



## New perspectives in diagnosing and managing dry eye

- incorporating TFOS DEWS II in clinical practice

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JS Wolffsohn Disclosures




### Objectives

- What** is dry eye?
  - Definition and Classification
- Who** is affected?
  - Epidemiology
- Why** does it occur?
  - Pathophysiology
- When** is it diagnosed as dry eye?
  - Diagnostic Methodology
- How** do we manage it?
  - Management and Therapy

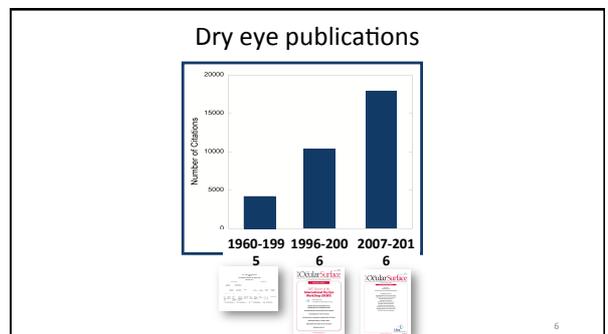



tfos

# DEWS II

## REPORT

www.tearfilm.org



### TFOS DEWS II Reports

Definition & Classification	Pathophysiology
Sex, Gender, & Hormones	Iatrogenic Dry Eye
Epidemiology	Diagnostic Methodology
Tear Film	Management & Therapy
Pain & Sensation	Clinical Trial Design

Introduction	Executive Summary
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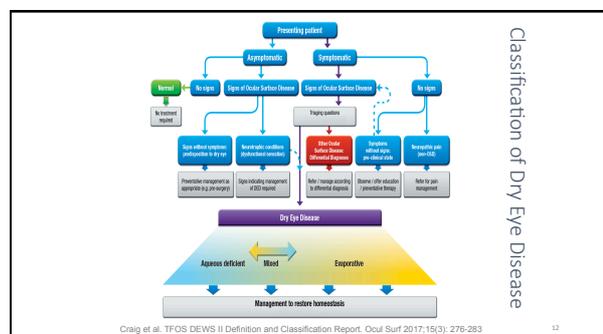
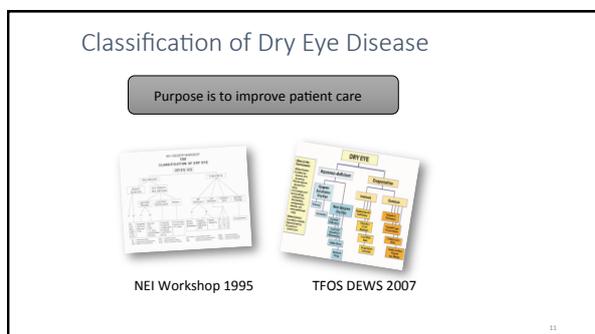
TFOS DEWS II Report. Ocul Surf 2017; 15(3): 269-649 – available free from www.nearfilm.org  
TFOS DEWS II Executive Summary. Ocul Surf 2017; 15(4) – also free via TFOS website

