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The epidemiology of dry eye disease in the UK: The Aston dry eye study

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ABSTRACT

Purpose: Cross-sectional studies on dry eye disease (DED) have relied on different diagnoses hindering conclusions about the disease epidemiology. This study offers an insight into DED epidemiology in the UK using prior and recent diagnostic recommendations.

Methods: Study participants comprised 282 volunteers from Birmingham, UK (median 40 years, range 18–88 years, 56% females). DED was defined by the Tear Film Ocular Surface Dry Eye Workshop II (TFOS DEWS II) criteria, based on a positive symptom score with the Dry Eye Questionnaire (DEQ-5) and Ocular Surface Disease Index (OSDI), and one of the following homeostasis markers: non-invasive tear break-up time of < 10 s (Oculus Keratograph 5M); the highest osmolarity value of ≥ 308 mOsm/L among eyes or an interocular osmolarity difference of > 8 mOsm/L (TearLab Osmolarity System); or > 5 corneal spots, >9 conjunctival spots or lower/upper lid-wiper-epitheliopathy staining of ≥ 2 mm length and $\geq 25\%$ width (Oculus Keratograph 5 M). In addition, the Women's Health Study (WHS) criteria, based on symptoms or a prior dry eye diagnosis, was assessed. DED risk factors were gathered using a self-administered questionnaire.

Results: DED prevalence by the TFOS DEWS II criteria was 32.1% (95% confidence interval 25.5–37.7% and 29.5% (95% confidence interval 24.4–35.1% by the WHS criteria. Female sex, systemic and/or ocular health conditions, short sleep duration and prolonged outdoor leisure time spent were significant DED risk factors ($p \leq 0.05$).

Conclusions: Approximately one-third of the adult UK population have DED, aligning with the prevalence reported in multiple counties globally. Female sex, systemic/ocular health conditions, short sleep duration and prolonged outdoor leisure time are positive predictors of DED.

1. Introduction

The epidemiology of dry eye disease (DED) aims to answer basic research questions – how many people are affected by the disease? What are the risk factors for the disease? What are the health care resources needed? These questions, however, encompass enormous methodological and interpretative complexity.

Researchers have assessed DED prevalence and risk factors differently, using a range of diagnostic criteria and risk factor assessment tools [1]. Inconsistencies across published cross-sectional studies have created barriers to interpreting the results. Moreover, the heterogeneity in the characteristics of the population studied has further complicated the research [1].

Historically, the most consistent diagnostic criteria for DED in the literature appears to be that first adopted by the Women's Health Study (WHS) [2-8]. The WHS criteria determines DED by the presence of self-reported symptoms of ocular dryness and irritation either often or constantly, or a previous disease diagnosis by a physician [2-8]. Other epidemiological studies have diagnosed DED either by the presence of its symptoms [9-18], signs [9,12,13,17,18] or both symptoms and signs [12,17-19].

In 2017, the Tear Film and Ocular Surface Dry Eye Workshop II (TFOS DEWS II) identified the most appropriate test battery to diagnose DED according to the updated disease definition [20]. The recommended diagnostic criteria is based on the presence of one ocular sign, determined either by assessing the tear film stability, tear film osmolarity, or ocular surface damage, in addition to a positive result from a validated questionnaire, either from the 5-item Dry Eye Questionnaire (DEQ-5) or the Ocular Surface Disease Index (OSDI).

The present study is the first cross-sectional UK-based study that estimates the prevalence and risk factors of DED following the TFOS DEWS II diagnostic recommendations. Moreover, it studied the disease

