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Clinical practice patterns in the management of dry eye disease: A TFOS international survey 2023-4

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Abstract

Aims: To understand current clinical management of dry eye disease (DED), based on its perceived severity and subtype by practitioners across the world.

Methods: The content of the anonymous survey was chosen to reflect the DED management strategies reported by the Tear Film and Ocular Surface Society (TFOS) 2nd Dry Eye Workshop (DEWS II). Questions were designed to ascertain practitioner treatment choice, depending on the subtype and severity of DED. It was first created in English and then translated/back-translated into 14 languages for online completion.

Results: Completed surveys were received from 905 eye care practitioners (52% optometrists and 42% ophthalmologists) from across the globe. Many treatment strategies for DED were observed to be utilised by respondents, independent of severity and subtype, the most common being advice (82%), low (82%) and high (81%) viscosity unpreserved lubricants and lid wipes/scrubs (79%). Several treatments were prescribed across all severity levels (scaled from 1 mild to 10 severe), such as advice (median 4.5, range 4.8), artificial tears (median 5.1, range 4.6) and nutritional supplements (median 5.3, range 4.2). Others were prescribed more frequently with increasing disease severity, for instance, biologics (median 8.2, range 2.8) and surgical approaches (median 8.1, range 2.2). While a similar number of practitioners reported prescribing advice, artificial tears and anti-inflammatories regardless of DED subtype, the majority reported approaches for aqueous deficient DED were punctal occlusion, therapeutic contact lenses and secretagogues, while the use of oral essential fatty acids, topical lipid-containing products, lid hygiene and lid warming were the preferred management choices for evaporative DED.

Conclusions: There remains great variability in clinical approaches to DED management and until research-evidence definitively informs improved guidance, data from this survey can be used by clinicians to benchmark their practice.

Keywords: Management; Therapy; Dry eye disease; Subtype; Severity; Ocular surface; Tear film

1. Introduction

Dry eye disease (DED) is common and symptomatic, affecting many millions of individuals worldwide [1]. It is a multifactorial condition characterised by a loss of tear film homeostasis, perpetuated by a vicious cycle of tear film instability, hyperosmolarity, and ocular surface damage and inflammation [2]. The nature and severity of symptoms vary widely, and can significantly impair quality of life [3] and increase anxiety and depression [4]. This results in considerable human and economic burden, through loss of productivity, and healthcare costs incurred by individuals and healthcare systems [5-7]. Considered in totality, the appropriate diagnosis and management of DED has a far-reaching impact and, as such, is of high importance.

As with other diseases, the type and severity of DED should be identified, in order to formulate an effective management plan [2, 8]. Dry eye disease can be subclassified into evaporative, aqueous deficient, or a combination of these elements [2]. Features of evaporative dry eye disease (EDE) include changes in meibomian gland secretions and morphology, and abnormal lipid layer thickness on interferometry, suggesting meibomian gland dysfunction [9]. In aqueous deficient dry eye disease (ADDE), there is reduced aqueous tear volume, apparent as a reduction in tear meniscus height [9].

Artificial tears are the mainstay management option for DED, being easily accessible in a wide range of formulations, and having a low risk-profile [8], with the addition of lipid-containing products being preferential in EDE management [10, 11]. With numerous products on the market, it can be difficult for patients and practitioners to ascertain the best option, which can result in a trial-and-error approach, accompanied by mounting frustration and expense [12]. Other common strategies may include patient education, modification of local environment, dietary modifications, such as oral essential fatty acid supplementation, modification/elimination of offending systemic and topical medications, and lid hygiene and warm compresses [8]. Numerous other treatments have been used in the management of DED, but as healthcare practitioners, it is essential that clinicians are guided by evidence from high quality research. The TFOS DEWS II Management and Therapy Report provided a staged management algorithm, with suggested treatments based on the best available evidence at the time [8]. It is intended that this be used following a positive diagnosis and subclassification of DED, in conjunction with other available clinical information regarding the dry eye nature and severity.

The TFOS DEWS II reports provided expert consensus recommendations for the diagnosis and management of DED. However, there remains limited evidence to guide practitioners as to which treatment may be expected to be most effective for each DED severity and subtype [8]. Previous studies have compared management patterns between certain countries [13], between different professions working within the same country [14-16] and have evaluated differences between clinical patterns and evidence-based guidelines across Australia [17] (Table 1). A recent study looked at the evolving landscape of optometry in the United Kingdom, in light of its increasing scope [18]. Nonetheless, there is still a dearth of studies comparing global trends [19].

The purpose of relaunching the TFOS international survey after 5 years was to re-evaluate clinical DED prescribing and management patterns of dry eye practitioners [20], and examine how this has changed since the reporting of TFOS DEWS II, with the aim of improving patient care. The aim of this study was to determine how clinical management patterns differed depending on disease severity and subtype. Data collected from practitioners across the globe also allowed differences in dry eye management approaches between continents to be identified. Furthermore, as the survey was conducted twice, it became possible to compare datasets, and reveal evolution in management strategies over time. This allows practitioners to compare their practice to that of their peers, and understand how management varies in different locations across the world. This is also important for industry, in terms of product development and in the provision of professional education and support.

Table 1: Previous studies on patterns of clinical diagnosis and management of dry eye disease (DED) (all anonymous internet surveys).

