The TFOS International Workshop on Contact Lens Discomfort: Report of the Subcommittee on Epidemiology

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See the tables in the Introduction for the members of the TFOS International Workshop on Contact Lens Discomfort.

The first citation in PubMed referencing the issue of comfort with contact lenses is a paper from 1960 linking hygienic contact lens care and comfortable lens wear.[1] Unfortunately, not all contact lens wearers are able to achieve acceptable comfort; and while tremendous developments in lens polymers, designs, replacement modalities, and care regimens have occurred over the past 50 years, the challenge of preventing or managing contact lens discomfort (CLD) is still common in clinical practice. Our limited understanding of the etiology and the correlation between signs and symptoms makes it more difficult for eye care practitioners (ECPs) to diagnose and manage CLD.

It has been estimated that there are currently more than 140 million contact lens wearers worldwide (Nichols JJ, written communication, 2013). It is much more difficult to estimate the number of individuals who have previously worn contact lenses and then abandoned lens wear as a result of CLD. Studies have reported that between 12% and 51% of lens wearers "drop out" of contact lens wear,[2–6] with CLD remaining the primary reason for discontinuation.[2,4]

EPIDEMIOLOGY

The World Health Organization defines epidemiology as "The study of the distribution and determinants of health-related states or events (including disease), and the application of this study to the control of diseases and other health problems."[7] While CLD is not considered a disease, it cannot be denied that it is a health-related state, which can have profound consequences for contact lens wearers, ECPs, and the ophthalmic industry. Contact lens wearers who persistently experience discomfort with their lenses may initially reduce their daily wearing time to cope with the condition; this could be followed by wearing lenses less frequently and ultimately discontinuing lens wear altogether.[2,4]

HISTORICAL CONTEXT

There has been increased interest in and reporting of CLD in the literature. A PubMed search for "contact lens" in the title or abstract fields elicited 7024 responses. When "comfort" or "discomfort" was added to the search terms, 406 reports resulted. If these data are broken down by decade, 2.6% of contact lens papers in the 1970s referred to comfort/discomfort in the title or the abstract (a similar percentage for the 1980s), rising to approximately 7.5% of the relevant literature since 2000.

Review of the literature suggests that there have been discrete periods of research interest in CLD. Since lens types,

modalities, and care regimens have changed radically over the past 25 years, it is important to reference the era in which data were collected when discussing the epidemiology of CLD. Much of the work reported in the 1980s and 1990s sought to describe the frequency and related symptomatology in CLD (Vajdic CM, et al. *IOVS* 1996;37:ARVO Abstract 5178).[8–13] With perhaps one notable exception,[14] work focusing on the determinants of CLD has been largely conducted over the last 15 years,[15–24] although few fully controlled studies have been undertaken. Around the turn of the millennium, the relevance of contact lens hydration and dehydration to CLD was reported by a number of authors.[25–29] Although silicone hydrogel lenses were introduced into the market in 1999, information on the effects of these materials (and directly or indirectly, their enhanced oxygen transmission characteristics) on CLD was reported only beginning in 2005.[30–36]

Even though lens storage systems have been a longstanding and fundamental part of contact lens wear, their impact on CLD and related phenomena has been primarily reported in the last 10 years,[37–45] with only a few earlier reports. More recently, studies investigating the possible benefits of "sustained-release" comfort-enhancing agents from daily disposable lenses have been reported.[46–48]

SCOPE OF REPORT

The goals of the Epidemiology Subcommittee of the CLD Workshop were to (1) provide a clinical context of CLD and to differentiate this condition from dry eye that can occur in both contact lens and non–contact lens wearers; (2) report on the frequency of CLD; (3) investigate the factors that are associated with CLD; (4) examine the impact of CLD from both a quality of life and economic perspective; and (5) consider future research directions for evaluating the epidemiology of CLD. The emphasis of this report is on CLD as a symptom, not as a sign, and on CLD that is not due to a specific pathophysiology to which it could otherwise be attributed.

The objective was to focus on associations that have been reported from clinical and epidemiological studies. The report was not intended to expound on the mechanistic or etiological considerations of CLD that are described in detail in the other workshop subcommittee reports. The epidemiology of CLD with disposable soft lenses was primarily considered within a historical context with respect to other lens types where relevant.

CLINICAL CONTEXT: THE CLINICAL PICTURE OF CLD

Eye care practitioners are all too familiar with patients presenting with the symptoms and sometimes the associated signs of CLD. However, the clinical picture of CLD is not as well represented in the literature as are the subjective and objective attributes of dry eye.

SYMPTOMS OF CLD

While the generic symptom "discomfort" may be the most frequently cited reason for discontinuing contact lens wear, what the term "discomfort" actually means to individuals is more complex. Reporting of CLD symptoms may be influenced by personal factors such as the motivation to wear contact lenses and personal economics. For example, patients who dislike wearing spectacles are less likely to complain about their contact lenses and may be more tolerant of their lenses. Creative approaches to this potential bias include subjective

assessment of symptoms in real time via text messaging and e-mail prompts on handheld Web-enabled devices.[49,50]

Dryness

In 1986, McMonnies and Ho[51] identified contact lens wear as a provocative factor in what was termed "marginal dry eye." Since then the frequent clinical use of the terms "contact lens induced dry eye" and "contact lens induced dryness" suggests that a sensation of "dryness" is the common interpretation of such discomfort. Dryness appears to diminish when lenses are removed[52] and to change during the wearing period, with increased symptoms observed in the afternoon and evening.[52–55]

Other Symptoms in CLD

Receptors on the ocular surface do not respond to dryness per se. The perception of symptoms of contact lens–related discomfort is complex and likely results from interactions across multiple psychophysical channels. The neurobiological mechanisms underlying perception of symptoms are discussed in the report from the Neurobiology of Discomfort and Pain Subcommittee. Other than dryness, "scratchy" and "watery" sensations have been reported 52% and 30% of the time, respectively, in daily hydroxyethyl methacrylate (HEMA) contact lens wearers.[56] Other symptoms have also been reported. Among a sample of 83 adapted contact lens wearers, blurry vision was a frequent symptom. Scratchiness and irritation were infrequent symptoms, and light sensitivity and eye soreness were seldom experienced.[54] In a large population-based study of dry eye (2500 subjects including some contact lens wearers), blurred vision was found to be the most commonly reported symptom.[57]

In a cross-sectional study examining the differences between spectacle wearers and those wearing rigid gas-permeable contact lenses (RGPCL) and soft contact lenses (SCL), there were no significant differences in the frequency of ocular symptoms between the SCL and RGPCL wearers, and the most common symptom was tired eyes. Symptoms of tiredness, itchiness, watering, pain, aching, excessive blinking, and burning had similar rates of occurrence for all three groups. However, symptoms of dryness and self-reported redness were reported more frequently in contact lens wearers compared to spectacle wearers.[13]

CLINICAL SIGNS IN CLD

The published literature contains many references to traditional clinical tests that may be helpful in the diagnosis of CLD. These include assessment of the pre-lens tear film,[16,58–60] meibomian glands,[61] bulbar and limbal hyperemia,[62] and corneal and conjunctival staining.[63–65] A recent multicenter study conducted by Young and colleagues[66] in the United States and Canada specifically investigated which tests commonly undertaken in ECP offices are helpful in the diagnosis of contact lens dryness. The symptomatic participants exhibited a wide range of clinical signs accompanying their CLD, but there was not one single common sign that was present in all participants. However, poor lens wetting was reported in 40%, and 39% of participants had rapid pre-lens noninvasive tear breakup times (NITBUT) and preocular fluorescein breakup times (FBUT). Further detailed discussion of the clinical signs reported to be associated with CLD can be found in the reports by the Contact Lens Interactions with the Ocular Surface and Adnexa and the Clinical Trial Design and Outcomes Subcommittees.

