50D in the vertical meridian. Horizontal visible iris diameter (HVID) ranged from 10.2 to 13.0 mm, with a mean ± SD of 11.7 ± 0.5 mm. Vertical palpebral aperture size (PAS) ranged from 7.0 to 15.0 mm, with a mean ± SD of 10.3 ± 1.5 mm. Table 2 presents these subject characteristics stratified on race and sex. The non-Asian group had significantly steeper corneas, on average, in both meridians ($p = 0.001$ for horizontal, $p = 0.020$ for vertical); however, the group average differences were of minimal clinical importance, being less than 0.5D. Non-Asians also had significantly wider HVID ($p < 0.001$), but only by approximately 0.4 mm on average. There were no significant racial differences in age or PAS, and there were no significant differences between sexes in age, corneal curvatures, HVID, or PAS. In terms of lens performance, we observed ranges of front surface deposit grades of 0 to 2.5, of wettability grades of 0.5 to 4.0, of lens lag grades of 0 to 2, of lens movement of 0 to 1.2 mm, and of push-up test tightness of 25 to 90%. We also observed vertical lens decentration ranging from 0.9 mm inferiorly to 0.6 mm superiorly, and horizontal lens decentration ranging from 1.0 mm nasally to 0.5 mm temporally. We observed grades of all ocular surface examination parameters ranging from 0 to 4, with the exception of temporal conjunctival indentation that ranged from 0 to 3 among our subjects.

## Comfort Rating

Higher comfort ratings 10 minutes after lens insertion were found to be significantly related to greater subject age ($p < 0.001$). No lens performance measures showed any significant or clinically relevant associations with postinsertion comfort rating, which was not unexpected after such a short duration of lens wear.

In contrast to comfort immediately after lens insertion, which older subjects tended to rate higher and was not influenced by lens performance variables, comfort after 3 hours of lens wear was related to a number of different factors. A lower grade of lens surface deposits ($p = 0.004$), greater wettability ($p = 0.014$), and less lens lag ($p = 0.039$) were all associated with significantly improved subjective comfort rating. The estimated differences in comfort ratings corresponding to the ranges of these variables that we observed in our subjects were approximately 8.0, 3.4, and 7.7 units on the 0 to 100 comfort scale for deposits, wettability, and lag, respectively. The factor with highest significance in subjective comfort after 3 hours of lens wear can be quantified either as millimeters of lens movement ($p < 0.001$) or lens tightness as graded by push-up test ($p = 0.003$), with less lens movement or a tighter lens being associated with improved lens comfort (see Discussion). The estimated differences in comfort rating corresponding to our observed ranges of movement and tightness were 8.7 and 6.9 units on the 0 to 100 comfort scale, respectively. Asian subjects rated comfort significantly lower ($p < 0.001$) on average, although the difference between ethnic groups was not large (an estimated 3.1 units on the 0 to 100 comfort scale). There also seemed to be a significant ($p = 0.014$) interaction between ethnicity and the impact of lens deposits on subjective comfort, such that Asian subjects with higher lens deposit grading tended to have more discomfort than non-Asians with an equivalent deposit grading. Lens type was not found to be significant in any model. Table 4 presents the final multivariate models for comfort rating at 3 hours after lens insertion.

**TABLE 4.**

Parameter estimates and p values for models of comfort rating at 3 hours after lens insertion

| | 3 hours of wear | | | |
|---|---|---|---|---|
| | Model 1 | | Model 2 | |
| | Estimate | p | Estimate | p |
| Intercept | 89.807 | <0.001 | 82.513 | <0.001 |
| Race | 1.742 | <0.001 | 1.946 | <0.001 |
| Movement (mm) | −7.244 | <0.001 | | |
| Tightness (%) | | | 0.106 | 0.003 |
| Deposits | −3.199 | 0.004 | −3.406 | 0.004 |
| Race: deposits | 3.360 | 0.014 | 3.709 | 0.007 |
| Wettability | 0.978 | 0.014 | 1.156 | 0.014 |
| Lag (mm) | 3.844 | 0.038 | 3.942 | 0.039 |

The two models are identical, except in that Model 2 includes push-up test tightness as an explanatory variable instead of millimeters of lens movement, with which it is highly correlated. The arbitrary reference group for Race in the models was Asian.