Study	Comparison	Topics	Surveyed	Professionals	Results	Comments
Downie et al., [17]	Australian practice versus [illegible] guidelines	- Practitioner demography [illegible] severity - Research evidence basis	144	Optometrists	- DED practitioners utilise more Dx [illegible] treatments - Mg: - Mild: ATs & lid hygiene - Moderate: Pres. free lubricants - Severe: Gels	- EFA recommended if [illegible]evere. - Steroids & anti-inflammatories also used in moderate & severe cases.
Downie et al., [13]	UK versus Australian practice patterns	- Practitioner demography - Dx & Mg at each severity - Research evidence basis	317	Optometristss	- Symptoms, MGE & FBUT key in UK & Australia for Dx - Mg: - Mild: Lid hygiene & lubricants - Moderate: Pres. free gels - Severe: Ointments & punctal plugs	- Dx: UK more use of TMH, LIPCOF, grading of conj. LG stain & OSDI - Dx: Australia FBUT often used - Severity: UK evaluation of symptoms - Mg: UK advise more EFA & more unpreserved ATs in mild dry eye. Australia uses steroids in moderate & severe dry eye
Sy et al., [19]	Global practice patterns	- Practitioner demography - mg of ADDE (case study) - Treatment availability - Mg algorithms	115	Cornea specialists (66 %), general ophthalmologists (16 %), non-clinical research (6 %), optometrists (6 %) & other (6 %)	Commonest mg included cyclosporine, FML, loteprednol & autologous serum. Commonest oral treatments included EFA supplements, weak doxycycline & flaxseed products, and punctal plugs	Treatment efficacy measured with corneal FL stain, symptoms of foreign body & burning.
Van Tilborg et al., [14]	Optometry & general practice in Holland	- Awareness - Dx methodology - Preferred Mg	231	Optometrists (138) & GPs (93)	- Dx: Variable GPs: Dx testing uncommon. - Mg: Agreement limited to gel/ointment products	- Mg: Optoms: use more pres. free ATs, eyelid hygiene & heat therapies GPs: use more preserved ATs
Williamson et al., [15]	Perceptions of optometrists & ophthalmologists in North Carolina	- Awareness of symptoms - Dx - Mg used	100	Optometrists & Ophthalmologists	- Dx: BUT, Fl stain - Mg: ATs, warm comps & eyelid cleansing	- Dx: combined BUT, NaFl & LG stain Optometrists: Fl stain & history Ophthalmologists: Schirmer
Xue et al., [16]	Protocols for diagnosis & management in New Zealand	- Practitioner demography - Dx methodology - Mg at each severity - Research evidence basis	203	Optometrists (174) & Ophthalmologists (29)	- Dx: Symptoms, MGE, FBUT Optometrists: MGE Ophthalmologists: NaFl stain - Mg: Mild: Preserved & pres. free ATs & lid hygiene Moderate: Lid hygiene, EFAs, pres. free ATs & gels Severe: Lid hygiene, pres. free ATs & gels	For severe DED pres. free gels, ointments, cyclosporine, steroids, oral tetracyclines, punctal plugs & autologous serum used by both professions
Casemore et al. [18]	Diagnosis & management patterns of UK	- Practitioner demographics - Diagnostic techniques	131	Optometrists in primary care setting, excluding	Optometrists in primary care setting have inadequate time	Increase in therapeutic management of

	optometrists in light of increased role in therapeutic management	- management & patterns of intervention - Therapeutic qualification & implementation		secondary & tertiary practice	treating DED. Therapeutically qualified Optometrists felt more confident treating DED. - Dx: Symptomatology, Fl staining, MGE, FBUT, TMH, screen use - Mg: Mild: Environmental modification, dietary advice, lid hygiene, unpreserved ATs Moderate: Ointments, liposomal sprays, light therapies, Severe: topical corticosteroids, punctal plugs, systemic tetracyclines	DED in UK, & stepwise approach is being implemented

AT – Artificial Tears, DED – Dry Eye Disease, GP – General Practitioner, Dx – Diagnosis, Mg – Management, MGE – Meibomian Gland Examination, FBUT – Fluorescein Tear BreakUp Time, LG – Lissamine Green, Fl – Fluorescein, BUT – BreakUp Time (method not defined), TMH – Tear Meniscus Height, LIPCOF – Lid Parallel Conjunctival Folds, OSDI – Ocular Surface Disease Index Questionnaire.

2. Methods

2.1. Survey design

The content of the survey (Figure 1) was chosen to reflect the dry eye management strategies reported by TFOS DEWS II [8]. The wording of the questions was designed to ascertain which treatments a practitioner would select, depending on the subtype and severity of DED. It was first produced in English, and then translated into 14 languages (Brazilian Portuguese, Chinese/Mandarin Chinese, Czech, French, German, Italian, Spanish, Polish, Portuguese, Rumanian, Russian and Serbian). In every instance, the translation underwent a process of back-translation and was subsequently reviewed by a native speaking eye care professional, ensuring that the intended meaning of the questions was preserved in each case. Once perfected, the anonymous survey was administered using the online Qualtrics platform (Utah/Seattle, Washington, USA).

Figure 1: Summary of questions presented in the survey

2.2. Ethics

This study adhered to the tenets of the Declaration of Helsinki and received ethical clearance from the University of Auckland ethics committee (Ref. 019870, protocol v1). Data were gathered anonymously and were handled confidentially. Prior to survey completion, a statement detailed the survey's duration, that submission of the questionnaire signified their consent to participate, and that due to the anonymity of the data, no modifications could be made once the responses were submitted. Participants could submit responses only once each, from a single device.

2.3. Participants

The online survey link was disseminated through various channels, including email, TFOS Ambassadors, conference seminars, professional colleges, and alumni university communities and by word-of-mouth. The survey remained accessible from July 2023, until data extraction in May 2024.

2.4. Data analysis

For the purpose of statistical analysis, countries were grouped into continents; Europe and the United Kingdom (EU), North America (NA), Latin America (LA), Australasia (AA), Asia/Middle East (AME) and Africa (A). In the 2018-19 survey, insufficient responses were received from participants in Africa to allow for statistical analysis of data from this continent.

SPSS Statistics (version 29, New York, USA) was employed for data analysis, and incomplete surveys (those where respondents reported using management options for patients with DED, but did not provide data on the subtype or severity they used them for) were excluded. Descriptive statistics, such as median and range, or mean and standard deviation, were utilised to portray the clinical severity and subtype of DED when examining practitioners' therapy approaches. Given the ordinal nature of the data and it differing from a normal distribution (Kolmogorov-Smirnov test $p<0.05$), the Mann-Whitney U test was used to compare data between continents. For usage data, Chi-squared test was applied. For categorical data, Fisher's exact test was employed. Regarding statistical significance, a p-value of 0.003 (0.05/16) or less was considered significant when comparing approaches to dry eye management between continents, based on a Bonferroni adjustment.

