Dry Eye: Age-related Prevalence, Correlation Between Symptoms and Diagnoses, and Significant Associations

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Abstract

This Canadian study determined the prevalence of dry eye (DE) symptoms and clinical diagnosis over the human lifespan, the correlation of symptoms with a diagnosis, and factors associated with DE. Data were abstracted from WatES, a retrospective file review (n=6397) of patient examinations at the University of Waterloo Optometry Clinic. The prevalence of DE symptoms and diagnosis were determined overall, in five-year age groups and for individual symptoms. With the use of logistic regression, each symptom was analyzed for a significant association with a DE diagnosis. Ocular and systemic factors and common medications were analyzed for associations with DE symptoms or diagnosis. Among all of the patients (0-93 years), 543 (8.5%) presented with DE symptoms. With respect to age groups, the highest prevalence was seen for patients aged 30<35 (11.4 %) and 75<80 years (13.7 %). DE was diagnosed in 1140 patients (17.8%). The prevalence increased by 3.0% per year of age. No sex-related differences in meibomian gland dysfunction (MGD) as a function of age were found. Less than half (43.5%) of symptomatic patients were diagnosed with DE. The following symptoms were associated with a DE diagnosis: dryness (OR= 7.56, 5.30-10.77 95% CI), injection (OR=3.62, 2.04-6.43 95%CI), burning/stinging/soreness (OR=2.67, 1.69-4.23 95%CI), and watery eyes/tearing (OR=1.66, 1.12-2.45 95%CI). Anterior blepharitis (OR=2.46, 2.05-2.95), female (OR=1.24, 1.06-1.40 95%CI), contact lens wear (OR=1.34, 1.06-1.70 95%CI), and environmental allergies (OR=1.18, 1.00-1.41 95% CI) were significantly associated with a diagnosis of DE. This study is unique in that it covers the entire human lifespan for dry eye diagnosis, symptoms and MGD and provides data on the prevalence of dry eye in Canada.

KEY WORDS:
dry eye diagnosis, dry eye symptoms, meibomian gland dysfunction, prevalence, risk factors

Dry eye represents a significant concern for many people in terms of its visual and physical ramifications. This multifactorial disease of the ocular surface causes a decrease in tear film homeostasis, resulting in symptoms and visual disturbance.[1,2] Dry eye has been shown to have a negative impact on many important tasks of daily living and quality of life.[3-7] As a result, a significant amount of research is being dedicated to understanding the pathogenesis of dry eye and developing more effective therapies.[8] Determining the frequency and risk factors of a disease is essential for understanding both the problem and the effectiveness of treatments. The reported prevalence of dry eye in large epidemiological studies varies from 5% to 58%,[5,6,9-26] depending on the population studied, the age group included, the clinical tests used and the definition of dry eye. Some prevalence studies included objective findings,[6,16,19-22,25,27] while others relied on patient reports of practitioner diagnosis.[15,16,18,28,29] Almost all of these studies have used self-reported symptoms, and participants had to have at least one or two symptoms to be considered as having dry eye. Although the symptoms included in these lists are variable, there is considerable overlap. Surveys were frequently used to achieve large numbers of participants, compared to performing examinations, and symptoms were considered to be a more repeatable measure than traditional clinical tests.[10,12,20,30] A poor correlation between reported symptoms and clinical test findings has been suggested in the literature.[9,10,13,20,30-32]

The epidemiology subcommittee for the first International Dry Eye Workshop (DEWS 2007) report reviewed the literature and reported compelling evidence for some risk factors, but found that evidence for other risk factors was inconsistent and warranted further study.[31] Age is a well-known risk factor for dry eye,[11,13,17,31] and most data regarding the prevalence of dry eye have only included people over 39 years of age.[6,19,20,22,24-29] A few studies from Asia, the United Kingdom, and the United States have included participants in early adulthood, with prevalence reported in 10-year (or greater) age groups.[5,14-16,18,23] A more detailed analysis of the impact of age on the prevalence of dry eye could provide important information for understanding the natural history of the disease. Meibomian gland dysfunction (MGD) is considered to be the leading cause of evaporative dry eye and is thought to be less symptomatic than dry eye in general.[2,9] The DEWS II report estimated that the prevalence of MGD increased by 5.3% per decade, but stated that information on the impact of sex and age on MGD is limited and encouraged further study in this area.[9]