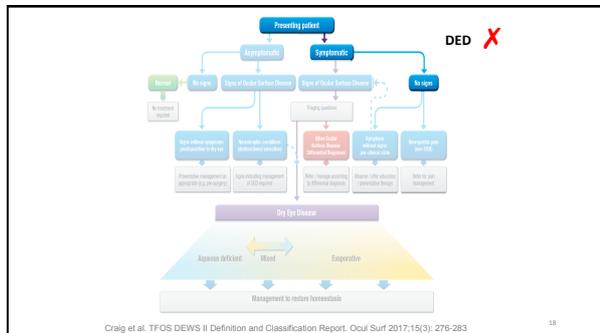
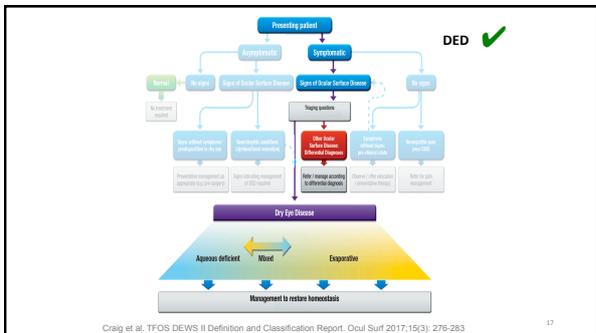
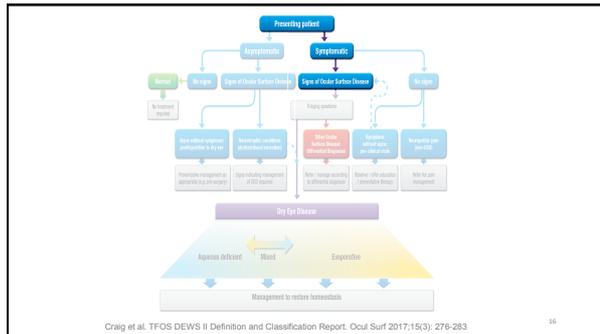
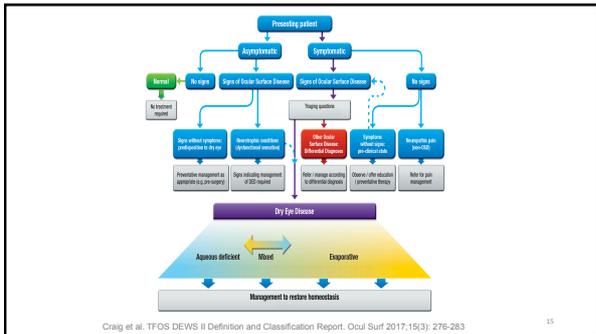
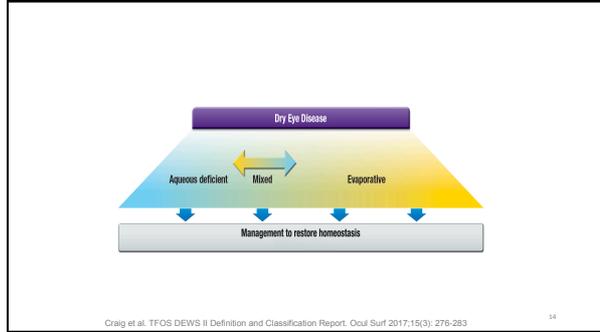
- ### What?
- **What** is dry eye?
    - Definition and Classification
  - **When** does it occur?
    - Epidemiology
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  - **How** do we manage it?
    - Management and Therapy
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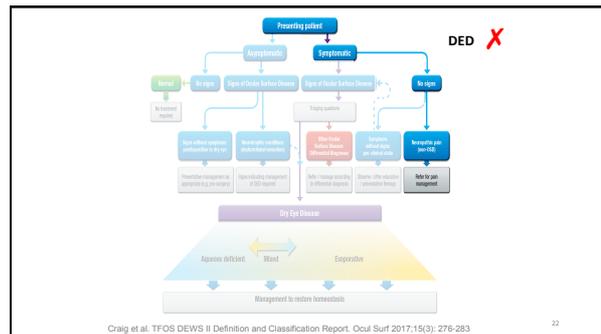
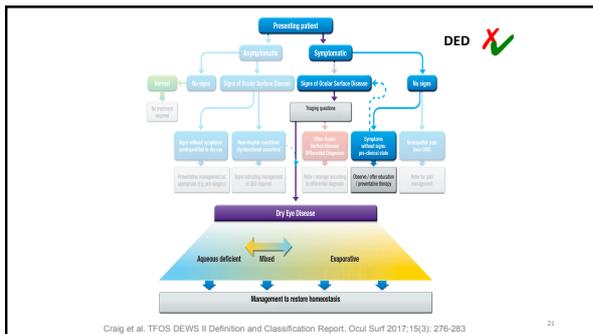
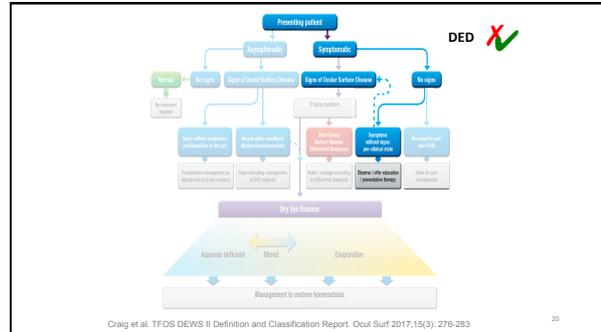
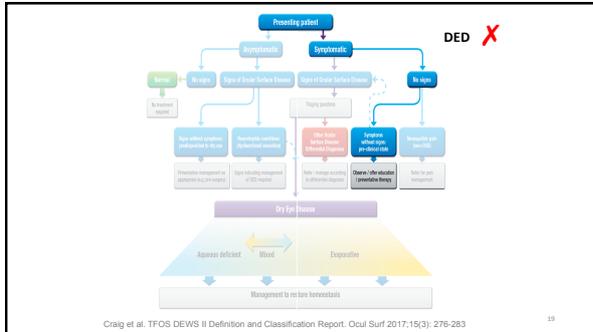
### TFOS DEWS II revised definition

“Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.”