3. Results

3.1. Practitioner demographics

Completed questionnaires were submitted by a total of 905 eye care professionals, (42% ophthalmologists, 52% optometrists and 6% opticians) from 56 countries across 6 continents:

• Europe/UK and Scandinavia (n = 410): Albania (n = 1), Austria (n = 6), Bulgaria (n = 42), Czech Republic (n = 4), Denmark (n = 4), France (n = 2), Germany (n = 14), Ireland (n = 4), Italy (n = 24), Moldova (n = 1), Netherlands (n = 13), Poland (n = 13), Portugal (n = 23), Romania (n = 5), Serbia (n = 3), Slovakia (n = 1), Spain (n = 26), Sweden (n = 2), Switzerland (n = 3), United Kingdom (n = 219).

• North America (n = 81): Canada (n = 57), United States of America (n = 24).

• Latin America (n = 169): Argentina (n = 17), Brazil (n = 8), Chile (n = 18), Colombia (n = 5), Dominican Republic (n = 1), Ecuador (n = 4), Guatemala (n = 1), Mexico (n = 67), Paraguay (n = 1), Peru (n = 46), St. Vincent and the Grenadines (n = 1).

• Australasia (n = 81): Australia (n = 34), New Zealand (n = 47).

• Asia and the Middle East (n = 114): China (n = 44), Georgia (n = 9), Hong Kong (n = 5), India (n = 10), Malaysia (n = 1), Philippines (n = 1), Russia (n = 1), Saudi Arabia (n = 1), Singapore (n = 2), South Korea (n = 14), Thailand (n = 26).

• Africa (n = 50): Botswana (n = 1), Cameroon (n = 1), Ethiopia (n = 2), Ghana (n = 9), Kenya (n = 1), Madagascar (n = 1), Nigeria (n = 15), Seychelles (n = 1), South Africa (n = 16), Uganda (n = 3).

The average years of clinical experience was 14.9 ± 7.8, being similar between professions (p = 0.573).

3.2. Types of patients examined

Of those who responded (n = 905), 827 practitioners detailed the severities of dry eye they manage; patients with mild (28%, n = 229/827) and moderate (26%, n = 210/827) symptoms were the most common. Although 11% (n = 89) predominantly managed those with severe symptoms, some 51% (n = 410) found these to be the least common.

3.3. Global management and therapeutic approach

Out of all the respondents, 7% (n = 62) stated they were unable to prescribe for DED but, of those, 21% (n = 13 / 62) were providing advice, such as diet, water intake and office conditions.

Numerous dry eye therapies [8] were found to be in usage. The commonest management approaches globally are advice (82%), low (82%) and high (81%) viscosity unpreserved lubricants and lid wipes/scrubs (79%). Figure 2 presents, the median, and range of severities (along the X-axis) and subtypes (along the Y-axis) practitioners identified each treatment to be most suitable for.

Figure 1: Global management of dry eye disease based on severity and subtype. Symbol positioned at median value and bars indicate average range.

Trends in management strategies were observed worldwide. Unpreserved products were prescribed by more commonly than preserved (1.45:1; n = 738 to 509, p<0.001). Unpreserved artificial tears with low and high viscosity were prescribed by similar numbers of practitioners (1.01:1; n = 628 to 619, p=0.646). Ointments were given more commonly (1.13:1; n = 691 to 612, p<0.001) than lipid-containing lubricants, and unpreserved high viscosity lubricants were used more than ointments (1.06:1; n = 733 to 691, p=0.016). Prescriptions for general lid wipes/scrubs outnumbered those with Anti-Demodex properties (1.33:1; n = 719 to 541, p<0.001). Patient applied anti-demodex wipes were given more commonly than in-office anti-demodex therapies (1.73:1; n = 541 to 313, p<0.001). Commercially available warm lid compresses/face masks are now recommended by more practitioners than home-made alternatives (e.g. hot flannels) (1.11:1; n = 603 to 541, p=0.003). With regard in-office lid hygiene, for example BlephEx or debridement, lid debridement was used by similar numbers (1.01:1; n = 320 to 318, p=0.921), however, therapeutic meibomian gland expression is still used by more practitioners (1.47:1; n = 466 to 318, p<0.001). Intense pulsed light therapy was used by more practitioners than LipiFlow (by 1.48 times; n = 245 vs 166, p<0.001). For tear preservation, punctal occlusion was utilised more frequently than moisture chamber spectacles/goggles (by 1.41 times; n = 364 to 259, p<0.001).

A similar number of prescriptions were written for topical compared to oral antibiotics (1.09:1; n = 419 to 385, p=0.108). There was an equal split between topical and oral azithromycin (1.01:1; n = 235 to 232, p=0.872). Topical secretagogues were used more than systemic forms (1.79:1; n = 145 to 81, p<0.001). Prescriptions for topical immunomodulatory agents, e.g. tacrolimus, greatly outnumbers those for lifitegrast (1.90:1; n = 169 to 89, p<0.001), however corticosteroids were favoured much more than tacrolimus (2.83:1; n = 478 to 169, p<0.001). Clinicians fit therapeutic contact lenses in favour of autologous/allogeneic serum (1.36:1; n = 363 to 267, p<0.001) and amniotic membrane (1.70:1; n = 363 to 214, p<0.001). Autologous/allogeneic serum was reported to be prescribed more commonly than amniotic membrane (1.25:1; n = 267 to 214, p=0.005). Finally, other surgical approaches are now performed by more responding clinicians than intraductal probing (1.32:1; n = 91 to 69, p=0.071).