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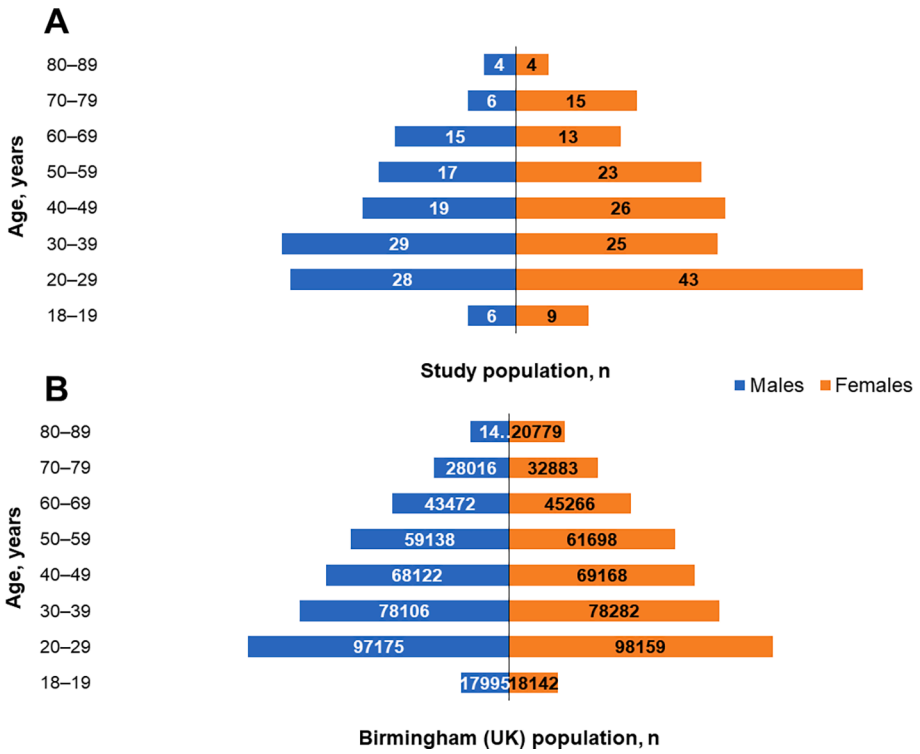

Fig. 1. Study population distribution versus Birmingham, UK population census 2016.

prevalence according to the WHS criteria [2-8].

2. Methods

The cross-sectional study conformed to the tenets of the Declaration of Helsinki. It received a favourable opinion by the ethical committee of Aston University and governance approval.

Two hundred and sixty-five participants were estimated to be an appropriate sample size, using the formula: n = (((1.962)P(1-P))/d2) [21]. An expected disease prevalence "P" of 22.1% was derived from a British female cohort study, where the reported dry eye prevalence was 20.8% (95% CI, 19.5–22.1) [19]. The upper confidence value was selected, to maximise the sample size and hence to be confidence in the results [21]. Moreover, an allowable error "d" of 5% was recommended when "P" takes values between 10% and 90% [21].

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 targetting of age and sex stratification to closely match the 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.

Room temperature and humidity (mean ± standard deviation) were 22.4 ± 2.0 °C and 49.3 ± 8.2%, respectively. A minimum of 15 min of adaptation time to the room conditions was scheduled prior to the collection of clinical measures.

In a single clinical session, participants were first asked to complete both DEQ-5 and OSDI questionnaires, followed by a tear film and ocular surface examination. Information about the exposure of DED risk factors was obtained through a self-administered survey of risk factors identified in past prevalence studies reported by the Epidemiology report of TFOS DEWS II [1]. Participants were also asked if they had experienced eye irritation, either rarely, sometimes, frequently or constantly, over the past month and a previous diagnosis of DED by a physician. The questions were asked to further diagnose DED according to the WHS criteria, as the most widely used previous diagnostic criteria in the epidemiology of DED [1].

In the following order, DED signs of non-invasive Keratograph tear break-up time (NIKBUT, Oculus Keratograph 5M (K5M, Oculus Optikgeräte GmbH, Wetzlar, Germany)), tear osmolarity (TearLab Osmolarity System, TearLab Corporation, California, USA) and ocular surface staining (K5M, Oculus Keratograph 5 M (Oculus Optikgeräte GmbH, Wetzlar, Germany)) were assessed. All DED signs were obtained from one eye, except for tear osmolarity, where both eyes were evaluated. NIKBUT was measured 3 times and the mean was recorded. Ocular surface staining included corneal fluorescein staining, conjunctival lissamine green staining, and upper and lower lid wiper epitheliopathy (LWE) lissamine green staining. Both fluorescein (Bio-Fluoro, Bio-Tech Vision Care Pvt Ltd, Gujarat, India) and lissamine green (Green Glo, Hub Pharmaceuticals Llc, California, USA) were applied via saline-wetted paper strips to the temporal eyelid canthus [20]. The former was instilled once (with the excess saline flicked off), whereas a whole drop of the latter (allowed to increase in concentration for 5 s) was instilled twice, 5 min apart [20]. Ocular surface staining images were analysed by counting corneal and conjunctival spots, rather than recording these live as the Oculus Keratograph 5M only has a digital display, and this allowed as this allowed for investigator masking with respect to participant demographics and promoted maximum consistency in assessment. Lastly, the length and width of the lower and upper lid margin staining were measured subjectively using digital callipers [20].