Craig et al. TFOS DEWS II Definition and Classification Report. Ocul Surf 2017;15(3): 276-283





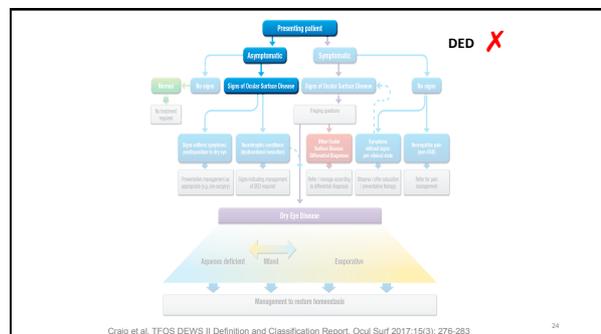


When is it not dry eye

**NOICEPTIVE PAIN:** Pain that arises from actual or threatened damage to tissues and is due to the activation of nociceptors (acute and chronic) (*pain with biological value*)

**NEUROPATHIC PAIN:** Pain caused by a lesion or disease of the somatosensory system (peripheral and central) (*pain without biological value*)

Belmonte et al. TFOS DEWS II Pain and Sensation Report. Ocul Surf 2017;15(3): 404-437. 23





### Who?

- **What** is dry eye?
  - Definition and Classification
- **Who is affected?**
  - Epidemiology
- **Why** does it occur?
  - Pathophysiology
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### Epidemiology

- Dry eye prevalence ranges from 5 to 50%
- Risk factors

	Consistent*	Probable +	Inconclusive #
<b>Non-modifiable</b>	Aging Female sex Asian race Meibomian gland dysfunction Connective tissue diseases Sjogren Syndrome	Diabetes Rosacea Viral infection Thyroid disease Psychiatric conditions Pterygium	Hispanic ethnicity Menopause Ache Sarcoidosis
<b>Modifiable</b>	Androgen deficiency Computer use Contact lens wear Hormone replacement therapy Hematopoietic stem cell transplantation Environment: pollution, low humidity, sick building syndrome Medications: antihistamines, antidepressants, anxiolytics, isotretinoin	Low fatty acids intake Refractive surgery Allergic conjunctivitis Medications: anticholinergic, diuretics, beta-blockers	Smoking Alcohol Pregnancy Demodex infestation Botulinum toxin injection Medications: multivitamins, oral contraceptives

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### Impact on quality of life

- Severe dry eye rated as equivalent to angina or dialysis
- Impact on productivity
  - absenteeism/presenteeism
- Association with depression
- Financial burden
  - personal / global





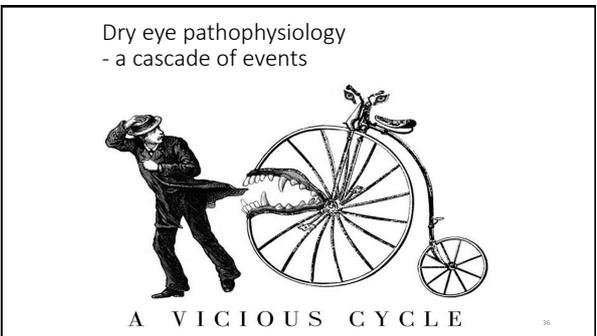
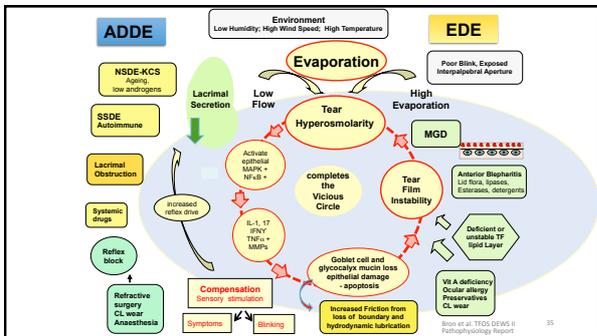

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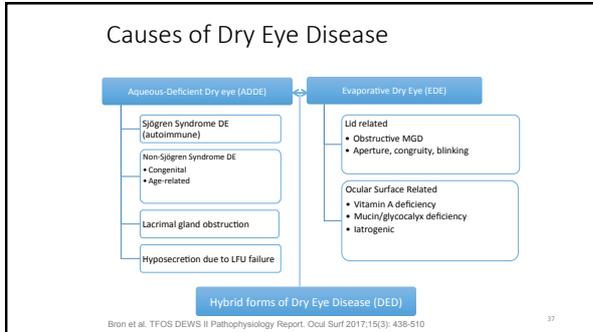
### Why?