**TABLE 5.**
Parameter estimates and p values for model of comfort rating at 6 hours after lens insertion

| | 6 hours of wear | |
|---|---|---|
| | Estimate | p |
| Intercept | 89.417 | <0.001 |
| Race | 3.645 | <0.001 |
| Movement (mm) | −4.411 | 0.032 |
| Corneal staining inferior | −2.068 | <0.001 |
| Conjunctival staining temporal | 1.033 | 0.001 |
| Conjunctival indentation temporal | 1.278 | 0.051 |

The arbitrary reference group for Race in the models was Asian. Corneal staining is graded in extent.

In addition to subjective ratings and a lens fit and performance evaluation, the ocular response to lens wear was assessed by fluorescein slitlamp examination after 6 hours of wear. Less lens movement ($p = 0.032$) and non-Asian ethnicity ($p < 0.001$) continued to be significantly associated with higher comfort ratings after 6 hours of lens wear, with higher estimated comfort ratings of approximately 5.3 and 3.6 units on the 0 to 100 comfort scale corresponding to our observed range of movement and non-Asian ethnicity, respectively. Inferior corneal staining over the range we observed in our subjects was significantly associated with an estimated lower comfort rating of approximately 8.3 units on the 0 to 100 comfort scale ($p < 0.001$). Staining was graded in terms of type, depth, and extent (area), and although all three measures were significant, a greater extent of inferior staining was most closely associated with decreased comfort in the multivariate models. Although the type, depth, and extent of corneal staining represent different aspects of the ocular surface response and are clinically distinguishable, they tend to be collinear; type, depth, and extent of corneal staining were significant, each in a separate model (not together in one model) due to this collinearity. Staining ($p < 0.001$) and indentation ($p = 0.051$) of the temporal conjunctiva were also significantly associated (or nearly so) with comfort rating. Interestingly, a *higher* grade of temporal conjunctival staining and indentation resulted in an estimated *higher* comfort rating, with estimated higher comfort ratings of 4.1 and 3.8 units on the 0 to 100 comfort scale for conjunctival staining and indentation, respectively. Lens type was not found to be significant in any model. Table 5 presents the final multivariate model for comfort rating at 6 hours after lens insertion.

## Dryness Rating

Subjects rated lens-associated dryness after 3 and 6 hours of lens wear. As with comfort rating, greater lens movement was an important factor associated with dryness rating at 3 hours after lens insertion ($p < 0.001$), with an estimated 11.7-unit higher dryness rating on the 0 to 100 scale across our observed range of lens movement. Asian subjects rated dryness after 3 hours of lens wear significantly higher than did non-Asians ($p < 0.001$) by approximately 3.3 to 4.3 units depending on the model (Table 6). Two statistically similar models showing increased dryness rating included Asian ethnicity and increased lens movement, along with either lower lens surface wettability ($p < 0.001$) or greater front surface deposit grade ($p < 0.001$). Lens deposits at the highest level we observed in our subjects (grade 2.5), compared with zero deposits, resulted in an estimated 9.4-unit higher dryness rating, whereas the poorest lens surface wettability we observed (grade 0.5), compared with complete wettability (grade 4.0), was associated with an estimated 11.3-unit higher dryness rating. Lens type was not found to be significant in any model. Table 6 presents the final multivariate models for dryness rating at 3 hours after lens insertion.

Lens movement continued to be significantly related to dryness rating after 6 hours of wear ($p < 0.001$), with an estimated 12.2-unit greater dryness rating over our observed range of movement. Greater vertical lens decentration in the inferior direction was associated with significantly higher dryness rating ($p = 0.001$) by an estimated 8.8 units on the 0 to 100 dryness scale. Interestingly, a higher grade of inferior corneal staining—particularly in extent of staining—seemed to have the strongest impact on higher dryness ratings ($p < 0.001$). The difference in estimated dryness rating over the 0 to 4 grade range we observed in inferior corneal staining extent was approximately 20.8 units on the 0 to 100 dryness rating scale. Asian ethnicity was also associated with increased dryness ratings ($p < 0.001$). A significant interaction was found between ethnicity and sex such that, among males, estimated dryness rating for Asians was approximately 6.5 units higher than for non-Asians, whereas among females, the difference was only 1.3 units on average. Table 7 presents the final multivariate model for dryness rating at 6 hours after lens insertion.