The prevalence and risk factors of DED were based on diagnosis according to the TFOS DEWS II diagnostic criteria [20]. The criteria defined the disease by an OSDI score of ≥ 13 and DEQ-5 score of ≥ 6 and at least one of the following homeostasis markers:

- NIKBUT of < 10 s;
- Tear film hyperosmolarity defined either by an osmolarity value of ≥ 308 mOsm/L in either eye or an interocular osmolarity difference of > 8 mOsm/L;

Table 1
Reported risk factors.

Risk factor	Category	Frequency (n)	Percentage (%)
Ethnicity	White	166	58.9
	South Asian	99	35.1
	Black	6	2.1
	Others	11	3.9
Sex	Male	124	44.0
	Female	158	56.0
Age (years)	18–19	15	5.3
	20–29	71	25.2
	30–39	54	19.1
	40–49	45	16.0
	50–59	40	14.2
	60–69	28	9.9
	70–79	21	7.4
	80–89	8	2.8
Residential area	Rural	40	14.8
	Urban	230	85.2
Education	Elementary or primary school	2	0.7
	Middle or secondary school	24	8.8
	High school or 6th form	49	17.9
	University or higher	199	72.6
Employment status	Unemployed	101	36.9
	Employed	173	63.1
Smoking	No	259	94.5
	Yes	15	5.5
Alcohol intake	No	111	40.5
	Yes	163	59.5
Contact lens wear	No	206	75.2
	Yes	68	24.8
Computer use (hours/day)	<3	61	22.3
	3–5	92	33.6
	6–8	95	34.7
	>8	26	9.5
Systemic/ocular health condition*	No	86	31.4
	Yes	188	68.6
Ocular surgery**	No	232	85.0
	Yes	41	15.0
Systemic/ocular medication***	No	142	51.8
	Yes	132	48.2
Nutritional supplement intake****	No	134	48.9
	Yes	140	51.1
Sleep duration (hours/night)	>8	14	5.1
	6–8	226	82.8
	<6	33	12.1
Outdoors activity (hours/leisure day)	<3	119	44.6
	3–4	84	31.5
	>4	64	24.0
Stress level	Minimally stressful	82	30.0
	Moderately stressful	173	63.4
	Extremely stressful	18	6.6

* Recorded systemic/ocular health conditions were migraine (n = 31), asthma (n = 31), eczema (n = 23), acne (n = 17), rosacea (n = 9), psoriasis (n = 3), dermatitis (n = 1), morphea (n = 1), vitiligo (n = 1), vitamin D deficiency (n = 28), iron deficiency (n = 11), anxiety (n = 25), depression (n = 15), rheumatoid arthritis (n = 28), hypertension (n = 27), hypercholesterolemia (n = 20), thyroid disease (n = 14), cancer (n = 13), polycystic ovary syndrome (n = 4), bladder irritation (n = 1), osteoporosis (n = 5), irritable bowel syndrome (n = 9), diabetes mellitus (n = 11), lymphatic drainage problem (n = 1), stroke (n = 4), prostatitis (n = 1), gout (n = 1), keratoconus (n = 1), pterygium (n = 1), insomnia (n = 2), Sjögren syndrome (n = 1), tuberculosis (n = 1), epilepsy (n = 1), Ehlers-Danlos syndrome (n = 1), sinusitis (n = 2), familial dilated cardiomyopathy (n = 1), Crown disease (n = 1), carpal tunnel syndrome (n = 1), glaucoma (n = 4), human immune deficiency virus (n = 1), multiple sclerosis (n = 1), thoracic outlet syndrome (n = 1), osteoperosis (n = 1), diverticulosis (n = 1), rhinitis (n = 1), bronchiectasis (n = 1), Best disease (n = 1), age-related macular degeneration (n = 1), Parkinson's disease (n = 1), traumatic glaucoma (n = 1), ulcerative colitis (n = 1), retinopathy (n = 1), spinal stenosis (n = 1). cataracts (n = 1), pain in joints (n = 1), back (n = 8), pelvis (n = 3) and hips (n = 1), and allergy to pollen (n = 44), grass (n = 3), dust (n = 12), penicillin (n = 11), pets (n = 7), nuts (n = 3), feathers (n = 2), flowers (n = 1), wool (n = 1), mould (n = 1), mites (n = 2), plasters (n = 2), antibiotics (n = 1), non-steroidal anti-inflammatory drugs (n = 1), gluten (n = 1), dairy (n = 1), soy (n = 1), fish (n = 1), eggs (n = 1), zinc (n = 1), statins (n = 1), trimethoprim (n = 1), ethylephrine (n = 1), morphine (n = 1) and opioids (n = 1).

