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Latin American Consensus on Ocular Lubricants and Dry Eye Disease (LUBOS): A Report on Severity Classification, Diagnosis, and Therapy

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Purpose: This consensus aims to establish a practical severity classification for applying a tailored stepladder treatment algorithm helpful to any clinician.

Methods: A modified Delphi methodology was used to establish a consensus on the definition, diagnosis, severity classification, and treatment algorithms for dry eye disease (DED) adapted to the needs of Latin America. The consensus focused on promoting the effective use of lubricants and providing straightforward, practical guidance for ophthalmologists treating dry eyes. Twenty-eight corneal specialists from representative Latin American countries reviewed the scientific evidence and drew on their expertise to answer specifically designed open-ended questions.

Results: A simple diagnostic algorithm (clinical history, DED questionnaire, and dry eye clinical tests) identified patients with the disease. A practical severity classification system of four grades: mild, moderate, severe, and LUBOS plus DED was based on four criteria: OSDI, film break-up time, Sjögren International Collaborative Clinical Alliance ocular surface staining score, and international workshop on meibomian gland dysfunction meibomian gland functionality test. For classification, ≥2 criteria of the highest severity grade from the worse eye were considered. A stepladder therapeutic algorithm aligned with disease severity consisted of 5 steps, each with proposed and recommended treatment alternatives. Patient education, lifestyle recommendations, adverse environment avoidance, lubricants, and eyelid therapy were reinforced during the therapy period.

Conclusions: The LUBOS expert panel consensus considered the diverse geoenvironmental, socioeconomic, cultural, and ethnic factors pertinent to Latin America. This consensus offers an

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ARG and MXN have full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Data related to this publication are available upon request.

All authors made a significant contribution to the consensus, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

The Colombian Association of Cataract and Refractive Surgery (ASOCYR) and the Pan American Corneal Society (Pancornea) endorsed the consensus study.

IRB approval does not apply to the present consensus report.

All figures and tables are original or have been modified substantially from the original and have been credited/referenced.

M. X. Núñez, A. Rodriguez-Garcia, J. A. Pereira-Gomes, M. A. Henriquez, M. Garza-Leon, and A. Aguilar designed and planned the project and created the open survey questions. M. X. Núñez coordinated the present and virtual sessions. A. Rodriguez-Garcia wrote the initial draft and edited all its versions. He also made all figures and tables. All principal authors edited and revised the manuscript in all its versions. M. X. Núñez contributed to the initiative, leadership, coordination, and identification of the financial support to perform the project.

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accessible and cost-effective tool, enabling professionals to detect, evaluate, and grade the severity of dry eye disease effectively for planning adequate therapeutic strategies that can be monitored with confidence.

Key Words: tear film, ocular surface, dry eye disease, OSDI, lubricant eye drops, artificial tears, Delphi consensus, Latin America

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Dry eye disease (DED) is a highly prevalent condition influenced by existing systemic and eye disorders and environmental, lifestyle, geographic, and socioeconomic factors.[1–3] Beyond globalization, it is essential to consider that regional differences can affect the expression of DED and its management.[4] Latin America is an extensive geographic region with social, cultural, ethnic, and environmental particularities that justify the fulfillment of an expert consensus, evaluating whether concepts created in other parts of the world can be applied in our communities.[5] Conducting a scientific consensus permits reviewing the scientific evidence and building practical knowledge for a particular ophthalmological community in decision making.[6–8] This consensus focuses on DED, a common, complex, and multifaceted condition presenting as a long-lasting and evolving disorder where lubricating eye drops are the first line of treatment.[9,10] However, no artificial tear fully replicates healthy natural tear film (TF), which is a complex mixture of water, electrolytes, proteins, and mucins that interact with lipids.[10–12] Moreover, tears are continuously produced, and their elements dynamically adjust to maintain ocular surface homeostasis. When different pathogenic pathways disrupt this balance, it can lead to varying degrees of DED, requiring more than adding lubrication to the eye.[13] Therefore, managing DED requires personalized treatment based on its specific subtype and severity. New topical lubricant formulations are constantly being developed, challenging ophthalmologists to update their availability and applications in different clinical situations.[9–12,14,15] This consensus aims to provide a simple diagnostic methodology and a practical DED severity classification for designing a personalized therapeutic approach for patients.

MATERIALS AND METHODS

Consensus Methodology

An expert panel consensus-based study was performed via a modified Delphi method[16] following the ACCORD (ACcurate COnsensus Reporting Document) guidelines.[17] This method allows a formal group consensus process that systematically and quantitatively combines an exhaustive evidence review with an expert opinion by asking panelists to rate, discuss, and rerate uncertain, incomplete, and adaptable DED knowledge.[16] The final goal was to maximize convergence and adaptability for managing DED in Latin America. For this purpose, panelists were equally included in randomized work groups to review the pertinent scientific evidence through specific open-ended questions by answering the following individual criteria: 1) objectivity, 2) practicality, 3) clinical applicability, 4) affordability, and 5) diagnostic and therapeutic capacity. Then, they participated in in-person and online discussions, exchanging opinions about their answers, voting to determine the extent to which they agreed on a particular question, and obtaining shared confirmation of their opinions. To reach an agreement, at least 75% of the panelists voted in favor of a proposal (concept definitions, inclusion or selection severity criteria, diagnostic methods, and therapeutic algorithm). A high level of consensus was set to 95% agreement.[16] To improve the methodology quality, consistency, and reliability, we followed the recommendations of the Conducting and REporting of Delphi Studies (CREDES) guidelines.[18]

Five working rounds were performed (see Supplemental Fig., Supplemental Digital Content 1, http://links.lww.com/ICO/B809). Directive committee members were designated for rounds 1 and 2. Round 1 consisted of planning the working strategy, the general and specific objectives and goals, and the selection and invitation of expert panelists. In round 2, specific open-ended questions were designed under the PECOT (patients, exposure, comparison, outcomes, and time) methodology.[19] Eleven questions were included in the consensus workshop regarding the general aspects (four questions), the diagnosis (two questions), the treatment of DED (four questions), and a final question summarizing the agreements (Table 1).