THE RELATIONSHIP BETWEEN SYMPTOMS AND SIGNS IN CLD

In populations with dry eye disease, the lack of association between clinical signs and symptoms is frequently reported.[67,68] The most common clinical signs have also been demonstrated to be poorly correlated with symptoms in CLD,[68] but this may be a reflection of the tests employed. Investigating symptoms in SCL wearers is likely to have more diagnostic value than conducting clinical tests. This is supported by Young and colleagues,[66] who reported that 23% of the symptomatic participants did not exhibit typical clinical signs of dryness. A set of tests combining both subjective and objective assessments may be more predictive for CLD or dryness than a single diagnostic test.[60,69]

DEFINITIONS FOR DRY EYE AND CLD

Dry eye disease is a common clinical presentation in eye care offices. The Tear Film & Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) report of 2007 established the working definition: "Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface."[70] The prevalence of dry eye disease varies with populations and the working definitions of dry eye and runs as high as 33%.[57,71-74]

Contact lens discomfort is also a common clinical presentation in contact lens practice and is found in greater numbers than dry eye itself.[75-77] The definition of CLD as set out by the Definition and Classification Committee is as follows: "Contact Lens Discomfort (CLD) is a condition characterized by episodic or persistent adverse ocular sensations related to lens wear either with or without visual disturbance, resulting from reduced compatibility between the lens and ocular environment, which can lead to decreased wearing time and discontinuation from lens wear."

HOW DO CLD AND DRY EYE INTERACT?

Clearly, the entities of dry eye and CLD can intertwine. Clinical wisdom suggests that those patients who have traditional signs and symptoms of dry eye disease are more likely to have CLD when fitted with contact lenses.[53] In addition, as the presence of dry eye disease increases with age,[78] it is likely that in some individuals not diagnosed with dry eye at the time of fitting, their CLD may instead be a manifestation of acquired dry eye disease.

HOW ARE CLD AND DRY EYE DIFFERENT?

There are many individuals without signs or symptoms of dry eye who suffer irritation when wearing their contact lenses and note relief with lens removal.[52] As reported in the recent study by Young and colleagues,[66] 23% of the subjects with CLD had no signs of dry eye. Conversely, practitioners often have patients with significant signs of dry eye who report being able to wear their contact lenses comfortably. The insertion of a contact lens introduces numerous factors that may be related to CLD, including surface deposits and wettability, disturbance of the tear film, stimulation of eyelids, oxygen availability, the trapping of debris under lenses, the loss of tear film under lenses, interaction of the lens material and design with the ocular tissues, interference with the blink, and the use of care solutions and lubricating drops. A single factor or a combination of these entities may contribute to CLD.

DIFFERENCES IN SYMPTOMS BETWEEN CLD AND DRY EYE

It is interesting to note the differences in the symptoms between dry eye and CLD. The ocular surface sensations that individuals experience are related to the innervation of the cornea, conjunctiva, and lids[79-81] and are discussed with respect to CLD in the report by the Neurobiology of Discomfort and Pain Subcommittee. Many questionnaires have been used to document the specific symptoms reported by individuals with dry eye and CLD. Using the McMonnies questionnaire, patients with dry eye most commonly reported symptoms of "dryness," "grittiness," and "burning."[82] Holly[83] related that in dry eye, "sandy" and "gritty" feelings were most common along with "burning" and a "foreign body sensation." In contrast, "dryness" is reported as the most common symptom in contact lens wearers, followed by "scratchiness" and "watery eyes."[54,56] There can be distinct differences between the symptoms reported by dry eye sufferers and those of contact lens wearers experiencing CLD.[52] Contact lens wearers report symptoms more frequently and with increased intensity late in the day.[76] Surprisingly, older contact lens wearers have been shown to experience fewer symptoms as they age compared to dry eye patients.[73,84,85]

DIFFERENCES IN SIGNS BETWEEN CLD AND DRY EYE

Dry eye patients can present with no observable signs of dry eye; however, most have some combination of low Schirmer scores, ocular surface staining, low tear breakup times, low tear meniscus heights, high tear osmolarity, and meibomian gland dysfunction (MGD).[70] Contact lens discomfort patients may have some of these characteristics, but they are often absent. Objective findings specific to CLD may relate to lid changes including lid wiper epitheliopathy (LWE).[86] Corneal staining has been associated with the use of some care systems and contact lenses,[38] although some amount of corneal staining is considered normal in contact lens wearers.[87]

In summary, patients with dry eye are more likely to have contact lens–related symptoms of discomfort. However, a significant number of contact lens wearers who suffer from CLD show no signs of dry eye disease. Clinicians have a difficult job in determining which factors have caused CLD and establishing if they are patient or contact lens related.

THE SPECTRUM OF CLD

As with many diseases and conditions, CLD is reported with varying levels of intensity, which may or may not impact the patient's contact lens wearing patterns. A representation of this "spectrum" of CLD is presented in Figure 1 in the report of the Definition and Classification Committee. However, it is important to recognize that some individuals may not progress from one "stage" to the next in a sequential manner. A large proportion of individuals may report symptoms of CLD and could be considered to be "strugglers." These individuals may continue to wear their lenses despite their discomfort, possibly with the use of contact lens rewetting drops or artificial tears.[53] Some wearers who are struggling with CLD may choose to decrease their daily wearing time, particularly if they experience increasing discomfort as the day progresses. Simply removing lenses has been anecdotally reported to greatly relieve CLD for many individuals. Decreased wearing time may

be followed by a decrease in the number of days each week that lenses are worn (the wearing frequency), and both of these behaviors have been reported by dissatisfied lens wearers.[4] A natural progression is from less frequent lens wear to extended periods when lenses are not worn at all. Temporary discontinuation of lens wear has been reported in the literature by several authors.[2,3,5,6] Unfortunately, the most dissatisfied contact lens wearers will eventually become former lens wearers with permanent discontinuation from lens wear, often called "dropout."[2,3]

FREQUENCY OF CLD

In order to gain a better understanding of CLD, it is important to recognize how often the condition occurs in the population. Clarification of the terminology that is used to report this problem is necessary. In some studies, "counts" are used to report the number of individuals who experience symptoms associated with CLD. "Incidence" is generally used to report the number of new cases of a condition that develop in a population within a specified period of time, and may not be the most appropriate term to use when referring to how often contact lens wearers experience discomfort. "Prevalence" is the term usually used in the contact lens literature and in this case represents the number of people who experience CLD in a defined population. "Frequency" is an overarching term that is used to describe counts, prevalence, and incidence.

ASSESSMENT METHODS AND EVALUATION OF CLD

As discussed earlier, CLD is primarily reported according to symptomatology as opposed to the observation of signs. While the precise etiology of CLD is yet to be determined, the use of symptoms as outcome measures is appropriate because it relates directly to the patients' experience with contact lenses and the motivation to seek and use treatment, regardless of the presence of observable signs. The frequency and intensity with which these symptoms are reported can be assessed with the use of questionnaires. McMonnies[82] and McMonnies and Ho[88] developed a questionnaire to evaluate, in part, ocular discomfort symptoms and reported its use in individuals wearing and not wearing lenses. A number of questionnaires have been developed to assess dry eye symptoms in non–lens wearers[89-91]; however, the first questionnaire developed specifically to assess symptoms in contact lens wearers was the Contact Lens Dry Eye Questionnaire (CLDEQ).[53,54] Both the McMonnies and CLDEQ questionnaires have been used as assessment tools in studies of CLD.[55,82] A short version of the CLDEQ has been reported to be more accurate in predicting CLD and better at discriminating a contact lens–related dry eye diagnosis than McMonnies' questionnaire. Using the full model parameters for the CLDEQ there appears to be a predictive efficiency of 1.50, with a sensitivity of 83% and specificity of 67%.[55] More recently, a revised version of the CLDEQ has been developed, the CLDEQ-8.[92] The scores from the CLDEQ-8 have been shown to correlate well with baseline CLD status and to be capable of measuring changes in CLD scores associated with refitting with different contact lens materials.[92]

POPULATION-BASED CLD STUDIES

Contact lens discomfort is commonly encountered in clinical practice and frequently reported in the literature. However, few studies have addressed the frequency of CLD in a natural population setting, as most studies investigate its occurrence in clinical practices or hospital settings. A PubMed search employing the keywords "contact lens discomfort," "population study," and "epidemiological study" revealed no prospectively designed epidemiological studies investigating the natural occurrence and evolution of CLD, dryness, or related symptomatology associated with contact lens wear in a population-based setting for adapted contact lens wearers or in individuals who started wearing contact lenses for the first time. Most of our knowledge of the magnitude of CLD in population-based investigations comes from epidemiological studies designed specifically for the investigation of the prevalence of dry eye disease. However, the majority of these studies were conducted in older populations, and contact lens wear was infrequently reported.