** Documented surgical ocular interventions were strabismus surgery (n = 4), refractive surgery (n = 13), dacryocystorhinostomy (n = 2), cyst removal (n = 7), corneal cross-linking (n = 1), cataract surgery (n = 11) and retinal surgery (n = 2).

*** Medication intake included the use of oral contraceptives (n = 18), antimigraine drugs (n = 4), antihistamine drugs (n = 22), pills for skin problems (n = 7), antihistamine inhaler (n = 11), anxiolytics (n = 3), steroids (n = 2), painkillers (n = 7), blood pressure pills (n = 19), antithyroid pills (n = 11), pills for asthma (n = 1), pills for digestive problems (n = 2), pills for bladder control (n = 4), cancer treatment (n = 2), antidepressant (n = 8), statins (n = 19), diuretics (n = 2), hormone therapy (n = 3), pills for irritable bowel syndrome (n = 1), diabetes treatment (n = 6), aspirins (n = 12), prostatitis treatment (n = 2), heart treatment (n = 1), pills for vertigo (n = 1), sleeping tablets (n = 5), dermatitis treatment (n = 1), arthritis treatment (n = 2), antibiotics (n = 2), glaucoma drops (n = 3), pills for palpitation (n = 1), beta blockers (n = 1), human immune deficiency virus treatment (n = 1), osteoporosis treatment (n = 1), stomach protector (n = 3), antifungal pills (n = 1), antihistamine nasal spray (n = 1), antihistamine eyedrops (n = 2), Parkinson treatment (n = 1), morphine (n = 1), epilepsy treatment (n = 1), sinusitis nasal spray (n = 1), gout treatment (n = 1), and contraceptive implant (n = 2).

**** Nutritional supplement intake include the use of vitamin D (n = 42), cod liver oil (n = 37), iron (n = 22), protein supplement (n = 4), multivitamins (n = 44), vitamin C (n = 16), vitamin B (n = 9), calcium (n = 5), zinc (n = 2), vitamin E (n = 1), weight gainer (n = 1), folic acid (n = 2), echinacea (n = 1), glucosamine (n = 11), hyaluronic acid (n = 1), probiotics (n = 1), herbal pills (n = 1), magnesium (n = 7), primrose oil (n = 1), caffeine (n = 1), essential amino acids (n = 1), electrolytes (n = 1), melatonin (n = 1), collagen (n = 1), lutein (n = 2), yin yang (n = 1), flaxseed oil (n = 1), lysine (n = 1), beetroot extract (n = 1), and turmeric (n = 1).

- Ocular surface damage defined either by > 5 corneal staining spots, >9 conjunctival staining spots, or a LWE staining of ≥ 2 mm length and ≥ 25% width.

Moreover, for comparison with previous studies, DED was determined by the WHS criteria, which defined the disease by the presence of self-reported symptoms of ocular dryness and irritation either often or constantly, or a previous dry eye diagnosis by a physician [2-8].

3. Statistical analysis

Statistical analysis was performed with SPSS version 23 (IBM Corp, released in 2015, New York, USA). All parameters were found to be significantly different from a normal distribution using Kolmogorov-Smirnov testing. Risk factors were treated as dichotomous and/or ordinal variables, and risk categories with low frequency of endorsement (<5%) were collapsed (rather than being excluded from the start) for the statistical analysis. DED prevalence rates were presented with 95% confidence intervals (CI). Correlations between DED symptoms and signs among DED participants were evaluated with Spearman's rank correlation coefficients. Univariate analysis, including Chi-square tests, initially determined the potential of all self-reported risk factors. Risk factors with p-values of<0.10 were considered for further multivariate analysis with non-hierarchical binary logistic regression. The strength and precision of the DED associations were summarised using odds ratios (OR) and 95% CIs, respectively. ORs with p-values of ≤ 0.05 were considered statistically significant. Correlations between the selected DED risk factors were evaluated with point biserial correlation coefficients (between dichotomous and ordinal risk factors), Spearman's rank correlation coefficients (between two ordinal risk factors) and phi coefficients (between two dichotomous risk factors).

