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Classification of dry eye disease subtypes

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ABSTRACT

Purpose: The current subclassifications of dry eye disease (DED) are aqueous deficient (ADDE) and evaporative (EDE) forms, but there lacks consistency in the clinical characteristics used to define each of these. This study used clinical data to inform cut-off values for the subclassification of ADDE and EDE, to allow more consistent study of the epidemiology of both DED subtypes.

Methods: The study enrolled 261 residents from the UK, extracted from a cohort with demographics representing the population (mean 42.4 ± 18.7 years, 56 % females). The TFOS DEWS II diagnostic criteria were used to identify those with DED. Meibomian gland loss/drop-out (from meibography), lipid layer thickness (LLT – from interferometry graded on the Guillon-Keeler scale), and tear meniscus height (TMH – Keratograph 5M) along with tear evaporation (Delfin Vapometer) were used to characterise the subclassification. The Dry Eye Risk Factor Survey was used to assess risk factors associated with each DED subtype.

Results: Compared to individuals who were not diagnosed with DED, EDE was characterized by signs of meibomian gland loss of > 28 %, LLT grade < 3 and tear evaporation > 46 g/m^2/h. In contrast, ADDE was best characterized by a reduced TMH < 0.2 mm. Based on these criteria, the prevalence of ADDE was 6.2 %, EDE was 64.2 %, and 11.1 % exhibited features of both ADDE and EDE, with 18.5 % unclassified despite having a DED diagnosis. Contact lens wear and computer use were risk factors for ADDE ($p < 0.05$), whereas age was a positive risk factor for EDE ($p < 0.01$). Meibomian gland loss (occurring in 27.9 %) was the most commonly observed sign in EDE.

Conclusions: Data driven-classification of DED confirms that the evaporative form is most prevalent and identified that in a generalisable UK population, ADDE alone occurs only in approximately 1 in 16 cases of DED.

1. Introduction

Dry eye (DED) is a multifactorial disease characterized by symptoms resulting from a homeostatic imbalance of the ocular surface and tear film. It has been classified into two main entities: evaporative (EDE) and aqueous deficient (ADDE) DED [1]. These subclassifications are used by clinicians to inform the most effective treatment plan for an individual patient and hence are critical to clinical practice [2]. A lack of standardisation makes it difficult to compare the results from clinical trials to inform evidence-based practice. Both EDE and ADDE have similar ocular symptoms and general DED signs; however, they have different primary causes and may be associated with different risk factors; therefore a different therapeutic approach is warranted [2].

DED consensus reports support the hypothesis that EDE and ADDE can coexist and that subclassification is an important stage of patient management between diagnosis and treatment [3]. Clinical tests that could inform ADDE and EDE subclassification include those that quantify the tear film volume (including Schirmer test, the Phenol Red Thread test (PRT) and tear meniscus height (TMH)), as well as lipid layer thickness (LLT), tear film evaporation and meibomian gland loss/drop-out [4]. These clinical assessments are not part of a formal diagnosis of DED, but should be used to inform selection of the most appropriate therapies for an individual patient to improve their quality of life through reducing DED symptoms [4].

While many combinations of clinical tests have been selected to differentiate EDE and ADDE in academic clinical trials, there is no apparent consistency in categorising both DED subtypes [2]. This causes problems, for example in understanding the epidemiology of DED, using differing subclassification test combinations and cut-off values, and hindering direct comparisons of the prevalence rates of EDE and ADDE [5–7] (see Table 1). In general, the selected criteria have been reported without any rationale, and the tests used to diagnose DED prior to

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Table 1
Previous large-scale clinical-population-based studies on DED subtypes.

Study	Population characteristics	DED subtypes			
		ADDE		EDE	
	Age (years) Sex (n)	Diagnosis	Prevalence (%[95 % CI])	Diagnosis	Prevalence (%[95 % CI])
Albietz 2000[A] [5]	3–96 ♀ 912 ♂ 672	Lipid layer without colour fringes and meibomian glands without particulate, frothy or cloudy meibum, and PRT test of < 10 mm/ 15 s and TMH of < 0.10 mm	1.7 [n/a]	Lipid layer with colour fringes and meibomian glands with particulate, frothy or cloudy meibum, and PRT test of ≥ 10 mm/ 15 s and TMH of ≥ 0.10 mm	4.0 [n/a]
Lemp et al. 2012[B] [8]	46.3 ± 16.9 ♀ 218 ♂ 81	MGD score of ≤ 5 and Schirmer test II of < 7 mm/5 min	10.3 [n/a]	MGD score of > 5 and Schirmer test II 7 mm/5 min	35.5 [n/a]
Rege et al. 2013[C] [6]	≥18 ♀ 2585 ♂ 2165	Meibomian glands without inspissated or toothpaste-like meibum, and Schirmer test II of < 10 mm/ 5 min	13.36 [n/a]	Meibomian glands with inspissated or toothpaste-like meibum, and Schirmer test II of ≥ 10 mm/ 5 min	14.48 [n/a]
Asiedu. Dzasimatu and Kyei 2019[D] [7]	17–35 ♀ 89 83 ♂	Meibomian glands without low expressibility and cloudy or toothpaste-like meibum. and Schirmer test I of ≤ 5 mm/5 min	5.2 [n/a]† 5.2 [n/a]‡	Meibomian glands with low expressibility and cloudy or toothpaste-like meibum. and Schirmer test I of > 5 mm/5 min	11.6 [n/a]† 7.0 [n/a]‡