## DISCUSSION

Dryness and discomfort are two primary subjective factors that are responsible for contact lens dissatisfaction and discontinuation.[21,22] A plethora of past studies highlights the complexities inherent in elucidating relationships among the numerous interrelated factors that can influence contact lens–related discomfort and dryness.[4–9] A number of studies have addressed small subsets of these factors, often with relatively small sample sizes or sampling from narrowly or ill-defined study populations. To the best of our knowledge, this study is the first to evaluate a wide range of factors that include subject demographics, ocular biometrics, contact lens clinical performance, and ocular health outcomes in a large-sample size, multivariate analysis of contact lens–related discomfort and dryness.

**TABLE 6.**
Parameter estimates and p values for models of dryness rating at 3 hours after lens insertion

| | 3 hours of wear | | | |
|---|---|---|---|---|
| | Model 1 | | Model 2 | |
| | Estimate | p | Estimate | p |
| Intercept | 8.078 | <0.001 | 18.948 | <0.001 |
| Race | −4.333 | <0.001 | −3.327 | <0.001 |
| Deposits | 3.752 | <0.001 | | |
| Wettability | | | −3.221 | <0.001 |
| Movement (mm) | 9.766 | <0.001 | 9.379 | <0.001 |

The two models differ in that Model 1 estimates higher dryness rating with more lens deposits, and Model 2 estimates lower dryness rating with better lens wettability. The arbitrary reference group for Race in the models was Asian.

**TABLE 7.**

Parameter estimates and p values for model of dryness rating at 6 hours after lens insertion

| | 6 hours of wear | |
|---|---|---|
| | Estimate | p |
| Intercept | 6.058 | <0.001 |
| Race | −1.669 | <0.001 |
| Movement (mm) | 12.229 | <0.001 |
| Asian: male | −1.409 | <0.001 |
| Non-Asian: male | −6.467 | |
| Corneal staining inferior | 5.205 | <0.001 |
| Vertical lens decentration (mm) | −5.868 | 0.001 |

The arbitrary reference group for Race in was Asian. Corneal staining is graded in extent. The interaction between race and sex estimates lower dryness ratings for non-Asians than for Asians in male subjects.

The strength of this analysis is that all studies that contributed to our database recruited from the same study population and adhered to the same study protocol, thus providing an opportunity to examine the relationships to subjective ratings of many potential explanatory variables in a large-sample size analysis, more comprehensive in scope than has been possible to date. However, the study design and protocol do present some potential limitations to the generalizability of the multivariate analysis. In these studies, only two silicone hydrogel lens materials fabricated on a proprietary lens design platform and a narrow power range were evaluated, thus making the results of the analysis less generalizable to lenses of different materials manufactured on different lens design platforms and/or outside the study lens power range. Another study design limitation is the 6 hours of contact lens wearing time, which is less than the daily wearing schedule of a typical contact lens patient. In addition, it should be kept in mind that the amount of unexplained variance in our models precludes them from being considered predictive or causative models, but rather providing information on significant associations of commonly assessed clinical parameters with subjective symptoms. Finally, the sets of models we examined were limited to linear models, and although linearity seemed to be an acceptable assumption based on our model diagnostics, it is possible that other nonlinear models could be found which provide a better fit, reducing any model selection bias.

To highlight the important findings that practicing clinicians should consider when fitting patients with contact lenses or when diagnosing the underlying problems of returning patients who express contact lens–related discomfort and dryness, the principal results of the current study are discussed below in four sections: demographics, contact lens fit, surface properties of the contact lens *in vivo*, and anterior segment ocular response to contact lens wear.

## Demographics

The subject population for these contact lens studies consisted of *successful* contact lens wearers who are able to wear study lenses for at least 6 hours. Older participants are likely to have had more years of contact lens experience than younger subjects. This inherent sampling bias partly explains the finding that increased age is associated with increased ratings of comfort on lens insertion. It has been previously reported that symptoms of dryness decrease with advancing age among lens wearers and that the diminishing proportion of older symptomatic lens wearers most likely stems from self-selection.[10] However, it is possible that changes in ocular physiology with age could also contribute to changes in subjective symptoms. It has been shown that there is a natural decrease in corneal and conjunctival sensitivity with age[23] and that prolonged contact lens wear further decreases corneal sensitivity.[24] It should be kept in mind that this study recruited from a university campus and surrounding area and thus is likely to have a subject sample skewed toward younger ages than might be typical in the contact lens–wearing population at large.