The DEWS II report also recommended that epidemiological studies should be performed in other geographical areas.[9] At the time of their review, most of the data were from the United States, Europe and Asia. Canadian data are scarce, and there has been only one other Canadian study to date.[12] In 1997, Doughty et al. published the results of a large survey (n=13,517) from optometric practices across Canada (CANDEES) and gave estimates of the prevalence of dry eye in patients of all ages in 10-year age categories. They solicited yes/no responses to various "symptoms of dry eyes". These symptoms were not broken down into any specific qualifiers (grittiness, dryness, etc.). In their study, 28.7% of patients who responded to the survey had dry eye symptoms. A bimodal distribution of prevalence across age was found, with peaks in the 21–30 year age group (38.1%) and in the oldest patients (40.8% at 80+ years). That study did not report dry eye-related clinical findings or diagnoses from optometrists.

Besides age, many other factors have been investigated for possible associations with dry eye. Factors that show the most consistent evidence include female sex, hormone replacement therapy, contact lens wear, systemic antihistamine use, antidepressant use, and connective tissue disease.[9] While there is evidence that other medications may be associated with dry eye, further study is required.[10,13,31,33] Whereas diabetes, refractive surgery and ocular allergies are considered to be probable risk factors,[9] the associations for other factors including smoking, gout, oral contraceptives and menopause are unclear.[10,13,31,33]

The purposes of this study were to determine 1) how often commonly related symptoms of dry eye present in clinic patients, 2) how often dry eye is diagnosed through clinic testing, and 3) how these two factors are correlated with each other and with age, and 4) to identify risk factors associated with dry eye symptoms or clinical diagnosis.

METHODS

Data used for this investigation, including patient age, sex, presenting chief complaint and dry eye-associated symptoms, ocular health including a history of ocular surgery, and systemic health including smoking, contact lens wear, and current medications, were abstracted from the Waterloo Eye Study (WatES) database. The methods for creating the WatES database, population representation, reliability of data abstraction and missing data rates have all been reported previously.[34] In brief, 6,397 clinic files were reviewed retrospectively for patients (age range: 0–93 years) examined at Primary Care or Paediatric clinics between January 2007 and January 2008 at the University of Waterloo, Optometry Clinic. Data from specialty clinics were not included. There were no other exclusion or inclusion

criteria. Intra- and inter-abstractor reliability were high for all of the abstracted data. Patient demographics were representative of Canadian optometric private practices in terms of age distribution and percentage of females (54.1%). This study was approved by the University of Waterloo, Office of Research Ethics.

The dry eye-associated ocular symptoms abstracted were intended to be reasonably exhaustive of factors in previous dry eye surveys: ocular dryness, burning/stinging/soreness, foreign body sensation/grittiness, itchiness, watery eyes/tearing, crusting/sticky lids, photosensitivity, blinking/transient blur/fluctuating vision, and ocular injection (red eyes).[31] In children under the age of 3, parental reports of redness, watery eyes/tearing, blinking, rubbing eyes (indicating discomfort), and crusting/sticky lids were abstracted due to the limited ability of young patients to report symptoms. The prevalence of each of these symptoms was determined for the entire study group. The prevalence of one or more of these symptoms was determined for five-year age groups across the entire lifespan.

Patients were classified as having a diagnosis of dry eye if dry eye, MGD or tear film dysfunction was recorded as a diagnosis in their clinic file. The frequency of a dry eye diagnosis was determined overall and for each five-year age group. The percentage of patients with symptoms who had a diagnosis of dry eye was calculated. While controlling for patient age, sex and other symptoms, each symptom was analyzed for a significant association with a diagnosis of dry eye through a logistic regression analysis. The percentage of patients diagnosed with dry eye who also presented with symptoms was determined. Each health condition and medication type was analyzed for an association with dry eye symptoms as well as a clinical diagnosis of dry eye while controlling for patient age and sex using a logistic regression analysis. Finally, a diagnosis of MGD alone was considered as a subset of a diagnosis of dry eye and age-related prevalence, sex difference and symptom rates were determined. Statistical significance was set at $p \leq 0.05$ with 95.0% confidence intervals for odds ratios.