DED = dry eye disease. ADDE = aqueous deficient dry eye. EDE = evaporative dry eye. PRT = phenol red thread. TMH = tear meniscus height.
A. DED was defined by at least one of five primary symptoms of the McMonnies questionnaire (soreness, scratchiness, dryness, grittiness and burning) either often or constantly, a fluorescein breakup time of < 10 s and a rose bengal score of ≥ 1 (van Bjisterveld staining score).
B. DED was defined by an Ocular Surface Disease Index (OSDI) score of ≥ 5 and at least two of five signs: fluorescein breakup time < 7 s, Schirmer test I < 7 mm/5 min, corneal staining > 0 (National Eye Institute/Industry Workshop scale), conjunctival staining > 0 (National Eye Institute/Industry Workshop scale) and meiboscore of > 5 (Bron/Foulks scoring system).
C. DED was defined by presenting a meibum quality score of ≥ 14.5.
D. DED was classified into symptomatic† and asymptomatic‡ DED. Symptomatic DED was defined by an OSDI score of ≥ 13 and fluorescein tear break-time of < 10 s or corneal and conjunctival fluorescein staining of ≥ 1 (Oxford grading scale). Asymptomatic DED was defined by an OSDI score of < 13 and fluorescein tear break-time of < 10 s or corneal and conjunctival fluorescein staining of ≥ 1 (Oxford grading scale).

Table 2
DED subclassification signs of non-DED participants (stratified by sex and the absence/presence of health conditions/problems).

Subclassification Signs (mean ± SD)	Non-DED participants				
	Without health conditions/ problems		With health conditions/ problems		
	♀ n = 20	♂ n = 26	♀ n = 26	♂ n = 27	
Tear evaporation (g/ m^2/h)	43.3 ± 2.8	37.4 ± 1.9	56.5 ± 7.1	46.1 ± 5.4	
TMH (mm)	0.28 ± 0.02	0.28 ± 0.02	0.26 ± 0.02	0.38 ± 0.03	***
LLT score	3.7 ± 0.3	3.3 ± 0.3	3.8 ± 0.3	3.3 ± 0.2	*
Lower MG loss (%)	19.3 ± 3.1	17.2 ± 2.5	21.2 ± 2.5	20.8 ± 2.3	
Upper MG loss (%)	23.5 ± 3.8	20.9 ± 2.1	30.2 ± 3.3	26.4 ± 2.7	

DED = dry eye disease. MG = meibomian gland. * p ≤ 0.05. *** p ≤ 0.001. ♀ = female. ♂ = male. n = sample size. SD = standard deviation.

subclassification can be somewhat variable [4].

To achieve an accurate disease subclassification, a standardized DED diagnosis is crucial. Accordingly, TFOS DEWS II identified an evidence-based DED diagnostic battery of tests and cut-offs [4] and advocated for subsequent subclassification of the disease in those diagnosed, including measurements of TMH, tear evaporation, LLT and meibomian gland loss [4]; however, evidence informing subclassification test cut-off values was lacking.

The present study is the first to propose a subclassification system for both ADDE and EDE (with evidence-informed cut-off values) for DED, based on the current diagnostic recommendations of the TFOS DEWS II. Once established, the subclassification system was used to determine the prevalence and risk factors of EDE, ADDE and those displaying elements of both DED subclassifications within the UK population.

2. Methods

The study conformed to the tenets of the Declaration of Helsinki and all participants gave their written, informed consent to take part. It received a favourable opinion by the ethical committee of Aston University and governance approval. To participate in the study, participants were required to be ≥ 18 years of age and have lived in the UK for at least the previous 5 years. Participants were invited from those attending routine eye care (not a specialist service), random sampling, with targeting of age and sex stratification to closely match the United Kingdom (UK) Birmingham population census. Less than 10 % declined and were replaced by participants of a similar age and sex. The participants were advised not to wear contact lenses or use any artificial tears or topical medication 24 h prior to the study.

DED was diagnosed based on the TFOS DEWS II criteria and a previous study described the methodology [9] used to assess the prevalence and potential risk factors of DED. Measurements of tear evaporation, TMH, LLT and lower/upper meibomian gland loss, were assessed in the order listed to inform the subclassification of DED, as suggested by the TFOS DEWS II [4].

The Delfin VapoMeter (Delfin Technologies Ltd, Kuopoi, Finland) was used to assess tear film evaporation rate. The humidity is measured within a swimming google piece that encloses the eye during measurement. Participants were required to keep their eyes open without blinking during the complete measurement, as specified by the equipment instructions. The average of three consecutive tear film evaporation readings were recorded.