In the current study, subjects of Asian ethnicity tended to have lower comfort and higher dryness ratings than non-Asian subjects after 3 or more hours of lens wear. This was a surprising finding given the fact that differences in average PAS, corneal curvatures, and HVID between the two racial groups were minimal. In *post hoc* analyses, it was found that a larger PAS ($p < 0.001$) and a larger HVID ($p = 0.001$) were significantly associated with the greater lens movement that was shown in our models to be the primary factor in contact lens–related discomfort. Since non-Asian subjects had slightly larger PAS and HVID on average, we would expect them to have somewhat greater lens movement and hence lower subjective comfort and higher dryness ratings than Asian subjects. However, it was found that non-Asian subjects had less significant lens movement ($p < 0.001$) on average than did Asian subjects; it was also found that subjects with steeper corneas had significantly less lens movement ($p < 0.001$), and non-Asian subjects did have slightly higher keratometry readings on average ($p = 0.020$). Nevertheless, the fact that even after adjusting for lens movement in the multivariate models, Asians still had significantly lower estimated comfort and higher estimated dryness ratings than non-Asians suggests that there are inherent differences between the two populations of subjects that were not captured with the ocular biometrics and lens performance measurements. For example, it has been proposed that Asians have greater lid tightness compared with non-Asians, which could easily affect the behavior of the lens on the eye during the blink cycle, thus impacting sensations of discomfort or dryness.[25]

There have been studies in the past that have found differences between the two subpopulations in ocular response to contact lens wear. One study using optical pachometry on a population of experienced lens wearers found that the post-lens tear film in Asian eyes was significantly thinner than that in non-Asian eyes.[26] A separate study evaluating endothelial bleb formation, an indicator of corneal response to stress, showed that Asian subjects had significantly higher grades of bleb formation than did Caucasian subjects.[11]A recent study has also shown that, compared with non-Asians, Asian subjects have a significantly greater increase in corneal epithelial permeability on awakening after 30 days of continuous wear with silicone hydrogel lenses.[12] Although not yet confirmed by a large-scale epidemiological study, there is some evidence that Asians present with more positive ocular findings with the slitlamp biomicroscope than do non-Asians.[13–15] Although these studies did not evaluate subjective responses, it is reasonable to conclude that these differences in ocular response to contact lens wear may have a negative impact on contact lens comfort and dryness.

## Contact Lens Fit

There is a general acceptance by many contact lens practitioners that excessive postblink lens movement is a common underlying cause of lens-related discomfort. The current study provides strong evidence that excessive lens movement is a valuable indicator of the likelihood of subsequent lower comfort and higher dryness ratings after periods of lens wear exceeding 3 hours. Movement is the only lens fitting characteristic that consistently remained a significant factor in all the multivariate models of both comfort and dryness ratings after 3 or more hours of contact lens wear. It is reasonable to suggest that minimizing lens movement would minimize its mechanical stimulus to the cornea, conjunctiva, and eyelids, although too tight a fit with virtually no lens movement could result in increased dryness symptoms due to poor tear exchange. *Post hoc* analyses revealed a clear range of preferred lens movement, with the highest percentage of subjects having comfort ratings above 90, or dryness ratings below 10, occurring in subjects with 0.1 to 0.4 mm of movement.

In one model for comfort rating at 3 hours after lens insertion, push-up test tightness could be substituted for millimeters of lens movement with minimal change in the fit of the model. Movement and tightness are highly collinear, and as with movement, there seems to be an ideal range for lens tightness. *Post hoc* analyses revealed that the highest percentage of subjects having comfort ratings above 90 occurred among those with push-up test tightness values above 40, up to 55. A linear regression of movement on tightness was significant; however, diagnostic plots reveal greater variance in movement at the lower end of the tightness scale. This means that, for a very tight-fitting lens, little postblink movement is consistently observed; however, for a lens fit that is low on the tightness scale, postblink movement may range from excessive to none. Thus, although push-up test tightness may act as a proxy for lens movement, it is not a good predictor of movement for looser fitting lenses, and therefore clinicians, should measure millimeters of lens movement directly to assess a lens fit for optimum comfort.