The large number of treatments were divided into the categories shown in Figure 1, in order to simplify visualisation. Numbers (percentage) of respondents prescribing specific treatments are listed below:

- Advice; n=805 (89%) such as on sleep or diet.
- Essential fatty acid supplements; n=697 (77%) in oral form.
- Artificial tears; n=805 (89%) – low and high viscosity, preserved and unpreserved.
- Ointments; n=715 (79%).
- Lipid containing lubricants (drops/spray); n=695 (77%).
- Lid hygiene; n=796 (88%).
- Moisture chamber spectacles /goggles; n=392 (43%).
- Punctal occlusion (with plugs); n=500 (55%).
- Warm compress; n=760 (84%) reported offering both in-office thermal pulsation as well as patient-admininstered lid warming.
- In-office techniques (e.g. intense pulsed light therapy); n=395 (44%).
- Topical antibiotics (e.g. azithromycin); n=433 (48%).
- Systemic antibiotics; n=444 (49%).
- Topical anti-inflammatory/immunosuppressants; n=525 (58%) prescribed dual anti-inflammatory options.
- Secretagogues; n=270 (30%) were prescribed both topically and orally.
- Biologic products; n=365 (40%) gave serum in addition to membranes.
- Therapeutic contact lenses; n=405 (45%).
- Surgical approaches; n=216, (24%) administered intraductal probing and/or other surgical approaches.

3.4. Severity

The choice of treatments deemed suitable for each disease severity are presented in Figure 2. Some therapies were applied roughly equally for all severity levels (scaled from 1 – mild to 10 – extreme), such as advice (median 4.5, range 4.8, 95% confidence interval 4.2), artificial tears (median 5.1, range 4.6, 95% confidence interval 2.8) and nutritional supplements (median 5.3, range 4.2, 95% confidence interval 4.0). Others were reserved for patients with more severe disease, for example biologics (median 8.2, range 2.8, 95% confidence interval 3.7) and surgical approaches (median 8.1, range 2.2, 95% confidence interval 4.5). There was no marked association between practitioner experience and the median severity or range of severity over which different DED treatments were prescribed (all $p<0.15$).

The analysis of the proportion of practitioners selecting a particular management approach based on varying severity levels revealed statistically significant differences across continents (Table 2). Advice was offered to patients with lower levels of disease severity in Africa, Asia/Middle East, Australasia and Europe/UK, than in Latin America. Practitioners in Latin America also reported reserving artificial tears for patients with higher DED severity than in North America, Asia/Middle East and Europe. Practitioners in Australasia prescribed lipid-containing lubricants for dry eye of lower severity than did their counterparts in Asia/Middle East, Latin America and Africa; as did those in Europe. Topical and systemic antibiotics were prescribed more readily in Africa, Latin America and Asia/Middle East than Europe; topical antibiotics more so in Latin America than in Australasia and systemic antibiotics most so in North America than in Europe. Topical anti-inflammatories/immunomodulators were used for dry eye of lower severity in Asia/Middle East and North America than in Europe and Australasia; and in Latin America compared to in Europe. Secretagogues were favoured for milder disease in Asia/Middle East and Latin America, than in Europe and Australasia.

Table 2. Differences in treatment choice between continents, by severity and subtype of DED.

Treatment	Severity	Sig. (p)	Subtype	Sig. (p)
Advice	A ⇨ LA	.001	Not significant	
	AME ⇨ LA	<.001		
	AA ⇨ LA	.001		
	EU ⇨ LA	<.001		
Essential fatty acid supplements	Not significant		Not significant	
Artificial tears	NA ⇨ LA	<.001	Not significant	
	AME ⇨ LA	<.001		
	EU ⇨ LA	.002		
Ointments	Not significant		LA → EU	<.001
			LA → A	<.001
Lipid containing lubricants (drops/		.001		
spray)	AA ⇨ AME	<.001	Not significant	
	AA ⇨ LA	<.001		
	AA ⇨ A	.008		
	EU ⇨ AME	<.001		
	EU ⇨ LA	.006		
	EU ⇨ A			
Lid hygiene	Not significant		A → AME	<.001
			EU → AME	<.001
			NA → AME	.001
Moisture chamber spectacles/ goggles	Not significant		Not significant	
Punctal occlusion (with plugs)	Not significant		Not significant	
Warm compresses	Not significant		Not significant	
In-office IPL therapy	Not significant		Not significant	
Topical antibiotics (e.g. azithromycin)	A ⇨ EU	<.001	Not significant	
	LA ⇨ AA	.0075		
	LA ⇨ EU	<.001		
	AME ⇨ EU	<.001		
Systemic antibiotics	A ⇨ EU	<.001	A → LA	<.001
	LA ⇨ EU	<.001	A → EU	<.001
	NA ⇨ EU	.006	A → NA	<.001
	AME ⇨ EU	.004	A → AME	<.001
			A → AA	<.001
Topical anti-inflammatory /		<.001	NA → AME	<.001
immunomodulators	AME ⇨ EU	<.001	NA → EU	<.001
	AME ⇨ AA	<.001	NA → AA	<.001
	NA ⇨ EU	.001	LA → AME	<.001
	NA ⇨ AA	<.001	LA → EU	<.001
	LA ⇨ EU		LA → AA	<.001
Secretagogues	AME ⇨ EU	<.001	LA → AME	<.001
	AME ⇨ AA	<.001		
	LA ⇨ EU	<.001		
	LA ⇨ AA	<.001		
Biologics	Not significant		Not significant	
Therapeutic contact lens approaches	Not significant		Not significant	
Surgical approaches	Not significant		EU → NA	<.001

EU=Europe/UK & Scandinavia, NA=North America, LA=Latin America, AA=Australasia, AME=Asia/Middle East, A=Africa. Black arrow (⇨) points towards more severe & orange arrow (→) points towards more evaporative DED.