In round 3, the questions and literature evidence shared by the support group were randomly assigned to the panelists' groups. Eight weeks were given to answer the questions and prepare a referenced written document with a final summary of the group's statements to be presented in round 4 for further deliberations, discussions, and voting during the 2-day in-person meeting held in Cali, Colombia, on June 6-7, 2023. The directive committee, panelists, and support group (clinical research coordinator and reviewers) agreed with the statements. MXN moderated the meeting, allowing everyone to speak and ensuring a fair distribution of the time allocated to each subject. The panelists were encouraged to express their opinions freely and enrich the discussion with reflections, criticisms, objections, and doubts based on their experience. At the end of each question discussed, the leader of each group pronounced a final statement, and the rest of the panelists could propose changes and additions based on voting and joint agreement. Each of these discussions was allocated the same amount of time and led to the definition of the final version of the LUBOS consensus document.

Finally, round 5, performed online, permitted the discussion and voting of the definitive results of question 11, containing the LUBOS severity classification and the diagnostic and therapeutic algorithms.

Literature Review Process

The clinical research coordinator (LMC) and the research reviewers (BEOL, MICM, and CAHT) initially performed an all-time comprehensive Spanish and English literature search via PubMed, Scopus, and Cochrane Library search engines. Combinations of the keywords "dry eye,"

TABLE 1. PECOT Methodology of Open Questions for the LUBOS Consensus on DED and Agreement Results*

General aspects	Round 4 No. votes (%) (N = 28)	Round 5* No. votes (%) (N = 28)
1. What are the components of the tear film and what is its function?	28/0 (100.0)	—
2. What is dry eye and how is the tear film found in DED?	26/2 (92.8)	—
3. What is the prevalence of DED and its impact on quality of life?	28/0 (100.0)	—
4. What is the burden of DED?	26/2 (92.8)	—
Diagnosis		
5. What are the etiologic causes of DED?	27/1 (96.4)	—
6. What are the levels of severity of DED according to its etiology?	10/18 (35.7)	26/2 (92.8)
Treatment modalities		
7. What are the functions of the components of lubricant eye drops?	26/2 (92.8)	—
8. What is the ideal tear for each type of DED according to its etiology and severity?	11/17 (39.2)	27/1 (96.4)
9. What is the role of non-pharmacological treatments for DED?	10/18 (35.7)	28/0 (100.0)
10. What pharmacological mechanisms of action complement the treatment of dry eye with lubricants?	15/13 (53.5)	28/0 (100.0)
Summary of agreements		
11. What are the diagnostic and therapeutic algorithms for the management of DED?	10/18 (35.7)	27/1 (96.4)

*During the fifth final round, those questions with less percentage (≤75%) of necessary votes to reach an agreement were revoted after final delivery, discussions, and content modifications to the consensuses on DED diagnosis, severity, and treatment modalities.

"dry eye disease," "ocular surface disease," "meibomian gland dysfunction," "aqueous-deficient dry eye," "evaporative dry eye," "mixed dry eye disease," "ocular surface disease index," "OSDI," "corneal fluorescein staining," "ocular surface staining," "SICCA," "tear break-up time," "Schirmer test," "dry eye clinical tests," "noninvasive dry eye tests," "dry eye severity," "dry eye diagnosis," "dry eye therapy," "Latin America," "dry eye consensus," "dry eye workshop," "lubricant eye drops," "artificial tears," "corticosteroids," "immunomodulators," and "dry eye surgery." The

directive committee and panelists were asked to review all publications shared in a drive and ensure that all relevant information for the questions assigned to them was included. Publications were selected according to 1) content relevance, 2) journal impact, 3) sample size, 5) methodology, and 6) results. Randomized clinical trials (RCTs), consensus studies, workshops, case series, case–control studies, and systematic reviews with meta-analyses were considered for analysis (see Supplemental Fig., Supplemental Digital Content 2, http://links.lww.com/ICO/B809).

Panelist Selection

The directive committee, consisting of six principal investigators (M.X.N., A.R.G., J.A.P.G., M.A.H., M.G.L., and A.A.), all of whom are expert opinion leaders in Latin America, was assigned by the consensus coordinator (M.X.N.). They played a crucial role in the designation of the expert panelists, ensuring that the following criteria were met:

1. Board-certified subspecialty in cornea and ocular surface disease.
2. At least 5 years of clinical experience attending DED.
3. Speaker in at least one academic or scientific meeting yearly.
4. Latin American origin (multinationality) with varied academic training backgrounds.

Panelists were invited via email detailing the study's aim, specific objectives, and methodology. All agreed to review the pertinent literature and answer the question assigned, attend in-person and online meetings, and comply with project timelines. Twenty-eight panelists agreed to participate in the study: four from Argentina, seven from Brazil, two from Chile, six from Colombia, six from Mexico, one from Costa Rica, one from Ecuador, and one from Peru (see the extended list of panelists below).

RESULTS

Analysis of Literature Evidence

To answer and discuss the formulated questions, we revised the pertinent literature in the English and Spanish languages, which became the scientific foundation for the consensus agreements (see Supplemental Fig., Supplemental Digital Content 2, http://links.lww.com/ICO/B809). Questions 6, 8, 9, 10, and 11, regarding DED diagnosis, severity classification, and treatment alternatives, did not reach the minimum percentage (75%) for agreement during round 4; therefore, after further panelist revisions and discussions, they reached a consensus at round 5 (Table 1).