We also found in this study that vertical lens decentration is a significant factor in dryness sensation after 6 hours of lens wear, with greater inferior decentration associated with higher average dryness ratings. Interestingly, inferior lens decentration was not associated with lower comfort ratings. We speculate that dryness symptoms arise from the lens dropping inferiorly during the interblink period sufficiently to expose the upper lens edge, which causes the upper lid wiper to repeatedly cross over the lens edge with each blink. There is evidence from the literature linking symptoms of dryness with lid wiper epitheliopathy in contact lens wear. The upper eyelid marginal conjunctiva plays a crucial role in wiping the bulbar surface and distributing the preocular tear film.[13] Alteration of the upper eyelid epithelium, a condition known as lid wiper epitheliopathy, was first characterized in soft contact lens wearers in a study that found that 80% of subjects who had dry eye symptoms displayed lid wiper epitheliopathy compared with only 13% of asymptomatic subjects.[27] The primary sensory mechanism for lens awareness and dryness sensation associated with an undamaged and well-fitted soft lens seems to be the blink-related action of the upper eyelid margin lid wiper over the CL surface,[28] possibly exacerbated by repeated contact with the edge of an inferiorly decentered lens. Future studies are needed to confirm the relationship between lid wiper epitheliopathy and inferior decentration of a CL.

## *In Vivo* Contact Lens Surface

After 3 hours of lens wear, lens surface wettability and deposits can influence comfort and dryness sensation. Higher lens surface wettability and less surface deposits are both independently associated with higher comfort ratings after 3 hours of wear. However, wettability is interchangeable with deposits in the model for dryness ratings. Either a higher wettability or lower surface deposit grade was associated with lower dryness ratings. The compartmentalization of the tear film in the presence of a CL into two layers, prelens and postlens, interferes with its normal structure and function. Tear film evaporation rate has been shown to increase significantly with contact lens wear.[29,30] Studies have also found that the presence of a lens on the eye destabilizes the tear film[31] and that the prelens tear thickness decreases significantly within half an hour of lens wear.[32] In fact, both a rapid prelens tear film thinning time[4] and reduced tear film breakup time[33] are important factors commonly observed in symptomatic contact lens wearers. In our study, wettability and lens surface deposits were found to be moderately negatively correlated (Pearson $\rho = -0.43$), suggesting that lenses with worse deposits are somewhat more likely to have poor wettability. It may be that poor lens wettability causes thinning and destabilizing of the tear film leading to dryness symptoms and that lens surface deposits merely act as a proxy variable in the model through collinearity. On the other hand, with the more generalized comfort ratings, poor wettability leads to decreased comfort through a similar mechanism to dryness, whereas front surface deposits contribute to an independent effect on comfort through some other mechanism, such as interaction of the lids with the front surface of the lens. Further study is needed to differentiate the effects of contact lens wettability and surface deposits on symptoms of discomfort and dryness.

## Anterior Segment Ocular Health Response to Contact Lens Wear

This analysis found that corneal staining, considered one of the most important clinical outcome measures for evaluating the safety of contact lenses, is also significantly associated with increased discomfort and dryness. More specifically, it was the extent of corneal staining in the inferior quadrant that had a large influence on discomfort and dryness sensation. Studies in the past have shown that lens material properties and design[34–36] are factors that impact the level of corneal staining, although few studies have established a link between staining and subjective symptoms.[37] There has been a growing interest in the relationship between the interaction of contact lenses and lens care solutions resulting in solution-induced corneal staining. One study reported the characteristic corneal staining over a 6-hour time course with various lens–multipurpose lens care product combinations but found no correlation between ocular comfort and corneal staining.[38] A separate study that also reported increased corneal staining with certain lens material–solution combinations, in contrast, found subject preferences generally followed objective staining results.[39] However, other findings suggest that contact lens factors such as water content, material, wearing time, and deposition are more strongly associated with corneal staining than are lens care solutions.[4] Regardless of the mechanism of contact lens–associated corneal staining, the frequency of corneal staining with lenses is high and has been reported to be approximately 54% of lens wearers sampled in a cross-sectional study.[4] Noteworthy was the moderate-to-severe staining extent (grade 3 or more on the Brien Holden Vision Institute grading scales) that was detected on 26% of the patients in the study. Although the current study did not evaluate the interaction between lens materials and care solutions and did not address the mechanisms of lens-induced corneal staining, the study findings do provide additional evidence that contact lens–associated corneal staining—particularly in the inferior quadrant—may be associated with symptoms of discomfort and dryness. This has important clinical implications because the highest incidence and severity of corneal staining occur in the inferior corneal region.[40]

