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DEVELOPING A MODEL OF A DRY EYE PRACTICE IN FINLAND

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ABSTRACT

Purpose
This study aims to build a dry eye practice model in Finland based on the information from four expert interviews and the Dry Eye Workshop literature reports.

Methods
A qualitative survey study using semi-structured and open-ended questionnaires was designed to identify evidence-based components of a practice model. Dry eye experts from Finland (n=1), Norway (n=1), and the UK (n=2) were invited to participate based on their long-term experience in dry eye practice and participation in education. Expert interviews were recorded and held online, transcribed, and inductive content analysis was performed, followed by deductive content analysis of literature.

Results
Based on the expert interviews, osmolarity measurement was routinely done in the UK but occasionally in Finland and Norway. Regarding the MMP-9 inflammatory test, the experts' opinions were dissenting. Advanced technology was highly valued and used among the experts. All agreed on the need for a therapeutic license for optometrists in Finland as a part of dry eye practice.

Conclusions
Considering the prevalence of dry eye, assessment and management require commitment, continuity, and cooperation with eye care professionals and the patient. The dry eye practice model helps to achieve the desired goal – quality dry eye care with better compliance in Finland. We need the therapeutic license for optometrists in Finland to manage dry eyes more efficiently. Standardization of dry eye practice could improve quality care in the future.

Keywords: dry eye, dry eye practice model, dry eye assessment, dry eye management, advanced technology

CONTENTS

1 INTRODUCTION

Smartphones, tablets, computers, and other technologies continue to increase the prevalence of dry eye disease. One aspect is that the population is aging, which is one significant risk factor for dry eye disease. Another fact is that dry eye symptoms are becoming more common among young people. This master thesis focuses on developing a dry eye practice model in Finland because we need to create a clear and basic concept for serving better eye care in the future.

Dry eye was first defined as a disorder; nowadays, it is a multifactorial disease. A comprehensive understanding of the ocular surface homeostasis and a systematic approach to assessing and managing dry eye disease is essential. One primary reason is that we are dealing with a chronic disease that needs constant management, and the compliance for warm compress management is poor. A quality management plan guarantees compliance with the management instructions.

In the future, we might need a therapeutic license for optometrists in Finland to take care of the inflammation of the ocular surface. Specialized training courses are also crucial for optometrists to insert punctal plugs and do lacrimal canal syringing independently as a part of dry eye management.

Optometrists already have some new technologies available for dry eye disease assessment and management, making recording the data more accessible and monitoring the management results more precisely. Investing in advanced technologies is one key aspect of developing a dry eye practice.

World Health Organization (2022) defines the quality of life as “an individual's perception of their position in life in the context of the culture and value systems in which they live and about their goals, expectations, standards, and concerns.” The impact of dry eye syndrome on vision-related quality of life was evaluated by Miljanović et al. (2007) concluded, that several everyday tasks of daily living, such as reading and driving, are adversely affected by dry eye syndrome. This makes DED a significant public health problem that deserves further studies.

2 THEORETICAL BACKGROUND

2.1 Prevalence of Dry Eye Disease

Dry Eye Workshop (DEWS) Epidemiology subcommittee of the Tear Film and Ocular Surface Society (TFOS) summarized the evidence on dry eye prevalence, incidence, risk factors, and impact. In 2017, in the DEWS II Epidemiology subcommittee, the prevalence of DED ranged from 5% to 50% (Stapleton et al. 2017, p. 336). According to recent study by Vehof et al. (2021, p. 92), DED symptoms are particularly prevalent among young adults.

According to Liu et al. (2014, p. 1), the prevalence of DED in China was 17.0%, less than in some other Asian regions. In Japan, the prevalence of DED based on symptoms and signs ranges from 9% to 30% and is considered an economic burden (Uchino 2018, p. 3).

Courtin et al. (2016, p. 7) evaluated the prevalence of dry eye disease in visual display terminal workers. According to DEWS II Epidemiology Report, females showed a higher prevalence with increased age than males. On the other hand, meibomian gland dysfunction (MGD) was more common in males in all age categories. However, it was not statistically significant, except over 80 years of age group (Stapleton et al. 2017, p. 347).

2.2 Risk Factors of Dry Eye Disease

Aging is the most consistent non-modifiable risk factor of dry eye disease. DEWS II Epidemiology Committee has summarized a broad spectrum of risk factors and categorized them into modifiable or non-modifiable in Table 1 (Stapleton et al. 2017, pp. 355-356).

Table 1. Risk factors for dry eye disease.

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

MGD=meibomian gland dysfunction
CL=contact lens

Adopted from Stapleton et al. 2017, p. 355.

Risk factors may vary with different diagnostic criteria. According to the DEWS II Epidemiology Report, the health service provision in other jurisdictions may cause variation in the risk factors that need to be considered (Stapleton et al. 2017, p. 357). Advanced age, female sex, and more considerable latitude were significant risk factors for DED by symptoms and signs (Song et al. 2018, p. 7). Song et al. (2018, p. 7) investigated dry eye disease prevalence variations by age, sex, and geographic characteristics in China. According to their systematic review and meta-analysis, only advanced age was positively associated with an increased prevalence of DED by symptoms.

The DEWS II Epidemiology Report Committee concluded that it is essential to distinguish dry eye from other symptomatic conditions, including allergic, infectious, inflammatory, and other chronic ocular surface diseases (Stapleton et al. 2017, p. 357).

Vehof et al. (2021, p. 92) investigated the prevalence and risk factors of dry eye in 79,866 participants in the population-based Lifelines cohort study in the Netherlands. They were the first to report persistent dry eye symptoms in young adults. Further studies among younger age groups are needed to determine long-term consequences and the influence of screen use in the future.

Liu et al. (2020, pp. 749-754) demonstrated an association between the serum vitamin D level and dry eye syndrome (DES). In DES patients, the serum vitamin D level was lower than healthy controls (Liu et al. 2020, p. 752). This is contradicted, because Jeon et al. (2017, p. 373) study found no association between serum vitamin D levels and DED.

According to Kojima et al. (2020, p. 23), recent basic and epidemiological studies have revealed that dry eye is a lifestyle disease requiring lifestyle interventions such as diet therapy and exercise. Nasiri et al. (2021, p. 107) conducted a systematic literature review and meta-analysis about ocular manifestations of COVID-19 (n=8,219 COVID-19 patients), and the most prevalent ocular manifestations were dry eye or foreign body sensation (16%), followed by redness (13%), and tearing (13%).

2.3 Definition and Classification of Dry Eye Disease

Over the years, the definition of dry eye disease (DED) has evolved significantly. It was first defined as a tear film disorder, but nowadays, it is a multifactorial disease of the ocular surface. Defining and classifying dry eye disease is essential to building a dry eye practice model in Finland.

1995 was the year that the National Eye Institute/Industry Workshop on Clinical Trials in Dry Eye defined and classified DED for the first time. (Craig et al. 2017, p. 277).

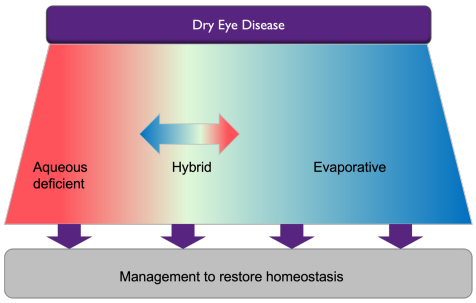
> "Dry eye is a disorder of the tear film due to tear deficiency or excessive tear evaporation, which causes damage to the interpalpebral ocular surface and is associated with symptoms of discomfort." (Craig et al. 2017, p. 277)

Based on the definition from the International Dry Eye Workshop (DEWS I) in 2007, DED is defined as "a multifactorial disease causing symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface". According to the DEWS I committee, "dry eye disease is accompanied by increased tear film osmolarity and ocular surface inflammation". (DEWS, 2007, p. 75)

The Tear Film Ocular Surface Society (TFOS) refined the global definition in DEWS II (2017) report as follows:

> "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. 2017, p. 278)

The etiological classification of DED is divided into two categories: aqueous deficient dry eye (ADDE) and evaporative dry eye (EDE). ADDE describes conditions affecting lacrimal gland function, and EDE includes both lid-related and ocular surface-related causes. Lid-related causes are, e.g., meibomian gland dysfunction (MGD) and blink-related; ocular surface-related, e.g., mucin and contact lens-related. However, mixed forms are common. (Craig et al. 2017, p. 281). The TFOS DEWS II Pathophysiology subcommittee (Bron et al. 2017, p. 441) refers to hybrid dry eye disease (Figure 1).



Adopted from Craig et al. 2017, p. 281.

Figure 1. The Etiological Classification of DED. Picture: Päivi Nokipii.

2.4 The Ocular Surface and Tear Film

The ocular surface is bathed by the tear film (Forrester et al. 2008, p. 201). It is the protective covering and improves the optics of the eye. The tear film comprises three layers: an oily surface layer, an aqueous layer, and a deep mucoaqueous layer (Forrester et al. 2008, p. 201; Willcox et al. 2017, p. 370). A lipid layer prevents loss of the aqueous layer through overspill and evaporation; an aqueous layer nurses ocular epithelium by providing lubricity, nutrients, antimicrobial proteins, and appropriate osmolarity, and a mucin layer covers the ocular surface and lowers the hydrophobicity of the epithelial cells. There are different compartments within the precorneal tear film, making it a dynamic functional unit. Tears are distributed in the fornical, the tear menisci, and the preocular tear film compartments when the eyes are open. The thickness of the tear film ranges from 2 to 5.5µm, and the average lipid layer thickness (LLT) is only 42nm. (Willcox et al. 2017, p.369-370).

Autonomic parasympathetic nerves innervate the secretion of the main lacrimal gland, which is reflex activated by sensory nerves of the ocular surface. Goblet cell secretion is evoked through unidentified efferent fibers (Belmonte et al. 2017, p. 407).

2.5 The Meibomian Glands

DED is primarily caused by dysfunction of the meibomian glands (MGD), which accounts for 86% of dry eye cases. Diagnostic evaluation of the meibomian glands and eyelid margins is crucial to determining whether MGD is present (Wu et al. 2021).

Meibomian glands are in the tarsus of the eyelids, and the glands' openings are located posterior to the eyelashes (Knop et al. 2011, p. 1938; Forrester et al. 2008, p. 85). Tear film´s outer layer is formed by the meibomian glands, which secrete oily or lipid substances that prevent the tear film from evaporating (Knop et al. 2011, p. 1938; Forrester et al. 2008, p. 91).

A single meibomian gland is composed of clusters of secretory acini, and the median number of glands in the upper lid is 31, and the lower lid median is 26 glands. Meibomian glands are influenced by hormonal and neural regulation and the mechanical forces of muscle contraction during blinking. After an absence or decreased blinking, researchers have found an increased amount of accumulated meibum secretion and repeated enforced blinks have significantly increased the LLT. Studies show a decrease of active glands by 50% from the age of 20 years to the age of 80 years. (Knop et al. 2011, p. 1939; p. 1942). Neural pathways that regulate meibomian gland secretion or mucins release have not been identified (Belmonte et al. 2017, p. 407).

2.6 Tear Film Osmolarity and pH

Tear film osmolarity indicates the balance between tear production, evaporation, drainage, and absorption, and it is determined by the concentration of electrolytes in the mucocutaneous layer (Willcox et al. 2017, pp. 372). The core mechanism of DED resulting in hyperosmolarity is tear film instability due to increased evaporation of tears (Akpek et al. 2019, p. 3024). According to recent studies, age, race, hormonal changes during the menstrual cycle, or oral contraceptive pill use seems to have no statistical or clinically relevant effect. Some studies show higher values in men

than women, but the influence of sex is contradictory. Plasma osmolarity and tear osmolarity has a positive correlation. (Willcox et al. 2017, pp. 372-373).

Factors influencing tear osmolarity are the following: body hydration, the tear film lipid layer, palpebral aperture width, blink interval, TBUT, and environmental issues. Tears are slightly hypotonic in the morning, and tonicity increases during the day because of the evaporative effect. Dehydration causes hyperosmolarity in the tear film: decreased tear film lipid layer and TBUT cause hyperosmolarity. The evaporative loss is approximately three times greater when looking up and straight compared to looking down because of the increased palpebral aperture width. Prolonged blink interval increases evaporation and has thereby positive correlation with osmolarity value. (Bron et al. 2017, pp. 452-453).

Tear film osmolarity can be measured with an osmometer such as TearLab (TearLab Corporation, Escondido, CA, USA), which collects a 50 nL sample and analyzes its electrical impedance. (Willcox et al. 2017, pp. 372-373). I-PEN (I-MED Pharma Inc., Dollard-des-Ormeaux, QC, Canada) tear osmolarity test is another method in which the disposable single-use sensor softly touches the palpebral conjunctiva from the lower eyelid at a 30-degree angle. Before the measurement, the eyes are gently closed for 30 s to get a reliable reading. (Wu et al. 2021). The advantage of the I-PEN osmolarity system is portability compared to the other osmolarity systems (Fagehi et al., 2021, p. 173). The typical mean values range from 270 to 315 mOsm/L. (Willcox et al. 2017, p. 373). Liu et al. (2009, p. 3678) study results suggest that the ocular surface may frequently be exposed to hyperosmolar conditions when local tear film thinning, or breakup occurs.

Tear film osmolarity correlates most strongly with the severity of DED in clinical dry eye tests, even though Baenninger et al. (2018) recommend interpreting the TearLab osmolarity results cautiously. The results of this test are occasionally challenging to diagnose and should be considered within the context of symptoms and other clinical findings (Akpek et al. 2019, p. 304).

In general, osmolarity increases with disease severity, classified as normal (302.2 ± 8.3 mOsm/L), mild-to-moderate (315.0 ± 11.4 mOsm/L) and severe (336.4 ± 22.3 mOsm/L) and the cut-off value of DED is 308 mOsm/L. Sensitivity varies depending on the cut-off values between 64% to 91% and specificity between 78% to 96% (Wolffsohn et al. 2017, p. 554). Willcox et al. (2017, p. 373) suggest future studies to establish consistent cut-off values for dry eye.

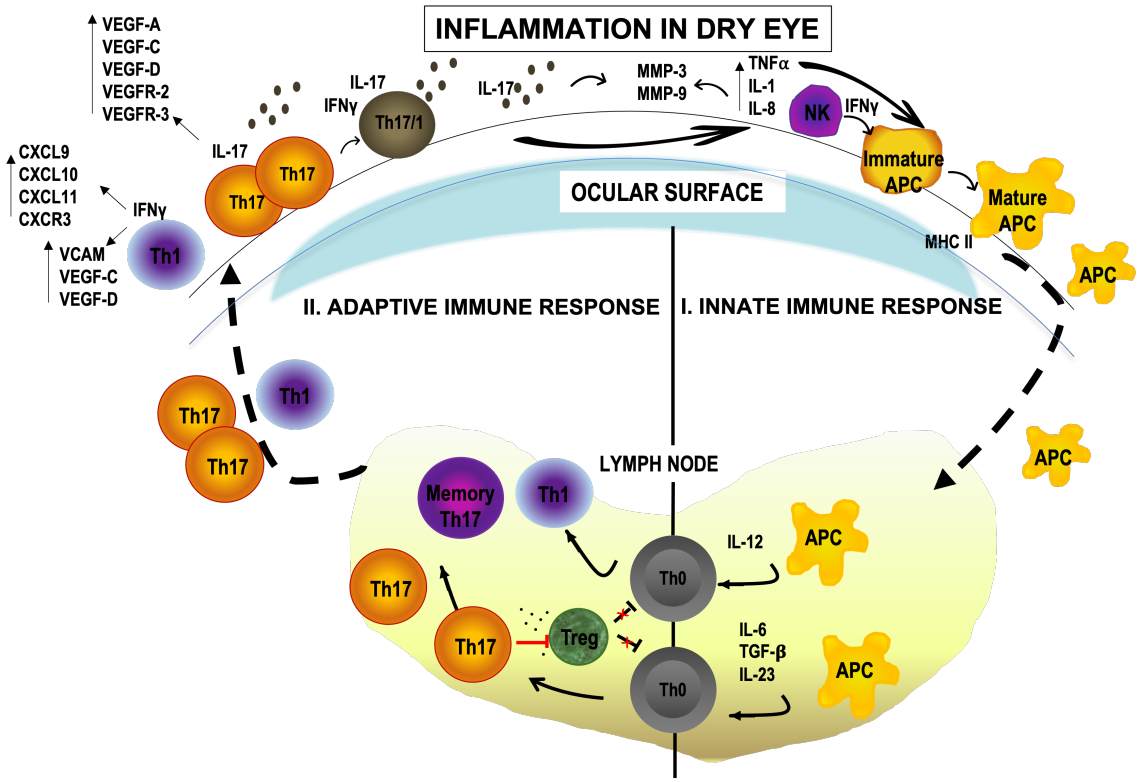
The mean pH of tear film range between 6.8 and 8.2. DED causes an alkaline shift of approximately 0,1 on pH. Sex seems not to affect the value, but age, time of day, eye closure, prolonged eye-opening, blinking, and reflex tearing, have. (Willcox et al. 2017, pp. 375-376).