RESULTS

Overall, 543 WatES patients (8.5%) reported symptoms that are commonly associated with dry eye. The most common symptom reported was a sensation of ocular dryness followed by watery eyes/tearing and then burning/stinging/soreness (Table 1). Dry eye symptoms were noted throughout childhood and adolescence (<20 years) at an average prevalence of 5.1% (Figure 1). In early adulthood, the prevalence of symptoms increased to a peak of 11.4% in 30<35-year-old patients. After 50 years of age, the prevalence of symptoms began to increase again to a maximum value of 13.7% in 75<80-year-old patients. There were 1140 WatES patients (17.8%) with a clinical diagnosis of dry eye. The odds of being diagnosed with dry eye increased at a rate of 3.0% per year of age (OR=1.03, 1.03–1.03 95% CI) and age was directly related to the prevalence of a clinical diagnosis of dry eye (Figure 1).

Figure 1: *Percentage of WatES (N=6397) patients in five year age groups with dry eye diagnosis and with dry eye symptoms. The number of patients in each age group is noted above the data.*

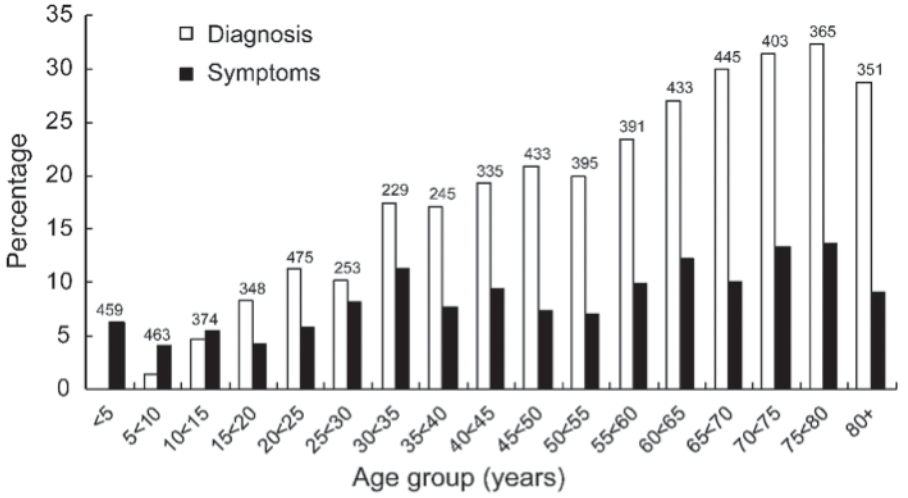


Table 1: *Symptoms of patients in the WatES database*

Symptom	A	B	C	
	# (%) Pts with the symptom	# (%) Pts with a diagnosis who had the symptom	% Pts with the symptom who had a diagnosis	OR (95% CI)
Ocular Dryness	164 (2.6)	109 (9.6)	66.5	7.56* (5.30–10.77)
Watery eyes / Tearing	143 (2.2)	56 (4.9)	39.2	1.66* (1.12–2.45)
Burning /Stinging / Soreness	106 (1.7)	51 (4.5)	48.1	2.67* (1.69–4.23)
Ocular Itch	70 (1.1)	35 (3.1)	50.0	1.69 (0.95–3.00)
Photosensitivity	68 (1.1)	10 (0.9)	14.7	0.53 (0.25–1.14)
Ocular Injection	65 (1.0)	33 (2.9)	50.8	3.62* (2.04–6.43)
Foreign Body Sensation / Grittiness	56 (0.9)	22 (1.9)	39.3	1.40 (0.77–2.53)
Blinking / Transient Blur / Fluctuating Vision	30 (0.5)	6 (0.5)	20.0	1.42 (0.51–3.98)
Crusting / Sticky lids	23 (0.4)	11 (1.0)	47.8	1.87 (0.75–4.64)
Any of the above	543 (8.5)	236 (20.7)	43.5	3.83* (3.15–4.65)
Total N	6397	1140	% (B/A)	