LUBOS Definition of Dry Eye Disease

The LUBOS agreement statements allow us to understand DED as a complex multifactorial pathology related to and influenced by the rest of the human body, our lifestyle, and our environment. Hence, 92.8% of the LUBOS panelists agreed with the DED definition as follows:

> *Dry eye* is a multifactorial disease that affects the ocular surface and is characterized by an alteration in the homeostasis of the tear film. It can have an evaporative, hyposecretory, or mixed origin. It is accompanied by varying degrees of ocular and visual symptoms and signs, where tear film instability and factors such as hyperosmolarity, inflammation, tissue damage, and neurosensory abnormalities play important roles in its etiopathogenesis. Lifestyle and environmental conditions are triggering or aggravating elements of the disease.

LUBOS Diagnostic Algorithm

During the first visit, clinicians identify a patient with DED by conducting a simple but systematized diagnostic algorithm composed of three elements: 1) clinical history, 2) DED questionnaire, and 3) slit-lamp examination, including clinical dry eye tests (see Supplemental Fig., Supplemental Digital Content 3, http://links.lww.com/ICO/B809). LUBOS considers Schirmer and noninvasive dry eye tests to be optional but is recommended when necessary and if available.

Clinical History

Demographic features, a brief directed patient interrogation about the reason for consultation, current condition, and intended questions such as the following: 1) Have you experienced daily persistent ocular dryness sensations? 2) Do you have recurrent foreign body sensations? 3) Do you frequently use tear substitutes? Help suspect DED during the first visit.[20] Nonpathological factors, including occupation, lifestyle, cosmetic use, daily digital screen use, sports practice, tobacco consumption, and alcohol consumption, are also relevant risk factors affecting DED. Systemic metabolic (ie, diabetes mellitus, thyroid dysfunction) and autoimmune (ie, rheumatoid arthritis and Sjögren syndrome) diseases and previous ocular surgeries (ie, corneal refractive, cataract extraction) are also crucial for understanding the context in which dry eye occurs. Other risk factors for DED, such as insomnia and medication intake (ie, antidepressants, antihistamines, diuretics), need to be investigated.[21]

Ocular Surface Disease Index (OSDI) Dry Eye Questionnaire

Validated dry eye questionnaires are essential for detecting and classifying the degree of dry eye involvement and patient-reported outcomes (PROs) for therapeutic efficacy evaluation.[22] Screening for dry eye symptoms should be performed initially, excluding other possibilities from the differential diagnosis.

LUBOS participants voted on the OSDI questionnaire, which is the most adequate instrument for measuring DED symptoms because it is the most validated (more than 600 records) and has been translated into Spanish and Portuguese.[23–26] It is complete and relatively brief, consisting of

three components (12 questions) that measure 1) symptom frequency, 2) impact on visual quality of life, and 3) environmental precipitation factors. The resultant score classifies dry eye symptoms from mild (13–22 points) to severe (33–100 points).[22] It has good concurrent validity, internal consistency, and test–retest reliability.[26,27]

Biomicroscopy

A thorough biomicroscopic examination of the eyelids and ocular surface is crucial for understanding the pathogenic mechanisms involved in DED and its etiology. Different clinical manifestations and specific signs can be observed while the patient is under a slit lamp, providing precise clues for diagnosing an underlying disease associated with dry eyes. In addition, most clinical dry eye tests (vital staining tests, film break-up time [FTBUT], and Meibomian gland function tests, among others) are performed under a slit lamp.[21]

LUBOS agreed by 96.4% that the FTBUT, the ocular surface staining score (OSS-SICCA), and the meibomian gland functionality test (IW-MGD) give the peer community a practical and low-cost set of tools for accurately identifying patients with the different subtypes of DED and are equally important for therapeutic decisions by grading their severity.[21,28] However, all other alternative and available clinical tests (ie, the Schirmer test) and noninvasive methods (ie, infrared meibography and lipid interferometry) should be performed when necessary to reassure or complement the evaluation of a specific case (see Supplemental Fig., Supplemental Digital Content 3, http://links.lww.com/ICO/B809).[21,29]

Fluorescein Tear Film Break-Up Time

A shortened TBUT because of TF thinning by hyposecretion, with or without thinning or absence of the oily layer in MGD, can be easily and quickly assessed by instilling fluorescein on the ocular surface. An FTBUT ≥10 seconds is usually considered normal.[21,30,31] However, studies of efficacy and FTBUT measurement verification suggest that the test has excellent diagnostic accuracy and that a 3- to 6-second cutoff point is optimal for differentiating between healthy and dry eyes.[30] Among the test disadvantages, fluorescein produces discomfort upon instillation and hinders the natural observation of the ocular surface; the TF rupture time depends on the amount of dye used (high variability), and the starting breakpoint may be challenging to determine (low reproducibility).[30] Therefore, the TFOS DEWS II recommends performing the NITBUT; however, this requires expensive equipment that is not readily available for all patients. On the other hand, investigators from the Sjögren International Collaborative Clinical Alliance (SICCA) still widely use the FTBUT, which is also recommended by the AAO Preferred Practice Patterns.[21] Another advantage of the FTBUT is the analysis of the rupture pattern, suggesting which phase of the TF is affected (Fig. 1).[32]

Ocular Surface Staining Score

The degree of ocular surface staining (fluorescein and lissamine green) is a critical diagnostic component of DED assessment, particularly for grading severity and monitoring management.[30] The staining parameters analyzed included 1) extent (dividing the cornea and conjunctiva into zones); 2) density (based on the number of staining spots); 3) confluence (staining patches); and 4) other parameters (pupillary zone involvement, presence of filaments).[30,33,34] Upon 0.5% fluorescein instillation, areas of damaged and absent epithelial cells were stained and observed under a cobalt blue light filter (450–490 nm), which appeared bright green.[30] An enhancing technique uses a Wratten yellow filter #12 (410–470 nm) over the cobalt blue.[34] 1% lissamine green staining captures areas devoid of mucin/glycocalyx and desiccated and damaged cells, as observed under white light, and is enhanced by a Hoya 25A red barrier filter.[35] The morphologic pattern and topographic distribution of the stain provide clues to the underlying etiology, and its density and extent allow the grading of dry eye severity and monitoring of therapeutic response.[28]