The tear meniscus was imaged using infrared light and 1.4 times magnification, with the software callipers used to measure the inferior TMH three times (Keratograph 5M). The lipid layer was imaged using interferometry (1.4 times magnification using the Keratograph 5M) and graded with the modified Guillon-Keeler scale [10]. Participants were instructed to look forward naturally while the instrument was set up for the next measure to ensure blinks were not forced. The predominant

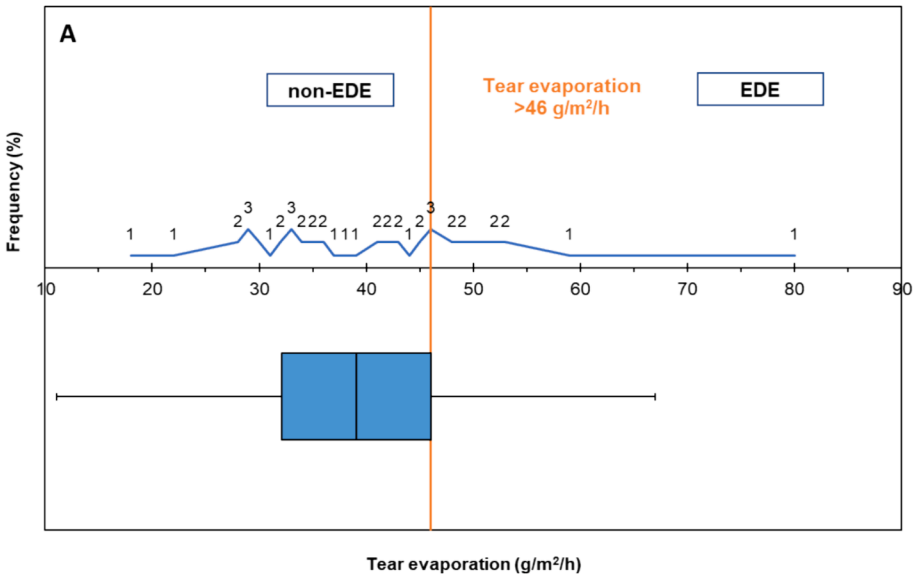

Fig. 1. Tear evaporation distribution of healthy non-DED participants (n = 46; numbers above line indicate number of participants) EDE = evaporative dry eye; DED = dry eye disease. (A) Frequency plot of tear evaporation measurements of healthy non-DED participants. (B) Box plot of tear evaporation measurements of healthy non-DED participants. First quartile = 32 g/m^2/h; Median = 39 g/m^2/h; Third quartile = 46 g/m^2/h; Minimum = 11 g/m^2/h; Maximum = 67 g/m^2/h. The tear evaporation cut-off value was set at 46 g/m^2/h. The cut-off value was based on the third quartile of the tear evaporation distribution referring 36 of 46 non-DED participants as non-EDE. The approach used allowed inference of the highest possible test specificity of 78 % (36/46).

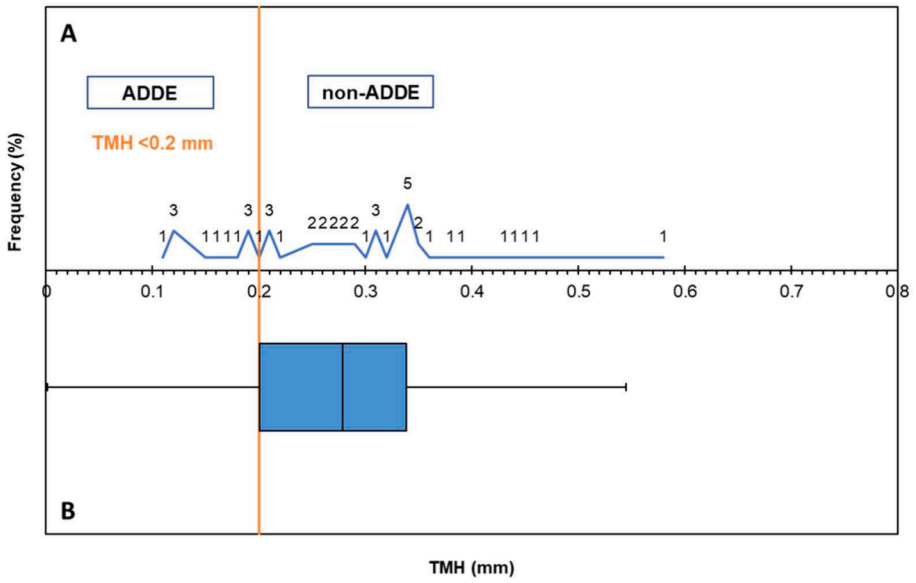

Fig. 2. TMH distribution of healthy non-DED participants (n = 46; numbers above line indicate number of participants). TMH = tear meniscus height; ADDE = aqueous deficient dry eye; DED = dry eye disease. (A) Frequency plot of TMH measurements of healthy non-DED participants. (B) Box plot of TMH measurements of healthy non-DED participants. First quartile = 0.20 mm; Median = 0.28 mm; Third quartile = 0.34 mm; Minimum = 0.00 mm; Maximum = 0.55 mm. The TMH cut-off value was set at 0.20 mm. The cut-off value was based on the first quartile of the TMH distribution referring 35 of 46 non-DED participants as non-ADDE. The approach used allowed inference of the highest possible test specificity of 76 % (35/46).

pattern was recorded when overlapping lipid layer patterns were observed. The areas of meibomian gland loss relative to the exposed palpebral area was calculated from infrared light images captured using the Keratograph 5M, with the glands outlined in ImageJ (https://imagej.nih.gov/ij/index.html) [11].