Number (#) and percentage (%) of WatES patients (total N=6397): A. patients presenting with a symptom related to dry eye, B. patients with a symptom and a clinical diagnosis of dry eye (N=1140), and C. the percentage (%) of patients with a symptom who had a diagnosis, and the Odds Ratio (OR) and 95% confidence interval (CI) of patients presenting with a symptom of dry eye who had a clinical diagnosis of dry eye.

Pts, patients * $p<0.05$

Of the patients with symptoms (N=543), 236 (43.5%) were diagnosed as having dry eye. Most of the patients (66.5%) presenting with ocular dryness were diagnosed with dry eye and, after controlling for patient age, sex and other symptoms, ocular dryness was strongly associated with a diagnosis of dry eye (OR=7.56, 95% CI 5.30–10.77). Ocular, burning/stinging/soreness and watery eyes/tearing were moderately associated with a diagnosis of dry eye (Table 1). Conversely, most of the patients (79.3%) who were diagnosed with dry eye did not report symptoms. Of those who did, ocular dryness was the most common symptom, followed by watery eyes/tearing, burning/ stinging/soreness, ocular itch, ocular injection, and foreign body sensation/grittiness (Table 1).

As seen in Table 2, even when controlling for age, female patients had 24% greater odds of presenting dry eye symptoms as well as being diagnosed with dry eye (OR=1.24, 1.08–1.42 95% CI) compared to male patients. Female patients accounted for 320 (58.9%) of those reporting dry eye symptoms and 662 (58.1%) of those diagnosed with dry eye. Furthermore, females contributed significantly more to the initial peak in symptoms (14.9% females in the 30<35 year age group compared to 7.4% males). When only those with a diagnosis of MGD (N=713) were considered (Figure 2A), the rate of MGD increased at a rate of 3.0% per year (OR=1.03, 1.03–1.03 95% CI) with no sex effect (OR=1.00, 0.85–1.17 95% CI). In comparison, for those diagnosed with dry eye without MGD (N=427) (Figure 2B), females had 63% greater odds of being diagnosed with dry eye than males (OR=1.63, 1.33–2.01) when controlling for age. This suggests that factors other than MGD cause sex-related difference in dry eye diagnostic rates. For the MGD subset, 72 of 385 (18.7%) females and 45 of 328 (13.0%) males reported symptoms. Among patients with dry eye without MGD, 76 of 277 (27.4%) females and 43 of 150 (28.7%) males reported symptoms.

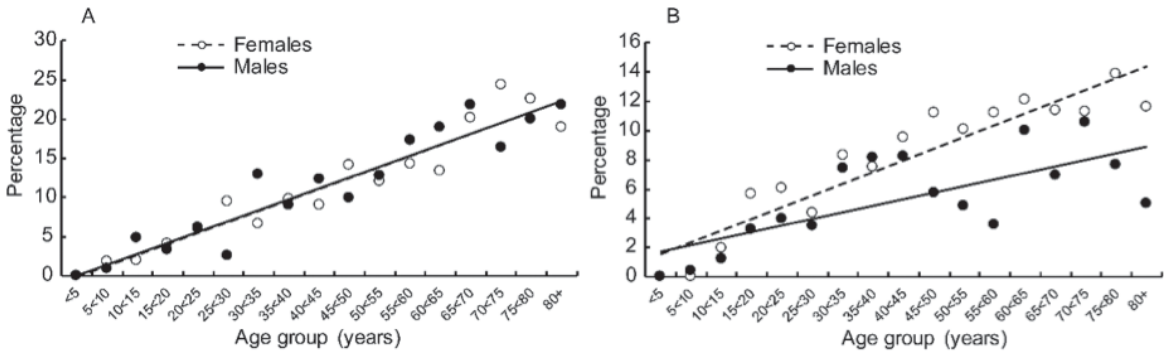
Table 2: *Odds ratios (OR) and 95% confidence intervals (CI) for patient age, sex, various ocular and systemic conditions, and medications and their association with dry eye-related symptoms and a clinical diagnosis of dry eye.*