The first population-based dry eye study to investigate dry eye symptoms in contact lens wear was conducted in Canada in the mid-1990s.[71] The purpose of the Canadian Dry Eye Epidemiology Study (CANDEES) was to determine the overall prevalence and severity of dry eye symptoms in a population ranging in age from younger than 10 years to older than 80 years and to obtain details regarding possible associated factors. In total, 13,517 questionnaires were returned, with 24.3% of these (3285) from contact lens wearers. Overall, 50.1% of the contact lens wearers had dry eye symptoms compared to 21.7% of the respondents who did not wear contact lenses.

More recently in the Japanese Koumi study, 2791 residents completed a dry eye questionnaire; 105 were contact lens wearers.[93] Contact lens use was found to be associated with a composite outcome of clinically diagnosed dry eye disease or severe symptoms of dry eye disease. The prevalence of severe dryness symptoms in contact lens wearers was found to be 28% in males and 35% in females. In another epidemiological study investigating the prevalence of dry eye disease among 3433 high school students, contact lens wear was reported by 1298 of the respondents; and, compared to findings in non–contact lens wearers, contact lens wear was associated with a significantly higher prevalence of severe dry eye symptoms (37%) in both boys (odds ratio [OR], 4.14; 95% confidence interval [CI], 3.42–5.00) and girls (OR, 4.68; 95% CI, 3.02–7.26).[94] A recent, similarly designed study from Shandong Province, China, reported a prevalence of dryness symptoms in 8.4% of the 1885 high school students evaluated and 32.8% of the 122 contact lens wearers.[95] In another study designed to estimate the prevalence of dry eye disease among 3549 Japanese office workers using visual display terminals (1349 contact lens wearers), contact lens wearers were more likely to report severe symptoms of dry eye (prevalence, 50.4%).[96]

It is important to recognize that there may be significant differences in the prevalence of CLD according to geographical location. The only population-based studies reported in the literature were conducted in Canada, Japan, and China; the results from these studies are summarized in Table 1.

CLINICAL PRACTICE/HOSPITAL–BASED CLD STUDIES

Although population-based studies are preferred in epidemiological research, more studies of CLD are performed in clinical practice, office, or hospital settings. Studies in these settings do not require the resources and complex sampling techniques that are required for population-based studies yet are still able to provide insight into symptoms of discomfort and dryness, which continue to be the most commonly cited reasons for discontinuation of contact lens wear.[2-6] Table 2 summarizes the prevalence of CLD that has been reported in clinical and research-based studies in the preceding quarter of a century. The results of such studies in limited populations may not be generalizable, and there may be issues of sampling, appropri-

TABLE 1. Prevalence of CLD From Population-Based Studies

Study	Location	Number of Contact Lens Wearers	Age	Sex	Symptom Assessment	Prevalence	References
CANDEES study	Canada	3285	10–80 y	Not reported for contact lens wearers	Presence or absence of dryness and severity rating	Overall: 50.1%	Doughty et al., 1997[71]
Koumi study	Japan	105	≥40 y	Male 24%, female 76%	Severe symptoms of both ocular dryness and irritation	Male 28%, female 35.0%	Uchino et al., 2011[93]
Japanese VDT users study	Japan	1390	≥22 y	Male 60%, female 40%	Severe symptoms of both ocular dryness and irritation	Overall: 50.4%	Uchino et al., 2008[96]
Japanese high school students study	Japan	1298	15–18 y	Male 77%, female 23%	Severe symptoms of both ocular dryness and irritation	Male 36.8%, female 37.4%	Uchino et al., 2008[94]
Chinese senior high school students study	China	122	Not mentioned	Not mentioned	Severe symptoms of both ocular dryness and irritation	Overall: 32.8%	Zhang et al., 2012[95]

ateness of controls, and other biases, which need to be considered in their interpretation.

In 1986, McMonnies and Ho[51] were the first to report that soft lens wearers had more frequent symptoms of dryness than both non–lens wearers and hard contact lens wearers. Brennan and Efron[56] conducted the first study to specifically investigate the extent of symptoms of discomfort associated with wearing soft HEMA lenses and to correlate patient and lens factors with these symptoms. A total of 104 SCL wearers in the contact lens clinic at the University of Melbourne, Australia, reported how frequently they experienced symptoms during contact lens wear. Dryness was the most frequently reported symptom; 75% of the patients surveyed reported experiencing this symptom to some extent.

Almost a decade passed before the next publication appeared in the literature reporting the prevalence of symptoms of discomfort during contact lens wear. In a study designed to investigate the preocular tear film characteristics of SCL wearers, Guillon and colleagues[97] in the United Kingdom assessed symptomatology with the McMonnies questionnaire and reported that 44% of the 184 SCL wearers in their study were symptomatic for CLD. Another study was conducted in Australia at a similar time involving 171 SCL wearers and 48 RGPCL wearers.[14] Once again, the lens wearers were asked to report the frequency of ocular symptoms: 13% of SCL wearers and 23% of RGPCL wearers experienced dryness either often or constantly.

With the exception of the dry eye study conducted by Doughty and colleagues[71] in 1997, the first studies to specifically report on the prevalence of CLD in North America started to appear in the literature in the year 2000. Begley and colleagues[54] reported a prevalence of dryness of 37% and evening discomfort during contact lens wear of 37% in a population of 83 patients in a private optometry office in Toronto, Canada. The questionnaire used in this study was the precursor to the CLDEQ. A larger study soon followed, conducted in optometric practices in Canada and the United States, the results of which were published in 2001 and 2006.[52,53] In this study 367 contact lens wearers (83% SCL, 17% RGPCL) completed the original CLDEQ. Ocular discomfort was reported by 79% of respondents and dryness by 77%. A study conducted during a similar time frame at the University of Waterloo in Canada used the Dry Eye Questionnaire (DEQ) to evaluate symptoms in presbyopes wearing SCLs and reported dryness in 68% of the study participants.[98]

Guillon and Maissa[75] conducted an additional larger study to evaluate dry eye symptomatology of lens wearers in the United Kingdom and reported their findings in 2005. In their study, 502 SCL wearers completed the McMonnies questionnaire; and overall, 43% reported dryness, with 28% reporting these symptoms to be moderate to severe compared to 15% in the age-matched nonwearers. About the same time, Nichols and colleagues[76] used a survey to evaluate self-reported dry eye disease and dryness symptoms across refractive modalities. They reported that 53% of the 393 contact lens wearers responded that they thought they had dry eye, and 68% reported symptoms of dryness while wearing their lenses.[76] After controlling for age and sex, the authors reported that contact lens wearers were 12 times more likely than emmetropes and five times more likely than spectacle wearers to report dry eye. This survey was followed by the Contact Lens and Dry Eye Study (CLADES). In this study Nichols and Sinnott[60] employed the CLDEQ and reported a prevalence of dry eye of 55.3% in a cohort of 360 contact lens wearers (91% SCL, 9% RGPCL).

The first study in the literature that investigated the prevalence of ocular surface symptoms in a sample of more than 1000 SCL wearers was reported in the literature in 2006.[99] This study was conducted across the United States and Canada in 82 optometry and two ophthalmology offices. Overall, 28% of respondents reported symptoms of dryness, 17% discomfort, and 31% reduced comfortable wearing time.

In a study conducted by Richdale and colleagues[4] that was designed to determine the frequency and factors associated with contact lens dissatisfaction and discontinuation, 453 current and lapsed SCL and RGPCL lens wearers completed a self-administered survey in which they reported the presence or absence of a series of symptoms while wearing contact lenses. Overall, 73% reported at least one symptom, with 76% of the reported symptoms being dryness and 67% discomfort. Thirty-five percent of the current wearers also reported dissatisfaction with their lens wear. In a smaller study

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TABLE 2. Prevalence of CLD From Clinical Practice/Hospital–Based Studies