2.7 Inflammation

Medical Definition of inflammation, according to the dictionary, is “a local response to cellular injury that is marked by capillary dilation, leukocytic infiltration, redness, heat, and pain that serves as a mechanism initiating the elimination of noxious agents and damaged tissue” (Merriam-Webster 2022). According to Craig et al. (2017, p. 277), inflammation is a recognized component of the pathophysiological mechanism of DED. The term “inflammation” is also included in the global definition of dry eye.

Conjunctival redness is the most common clinical sign of ocular surface inflammation. Non-specificity makes it problematic because conjunctival redness is associated with many other conditions such as allergy, infections, or other systemic diseases with inflammation. (Wolffsohn et al. 2017, p. 557)

Innate and adaptive immune system pathways play an important role in DED (Palomar et al. 2019). The innate immune response is mediated by, e.g., natural killer (NK) cells that secrete proinflammatory cytokines such as interferon-gamma (IFN- γ). Interleukin (IL)-1, IL-6, and tumor necrosis factor-alpha (TNF- α), promote the maturation of antigen-presenting cells (APCs), leading eventually to matrix metalloproteinases (MMPs) production in epithelial cells (Figure 2).



Adopted from Tsubota et al. 2020.

Figure 2. Inflammation in DED. Picture: Päivi Nokipii.

Then the adaptive immune response is activated when the APCs drain to the lymph nodes to initiate prime naïve T cells (Th0) differentiation into IL-17- secreting Th17 cells and IFN- γ – secreting Th1 cells. IL-17 inhibits the suppressive function of regulatory T cells (Tregs) and stimulates MMP-3 and MMP-9 production, eventually leading to epithelial cell damage. (Tsubota et al. 2020). DED is characterized by an inflammatory process, manifested by an increase in inflammatory cells as well as the expression of immune activation molecules, cytokines, and chemokines such as T-helper type 1 (Th-1) and Th-17 (Wu et al. 2021).

Palomar et al. (2019) also investigated the role of cytokines and chemokines in shaping the immune response in ocular diseases. A vital role is played by dendritic cells (DCs) in the maintenance of activating the differentiated T cells in different ways, mediating through many chemokines and cytokines, thus triggering the inflammatory cascade. (Palomar et al. 2019). Kodati et al. (2014, p. 5876) have found that chemokine receptor (CCR)-7-mediated APC trafficking drives Th17 immunity in DED, and that CCR7 blockade suppresses the immunopathogenic mechanisms. In the future,

growing concern about inflammation and nerve damage has made it essential to identify new biomarkers in DED.

In patients with DED, a targeted lipidomics case-control study identified increased levels of prostaglandin E_2 (PGE_2), a proinflammatory mediator, but the prostaglandin D_2 (PGD_2), a resolving mediator, was decreased (Khanna et al. 2022, p. 1235). Navel et al. (2022) compared oxidative stress markers and antioxidants in DED with healthy subjects. Those dysregulated in DED formed a local oxidative environment in tears, conjunctival cells, and tissues. Rowsey & Karamichos (2017) focused on lipid-based therapies for DED, providing encouraging results despite the limited options.

TFOS DEWS II Tear Film Subcommittee report contains a long list of humans 'extracellular' (n=102) and 'intracellular' (n=20) tear proteins that are reported whether to increase or decrease during ocular surface pathology depending on the cause (e.g., ADDE, MGD or conjunctivochalasis) (Willcox et al. 2017, pp. 386-389). According to Willcox et al. (2017, p. 389), there are only two methods to investigate tear film biomarkers and follow-up patients more accurately: InflammaDry® (MMP-9) and TearScan™ Lactoferrin Diagnostic Test Kit.

The extracellular matrix (ECM) is remodeled by MMP-9, an endopeptidase (Wu et al. 2021). A sample collector tip is inserted multiple times along the palpebral conjunctiva and placed in a cassette provided. After 10 minutes, a blue line represents a valid test on the display, and the result is positive with blue and pink stripes and negative with only a blue line present. (Wu et al. 2021). InflammaDry® test can detect MMP-9 biomarker in the tear film with detection of 40ng/mL, showing a sensitivity of 85% and specificity of 94% (Wu et al. 2021; Sambursky et al. 2013). Sensitivity range is depending on the study. Studies suggest that the InflammaDry® test is better at detecting moderate to severe DED (Willcox et al. 2017, p. 389).

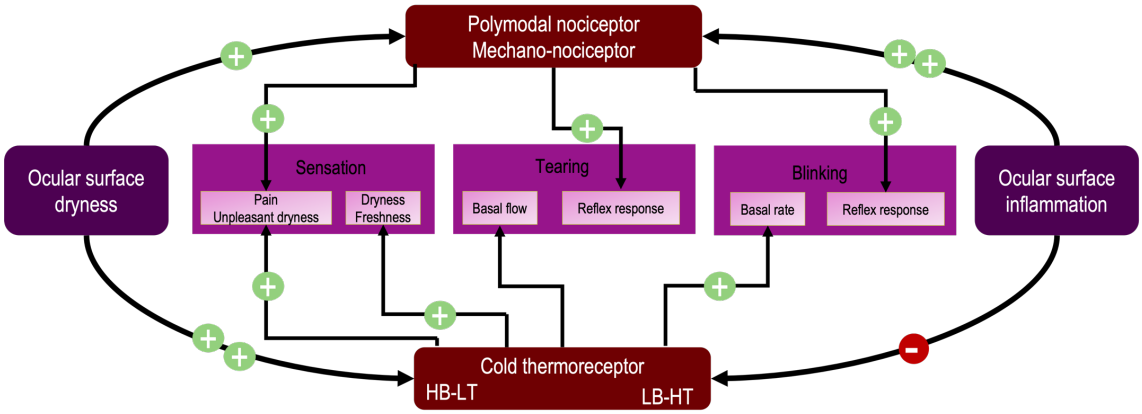
Lactoferrin is a functional glycoprotein participating in antioxidant, antibacterial, antiviral, and anti-inflammatory activities (Zhang et al. 2021). Lactoferrin is decreased in ADDE and MGD (Willcox et al. 2017, p. 388).

2.8 Pain and Sensation

It is well substantiated that the sensory nerves of the ocular surface display an essential role in the structural and functional changes in DED. The intensity of adverse symptoms varies from mild discomfort to burning pain. (Belmonte et al. 2017, p. 409). Reduced tear secretion in DED leads to inflammation and peripheral nerve damage (Belmonte et al. 2017, p. 420). Further, inflammation causes sensitization of polymodal and mechano-nociceptor nerve endings and an abnormal increase in cold thermoreceptor activity, resulting in dryness sensations and pain (Belmonte et al. 2017, p. 412).

Report of the TFOS DEWS II Pain and Sensation Subcommittee provides a comprehensive review of DED focused on pain. Pain is one of inflammation's five cardinal signs (dolor) (Tracy 2006, p. 1051). The International Association for the Study of Pain (IASP) defines pain as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage” (IASP 2021). Nociceptive pain and neuropathic pain can be distinguished. The IASP defines neuropathic pain as” pain caused by a lesion or disease of the somatosensory nervous system.” In patients with DED who remain symptomatic despite adherence to treatment, neuro-sensory dysfunction may be responsible for the lack of association between signs and symptoms (Kaido et al. 2016, p. 918). Nociceptive pain occurs when nociceptors are activated in response to actual or threatened damage to non-neural tissue (IASP 2021).

Pain associated with mechanical and chemical irritation of the eye surface is mediated by the peripheral axons of trigeminal ganglion (TG) neurons innervating the cornea and conjunctiva, where they form subepithelial nerve plexus in the stroma. The ascending branches penetrate Bowman's layer, and the unit terminates within the surface of the epithelium layer. There are three types of corneal sensory neurons (Figure 3): polymodal nociceptors (70%), specific mechano-nociceptors (20%), and cold thermoreceptor neurons (10%). (Belmonte et al. 2017, p. 408; Cruzat et al. 2017). Cold thermoreceptors detect wetness and reflexively maintain basal tear production and blinking rate (Belmonte et al. 2017, p. 407).



Adopted from Belmonte et al. 2017, p. 423.

Figure 3. The interactive influences of dryness and inflammation on the activity of ocular surface sensory receptors on sensation, blinking, and tearing. (HB=high background, LT= low-threshold, LB= low background, HT=high-threshold). Picture: Päivi Nokipii.

Typically, polymodal nociceptors are silent and respond to chemical, mechanical and thermal stimuli. Ocular surface injury induces the release of inflammatory mediators that induces sensitization of the polymodal nociceptors. (Belmonte et al. 2017, p. 430). The normal responsiveness of nociceptors ('sensitization') is modified by inflammatory mediators, decreasing their threshold for activation and increasing suprathreshold responses. (Belmonte et al. 2017, p. 408).

Mechano-nociceptors respond only to mechanical forces through mechanosensitive ion channels. Inter-blink tear evaporation causes cooling of the ocular surface, augmenting tear osmolarity, and increasing basal activity of cold thermoreceptors. (Belmonte et al. 2017, p. 430). Corneal polymodal receptors are insensitive to innocuous cooling (Gallar et al. 1993, p. 620), but they are activated by hyperosmotic solutions (Liu et al. 2009, p. 3678). The transduction channel (TRPM8) for cooling or cold is also sensitive to changes in osmolarity (Belmonte et al. 2017, p. 430).

Kovács et al. (2016, p. 412) found that selective stimulation of corneal cold sensory fibers in healthy humans evokes distinct sensations of eye discomfort. That reinforces the suggestion that cold thermoreceptors could play an essential role in signaling potentially injurious ocular surface desiccation. Belmonte & Gallar (2011, p. 3890) illustrates that a conscious sensation of eye dryness of a magnitude proportional to the number and firing rate of cold receptor afferents can be expected when enough ocular cold sensory fibers firing at higher frequencies are recruited.

Cold receptor activity affects the dryness sensation when evaporation increases and corneal surface temperature decreases. Dryness sensation increases more in aged and injured people compared to expected. (Belmonte & Gallar 2011, p. 3890).

The results from the study by Liu et al. (2009, p. 3678) suggest that hyperosmolar stress is potentially injurious to the epithelium and thus is protected by the pain response. The purpose of corneal neurons is to protect the epithelial tissue from damage or injury. They measured the responses because changing tear osmolarity, epithelial cells, and underlying sensory neurons affected the two main corneal cell types. According to Liu et al. (2009, p. 3678), tear film osmolarity is likely to spike transiently during periods of tear instability, causing discomfort and proinflammatory signaling sensations.

Decreased tear secretion in DED leads to peripheral nerve damage. According to the TFOS DEWS II report, Pain and sensation subcommittee pain can be evaluated with questionnaires and corneal sensitivity with esthesiometry and in-vivo confocal microscopy. (Belmonte et al. 2017, p. 407). A gas esthesiometer applies controlled mechanical, chemical, and thermal stimuli to the corneal surface, which can be used to experimentally explore corneal sensations in humans (Belmonte, Acosta & Gallar 2004). The Cochet-Bonnet esthesiometer only stimulates mechanosensitive nerve fibers (Kaido et al. 2016, p. 917). A handheld device or a slit lamp can be used to use this device.

Kaido et al. (2016) concluded that corneal sensitivity for blinking and pain evoked by increased stimuli was higher in the symptomatic group (subjects with short break-up time dry eye) than in subjects with no dry eye symptoms despite decreased tear stability. Xu et al. (2021) systematic review and meta-analysis showed a significant increase in central corneal dendritic cell density in dry eye patients, while corneal nerve fiber density and corneal nerve fiber length were lower. According to Belmonte et al. (2017, p. 426), neuropathic pain should not be diagnosed as DED, but the management of neuropathic pain needs further research when it manifests as dry eye symptoms.

2.9 Dry Eye Assessment

2.9.1 Introduction

With the recent advances in technology, dry eye assessment has rapidly progressed into more targeted point-of-care tests, and imaging technologies help clinicians to evaluate the type and severity of dry eye more effectively. According to Wolffsohn et al. (2017, p. 545), dry eye examination must be based on tests available in clinical practice. The purpose of dry eye assessment is to preserve and improve vision, prevent, or minimize structural damage to the ocular surface, and improve patient comfort (Akpek et al. 2019, p. 294). External examination and slit lamp biomicroscopy are essential in documenting the signs of dry eye, assessing the quality, quantity, and stability of the tear film, and determining other causes of ocular irritation (Akpek et al. 2019, p. 302).

2.9.2 Screening, Patient History, and Risk Factor Analysis

The purpose of screening is prevention, aiming to identify people with a higher risk of a disorder (The Definition and Classification of Dry Eye Disease 2007, p. 112). Screening tests should be rapid and straightforward but also maximize sensitivity and prevent dry eye overdiagnosis (The Definition and Classification of Dry Eye Disease 2007, p. 119-120). Customers often do not recognize the symptoms except when asked. (Wolffsohn et al. 2017, p. 549). Identification of the causative factors, such as adverse environments (e.g., decreased humidity) and prolonged visual efforts (e.g., reduced blink rate while using a computer or reading), is essential (Akpek et al. 2019, p. 299).

Patient history in dry eye assessment should focus on symptoms and signs, exacerbating conditions, duration of symptoms, and both ocular and medical history (Akpek et al. 2019, p. 301-302). According to Akpek et al. (2019, p. 301), the list of symptoms and signs is, e.g., the following: irritation, itching, burning, tearing, stinging, dry or foreign body sensation, photophobia, blurry vision, redness, increased frequency of blinking, eye fatigue, contact lens intolerance, diurnal fluctuations and any symptoms that worsen during the day. Wolffsohn et al. (2017, p. 549) recommend validated symptom questionnaires to enhance clinical research and practice

standardization. Ocular Surface Disease Index (OSDI) is the most widely used questionnaire, which measures ocular symptoms, vision-related functions, and environmental triggers. (Wolffsohn et al. 2017, p. 562-563). In the OSDI questionnaire, screening criteria for DED are scored as mild (13-22), moderate (23-32 or severe (≥33) (Tsubota et al. 2020). DEQ-5 is also commonly used because of its short length and measures the frequency of eye discomfort, dryness, and watery eyes (Wolffsohn et al. 2017, p. 562-563). Shiraishi & Sakane (2018) suggest the development of a global standard questionnaire for DED with translations and cross-cultural adaptations, and Grubbs et al. (2014) offer the quality-of-life measures in future questionnaires for the monitoring and management of DED. According to Recchioni et al. (2021), The Impact of Dry Eye on Everyday Life (IDEEL) questionnaire presented the highest scores in evaluating its psychometric properties.