			Dry eye symptoms	Dry eye clinical diagnosis
		N	OR (95% CI)	OR (95% CI)
	Patient age	6397	1.01* (1.01-1.02)	1.03* (1.03-1.03)
	Female sex	3459	1.24* (1.04-1.49)	1.24* (1.08-1.42)
Ocular Conditions	Blepharitis	663	1.84* (1.44-2.34)	2.46* (2.05- 2.95)
	Contact lens wear	627	0.54* (0.36-0.80)	1.34* (1.06-1.70)
	History of refractive surgery	19	2.07 (0.60-7.15)	1.40 (0.46-4.30)
	Ocular allergies	238	1.83* (1.26-2.67)	1.30 (0.94-1.80)
Systemic Conditions	Hypertension	1177	0.97 (0.77-1.23)	1.01 (0.86-1.20)
	Asthma	315	1.44* (1.01-2.05)	0.91 (0.67-1.24)
	Diabetes	512	1.30 (0.98-1.73)	0.94 (0.75-1.17)
	Smoking	310	1.02 (0.68-1.52)	1.12 (0.84-1.49)
	Environmental allergies	1040	1.07 (0.85-1.34)	1.18* (1.00-1.41)
	Connective tissue disease	52	0.50 (0.16-1.63)	0.93 (0.48-1.78)
	Gout	56	1.47 (0.68-3.15)	0.93 (0.51-1.70)
	Thyroid disease	354	1.06 (0.75-1.50)	1.08 (0.84-1.38)
Medications	Antihistamines	157	1.94* (1.23-3.06)	1.34 (0.89-2.01)
	Selective serotonin reuptake inhibitors	242	1.83* (1.27-2.62)	0.91 (0.66-1.27)
	Diuretics	386	1.04 (0.74-1.46)	0.75* (0.59-0.97)
	Beta-blockers	351	1.10 (0.78-1.56)	0.93 (0.73-1.20)
	Tricyclic antidepressants	58	0.97 (0.41-2.27)	1.03 (0.57-1.87)
	Statins	747	1.24 (0.96-1.61)	0.88 (0.73-1.06)
Other	Hormone replacement therapy	67	1.06 (0.50-2.25)	0.87 (0.49-1.52)
	Oral Contraceptives	196	0.71 (0.38-1.33)	1.40 (0.93-2.12)

*$p<0.05$

Anterior blepharitis was also strongly associated with both dry eye symptoms and a clinical diagnosis of dry eye. Anterior blepharitis was common in WatES patients and its prevalence increased in a near-linear manner with age. The mean age for contact lens use in WatES patients was 32 years, with a peak at 22 years. While contact lens wear and environmental allergies were associated with a dry eye diagnosis, ocular allergies and asthma increased the odds of common dry eye symptoms. Of the medications considered, antihistamine and selective serotonin reuptake inhibitor use were significant for a positive association with dry eye symptoms and the use of diuretics was negatively associated with a clinical diagnosis of dry eye.

Figure 2: *Percentage females and males in five year age groups A. with meibomian gland dysfunction and dry eye diagnosis (females y=1.399x-1.505 R2=0.9138, males y=1.385x-1.249 R2=0.8978) and B. without meibomian gland dysfunction and dry eye diagnosis (females y=0.799x+0.803 R2=0.8674, males: y=0.455x+1.298 R2=0.506).*



DISCUSSION

Dry eye is known to be a prevalent disease in the elderly. The results of this study illuminate the fact that patients of all ages are affected. Similar to the results reported by Doughty,[12] we found a bimodal age distribution in dry eye symptoms, with peaks in early adulthood and the senior years. Vehof et al.[15] looked at the prevalence and risk factors of dry eye disease in a British all-female cohort 20–87 years of age in 10-year age groups. In agreement with the current study, their data also suggested a bimodal distribution in dry eye symptoms and a linear increase in a diagnosis of dry eye, although data for adolescents and children were not available. Very few other studies cover the entire lifespan. The DEWS II epidemiology subcommittee performed a meta-analysis of published prevalence data and found that while both symptoms and signs increased with age, signs showed a greater increase per decade than symptoms.[9]