In line with current definitions of EDE and ADDE [3], ADDE was chosen by the authors based on prior approaches to be described by a reduced TMH, whereas EDE was described by a reduced LLT or an increased tear evaporation or lower/upper meibomian gland loss [4].

Meibomian gland dysfunction has been previously graded by the quality of the meibum, more specifically, by its expressibility and appearance [5–7]. In the present study, the condition was defined by meibomian gland dropout, which has been previously correlated with altered meibum [12,13] and is generally less invasive and easier to quantify than gland expression.

Sex, age, employment status, health conditions/problems, medication intake, sleep quality, and outdoor activity were gathered by the Dry Eye Risk Factors Survey (DERFS) [9] and the results used to inform the risk factor analysis of both DED subclassifications. These factors have been shown to be significant risk factors of (TFOS DEWS II diagnosed)

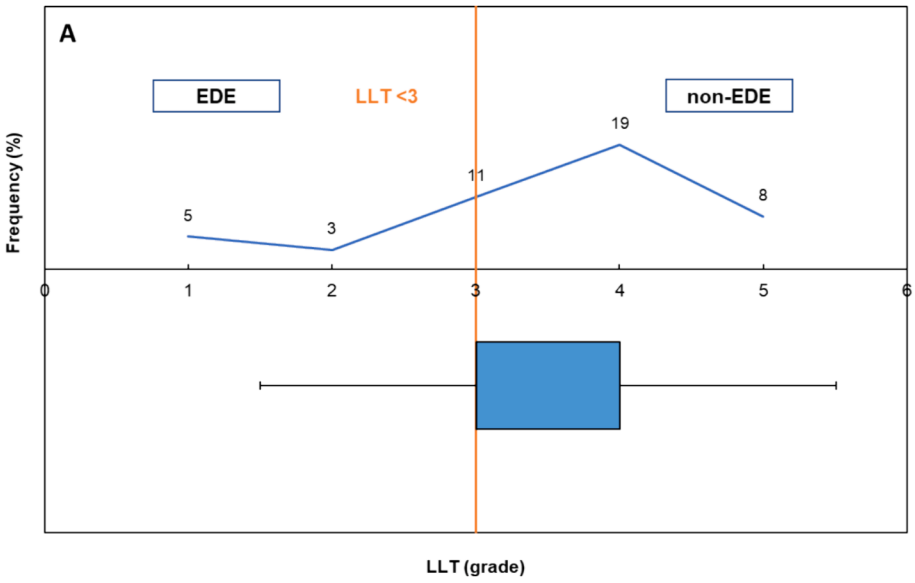

Fig. 3. LLT distribution of healthy non-DED participants (n = 46; numbers above line indicate number of participants). LLT = lipid layer thickness; EDE = evaporative dry eye; DED = dry eye disease. (A) Frequency plot of LLT measurements of healthy non-DED participants. (B) Box plot of LLT measurements of healthy non-DED participants. First quartile = 3.0; Median = 4.0; Third quartile = 4.0; Minimum = 1.5; Maximum = 5.0. The LLT cut-off value was set at a grade of 3.0. The cut-off value was based on the first quartile of the LLT distribution referring 38 of 46 non-DED participants as non-EDE. The approach used permitted inference of the highest possible test specificity of 83 % (38/46).

DED and, amongst these, sex and health conditions/problems had the greatest statistical significance [9].

Dry eye subclassification test cut-off values were determined from TMH, tear evaporation, LLT and meibomian gland loss readings, ensuring a high level of specificity in the excluding of non-DED participants. The readings were first stratified by sex and subsequently by the presence or absence of health conditions or problems, to understand whether either factor might have confounded normal tear film characteristics. The study aimed to adopt cut-off values that were as specific as possible, since parallel testing of highly specific tests gives greater confidence in the differential diagnosis of DED [4].

2.1. Statistical analysis

Statistical analysis was performed with SPSS version 23 (IBM Corp, New York. USA). Kolmogorov-Smirnov tests confirmed all ocular parameters as being statistically different to a normal distribution. Differences between EDE and ADDE signs of both male and female non-DED participants, both with and without health conditions were analysed with U-Mann Whitney tests [14]. The prevalence rates of DED subclassifications were presented along with 95 % confidence intervals. Associations between EDE and ADDE signs and between the subclassification symptoms and signs of DED participants were evaluated with Spearman's rank correlation coefficients. Finally, within DED participants, risk factors of individuals who had been identified with purely EDE or ADDE characteristics were determined through phi (for dichotomous risk factors) and point biserial correlation coefficients (for ordinal risk factors).