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### When?

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### What is the purpose of a diagnosis?

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### TFOS DEWS Definition

**Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film & inflammation of the ocular surface.**

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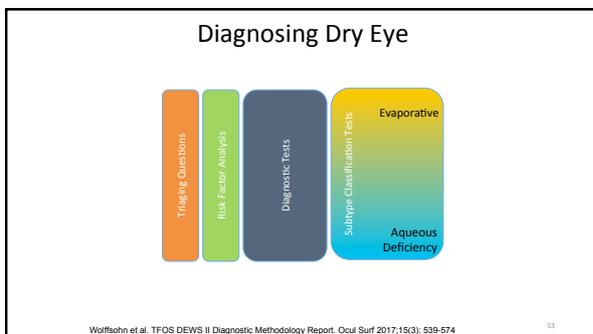
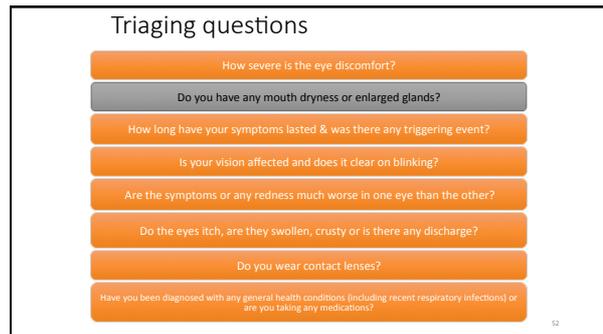
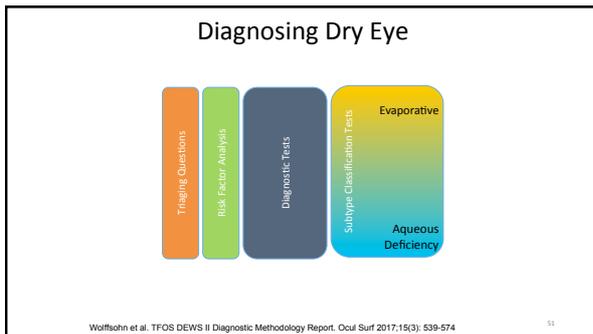
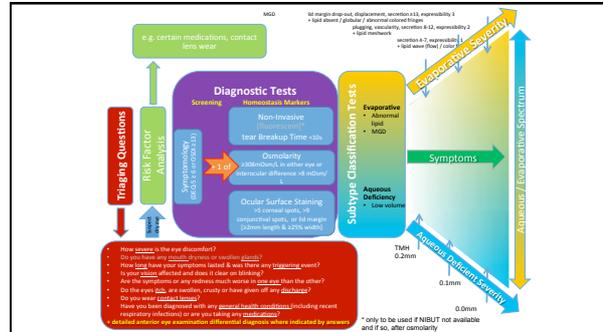
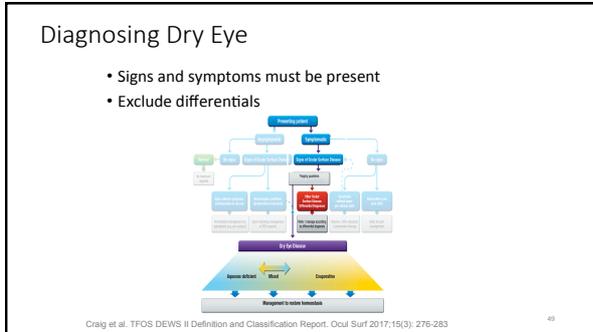
- ### Recommendations for Diagnosis TFOS DEWS
- Symptomology questionnaire
  - Osmolarity
  - Non-invasive TFBUT
  - Tear function Index – diagnostic value Sjögren's
    - fluorescein-coated tear strip placed over the lower lid margin
    - 1. eye closed - strip in place for 3 minutes
    - 2. wetting distance measured
    - 3. strip air dried and intensity of staining compared to calibrated panel of dilutions = tear clearance rate
    - 5. The TFI is defined as the quotient of the Schirmer test and the TCR.
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### Prevalence