4. Results

Two-hundred and eighty-two participants (mean age 40 years, range

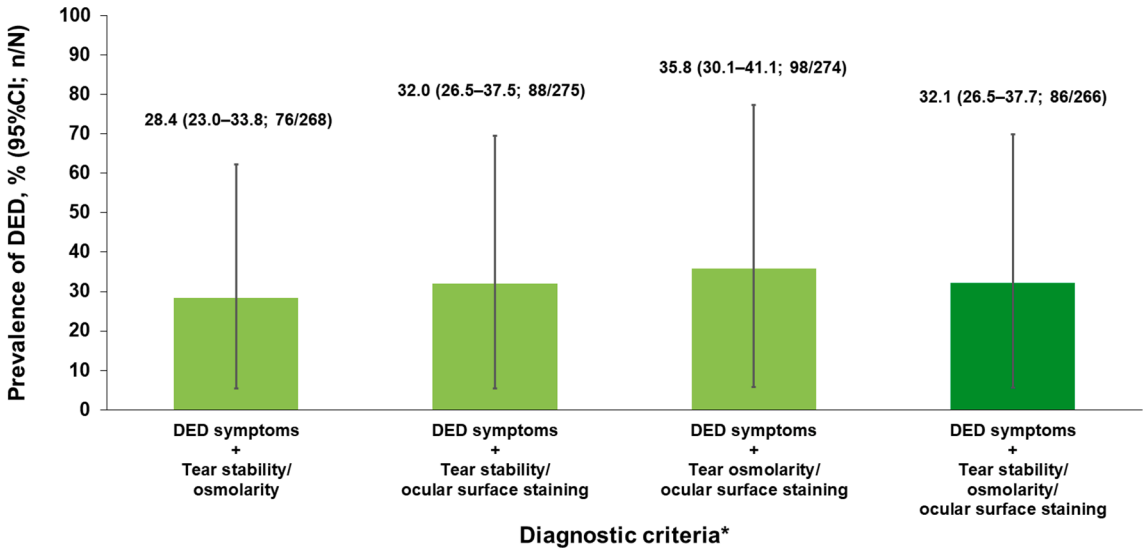

Fig. 2. DED prevalence, based on the inclusion of different combinations of the TFOS DEWS II recommended homeostasis markers. DED = dry eye disease. NIKBUT = non-invasive Keratograph tear break-up time. LWE = lid wiper epitheliopathy. CI = confidence interval.

Table 2
Correlations between DED signs/symptoms of DED participants.

Ocular signs/symptoms	DEQ-5 score	OSDI score
	Spearman's rank coefficient	Spearman's rank coefficient
NIKBUT mean value (s)	−0.177*	−0.175*
Interocular osmolarity difference (mOsm/l)	−0.114	−0.107
Highest osmolarity value (mOsm/l)	−0.057	−0.034
Corneal staining spots	0.124	0.095
Conjunctival staining spots	0.058	0.091
Upper LWE length (mm)	0.070	−0.046
Upper LWE width (%)	0.066	0.015
Lower LWE length (mm)	−0.006	−0.026
Lower LWE width (%)	−0.040	−0.047
DEQ-5 score	GRAY SHADING	0.518**
OSDI score	0.518**	GRAY SHADING

DED = dry eye disease. DEQ-5 = 5-item Dry Eye Questionnaire. OSDI = Ocular Surface Disease Index. NIKBUT = non-invasive Keratograph tear break-up time. LWE = lid wiper epitheliopathy.
* p-value ≤ 0.05.
** p-value ≤ 0.01.

18–88 years; 56% female) took part in the study, matched for age and sex to the UK Birmingham population census for 2016 (Fig. 1, Table 1). Up to 5% (n = 15) of participants did not respond to each of the risk factor questions.

The prevalence of DED according to the TFOS DEWS II criteria was 32.1% (95 %CI 25.5–37.7%; Fig. 2) and remained relatively similar when combining symptoms with the different DED signs indicating a loss of homeostasis (Fig. 2). The most common contributing signs were tear instability and conjunctival or LWE staining (Fig. 2). DED prevalence according to the WHS criteria was 29.5% (95 %CI, 24.4–35.1).

Among all DED participants, NIKBUT values were significantly correlated with the DEQ-5 and OSDI scores (Table 2). Both symptom questionnaires were found to be significantly associated with each other (Table 2).