Several staining techniques are available to assess the degree of damage to the ocular surface in DED.[30] The LUBOS panelists recommend the SICCA "Ocular Surface Staining" (OSS) score for DED diagnosis and severity grading.[33,36] This validated scale, known for its objectivity, combines fluorescein (corneal) with lissamine green (conjunctival) staining (modified van Bijsterveld technique). The OSS-SICCA assesses conjunctival damage by weighing severity from 0 to 3 by staining points ranging from 0 to 9 (grade 0), 10 to 32 (grade 1), 33 to 100 (grade 2), and >100 points (grade 3) (Fig. 2).[33] The combination with corneal fluorescein staining (CFS) (0–6 points) yields a score range of 0 to 12 points by adding 3 extra points for staining coalescence (patchiness), visual axis (pupil) involvement, and the presence of filaments to the original weighting of 3 points of the CFS score (Fig. 2).[33] The presence of one or more additional corneal points is highly predictive of Sjögren syndrome classification (sensitivity = 0.56; specificity = 0.75; Youden J = 0.31).[37,38]

Meibomian Gland Functionality

Because MGD is highly prevalent (accumulate prevalence ≈35.9%), with signs observed in 70% to 90% of patients with DED, representing the leading cause of evaporative and mixed subtypes, the assessment of glandular function is mandatory for any patient.[39,40]

Following its principles, the LUBOS panelists agreed with the recommendation of a testing methodology for diagnosing MGD-related DED that is suitable for any practitioner. The MGD classification by the International Workshop on Meibomian Gland Dysfunction (IW-MGD) focuses on assessing morphologic lid features and meibomian gland expression to quantify meibum expressibility and quality, accompanying symptoms and the grade of CFS (Fig. 3).[41] Expressibility can be graded by assessing the inferior glands with digital pressure or with a swab on the tarsal plate to determine the percentage of functional glands. The quality of meibum can be assessed as fluid and transparent, cloudy, cloudy with particles, and dense and pasty.[39,41]

Dry Eye Disease Severity Classification

Identifying the etiology and extent of damage or severity of the disease forms the cornerstone of treatment

selection and monitoring disease progression. This understanding is particularly vital in DED, where a proper treatment approach can significantly improve the quality of life of patients.[42]

To create a simple and practical severity classification accessible to any ophthalmologist in Latin America, the LUBOS expert panel decided to use the OSDI, TFBUT, OSS-SICCA, and IW-MGD functionality tests as the primary clinical criteria for determining the severity of DED (92.8% agreement).[22,30,33,41] This classification will help develop an effective treatment plan and accurately monitor its effects. However, all other clinical diagnostic tools, including non-invasive imaging methods, should also be used when available or necessary.[21,29]

Figure 4 depicts the DED severity classification proposed by the LUBOS consensus. The scale ranges from LUBOS-I (mild) to LUBOS-III (severe) grades, with an additional category, LUBOS-IV or Plus, which includes LUBOS-III grade parameters plus any of the following clinical findings: irreversible damage, Schirmer test = 0 mm, lagophthalmos with epithelial erosion or defects, symblepharon formation (≥50% of the corneal surface), corneal anesthesia, and corneal keratinization (≥50%). The severity weighting includes ≥2 criteria with the highest scores from the worse eye.

Formulation Components and Function of the Ideal Tear Substitute

A distinguishing aspect of the LUBOS consensus (92.8% agreement) is the study of current lubricant eye drop formulations, their components, and functions in the pursuit of an ideal tear substitute and considerations of the type of formulation based on a particular subtype and severity of dry eye.[10,15] Making awareness in the ophthalmic community of the importance of recognizing the physicochemical properties and the main functions of the available lubricant formulations will allow practitioners to improve treatment by choosing an adequate combination of lubricant drops.[10,12,15]

Creating an ideal "artificial tear" represents a massive challenge for the pharmaceutical industry. Like other replenishment strategies for specific functions of the human body,