Risk factor analysis is part of the DED diagnostic battery, which may inform management options (Wolffsohn et al. 2017, p. 561). Risk factors for dry eye are categorized into non-modifiable and modifiable and divided into consistent, probable, and inconclusive factors, as seen in Table 2 (Stapleton et al. 2017, p. 355). Discussion concerning ocular history, e.g., topical medications and their associated preservatives, eyelid and eyelash hygiene, ocular surgical history (e.g., LASIK), contact lens history, allergic conjunctivitis, eyelid surgery (e.g., entropion/ectropion repair) and ocular surface diseases, should be covered. Medical history should concentrate on systemic diseases (e.g., Sjögren syndrome, SLE, rheumatoid arthritis, sarcoidosis) and medications (e.g., antihistamines, antidiuretics, hormones, isotretinoin, and any drug with anticholinergic effects), smoking, dermatological diseases (e.g., rosacea, psoriasis), atopy, neurological conditions (e.g., Parkinson disease, Bell´s palsy), trauma, chronic viral infections, and menopause (Akpek et el. 2019, pp. 301-302).

2.9.3 Diagnostic Tests

TFOS DEWS II Diagnostic Methodology Subcommittee developed a clinical protocol for dry eye diagnostic and monitoring test battery, which will be considered in detail in chapter 2.10.2 DEWS II. It is important to note that if there are chronic symptoms but limited signs, the neuropathic pain should be considered instead of DED. (Wolffsohn et al. 2017, p. 560). The tests should be conducted from the least invasive to the most intrusive, and alternation of blinking and bright illumination can affect the results (Wolffsohn et al. 2017, p. 548).

Tear film volume is essential for ocular health, and aqueous deficiency causes loss of homeostasis, which can be one of the fundamental pathogenic mechanisms in DED. Meniscometry means the assessment of tear meniscus: height (TMH), curvature (TMR), or cross-sectional area (TMA). (Wolffsohn et al. 2017, p. 553). Tear meniscus contains 75-90% of the aqueous tear volume and correlates positively with the lacrimal secretory rate. (Wu et al. 2021). The tear film quantity can be measured by evaluating the tear meniscus height (TMH) with the slit-lamp. Still, even though it correlates positively with other DED tests, it is operator-dependent (Wolffsohn et al. 2017, p.553). Normal TMH ranges between 0.2mm and 0.4mm, but for elderly individuals' the normal range is lower, between 0.1mm and 0.3mm (Doughty et al. 2002).

Phenol red thread test (PRT) is pH sensitive test to measure tear film volume. Usually, the thread turns red because of the slightly alkaline physiological pH of tears, but in DED, the thread postulates a yellow color. The thread is folded and held for 15s over the lateral one-third of the lower eyelid margin. Compared to Schirmer's test without anesthesia, it is more comfortable because the thread is thin. The typical PRT result is 20mm or over to differentiate DED with or without aqueous deficiency (Wolffsohn et al. 2017, pp. 553-554). Kashouli et al. (2010) discovered that a shorter 1-min Schirmer test with anesthesia saved time, decreased patient discomfort, and increased reliability. A cut-off value of 10mm gives only 25% sensitivity and 93% specificity. (Wolffsohn et al. 2017, pp. 553-554).

Schirmer test without anesthesia estimates stimulated reflex tear flow, and it is a well-standardized and straightforward test with no requirements for special equipment. Disadvantages are a lack of high-level evidence data on repeatability, sensitivity, and specificity. The Schirmer paper strip is folded and placed in the same way as the PRT test strip for 5 minutes. (Wolffsohn et al. 2017, p. 554). Typical Schirmer test result is >10mm, <10mm marginally dry eyes, and <5mm is considered to indicate dry eyes (Wu et al. 2021). The combination of PRT and Schirmer tests has also been proposed in aqueous deficient dry eye (ADDE), but the Schirmer test is recommended for severe ADDE such as Sjögren syndrome (Wolffsohn et al. 2017, p. 554; de Monchy et al. 201, p. 5172).

Strip meniscometry is an alternative method instead of the Schirmer test to measure the retained tear volume in the tear meniscus only in 5s using a unique water-absorbing material. Strip meniscometry tube is put on the lateral side to avoid irritation to the cornea, and binocular measurement is possible with one strip. The cut-off value for diagnosing dry eyes is ≤ 4 mm,

sensitivity 93%, and specificity 73%. In the future, strip meniscometry could be used to measure tear protein concentrations. (Kojima et al. 2020, pp. 5-6).

According to Khanna et al. (2022, p. 1230), tear sampling should be performed first to avoid reflex tearing and at least 2 hours after awakening because there are four types of tears: basal, reflex, emotional, and closed eyes. Tears produced during sleep ensure nutrition to the ocular surface, while basal tears provide permanent protection. Emotional tears of healthy eyes contain small amounts of pro-inflammatory mediators, ranging from 27pM to 2.7nM (e.g., prostaglandins, leukotrienes). (Khanna et al. 2022, p. 1233).

The tear film lipid layer is assessed with a slit lamp using specular reflection and diffuse filter, but it is operator-dependent. The interference color of the precorneal lipid layer changes from gray to red (and multiple colors) under a biomicroscope, indicating thickened lipid layer. Table 2 shows the scale, where grades 1 and 2 are seen in normal eyes. (Yokoi, Takehisa and Kinoshita 1996, p. 822).

Table 2. Tear film lipid layer interferometry grading patterns.

A: Grade 1	Gray, uniform
B: Grade 2	Gray, non-uniform
C: Grade 3	Few colors
D: Grade 4	Many colors
E: Grade 5	Partly exposed corneal surface

Adopted from Yokoi, Takehisa and Kinoshita 1996. p. 821.

Tear film stability is assessed with a tear breakup time test (TBUT): invasive (FBUT) or noninvasive (NIBUT). In FBUT, a sterile fluorescein strip moistened with normal saline is instilled inside the far lower temporal lid in an upgaze with the lower eyelid pulled slightly temporally of the eye. After instillation, instructions are given to blink naturally three times and then cease blinking until instructed otherwise (Figure 4). Normal FBUT is >10 s and cut-off time <10 s. Disadvantages are dependence on subjective assessment of the observer and fluorescein interfering with the normal homeostasis and stability of the tear film (Wolffsohn et al. 2017, p. 551; p. 563). The sensitivity of

the TBUT test is 72%, and the specificity is 61% (Mou et al. 2021). NIBUT is being considered in the advanced technology chapter.

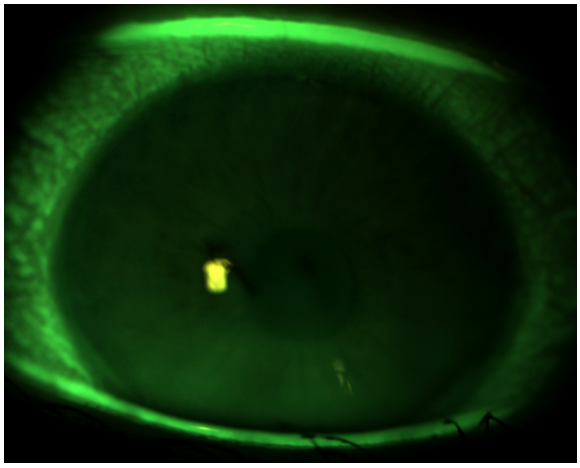


Figure 4. Fluorescein tear breakup time. The picture was taken when the first breakup appeared, shown as black streaks. Picture: Päivi Nokipii.

In addition, the fluorescein breakup pattern (Table 3) can be used to confirm the abnormalities in each tear film component to evaluate which layer is the dominant abnormality. (Kojima et al. 2020) One problem is that the tear breakup time is reduced regardless of the dry eye subtype when the dry eye and meibomian gland dysfunction (MGD) are diagnosed simultaneously (Kojima et al. 2020).

Table 3. Typical fluorescein break-up pattern.

Breakup pattern	When breakup occurs	Suspected abnormality in tear film
Area break	Before complete eye opening	Severe aqueous deficiency
Spot break	Before complete eye opening or immediately after eye opening	Decreased wettability
Line break	During the UMF	Mild to moderate aqueous deficiency
Dimple break	During the UMF	Mild to moderate decreased wettability
Random break	After the cessation of UMF	Increased evaporation

UMF= upward movement of fluorescein stained aqueous tears

Adopted from Kojima et al. 2020.

Ocular surface staining with sodium fluorescein (+cobalt blue light), lissamine green and rose bengal are mainly used dyes. Disruption in the tight junctions between superficial epithelial cells results in fluorescein staining. Lissamine green is a vital dye that only stains epithelial cells if the cell membrane is damaged. A yellow filter with fluorescein and a red filter with lissamine green is

recommended to enhance staining visibility. (Wolffsohn et al. 2017, p. 555). Delaveris et al. (2018, p. 23) study shows significant variations in clinical performance between lissamine green solutions from different manufacturers' strips showing the highest amount of LWE staining with GreenGlo and the least with Lissaver while Biotech and OPGreen were somewhere in between.

Optimal viewing after fluorescein instillation is between 1-3min. After lissamine instillation, viewing is recommended between 3-6 min after two repeat and separate strips installation (Wolffsohn et al. 2017, p. 563). Corneal and conjunctival staining are informative markers of severity in severe DED, but the correlation is poor in mild to moderate DED. The following should be noted: in some countries, ophthalmic stain strips are registered as medical devices instead of pharmaceuticals. (Wolffsohn et al. 2017, p. 555).

The severity of the ocular surface damage is related to the degree and area of staining (Wu et al. 2021). Grading scales for ocular surface staining (e.g., National Eye Institute/ Industry Workshop guidelines) are recommended. Still, it's important to note that DED severity can change with the time of day (Wolffsohn et al. 2017, p. 563).

Lid parallel conjunctival folds (LIPCOF) are in the temporal side of the bulbar conjunctiva, parallel to the lower lid margin (Figure 5). The severity of LIPCOF is associated with decreased mucin production, and the cut-off value is 2. If the LIPCOF is evaluated by the number of folds instead of fold height, the sensitivity of LIPCOF is 70% and specificity 91%. Grade 0 means no folds; Grade 1 means one fold, Grade 2 means two folds, and grade 3 > two folds. Compared to conjunctivochalasis, the cross-sectional area of LIPCOF is smaller. (Wolffsohn et al. 2017, pp. 555-556).

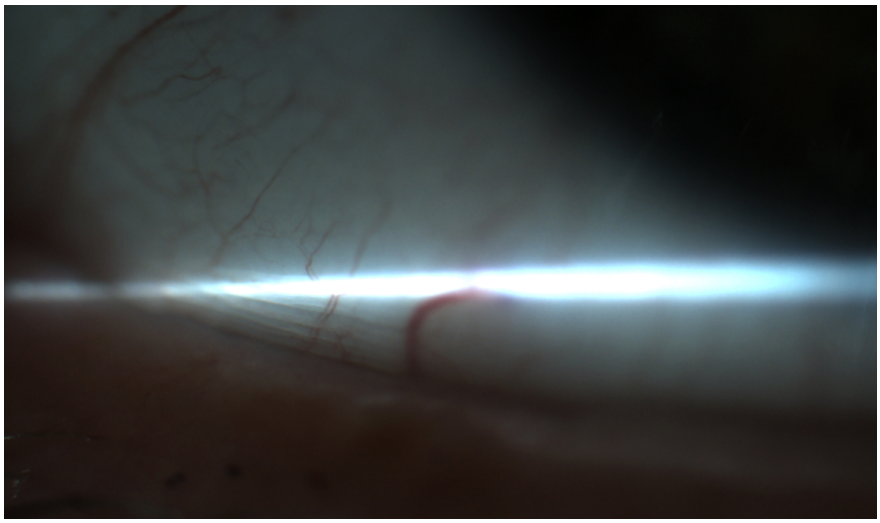


Figure 5. Lid parallel conjunctival folds (LIPCOF), right eye. Picture: Päivi Nokipii.

Eyelid aspects are an essential part of dry eye assessment. According to Akpek et al. (2019, p. 303), incomplete closure/malposition, incomplete or infrequent blink, eyelid lag or retraction, erythema of eyelid margins, abnormal deposits or secretions, entropion or ectropion should be paid particular attention to during the external examination. Especially anterior and posterior eyelid margins: abnormalities of meibomian glands (e.g., atrophy, reduced meibum expression, meibum quality), eyelid margin hyperemia, scarring, keratinization, or vascularization crossing the mucocutaneous junction (Akpek et al. 2019, p. 303).

Meibomian gland health evaluation with a slit lamp includes visualization of the glands with infrared light to detect possible drop-outs in the quantity of the glands, inspection of possible orifice plugging and telangiectasia, and gentle meibomian gland expression to evaluate the quality of meibum, which should be clear in color. Individuals with MGD have opaque, viscous, or even toothpaste-like meibum that is difficult to express. (Kloosterboer, Dermer and Galor 2019).

Blinking is essential in maintaining optical performance and the health of the ocular surface, as well as clearing debris, providing mechanical protection, re-forming tear film lipid layer, and distributing meibum (Wolffsohn et al. 2017, pp. 560). Spontaneous blinks are thought to be generated in the brainstem (“blink generator”) and modified by reflex inputs from the ocular surface (Bron et al. 2017, p. 451). Average blink rate while speaking varies between 15.5 ± 13.7 blinks per minute, but it is significantly reduced while reading and during computer work to only 5.3 ± 4.5 blinks per minute (Freudenthaler et al. 2003).

According to the TFOS DEWS II Pathophysiology subcommittee (Bron et al. 2017, p. 451), low humidity, cold and high wind speeds increase the blink rate. Cold-sensitive fibers contribute to the reflex control of basal tear production and blinking. (Belmonte et al. 2017, p. 430). Incomplete blinking may contribute to DED and exposure to keratopathy (Wolffsohn et al. 2017, p. 560).

Lid-wiper epitheliopathy (LWE) is a diagnostic sign of DED. In a normal eyelid wiper, the marginal conjunctiva contacting surface at the lid margin is rich in goblet cells. (Wolffsohn et al. 2017, p. 558). Suitable boundary lubrication reduces friction between the lids and globe through the cross-linked mucin exodomains of the healthy glycocalyx that act as hydrophilic polymer brushes (Bron et al. 2017, pp. 453-454).

The staining of the lid wiper with fluorescein and lissamine green is called LWE, mostly studied in the upper lid margin. LWE grading is based on the staining's horizontal length and sagittal width. LWE sensitivity is 48% and specificity 96% using the cut-off value of grade 1. Grade 0 means horizontal length of staining <2 mm and sagittal width of staining <25% of the lid wiper, grade 1 means 2-4 mm and 25% - <50%, grade 2 means 5-9 mm and 50% - <75% and grade 3 >10 mm and ≥75% of the lid wiper. (Wolffsohn et al. 2017, pp. 558-559).

2.10 Dry Eye Management

2.10.1 Introduction

Understanding DED's risk factors, etiology, and pathophysiology has advanced and contributed to an evolution in dry eye management. Most people with symptoms related to DED suffer from variable combinations of abnormal meibomian gland physiology and tear underproduction, leading to comprehensive dry eye management (Jones et al. 2017, p. 582). The multifactorial etiology of DED results in versatile management that aims to restore ocular surface homeostasis.

Concerning the DED management options, tear replacement approaches are excluded from this study because of the well-existing awareness among clinicians of the role of ocular lubricants in managing tear insufficiency. The use of ocular lubricants alone is unsuccessful if additional

causative factors are not concurrently addressed (Akpek et al. 2019, p. 306). Patient education and tear conservation approaches are more detailed in the following chapters.

2.10.2 Patient Education

One of the critical elements of DED management is patient education, including environmental issues, blinking habits, diet, and medication. Setting realistic and individual goals is also essential to the management plan. (Akpek et al. 2019, p. 306).

Ambient environmental effects increase tear film evaporative loss, and thereby hyperosmolarity increases. Conditions of low humidity or increased airflow, whether indoor (e.g., air conditioning, ceiling fans) or outdoor (e.g., wind), should be avoided, even though Byber et al. (2021) suggest dryness symptoms of the eyes may not be affected by indoor air humidification at the workplace (Bron et al. 2017, p. 453). Akpek et al. (2019, p. 308) suggest avoiding potentially exacerbating exogenous factors such as cigarette smoking and exposure to second-hand smoke. Increased air pollution is also associated with DED (Jones et al. 2017, p. 612).