We also found an inverse relationship between comfort rating and temporal conjunctival staining and indentation. A recent study investigating the edge designs of different silicone hydrogel lenses also reported this finding.[41] That study found that a rounded edge that produced the lowest circumlimbal staining was associated with low comfort, whereas a knife-edge lens that induced the highest circumlimbal staining was associated with higher comfort levels. It was proposed that the knife-edge design was in close apposition to the ocular surface, whereas the thicker, rounded edge design had an apex pointing away from the ocular surface. Interestingly, all lenses in the current study used the same rounded edge profile. We also found in a *post hoc* analysis that conjunctival staining and indentation were not significantly associated with push-up test tightness, suggesting that the effect of the lens on the conjunctiva was not simply due to an ill-fitting lens. Together, these results suggest that, although a greater interaction of the lens with the ocular surface may cause more conjunctival staining, close conformity to the surface in fitting a lens provides better subjective comfort. It is possible to achieve this in ways other than altering edge design. Steepening lens base curve is the most common and effective method of conforming the lens edge to the eye. This also alters the way in which applied pressure is absorbed by the eye. Steepening the lens results in increased transmittance of the pressure load to the rim of the lens rather than to the central portion of the lens, as is found with flatter lenses.[42] It is known that the conjunctiva is less sensitive than the cornea.[43] It is therefore possible that increased comfort is the result of the redistribution of the mechanical forces generated during a blink away from the cornea to the less-sensitive conjunctiva. The redistribution of this reaction pressure is manifested as conjunctival staining. Although there is evidence suggesting that better comfort can be achieved by having close apposition to the ocular surface and the lens edge, it is unclear how this close conformity affects postlens tear mixing. Maintaining sufficient tear mixing is important to inflammatory mediators accumulating underneath a CL being flushed out. Therefore, future studies are needed to suggest strategies for striking a balance between lens-wearing comfort and postlens tear mixing.

Interestingly, models of subjective comfort and dryness after 6 hours of lens wear, at which point ocular surface response was also evaluated, were a better fit than models for initial and 3-hour lens wear. Thus, evaluating ocular surface integrity along with contact lens fit is crucial in determining the underlying causes of contact lens–related discomfort and dryness. In addition, our diverse study population allowed us to examine racial or ethnic differences in subjective symptoms. Whether these differences are due solely to cultural differences in symptom perception and/or how symptoms are reported to clinicians or whether there are underlying physiological differences leading to differential symptoms is currently being investigated. Nevertheless, it is clear that a better understanding of these racial or ethnic differences would assist clinicians in achieving optimum ocular surface health and subject comfort as contact lens wear becomes more pervasive outside the United States and Europe.

In conclusion, this multivariate analysis has identified key factors associated with subjective comfort and dryness symptoms that practicing clinicians should keep in mind during a contact lens exam. A patient's age and ethnicity are important indicators of whether he or she will have contact lens–related complaints. Older subjects in this study population, who most likely had more years of contact lens wearing experience, had higher comfort and lower dryness ratings than younger subjects did. This study found that Asian subjects will tend to have lower comfort and higher dryness ratings on average. In addition, several contact lens performance measures significantly impacted subjective ratings. Excessive lens movement, inferior lens decentration, and lower surface wettability or more lens surface deposits are all measures associated with decreased comfort and increased dryness. Through evaluating the ocular health response to contact lens wear, we have shown that the location and extent of corneal staining significantly influenced subjective ratings. Subjects with a greater extent of inferior corneal staining were more likely to have lower comfort and experience more dryness. However, greater contact lens–related temporal conjunctival staining and indentation were inversely related to dryness ratings. Lastly, it is important to note that models of subjective comfort and dryness after 6-hour lens wear were a better fit than models for initial and 3-hour lens wear. Thus, considering patient demographics and evaluating ocular surface integrity along with contact lens fit are crucial in achieving a successful, comfortable contact lens fit with the best chance of maintaining optimal ocular surface health.