Study	Location	Number and Type of CL Wearers	Age	Sex	Symptom Assessment	Prevalence	References
Marginal dry eye diagnosis: history versus biomicroscopy	Australia	177 non-CL 163 SCL 160 rigid	Not reported	Not reported	Dryness, grittiness, burning, soreness, scratchiness (McMonnies questionnaire)	CL wearers reported symptoms more frequent than non-CL; SCL > rigid	McMonnies and Ho, 1986[51]
Symptomatology of HEMA CL wear	Australia	104 SCL	24 ± 9 y	Male 48% female 52%	Self-reported often or seldom	Dryness 75%	Brennan and Efron, 1989[96]
Preocular tear film characteristics	United Kingdom	184 SCL	31 ± 7 y	Male 46% female 54%	McMonnies questionnaire	44% symptomatic	Guillon et al., 1997[97]
Frequency of ocular symptoms	Australia	171 SCL 48 RGP	17–67 y	Male 33% female 67%	Self-reported often or constantly	Dryness 13%–23% (SCL-RGP)	Vajdic et al., 1999[13]
Responses of CL wearers to a dry eye survey	Canada	68 SCL 15 RGP	18–78 Average 41 ± 13 y	Male 31% female 69%	Questionnaire (preliminary version of CLDEQ)	Dryness 37% evening discomfort 37%	Begley et al., 2000[54]
Optometric practices in North America	United States and Canada	305 SCL 62 RGP	18–94 Average 39 y	Male 36% female 64%	CLDEQ Ocular discomfort Dryness Visual changes	Ocular discomfort 79% dryness 77%	Begley et al., 2001[53]; Chalmers and Begley, 2006[52]
Symptoms in presbyopes following 6 mo lens wear	Canada	141 SCL	40–71 Average 51.5 ± 6.3 y	Male 21% female 79%	DEQ	Dryness 68%	du Toit et al., 2001[98]
Dry eye symptomatology of SCL wearers	United Kingdom	502 SCL	17–69 Average 34 ± 10 y	Male 33% female 67%	McMonnies questionnaire	43% (28% moderate to severe symptoms)	Guillon and Maissa, 2005[75]
Self-reported dry eye disease across refractive modalities	United States	393 (type not reported)	Average 30.3 ± 10.7 y	Male 33.9% female 66.1%	Self-reported dry eye Dryness (occasionally to constantly)	Dry eye 52.7% dryness (occasionally; frequently; or constantly) 68.1%	Nichols et al., 2005[76]
CLADES	United States	327 SCL 33 RGP	Average 31.1 ± 11.5 y	Male 32% female 68%	CLDEQ	55.3%	Nichols and Sinnott, 2006[60]
Prevalence of ocular surface symptoms in CL wearers	United States and Canada	1092 SCL	18–42 Average 28 y	Male 30% female 70%	CLDEQ	Dryness 28% discomfort 17% reduced comfortable WT 31%	Riley et al., 2006[99]
Frequency and factors associated with CL dissatisfaction and discontinuation	United States	453 (current and lapsed SCL and RGP wearers)	Average 32.1 ± 11.0 y	Male 36% female 64%	Self-administered survey presence/absence of symptoms	73% reported one or more symptoms (76% dryness, 67% discomfort) 35% of current wearers reported dissatisfaction	Richdale et al., 2007[4]
Symptoms of CL wearers using VDTs, Portugal	Portugal	71 SCL	19–38 Average 24.9 ± 5.5 y	Male 31% female 69%	Presence/absence of symptoms	Symptoms often 24%	Gonzalez-Meijome et al., 2007[100]
CL dryness symptoms in UK wearers	United Kingdom	932 SCL	<20 to >61 y	Male 30% female 70%	CLDEQ (modified scoring)	Dryness 31% (plus marginal 13%)	Young et al., 2011[101]

CL, contact lens; WT, wearing time.

conducted in Portugal, the prevalence of CLD was investigated among 71 SCL wearers who were using visual display terminals (VDTs). Symptoms were reported to occur "often" by 24% of the study participants.[100]

The majority of studies investigating the prevalence of CLD were conducted prior to the widespread use of contemporary contact lens materials. However in 2011, Young and colleagues[101] reported on the prevalence and factors associated with contact lens–related dryness in a large cohort of contact lens wearers in the United Kingdom. The CLDEQ was self-administered to 932 SCL wearers at 12 clinical sites; 37% were wearing silicone hydrogel lenses and 30% daily disposable lenses. Both frequency and late-day intensity of dryness were considered in the analysis of the results. Overall, 31% of the wearers reported dryness consistent with contact lens–related dry eye (CL-DE) with a modified scoring technique, and 13% reported marginal CL-DE. The class of lens materials was not significantly related to CL-DE status. Further discussion of the possible role of lens material and replacement frequency on the prevalence of CLD is provided in the section on lens-related factors and the TFOS Subcommittee report on materials, design, and care.

In those who continue to wear contact lenses, the prevalence of CLD and dryness symptoms in the literature has been remarkably consistent, with rates averaging around 50% (Table 2). This is significantly greater than the rates that have been reported in non–lens wearers.[13,55,71,75,102]

Factors Associated With CLD

In contrast to dry eye and other ocular diseases, relatively little is known regarding the factors that may be associated with CLD. This section discusses the literature evidence for factors relating to the patient, the contact lenses, and the environment in which they are worn.

Patient-Related Factors

Nonmodifiable Factors Associated With CLD. *Sex*. The evidence supporting a strong association for sex effects in CLD is mixed. Chalmers and colleagues[52] evaluated 1054 patients with a mean age of 39 years for symptoms of CLD. Using the CLDEQ, they found no difference in either the frequency or intensity of dryness associated with contact lens between males and females. Young and colleagues[101] also reported on dryness symptoms in 932 SCL wearers across the United Kingdom (ages ranging from younger than 20 to older than 61 years). In agreement with Chalmers and colleagues, sex was not associated with dry eye status in contact lens wearers. In contrast, du Toit and colleagues[98] reported a sex effect in their study of 150 neophyte and established presbyopic contact lens wearers aged 40 and older. Using the DEQ to assess dryness symptoms, they reported that females had higher overall dryness ratings and experienced more frequent symptoms than males. In addition, Nichols and Sinnott[61] showed, in the 360 lens wearers in CLADES, that female sex was associated with contact lens dry eye status, even after controlling for confounding factors. Similarly, González-Meijome and colleagues[100] evaluated 71 contact lens wearers within an academic population and concluded that females were more likely to report symptoms of scratchiness compared to males. Riley and coworkers[99] also reported on 1092 established soft lens wearers, from two ophthalmology and 82 optometric practices in North America, ranging from 18 to 39 years of age. In their study, patients were separated into one of two groups using the CLDEQ, "problem patients" and "problem-free patients." In the problem patients group, there was a

statistically significant increase in the proportion of women compared to the problem-free group. Lastly, in CLADES, Nichols and Sinnott[60] showed that female sex was predictive of contact lens dry eye, after controlling for multivariate factors.

While studies indicate that women may be more likely to report symptoms of contact lens dryness and discomfort, female sex does not appear to be a consistent factor relating to lens dropout. Pritchard and colleagues[3] reported on 1444 surveys completed by established and lapsed lens wearers in Canada and found no association between male or female sex and lens discontinuation. More recently, Dumbleton and colleagues[2] surveyed 4207 patients across Canada and again found no difference in sex distribution between current and lapsed wearers. In contrast to these reports, Richdale and colleagues[4] surveyed 730 subjects from a university-based population and identified male sex as a significant factor associated with lens discontinuation. The findings from this latter study may reflect differences in motivation to continue lens wear as opposed to sex differences leading to discomfort.

Age. Age has been shown occasionally to be associated with CLD. The strongest piece of evidence supporting an association between age and symptomatic contact lens wear stems from a study by Chalmers and colleagues,[103] who reported that dryness associated with contact lens wear was inversely correlated with age, with more symptoms reported by younger wearers.[52] In contrast to non–contact lens wearers with dry eye, dryness was greatest in patients 20 to 40 years old and reported less often in the older age groups. Similarly, in the presbyopic study by du Toit and colleagues,[98] the authors reported that younger wearers (40–51 years old) experienced dryness 1.4 times more frequently than older wearers (52–71 years old). In 882 young adults recruited from various clinical sites in North America, Chalmers and colleagues[103] reported that hydrogel lens wearers had more frequent dry eye symptoms, increasing as a function of age up to 35 years old. However, this age effect was not evident for silicone hydrogel lens wearers. Since more silicone hydrogel wearers in this study reported a previous dry eye diagnosis than hydrogel wearers, the authors speculated that the silicone hydrogel lens cohort likely included unsuccessful hydrogel patients who had been refitted with silicone lenses, potentially confounding the relationship between lens dryness and age in this latter group. Lastly, Nichols and Sinnott[60] did not show age to be related to contact lens dryness in CLADES when controlling for multiple other factors.

Ethnicity. In contrast to dry eye, where there is an increased incidence of disease in Hispanic and Asian populations,[84] a clear association between ethnicity and CLD has not been identified.[60] A steeper corneal curvature in Chinese subjects has been shown to adversely affect lens fit for SCL.[104] Differences in tears, including a reduced tear volume and changes in rheological properties, have also been reported for Asians compared to non-Asians (Lin M, Svitova T. *IOVS* 2010;51:ARVO E-Abstract 4155).[105] While these differences may impact lens comfort and dryness symptoms, there are no definitive studies that establish a linkage between them.