Blink interval plays a vital role because the tear film must be constantly replenished by blinking to maintain optical quality. In recent studies, working at a video display terminal, reading, and operating monitor-based and handheld video games have decreased blink intervals. (Bron et al. 2017, p. 452). Akpek et al. (2019, p. 308) recommend lowering the computer screen below the eye level to decrease lid aperture, scheduling regular breaks, and increasing consciously blinking. Incomplete blinking or the inability to close the eyes properly during sleep can sometimes cause the symptoms and signs (Jones et al. 2017, p. 597).

Dietary modifications and nutritional supplementation are growing evidence to be part of dry eye management. Taking care of the whole body's hydration positively reduces the clinical expression of DED. Still, more studies are needed to assess the efficacy and safety of optimizing hydration status (Jones et al. 2017, p. 607). Alcohol consumption has shown to aggravate both symptoms and sign of DED, and reducing oxidative stress with orally administered antioxidants (containing beta-carotene, vitamins E, C, B, B6, D, zinc, and copper) have shown improvement in tear film stability, goblet cell density and squamous metaplasia (Jones et al. 2017, p. 611). Oral lactoferrin

has also reduced oxidative damage and suppressed gland inflammation. Essential fatty acids, omega-3s (EPA and DHA), are found in high concentrations in oily fish, and omega-6s are derived from vegetable oils, but recent studies are contradicted regarding the benefit. (Jones et al. 2017, p. 607). A more detailed review is excluded from this study because future studies are needed before finding a consensus on optimal management protocol concerning the dose, composition, and duration.

Medications, both topical and systemic, have been implicated in DED. Especially topical medicines that contain preservatives such as benzalkonium chloride (BAK) if used long-term, like in glaucoma treatment. Systemic medications causing a higher incidence of dry eye are the following: antihistamines, beta-blockers, antidepressants, diuretics, anxiolytics, antipsychotics, anti-Parkinsonian drugs, isotretinoin, estrogen therapy, and systemic chemotherapy. (Jones et al. 2017, pp. 611-612).

2.10.3 Lid Hygiene, Warm Compress, and Forceful Expression

Lid hygiene reduces lipid by-products and lipolytic bacteria associated with various lid conditions that result in dry eyes. A dedicated lid cleanser reduces ocular surface MMP-9 levels, improves lipid layer quality, and is well-tolerated compared to lid scrubs with baby shampoo. Problems are poor compliance with following lid hygiene instructions and a lack of universally accepted guidelines for lid cleansing. (Jones et al. 2017, p. 593).

Warm compresses share the same problem with following the lid hygiene instructions – poor compliance. The main reasons for poor compliance are lack of time and difficulty maintaining the compress's temperature. The time and the temperature required for melting obstructive material within the meibomian glands' excretory duct depend on the meibum's content. Some evidence recommends a temperature of ≥40°C in the palpebral conjunctiva and the meibomian gland. A problem is how to prevent over-heating and thermal skin damage because the eyelid skin should not be heated more than 45°C and the only safeguard is the individuals´ pain response. Rubbing should be avoided if the corneal temperature is elevated to prevent corneal deformation and visual blur. (Jones et al. 2017, p. 594).

In forceful expression, force is applied either by squeezing the eyelids against each other with examiners´ fingers or utilizing a rigid object on the inner and outer surface of the eyelid to apply force. (Jones et al. 2017, p. 596). Meibomian glands of both upper and lower eyelids of each eye can be expressed using a meibomian gland forceps after topical 0,4% oxybuprocaine hydrochloride anesthetic drops are administered (Moon et al. 2021). Meibomian gland expression (MGX) is a physical management method. It should not be confused with diagnostic expression, which is done during meibomian gland assessment to evaluate if the glands are functional. The number of expressible glands, quality of meibum, and lipid layer thickness have improved after four in-office forceful expressions over six months in combination with daily warm compress therapy. (Jones et al. 2017, p. 596). More advanced methods of physical treatments such as LipiFlow and IPL are discussed in the Advanced Technology chapter.

2.10.4 Punctal Occlusion with Plugs

Punctal occlusion is a mechanical blockage of the tear drainage system to preserve natural tears on the ocular surface. According to Jones et al. (2017, p. 590), indications for the use of punctal occlusion are the following conditions: dry eye associated with a rapid TBUT, ADDE secondary to a variety of systemic diseases (e.g., Sjögren syndrome, autoimmune diseases), symptomatic contact lens wear, dry eye related to refractive surgery, systemic medications that reduce tear film production, superior limbic keratoconjunctivitis, any corneal irregularities or scarring that affect tear stability, lid palsy or lid closure abnormalities and toxic epitheliopathy. Akpek et al. (2019, p. 310) recommend punctal plugs after achieving tear homeostasis.

In their systematic review, Ervin, Law, & Pucker (2017) assessed the effects of punctal plugs versus no plugs, including five trials. He concluded that improvements in symptoms and commonly tested dry eye signs are inconclusive even though many investigators of the individual trials concluded that punctal plugs effectively manage dry eye signs and symptoms. Punctal plugs are considered a relatively safe management option, but there are some potential complications, e.g., epiphora, punctal plug loss, or rarely dacryocystitis (Erwin, Law & Pucker 2017). According to Jones et al. (2017, p. 590), they are treating the inflammation before occlusion is recommended. Tong et al. (2016, p. 239) concluded that the overall tear cytokine levels were not significantly altered following

the insertion of punctal plugs. Still, they suggest dry eye patients may benefit from earlier or concurrent treatment of anti-inflammatory agents with punctal plugs to manage their disease.

Punctal plugs are divided into absorbable and non-absorbable devices, and both are inserted into the upper, lower, or both puncta (Ervin, Law & Pucker 2017). Collagen-based plugs are most used, which absorb in one to 16 weeks, depending on the patient. Non-absorbable plugs are often silicone-based. (Jones et al. 2017, p. 590). Clinicians typically first prescribe collagen plugs to test whether the patient founds symptomatic relief with them, followed by the silicone plugs if permanent treatment is needed. On a short-term basis, temporary collagen plugs appear similarly effective as silicone plugs. (Ervin, Law & Pucker 2017).

Complications are related to punctal occlusion; spontaneous plug extrusion is the most common. Other reported complications include infections (more commonly with intracanalicular devices), canalicular migration of the plug, pyogenic granuloma, punctal enlargement, and rarely tumors. Less severe complications include subconjunctival hemorrhage, chemosis, epiphora, punctal erythema, discomfort, and foreign body sensation (Jones et al. 2017, p. 590). A permanent punctal occlusion is also an option, but it´s excluded from this study because optometrists do not perform it in Finland.

2.11 Advanced Technology in Assessment and Management of Dry Eye

Over the past few years, many advanced technologies have been introduced in dry eye practice, both in assessment (e.g., Idra, LipiView, Myah, Oculus Keratograph 5M, anterior segment OCT) and management (BlephEx, IPL (e.g., E>Eye, M22 Optima), IPL+MGX (e.g., LipiFlow, Eye-Light)) of dry eye. Functions that are most commonly included in dry eye diagnostic devices are interferometry (to assess lipid layer thickness), tear meniscus (to assess tear volume), NIBUT (to evaluate tear film stability), meibography (to assess meibomian glands), blinking (to assess blinking quality and frequency) and ocular redness classification. Restoring data helps optometrists demonstrate the patient's situation and follow up more precisely. Osmolarity measurement is discussed in Tear Film Osmolarity Chapter, and the esthesiometer is discussed in the Pain and Sensation Chapter.

Tear film stability is measured non-invasively with NIBUT utilizing different devices (e.g., Tearscope). Most involve the observation of the specular reflection of an illuminated grid pattern from the tear film. Corneal topographers can also measure NIBUT by observing the Placido disc images reflected from the eye's anterior surface. Oculus Keratograph 5M utilizes automated assessment of tear film stability by detecting and mapping the locations of tear break-up over time. (Wolffsohn et al. 2017, p. 551).

Tear film instability and loss of homeostasis are the core mechanisms of dry eye. Kojima et al. (2020) investigated advances in diagnosing and treating dry eye, referring to the Japanese Dry Eye Society and Asia Dry Eye Society's concept of tear film-oriented diagnosis (TFOD) and therapy. TFOD focuses on the layers where the abnormalities are, and topical eye therapy is chosen after the clinician has found the target layer for therapy. Kojima et al. (2020) evaluate the lipid layer with interferometry, and the Schirmer test measures aqueous quantity, strip meniscometry, or anterior segment optical coherence tomography (OCT).

Interferometry allows an estimate of the tear film lipid layer thickness (LLT). Tearscope (Keeler Tearscope-Plus™) is a subjective method, and Oculus® Keratography 5M, LipiView®, and Myah (Topcon) are objective methods to measure LLT. The LipiView instrument, for example, has a sensitivity of 66% and specificity of 63% (Wolffsohn et al. 2017, pp. 558-559).

Meibography allows observation of meibomian glands' structure. With advanced technology, the grading of dropouts at baseline and follow-up examinations can be used to track the long-term progression of MGD (Wu et al. 2021). The development of recent technological advances has led to the creation of multiple mobile and handheld systems with infrared light-emitting diodes (LEDs) fixed to infrared cameras (Wolffsohn et al. 2017, p559). Meibography can be performed using transillumination (contact), direct illumination (non-contact), interferometry, or anterior segment optical coherence tomography (AS-OCT). There are six commercially available meibography devices: EyeTop Topographer (Costruzione Strumenti Oftalmici, Florence, Italy), LipiScan™ with Dynamic Meibomian Imaging™ (TearScience, Morrisville, North Carolina, USA), LipiView II (TearScience, Morrisville, North Carolina, USA), Oculus Keratograph 5M (Oculus, Wetzlar, Germany), Topcon slit-lamp microscope (Topcon Cooperation, Tokyo, Japan) and Sirius Scheimpflug Camera and Cobra Fundus Camera (bon Optic Vertriebs GmbH, Lübeck, Germany). (Yanoff and Duker 2019, p. 164).

Normal meibomian glands appear hyperilluminated and adjacent areas between the meibomian glands as hypoilluminated. Meibography helps differentiate the ADDE from EDE related to MGD. In MGD, acinar density and wall homogeneity decrease, while acinar and duct diameter increase. Meibomian gland dropout is assessed using MGD grading systems (Table 4). (Yanoff and Duker 2019, pp. 164-165).

Table 4. MGD grading system.

Characteristics	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Gland dropout	None	33%	34-66%	>66%	-
Partial glands	None	<25% of image	25-75% of image	>75% of image	-
Loss of total meibomian gland area	None	<1/3	1/3 – 2/3	>2/3	-
Area of loss	0%	25%	25-50%	51-75%	75%

Adopted from Yanoff and Duker 2019, p. 164.

BlephEx® (RySurg, Fort Worth, FL, USA) system is designed for lid debris debridement to exfoliate the eyelid margin with a rapidly spinning sponge-tipped micro brush and a foam cleanser. The procedure takes approximately 1-2 minutes to remove the bacterial biofilm, lid debris, and Demodex folliculorum mites with four disposable brushes. (Moon et al. 2021). According to Moon et al. (2021), telangiectasia, meibomian gland plugging, and thickness improved significantly four weeks after the procedure in moderate to severe MGD when BlephEx was combined with MGX. Lid margin telangiectasia is associated with vascular dilatation due to inflammatory mediators, and MMP-9 levels were also decreased in their study (Moon et al. 2021).

Intense pulsed light (IPL) therapy is a handheld and computer-controlled flashgun that uses the high-output flash lamp to deliver intense pulses of non-coherent light from 500nm to 1200nm. The first IPL device was approved by the Food and Drug Administration (FDA) in the US in 1995 for treating lower extremity telangiectasias. There has been rapid development of technology in many areas of medicine, and nowadays, specific IPL devices are developed for dry eye management. The two primary devices are the E>Eye device (E-Swin, France) and the M22 Optima device (Lumenis Ltd, US). IPL devise for the MGD management is applied to multiple locations under the inferior eyelids, starting from the nasal side and finishing temporally and delivering light pulses ranging from 9 J/cm^2 to 16 J/cm^2 depending on the device. Most commonly, three or four sessions over four months are recommended. (Cote et al. 2020).

People with darker skin tones are not eligible for the IPL procedure because of the risks of inducing hypopigmentation and scarring. The optometrist and the patient must wear eye shields to prevent potentially permanent eye injury. The Fitzpatrick Classification of Skin Types I through VI (Table 5) (Ward et al. 2017, p. 83) is used to determine whether IPL may be an appropriate intervention option and whether people with types V to VI are not good candidates. (Cote et al. 2020).

Table 5. The Fitzpatrick Classification of Skin Types I through VI.

Type I	Type II	Type III	Type IV	Type V	Type VI
White skin Always burns, never tans.	Fair skin Always burns, tans with difficulty.	Average skin Sometimes mild burn, tan about average.	Light-brown skin Rarely burns, tans easily.	Brown skin Never burns. Tans easily.	Black skin Heavily pigmented. Never burns, tans very easily.
					

Adopted from Ward et al. 2017, p. 83.

The potential mechanisms of action of IPL in treating MGD, according to Cote et al. (2020), are thought to be the following:

- Inducing thrombosis of telangiectatic blood vessels in the eyelids
- Liquification of meibum
- Reducing *Demodex* eyelid infestation
- Promoting changes to meibomian gland architecture
- Photomodulation

Risks related to IPL therapy are damage to the periocular skin (e.g., depigmentation, swelling, redness), hair or eyelash loss, and permanent intraocular injury (e.g., iris transillumination) (Cote et al. 2020). According to Cote et al. (2020), there is a need for future research to search the effectiveness and safety of IPL therapy for MGD. They suggest developing a “core outcome set” for dry eye clinical trials to improve the consistency of outcome reporting. Pang et al. (2019) studied the efficacy of vectored thermal pulsation (VTPT) and warm compress treatments (WCT) in MGD. They concluded that a single 12-minute VTPT was more efficacious than WCT in objective and subjective measurements.

IPL therapy improves non-invasive break-up time (NIBUT) but does not affect SPEED scores (Liu et al. 2020, p. 1815). According to Cote et al. (2020), IPL improved some of the clinical signs, like tear stability and tear composition, of MGD. Uncertainty exists concerning the effect of IPL on meibomian gland blockage or corneal sodium fluorescein staining (Cote et al. 2020).

LipiFlow® (TearScience, Morrisville, NC, USA) – Lipiflow Thermal Pulsation (LTP) system procedure of 12 minutes combines IPL and meibomian gland expression (MGX), has been safe and effective for managing MGD (Jones et al. 2017, p. 596). The so-called activator covers the front and back of the eyelids. The rear portion applies heat to the meibomian glands (heating the glands to therapeutic levels of 42.5 °C), while the front portion of the activator is inflated by air pressure compressing the glands (Jones et al. 2017, p. 596; Finis et al. 2014). Compared to twice-daily warm compress treatment combined with lid massage and lid hygiene, a single LTP procedure performs at least as well. (Finis et al. 2014).

IPL therapy with MGX seems to be a promising therapy for MGD, but it cannot improve all symptoms. Sambhi et al. (2020) meta-analysis indicated a significant increase in tear break-up time (TBUT) post-treatment follow-ups. Long-term therapy should be considered because the efficacy of IPL may decrease within six months after the last treatment (Leng et al. 2021). According to Hu et al. (2022), Lipiflow® not only significantly improved subjective parameters such as ocular surface disease index (OSDI) and standard patient evaluation of eye dryness (SPEED) but also showed significant improvement in the objective values concerning meibomian glands secretion compared with the control group.

The third IPL device available is Eye-Light® which is a combination of Optimal Power Energy (OPE®) -IPL and Light Modulation® Low-Level Light Therapy (LLLT). The advantage is shorter (3 minutes) therapy time and no need for gel application compared to the E>Eye system. According to D'Souza et al. (2021), combined light therapy shows promising results in chronic MGD and DED patients with a significant increase in TBUT and meibomian gland expressibility score and a significant reduction in inflammatory biomarkers (e.g., IL-1ß, IL-17F, and MMP-9).