3. Results

Two-hundred and sixty-one Birmingham, UK residents (median age 40 years, range 18 to 88 years, 56 % females) participated in the study. The participants were extracted from a cohort stratified by both age and sex to reflect the population of the UK [9]. One hundred and sixty-two participants had been diagnosed with DED based on the TFOS DEWS II criteria and 99 did not exhibit any positive characteristics of DED or ocular surface disease.

Measurements of tear evaporation, TMH, LLT and lower/upper meibomian gland loss of non-DED participants with health conditions/problems differed significantly between females and males; however, this was not the case for non-DED participants without health conditions/problems (Table 2).

The cut-off values of the subclassification tests were based on the distribution of TMH, tear evaporation rates, LLT and upper/lower meibomian gland loss of non-DED participants without health conditions or problems using an upper (tear evaporation and meibomian gland loss) or a lower (TMH and LLT) quartile boundary approach (Figs. 1–4).

Therefore, ADDE was defined as DED participants with a TMH of $<$ 0.2 mm along with a normal LLT (a grade of $\geq$ 3), lower/upper meibomian gland loss ($\leq$28 %) and tear evaporation rate ($\leq$46 g/m^2/h). EDE was identified by a LLT of grade $<$ 3, lower/upper meibomian gland loss of $>$ 28 % and a tear evaporation rate of $>$ 46 g/m^2/h, but a normal TMH ($\geq$0.2 mm). Using these criteria, 64.2 % of individuals diagnosed with DED had EDE alone, 6.2 % ADDE alone and 11.1 % showed features of both ADDE and EDE; this left 18.5 % of those meeting the TFOS DEWS II criteria for a diagnosis of DED as unclassified (not meeting either subclassification criteria identified in the study; Fig. 5). Those classified as having ADDE were younger (33.5 $\pm$ 13.8 years) than those with EDE (42.1 $\pm$ 15.0 years; $p = 0.030$). Ocular Surface Disease Index assessed symptoms were similar ($p = 0.927$) between those classified as EDE (20.1 $\pm$ 14.7) and ADDE (19.8 $\pm$ 11.9).

Tear evaporation rate was significantly, but weakly positively correlated with TMH, as well as with meibomian gland loss in the lower eyelid (Table 3). TMH was also weakly correlated with upper meibomian gland loss. LLT grade did not significantly correlate with any other signs specific to ADDE or EDE (Table 3).

Within individuals diagnosed with DED, higher symptoms identified by the 5-item Dry Eye Questionnaire (DEQ-5) and Ocular Surface Disease Index (OSDI) were significantly associated with greater tear evaporation (Table 4). However, no other EDE or ADDE associated signs were significantly related to DED symptoms (Table 4).

EDE was more common with increasing age ($p < 0.01$), whereas ADDE was more common in contact lens wearers and in those with high levels of computer use. Sex, smoking habits, education, sleep quality, outdoor activity and health conditions or problems were not identified as significant risk factors of either ADDE or EDE ($p > 0.05$) in this cohort.