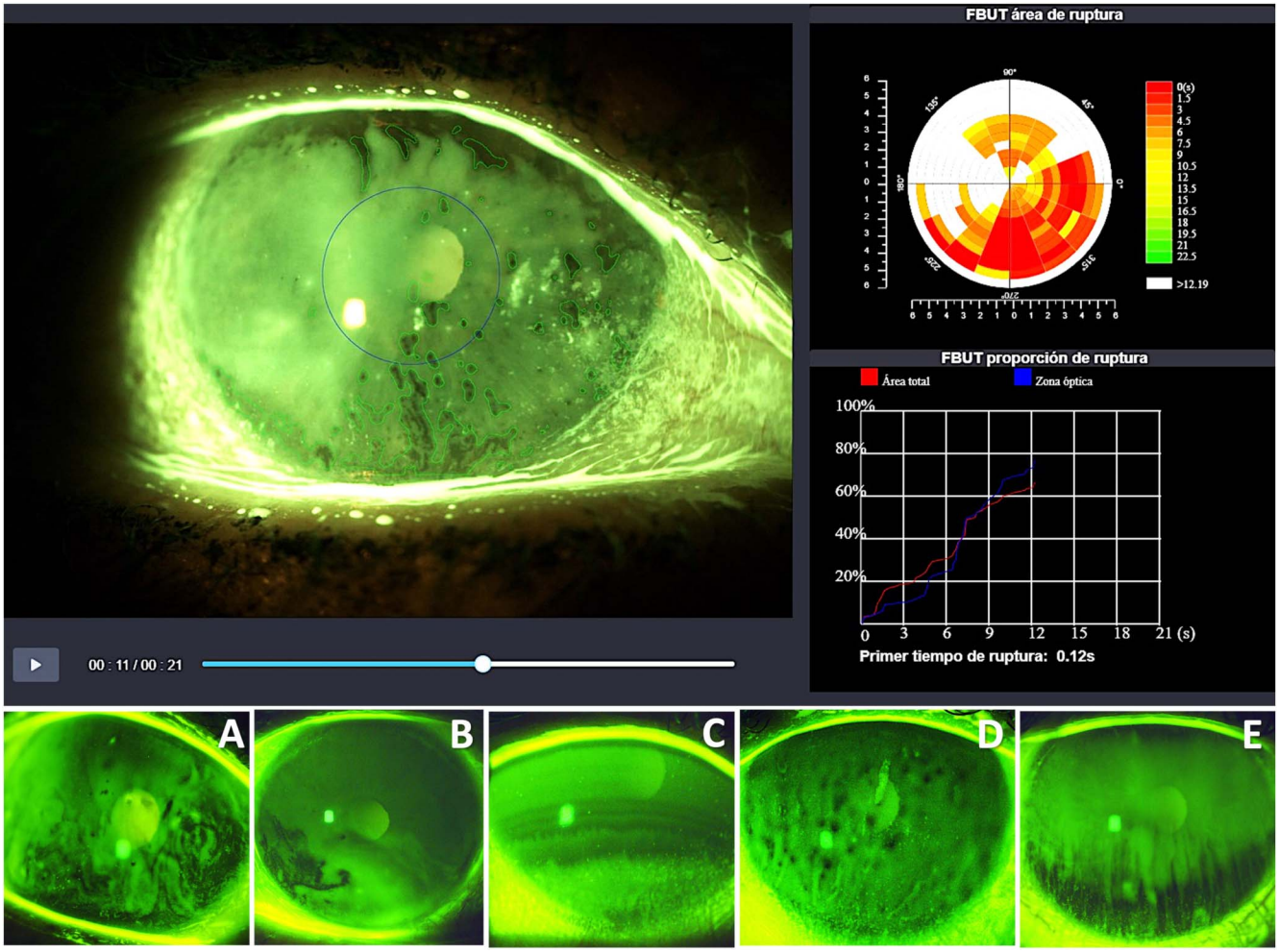
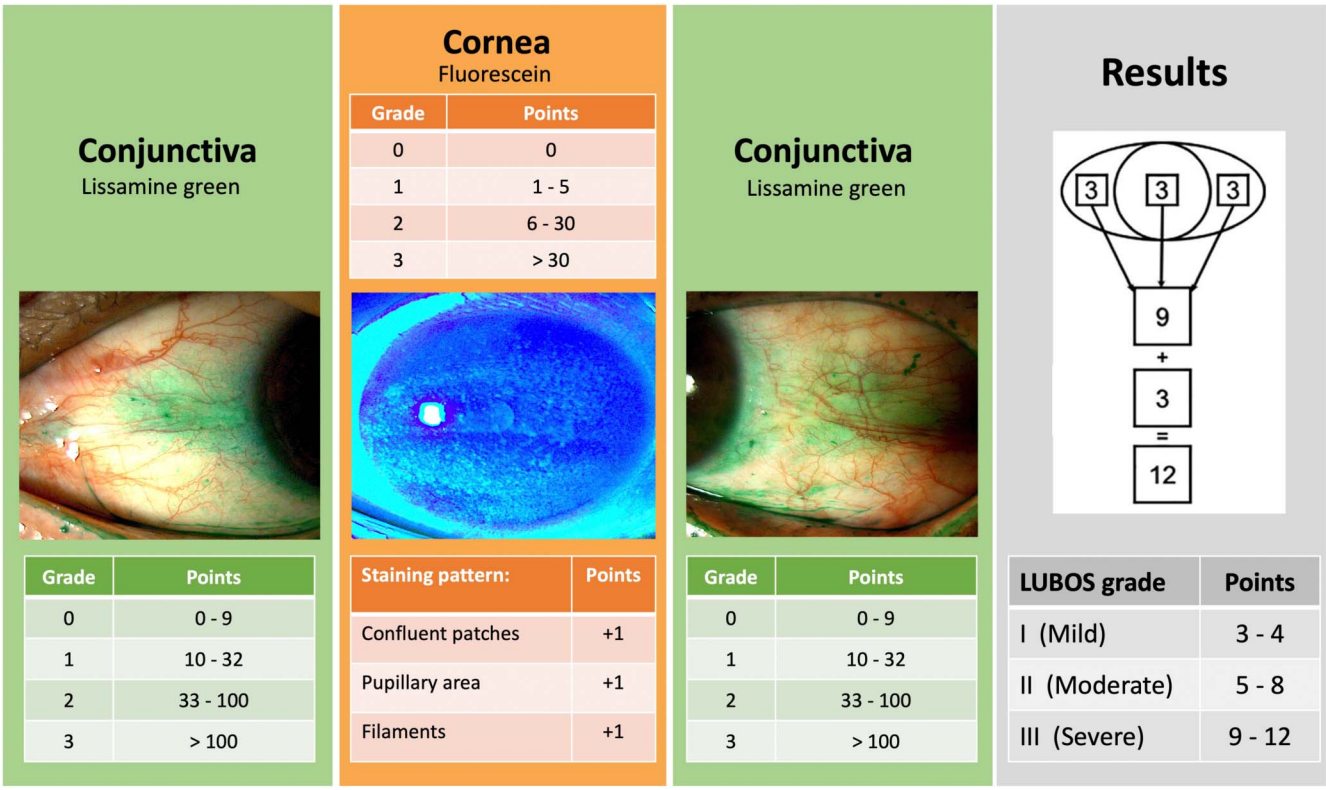


FIGURE 1. Fluorescein tear FTBUT and its different break-up patterns. *According to Yokoi et al.[32] A, Random; (B) dimple; (C) area; (D) spot; and (E) line.



