TFOS DEWS III: **Diagnostic Methodology Summary**

Stephanie Wong, Centre for Ocular Research & Education (CORE) School of Optometry & Vision Science, University of Waterloo, Canada

Wolffsohn JS, Benítez-del-Castillo JM, Loya-Garcia D, et al. TFOS DEWS III: Diagnostic Methodology. *American Journal of Ophthalmology.* 2025; doi: 10.1016/j.ajo.2025.05.033

The TFOS DEWS II Diagnostic Methodology report[1] was published in 2017 and standardized the testing procedures used to diagnose dry eye disease (DED). As our knowledge of DED has increased over the years, the TFOS DEWS III: Diagnostic Methodology[2] report was created to reflect the latest body of evidence. The report provides a revised definition of DED, updated recommendations for diagnostic testing, and an expanded subclassification of DED.

Revised Definition of Dry Eye Disease

The definition of dry eye has been updated to:

Dry eye is a multifactorial, symptomatic disease characterized by a loss of homeostasis of the tear film and/or ocular surface, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities are etiological factors.

It is helpful to understand the rationale for including specific words in the revised definition of DED. These key words are summarized in ***Table 1.***

Key words	Updated from TFOS DEWS II?	Rationale
"Multifactorial"	No	DED is complex, and the ocular surface is affected by genetics, lifestyle, and environmental factors.
"Symptomatic"	No	DED has a wide range of symptoms, including discomfort and visual problems.
"Disease"	No	Continues to acknowledge that dry eye is a disease, and not a syndrome.
"Loss of homeostasis of the tear film and/or ocular surface"	Yes	Updated recognition that the 'loss of homeostasis' can apply not only within the tear film but also the ocular surface microenvironment.

Table 1: *Key words in the definition of DED*

History Taking

Signs and symptoms similar to those of DED also occur in several other conditions. Practitioners must take a thorough history to identify any general health conditions, medications, use of cosmetics, or known risk factors that can be associated with or mimic DED.[3,4] Important questions that can aid in the differential diagnosis of DED appear in ***Table 2.***

Question	Rationale
Do you feel eye pain rather than discomfort?	Pain is not commonly reported in mild-to-moderate DED.
Do you have any facial flushing/redness, mouth dryness, or enlarged salivary glands?	Warrants further investigation for rosacea, sarcoidosis, or Sjögren's disease.
When did your symptoms start, and can you recall any triggering event?	Dry eye is chronic. Sudden onset may be due to infection or trauma.
Is your vision affected, and if so, does it improve on blinking?	Sudden onset of decreased vision that does not improve with blinking requires urgent investigation for other causes (e.g. vascular occlusions).
Are the symptoms or any redness much worse in one eye than the other?	Dry eye is generally bilateral.
Do the eyes itch, are they swollen or crusty, or is there any discharge?	Itching is likely to be caused by allergies, but can be associated with anterior blepharitis if reported along the lash line. Mucopurulent discharge can be a sign of infection.

Table 2: *Questions to aid in the differential diagnosis of DED*

Common Symptoms

Frequently reported symptoms associated with DED include grittiness, burning, photophobia, and dryness. The severity of symptoms changes over the day, with dryness typically being worse upon waking compared to later in the morning.

Updated Screening Questionnaire

The recommended screening questionnaire for DED is now the shortened Ocular Surface Disease Index-6 (OSDI-6).[5] The OSDI-6 consists of six questions that assess symptoms over the past month compared to the original 12-item OSDI questionnaire, which investigates symptoms experienced only over the previous week.

The OSDI-6 questionnaire appears in ***Figure 1.*** The diagnostic cut-off value for symptoms of dry eye is a summed score ≥4. The overall OSDI-6 score is classified as normal (0-3 points), mild-to moderate DED (4-8 points), or severe DED (9-24 points).

Ocular Examination

Once the presence of dry eye symptoms has been confirmed with the OSDI-6, the tear film and ocular surface must be examined for a loss of homeostasis. The diagnostic tests and criteria used to assess the eye for signs of DED are the same as previously reported in the TFOS DEWS II Diagnostic Methodology report,[1] and a summary is shown in ***Figure 1.*** At least one sign that demonstrates the loss of homeostasis must be observed to diagnose DED. The order of tests should be performed from least invasive to most invasive.