The identified significant univariate risk factors (using $p < 0.10$) of sex, age, employment status, systemic/ocular health, systemic/topical medication use, hours of sleep and leisure time spent on outdoors activities (Table 3) were considered for the multivariate analysis (Table 3). Risk factors which did not initially reach significance included ethnicity, residential area, education, smoking, alcohol intake, contact lens wear, daily hours of computer use, nutritional supplement intake, prior ocular surgery and stress level (Table 3).

DED associations that remained statistically significant in the multivariate analysis were female sex, the presence of any systemic/ocular co-morbidity, short sleep duration and prolonged leisure time spent on outdoor activities (Table 4).

5. Discussion

The primary importance of epidemiological studies is to gain an understanding of a disease burden to plan and allocate health sources. In DED, the disease epidemiology has been challenged by the lack of a standardised diagnostic method to rely on [1]. The present study is the first to determine the prevalence and risk factors of DED in the UK conforming to the TFOS DEWS II diagnostic criteria [20]. The criteria are from a consensus on the evidence-base and currently recommended to be globally applied in DED research [20]. In addition, the prevalence of DED was estimated by the WHS criteria [2-8].

The prevalence of DED by the TFOS DEWS II diagnostic criteria of 32.1%, aligned to the worldwide DED prevalence rates reported by the TFOS DEWS II epidemiology report [1]. Amongst the DED signs assessed, conjunctival staining was the most common sign, followed by reduced NIKBUT, lower/upper LWE staining, corneal staining and signs of tear hyperosmolarity. However, the prevalence of dry eye remained remarkably consistent if any of the loss of homeostasis markers was omitted, indicating the robustness of the TFOS DEWS II diagnostic approach.

Previous research has noted that ocular surface staining might not only be an intrinsic feature of DED, but may also present in other conditions with eventual DED symptoms [1]. This might explain the high DED prevalence rates obtained where conjunctival and LWE staining signs were assessed individually. Further research is needed to understand which staining thresholds are best to distinguish DED from other symptomatic ocular diseases.

Significant (but low) negative correlations observed between NIKBUT and DED symptoms strengthened the diagnostic suitability of tear film stability in assessing DED by the TFOS DEWS II criteria. However, the cut-off specified by TFOS DEWS II used was derived from subjective techniques, but benchmarking for automated K5M data [20,22], where the detection of tear break-up times has been shown to occur 2 s earlier [23], may be appropiate. The low correlations between signs and symptoms suggest they are largely independent, at least in this Birmingham cohort.

Table 3
Distribution of risk factors among participants with or without DED‡.

Risk factor	Category	NDED	NDnon-DED	NTotal	X2	p-value
Ethnicity	White	58	97	155	0.893	0.640
	South Asian	42	55	97		
	Black and others	6	10	16		
Sex	Male	58	59	117	8.721	0.003*
	Female	48	103	151		
Age (decades)	18–19	11	4	15	12.201	0.058*
	20–29	33	37	70		
	30–39	15	36	51		
	40–49	16	27	43		
	50–59	12	23	35		
	60–69	10	16	26		
	70–79 and 80–89	9	19	28		
Residential area	Rural	14	25	39	0.439	0.509
	Urban	91	128	219		
Education	Elementary, primary, middle or secondary school	8	16	24	1.524	0.467
	High school or 6th form	16	30	46		
	University or higher	82	110	192		
Employment status	Unemployed	48	51	99	4.256	0.039*
	Employed	58	105	163		
Smoking habits	No	103	145	248	2.223	0.136
	Yes	3	11	14		
Drinking habits	No	40	67	107	0.710	0.399
	Yes	66	89	155		
Contact lens wear	No	83	116	199	0.537	0.464
	Yes	23	40	63		
Systemic/ocular health condition	No	46	38	84	10.501	0.001*
	Yes	60	118	178		
Ocular surgery	No	90	133	223	0.041	0.839
	Yes	16	22	38		
Systemic/topical medication	No	62	75	137	2.744	0.098*
	Yes	44	81	125		
Nutritional supplement intake	No	58	72	130	1.851	0.174
	Yes	48	84	132		
Computer use (hours/day)	<3	23	36	59	2.438	0.487
	3–5	41	47	88		
	6–8	34	56	90		
	>8	8	17	25		
Sleep duration (hours/night)	>8	9	5	14	5.324	0.070*
	6–8	87	128	215		
	<6	9	23	32		
Outdoors activity (hours/leisure day)	<3	51	66	117	4.923	0.085*
	3–4	34	43	77		
	>4	17	44	61		
Stress level	Minimally stressful	29	52	81	4.284	0.117
	Moderately stressful	72	90	162		
	Extremely stressful	4	14	18		