Poor Tear Film Quality/Quantity. Expert clinicians argue that, in a prefitting examination, reduced tear volume, shortened breakup time, and reduced tear production, as measured by Schirmer tests, are predictors for symptomatic contact lens wear. Evidence provided by Glasson and colleagues[59] support that the tear film of contact lens wearers is important in understanding CLD and achieving success with lens wear. In their early study, they evaluated 10 soft lens wearers, split equally into tolerant and nontolerant groups. Comfort was assessed using the McMonnies questionnaire. The

results of this pilot study indicated that tolerance was associated with tear breakup time and tear flow rate, with tolerant wearers demonstrating greater tear stability and faster tear flow. In a subsequent study to further examine these findings, 38 tolerant and intolerant lens wearers were assessed for clinical changes in tear film before and after lens wear.[16] For the purposes of this study, the authors defined patients as intolerant if they were able to wear lenses for only 6 hours or less; comfort symptoms were once again assessed using the McMonnies questionnaire. Baseline patient characteristics that were correlated with tolerance to lens wear included the maximum blink interval, NITBUT, pattern of tear film breakup, phenol red thread test, and tear meniscus area and height. The authors concluded that the tear film of tolerant and intolerant wearers is different in the absence of a contact lens.

Blink Rate and Completeness of Blinking. Little evidence exists to support an association between changes in blink rate and comfort with lens wear. It has been proposed that longer blink intervals and incomplete blinking may lead to drying of and deposits on the front surface of the lens during wear.[106] However, wear of noncontemporary lens materials has been reported to increase blink rate when compared to that of non–lens wearers.[107] It is theorized that an increased blink rate occurs as a result of irritation of the eyelid and/or ocular surface during lens wear. A recent study by Ishak and colleagues[108] confirmed a lens-induced increase in blink rate in subjects wearing contemporary silicone hydrogel and hydrogel lens materials. Using video recordings, blink rate was measured at baseline and after 1 and 2 months of lens wear. After 2 months, the mean blink rate was found to be 20 and 22 blinks per minute for silicone hydrogel and hydrogel lens wearers, respectively, which was significantly increased compared to 15 blinks per minute for the non–lens-wearing controls. There was no difference in the completeness of the blink between groups.

The impact of blink rate on CLD becomes important during near tasks in which concentration can negatively influence blink rate. Jansen and coworkers[109] reported on 15 established soft lens wearers and determined the interblink interval with and without lenses during listening to music compared to playing a video game. Only non–lens wearers demonstrated the expected increase in the interblink interval associated with a near task, while the interblink interval in lens wearers was not significantly altered. Contact lens wearers did, however, show greater tear breakup than non–lens wearers, which correlated with lens discomfort. These findings suggest that changes in tear film stability during the blink may be a more important parameter influencing lens wear than blink rate. In support of this view, Bitton and colleagues[110] further evaluated tear film changes that occur in the interblink interval during lens wear. Using optical coherence tomography, the authors investigated changes in tear meniscus height in 25 soft lens wearers and 25 non–lens wearers. After approximately 9 hours of lens wear, a reduction in tear meniscus height and volume during the interblink interval was moderately associated with grittiness. No correlation was evident for dryness. While this is suggestive of a relationship between tear film changes during the interblink interval and CLD, these findings should be interpreted with caution, as the lenses were removed prior to performance of tear meniscus measurements.

Systemic Disease. There is very little evidence in the literature to indicate that systemic disease impacts comfort or dryness symptoms during contact lens wear. One study evaluated a potential relationship between systemic factors (including thyroid conditions, diabetes, hypertension, cancer, heart disease, osteoporosis, and arthritis) and contact lens dry eye, but failed to detect any significant associations.[60] However, a subsequent study did report an association between polycystic ovary syndrome and contact lens intolerance.[111]

Seasonal Allergies. Patients with seasonal allergic conjunctivitis have been shown to have alterations in the tear film and ocular surface.[112] In a study by Chalmers and Begley,[52] symptoms of dryness were investigated in 367 current contact lens wearers using the CLDEQ. In this cohort, 42.6% of wearers reported a positive history for seasonal allergies. However, this was a not a factor associated with dryness during lens wear. In contrast to this, Nichols and Sinnott[60] reported on 360 patients who completed the CLDEQ. In their univariate analysis, they reported that dryness was statistically associated with seasonal allergies, but this was not significant in the final multivariate model. Two other reports investigated the use of topical antiallergy agents in enhancing comfort in patients with seasonal allergies. The first evaluated the use of olopatadine hydrochloride 0.1% ophthalmic solution in 20 SCL wearers who had a history of allergic conjunctivitis without any current signs or symptoms.[113] Patients were treated with a single drop of the study medication or a placebo control prior to lens insertion and then underwent allergen challenge. There was a significant improvement in comfort for patients undergoing treatment at all time points, and reported wearing time was longer. In a second study, the effects of epinastine 0.05% ophthalmic solution on contact lens comfort in patients with current seasonal allergies was evaluated in daily SCL wearers over a 7-day period.[114] For this study, 76 patients received the test agent, and 71 received the placebo control. Similar to what occurred in the prior study, use of the test agent resulted in enhanced comfort and a 1.33 hours per day increase in comfortable wearing time. Collectively, these findings indicate that, at least for a subset of allergy sufferers, the ocular response to seasonal allergies may be associated with reduced lens comfort.

Modifiable Factors Associated With CDL. *Medication.* There are several early reports in the literature of contact lens intolerance in women using oral contraceptives.[115-117] However, Brennan and Efron[56] were the first to report a relationship between the use of systemic medication and CLD in SCL wearers. In their study of 104 soft lens wearers, use of oral contraceptives was shown to be statistically associated with symptoms of scratchiness and dryness. In support of this work, Chen and colleagues[118] investigated symptoms of dry eye in 97 women using the Symptom Assessment in Dry Eye (SANDE) and Ocular Surface Disease Index (OSDI) questionnaires. Of the 48 contact lens wearers evaluated, the authors found that there was a significant increase in dry eye symptoms in patients who reported using oral contraceptives. In contrast to this study, in a sample of 360 contact lens wearers, Nichols and Sinnott[60] reported that use of over-the-counter pain medication was associated with contact lens dry eye status. However, there was no statistical association with any other systemic medication, including oral contraceptives, hormone replacement therapy, and antihistamines.[60] Fraunfelder and coworkers[119] evaluated 2379 possible adverse events relating to the use of isotretinoin. All reports received prior to March 1999 were compiled and sent to the National Registry of Drug-Induced Ocular Side Effects for review. The likelihood of adverse events arising from the use of isotretinoin was determined using the World Health Organization definitions for causality assessment of suspected adverse reactions. In total, the authors found 38 documented cases of intolerance to contact lens wear after initiation of drug use. From this study, decreased tolerance to contact lens wear was classified as a "certain" clinical event. While dry eye was also classified as "certain," a small percentage of dry eye cases were determined to be permanent. The long-term effects of isotretinoin use on CDL have not been established.

Diet, Hydration, and Alcohol Intake. Factors such as diet, hydration status, and alcohol intake have been shown to be associated with dry eye, but few studies have begun to investigate the relationship between these factors and CLD. Kokke and colleagues[120] evaluated the effects of omega-6 fatty acids taken orally for the treatment of contact lens–associated dry eye. Evening primrose oil containing gamma-linolenic acid and linoleic acid was given six times a day to 76 females wearing frequent-replacement soft lenses over a 6-month period. Participants were classified as symptomatic for contact lens–induced dry eye using the McMonnies questionnaire. After 6 months of treatment, dryness during lens wear had improved. Lazon de la Jara and colleagues[121] also investigated the effects of oral omega-3 supplements on comfort during contact lens wear in a non–placebo-controlled study. In this study, 45 patients were assessed for ocular comfort during lens wear over a 6-week treatment period. While the authors found a significant improvement in end-of-day comfort in non–lens wearers, this effect was not evident while wearing lenses.[121] Ramamoorthy and colleagues[22] evaluated the effects of alcohol consumption on CL-DE as part of a larger, cross-sectional survey involving 360 patients. While the percentage of patients reporting dry eye the day after alcohol consumption was increased, this finding was not statistically significant. There are no available data on the effects of adequate hydration on CLD.