Study	N	Age range	Dry eye assessment	Prevalence
<b>US Studies</b>				
Salisbury Eye Study <sup>24</sup>	2420	≥ 65 y	At least 1 of 6 symptoms (dryness, gritty/scratchiness, burning, redness, crusting on lashes, eyes stuck shut in morning), occurring at least often.	14.6%
Beaver Dam <sup>25</sup>	3722	≥ 48 y	"For the past 3 months or longer have you had dry eyes?" (if needed, described as foreign body sensation with itching, burning, sandy feeling, not related to allergy.)	14.4%
Women's Health Study <sup>26</sup>	36995	≥ 40 y	Severe symptoms of dryness and irritation, either constantly or often, and/or the physician's diagnosis of dry eye as volunteered by the patient.	7.8%
Physician's Health Studies I and II <sup>24,24</sup>	25655	≥ 50, 55 y	Severe symptoms of both dryness and irritation either constantly or often and/or the physician's diagnosis of dry eye as volunteered by the patient.	
<b>Australian Studies</b>				
Blue Mountains <sup>27</sup>	1075	≥ 50 y	At least 1 of 4 symptoms regardless of severity, or at least 1 symptom with a moderate to severe rating (dryness, grittiness, itchiness, discomfort).	10.0% (at least 1 symptom) 15.3% (2 or more symptoms)
Melbourne Visual Impaired Project <sup>28</sup>	926	≥ 40 y	At least 1 of 6 "severe" symptoms, not attributed to the subject to have fever (discomfort, foreign body, itching, tearing, dryness, photophobia).	5.0%
<b>Asian Studies</b>				
Shanghai <sup>29</sup>	2038	≥ 65 y	At least 1 of 6 symptoms, often or all of the time (dryness, gritty/scratchiness, burning, itching, tearing, redness, discharge, eyes stuck shut in morning).	33.7%
Sunata <sup>30</sup>	1058	≥ 21 y	At least 1 of 6 symptoms, often or all of the time (dryness, gritty/scratchiness, burning, redness, crusting on lashes, eyes stuck shut in morning).	27.5%

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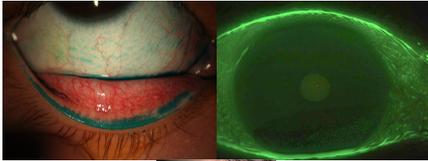


### Risk factor questions

	Consistent*	Probable +	Inconclusive #
Non-modifiable	Aging	Diabetes	Hispanic ethnicity
	Female sex	Rosacea	Menopause
	Asian race	Viral infection	Acne
	Meibomian gland dysfunction	Thyroid disease	Sarcoidosis
	Connective tissue diseases	Psychiatric conditions	
	Sjögren Syndrome	Pterygium	
Modifiable	Androgen deficiency	Low fatty acids intake	Smoking
	Computer use	Refractive surgery	Alcohol
	Contact lens wear	Allergic conjunctivitis	Pregnancy
	Hormone replacement therapy		Demodex infestation
	Hematopoietic stem cell transplantation		Botulinum toxin injection
	Environment: pollution, low humidity, sick building syndrome		
	Medications: antihistamines, antidepressants, anxiolytics, isotretinoin	Medications: anticholinergic, diuretics, beta-blockers	Medications: multivitamins, oral contraceptives



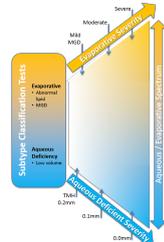
### Ocular Surface Staining: Fluorescein and Lissamine Green



- Corneal punctate spots >5
- Conjunctival spots >9
- Lid margin >2mm length & 25% width

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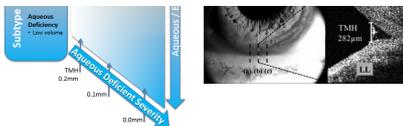
### Subtype Classification



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### Aqueous Deficient DED: Diagnostics

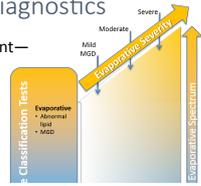
- Tear volume tests
  - Tear meniscus height measurement
  - Schirmer test
  - Phenol red test



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### Evaporative DED: Diagnostics

- Meibomian gland assessment—expressibility & oil flow
- Meibography
- Interferometry
- Blink and lid closure
- Lid margin keratinisation




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### Diagnostic Videos



1. **Tear film stability** assessment via calculation of tear film break up time, using both non-invasive and invasive (fluorescein) methods.
2. Evaluation of the **osmolarity** of the tear film in the tear meniscus region.
3. Examination of **ocular surface damage** using sodium fluorescein and lissamine green ophthalmic dyes.
4. Visualisation and thickness estimation of the **tear film lipid** layer.
5. **Eversion** of the upper and lower eyelids.
6. Evaluation of the **lids and lid margins**, diagnostic meibomian gland evaluation and meibography.
7. **Tear volume** assessment via determination of the lower tear meniscus height, Schirmer strip and phenol red thread.
8. **Ocular surface inflammation** presence detection using MMP-9.