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## REFERENCES

1. Bruce AS, Little SA. Soft lens design, fitting and physiologic response. In: Hom MM, Bruce AS, eds. Manual of Contact Lens Prescribing and Fitting. 3rd ed. Boston, MA: Butterworth Heinemann; 2006:277–312.
2. Terry RL, Schnider CM, Holden BA, Cornish R, Grant T, Sweeney D, La Hood D, Back A. CCLRU standards for success of daily and extended wear contact lenses. Optom Vis Sci 1993;70:234–43.
3. Young G. Evaluation of soft contact lens fitting characteristics. Optom Vis Sci 1996;73:247–54.
4. Nichols JJ, Sinnott LT. Tear film, contact lens, and patient factors associated with corneal staining. Invest Ophthalmol Vis Sci 2011;52:1127–37.

5. Glasson MJ, Stapleton F, Keay L, Willcox MD. The effect of short term contact lens wear on the tear film and ocular surface characteristics of tolerant and intolerant wearers. Cont Lens Anterior Eye 2006;29:41–7.
6. Dumbleton KA, Chalmers RL, McNally J, Bayer S, Fonn D. Effect of lens base curve on subjective comfort and assessment of fit with silicone hydrogel continuous wear contact lenses. Optom Vis Sci 2002;79:633–7.
7. Santodomingo-Rubido J, Rubido-Crespo MJ. The clinical investigation of the base curve and comfort rate of a new prototype silicone hydrogel contact lens. Eye Contact Lens 2008;34:146–50.
8. Dumbleton K, Keir N, Moezzi A, Feng Y, Jones L, Fonn D. Objective and subjective responses in patients refitted to daily-wear silicone hydrogel contact lenses. Optom Vis Sci 2006;83:758–68.
9. Maldonado-Codina C, Efron N. Impact of manufacturing technology and material composition on the clinical performance of hydrogel lenses. Optom Vis Sci 2004;81:442–54.
10. Chalmers RL, Begley CG. Dryness symptoms among an unselected clinical population with and without contact lens wear. Cont Lens Anterior Eye 2006;29:25–30.
11. Hamano H, Jacob JT, Senft CJ, Hamano T, Hamano T, Mitsunaga S, Kotani S, Kaufman HE. Differences in contact lens-induced responses in the corneas of Asian and non-Asian subjects. CLAO J 2002;28:101–4.
12. Lin MC, Yeh TN, Graham AD, Truong T, Hsiao C, Wei G, Louie A. Ocular surface health during 30-day continuous wear: rigid gas-permeable versus silicone hydrogel hyper-$O_2$ transmitted contact lenses. Invest Ophthalmol Vis Sci 2011;52:3530–8.
13. Knop E, Korb DR, Blackie CA, Knop N. The lid margin is an underestimated structure for preservation of ocular surface health and development of dry eye disease. Dev Ophthalmol 2010;45:108–22.
14. Foulks GN, Nichols KK. Meibomian gland dysfunction: understanding and implementing the new consensus definition and treatment regimens into your optometric practice. Rev Optom 2012. COPE Course ID 34224-AS:1-16. Available at: http://mededicus.com/downloads/Meibomian_Gland_Dysfunction.pdf. Accessed October 11, 2013.
15. Tagliaferri A. Risk factors for contact lens induced papillary conjunctivitis associated with silicone hydrogel contact lens wear [Master's thesis]. Case Western Reserve University; 2012.
16. Moodie EE, Stephens DA. Using directed acyclic graphs to detect limitations of traditional regression in longitudinal studies. Int J Public Health 2010;55:701–3.
17. Shrier I, Platt RW. Reducing bias through directed acyclic graphs. BMC Med Res Methodol 2008;8:70.
18. UC Berkeley Office of Planning and Analysis. UC Berkeley Fall Enrollment Data. Available at: http://opa.berkeley.edu/statistics/enrollmentData.html. Accessed October 10, 2012.
19. Terry RL, Schnider CM, Holden BA, Cornish R, Grant T, Sweeney D, La Hood D, Back A. CCLRU standards for success of daily and extended wear contact lenses. Optom Vis Sci 1993;70:234–43.
20. Martin DK, Boulos J, Gan J, Gavriel K, Harvey P. A unifying parameter to describe the clinical mechanics of hydrogel contact lenses. Optom Vis Sci 1989;66:87–91.