Grade	Points
0	0 - 9
1	10 - 32
2	33 - 100
3	> 100

Grade	Points
0	0
1	1 - 5
2	6 - 30
3	> 30

Staining pattern:	Points
Confluent patches	+1
Pupillary area	+1
Filaments	+1

Grade	Points
0	0 - 9
1	10 - 32
2	33 - 100
3	> 100

LUBOS grade	Points
I (Mild)	3 - 4
II (Moderate)	5 - 8
III (Severe)	9 - 12

FIGURE 2. OSS was determined by the SICCA. The LUBOS severity score weight is shown on the lower right cell. *Modified from the SICCA report.[33].

tear film has many complex properties that are impossible to emulate or substitute.[10,43] The most difficult one is likely the continuous and reactive (reflex) tear production rate, which is translated to the "residence" or "retention time" on the ocular surface by a lubricant eye drop.[11,15] The shearing blinking force, potentiated by a more frequent rate in patients with DED, accelerates the elimination of any eye drop from the ocular surface, hence causing it to lose its function.[11] Because natural continuous and reflex tear production cannot be performed in parallel by applying it manually from a drop bottle, different formulation strategies have been designed to overcome this challenge. They are all efforts to improve the retention time and therapeutic efficacy from higher viscosity and mucoadhesive properties to non-Newtonian polymeric components.[44]

Water-soluble polymers or excipients, such as polyvinyl alcohols, hydroxyethyl and carboxymethylcellulose, hyaluronic acid, gums (HP-guar, Gellan, Xantana), carbomers, and polyacrylic acid, are all used to solve formulation problems and improve retention.[44–46]

The LUBOS agreements (96.4% agreement) for the essential functions, formulation properties, and component functions of lubricant eye drops are summarized in (see Supplemental Table, Supplemental Digital Content 1, http://links.lww.com/ICO/B809). Ophthalmologists should also be aware that the ingredients in makeup tear substitutes can negatively affect the leading etiological causes of DED. For example, using preserved formulations (ie, benzalkonium chloride) for patients requiring continuous and frequent use will induce significant ocular surface toxicity.[47] Similarly, lipid-containing lubricants induce "saturation" on the ocular surface when frequently prescribed, resulting in patient discomfort.[46] Therefore, the choice and concentration of each ingredient must be carefully selected to provide a safe and effective product for the patient.[48] The LUBOS agreements (100% agreement) regarding the use of tear substitute formulations are shown in (see Supplemental Table., Supplemental Digital Content 2, http://links.lww.com/ICO/B809).

Therapeutic Algorithm for Dry Eye Disease

Following the LUBOS diagnostic algorithm and severity classification system, we propose a systematic and practical therapeutic algorithm (96.4% agreement) designed to adjust the patient's DED status and therapeutic response. The algorithm is organized in progressive steps according to the severity of dryness and symptomatology, and each step is divided into recommended and complementary therapies (Fig. 5).

Lubricant eye drops represent the first and baseline treatment steps (see Supplemental Table, Supplemental Digital Content 3, http://links.lww.com/ICO/B809). Unpreserved or mild preservative formulas are favored in all cases, adding lipid compositions in cases of evaporative DED.[49] As DED severity and worsening of symptoms occur, therapy should be escalated to high-viscosity agents (increased

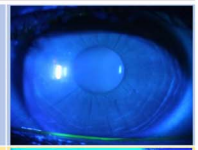
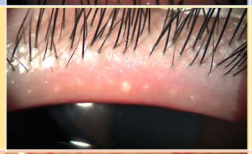
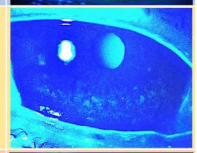
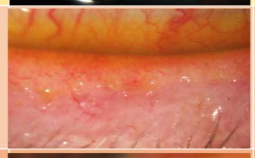
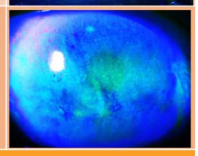
Stage	Grade of Meibomian Gland Dysfunction		Symptoms	Corneal Staining	
1	+ (minimally altered expressibility and secretion quality)		None	None	
2	++ (mildly altered expressibility and secretion quality)		Minimal to mild	None to limited	
3	+++ (moderately altered expressibility and secretion quality)		Moderate	Mild to moderate, mainly peripheral	
4	++++ (severely altered expressibility and secretion quality)		Marked	Marked; central in addition	
Plus disease	Co-existing or accompanying disorders of the ocular surface and/or eyelids				

FIGURE 3. Meibomian gland functionality grading system. *Adapted from the international workshop on meibomian gland dysfunction (IW-MGD).[39].

polymer concentrations, gels, and ointments).[49,50] As the disease progresses to moderate to severe disease, short-term topical surface corticosteroids and longer-use immunomodulators (ie, cyclosporine-A and lifitegrast) should be added to the regimen.[51] In addition, at this stage, blood products (ie, autologous serum, plasma rich in growth factors), oral secretagogues, and insulin (IGF-1) eye drops are added (100% agreement).[52–54] Finally, in severe or refractory DED, interventional procedures (ie, prosthetic replacement of the ocular surface ecosystem (PROSE), amniotic

Criteria	Disease Severity Grade*			
	LUBOS – I Mild	LUBOS – II Moderate	LUBOS – III Severe	LUBOS – IV Plus
OSDI questionnaire	13 – 22 points	23 – 32 points	33 – 100 points	LUBOS – III, plus any of these criteria: ▪ Irrevesible damage to the ocular surface ▪ Schirmer-I test = 0mm / 5 min ▪ Eyelid margin keratinization and fibrosis ▪ Moderate-severe corneal hypoesthesia ▪ Symblepharon formation ▪ Lagophthalmos / epithelial defect
Fluorescein tear break-up time (FTBUT)†	8 – 10 sec	5 – 7 sec	< 5 sec	
Ocular surface staining (OSS-SICCA) score‡	3 – 4 points	5 – 8 points	9 – 12 points	
Meibomian gland functionality§	+ / ++	+++	++++	