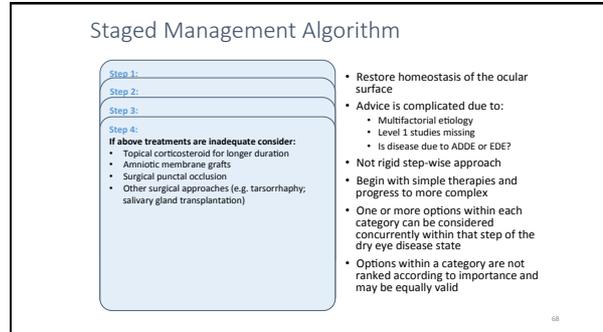
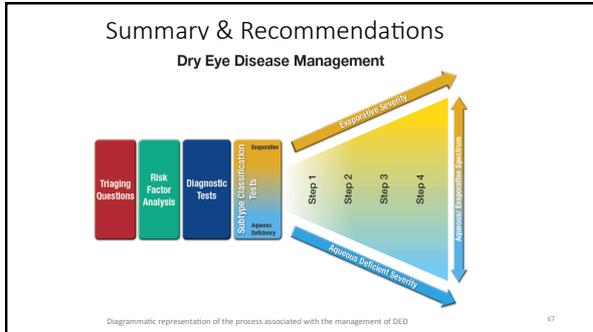
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### Step 1 Treatment

STEP	TFOS DEWS II recommendations for the staged management and treatment of DED
1	<ul style="list-style-type: none"> <li>• Education regarding the condition, its management, treatment and prognosis</li> <li>• Modification of local environment</li> <li>• Education regarding potential dietary modifications (including oral essential fatty acid supplementation)</li> <li>• Identification and potential modification (elimination of offending systemic and topical medications)</li> <li>• Ocular lubricants of various types (if MGD is present, then consider lipid-containing supplements)</li> <li>• Lid hygiene and warm compresses of various types</li> </ul>

### Environmental Modifications

- Locally placed humidifiers
  - USB-driven for laptops now available
- Minimise direct exposure to draughts/air conditioning
  - office
  - in-car vents/blowers
  - draughts

### Simple Dietary Modifications

- Increase water consumption
- Avoid excessive intake of foods and fluids that dehydrate the body
  - salty snacks
  - chips
  - popcorn
  - french fries
  - cured meats
  - alcohol
  - coffee
  - soy sauce

### Essential Fatty Acids & Dry Eye Reviews

1. Mardianpour-Kandari M, et al. Essential fatty acids for dry eye. *Am J Ophthalmol*. 2012; 154(1): 10-15.

2. Mardianpour-Kandari M, et al. Essential fatty acids for the treatment of dry eye. *Am J Ophthalmol*. 2012; 154(1): 10-15.

3. Mardianpour-Kandari M, et al. Essential fatty acids for the treatment of dry eye. *Am J Ophthalmol*. 2012; 154(1): 10-15.

4. Mardianpour-Kandari M, et al. Essential fatty acids for the treatment of dry eye. *Am J Ophthalmol*. 2012; 154(1): 10-15.

5. Mardianpour-Kandari M, et al. Essential fatty acids for the treatment of dry eye. *Am J Ophthalmol*. 2012; 154(1): 10-15.

### Studies on Dry Eye & EFA

- Protective role for omega-3 EFA (DHA) in cases of dry eye.<sup>1</sup>
- Women consuming highest amounts of omega-3 (mainly tuna) had lowest rate of dry eye.<sup>2</sup>
- Targeted omega-6 intake was beneficial in those with dry eye.<sup>3</sup>
- Topical use of EFA drops reduced ocular inflammation in mouse model of dry eye.<sup>4</sup>



1. Osholm et al. Prostaglandins Leukot Essent Fatty Acids 1996; 55:4: 239-45.  
2. Mijanovic et al. Am J Clin Nutr 2005; 82:4: 887-93.  
3. Barabino et al. Cornea 2003; 22:2: 97-101.  
4. Rashid et al. Arch Ophthalmol 2008; 126:2: 219-25.