DED = dry eye disease. n = sample size. X^2 = Chi-square test. ǂ DED was diagnosed by an Ocular Surface Disase Index score of ≥ 13 and a 5-item Dry Eye Questionnaire score of ≥ 6 and at least one of the following homeostasis markers: non-invasive Keratograph tear breakup time < 10 s, tear film hyperosmolarity ≥ 308 mOsm/L in either eye or an interocular osmolarity difference of > 8 mOsm/L) and ocular surface damage (defined either by > 5 corneal staining spots, > 9 conjunctival staining spots, or a LWE staining of ≥ 2 mm length and $\geq 25\%$ width).

* Selected for logistic multivariate analysis.

DED prevalence by symptoms and signs has also been reported in other European countries, although using different diagnostic criteria and clinical-based populations. Malet et al., describing DED in an elderly population (aged over 73 years) by an OSDI score of ≥ 23 or the use of daily artificial tears, determined a disease prevalence of 21.9% in France; 27.1% in females and 13.6% in males [18]. Another diagnostic method, involving symptom self-reporting and the assessment of ocular surface staining or tear film stability, was used in Spain and estimated a disease prevalence of 11.0%, with females more affected than males (11.9% vs. 9.0%) [12].

The WHS criteria has previously been the most consistently applied DED diagnostic method [1]. In the present study, the prevalence of DED by the WHS criteria was 29.5%. The rate falls within the calculated TFOS DEWS II DED prevalence range, and is comparable to previous WHS DED estimates [2-8].

Age, employment status, medication intake, female sex, the presence of any systemic/ ocular co-morbidity, short sleep duration and prolonged leisure time spent on outdoor activities were identified as potential risk factors for DED (p-values < 0.10). The last four factors were confirmed to reach statistical significance in the multivariate analysis (p-values ≤ 0.05).

Females were 2.4 times significantly more likely to be diagnosed with DED than males, reflecting the importance of sex hormones in the disease predisposition. Male-specific sex hormones are believed to regulate both tear lipid and aqueous secretions, as well as the immune responses of corneal and conjunctival cells [24]. In contrast, female-specific sex hormones appear to antagonise these functions [24].

Systemic diseases, including hypertension, hypercholesterolemia, thyroid disease, asthma, eczema, any allergy, rheumatoid arthritis, stroke, migraine, irritable bowel syndrome and pelvic pain, have previously been recognised to be significant DED risk factors [5,19]. The same range of diseases was reported in the present study. Nevertheless, the rationale behind the relationship between the individual diseases and DED is difficult to ascertain, as aggregate data were studied.

Sleeping<6 h/night was significantly associated with DED (OR = 5.05), as has been observed previously [5]. Short sleep duration is

Table 4
DED risk factor assessment.