Smoking. Ward and colleagues[122] investigated the effects of passive cigarette smoke exposure on the ocular surface and tear film in SCL wearers. The authors observed that even brief passive cigarette smoke exposure significantly destabilized the tear film and resulted in an increase in the vital staining scores in both contact lens wearers and nonwearers. While acute smoke exposure caused only an insignificant increase in symptom visual analogue scale scores in contact lens wearers, the authors concluded that repeated and/or chronic smoke exposure would likely be associated with significant symptomatology. This is an issue that needs to be addressed in future studies.

Cosmetics. Expert clinical evidence suggests that use of specific soaps, lotions, and cosmetics may contribute to CLD. While practitioners frequently express concern with respect to the use of these products by contact lens wearers, there is little scientific evidence available to support their role in CLD. A recent study by Luensmann and colleagues[123] assessed the effects of commonly used cosmetics (including mascara, hand lotion, and eye makeup remover) on the physical parameters of silicone hydrogel lenses in vitro, but assessment of CLD was not part of the study design.

Compliance. Dumbleton and colleagues[124] reported on the effects of patient compliance with the manufacturers' recommended replacement frequency on lens comfort. This observational study consisted of 1344 patients from 158 ECPs in the United States. All patients were established silicone hydrogel lens wearers and replaced lenses at either 2-week or 1-month intervals. Patients were asked to complete an anonymous survey regarding both their replacement frequency and comfort with current lenses. Patients were considered noncompliant if lenses were worn for more than 17 days for 2-week replacement lenses and more than 31 days for 1-month replacement lenses, irrespective of whether or not the lenses had been prescribed based on the manufacturer's recommended replacement schedule. The authors found that patients who reported poor compliance with replacement frequency had both reduced comfort and vision ratings at the end of the day and when lenses needed to be replaced compared with compliant patients.

Psychological/Fatigue. Psychological factors, including end-of-day fatigue, have been suggested as causative factors for CLD. In a recent article by Santadomingo-Rubido and colleagues,[49] the authors evaluated ocular surface comfort in 88 subjects including contact lens and non–contact lens wearers. The study findings indicated that end-of-day comfort was reduced in all subjects, regardless of lens status. While they provided no definitive evidence to support it, the authors speculated that ocular and/or physical fatigue might contribute to end-of-day symptomatology. In CLADES, Nichols and colleagues[125] also evaluated mood or affect as it relates to contact lens dry eye—including both positive and negative scales of affect using the Positive and Negative Affect Schedule (PANAS). In this study, they showed neither dimension of affect to be related to contact lens dry eye. Other psychological factors may contribute to CLD, such as a potential for a poor initial fitting experience. However, there is not sufficient evidence to support this theory.

Summary of Patient-Related Factors. The evidence from the literature supports some occasional but not entirely consistent patient-related factors as associated with CLD, including female sex, younger age, poor tear film quantity and quality, seasonal allergies, and the use of some systemic medications. However, there is little evidence to support that ethnicity, blink rate and blinking patterns, systemic disease, diet, alcohol, smoking, cosmetic use, or psychological factors play a role in CLD.

Factors Secondary to Lens Wear. Contact lens wear has been shown to be associated with a decrease in pre-lens tear film thickness[60,126] and stability,[17,26,66,127,128] increased tear osmolality,[24] loss or shortening of the meibomian glands,[61,129] alterations in corneal sensitivity,[130,131] and cellular changes in the corneal and conjunctival epithelia.[132-135] These changes and their potential impact on CLD are described in detail in the reports from the Contact Lens Interactions with the Ocular Surface and Adnexa Subcommittee and the Contact Lens Interactions with the Tear Film Subcommittee. In a recent publication, Young and colleagues[66] reported that approximately one-quarter of symptomatic wearers do not have any clinical signs. This suggests that etiologies other than changes to the ocular surface and tear film are responsible.[66] A subsequent study by Spyridon and colleagues[136] investigated 2154 established contact lens wearers who were grouped into either a sensitive eye or a nonsensitive eye category. The authors found that patients with sensitive eyes were more likely to report symptoms of dryness without any accompanying clinical signs than nonsensitive eye patients. The intermixing of different patient groups such as those classified as "sensitive" or patients with undiagnosed or subclinical dry eye etiologies may mask the identification of true clinical factors associated with CLD.

Environmental Factors. Although clinical experience may suggest that many environmental factors can impact the comfort of contact lenses, the literature is mostly devoid of good evidence to support this. There are a number of observational studies and larger surveys, but only a few small well-controlled trials. Often, multiple environmental factors are changing at the same time, making conclusions about specific effects more difficult.

To characterize the problems facing contact lens wearers, Young and colleagues[137] surveyed 496 hydrogel contact lens wearers in the United States, and reported their comfort ratings in challenging environments such as high altitude, airplanes, dusty or polluted or smoky environments, low humidity, windy conditions, and air-conditioned or heated cars. A high percentage of survey participants (varying between approximately 40% and 70%) self-reported comfort challenges while wearing their contact lenses in such environments. These data

represent the perceptions of the patients surveyed, as they were acquired from the patient's memory rather than during the actual challenging activity or environment. These data represent a snapshot of the issue at hand, but do not clearly make a definitive link between the specific environmental condition and CLD.

Low Humidity. A few well-controlled experiments that studied the effect of humidity, specifically low-humidity environments (defined in most studies as relative humidity [RH] lower than 30%), have contributed to a body of evidence that supports this factor as clearly connected to CLD. Observational studies first suggested this relationship with increased CLD, deposits, and tear breakup time when the RH in the subject's workplace was lower than 31%.[12] This original study suggested lens deposition as a major factor and was conducted prior to the advent of frequent-replacement and daily disposable lenses. Although lens deposition has not been eliminated in contemporary disposable lenses, it is much reduced compared to that with conventional (nonreplaced) lens wear.

Environmental effects have been studied more recently in controlled environmental chambers where humidity, temperature, and, in some cases, wind speed can be well controlled and varied.[100,138–140] Maruyama and colleagues[139] compared tear meniscus height and tear interferometry patterns, NITBUT, and symptoms in subjects who wore hydrogel contact lenses and those who did not wear lenses. A controlled adverse environment, where temperature and RH were well controlled and recorded, was used for the study. As air temperature and RH were concurrently decreased, there was no change in meniscus height (as a measure of tear volume), but the pre-lens tear film thinned, NITBUT decreased, and subjective dryness scores increased. The results suggested that the symptoms of CLD are related to pre-lens tear film thinning (rather than a reduction in tear volume), and that temperature and RH together can contribute to the effect.

In another controlled environmental chamber experiment, Gonzáles-García and colleagues[138] studied subjects with minimally symptomatic dry eye, defined as subjects who reported only dry eye with contact lenses and who were otherwise healthy. The researchers exposed their subjects to controlled temperature and reduced humidity (20°C, 20% RH) for 2 hours with and without hydrogel contact lenses and then exposed them to a more "normal environment" with similar temperature and higher humidity (24°C, 34% RH). Subjects were instructed to perform a standardized task (reading) during the experiment (wind was not introduced into the environment). Symptoms and signs were exacerbated by the low-humidity environment with and without contact lens wear, providing perhaps the most compelling evidence that low RH is a key environmental factor that influences CLD. The authors of this experiment also concluded that in normal humidity, contact lenses can act as a stressor and can induce symptoms not noted in non–contact lens wearers.