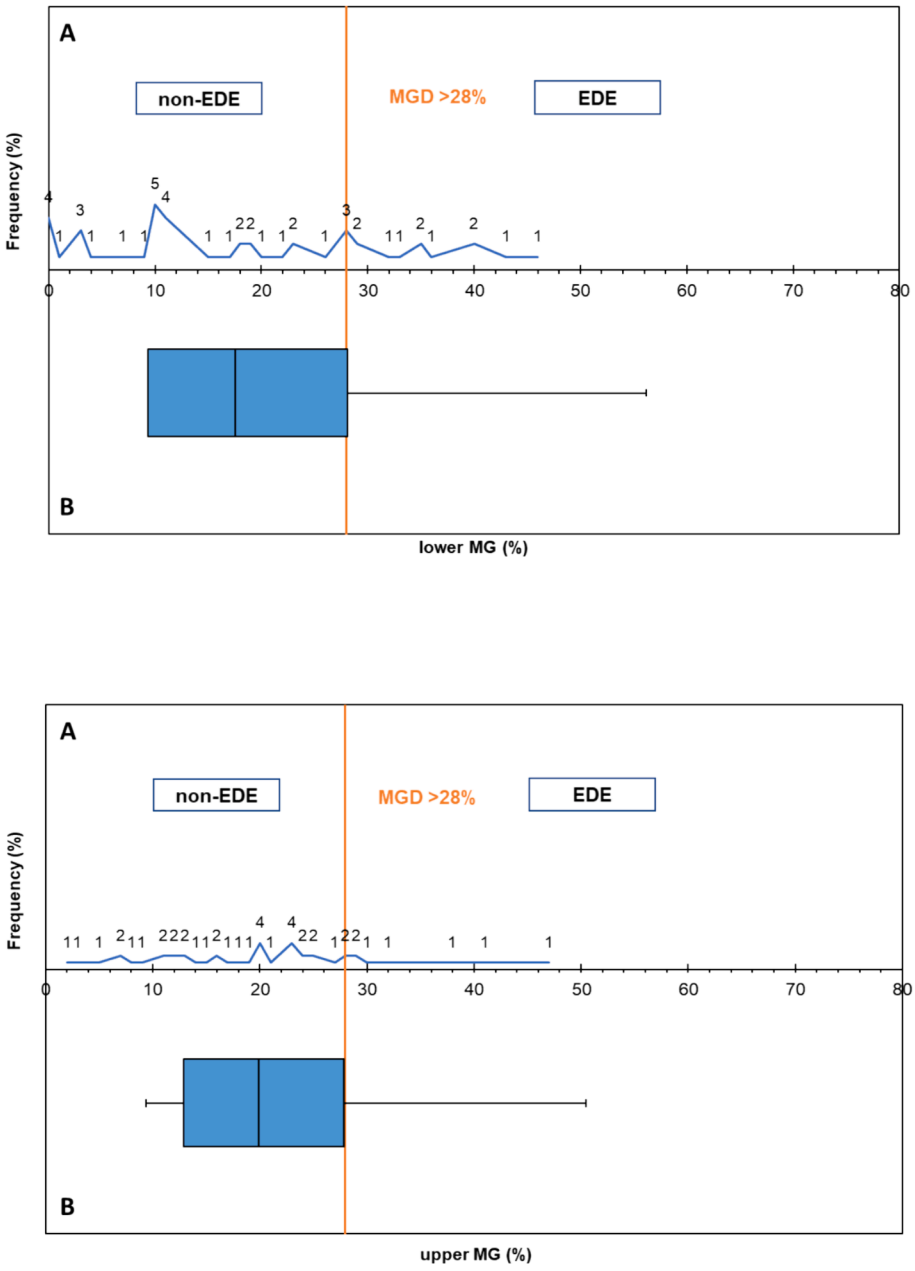

Fig. 4. Meibomian gland loss distribution of healthy non-DED participants (n = 46; numbers above line indicate number of participants). MG = meibomian gland loss; EDE = evaporative dry eye; DED = dry eye disease. (A) Frequency plot of lower/upper MG loss measurements of healthy non-DED participants. (B) Box plot of lower/upper MG loss measurements of healthy non-DED participants. For lower MG loss: First quartile = 9.3 %; Median = 17.5 %; Third quartile = 28.0 %; Minimum = 18.9 %; Maximum = 56.1 %. For upper MG loss: First quartile = 13.0 %; Median = 20.0 %; Third quartile = 28.0 %; Minimum = 9.5 %; Maximum = 50.5 %. The MG loss cut-off value was set at a grade of 28.0 %. The cut-off value was based on the third quartile of the lower MG loss and upper MG loss distribution referring 35/46 and 36/46 of non-DED participants as non-EDE, respectively. The approach used allowed the highest possible test specificity of 76 % (35/46) for lower MG loss and of 78 % (36/46) for upper MG loss to be inferred.

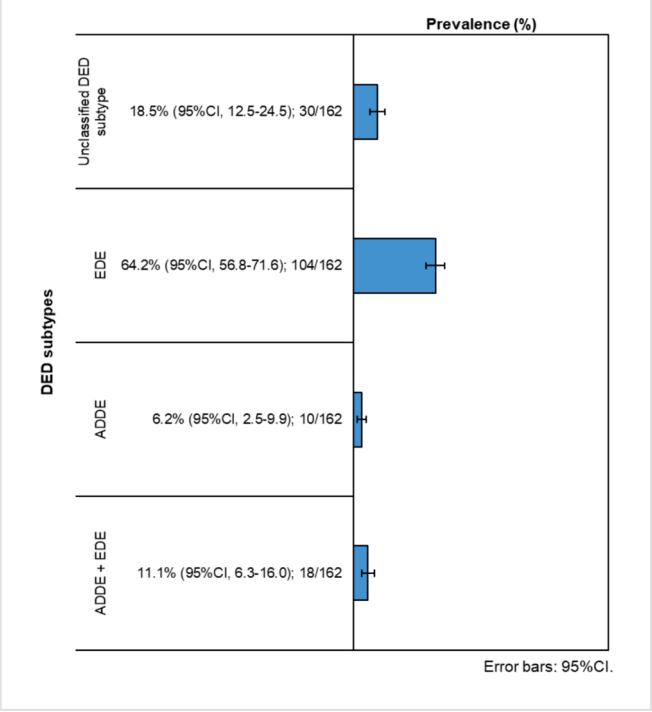

Fig. 5. Prevalence of DED subtypes. Error bars: 95 % CI. DED = dry eye disease. EDE = evaporative dry eye. ADDE = aqueous deficient dry eye. Upper/lower meibomian gland loss was the most common sign observed in EDE participants (27.9 %), followed by altered tear evaporation (20.2 %) and decreased LLT (6.7 %) (Fig. 6).