2.12 Clinical Practice Model Guidelines

There is currently no dry eye practice model or care recommendations for dry eye in Finland for optometrists or ophthalmologists. In the UK, the College of Optometrists has developed clinical management guidelines for dry eye (Keratoconjunctivitis sicca) and included a chapter concerning management by an optometrist. According to the College of Optometry Clinical Management Guidelines (2022), practitioners should recognize their limitations and if necessary, seek further advice or refer the patient elsewhere. The main categories in non-pharmacological management are patient education, environmental issues, oral EFA supplements (omega-3 and omega-6), tear conservation with punctal plugs, lid hygiene with warm compresses for MGD, and protection with therapeutic contact lenses. Pharmacological management by optometrists includes tear supplements (preferably unpreserved), topical steroids (such as fluorometholone or loteprednol) and cyclosporine (The College of Optometry 2022).

2.12.1 Dry Eye Syndrome Preferred Practice Pattern®

American Academy of Ophthalmology (AAO) approved the 2018 Dry Eye Syndrome Preferred Practice Pattern® (Akpek et al. 2019), which follows the recommendations from the TFOS DEWS II management and therapy report (Jones et al. 2017). All Preferred Practice Guidelines® are intended for the use of ophthalmologists, valid for five years from the “approved by” date to ensure they are current unless superseded by a revision (Akpek et al. 2019, p. 291).

In Table 6, Akpek et al. (2019) have summarized the characteristic findings related to DED; otherwise, they are mainly following the recommendations from the DEWS II report. The patient outcome criteria include reducing and alleviating signs and symptoms, maintaining or improving visual function, and reducing or preventing ocular surface damage (Akpek et al. 2019, p. 299).

Table 6. The characteristic finding in DED assessment.

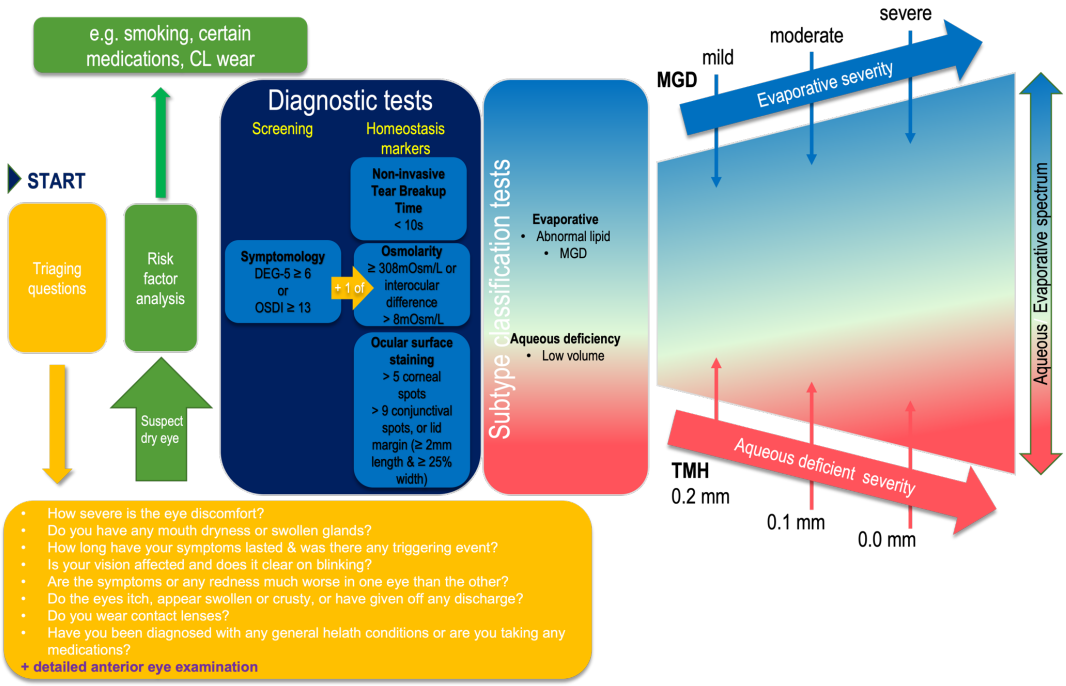
Test	Characteristic Findings
Tear osmolarity	Elevated; test-to-test variability; intereye differences considered abnormal
Matrix metalloproteinase-9	Indicates presence of inflammation which dictates treatment
Aqueous tear production (Schirmer test)	10 mm or less considered abnormal
Fluorescein dye disappearance test	Test result is compared with a standard color scale
Tear break-up time	Less than 10 seconds considered abnormal
Ocular surface dye staining	Staining of inferior cornea and bulbar conjunctival typical
Lacrimal gland function	Decreased tear lactoferrin concentrations

Adopted from Akpek et al. 2018, p. 305.

2.12.2 DEWS II

Dry eye assessment is complicated because of the multifactorial nature of dry eye disease (DED). This study uses dry eye assessment and dry eye diagnostics as synonyms. TFOS DEWS II Diagnostic Methodology report (Wolffsohn et al. 2017) proposes the most appropriate order to conduct the selected tests in a clinical setting to diagnose and monitor DED.

First are triaging questions and risk factor analysis as a part of routine eye examination patient history (Figure 6). Diagnostic tests, according to Wolffsohn et al. (2017, p. 561), include screening with the Dry Eye Questionnaire (DEQ-5) or with the Ocular Surface Disease Index (OSDI) followed with at least one of the homeostasis markers: non-invasive tear breakup time (NIBUT), osmolarity and ocular surface staining (corneal, conjunctival and lid margin). If NIBUT is unavailable, fluorescein tear breakup time (FBUT) can be used after osmolarity measurement (Wolffsohn et al. 2017, p. 561). Tests that inform subtype classification etiologies are meibomian gland dysfunction (MGD) imaging/observation and expression, lipid thickness, and tear volume tests (Figure 6) (Wolffsohn et al. 2017, p. 569).

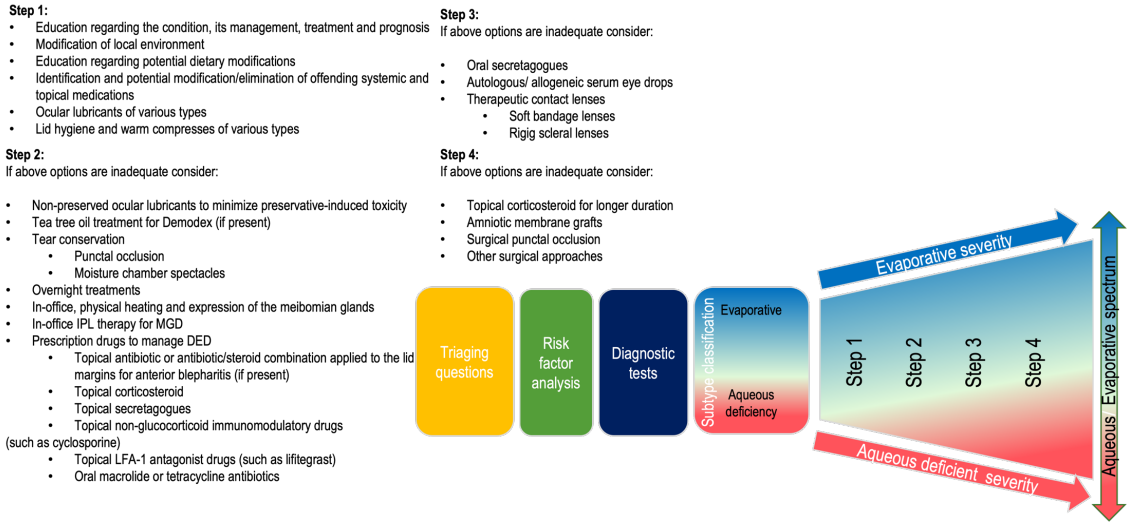


Adopted from Wolffsohn et al. 2017, p. 561.

Figure 6. TFOS DEWS II Diagnostic Methodology report description of DED diagnostic test battery. Picture: Päivi Nokipii.

TFOS DEWS II management and therapy report (Jones et al. 2017, pp. 575-628) gives a comprehensive picture of dry eye disease management (Figure 7) (Jones et al. 2017, pp. 614-615). It starts with triaging questions, which are presented in detail in the TFOS DEWS II Diagnostic Methodology report description of the DED diagnostic test battery (Figure 6) (Wolffsohn et al. 2017, p. 561).

Jones et al. (2017, p. 615) have proposed the following 4 step management algorithm (Figure 7) to assist eye care practitioners, even though DED varies in severity and character from patient to patient.



Adopted from Jones et al. 2017, pp. 614-615.

Figure 7. The process is associated with the management of DED. Picture: Päivi Nokipii.

2.13 Rules and Legislation

Act on the Status and Rights of Patients (785/1992) states that patients have a right to good quality health care. It also obligates optometrists, as health care professionals, to inform the examinee about the findings and conclusions and, if needed, to refer the patients to medical care.

Regarding the practice of opticianry in Finland, section 16 of the Decree of the Ministry of Social Affairs and Health on Health Care Professionals (564/1994) states:

> "A licensed optician may not prescribe spectacles independently to:
>
> 1) a child under the age of eight years
> 2) a person who has previously undergone an operation involving the eyeball
> 3) a person suffering from an obvious eye disorder
> 4) a person whose vision cannot be normalized with spectacles."

Health Care professionals Act (559/1994) obligates optometrists in section 18 to take part in further training to maintain and improve their professional knowledge and skills required to carry on their professional activity. Diagnostic privileges are nowadays included in the Bachelor of Health Care

(Optometry) degree, and in 2019 approximately 48% of working optometrists in Finland are called opticians without diagnostic privileges (Näery 2022).

The Decree of the Ministry of Social Affairs and Health on prescribing medicine (2.12.2010/1088) states the following:

> "Optician may prescribe from the pharmacy the medicinal products listed in Annex 2 needed for the reception activities. An optician does not have the right to prescribe medication to patients."

Annex 2 (19.9.2019/992) was later updated and came into force at the beginning of January 2020. The main renewal was adding ATC-class S01JA51, fluorescein, and combination products (fluorescein + oxybuprocaine hydrochloride) into the list that already contained the following: oxybuprocaine hydrochloride, tropicamide, cyclopentolate, and phenylephrine. Topical corticosteroids such as fluorometholone and loteprednol may be used to modulate anterior segment inflammation (Jones et el. 2017, p. 599). The available studies suggest that loteprednol etabonate is a safe and effective treatment for DED with a low risk of elevated IOP or cataract formation (Beckman et al. 2020, p. 509). In Finland, optometrists lack therapeutic privileges.

As eye care professionals, optometrists and opticians must act according to health care laws and regulations, following the general ethical principles. The Ethical Council of Optometry in Finland has created basic guidelines for good practice for eye examination and contact lens fitting (Ethical Council of Optometry n.d.). The procedures for comprehensive eye examination include diagnostic privileges.

The World Council of Optometry (WCO) defines optometrists as "the primary healthcare practitioners of the eye and visual system". An optometrist provides "comprehensive eye and vision care that includes refraction, dispensing detection/diagnosis, management of disease in the eye, and the rehabilitation of conditions in the visual system". (World Council of optometry n.d.).

3 CONCLUSIONS OF THE LITERATURE REVIEW

The study has been designed to focus on developing a model of dry eye practice in Finland. Hence, the research gap that the paper aims to fill is the achievement of a comprehensive understanding of the best assessment and management tools without or with advanced technology in combination with the limitations set by the Finnish legislation.

A literature review is essential in this thesis project to collect evidence-based data that is brought together on dry eye practice. It is necessary to form a coherent view of this topic because the findings of a single research paper are not enough to influence the development dry eye practice model (Aveyard 2019, p. 6).

Hyperosmolarity and inflammation are included in the definition of the DED, which makes sense because increased tear film evaporation and poor quality of LLT increase hyperosmolarity resulting in a vicious cycle and ocular surface inflammation.

The prevalence of DED ranged from 5% to 50% (Stapleton et al. 2017, p. 336). Most studies use different criteria, making comparing the results difficult. Nevertheless, DED has and will be increased in the future along with the aging population and the emerging use of intelligent devices. Vehof et al. (2021, p. 92) reported that young adults' dry eye symptoms are persistent. Research shows that this may be a new challenge for dry eye practice in the future.

The population is aging and becoming increasingly diverse, one of the highlight five trends in Sitra´s Megatrends 2020 update (Sitra 2022). Identifying the risk factors is an integral part of dry eye practice because age and female sex are the major risk factors for DED (Zhang et al. 2020). Another aspect is that the immune system ages along with the increasing life expectancy (Zhang et al. 2020). Studies show a decrease of active meibomian glands by 50% from the age of 20 years to the age of 80 years. (Knop et al. 2011, p. 1942). Maybe this should be taken into consideration resulting in age-corrected values. For example, normal TMH ranges between 0.2mm and 0.4mm, but for elderly individuals' the normal range is lower, between 0.1mm and 0.3mm (Doughty et al. 2002).

Risk factors of DED are divided into modifiable and non-modifiable. MGD is classified as a non-modifiable risk factor of DED. (Stapleton et al. 2017, p. 355). The classification will likely change in the future as science evolves. Could stem cell implementation grow new meibomian glands?

The serum vitamin D level in dry eye syndrome patients was lower than healthy controls (Liu et al. 2020, p. 752). This is important, mainly due to Finland´s northern location and camouflage, to support additional vitamin D intake.

Bron et al. (2017, p. 441) refer to the term hybrid dry eye disease, which best describes the multifactorial nature of DED.

The precorneal tear film is a single dynamic functional unit with different compartments (Willcox et al. 2017, p.369). A comprehensive understanding of the single available unit requires a deep understanding of the pathophysiology of the separate rooms.

Blinking habits matter in dry eye practice. After an absence or decreased blinking, researchers have found an increased amount of accumulated meibum secretion, and repeated enforced blinks have significantly increased the LLT. (Knop et al. 2011, p. 1939). Prolonged blink interval also increases evaporation and has thereby positive correlation with osmolarity value. (Bron et al. 2017, pp.452-453).

The neural pathways that regulate meibomian gland secretion or mucins release have not been identified (Belmonte et al. 2017, p. 407). Future studies in this area are needed.

The osmolarity of tear films is correlated most strongly with the severity of DED in clinical dry eye tests. Plasma and tear osmolarity positively correlate (Willcox et al. 2017, p. 372). Further research on this is suggested to develop a device that could measure plasma osmolarity from the tear film or vice versa.

Studies show that dehydration causes hyperosmolarity in the tear film (Bron et al. 2017, p.452). A topic that could be included in dry eye practice conversations is drinking water and staying hydrated

Studies suggest that the InflammaDry® test is better at detecting moderate to severe DED (Willcox et al. 2017, p. 389). In the future, we need to develop a device that could detect mild to moderate DED.

Inflammation plays a vital role in dry eye etiology; thereby, maintaining ocular surface homeostasis is critical in dry eye practice. During inflammation, polymodal and mechano-nociceptor nerve endings become sensitized, and cold thermoreceptor activity increases abnormally, causing pain and dryness sensations (Belmonte et al. 2017, p. 407). Could the increase in cold thermoreceptor activity be due to "freezing of the eye" caused by the decreased LLT and increased evaporation because the ocular surface lacks insulation material?

In DED patients who remain symptomatic despite adherence to therapy, neurosensory dysfunction may be responsible for the lack of association between signs and symptoms (Kaido et al. 2016, p. 918). This is an important thing to be taken into consideration during dry eye practice because the purpose of corneal neurons is to protect the epithelial tissue from damage or injury.

Pain can be evaluated with questionnaires and corneal sensitivity with esthesiometry (Belmonte et al. 2017, p. 407). The problem is that, e.g., the Cochet-Bonnet esthesiometer stimulates only the mechanosensitive nerve fibers (Kaido et al. 2016, p. 917). Corneal sensory neurons can be classified as polymodal nociceptors, specific mechano-nociceptors, or cold thermoreceptor neurons (Belmonte et al. 2017, p. 408). That is one crucial point to consider. According to Kovács et al. (2016, p. 412), selective stimulation of corneal cold sensory fibers in healthy humans evokes distinct sensations of eye discomfort. That also confirms that to assess corneal sensitivity precisely, we need to develop a device that could efficiently measure corneal cold sensory neurons and implement it in dry eye practice assessment and follow-up.