3.5. Subtype

Worldwide, practitioners appear to have clearly established management algorithms for treating dry eye of each subtype based on their data in which they reported criteria differed for ADDE compared to EDE. While practitioners reported prescribing advice, artificial tears and anti-inflammatories for both DED subtypes, the key approach for aqueous deficient DED involved punctal occlusion, therapeutic contact lenses and secretagogues, whereas, products containing essential fatty acids, lipids, lid hygiene, lid warming, in-office treatments and antibiotics were central to the treatment of evaporative DED (Table 3). There was no marked association between practitioner experience and the median subtype for which different DED treatments were prescribed (all $p<0.15$). However, there was marked positive association between practitioner experience and the subtype range for which anti-inflammatory / immunosuppressants ($r=0.20$, $p<0.001$) and secretagogues ($r=0.24$, $p<0.001$) were prescribed for, whereas for all other treatments, the association was weak ($p<0.15$).

Table 3. Proportion of practitioners that only use each therapy for a particular subtype of DED.

	ADDE	EDE
Essential fatty acids	2%	18%
Artificial tears	15%	7%
Ointments	7%	9%
Lipid based products	1%	23%
Lid hygiene	2%	6%
Moisture chamber goggles	13%	11%
Punctal occlusion	32%	4%
Eyelid warming	2%	13%
In-office treatments	1%	14%
Topical antibiotics	2%	12%
Systemic antibiotics	1%	8%
Anti-inflammatories/Immunosupressants	7%	3%
Secretagogues	7%	1%
Biologics	9%	8%
Therapeutic contact lenses	17%	2%
Other surgical approaches	4%	3%

ADDE = pure aqueous deficient dry eye; EDE = pure evaporative dry eye.

Some patients present with mixed DED, and display elements of both ADDE and EDE [9]. These patients can be located anywhere along a continuum between the two extremes of pure ADDE or EDE. Between continents (Table 2), practitioners in Latin America reported prescribing ointments for patients with a greater aqueous deficient element, compared to those practising in Europe and Africa. Those in Africa, Europe and North America, recommended lid hygiene for patients with less severe evaporative disease than respondents in Asia/Middle East. Systemic antibiotics were prescribed for ADDE more in Africa, than in any other continent. Practitioners in North America and Latin America reported prescribing topical anti-inflammatories/ immunomodulators for patients with a greater degree of ADDE than those in Asia/Middle East, Europe and Australasia. Secretagogues were prescribed for aqueous deficient patients more in Latin America than in Asia/Middle East. Finally, surgical approaches were performed for more ADDE more commonly in Europe than in North America.

3.6. Management trends

Preservation of the survey format used in the original analysis allowed comparison of global practice patterns over time. Data extraction for the first survey took place in August 2019, and that of the current survey took place in May 2024. Table 4 provides a summary of the changes in practice patterns over nearly 5 years, many of which were statistically significant. A higher proportion of respondents reported prescribing ointments, lipid containing lubricants, lid hygiene, warm compresses and in-office therapies, as well as pharmaceuticals, such as systemic antibiotics, topical anti-inflammatories/ immunosuppressants, secretagogues and biologics, compared to 2018-19. Practitioners are also prescribing systemic antibiotics for lower severities of DED than previously, but largely the severity at which treatments are being prescribed had changed by less than 5%. There were no statistically significant changes in the DED sub-classification each treatment was considered to be appropriate for.

Table 4: Overall change in prescribing patterns & changes in DED severity & subtype for which each treatment was considered appropriate, between 2019 & 2024 analyses. P<0.003 considered significant with Bonferroni correction for multiple testing.

Treatment	Change in use (%)	Significance (p)	Severity change (%)	Significance (p)	Subtype change (%)	Significance (p)
Advice	-4	.059	+5	.121	-1	.753
Essential fatty acid supplements	+3	.456	0	.639	+1	.696
Artificial tears	-4	.014	+1	.339	-2	.236
Ointments	+11	<.001	-2	.179	-2	.149
Lipid containing lubricants	+12	<.001	-5	.050	0	.964
Lid hygiene	+18	<.001	+1	.923	0	.117
Moisture chamber spectacles/ goggles	+5	.482	0	.698	-4	.152
Punctal occlusion	+9	.132	+1	.843	-2	.330
Warm compresses	+31	<.001	0	.450	+1	.642
In-office therapies	+175	<.001	-2	.123	-1	.338
Topical antibiotics	+10	.055	-3	.120	-2	.178
Systemic antibiotics	+19	<.001	-5	.002	0	.208
Topical anti-inflammatory/ immunosuppression	+36	<.001	-1	.364	0	.825
Secretagogues	+43	<.001	-3	.513	0	.808
Biologics	+30	<.001	-4	.004	-1	.264
Therapeutic CLs	+9	.125	-2	.294	-5	.234
Surgical approaches	+11	.329	-1	.826	-1	.601

For subtype change, '–' indicates more aqueous deficient dry eye and '+' more evaporative.

4. Discussion

The aim of this study series was to determine how clinical management patterns differed depending on disease severity and subtype. Data collected from practitioners across the globe also allowed differences in dry eye management approaches between continents to be identified [20]. Furthermore, as the survey was conducted twice, it became possible to compare datasets, and reveal evolution in management strategies over time. Survey responses encompassed a broad spectrum of clinicians from over 50 countries, across 6 continents, ranging from newly qualified to seasoned practitioners with decades of experience. To our knowledge, this is a first series of studies to have tracked and compared the dry eye management patterns of eye care professionals around the world.

Completed surveys were received from 905 practitioners from across the globe, with a balance between optometrists and ophthalmologists, each with around 15 years of clinical practice experience, on average. The reason practitioners from some countries participated more in this unpaid survey than others is uncertain, and could be due to workload how often they receive other survey invites. As found previously [20], the most commonly seen patients were those with mild symptoms, and least common were those with severe symptoms. Interestingly practitioner experience (as assessed by the number of years since qualification) had limited impact on the median severity or subtype over which different DED treatments were prescribed. However, more experienced practitioners prescribed anti-inflammatory / immunosuppressants and secretagogues over a wider range of subtypes, perhaps due to move confidence over their general effectiveness over time.