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### Identify & Eliminate/Modify Drugs Causing DED

- Antihistamines
- Acne meds (isotretinoin)
- Anticholinergics
- Barbiturates
- Beta blockers
- Diazepam (valium)
- Oral contraceptives
- Tricyclic antidepressants



Gomes et al. TFOS DEWS II Iatrogenic report. Ocul Surf 2017; 15:3: 511-538

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### Ocular Lubricants

- Mainstay of therapy
  - numerous topical formulations available
- **Avoid preservatives in severe dry eye**
- **Very few** RCT have compared the relative superiority of a particular OTC product to others for DED<sup>1</sup>



- Viscosity enhancing agents
  - HPMC; CMC; HA; CMC+HA; HP-guar; HA+HP-guar
- Osmotic agents
  - L-carnitine; betaine; trehalose
- Osmoprotectants
- Antioxidants
- Preservatives
- Inactives
  - Buffers; excipients; electrolytes
- Lipid-containing drops
  - nanoemulsions
  - types/props of lipids

1. Packer et al. Over the counter (OTC) artificial tear drops for dry eye syndrome. Cochrane Database Syst Rev 2016; 1: CD010720

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### Lid Hygiene

- Appropriate lid hygiene is important in the management of a variety of lid conditions that result in DED
  - particularly blepharitis
  - if used appropriately can reduce lipid by-products and lipolytic bacteria associated with these conditions
- Proprietary lid scrubs better than dilute baby shampoo applied with cotton buds
- No universally accepted guidelines for lid cleansing and peer-reviewed evidence for such advice is lacking
  - an area worthy of study



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### Commercial Warm Compresses

- MGDRx EyeBag
  - [www.eyebagcompany.com](http://www.eyebagcompany.com)
  - flax seeds in a silk bag
  - warmed in microwave
- Bruder mask
- Blephasteam
  - swimming goggle that plugs into electrical socket
- Tranquileyes Moist Heat Therapy goggles
  - <http://www.ocusoft.com/>



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### Step 2 Treatment

STEP	TFOS DEWS II recommendations for the staged management and treatment of DED
2	<p><b>If above options are inadequate consider:</b></p> <ul style="list-style-type: none"> <li>• Non-preserved ocular lubricants to minimize preservative-induced toxicity</li> <li>• Tea tree oil treatment for Demodex (if present)</li> <li>• Tear conservation                             <ul style="list-style-type: none"> <li>o Punctal occlusion</li> <li>o Moisture chamber spectacles/goggles</li> </ul> </li> <li>• Overnight treatments (such as ointment or moisture chamber devices)</li> <li>• In-office, physical heating and expression of the meibomian glands (including device-assisted therapies)</li> </ul> <ul style="list-style-type: none"> <li>• In-office intense pulsed light therapy for MGD</li> <li>• Prescription drugs to manage DED                             <ul style="list-style-type: none"> <li>o Topical antibiotic or antibiotic/steroid combination applied to the lid margins for anterior blepharitis</li> <li>o Topical corticosteroid (limited-duration)</li> <li>o Topical secretagogues</li> <li>o Topical non-glucocorticoid immunomodulatory drugs</li> <li>o Topical lymphocyte function-associated antigen-1 antagonist drugs</li> <li>o Oral macrolide or tetracycline antibiotics</li> </ul> </li> </ul>

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### Tea Tree Oil for Demodex

- The active component of TTO is 4-Terpineol
- Various proprietary formulations are now commercially available
  - various concentrations
    - foams
    - pre-formulated wipes
- Relatively limited information exists in relation to the positive impact of TTO on dry eye symptoms and signs and more studies are needed on this topic

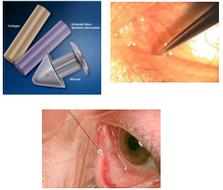


Carson et al (2006). Multitask efficacy of Tea Tree Oil: a Review of Antimicrobial and Other Medicinal Properties. Clin Microbiol Rev 20(2): 5-42

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### Punctal Occlusion

- Many different designs
- Punctal occlusion
  - Collagen plugs
    - dissolve
  - Silicone plugs
    - "permanent"
- Punctal occlusion may be most successful when combined with other DED treatments
- To date, no large scale Level 1 studies to support the contention that punctal occlusion of any form is effective in the management of DED.
  - but many Level 2 studies exist



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### Moisture Chamber Specs

- Specially designed eyeglasses made to slow evaporation of the tears, provide a humid environment and minimize airflow over the ocular surface
  - number of such devices available
- Level 3 evidence only



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### Ointments

- Severe dry eye
- Nocturnal lagophthalmos
- Typically contain mineral oil and petrolatum
  - some contain lanolin
  - Many options available



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### Prescription Drug Options

- **Topical**
  - Topical antibiotic
  - Topical corticosteroid
  - Topical combo antibiotic/steroid
  - Topical non-glucocorticoid immunomodulatory
  - Topical LFA-1 antagonist
- **Systemic**
  - Oral macrolide antibiotics

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### Anti-Inflammatory Therapy