Dry eye assessment consists of screening, patient history, risk factor analysis, and diagnostic tests according to individual needs. Optometrists play a vital role in all aspects of dry eye assessment. Patient history in dry eye assessment should focus on symptoms and signs, exacerbating conditions, duration of symptoms, and both ocular and medical history (Akpek et al. 2019, p. 301-302). According to the literature review, the symptom questionnaire should be consistent and uniform to provide quality knowledge for optometrists and researchers. OSDI and DEQ-5 are the most widely used symptom questionnaires. Risk factor analysis is a part of the DED diagnostic

battery (Wolffsohn et al. 2017, p. 561. Should it be included also in the screening for everybody who enters the optical store?

Diagnostic tests are used to either measure tear film volume, tear film stability and ocular surface staining. According to Wolffsohn et al. (2017, p. 548), the tests are recommended to perform from the least invasive to the most invasive. If tear film volume is measured by evaluating the tear meniscus height (TMH) with the slit-lamp, the downside is that it is operator-dependent. Advanced technology can offer more precise measurements and documentation of the results for further follow-up.

Evaluate ADDE with strip meniscometry with the cut-off value of ≤ 4 mm, which shows very high sensitivity (93%) and specificity (73%) (Kojima et al. 2020, pp. 5-6). Both Schirmer and Phenol Red Thread tests show lower values in sensitivity, suggesting using strip meniscometry in tear film volume assessment. The Shirmer test, however, has higher specificity (93%), which is why it is used in the diagnosis of Sjögren Syndrome. (Wolffsohn et al. 2017, p. 554). Khanna et al. (2022, p. 1230) suggest tearing sampling to be performed first to avoid reflex tearing and at least 2 hours after awakening, which is essential to consider.

To evaluate EDE with tear breakup time, the problem is that TBUT is reduced regardless of the dry eye subtype when dry eye and meibomian gland dysfunction (MGD) are diagnosed simultaneously (Kojima et al. 2020). The sensitivity of the TBUT test is 72%, and the specificity is only 61% (Mou et al. 2021). According to studies, TBUT and tear break-up patterns followed by ocular surface staining and LIPCOF are recommended to be evaluated.

Lid aspects and blinking habits must be considered part of dry eye assessment. According to Wolffsohn et al. (2017, p. 558), LWE is a diagnostic sign of DED, which suggests it be included in the dry eye practice model. LWE sensitivity is poor (48%), but specificity is high (96%).

Dry eye management done by optometrists should consist of patient education, lid hygiene, warm compresses, forceful expression, and punctal occlusion with plugs, according to individual needs. According to Akpek et al. (2019, p. 306), setting realistic and personal goals concerning the management plan is essential. This suggests a written format could be given for the customer to increase compliance. Optometrists should also educate the patient about the chronic nature and the lifelong management strategy. According to Jones et al. (2017, p. 593), poor compliance is also

a problem with following lid hygiene instructions and warm compresses. They suggest universally accepted guidelines for lid cleansing as one solution. This thesis presents, that optometrists in Finland could develop a lid cleansing and warm compress instruction brochure if dry eye management is performed in a conventional method.

According to Bron et al. (2017, p. 452), recent studies have shown that working at a video display terminal, reading, and operating monitor-based and handheld video games decrease blink interval. Optometrists should develop a brochure with physiotherapists to improve patient education in the display of terminal work concerning the dry eye.

The punctal plugs are associated with conflicting studies concerning the management order. Akpek et al. (2019, p. 310) recommend punctal plugs after achieving tear homeostasis. Still, Tong et al. (2016, p. 239) concluded that the overall tear cytokine levels were not significantly altered following the insertion of punctal plugs. The combination of punctal plugs and anti-inflammatory medication could be one solution in the future in dry eye management. This thesis suggests punctal plugs as a part of dry eye management by an optometrist in Finland if adequate competency has been achieved with an additional education certificate.

Advanced technology has brought more opportunities and reliability to dry eye assessment and management. Interferometry, tear meniscus, NIBUT, meibography, blinking, and ocular redness classification can be evaluated as a part of dry eye assessment and lid hygiene, warm compresses and forceful meibomian gland expression can be replaced with, e.g., BlephEX, IPL or IPL+MGX devices. Pang et al. (2019) concluded that a single 12-minute VTPT was more efficacious than WCT in objective and subjective measurements. According to D'Souza et al. (2021), combined light therapy shows promising results in chronic MGD and DED patients. Considering these studies with poor compliance to WCT and the chronic nature of DED, this thesis highly suggests using advanced technology in MGD management. Restoring data also helps optometrists to demonstrate the situation for the patient and follow up more precisely, which takes dry eye practice to a higher level.

One problem is that there are currently no simple clinical examination methods for evaluating the ocular surface mucins, which needs improvement in the future development of advanced technology.

4 THE PURPOSE, OBJECTIVES, AND TASKS OF THE RESEARCH DEVELOPMENT WORK AND THE DIFFERENT STAGES

4.1 Statement of the Research Question

What are the evidence-based components of a dry eye practice model?

4.2 Summary Description of the Experimental Design

A qualitative survey study using semi-structured and open-ended questionnaires was designed to identify evidence-based components of a practice model. Dry eye experts from Finland (n=1), Norway (n=1), and the UK (n=2) were contacted via email to participate. Subject selection criteria included almost ten years of dry eye practice experience and education participation.

The student investigator interviewed all four subjects online using Zoom as a videoconferencing platform. Semi-structured and open-ended questionnaires with 24 questions were used as the body of the interview. All four interviews were recorded, transcribed, and finally, the recordings were destroyed. All survey participants were permitted to publish their names in this master thesis in the beginning of the online interview.

The final dry eye practice model development is based on the deductive content analysis, inductive content analysis, and Engeström´s activity system model, and combining them with consideration of the limitations set by the Finnish legislation.

4.3 Methodology

4.3.1 Survey Design

A survey study was chosen as the research method because the study aimed to develop a dry eye practice model in Finland. The data collection method was an online expert interview to gather evidence-based knowledge of dry eye practice models from three different countries.

Semi-structured and open-ended questionnaire (Appendix 1), including a total of 24 questions, was designed and approved by master thesis instructor Dr. Robert Andersson in March 2021. Research questions were categorized, and related questions can be seen in Table 5. Background information was the focus of the first four questions (education, work setting, work experience, dry eye practice experience).

The second section of the interview dealt with dry eye practice setting, including six questions, and the third section dealt with dry eye assessment (symptom questionnaire, ocular surface staining, measuring tear volume and tear film quality, MGD, osmolarity, blink/lid closure, inflammation, patient education) with ten questions. The fourth section dealt with dry eye treatment (treatment methods and MGD treatment), including two questions.

All four sections consisted of a total of 22 semi-structured questions with four open-ended questions including an explanation of “why” and one question with additional open-ended answers including “interval” and “results.” The second last question was an opinion about the therapeutic license, and the final open-ended question was about discussing a possible important topic/s that was not already included in the questionnaire.

Table 7. Research question categories and corresponding questions in the questionnaire. Table: Päivi Nokipii.

Research question categories	Question nro
Background information	1, 2, 3, 4
Dry eye practice setting	5, 6, 7, 8, 9, 10
Dry eye assessment	11, 12, 13, 14, 15, 16, 17, 18, 19, 20
Dry eye treatment	21, 22
Should optometrists be allowed to use therapeutics to be able to treat dry eye disease?	23
Is there something that you want to add considering about your dry eye practice, that I forgot to ask?	24

Study End-points: In order to evaluate were the questions worded correctly, study end-points are listed in Table 8.

Table 8. Study end-points listed with question number/s (nro). Table: Päivi Nokipii.

Study end-points	Question nro
Education	1
Work setting	2
Overall experience after graduation	3
Experience in dry eye practice	4
Frequency of the assessment	5
Duration of the work-up	6
Frequency of the post-assessment	7
Who is the performer of the assessment?	8
How dynamic is it to perform the assessment?	9
Is advanced technology used for the assessment?	10
Mainly used symptom questionnaire	11

Diagnostic dye used in ocular surface staining	12
Method to measure tear volume (quantity)	13
Method to measure tear film quality	14
Method to assess MGD	15
Opinion why/why not measure osmolarity	16
Evaluation of blink rate	17
Method to evaluate inflammation of the ocular surface	18
What other test are used in assessment?	19
Patient education and compliance	20
Dry eye management methods	21
Management methods in MGD	22
Opinion about therapeutics license for optometrists to manage DED	23
Is there something relevant that student investigator forgot to ask?	24

4.3.2 Gathering of the Background information

In the field of eye care in Finland, there exists a need to develop a dry eye practice model that can be implemented all over Finland. The purpose of this literature review is to evaluate the prevalence of dry eye, define and classify dry eye disease (DED), research the risk factors, summarize different dry eye disease practice models, various tools and advanced technologies used in dry eye disease assessment and management and consider the legislation of dry eye practice in Finland. This literature review aims to gather all the puzzle pieces together, considering the best assessment and treatment methods from various studies without and with advanced technology.

The Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) I and II studies are the primary source in this literature review. American Academy of Ophthalmology`s (AAOs) Dry Eye Syndrome Preferred Practice Pattern is also used as a baseline.

Literature search: First electronic literature search was conducted using PubMed in September 2020, and the final search in March 2022. The database was searched using the terms ´dry eye AND prevalence´, ´dry eye AND (classification OR definition) ´, `dry eye AND risk factor*´, `dry eye AND meibomian gland*´, `dry eye AND osmolarity´, `dry eye AND (inflammation OR biomarkers)´, dry eye AND (pain OR sensation)´, dry eye AND blink rate´, ´dry eye AND (assessment OR diagnostic*) ´, ´dry eye AND (management OR treatment)´, `dry eye AND advanced technology)´, `dry eye AND (clinical practice model OR clinical practice pattern)´ and 'dry eye AND (contact lens OR scleral lens)'. The search was limited to systematic reviews and guidelines written in the English language. The literature review was conducted without time limitations. The total result (n=536) consisted of one guideline (n=1) and mainly systematic reviews (n=535).

Table 9. Literature review results by different search terms (situation in week 38/2020; Pubmed database was searched again in week 10/2022). Table: Päivi Nokipii.

Search term	Total Results (n)	Relevant Results (n)
dry eye AND prevalence	74	4
dry eye AND (classification OR definition)	20	0
dry eye AND risk factor*	33	5
dry eye AND meibomian gland*	18	8
dry eye AND osmolarity	7	1
dry eye AND (inflammation OR biomarkers)	35	3
dry eye AND (pain OR sensation)	26	4
dry eye AND blink rate	0	0
dry eye AND (assessment OR diagnostic*)	130	7
dry eye AND (management OR treatment)	164	16
dry eye AND advanced technology	3	1
dry eye AND (clinical practice model OR clinical practice pattern)	19	1
dry eye AND (contact lens OR scleral lens)	7	0
Duplicates (n)	-	19
TOTAL (n)	536	31
TOTAL (n) systematic reviews	535	30
TOTAL (n) guidelines	1	1

Professional literature from books was also included in deductive content analysis. Rules and legislation were searched mainly from Finlex Data Bank, an online database for up-to-date legislative and other judicial information on Finland. Valvira is the National Supervisory Authority for Welfare and Health operating under the Ministry of Social Affairs and Health, which is also used as a reference in the rules and legislation paragraph.

Literature selection: The first approach to the topic was made in October 2020 by reading the TFOS DEWS I and DEWS II reports. Especially the report of the TFOS DEWS II Diagnostic Methodology subcommittee (Wolffsohn et al. 2017, pp. 539–574) was the most important source of information. Relevant studies (n=50) were filtered by reading their titles and some by reading their abstracts, and duplicates (n=19) were removed, resulting in a total of 30 systematic reviews and one guideline (Table 9). Sjögren syndrome-related dry eye, acupuncture treatment, Demodex, omega supplements, biological tear substitutes, ocular lubricants, and therapeutics-related studies were excluded from the total results.

Pre-survey content expert meeting: In December 2020, a meeting was organized with the instrument manager Jouni Pekkanen from Essilor Oy, Finland. He gave a very comprehensive education about the advanced technology in the assessment and management of dry eye, including Idra and IPL (E-Eye). Information about dry eye experts was also discussed, who could later be invited for the expert interview.

4.4 Planning of the Expert Interviews

Subject selection criteria included almost ten years of dry eye practice experience and education participation. The process started in a pre-survey content expert meeting followed by discussions with multiple eye care practitioners in Finland to determine long-term dry eye experts to be eligible candidates included in expert interviews.

The first contact was taken via email in December 2020. Aija Hirsimäki from Finland, Erik Robertstadt from Norway, and one from the UK invited and accepted the invitations. They all agreed to be informed of the details a bit closer to the interview, which was scheduled for the late spring or the beginning of summer 2021.

In May 2021, scheduling the appointments for the expert interviews started. Nicholas Rumney from the UK was invited via e-mail because the first contacted person didn´t reply to emails anymore. Also, my mentor, Pia Mäkelä and Nicholas Rumney suggested getting Sarah Farrant from the UK, and she accepted the invitation with short notice.

The expert interviews were recorded and held online using Zoom as a videoconferencing platform on the 5th (n=3) and the 22nd (n=1) of June 2021. All interviewees were granted permission to record the interviews for later transcribing. After transcribing, the recordings were deleted, and transcriptions were analyzed during the summer.

4.5 Specific Aims

The first specific aim was to interview optometrist and dry eye specialist Aija Hirsimäki, a long-term dry eye practice expert in Finland. The interview was scheduled for 9 am EET Tuesday, 15 June 2021, and was held in the Finnish language via Zoom. The duration of the discussion was 40 minutes.

The second specific aim was to interview IP optometrist Professor Nicholas Rumney, who has over 40 years of experience in eye care in the UK. The interview was scheduled for 11.30 EET Tuesday, 15 June 2021, and held in the English language via Zoom. The duration of the discussion was 54 minutes.

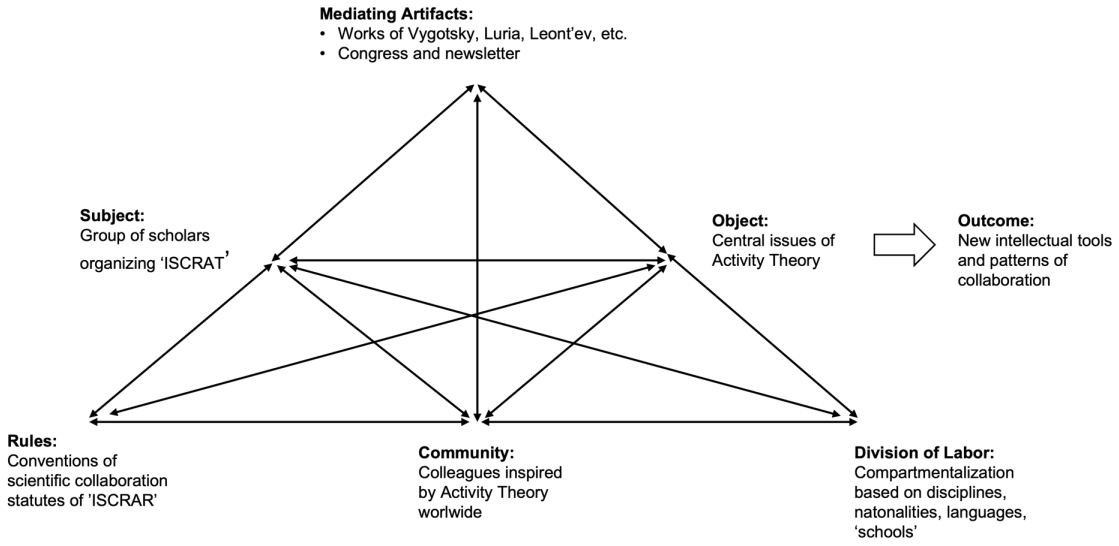
The third specific aim was to interview optometrist and lecturer Erik Robertstadt, who has over 20 years of experience in eye care, and who started in the UK and in 1998 in Norway. The interview was scheduled for 14.45 EET Tuesday, 15 June 2021, and held in the English language via Zoom. The duration of the discussion was 69 minutes.