4. Discussion

This study aimed to propose a subclassification system for both ADDE and EDE (with evidence-informed cut-off values) for DED, based on the current diagnostic recommendations of the TFOS DEWS II. The TFOS DEWS II global, evidence-based, consensus states that a DED diagnosis requires above a pre-defined symptom score (using either the OSDI or DEQ-5 questionnaire) together with one or more signs indicating a break-down of tear film homeostasis (a reduced non-invasive tear breakup time, tear hyperosmolarity or ocular surface staining) [4]. DED is traditionally classified into EDE and ADDE, where the lipid layer production and distribution, or aqueous volume of the tear film tend to be altered, respectively [3]. Establishing the subtypes of DED can be challenging as they have similar symptoms and general signs; however, distinguishing between the subclassifications is important to inform DED management and therapy decisions [2].

The resulting subclassification scheme, establishing cut-offs for each of TMH, LLT and upper/lower meibomian gland dropout, was used to identify the prevalence and risk factors of both ADDE and EDE among a cohort that is representative of the population of UK. These parameters were mentioned in TFOS DEWS II as tests to inform subclassification [4], however, no established diagnostic cut-off values were available at that time. In the present study, therefore, cut-off values were established from clinical data of non-DED participants with no known health conditions or problems (as these can significantly confound normal tear film functions) [15,16]. Cut-off values producing the highest possible diagnostic specificities of the subclassification tests were selected to allow greater confidence in the differential diagnosis of the disease [4]. A TMH of < 0.2 mm was found to best identify DED participants with ADDE. In contrast, tear evaporation rate of > 46 g/m^2/h, LLT grade of < 3, or lower/upper MG loss of > 28 % were most indicative of EDE. The TMH cut-off value identified was consistent with that reported by Uchida et al. [17]. The cut-off values for tear evaporation, LLT and meibomian gland loss were also in good agreement with previous studies, which found a tear evaporation rates of 48.9 $\pm$ 23.5 g/m^2/h (despite differences in instrumentation and accounting for skin evaporation) [18], LLT of ≥ 75 nm [19] and meibomian gland dropout of 30.1 $\pm$ 17.4 % [20] in non-DED individuals. A research communication in 2020 proposed similar cut-off criteria to this study for in-common assessments, despite using a combined sensitivity and specificity cut-off selection choice [21].

Based on the study classification, EDE was the most common form of DED in the UK population, with a prevalence rate of 64.2 %. The findings were in accordance with previous research [5–7] and suggest that, in a general population, those with DED are likely to have a lipid layer that is compromised more commonly than a deficient aqueous layer. Indeed, increased tear evaporation rate was the second most frequently occurring subclassification sign, surpassed only by upper lid meibomian gland loss, which gives the subclassification face validity.

It should be noted that 18.5 % of DED participants had no obvious clinical signs of ADDE or EDE. Unclassified DED has been observed in other studies attempting DED classification. For instance, Asiedu et al. reported 23.8 % of symptomatic DED participants and 25 % of asymptomatic participants with ocular surface disease could not be classified [7]. Lemp et al. also were unable to categorise 29 % of their study participants into EDE, ADDE or a mixed DED category [8]. Watery eyes (triggered by tear film instability secondary to meibomian gland dysfunction) has been suggested to possibly mask an ADDE subclassification [22]. Moreover, as the tear film is variable over time, more so in diseased eyes, it might be possible that the lack of evidence of the subclassification clinical signs was caused by stochastic or measurement noise. In addition, there are no easy ways to assess ocular surface quality clinically, so goblet cell loss or poor glycocalyx quality could be a key feature contributing to DED in those unclassified by the current subclassification.

Coexistence of both DED subclassifications in an individual with DED has been associated with increasing disease severity [3]. However, severity matrices, such as those proposed by Bron and colleagues [23], can result in individuals falling into different severity categories across distinct elements of the matrix. Hence, current consensus is that DED severity should be assessed from the participants' perspective by using symptom self-reports in DED [4]. Sullivan et al. described disease severity as a continuum rather than in distinct grades [24]. The significant associations between tear evaporation, MG loss and TMH underline their combined diagnostic contributions. The counterintuitive increase in TMH with increased evaporation could be due to triggered reflex tearing. A limitation of this study was that meibomian gland expression was not assessed, which could aid the classification of EDE.

Overall, the primary goal of management and therapy for DED is to restore tear film homeostasis [2]. It is clear that practitioners utilise different treatments for DED patients based on subclassification as well as severity [25]. Two studies have shown that DED subclassification (although using different subclassification algorithms) can help to predict effectiveness of different artificial tears formulations in individuals with DED [26,27]. Future studies are needed to differentiate other dry eye treatments / strategies to inform clinical practice to optimise patient treatment.

Having established the subclassification system, it was used to determine the prevalence and risk factors of EDE, ADDE and those displaying elements of both DED subclassifications within the UK population. In general, large-scale population-based studies establish risk factors for DED as a whole, rather than specific to its subtypes [28]. In the present study, EDE was found to be significantly related to age, which is consistently reported as a risk factor for DED as a whole [29], perhaps attributable to functional and structural changes of meibomian glands occurring with increasing age [30]. In contrast, ADDE was associated with contact lens wear, which is known to reduce TMH even with modern materials [31] and computer use, which has also been associated with a lower TMH after as little as 20 min use [32].