FIGURE 4. LUBOS dry eye disease severity classification. *Grade weighing: ≥2 criteria of the worst eye's highest severity grade. †Under fluorescein staining, the patient is asked not to blink while the tear film is observed under a broad beam of cobalt blue illumination. The TFBUT is recorded as the number of seconds between the last blink and the appearance of the first dry spot in the tear film. ‡Combined corneal fluorescein (465–495 nm cobalt blue filter after 4–8 minutes) and conjunctival lissamine green staining (neutral density filter, immediately -2 minutes).[33] §Altered expressibility and secretion quality according to the IW-MGD.[39]

membrane transplantation, salivary gland transplantation, and tarsorrhaphy) may be needed to improve ocular surface conditions (Fig. 5).[55,56]

There are several nonpharmacologic therapeutic options that ophthalmologists should be aware of, as they may be critical to the treatment of DED (94.6% agreement). Generally, most device-mediated dry eye therapies complement pharmacological treatment recommendations for lifestyle and proper nutrition (100% agreement).[49,57] The use of devices and the prescription of nutrition products in each country must be appropriately registered by health regulatory agencies to avoid inappropriate indications or unauthorized use. For devices authorized in your region, adhering to the manufacturer's indications for use is essential. Concerning nutritional supplements, consultation with a nutrition specialist is advised to select the appropriate proportion of nutrients not always available in multivitamin formulations.

DISCUSSION

DED is one of the most common reasons for ophthalmic consultation worldwide.[42,58] Multiple studies have acknowledged its global impact on quality of life and humanistic and economic burdens.[59–61] Latin America is not exempt from such an impact, representing a real eye health problem.[62–67] This situation creates concerns regarding the necessity of adequate and efficacious clinical assistance to the broad population.[68] LUBOS was designed to contribute to solving this eye health challenge by revising the current scientific evidence and applying the panelists' expertise. This study proposes a simple, practical, straightforward, and low-cost alternative for the early detection and accurate diagnosis of DED in Latin American populations. This cost-effective approach suggests that the most efficacious treatment can be applied according to its severity. Previous DED workshops and consensuses have provided extensive and solid evidence on all aspects of the disease to improve its management; nevertheless, few studies have focused on providing practical diagnostic strategies and a management approach based on DED severity classification systems.[57,69] We believe that a simple and helpful severity classification is essential to put the patient into perspective upon disease expectations, apart from permitting the planning of an efficacious therapeutic strategy and monitoring disease response. The DEWS-I (2007) provides a four-level classification system based on increased frequency and intensity of symptoms and signs of dry eye; however, because weighting requires both parameters for grading, its results are unreliable for patients with marked symptoms and signs of discordance, a frequent situation observed in patients with dry eye.[70] The ODISSEY European Consensus (2014) proposed a two-step scoring algorithm for diagnosing severe DED.[71] The first step requires prominent symptoms (OSDI score $\geq$33) and a sign (CFS score or Oxford scale score $\geq$3) to diagnose severe dry eye. If discordant symptoms and signs occur, the second step applies, consisting of three different discordance scenarios. Depending on the scenario assigned, additional recommended criteria, including aberrometry, confocal microscopy, tear inflammatory markers, and refractory to standard treatment, apply to evaluate DED severity further.[71] The latter makes the system complex and, in many instances, inapplicable owing to the costly equipment needed, making it unaffordable for the general population, particularly in Latin America. More recently, the Italian Dacryology & Ocular Surface Society (SIDSO) reported a DED severity classification characterized by the frequency and duration of symptoms and the restoration capacity of the ocular surface. The latter is an objective and accurate measure of disease severity.[72] Finally, the Mexican DED Expert Panel proposed a practical but customized approach to DED severity classification. This approach requires two constant criteria, symptom frequency and ocular surface restoration capacity, for all clinical DED evaluations and one or more of seven complementary criteria: the DEQ-5, the FTBUT, the CFS score, the Oxford scheme, the Schirmer-I test, conjunctival hyperemia, and eyelid involvement.[42] By allowing the clinician to customize the selection of at least one of the remaining clinical tests to complement the evaluation, this methodology provides a high degree of flexibility in assessing DED according to subtype and cause, providing accurate disease severity.[42]

LUBOS panelists have also focused on simple and practical low-cost dry eye evaluations based on basic methods. The clinical history focuses on detecting DED risk factors. The frequency and severity of symptoms, visual disturbances, and environmental factors affecting quality of life are evaluated with the OSDI, a validated survey instrument translated into Spanish and Portuguese with excellent reliability and an internal consistency profile.[26] Finally, the slit-lamp examination permits a thorough evaluation of the eyelids and the ocular surface, complemented with the OSS-SICCA, FTBUT, and IW-MGD functionality scores. In most cases, these practical DED clinical tests permit detection, subtype diagnosis, and grading of disease severity (Fig. 4).[33,41,73] The proposed DED severity grading system simplifies classification, aiding in treatment planning and monitoring. However, its lack of validation is a current limitation, which is the next task of the LUBOS. On the other hand, the OSDI questionnaire may show discordance between subjective symptoms, disease-related quality of life, and clinical findings, challenging the diagnosis and disease severity in many patients.[21,74,75] In addition, psychological factors, such as depression, anxiety, and posttraumatic stress disorder, play a preponderant role in the perception of dry eye symptoms.[76]

The clinical tests recommended by the LUBOS panelists to evaluate evaporative DED (FTBUT and IW-MGD functionality scores) are crucial because MGD is highly prevalent in these patients; hence, assessing glandular function by quantifying meibum expressibility and quality in a standardized form is essential for diagnosis and therapeutic follow-up (Figs. 1 and 3).[31,77] The same is true for the OSS-SICCA score, which has high sensitivity and specificity in measuring the ocular surface damage seen in different forms of dry eye, especially in aqueous-deficient subtypes, such as Sjögren syndrome (Fig. 2).[28,33,78]

The LUBOS therapeutic algorithm follows most of the principles previously reported by other groups.[6,9,10,42,49] However, we emphasize the need to accurately grade DED severity before planning a therapeutic strategy to focus on the