The fourth specific aim was to interview Sarah Farrant, director, IP optometrist, dry eye specialist, industry consultant, and lecturer from the UK. The interview was scheduled for 14.30 EET Tuesday, 22 June 2021, and held in the English language via Zoom. The duration of the discussion was 43 minutes.

4.6 Data Analysis

Engeström, Miettinen, and Punamäki (1999, p. 31) have developed an activity system complex model. The lightning-shaped arrows between the object and mediating artifacts, as well as between

object and division of labor, indicate contradictions between central components of the activity system (Engeström, Miettinen, and Punamäki, 1999, p. 31). This model consists of three separate triangles that are interconnected, resulting in an outcome. The object is between the subject and the outcome. All the lines are double-arrowed, so every component is somehow connected. Using their complex activity system model (Figure 8) (Engeström, Miettinen and Punamäki, 1999, p. 31) as a baseline, developing a model of dry eye practice started.



Adopted from Engeström, Miettinen and Punamäki, 1999, p. 31.

Figure 8. A complex model of an activity system. Picture: Päivi Nokipii.

5 IMPLEMENTATION OF THE RESEARCH DEVELOPMENT WORK

5.1 Specific Aim 1

5.1.1 Introduction

Aija Hirsimäki is an optometrist who has working experience in eye care for over 30 years and about ten years in dry eye practice in Finland. Since 2016 she has been working in private dry eye practice without assistance. Before working only in dry eye practice, she assessed dry eye as a part of the routine eye examination.

5.1.2 Results

A dry eye examination lasts 1hour, and a post-control appointment is always scheduled. All the instruments and tools are set in the same room, including advanced technology. Advanced technology, Oculus Keratograph 5M, is used in patient education and motivation and in monitoring the treatment outcomes. TMH, NIKBUT, meibography, and video without and with fluorescein are used to assess the tear film quality.

With many years of dry eye practice experience, she developed her symptom questionnaire consisting of questions about symptoms, medications, allergies, artificial tears, ophthalmologist diagnosis of dry eyes, and when the last visit to the ophthalmologist was. Occupation and environmental issues have also been discussed.

Ocular surface staining is evaluated mainly with fluorescein and occasionally with lissamine green. Tear volume (TMH) is estimated mainly with advanced technology, Oculus Keratograph 5M. If Sjögren syndrome is suspected, Phenol Red Thread Test (PRT) is used. The u-Tube instrument is also occasionally used. Tear film quality is assessed with Oculus Keratograph 5M by measuring NITBUT and with the slit lamp by measuring FBUT.

Meibomian glands are evaluated with Oculus Keratograph 5M with meibography on both upper and lower lids. The tear film lipid layer is assessed by looking at the color. Meibomian gland orifices are evaluated with the slit lamp and obstructed glands by the lipid content from the glands when compressed.

Tear film osmolarity is measured only occasionally because of the high price of the tips. If measured, an extra fee of 25€ is charged from the examinee.

Blink/lid closure is evaluated. The redness of the conjunctiva evaluates inflammation of the ocular surface. LWE is evaluated occasionally, but LIPCOF from everyone.

Dry eye management consists of adding moisture to the air with a cool mist humidifier, drinking water to stay hydrated, omega-7 and omega-3 supplements, lid hygiene, artificial tears, and moisture retaining eyeglasses (if needed). Scleral lenses are not fitted, and punctal plugs are not inserted as a part of dry eye management. Corticosteroid eye drops are not used because of limitations set by the Finnish legislation.

Warm compresses and BlephEX are part of the MGD management, followed by home-management instructions. Warm compress interval is once or twice a day for 10 minutes, and in-office BlephEX management every 3-4 months. The post-control appointment is scheduled after one month. IPL is done first three times every two weeks and the fourth after one month. Further data is not available for the IPL management results.

The last open-ended question addressed something that interview did not include but is related to my dry eye practice. Hirsimäki mentioned Demodex as a common problem among dry eye cases. Last, she highlighted that optometrists in Finland should be trained to insert punctal plugs and to do syringing. Optometrists should also be allowed to use therapeutics in the future in Finland to manage dry eye disease comprehensively.

5.1.3 Discussion

Assessment consists of a symptom questionnaire, Oculus Keratograph 5M (TMH, NITBUT, meibography), and slit lamp examination (redness, FBUT, fluorescein staining, meibomian glands, blink/ lid closure, LWE, and LIPCOF). Management includes environmental issues like adding moisture to the air with a cool mist humidifier, drinking water to stay hydrated, omega-7 and omega-3 supplements, lid hygiene, artificial tears, and moisture retaining eyeglasses (if needed). MGD treatment includes warm compresses, BlephEX, and IPL. Recent studies are contradicted regarding the benefit of omega-3 supplement (Jones et al. 2017, p. 607). According to Marsiñach and Cuenca (2019) sea buckthorn oil has a very strong correlation between health and its diverse composition of fatty acids, especially omega-7 fatty acids. These fatty acids are very important in human health, but more studies are necessary to certify the clinical effects on DED.

Tear film osmolarity is measured only occasionally, and an extra fee is charged if measured. Why it is measured only occasionally was an additional question, and the high cost justified the answer. According to the DEWS II report, osmolarity is a valid part of the diagnostic workup.

Advanced technology is essential in assessing and managing dry eye practice. Monitoring the treatment outcomes and as an essential part of patient education. Both in-office and home treatments are used to get the best results.

The last open-ended questions brought an exciting point: optometrists in Finland should be trained to insert punctal plugs and do syringing. That is a relevant point to consider while thinking about future education on dry eye. Punctal plugs and syringing are now included in the Master´s Degree in Health Care, Clinical Optometry education program, which started in Autumn 2020.

5.2 Specific Aim 2

5.2.1 Introduction

Professor Nicholas Rumney is an IP optometrist who has been working as a registered optometrist for over 40 years and about 5-10 years in dry eye practice in the UK. He is working in private practice in Hereford, UK.

5.2.2 Results

Every patient that comes for an eye examination will have a dry eye score of symptoms. A dry eye questionnaire based loosely on the SPEED questionnaire is used. The optometrist will discuss with the patient, and if it is felt that they have a dry eye problem, they will be encouraged to come back for a complete examination that takes 40 minutes. Optometrists in the clinic try to void giving basic advice on the dry eye even during the first examination.

The clinic has a clinical assistant who takes care of the automated tests in a separate room. They use two diagnostic tests, one is called LipiView from TearScience, which is a dynamic assessment of the tear film, and the other one is the new device from Topcon called the Myah. Myah works very similarly to the Oculus Keratograph 5M, so it does the topographical map of the cornea and measures the breakup time and the dry parts.

Their practice is configured because they have eight rooms with dedicated dry eye treatments and one dedicated diagnostic suite. The diagnostic suite has iCare from Finland, Optos fundus camera, visual fields, and the Myah. That´s the domain of the clinical assistant. The optometrist doesn´t usually do any of those tests because they are typically done for them.

When asked for more information about utilizing the Myah, it is used for topography, tear breakup time, objective autorefraction, and axial length measurement, if needed. Myah combines the need for dry eye and myopia management in the same instrument.

When asked why they are using advanced technology as a part of their dry eye practice, Professor Rumney states that it´s essential to identify the underlying cause of the ocular surface disease or the dry eye.

> "The most common is the evaporative, slightly less common is aqueous, but a significant group of people has a component of both. And if you treat only the evaporative and ignore the aqueous, or you treat only the aqueous and ignore the evaporative, you won´t solve that patient's problem satisfactorily. You need a very careful diagnosis and approach it from an evidence-based perspective. The technology gives you the evidence of what you are looking for."

Dry eye assessment is routinely done in regular eye examination using the adapted SPEED questionnaire. When the patient returns for the entire assessment to evaluate their dry eye, optometrists use the OSDI scale because it´s more targeted. Afterward, they would list procedures, starting with the least invasive.

> "The first thing we do is tear film osmolarity with the TearLab. That´s because you are only just touching the eye, then we would look with the slit lamp with white light, and then we would go into the staining."

Osmolarity is tested for everyone who comes for the dry eye workup. It is measured because it gives a numerical value that they can present to the patient when they see them in follow-up to say:

> "You have gone from tear film osmolarity of 325 to 305 with the treatments you are doing. You must keep going to get down to 295, which would be normal."

This gives an objective test that sits alongside the questionnaire so they can be confident that patients´ symptoms have improved. The machine is calibrated daily to ensure proper usage if needed. Osmolarity measurement is included in the total price of the dry eye workup. The total cost for the patient for the dry eye work-up is 60€.

Ocular surface staining is evaluated first with the fluorescein and then with lissamine green. Barrier filters, the yellow filter with fluorescein and the deep red filter with lissamine, are used.

Tear volume is assessed in the initial eye examination evaluating both the tear prism height and the length. Professor Rumney likes using Schirmer tests because that allows him to show the patient the results. Most commonly, he does it without an anesthetic, but occasionally with a drug if he feels it was an issue of trying to establish a baseline level of moisture instead of reflex tearing.

Tear film quality is measured with advanced technology, Myah and Lipiview. LipiView gives the measurement of the thickness of the lipid layer and the measurement of the stability of the tear film (NIBUT). And the blinking patterns, how much the patient blink. According to Professor Rumney, the lipid layer is one of the essential things in assessing the quality of the tear film. FBUT is always routinely done after non-invasive tests, even though he is aware of the problem that fluorescein itself is a solvent for meibomian gland oils.

> "If you aren´t controlled in the quantity of fluorescein that you are instilling into the eye, you can completely disrupt the tear film by effectively dissolving the way the oils."

MGD is assessed with advanced technology. The clinical assistant takes the measurements with the Myah and Lipiview (lipid layer thickness), and optometrists look at the meibomian glands with infrared meibometry. Optometrists also observe the ducts with an instrument from Tearscience that provides the same force against the meibomian glands as the muscle blinking.

> "If you would just go and squeeze them with your fingers, you are putting a lot more force than the blink, and that´s when you start to get more greasy, waxy discharge from the glands.

They are also using paddle tweezers with anesthetics to give a more controlled squeeze more profound into the tissues, but nowadays, they are mainly using Lipiflow.

Inflammation of the ocular surface is evaluated with ocular/conjunctival redness and the symptoms. LWE is evaluated for everyone. LIPCOF is assessed and graded as no folds, 0-5 folds, or greater than five folds. Patient education is done by using slit lamp photographs.

Dry eye management is divided into three tears in their clinic. Tearing is based on what the patient wants, but also in terms of what specialty you have available. Tear one is basic lid hygiene, wipes, and lubricants. Tear two is the more direct in-office treatments, like BlephEX, punctal plugs, and Demodex treatments, that don´t require highly complex equipment but are taken to another

management level. Tear three is advanced dry eye treatment, which includes independent prescribing therapeutics for steroid drops, LipiFlow and IPL. At the end of the dry eye examination, the patient will get a report about three different treatment options stages (tears), and the cost increases along with the number of tears. The total price is just the products and the cost for re-evaluation after three weeks to see how they are getting along and for follow-up. Tear two is the cost of the consumables for the BlepEX and the cost of the time to go through three in-office treatments and then one follow-up. And in tear three, they offer patients either IPL or IPL+ LipiFlow. According to professor Rumney, LipiFlow is always combined with IPL, but IPL is sometimes done independently. IPL is done in three treatments ten days apart. They have also realized that LipiFlow is the best way of managing MGD because it covers both upper and lower eyelids.

As a part of dry eye management, Professor Rumney agrees that they talk about drinking water to stay hydrated. They also speak of omega-3s and omega-7, changing the diet, environmental things like air conditioning, etc. They are also stratifying their lubricants. For example, hycosonshield works very well to supplement the meibomian gland, whereas hyaluronate doesn´t do that.

Lid hygiene is also discussed, and it depends on the diagnosis. If there is evidence of Demodex, Ocusoft Demodex treatment or Blephademodex, is used. But if there is no Demodex, then something like Blephaclean. BlephEX is also used as a treatment for MGD, and a follow-up visit is scheduled after six months of initial therapy and repeated during the follow-up if needed. Scleral lenses are fitted in the clinic by a specialist contact lens practitioner who has much experience in fitting scleral lenses. In some cases, they need to involve the family doctor to test the patient for Sjögrens factors in the blood test.

In terms of steroids, they have access to powerful steroids like dexamethasone, prednisolone, and fluorometholone, in the UK. In the dry eye clinic, they use fluorometholone quite a lot because it comes in a liquid-film carrier and helps to lubricate. They also have preservative-free hydrocortisone, marketed as a Softacort, that they use often.

Professor Rumney agrees that optometrists should be allowed to use therapeutics to manage DED because management can be taken only as far as you are licensed. He thinks that one of the challenges is that if you are setting yourself up as a dry eye specialist clinic, you will get people coming to you who have been to see everybody else, so their problems are pretty severe.

> "Many of those will have active inflammation when they come to see you. You must kill that active inflammation before you can do anything else. If you establish yourself as a specialist dry eye clinic, you must somehow find access to treat inflammation."

According to Professor Rumney, dry eye practice needs to be taken to the next level, not just talking about it during routine eye examinations and suggesting lubricants without any follow-up.

The last open-ended question addressed something that interview did not include but is related to my dry eye practice. Professor Rumney mentioned the importance of dry eye management before cataract surgery to get stable refraction and accurate biometry for the cataract surgeon.

5.2.3 Discussion

Assessment consists of a symptom questionnaire (OSDI) and dry eye analyzers (LipiView and Myah) to evaluate NIBUT, TMH, LLT, blinking pattern, and meibography, followed by osmolarity measurement. With the slit lamp redness, LIPCOF, both tear meniscus height and width, FBUT, ocular surface staining (fluorescein+lissamine green), LWE, and meibomian glands are assessed.

Meibomian gland assessment is done first with a dry eye analyzer (infrared meibometry). The ducts observation with the Korb Meibomian Gland Evaluator by Tearscience provides the same force against the meibomian glands as the muscle blinking. Optometrists sometimes use paddle tweezers with anesthetics to give a more controlled squeeze deeper into the tissues, but they mainly use Lipiflow.

Management is divided into three levels (tears), all introduced at the end of the dry eye assessment to the patient in a report form. The basic level (tear one) consists of lid hygiene, wipes, and lubricants. The second level (tear two) is the more direct in-office management with, e.g., BlephEX, punctal plugs, scleral lenses, and Demodex treatments. The third level (tear three) is advanced dry eye treatment, including independent prescribing (IP) therapeutics for topical steroids, LipiFlow+IPL, or IPL alone. Management also includes discussing omega-3s and omega-7, drinking water to stay hydrated, changing the diet, environmental things like air conditioning, etc. If there is evidence of Demodex, Ocusoft Demodex treatment or Blephademodex, is used. But if there

is no Demodex, then something like Blephaclean. Unfortunately, Demodex was excluded from the literature review. Both soft bandage contact lenses and scleral lenses were also excluded because of the lack of relevant systematic reviews related to those topics.

According to Professor Rumney, the lipid layer is one of the essential things in assessing the tear film quality, which correlates with the literature review results. Professor Rumney states that it´s essential to identify the underlying cause of the ocular surface disease or the dry eye, which strongly agrees with the DEWS II report. He also points out the importance of follow-up, which correlates with the literature findings.

The last open-ended questions brought an interesting point out. Rumney mentioned the importance of dry eye management before cataract surgery to get stable refraction and accurate biometry for the cataract surgeon. That is an important note for all optometrists doing regular eye examinations with dry eye indications if cataract surgery is becoming relevant soon.

5.3 Specific Aim 3

5.3.1 Introduction

Optometrist and lecturer Erik Robertstadt, from Norway, who has over 20 years of experience in eye care, was interviewed. He has been dealing with dry eyes for 20 years and started more targeted treatments about 5-6 years ago.

5.3.2 Results

Dry eye assessment is not routinely done for everyone in general eye examinations. Only targeted questions are asked to pick up dry eye and reschedule customers for dry eye assessment for 30 minutes appointments. Both SPEED and DEQ-5 questionnaires are used in dry eye assessment.