Risk factor	Univariate analysis			Multivariate analysis*		
Category	OR	95 %CI	p-value	OR	95 %CI	p-value
Ethnicity						
White	1.000			n/a	n/a	n/a
South Asian	0.783	0.467–1.313	0.354			
Black and others	0.997	0.344–2.885	0.995			
Sex						
Male	1.000			1.000		
Female	2.109	1.281–3.473	0.003	2.380	1.341–4.226	0.003
Age (years)						
18–19	1.000			1.000		
20–29	3.083	0.895–10.621	0.074	1.723	0.448–6.624	0.429
30–39	6.600	1.811–24.053	0.004	3.185	0.707–14.342	0.131
40–49	4.641	1.264–17.041	0.021	1.640	0.362–7.421	0.521
50–59	5.271	1.380–20.138	0.015	1.658	0.336–8.191	0.535
60–69	4.400	1.095–17.676	0.037	2.081	0.427–10.153	0.365
70–79 and 80–89	5.806	1.443–23.363	0.013	2.880	0.615–13.491	0.179
Residential area						
Rural	1.000			n/a	n/a	n/a
Urban	0.788	0.388–1.598	0.082			
Education						
Elementary, primary, middle or secondary school	1.000			n/a	n/a	n/a
High school or 6th form	0.938	0.330–2.661	0.903			
University or higher	0.671	0.274–1.642	0.382			
Employment status						
Unemployed	1.000			1.000		
Employed	1.704	1.025–2.832	0.040	1.826	0.850–3.923	0.123
Smoking habits						
No	1.000			n/a	n/a	n/a
Yes	2.605	0.709–9.570	0.149			
Alcohol intake						
No	1.000			n/a	n/a	n/a
Yes	0.805	0.486–1.334	0.400			
Contact lens wear						
No	1.000			n/a	n/a	n/a
Yes	1.244	0.693–2.234	0.464			
Systemic/ocular health condition						
No	1.000			1.000		
Yes	2.381	1.410–4.046	0.001	2.719	1.395–5.299	0.003
Ocular surgery						
No	1.000			n/a	n/a	n/a
Yes	0.930	0.463–1.869	0.839			
Systemic/topical medication						
No	1.000			1.000		
Yes	1.522	0.925–2.504	0.098	1.202	0.639–2.263	0.568
Nutritional supplement intake						
No	1.000			n/a	n/a	n/a
Yes	1.410	0.859–2.313	0.174			
Computer use (hours/day)						
<3	1.000			n/a	n/a	n/a
3–5	0.731	0.375–1.432	0.362			
6–8	1.052	0.536–2.066	0.882			
>8	1.358	0.505–3.653	0.545			
Sleep duration (hours/night)						
>8	1.000			1.000		
6–8	2.648	0.858–8.171	0.090	2.471	0.660–9.256	0.179
<6	4.600	1.207–17.524	0.025	5.050	1.039–24.536	0.045
Outdoors activity (hours/leisure day)						
<3	1.000			1.000		
3–4	0.977	0.547–1.745	0.938	0.968	0.505–1.856	0.968
>4	2.000	1.025–3.902	0.042	2.369	1.108–5.066	2.369
Stress level						
Least stressful	1.000			n/a	n/a	n/a
Moderately stressful	0.697	0.402–1.208	0.198			
Extremely stressful	1.952	0.588–6.484	0.275			

DED = dry eye disease. OR = odds ratio. CI = confidence interval. n/a = not applicable.
* Included DED risk factors with initial significance of p-value ≤ 0.10 (Chi-square tests, Table 3).

thought to decrease parasympathetic activity [25]. The lacrimal gland is innervated to a greater extent by the parasympathetic nervous system [26], and hence any kind of sleep disturbance may be expected to affect tear secretion.

Participants regularly engaging in more than four hours of outdoor activity on a weekend day were 2.4 times significantly more prone to DED. The impact of outdoor activity can be related to environmental conditions, such as high altitude, sunlight exposure, temperature,

humidity, wind, precipitation and air pollution that have been associated with symptomatic and clinically diagnosed DED [7,9,13].

Importantly, previously reported risk factors which did not reach significance in the initial univariate analysis, including ethnicity, residential area, education, contact lens wear, daily hours of computer use, prior ocular surgery and stress level, might have been confounded by the limited range within the sample. The participants enrolled were predominantly non-contact lens wearers, computer users and non-smokers, reporting moderate stress and no history of ocular surgery. However, this reflected the UK population in which these factors could only be fully explored with a much larger sample size.

The main limitations of this study are intrinsic to the study design. The association and certainty of the obtained cross-sectional risk factors of DED would be stronger in a longitudinal study. The sample size calculation might be limited as it was based on a British female cohort; nevertheless, this was the only available UK reference DED data at the time of the study. Moreover, the DED prevalence rates and risk factors obtained are specific to the population studied. The study was also powered to assess the prevalence and not risk factors for dry eye. However, larger European studies were focused on limited age ranges, participants were not stratified by population demographics and based diagnosis on symptoms alone (with or without artificial tear use)[18] or in combination with invasive signs [27] which do not meet the current consensus criteria. Causality cannot be inferred in a cross-sectional study so it is possible that dry eye caused factors such as a reduction in sleep or outdoor activity rather than the other way around.

In conclusion, this study serves as an insight into DED prevalence rates and risk factors of a single population in the UK, following the TFOS DEWS II diagnostic criteria. The prevalence of DED was just under one-third of the adult population, aligning with the prevalence identified in multiple counties worldwide [1]. Female sex, the presence of any systemic and/or ocular diseases, short sleep duration and prolonged leisure time spent on outdoor activities were significant DED risk factors.

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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Disclosure statements

The authors have no commercial or proprietary interest in any concept or product described in this paper.

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