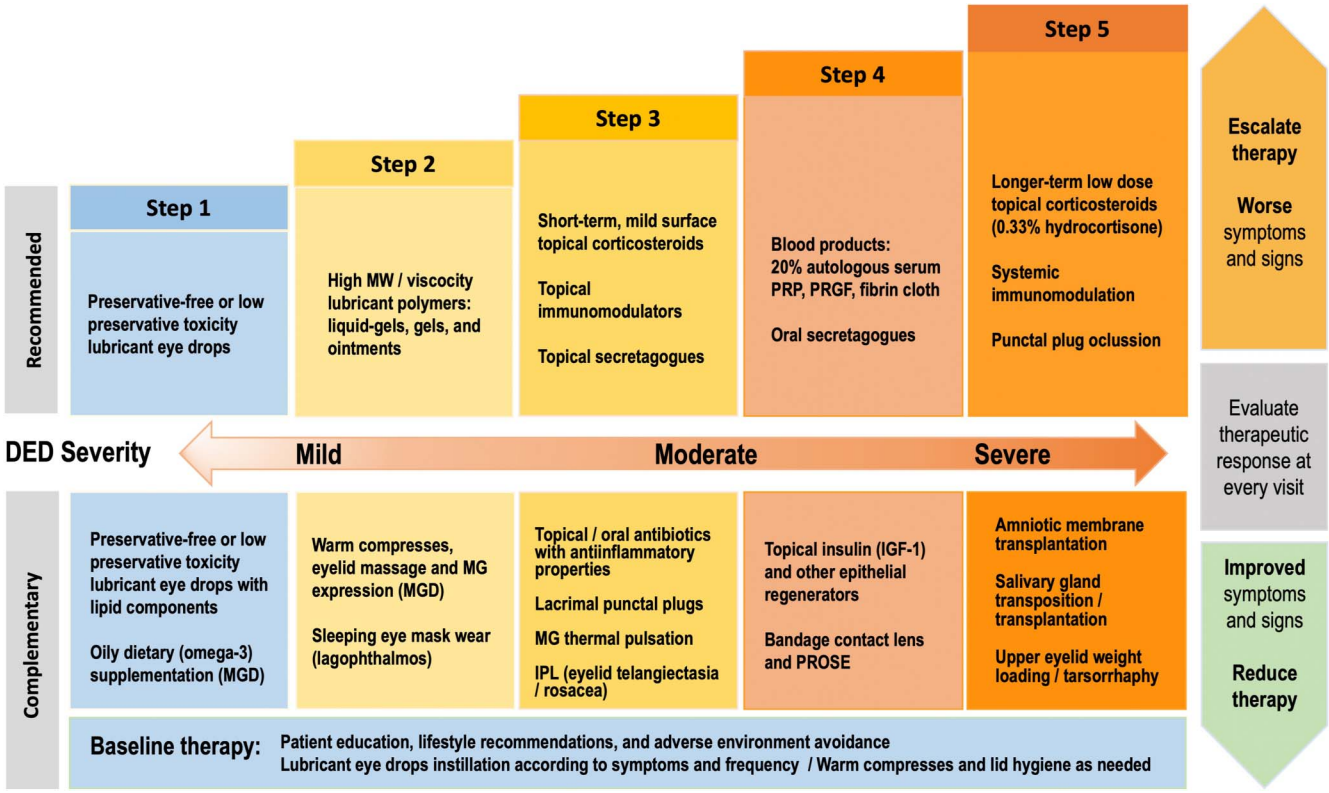


FIGURE 5. LUBOS dry eye disease stepladder therapeutic algorithm. *Adapted from the Mexican dry eye disease expert panel report.[42] IGF-1, Insulin-like growth factor-1; IPL, Intense pulse light; MG, Meibomian glands; MW, molecular weight; PRP, Platelet-rich plasma; PRGF, Plasma reached in growth factors; PROSE, Prosthetic replacement of the ocular surface ecosystem.

most appropriate remedies for patients and monitor their response (Fig. 5). We are aware that not all therapeutic modalities are available to the entire population suffering from dry eyes. Some may be unaffordable for patients without health insurance coverage, and others are unavailable or unapproved by national health regulation agencies in some countries.[79]

We are convinced that patient education is crucial to conscientize and bring patients into perspective about their situation, lifestyle, and environmental and social factors that influence their condition.[57] Because tear substitutes are the mainstay therapy for DED, preservative-free formulations are preferred to avoid further toxicity and damage to the ocular surface, particularly for patients requiring long-term treatment.[15,80] This preference is critical in patients with DED and is associated with other chronic and severe hypersensitivity or autoimmune ocular surface disorders.[28,54,81]

We recommend warm eyelid compresses and massage for chronic blepharitis and MGD throughout the clinical course of the disease (Fig. 5). In more severe cases, higher viscosity and mucoadhesive formulations, epithelial healing promoters (ie, hyaluronic acid–based and trehalose), neurotrophin-containing compounds (ie, autologous serum, insulin-IGF-1) for neurotrophic pathologies, and oral and topical secretagogues, immunomodulators, and biologic agents could be added to the regimen for severe DED.[54,82] Finally, interventional and surgical procedures may be needed for complex and irreversible cases, including punctal plug occlusion, weight loading, AMT, salivary gland transposition/transplantation, and tarsorrhaphy.[83,84]

The limitations of an expert panel consensus relate to the conditional reliability of published evidence, which directly affects the decisions and agreements that rely partly on the expert panel's clinical experience in evaluating, diagnosing, and treating patients. In addition, the multifactorial nature of DED and its wide range of clinical scenarios challenge the agreements reached. Therefore, clinicians must consider many other clinical and nonclinical factors beyond those addressed in our statements.

In conclusion, the LUBOS consensus on the diagnosis, disease severity, and treatment algorithms for DED subtypes aims to contribute to the peer community by developing practical concepts. These concepts are designed to enhance the daily clinical practice of ophthalmologists in Latin America. However, we also hope that this material could benefit the global ophthalmic community, as it holds the potential for partial or total inclusion, with corresponding adaptations in other regions to improve dry eye clinical practice.

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