Many treatment options for DED were observed to be utilised by respondents. As environment and iatrogenic factors, such as air conditioning and contact lens wear can disrupt the homeostasis of the tear film, advice is critical at all levels of DED severity, as identified in the TFOS DEWS II Management and Therapy Report [8]. Indeed, independent of severity and subtype, the most common management approaches were offering advice (82%) and recommending over-the-counter, low and high viscosity unpreserved lubricants and lid wipes/scrubs. “Step 1” interventions in the TFOS DEWS II management algorithm include patient education/advice, dietary advice, artificial tears and warm compresses [8], as they are conventional, low risk, and widely available management approaches suitable for early-stage disease. This study identifies these as the most commonly recommended management approaches, as reported in other studies [13, 15-17].

There was an increase in the preference for unpreserved artificial tears, versus preserved, with the ratio of prescriptions increasing from 1.3:1 in the 2018-19 survey, to 1.5:1 in 2023-24. This is supported by TFOS DEWS II guidance, which advises the use of preservative free products where possible [8], and is facilitated by a wider range of unpreserved artificial tears having come to market in recent years. A greater proportion of lid wipes/scrubs was made up by those developed specifically for Demodex control, rather than those for general lid cleansing. This may reflect greater product availability. There was also an increase in the use of commercial warm compresses, over home-made alternatives such as hot flannels which have been shown to rapidly fall below an effective temperature [21, 22], to the point where this is now advised by the majority of practitioners. The number of practitioners using mechanical spinning brush tools for lid hygiene increased, matching that of lid margin debridement, which was previously favoured, however therapeutic expression was still used by more respondents. Another change was seen in the relative adoption of in-office treatments such as intense pulsed light therapy and combined inner lid warming and massage devices. Five years ago, a slightly greater proportion of practitioners were performing the latter, but this has reversed, and the balance is now 1.5 times in favour of light therapies. Intense pulsed light and low level light therapy [23] have been shown to be effective in improving symptoms and signs of DED [24], and an increasing number of clinics appear to be offering light therapies to their patients.

Practitioners licensed to prescribe ocular therapeutics appear to have refined their prescribing profiles since the previous survey. The global use of topical tacrolimus increased significantly, relative to lifitegrast (1.9:1 in 2024 versus 1.2:1 in 2019) and topical steroids (0.4:1 in 2023-24 versus 0.2:1 in 2018-19), which is presumed to be due to its favourable risk/benefit profile and availability. Therapeutic contact lenses were still used by more respondents than autologous/allogeneic serum and amniotic membrane, but the gap has closed somewhat, again possibly due to greater availability of biologic therapies. Finally, a greater number of respondents reported performing surgical procedures rather than intraductal probing, compared to the previous survey.

Some treatments were prescribed across all severity levels (scaled from 1 mild to 10 severe), such as advice (median 4.5, range 4.8), artificial tears (median 5.1, range 4.6) and nutritional supplements (median 5.3, range 4.2). Others were prescribed more frequently with increasing disease severity, for instance, biologics (median 8.2, range 2.8) and surgical approaches (median 8.1, range 2.2). This aligns with the principles of conservative medicine, where invasive and higher risk treatments are reserved for incalcitrant cases, or for those patients most debilitated by their symptoms.

While a similar number of practitioners reported prescribing advice, artificial tears and anti-inflammatories, regardless of DED subtype, the major reported approaches for managing aqueous deficient DED were punctal occlusion, therapeutic contact lenses and secretagogues. In contrast, the use of oral essential fatty acids, topical lipid-containing products, lid hygiene and lid warming were the preferred management choice for evaporative DED (Table 3). Although some patients present with mixed dry eye, the vast majority are predominantly evaporative in nature, due to meibomian gland dysfunction [2, 25, 26]. The combination of increased melting point/viscosity of meibum [22], and excessive keratinization of the ductal epithelium in meibomian gland dysfunction [27], results in terminal duct obstruction [28] and a defective tear lipid layer. Treatments which address this deficiency are therefore important, in order to facilitate the normal functioning of the meibomian glands, restore tear film and ocular surface homeostasis and reduce evaporation of the underlying aqueous tear film.

Differences in management that respondents felt were appropriate for each severity and subtype of DED were noted between continents (Table 2), most notably with respect to less common advice or artificial tear prescribing in Latin America, lesser use of lipid based products (shown to be beneficial in those with more EDE [10, 11]) outside Europe and Australasia and fewer prescriptions for antibiotics in Europe and anti-inflammatories along with secretagogues in Europe and Australasia. There were less intercontinental differences in prescribing according to subtype, with ointments used more for ADDE in Latin America, lid hygiene being used more for EDE in Asia and the Middle East, systemic antibiotics being used less commonly for evaporative type dry eye in Africa and topical anti-inflammatories and immunomodulators being used less frequently for EDE in North and Latin America.

Retention of the original survey format allowed direct comparison of new data with the 2018-19 survey outcomes. It was found in the current survey that more respondents reported prescribing ointments, lipid containing lubricants, lid hygiene, warm compresses and in-office therapies, as well as pharmaceuticals, such as systemic antibiotics, topical anti-inflammatories/immunosuppressants, secretagogues and biologics. It may be that practitioners, increasingly, are attempting to treat the root causes of DED, in addition to the symptoms. Examples include treating meibomian gland dysfunction with warm compresses, lid hygiene and with systemic antibiotics, such as low dose doxycycline. Lipid-containing drops and sprays have gained greater popularity and enjoyed more widespread availability in recent years, as the importance of meibomian gland dysfunction and evaporative DED has become clearer [11, 12]. Practitioners are also prescribing systemic antibiotics at a lower DED severity threshold than previously, but largely the severity for which treatments are being prescribed experienced less than 5% change. There were no statistically significant changes in the treatments considered appropriate for specific DED sub-classification categories, suggesting that clinicians consistently have a battery of treatments suited to each dry eye subtype.

Surveys are intrinsically susceptible to selection bias, as those choosing to respond are likely to be practitioners with more knowledge and experience of managing the condition, compared to their peers. There will always be significant variation in management approaches between practitioners, not least because each patient presents with their own unique challenges. In addition, the practitioner cohort will have differed between 2018-19 and 2023-24, creating noise in the comparison over time. However, despite this, the findings significantly enhance our understanding of an important research area, and allow clinicians to benchmark their clinical practice against world norms, for the benefit of their patients.