21. Schlanger JL. A study of contact lens failures. J Am Optom Assoc 1993;64:220–4.
22. Richdale K, Sinnott LT, Skadahl E, Nichols JJ. Frequency of and factors associated with contact lens dissatisfaction and discontinuation. Cornea 2007;26:168–74.
23. Acosta MC, Alfaro ML, Borras F, Belmonte C, Gallar J. Influence of age, gender and iris color on mechanical and chemical sensitivity of the cornea and conjunctiva. Exp Eye Res 2006;83:932–8.
24. Murphy PJ, Patel S, Marshall J. The effect of long-term, daily contact lens wear on corneal sensitivity. Cornea 2001;20:264–9.
25. Swarbrick HA, Holden BA. Rigid gas-permeable lens adherence: a patient-dependent phenomenon. Optom Vis Sci 1989;66:269–75.
26. Lin MC, Chen YQ, Polse KA. The effects of ocular and lens parameters on the postlens tear thickness. Eye Contact Lens 2003;29:S33–6.
27. Korb DR, Greiner JV, Herman JP, Hebert E, Finnemore VM, Exford JM, Glonek T, Olson MC. Lid-wiper epitheliopathy and dry-eye symptoms in contact lens wearers. CLAO J 2002;28:211–6.
28. McMonnies CW. Incomplete blinking: exposure keratopathy, lid wiper epitheliopathy, dry eye, refractive surgery, and dry contact lenses. Cont Lens Anterior Eye 2007;30:37–51.
29. Guillon M, Maissa C. Contact lens wear affects tear film evaporation. Eye Contact Lens 2008;34:326–30.
30. Thai LC, Tomlinson A, Doane MG. Effect of contact lens materials on tear physiology. Optom Vis Sci 2004;81:194–204.
31. Faber E, Golding TR, Lowe R, Brennan NA. Effect of hydrogel lens wear on tear film stability. Optom Vis Sci 1991;68:380–4.
32. Nichols JJ, King-Smith PE. The impact of hydrogel lens settling on the thickness of the tears and contact lens. Invest Ophthalmol Vis Sci 2004;45:2549–54.
33. Fonn D, Situ P, Simpson T. Hydrogel lens dehydration and subjective comfort and dryness ratings in symptomatic and asymptomatic contact lens wearers. Optom Vis Sci 1999;76:700–4.
34. Holden BA, Sweeney DF, Seger RG. Epithelial erosions caused by thin high water content lenses. Clin Exp Optom 1986;69:103–7.
35. Orsborn GN, Zantos SG. Corneal desiccation staining with thin high water content contact lenses. CLAO J 1988;14:81–5.
36. Little SA, Bruce AS. Role of the post-lens tear film in the mechanism of inferior arcuate staining with ultrathin hydrogel lenses. CLAO J 1995;21:175–81.
37. Andrasko G, Ryen K. Corneal staining and comfort observed with traditional and silicone hydrogel lenses and multipurpose solution combinations. Optometry 2008;79:444–54.
38. Garofalo RJ, Dassanayake N, Carey C, Stein J, Stone R, David R. Corneal staining and subjective symptoms with multipurpose solutions as a function of time. Eye Contact Lens 2005;31:166–74.
39. Lebow KA, Schachet JL. Evaluation of corneal staining and patient preference with use of three multi-purpose solutions and two brands of soft contact lenses. Eye Contact Lens 2003;29:213–20.
40. Begley CG, Barr JT, Edrington TB, Long WD, McKenney CD, Chalmers RL. Characteristics of corneal staining in hydrogel contact lens wearers. Optom Vis Sci 1996;73:193–200.
41. Maissa C, Guillon M, Garofalo RJ. Contact lens–induced circumlimbal staining in silicone hydrogel contact lenses worn on a daily wear basis. Eye Contact Lens 2012;38:16–26.
42. Funkenbusch GM, Benson RC. The conformity of a soft contact lens on the eye. J Biomech Eng 1996;118:341–8.
43. Stapleton F, Tan ME, Papas EB, Ehrmann K, Golebiowski B, Vega J, Holden BA. Corneal and conjunctival sensitivity to air stimuli. Br J Ophthalmol 2004;88:1547–51.

**Meng C. Lin**
*Clinical Research Center*
*School of Optometry*
*University of California, Berkeley*
*Berkeley, CA 94720-2020*
*e-mail: mlin@berkeley.edu*