- **Topical glucocorticoids**
  - 9 RCT
  - Complications: IOP raise, cataracts, infection
- **Non-glucocorticoid immunomodulators**
  - Cyclosporine
  - Tacrolimus
  - NSAIDs
  - Biologics
- **LFA-1 antagonist**
- **Inflammatory modulation with systemic & topical antibiotics**
  - tetracyclines
- **Macrolide treatments**
  - azithromycin



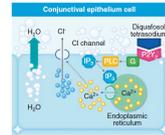
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### Steps 3 & 4 Treatment

STEP	TFOSS DEWS II recommendations for the staged management and treatment of DED
<b>3</b>	<p><b>If above options are inadequate consider:</b></p> <ul style="list-style-type: none"> <li>Oral secretagogues</li> <li>Autologous/allogeneic serum eye drops</li> <li>Therapeutic contact lens options                             <ul style="list-style-type: none"> <li>Soft bandage lenses</li> <li>Rigid scleral lenses</li> </ul> </li> </ul>
<b>4</b>	<p><b>If above options are inadequate consider:</b></p> <ul style="list-style-type: none"> <li>Topical corticosteroid for longer duration</li> <li>Amniotic membrane grafts</li> <li>Surgical punctal occlusion</li> <li>Other surgical approaches (eg tarsorrhaphy, salivary gland transplantation)</li> </ul>

### Secretagogues

- Secretagogues**
  - Topical**
    - Aqueous stimulation**
      - diquafofol tetrasodium; lacritin
    - Mucin stimulation**
      - diquafofol tetrasodium; rebamipide
    - Lipid stimulation**
      - insulin-like growth factor 1 (IGF-1)
  - Oral**
    - pilocarpine; cevimeline
      - best for oral dryness (Sjogren syndrome)



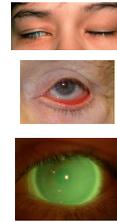
### Biological Tear Substitutes

- Autologous serum**
- Adult allogeneic serum**
- Umbilical cord serum**
- Platelet preparations**
  - generally positive results
  - non-standard preparation methods
  - difficult to directly compare results between studies



### Contact Lens Options

- Often used for variations of "corneal exposure"
  - lagophthalmos / nocturnal lagophthalmos
  - Bells palsy
  - Entropion and ectropion
- Treatments**
  - soft bandage lenses
  - RGP scleral lenses



### Amniotic Membrane Grafts

- Human amniotic membrane is a unique collagenous membrane derived from the innermost submucosa of the placenta
- Amniotic membrane contains collagen types I, III, IV, V, and VII, and specialized proteins such as fibronectin, laminins, proteoglycans, and glycosaminoglycans
- Also contains essential, active, growth factors such as epidermal growth factor (EGF), transforming growth factor beta (TGF-β), fibroblast growth factor (FGF), and platelet-derived growth factor (PDGF) that promotes and accelerates epithelialization
- Commercially available forms now available
  - typically dissolve in approximately one week and the conformer ring / contact lens can then be removed



### Surgical Approaches

- Tarsorrhaphy**
- Surgical treatment for conjunctivochalasis**
- Essential blepharospasm treatment with botulinum neurotoxin**
- Lid corrections**
  - Dermatochalasis
  - Blepharoptosis (ptosis)
  - Lower lid blepharoplasty
- Conjunctival surgery**
- Mechanical dacryoreservoirs**
- Major salivary gland transplantation**
  - Parotid duct transposition
  - Microvascular submandibular gland transplantation
- Minor salivary gland autotransplantation**





**Therapeutic Treatment Videos**

- Over-refraction**  
Detailed method of over-refraction using the contact lens technique of refraction for the patient with astigmatism.
- Over-refraction**  
Detailed method of over-refraction using the contact lens technique of refraction for the patient with astigmatism.
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### Incorporating TFOS DEWS II in clinical practice



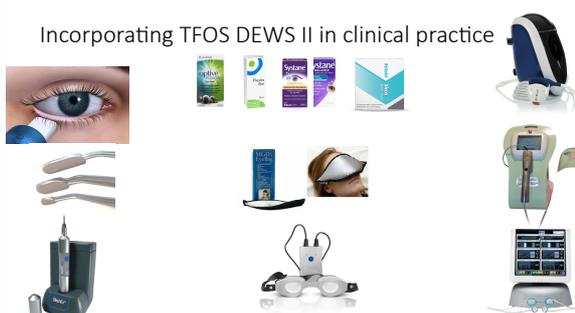
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### Incorporating TFOS DEWS II in clinical practice



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### Incorporating TFOS DEWS II in clinical practice



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### New perspectives in diagnosing and managing dry eye

- incorporating TFOS DEWS II in clinical practice

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