In conclusion, this study has confirmed that EDE, as characterized by

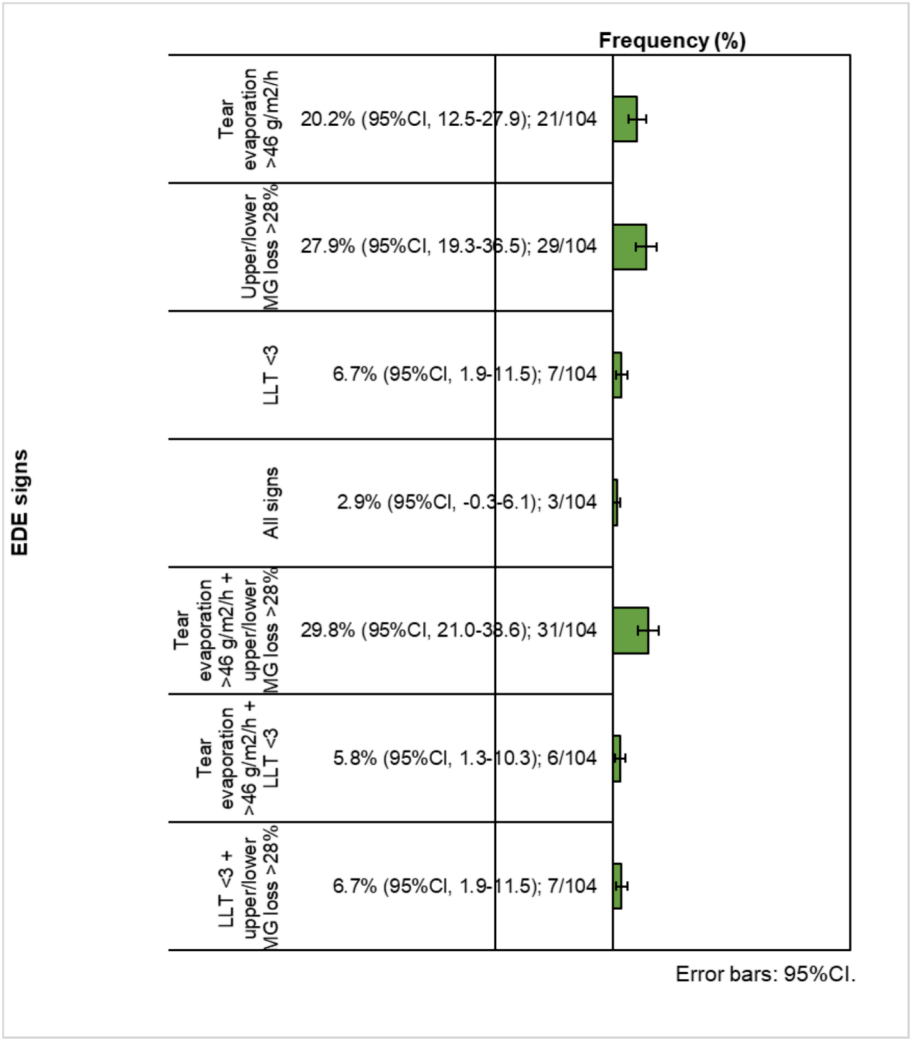

Fig. 6. Frequency of individual and combined EDE signs in EDE participants EDE = evaporative dry eye. LLT = lipid layer thickness. MG = meibomian gland.

Table 3
Correlations of subclassification signs in n = 162 DED participants.

Correlation of subclassification DED signs (r_s)	LLT grade	TMH (mm)	Lower MG loss (%)	Upper MG loss (%)
Tear evaporation ($g/m^2/h$)	−0.122	0.235**	0.171*	0.003
LLT grade		0.028	−0.017	0.021
TMH (mm)			0.065	0.197*
Lower MG loss (%)				0.133

DED = dry eye disease. LLT = lipid layer thickness. TMH = tear meniscus height. MG = meibomian gland loss. * p-value ≤ 0.05. ** p-value ≤ 0.01.

Table 4
Correlations of subclassification of DED signs and symptoms in n = 162 DED participants.

Correlation of DED Symptoms (r_s)	**Tear evaporation ($g/m^2/h$)**	**LLT grade**	**TMH (mm)**	**Lower MG loss (%)**	**Upper MG loss (%)**
DEQ-5 score	0.209**	−0.075	0.017	0.035	0.077
OSDI score	0.178*	0.020	−0.017	0.046	0.132

DED = dry eye disease. LLT = lipid layer thickness. MG = meibomian gland loss.
DEQ-5 = 5-item Dry Eye Questionnaire. OSDI = Ocular Surface Disease Index.
* p-value ≤ 0.05.

signs of tear evaporation, lipid thickness changes and meibomian gland loss, is much more common than ADDE in a UK population, consistent with existing research literature. The risk factors independently associated with the subclassifications differ, being age for EDE compared to contact lens wear and computer use for ADDE. Research into the best way to further subclassify individuals with dry eye to optimise individual patient DED treatment plans is warranted.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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