If the first test conducted is not positive for dry eye, clinicians can now be confident in confirming the presence or absence of

dry eye by performing two of the three tests of homeostasis; tear film stability OR tear osmolarity, plus comprehensive ocular surface staining (of the cornea, conjunctiva and lid margin).

Although a non-invasive measurement of break-up time remains the preferred method of examining tear film stability, the report clarifies that a fluorescein break-up time of <5 seconds is indicative of dry eye. The optimal time to assess corneal staining is 1 to 4 minutes after instilling fluorescein, whereas conjunctival and lid margin staining should be viewed 1 to 5 minutes after applying lissamine green. Lid wiper epitheliopathy is typically an earlier sign of ocular surface damage than corneal staining which tends to be observed only in more severe cases of dry eye.

After DED has been diagnosed, additional dry eye tests may be used to help identify risk factors and to aid in selecting the most appropriate treatment.[6]

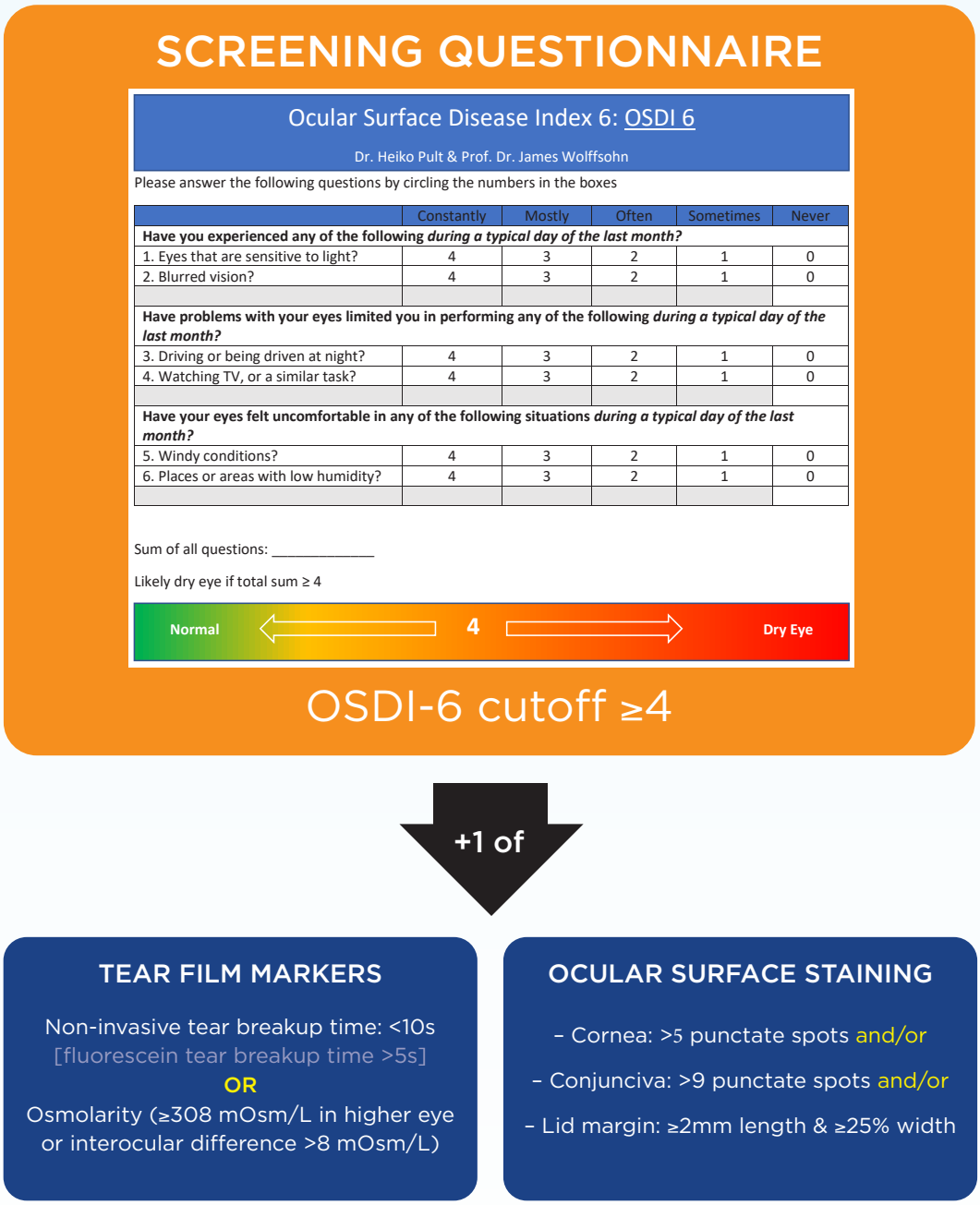

Figure 1: *Recommended screening questionnaire and follow-up tests to assess for symptoms and signs of dry eye disease*