The peak in dry eye prevalence in later adult years is not surprising. Changes in eyelid position, conjunctivochalasis, the cumulative loss of goblet cells and meibomian glands with age, an increased risk for systemic inflammatory conditions, as well as the increased use of systemic and topical ocular pharmaceuticals have all been cited as contributing factors to the high prevalence of dry eye in the elderly.[11] The small dip in the prevalence of dry eye symptoms in the WatES 80+ age group may be related to the low number of patients in that age group (N=351) as opposed to a true decreasing prevalence. Alternatively, corneal anesthesia, which is known to occur in the later years of life along with worsening dry eye disease, may lead to decreased reporting of symptoms in the oldest age groups.[11]

More intriguing is the initial peak in dry eye symptoms in the 30<35 year age group. The work environment in this age group may contribute to this peak. While occupational data were not abstracted as part of the WatES database, a study by Li et al,[16] found that younger Chinese adults in the workforce, especially those who worked on computers and in offices, had dry eye largely attributable to adverse environmental conditions. Increased contact lens use in this age group should be considered as it was found to be significantly associated with a diagnosis of dry eye. Contact lenses are thought to cause hyperosmolarity of the tear film, but the nature of this association is still being investigated.[13] Interestingly, only 28 contact lens wearers (4.5%) presented any dry eye symptoms, while 98 (15.6%) were diagnosed with dry eyes. This may be due to the fact that patients presenting for a routine eye examination in the Primary Care Clinic are not there to have their contact lenses assessed (this is done in a specialty clinic) and may not report contact lens-related dry eye symptoms. Alternatively, those who wear contact lenses are likely to not have symptoms, as those with symptoms tend to discontinue wear. Regardless, the peak in symptoms in this younger age group should be further investigated, especially in light of the increased use of mobile electronic devices.

The overall prevalence of dry eye symptoms in the current study (8.5%) is considerably lower than that in the CANDEES study (28.7%).[12] One might expect more positive responses regarding the occurrence of symptoms among patients who are specifically asked to reply to a survey about having any symptoms (CANDEES) than among those

attending an eye examination and reporting only symptoms that are problematic and/or severe enough for them to mention (WatES). American and Australian population-based studies that required the presence of severe symptoms reported a dry eye prevalence of 7.8% (Women's Health Study, age ≥49 y)[28] and 5.5% (Melbourne Visual Impairment Project, age ≥40 y),[25] which are lower than those in studies with symptoms of varying severity; i.e., prevalence of 14.6% (Salisbury Eye Study, age ≥65 y),[20] 14.4% (Beaver Dam, age ≥48 y)[24] and 16.6% (Blue Mountains, age ≥50 y).[26] When WatES patients are similarly grouped with respect to age, the prevalence of dry eye symptoms ranges from 9.2% in patients aged ≥40 years to 10.7% in those aged ≥65 years.

Historically, the symptoms included in dry eye surveys have been at the discretion of the investigator. Most commonly, these have included dryness, foreign body sensation, grittiness, and burning, stinging or discomfort. Less commonly, studies have included symptoms of watery eyes or tearing, crusting, stuck lids, photosensitivity, ocular injection, itching and transient fluctuations in vision with blinking. Even with well-tested, validated questionnaires, there is some variation in the symptoms screened.[9,31] The results of the current study suggest that symptoms of dryness, burning/stinging/soreness, watery eyes/tearing, and ocular injection (redness) are closely associated with dry eye and should be included in dry eye screening questionnaires.