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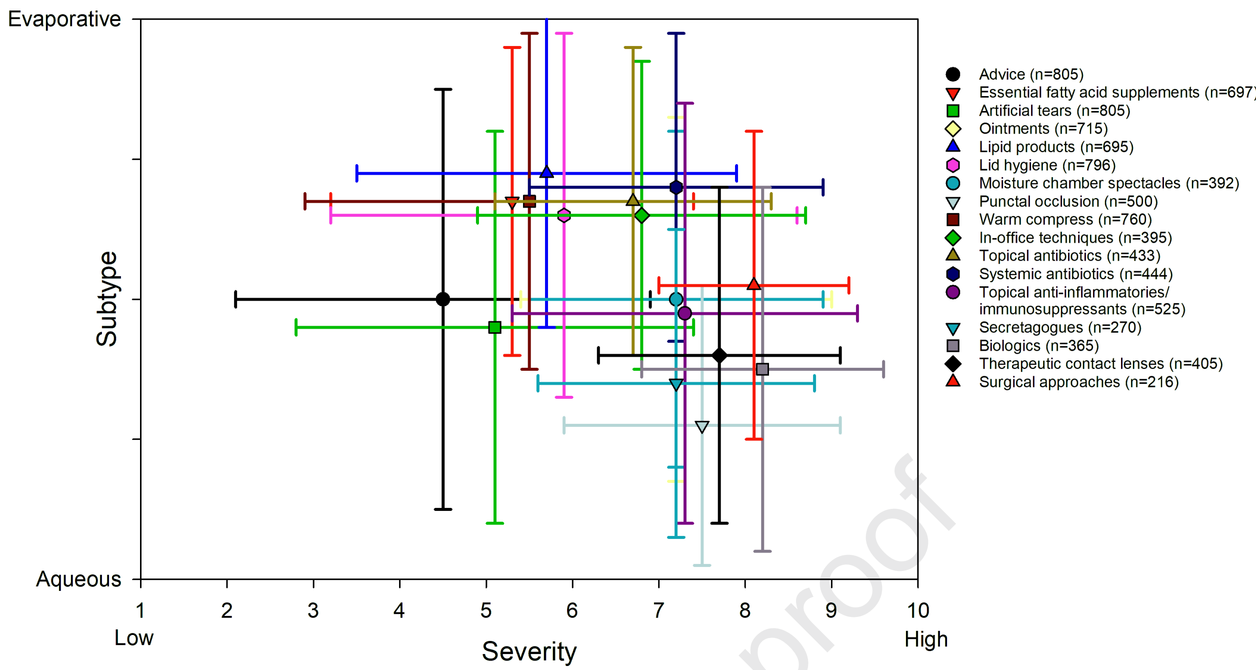
References

[1] Stapleton F, Alves M, Bunya VY, Jalbert I, Lekhanont K, Malet F, et al. TFOS DEWS II Epidemiology Report. Ocul Surf. 2017;15:334-65.
[2] Craig JP, Nichols KK, Akpek EK, Caffery B, Dua HS, Joo C-K, et al. TFOS DEWS II Definition and Classification Report. Ocul Surf. 2017;15:276-83.
[3] Schiffman RM, Walt JG, Jacobsen G, Doyle JJ, Lebovics G, Sumner W. Utility assessment among patients with dry eye disease. Ophthalmology. 2003;110:1412-9.
[4] Li M, Gong L, Sun X, Chapin WJ. Anxiety and depression in patients with dry eye syndrome. Curr eye res. 2011;36:1-7.
[5] Luo Y, Yang W, Qi M, Wang Y, Li S, Wang M, et al. Annual direct economic burden and influencing factors of dry eye disease in Central China. Ophthal Epidemiol. 2021.
[6] McDonald M, Patel DA, Keith MS, Snedecor SJ. Economic and Humanistic Burden of Dry Eye Disease in Europe, North America, and Asia: A Systematic Literature Review. Ocul Surf. 2016;14:144-67.
[7] Morthen MK, Magno MS, Utheim TP, Snieder H, Hammond CJ, Vehof J. The physical and mental burden of dry eye disease: A large population-based study investigating the relationship with health-related quality of life and its determinants. Value Health. 2021;21:107-17.
[8] Jones L, Downie LE, Korb D, Benitez-del-Castillo JM, Dana R, Deng SX, et al. TFOS DEWS II Management and Therapy Report. Ocul Surf. 2017;15:575-628.
[9] Wolffsohn JS, Arita R, Chalmers R, Djalilian A, Dogru M, Dumbleton K, et al. TFOS DEWS II Diagnostic Methodology report. Ocul Surf. 2017;15:539-74.
[10] Essa L, Laughton D, Wolffsohn JS. Can the optimum artificial tear treatment for dry eye disease be predicted from presenting signs and symptoms? Contact Lens Anterio. 2018;41:60-8.
[11] Craig JP, Muntz A, Wang MTM, Luensmann D, Tan J, Huarte ST, et al. Developing evidence-based guidance for the treatment of dry eye disease with artificial tear supplements: A six-month multicentre, double-masked randomised controlled trial. Ocul Surf. 2021;20:62-9.
[12] Semp DA, Beeson D, Sheppard AL, Dutta D, Wolffsohn JS. Artificial Tears: A Systematic Review. Clin Optom (Auckl). 2023;15:9-27.
[13] Downie LE, Rumney N, Gad A, Keller PR, Purslow C, Vingrys AJ. Comparing self-reported optometric dry eye clinical practices in Australia and the United Kingdom: is there scope for practice improvement? Ophthal Physl Opt. 2016;36:140-51.
[14] van Tilborg MMA, Murphy PJ, Evans KSE. Agreement in dry eye management between optometrists and general practitioners in primary health care in the Netherlands. Contact Lens Anterio. 2015;38:283-93.
[15] Williamson JF, Huynh K, Weaver MA, Davis RM. Perceptions of Dry Eye Disease Management in Current Clinical Practice. Eye Contact Lens. 2014;40:111-5.
[16] Xue AL, Downie LE, Ormonde SE, Craig JP. A comparison of the self-reported dry eye practices of New Zealand optometrists and ophthalmologists. Ophthal Physl Opt. 2017;37:191-201.
[17] Downie LE, Keller PR, Vingrys AJ. An Evidence-Based Analysis of Australian Optometrists' Dry Eye Practices. Optometry Vision Sci. 2013;90:1385-95.
[18] Casemore RK, Wolffsohn JS, Dutta D. Dry eye clinical practice patterns of UK optometrists. Contact Lens Anterio. 2023;46:101889.
[19] Sy A, O'Brien KS, Liu MP, Cuddapah PA, Acharya NR, Lietman TM, et al. Expert opinion in the management of aqueous Deficient Dry Eye Disease (DED). BMC Ophthalmol. 2015;15:6.
[20] Wolffsohn JS, Huarte ST, Jones L, Craig JP, Wang MTM, Ambassadors T. Clinical practice patterns in the management of dry eye disease: A TFOS international survey. Ocul Surf. 2021;21:78-86.
[21] Bitton E, Lacroix Z, Leger S. In-vivo heat retention comparison of eyelid warming masks. Contact Lens Anterio. 2016;39:311-5.
[22] Borchman D. The optimum temperature for the heat therapy for meibomian gland dysfunction. Ocul Surf. 2019;17:360-4.