OSDI-6: Ocular Surface Disease Index-6; s: seconds; mOsm/L: milliosmoles per liter; mm: millimeters.

Sub-classification of Dry Eye Disease drivers

DED is classified by etiology and can be caused by tear film deficiencies (lipid, aqueous, and/or mucin/glycocalyx), eyelid anomalies (blink/lid closure and/or lid margin), ocular surface anomalies (anatomical misalignment, neural dysfunction, ocular surface cellular damage/disruption, and/or primary inflammation/oxidative stress), or systemic conditions. ***Table 3*** provides information on standard tests that can be performed to classify DED. Please refer to ***Table 6*** in the report for diagnostic cut-off values and advanced testing techniques.

		Standard Tests
Tear Film Deficiencies	Lipid	Interferometry
		Meibum expressibility/quality
	Aqueous	Meniscometry (tear meniscus height)
	Mucin/glycocalyx	Rose bengal or lissamine green staining
Eyelid Anomalies	Blink/lid closure	Partial blinking observation Lagophthalmos/inadequate lid seal
	Lid margin	Anterior blepharitis observation Meibomian gland dysfunction (meibography, gland plugging, telangiectasia, gland expressibility) Keratinization (slit lamp biomicroscopy) Ocular rosacea (slit lamp biomicroscopy)
Ocular Surface Abnormalities	Anatomical misalignment	Slit lamp biomicroscopy
	Neural dysfunction	Sensation to a puff of air or physical contact
	Ocular surface cellular damage/disruption	Corneal fluorescein staining Conjunctival lissamine green staining Lid wiper staining
	Primary inflammation/oxidative stress	Bulbar conjunctival hyperemia
Systemic Drivers		Check for systemic conditions

Table 3: *Standard tests to classify the type of DED (adapted from TFOS DEWS III: Diagnostic Methodology[2] report)*

Only Symptoms or Only Signs of Dry Eye

Both symptoms and signs of DED must be present to diagnose DED. Patients complaining of significant symptoms who do not show clinical signs, or, as it is commonly referred to, *"pain without stain,"* may have neuropathic corneal pain. Conversely, significant corneal staining without pain (or *"stain without pain"*) may be due to neurotrophic keratopathy.

Summary

The TFOS DEWS III: Diagnostic Methodology[2] report provides a streamlined testing approach to diagnose and classify the drivers of dry eye disease. An accurate diagnosis will allow clinicians to choose the most appropriate therapy option from the evidence-base for each of their patients.

Key References

1. Wolffsohn JS, Arita R, Chalmers R, et al. TFOS DEWS II Diagnostic Methodology Report. *Ocular Surface.* Jul 2017;15(3):539-574.
2. Wolffsohn JS, Benitez-Del-Castillo JM, Loya-Garcia D, et al. TFOS DEWS III: Diagnostic Methodology. *Am J Ophthalmol.* May 30 2025;279:387-450.
3. Sullivan DA, da Costa AX, Del Duca E, et al. TFOS Lifestyle: Impact of Cosmetics on the Ocular Surface. *Ocular Surface.* July 2023;29:77-130.
4. Stapleton F, Argueso P, Asbell P, et al. TFOS DEWS III: Digest. *Am J Ophthalmol.* Jun 4 2025;279:451-553.
5. Pult H, Wolffsohn JS. The Development and Evaluation of the New Ocular Surface Disease Index-6. *Ocular Surface.* Oct 2019;17(4):817-821.
6. Jones L, Craig JP, Markoulli M, et al. TFOS DEWS III: Management and Therapy. *Am J Ophthalmol.* Jun 2 2025;279:289-386.

Alcon

SEE BRILLIANTLY