This study also supports the finding that symptoms and traditional clinical signs are poorly correlated. Only half the patients with symptoms were diagnosed with dry eye. A review of recent studies using objective measurements found that less than 60% of subjects with clinical signs of dry eye are symptomatic.[13] Despite this, dry eye symptoms will remain the driving force behind patients seeking eye care and complying with recommended treatment. Recently, the DEWS II report committee proposed a new definition for dry eye that includes a loss of tear film homeostasis with accompanying ocular symptoms, demonstrating the importance of including symptoms. They acknowledged subcategories of "symptoms without signs" as being a pre-clinical dry eye state if no neuropathic pain could be diagnosed. They further acknowledged "signs without symptoms" as either a predisposition to dry eye or dry eye in the presence of decreased corneal sensitivity, which is common when the disease is longstanding.[2]

Besides age, female patients and those with anterior blepharitis had greater odds of having both dry eye symptoms and a diagnosis. Several studies have demonstrated an increased risk of dry eye in women.[13,31] The DEWS II report cites the effects of sex steroids and sex-related differences in anatomy, immunity and physiology of the ocular surface and adnexa as contributors.[35] Females taking birth control pills have been known to report greater dry eye symptoms, and an association between hormone replacement therapy and dry eye has been well documented.[13] The current data did not support either of these findings, perhaps due to the low numbers of patients with these factors. Finally, the results suggest that the sex difference in dry eye diagnoses is not due to MGD, as there was no sex-related difference in MGD diagnosis with age. Anterior blepharitis was common in WatES patients, as previously noted. Anterior blepharitis involves an inflammatory process that results in hyperosmolarity. It may be thought of as a separate disease process from dry eye with overlapping signs and symptoms, or more recently as a possible continuum, where chronic anterior blepharitis leads to dry eye (dry eye blepharitis syndrome).[36,37]

The significant association between asthma and dry eye symptoms is interesting and has been infrequently investigated.[15,26] Recently, Vehof[15] found a significant positive relationship between asthma and both dry eye symptoms and patient-reported clinical diagnosis of dry eye. Further study of this association is recommended, with particular interest in separating the effect of the condition itself from its treatment, especially the use of corticosteroid pharmaceuticals.

Some previous dry eye studies did not include dry eye-related symptoms that could also be attributed to ocular allergies.[15,24,25] However, ocular allergies can contribute to dry eye by creating an inflamed ocular surface that reduces tear function.[33] Antihistamines have been consistently associated with dry eye[5,31,33] and the use of antihistamines was significantly associated with dry eye symptoms in this study. All other medications (except statins) included in this study were listed in the DEWS II report as having some association with dry eye.[9] Only selective serotonin reuptake inhibitors had a significant positive association with dry eye symptoms, and this association was almost as strong as that with antihistamines. Given the increasing use of these pharmaceuticals, further study into this association is warranted.[38]

The strength of this study lies in its large sample size and wide age range, including children and adolescents. Presumably, the low prevalence of dry eye diagnosis in the youngest patients (≤7 years) is influenced by the lim-

ited ability to perform diagnostic testing in this age group. However, this study also has some limitations. As a cross-sectional study, these data can highlight associations, but cannot show causation. Furthermore, there will be some inter-practitioner variability in diagnostic criteria and not all patients who have symptoms will report them. Finally, clinic populations are not representative of the general population. The assumption is that symptomatic conditions would be more prevalent in patients seeking care than in the general population. While this would cause an upward shift in the prevalence values, the age-related trend should still exist. The data were collected in 2007-8, and the factors that influence the dry eye prevalence may have changed since then. Further studies to determine the dry eye prevalence change following the widespread use of mobile devices would be of interest, and these data will be valuable for comparison.

In summary, symptoms of dryness, ocular injection, discomfort (burning/stinging/ soreness) and watery eyes/tearing are good predictors of a dry eye diagnosis, but many patients who are diagnosed with dry eye do not report symptoms. Furthermore, dry eye symptoms are not limited to adults, and also occur in children and adolescents. Increasing age, female sex, anterior blepharitis, contact lens wear, allergies, use of antihistamines, and the use of selected serotonin reuptake inhibitors appear to be associated with either dry eye symptoms and/or a clinical diagnosis. The sex difference in dry eye diagnosis is not likely to be due to MGD, since no sex-related difference in MGD diagnosis with age was found. ●

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