[23] Giannaccare G, Pellegrini M, Carnovale Scalzo G, Borselli M, Ceravolo D, Scorcia V. Low-Level Light Therapy Versus Intense Pulsed Light for the Treatment of Meibomian Gland Dysfunction: Preliminary Results From a Prospective Randomized Comparative Study. Cornea. 2023;42:141-4.
[24] Xue AL, Wang MTM, Ormonde SE, Craig JP. Randomised double-masked placebo-controlled trial of the cumulative treatment efficacy profile of intense pulsed light therapy for meibomian gland dysfunction. Ocul Surf. 2020;18:286-97.
[25] Vidal-Rohr M, Craig JP, Davies LN, Wolffsohn JS. Classification of dry eye disease subtypes Cont Lens Anterior Eye. 2024:In Press.
[26] Lemp MA, Crews LA, Bron AJ, Foulks GN, Sullivan BD. Distribution of aqueous-deficient and evaporative dry eye in a clinic-based patient cohort: a retrospective study. Cornea. 2012;31:472-8.
[27] Dietrich J, Garreis F, Paulsen F. Pathophysiology of Meibomian Glands - An Overview. Ocul Immunol Inflamm. 2021;29:803-10.
[28] Asbell PA, Stapleton FJ, Wickström K, Akpek EK, Aragona P, Dana R, et al. The international workshop on meibomian gland dysfunction: report of the clinical trials subcommittee. Invest ophthal vis sci 2011;52:2065-85.

Question Categories	Possible Responses
Practitioner demographics	Mode of practice; ophthalmologist, optometrist or other Years of clinical experience Country of practice
Type of dry eye patients managed (ranking)	1. No presenting specific symptoms: identified incidentally on questioning 2. Intermittent presenting symptoms: occasional effect on quality of life 3. Mild symptoms: low impact on quality of life 4. Moderate symptoms: frequent impact on quality of life 5. Severe symptoms: constant debilitating effect on quality of life
Are you LICENSED to use this within your scope of practice in your country? Do you ever PRESCRIBE this option? What SUBTYPE(S) of dry eye disease do you consider this treatment appropriate for (select as many as apply)? What SEVERITY(S) of dry eye disease do you consider this treatment appropriate for (select as many as apply)?	1. Advice 2. Essential fatty acid supplements 3. Artificial tears a. Low viscosity-enhancing lubricant PRESERVED b. High viscosity-enhancing lubricant PRESERVED c. Low viscosity-enhancing lubricant UNPRESERVED d. High viscosity-enhancing lubricant UNPRESERVED 4. Ointments 5. Lipid containing lubricants (drops/spray) 6. Lid hygiene a. Lid wipes/scrubs b. Demodex cleansing lid wipes c. In-office demodex lid control d. Lid margin debridement e. In-office lid hygiene (e.g. BlephEx) f. Therapeutic meibomian gland expression 7. Moisture chamber spectacles/ goggles 8. Punctal occlusion (with plugs) 9. Warm compresses a. Home-made warm lid compress, such as face-cloth b. Commercially available warm lid compress/face mask c. In-office thermal pulsation of lids (e.g. LipiFlow) 10. In-office techniques (e.g. intense pulsed light therapy) 11. Topical antibiotics (e.g. azithromycin) 12. Systemic antibiotics a. Systemic azithromycin b. Oral antibiotics (e.g. doxycycline) 13. Topical anti-inflammatory/ immunosuppression a. Topical corticosteroids b. Topical cyclosporine c. Topical tacrolimus d. Topical lifitegrast 14. Secretagogues a. Topical secretagogues b. Oral secretagogues 15. Biologics a. Autologous/allogeneic serum b. Amniotic membrane 16. Therapeutic contact lenses 17. Surgical approaches a. Intraductal probing b. Other surgical approaches


Evaporative
Subtype
Aqueous
1
Low
2
3
4
5
6
7
8
9
10
High
Severity
Advice (n=805)
Essential fatty acid supplements (n=697)
Artificial tears (n=805)
Ointments (n=715)
Lipid products (n=695)
Lid hygiene (n=796)
Moisture chamber spectacles (n=392)
Punctal occlusion (n=500)
Warm compress (n=760)
In-office techniques (n=395)
Topical antibiotics (n=433)
Systemic antibiotics (n=444)
Topical anti-inflammatories/
immunosuppressants (n=525)
Secretagogues (n=270)
Biologics (n=365)
Therapeutic contact lenses (n=405)
Surgical approaches (n=216)