These findings are supported by the work of Guillon and Maissa,[141] who studied tear evaporation using a closed environment (goggle-type apparatus) around the eyes, where temperature and RH were well controlled. Their experiment, which involved 379 subjects in total, evaluated tear film evaporation of contact lens wearers 1 day after lens removal compared to non–contact lens wearers. The authors defined normal RH as 40% (range, 35%–45%) and low RH as 30% (range, 25%–35%). The tear evaporation rate with contact lenses at higher RH was similar to the precorneal tear film evaporation of nonwearers at low RH. The authors concluded that contact lenses stress the tear film system and that their experiment supported increased tear evaporation as a mechanism for CLD. Other authors have studied lens dehydration in

controlled adverse environment (CAE) conditions, and have not found bulk water loss from hydrogel lenses to be impacted by extremes of low RH and temperature, supporting surface evaporation and tear thinning as potential mechanisms for CLD.[29,139]

More recently, the effects of controlled simulated wind, along with temperature and low RH, on contact lens wearers' symptoms and measurable ocular signs (tear evaporation, osmolarity, and breakup time) were studied in hydrogel and silicone hydrogel daily disposable lens wearers.[140] Thirty-one subjects participated in the experiment, which involved just 20 minutes in a CAE at 18°C with a very low RH of 18%. Wind flow, controlled with fans blowing at the research subjects at wind speeds of 1.2 m/s, was an added environmental factor mimicking the conditions of a dry, windy day. Subjects wearing the hydrogel contact lenses showed more worsening of both subjective symptoms and clinical signs in the CAE conditions than those wearing silicone hydrogel lenses. Blink rate increased significantly with hydrogel lens wear but not with silicone hydrogel lens wear, suggesting that the subjects were reacting to induced environmental stresses. These authors measured a reduction in tear meniscus height with the hydrogel lens wearers, acknowledging that this finding differed from the results of Maruyama and colleagues.[139] The introduction of wind to this specific experiment was suggested as a probable reason for the difference and further suggested wind and airflow as additional factors that exacerbate evaporation from the ocular surface.

Temperature. Although it is hypothesized that increased temperature would increase tear evaporation and lead to increased CLD,[142] there does not appear to be a well-controlled study that has looked at varying only temperature while keeping RH constant.

Climate. The connection between CLD and climate is well known clinically, with discomfort symptoms increasing in desert (hot and dry) or arctic (cold and dry) conditions compared to tropical climates. However, it is likely that low humidity is the main factor in such situations, perhaps aggravated by the addition of wind flow; but there are no well-designed or controlled studies conducted outdoors to substantiate the clinical experience.

Pollution and Air Quality. Although approximately 70% of hydrogel contact lens wearers in the survey conducted by Young and colleagues[137] in 2007 reported that they were "always or frequently" uncomfortable in contact lenses in smoky environments, there is little additional evidence that connects smoky environments with CLD. Eng[9] cited smoky aircraft cabins as an occupational hazard for flight attendants who wore contact lenses. In these circumstances, low-humidity cabin air was almost certainly also a factor; and this study, published in 1979 when smoking was still common in aircraft cabins, does not represent the contemporary challenge of contact lens wearers.[9] In a later study, Vajdic and colleagues[13] surveyed contact lens wearers and spectacle wearers. They did not find that smoking (as opposed to a smoky environment) had a significant effect on the reporting of ocular symptoms. They also did not find a difference in the frequency of reporting symptoms between wearers of rigid gas-permeable and soft lenses, suggesting low sensitivity of the data collection methods used.

Occupational Factors. Airline crew members unquestionably work in an environment with low humidity and sealed air circulation. In 1982, Eng and colleagues[10] set up a laboratory on a McDonnell Douglas DC-10 flying between Oakland, California, and Honolulu, Hawaii. They recorded a decline in humidity from 47% to 11% within 30 minutes of takeoff and

concluded that low cabin humidity is likely the most significant factor in discomfort for contact lens wearers during flight.

The majority of today's office workers use computers; the use of VDTs with contact lens wear has been shown to increase symptoms of "scratchiness."[100] The number of hours of VDT use has also been associated with an increase in "burning sensations" in contact lens wearers.[100] These findings have been supported by additional studies in which office workers who wore contact lenses and spent more than 4 hours engaged in VDT work had a lower tear meniscus volume with significant dry eye and visual symptoms.[143] Other researchers have reported more than 4 hours per day of VDT use to be a risk factor in dry eye disease, and contact lens wear to be an additional risk factor.[96] The mechanism involved is believed to be related to the reduced blink rate that occurs during VDT work, which reduces tear spreading, and the longer interblink interval that allows contact lens surface drying, leading to increased lid sensation and symptoms.[144]

Air Conditioning and Heating/Internal Environments. One study has reported that symptoms associated with discomfort increase in contact lens wearers in environments that are air conditioned or heated.[100] It is thought that this may be due to variations in humidity or airflow rather than temperature alone. Others have surveyed occupants of office buildings and reported that 29% complained of ocular discomfort, although this survey was not specifically conducted in contact lens wearers.[145] In this study, the investigators measured various aspects of indoor air quality including carbon dioxide, formaldehyde, temperature, and humidity. The same authors also evaluated air quality in aircraft and recommended optimal conditions for RH and temperature of cabin air of 40% to 60% and 20°C to 24°C, respectively.[146]

Altitude/Atmospheric Pressure. Experiments to evaluate the effect of low atmospheric pressure and simulated high altitudes were conducted by Castren[147] and Castren et al.[148] in 1984 and 1985 (these studies were specifically interested in aviation). In a first experiment, Castren[147] used a decompression chamber with 560 millibars of pressure (similar to that expected at an altitude of 4000 meters above sea level). Contact lens comfort was negatively impacted, although there was no control of RH in this experiment and it was conducted in a very low RH environment (20%–22%). The same author conducted an additional experiment ($n = 7$ subjects) in which only atmospheric pressure changed.[148] The subjects spent 4 hours in a decompression chamber where atmospheric pressure was lowered from the normal value of 1000 millibars (750 mm Hg) to 560 millibars (420 mm Hg). Keeping other key factors constant, such as humidity and temperature, subjects were tested with and without contact lenses. All subjects wearing contact lenses suffered subjective ocular discomfort, and some developed objective signs. The control group without contact lenses did not develop any symptoms during the test. The authors concluded that the effects were caused by hypoxia.

Summary of Environmental Factors. It is evident from the literature that CLD symptoms can occur due to an increased tear evaporation rate from the lens surface brought about by a reduction in RH. In addition to RH, variables such as air movement (wind) and blink rate–altering visual activities, such as VDT use, may exacerbate signs and symptoms of CLD. There is little solid evidence to support or dispel the connection between other environmental factors such as temperature, altitude, smoky environments, air conditioning or indoor heating, and CLD, although clinically, many of these factors are reported as stressors to contact lens wearer comfort. Any variation in the prevalence of CLD in different geographical regions due to climate or seasonality is not supported by solid evidence, and is likely secondary to the effects of humidity and wind.

Impact or Morbidity of CLD

Contact lens discomfort can have profound effects for the patient, the ECP, and ophthalmic industry. The impact on each of these constituents is considered in turn.

The Patient. As described earlier, contact lens wearers who experience CLD may respond in a number of different ways depending on the frequency and severity of their symptoms. Initially they may simply report CLD as an occasional inconvenience, but do not adjust their wearing habits as a consequence of it. With greater severity or frequency, however, individuals may start to struggle with their lens wear and reduce the number of hours each day and days each week during which they wear lenses.[2,4] Ultimately, periods of time may pass when these "strugglers" temporarily discontinue lens wear; a proportion of these may permanently drop out of lens wear and either wear spectacles or undergo refractive surgery.

There is good evidence that discontinuation from contact lens wear is more complex than the situation in which a lens wearer uses lenses for a period of time and then ceases wear permanently. In the most detailed assessment of the "natural history" of lens wear reported in the literature, Pritchard and colleagues[3] described their survey of over 1400 contact lens wearers who had used lenses for an average of 5 years. One-third of their sample reported ceasing lens wear on at least one occasion, but 77% of this discontinuing group started using contact lenses for a second time. Approximately half of this resuming-wear group then stopped using contact lenses for a second time, but again, most commenced lens wear for a third time. Dumbleton and colleagues[2] report a similar pattern in 4207 current and lapsed lens wearers, with 40% reporting lapsing for a period of at least 4 months. However, although 62% resumed lens wear, 32% eventually discontinued lens wear. These findings demonstrate that many contact lens wearers enter and exit the market repeatedly over a few years. This suggests that these wearers have periods during which lens wear is successful, meeting their daily requirements, but eventually they may discontinue wear, often due to CLD.

Quality of Life. Contact lens discomfort can interfere with a patient's everyday life, whether this is during daily activities or work. Clinical assessments and measurements are often unable to evaluate these important aspects relating to CLD and the ultimate success of patients with contact lenses. Therefore alternative methods of evaluating patient-reported outcomes might be extremely important. Research investigating patient-centered outcomes is widespread in health care and can be used both to identify patients needing particular attention and to assess the results of interventions.[149] These quality of life (QOL) assessments have been mainly used in ophthalmic research to compare different types of vision correction.[150-154] Pesudovs and colleagues[155] specifically developed a QOL questionnaire for contact lens wearers. Quality of life assessments have also been used to investigate the impact of dry eye,[89,156] but have not been widely used to assess the impact of CLD. One study was conducted by Jutai and colleagues,[157] in which a psychosocial assistive devices scale was reported to be able to predict retention and discontinuation of contact lens wearers, although the specific reasons for discontinuation were not evaluated.

Economic Impacts. In discussions of the economic impact of CLD and discontinuation from contact lens wear, the consequences for the ECP and the industry are always considered, while little attention is given to the contact lens wearer. Contact lens wearers who experience CLD may initially try to alleviate their symptoms by simply purchasing

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over-the-counter lubricating drops. When this approach does not provide sufficient relief, they may visit their ECP for advice and possible refitting with alternative lens types. There are no reports in the literature on the actual costs to the patient; these cannot be ignored and could be substantial when the patient's time is also taken into account.

The Eye Care Practitioner

Contact lens discomfort is a regular and ongoing problem in eye care practices. Somewhere between 50% and 94% of contact lens–wearing patients present with problems related to their contact lenses.[53,71,75,76] Of equal importance are those patients who no longer return to the office because of dissatisfaction or silently discontinue lens wear. In the United States, it has been estimated that 3 million contact lens wearers drop out of lens wear each year.[15] While there is very little evidence of the effects of CLD on patient retention at ECP offices, chair time, and overall economic impact to the ECP, there is value in discussing the possible influence of CLD on these factors.

Patient Retention. The problem of patient retention is critical to the ECP. Practitioners see themselves as problem solvers and pride themselves in providing their patients with contact lenses that afford good visual acuity and comfort. A significant amount of time is spent fitting lenses, teaching patients to handle and care for lenses, and optimizing lens and solution choices. When patients subsequently present with CLD, the complexity of this clinical entity requires much time and effort on the part of both patients and practitioners. The differential diagnosis of the etiology of symptoms includes dry eye disease,[53] lens fit and movement,[158] lens dehydration,[26,159] protein and lipid deposits,[127,160] solutions used in cleaning and storing,[161,162] tear osmolarity,[24] and wearing time and replacement schedules.[46] To understand the cause in each particular individual requires a full analysis of the ocular surface and the contact lens/solution interactions. Ideally one change at a time should be made to determine the cause of the patient's CLD, but this can require multiple visits with expensive and time-consuming refits. Patients may become discouraged and simply drop out of lens wear.

Patient Evaluation. In order to process the presenting problem of CLD, a thorough history must be undertaken that includes details of wear time, care and handling, replacement schedules, work habits, and the patient's environment. This should be followed by a careful evaluation of the contact lenses on the eye: movement, centration, lens condition, and pre-lens tear breakup time. Removal of the lenses will then allow for a full tear film and ocular surface assessment that ideally includes tear flow testing with Schirmer or phenol red thread tests, fluorescein staining of the cornea, tear film breakup time, lissamine green staining of the conjunctiva, and an investigation of the superior tarsal conjunctiva, along with any other dry eye tests that the practitioner feels appropriate, including tear osmolarity, tear meniscus height, and looking for conjunctivochalasis. There are two important issues to consider concerning the validity of these tests and observations: the fact that the patient has just removed his or her contact lenses and the poor association between CLD and ocular signs.[66] Ideally the dry eye workup should be conducted after the patient has stopped lens wear for some days. However, this adds further chair time, requiring several hours or days in the quest to determine the cause and solve the problem of CLD.

Economic. Practitioners often find that the time and expense of trying to solve CLD are a detriment to their income. The dropout rate of patients whose CLD is not solved is also an economic burden to the practitioner. There is not much evidence in the literature concerning the magnitude of the economic impact of CLD on the ECP. Rumpakis[163] estimated that a single patient dropping out of lens wear could result in a lifetime loss of income of almost \$20,000. Another study has reported that contact lens patients are 60% more profitable for the ECP than patients who wear only spectacles.[164] Further research into CLD should help to reduce the prevalence and economic burden of CLD for patients and practitioners.

The Contact Lens Industry

Contact lens discomfort can also have a significant impact on the investment in research and development and product development within the contact lens industry.

Impact of Product Technology Advances. Over the last several decades, the contact lens industry has seen continuous improvement in contact lens technology. The introduction of soft and frequent-replacement contact lenses, the advancement of silicone hydrogel lenses, and the development of improved care regimens raised the expectations that these novel products would address issues related to contact lens wear and improve the overall lens wearing experience. While there is certainly evidence to suggest improvement, it remains unclear if these enhancements have impacted the prevalence of CLD, the primary complaint associated with contact lens discontinuation.[2-5]

Several factors impede the ability to show significant improvements when one compares newer lens technologies. First, lenses of any unique material have exclusive properties with respect to dehydration, oxygen transmission, deposition profile, fit, modulus, and surface qualities. Any clinical trial utilizing available lenses is constrained by the fact that these features are predetermined by the lens material and cannot be studied in isolation.[138] Consequently, multiple factors change with each product introduction, making it difficult to isolate the factors that may be responsible for improvement. An additional potential confounding factor, the lens care regimen, is rarely controlled for in lens studies and often ignored in the analyses. In a survey conducted in Canada and the United States, 47% of contact lens wearers reported that removing their lenses provided a complete resolution of their CLD.[53] Therefore, for approximately half of those surveyed, there appeared to be other confounding factors contributing to CLD.

Impact on the Contact Lens Market. Despite technological advances in lens designs, materials, and lens care solutions, approximately 25% of contact lens wearers eventually discontinue lens wear, primarily as a result of CLD.[2,4,49] Nichols[165] has recently reported that growth in the actual number of contact lens wearers in the United States has been consistently flat for the past several years, with as many people discontinuing contact lens wear as people entering the market. The same report indicated that several of the larger contact lens markets have shown little growth over the last 10 years, although in the United States there was a trend toward modest growth in 2012, with new technologies in silicone hydrogel, daily disposable, and multifocal lenses believed to be responsible.

Understanding that the impact that CLD has a significant effect on the industry, it is not surprising that contact lens and contact lens solution companies fund a great deal of the research in this area. Of the papers referenced in this section, nearly 80% were sponsored by industry.

FUTURE RESEARCH DIRECTIONS

As reviewed above, CLD is a major issue for contact lens wearers, practitioners, and industry alike. A major deficiency in the literature is the lack of information derived from contact lenses that differ in only one parameter. While it remains

impossible to conduct prospective studies of this form with marketed products, the community would greatly benefit from an analysis of custom-made lenses that would allow for the generation of such a dataset. This would require significant input (and financial investment) from one or more lens manufacturers, but would represent a major advance in our understanding.

An alternative approach that can be used is to collect data from *noninterventional* or *registration* trials. Rather than using a very careful a priori clinical study design, such approaches derive their power from the large number of data points that they can accrue. Assuming that the key clinical data are collected in a consistent manner (which may or may not be the case), appropriate statistical modeling could be employed to determine the relationship between various lens-related factors and CLD. Noninterventional trials do require a wide mixing of all lens parameters such that each combination is represented within the collected dataset. In fact, this remains a significant problem within the contact lens area because any single manufacturer tends to offer only a small range of parameters, often with great similarity, so achieving the desired range across all lens types is likely to be difficult.

SUMMARY AND CONCLUSIONS

The epidemiological assessment of CLD faces many challenges, not least of which is the accurate assessment of the prevalence of the condition. The tools used to diagnose CLD and the expectations of contact lens wearers themselves continually change, making it difficult to draw conclusions over time and to compare results from multiple studies. There are few validated instruments for assessing comfort in contact lens populations, and these tend to produce data that are highly variable, as most rely on a patient's recall. In addition, the lack of postmarket surveillance studies, which would address many of the issues related to CLD, prevents us from drawing meaningful conclusions regarding the impact of technological advances on this issue. Future epidemiological work designed to clarify the natural occurrence and evolution of CLD in rural or urban population-based settings in various countries and races appears to be very much needed to enrich our understanding of CLD, since it is such a common clinical complaint.

Unfortunately, CLD remains a demanding problem affecting short- or long-term success with contact lens wear. Lens wearers address the problem mostly by removing their lenses—a relatively inconvenient measure that may suggest ineffective use of current treatments. In the near term, clinicians and researchers in the clinical field should continue to manage contact lens–related dryness through thoughtful choice of lens material, lens care, and rewetting systems, along with assessment of patient-related risk factors, management of environmental triggers, and other associated factors that may contribute to dryness symptoms.

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