Nowadays, Robertstadt does dry eye procedures without an assistant, and all equipment is placed in the same room. Considering advanced technology like Idra and IPL, they transfer them between

four rooms. They have meibum expression, masks, Blephasteam, a cabin full of different punctal plugs, BlephEX, etc.

Advanced technology is routinely used in dry eye examinations. According to Robertstadt, the primary benefit is that technology can be used to track progress with objective measurements.

Robertstadt points out that as a part of dry eye, we´re dealing with neuropathy and different types of neuropathies. Some patients have severe symptoms, but they can´t notice or can´t feel the improvement. It can also be vice versa that the patients will feel better, but objective measurements don´t show any progress. It´s a bit of a complexity that we are dealing with.

Dry eye assessment starts with utilizing advanced technology, the Idra, including the DEQ-5 symptom questionnaire. At the same time, Robertstadt is testing and evaluating various symptom questionnaire methods.

Ocular surface staining is evaluated by simultaneously instilling the fluorescein and lissamine green. Because of the time laps, he finds it practical to use them simultaneously. He starts with blue and yellow filters and then switches to white light to look at the lid margins to see if lissamine green shows LWE or bulbar staining. Robertstadt brings up an issue related to lissamine green quality in Nordic countries: too large molecular size shows less staining.

Tear volume is measured with TMH in three different spots and calculated the average with Idra. Sometimes Schirmquick (PRT) or Schirmer without anesthetic is used, depending on the situation. The Schirmer test is part of the diagnosis of Sjögren's Syndrome, so it is measured if the report is sent to a rheumatologist or a general doctor. Otherwise, Robertstadt prefers the PRT test, especially if advanced equipment is unavailable.

Tear film quality is measured with Idra by measuring NIBUT. Robertstadt sees that advanced technology gives the advantage of showing and explaining the situation to the patient from the video recording. FBUT is done only rarely. Tear film quality is also assessed with the slit lamp.

MGD assessment with meibography is done with the Idra and the slit lamp, which has infrared illumination. Lipid layer thickness and blink rate are evaluated with Idra. With the slit lamp, duct observation and gland expression are done together with grading the meibum quality and how

many glands express. Blink quality and blink rate are also measured. Blackie-Korb method of folding a light on the closed eye to see whether the lids are sealed or not is graded and used in dry eye examinations. During the slit lamp examination, elasticity, small or vague signs of ectropium, and blepharochalasis are evaluated.

Tear film osmolarity is measured occasionally. Before, osmolarity was always measured, but because of the variability of the results, they´ve been discontinued. Taking valid measurements without touching the conjunctiva, especially with people with aqueous deficiency, has been one reason to stop. The other problem was a patient's movement during the measurement, allowing oxygen into the bulk, making the test result invalid.

Instead of osmolarity, Robertstadt has started to measure inflammation with the MMP-9 inflammatory test before using fluorescein. Once there is a high level of MMP-9 in tears, it will tell that the eye is releasing inflammatory mediators and gives more information about the severity of the dry eye.

> "When you know the severity, you know that you must use more tools or put a more aggressive treatment."

Inflammation is also assessed by evaluating the ocular/ conjunctival redness. Robertstadt highlights that there can be a high level of MMP-9 but no staining and no keratopathy, even though keratopathy is a sign of inflammation. There can be keratopathy without an increased level of MMP-9, so according to Robertstadt, it´s not an absolute sign.

LWE is evaluated with lissamine green. LIPCOF is temporally assessed and graded. Conjunctivochalazias is also considered a more advanced form of LIPCOF because the chalazia can cover the puncta resulting in watering eyes.

Dry eye treatment consists of talking about lifestyle and recommendations connected to lifestyle. Air quality, air conditioning, computer screen use, breaks and pauses from screen use, blinking, and how screens affect blinking. He is talking about outdoor time and recommends that people with dry eyes spend more time outdoors. According to Robertstadt, talking about diet, drinking habits, coffee, tea, water, alcohol, and smoking is integral to dry eye treatment. Omega-3 supplements with a high EPA content of 1000mg per day are also recommended. Robertstadt also prefers the balance between omega-3 and omega-6.

Lid hygiene, artificial tears, moisture-retaining eyeglasses, and scleral lenses are also part of the dry eye treatment. Sometimes scleral lenses are fitted for neuropathy and Sjögrens patients, and soft bandage lenses are used. Robertstadt doesn´t prefer a warm compress and reminds us that dry eye is a chronic disease that will not disappear.

"It´s chronic. You can´t cure it. You can only make life better by adding therapies that work."

For MGD treatment, some patients consistently use Blephasteam, which includes heat and massage. But with experience, Robertstadt has ended up offering the patients the opportunity to have in-house in-practice treatments for MGD. In the case of settling for a warm compress, he highlights the importance of the correct dry eye diagnosis because selling the eye bag to patients with inflammation will only make things worse. Diagnosing inflammation and MGD is crucial before sending the patient home with a warm compress. A lukewarm washcloth is a safer option with a gentle massage.

Expression with a spatula is often combined with IPL in dry eye practice. If meibomian glands are severely obstructed, heating is done in practice by using an eye bag for seven minutes and then exchanging the eye bag for another seven minutes, followed by expression and finally use of IPL.

BlephEX is mainly used as a part of MGD treatment, sometimes only once. Thorough instructions are given for home treatment, including basic lid hygiene and Demodex collarette removal if needed. In the case of Demodex, the patient follow-up visit is after two weeks for re-treatment. Robertstadt points out that considering the lid hygiene, it´s possible to get the same result without the BlephEX, but it takes more time. First heating for 5 minutes, putting an eye bag and then massaging Blephagel into the lid margin and between the lipid lashes. Then thoroughly rinse with the lid towelette. Maybe crusts sometimes need to be removed with the forceps and then scrubbed with the lid towelette. With BlephEX, the same procedure is done faster.

IPL is also part of MGD treatment. There is a one-week interval between the first and second treatments, the second and third two weeks, and the fourth treatment is done after three weeks of the third treatment. Re-treatment is usually done between 9 to 12 months, depending on the severity.

As an AAO fellow, Robertstadt has been into many courses about inserting punctal plugs and independently inserting them for seven years. He uses lacrimal syringing, for example, to diagnose people with watery eyes. After making sure that the lacrimal is draining properly by syringing, plugs are inserted.

In Norway, optometrists don´t have the license to use therapeutics. If there is a need for anti-inflammatories, optometrists write a letter to the patient´s general practitioner or an ophthalmologist to get the patient's prescription. According to Robertstadt, often unpreserved Softacort is enough to get the patient out of the vicious circle, depending on the severity. He also highlights that IPL is known to reduce inflammation, and not always corticosteroids are needed to calm down the inflammation.

The last open-ended question about something that was not included to dry eye practice brought up an esthesiometer and measured the sensation of the cornea. Bonnet Aesthesiometer looks like a fish thread. If the thread is long, it will hit, and it´s soft, and you will not notice it. When you shorten the thread, it will be harder and cause more pain, Robertstadt explains.
Robertstadt believes there will be other future methods for quantifying sensation and pain. Another point that Robertstadt highlights are the importance of optometrists understanding neuropathy because it´s quite a large part of dry eye practice. Many patients have some level of neuropathy, and some patients will have only neuropathy. They have only symptoms and no clinical findings of dry eye, but they have all the classic symptoms.

5.3.3 Discussion

Assessment consists of a symptom questionnaire (SPEED, DEQ-5) and a dry eye analyzer (Idra) to evaluate NIBUT, TMH, LLT, blink rate, and meibography. Slit lamp examination consists of redness, LIPCOF, ocular surface staining (fluorescein + lissamine green), LWE, FBUT (rarely), meibography, ducts observation, gland expression, and blink quality. Conjunctivochalazias are also evaluated because they can result in watery eyes if puncta are covered. Occasionally PRT or Schirmer without anesthetic is used to assess tear film volume. Schirmer test is part of the diagnosis of Sjögren's Syndrome, which explains why it is used in some situations.

Considering dry eye assessment, Robertstadt brings up an issue related to lissamine green quality in Nordic countries: too large molecular size shows less staining. Delaveris et al. (2018, p. 23) study shows significant variations in clinical performance between lissamine green solutions from different manufacturers' strips showing the highest amount of LWE staining with GreenGlo and the least with Lissaver while Biotech and OPGreen were somewhere in between. Robertstadts' finding correlates with the study.

Interestingly Robertstadt mentioned the use of Blackie-Korb method of folding a light on the closed eye to see whether the lids are sealed or not as a part of the dry eye examination. Osmolarity is measured only occasionally, and the MMP-9 test has replaced it even though the DEWS II report has included osmolarity in its diagnostic test battery. Kook et al. (2020, p. 185) found out that it may be helpful to combine tear osmolarity and MMP-9 test results to determine the severity of dry eye associated with Sjögren's Syndrome. According to Robertstadt MMP-9 test gives more information about the severity of the dry eye. He highlights that it´s essential to be able to diagnose inflammation and MGD before sending the patient home with a warm compress because the heat will make it worse.

Management consists of patient education (diet, both omega-3 and omega-6, drinking habits, smoking, air quality, air conditioning, computer, and screen use, blinking, outdoor time), lid hygiene, Demodex collarette removal, artificial tears, moisture-retaining eyeglasses, and both scleral and soft bandage contact lenses, meibum expression, masks, Blephasteam, punctal plugs, BlephEX and IPL. Considering the lid hygiene, it´s possible to get the same result without the BlephEX, but it takes more time, which is one reason he doesn´t prefer warm compresses.

Robertstadt highlights that IPL is known to reduce inflammation, and not always corticosteroids are needed to calm down the inflammation. This is an interesting point to consider concerning the management order which one needs to be done first, treat inflammation, or perform IPL. If the MMP-9 test gives a positive value, should corticosteroids be used before the IPL, or is just IPL reducing inflammation enough? Future studies are needed on this topic.

From Robertstad's point of view, technology's primary benefit is the ability to track progress with objective measurements in dry eye follow-up.

Robertstadt points out that as a part of dry eye, we´re dealing with neuropathy and different types of neuropathies. Some patients have severe symptoms, but they can´t notice or can´t feel the improvement.

The last open-ended questions brought an exciting point: Robertstadt mentioned the esthesiometer and measuring the sensation of the cornea. He also highlights the importance of optometrists in understanding neuropathy because it´s quite a large part of dry eye practice. According to the literature review, esthesiometry still needs future development considering the devices, and it´s not included in the dry eye practice model even though Robertstadt pointed it out.

5.4 Specific Aim 4

5.4.1 Introduction

IP optometrist, lecturer, and private practice owner, Sarah Farrant, from the UK, who has almost 20 years of experience in eye care, was interviewed. She set up her dry eye clinic in 2005 or 2006 and has been dealing with dry eyes since then.

5.4.2 Results

Everyone who enters is screened for dry eye by filling out a questionnaire. If the patient has symptoms during a routine eye examination, they will be introduced to the concept of a dry eye clinic. The patient is given information via email or directed to their website to learn what the dry eye clinic can do for them. If the patient enters to dry eye clinic, they have either written, email, or online material, depending on which service suits the patient best. After that, they will let the patient go away, digest the information, and decide if they want to take it further.

The first dry eye appointment is one hour, and the routine regular assessment after that is half an hour. Post control is always booked because patients need long-term management considering the chronic condition, dry eye. Optometrists are doing all procedures by themselves at the clinic without assistants. The clinic has three consulting rooms and one imaging room, where all the advanced

technologies, the Myah, OCT, Optomap, etc., are. Advanced technology is utilized mainly to make assessment more objective, produce an accurate record that can be used to compare the treatments, and visualize the patient's situation.

DEQ-5 questionnaire is a part of dry eye assessment, mainly because it´s quick and easy. Farrant also has long-term records, so comparing the results is more straightforward if the format stays the same.

Ocular surface staining is evaluated mainly with fluorescein because Farrant finds lissamine green, which is inadequate for proper staining. Tear film volume was estimated to be low, medium, or excessive before the Myah. Neither the Schirmer test nor PRT test is not routinely used. Tear film quality is measured with the Myah (NITBUT, LLT) and the slit lamp with specular reflection and diffuse filter. Farrant also measures FBUT and break-up patterns.

MGD assessment is done with the Myah because it does meibography and grades that as a percentage loss. After that, she looks at the glands and uses meibomian gland forceps to express. Both as a diagnostic and therapeutic treatment. Grading the viscosity of the glands and the number of the glands expressing is essential. Also, the location of the glands if there exists any posterior migration. Farrant points out that even if the meibomian glands are visible in meibography, they might not be expressing at that point. She looks at the orifices to see if there are any cicatricial changes in the orifice structure or whether there is just la ot of posterior migration or age-related migration because those impact quite significantly on how the outflow spreads to the tear prism. Farrant also will deprive of the gold flap, and they have IPL in the clinic. She also evaluates telangiectasia and grades it visually.

Tear film osmolarity is measured with Tearlab. According to Farrant, sometimes it´s hard to gather enough of a sample, or the sample reads an error because of an air bubble in it. Touching the conjunctiva is inevitable during the measurement, Farrant concludes. Osmolarity is measured to validate the diagnosis, setting a baseline and follow-up improvement by showing the numbers to the patient.

Blink/lid closure is evaluated with the Myah and the slit lamp. Myah does an ocular protection index calculation automatically, but it doesn´t look at the pattern of the blinks, so an incomplete blink

pattern is evaluated with the slit lamp. Farrant finds esthesiometer also a hot topic that is interesting to understand in the future.

Inflammation of the ocular surface is evaluated by hyperemia and telangiectasia because Farrant finds those as the key elements to giving patients some sort of anti-inflammatory therapy. Both LWE and LIPCOF (temporally) are evaluated.

Farrant finds patient education massively vital and does it about a third of her time with the patient. She talks about environmental issues like air conditioning and pollution, drinking alcohol and coffee consumption, artificial tears, and especially blinking habits. Farrant also prefers omega-3 supplements, and she points out an interesting new supplement, turmeric, that has an anti-inflammatory effect that she is now following but not yet recommending. Lid hygiene is taken care of with advanced technology, NuLids, and BlephEX, mainly NuLids because of less aerosol generating, in six months intervals. She also inserts punctal plugs, but occasionally, if the patient is just aqueous deficient and there are no signs of inflammation.

MGD is treated in the clinic, and she oversees expression and debridement regularly once every 4-6 months, often followed by IPL with Eye-Light. IPL treatment is divided into four sessions spread apart by one month each time and re-evaluated after six months after the fourth session. After that, one session is done every six months as a long-term treatment. Warm compresses are also offered, and the recommendation considering the use is ten minutes once a day.

As an IP optometrist, Farrant uses corticosteroids as a part of dry eye treatment. Most used are Softacort and FML, or Maxitrol if there are indications of an overburden of bacterial growth. Follow-up visits after prescribing steroids are two weeks to check the intraocular pressure. Her opinion is that optometrists should be allowed to use therapeutics to treat dry eye disease.

5.4.3 Discussion

Assessment consists of a symptom questionnaire (DEQ-5) and a dry eye analyzer (Myah) to evaluate NIBUT, TMH, LLT, meibography, and blink rate; also, osmolarity is measured. Slit lamp examination consists of tear film quality evaluation with specular reflection and diffuse filter,

LIPCOF, redness, telangiectasia evaluation, ocular surface staining (fluorescein), FBUT, LWE, and break-up pattern.

Farrant points out that even if the meibomian glands are visible in meibography, they might not be expressed at that point. This is essential to note that optometrists should constantly assess the expressibility of the glands and not just rely on meibography.

Management consists of patient education (air conditioning, air pollution, drinking alcohol, coffee consumption, artificial tears, blinking habits, omega-3, and turmeric), punctal plugs, lid hygiene with mainly NuLids or BlephEX, warm compresses and IPL (Eye-Light), and corticosteroids. The core of dry eye management is to engage patients in it, and Farrant values good patient selection first.

Advanced technology is utilized mainly to make assessment more objective, produce an accurate record that can be used to compare the treatments, and visualize the patient's situation.

6 CONCLUSIONS FROM SPECIFIC AIMS

The first four questions in the expert interview addressed background information. All were optometrists and worked in private practice. Three interviewees have worked for over 20 years after graduation and one for 19 years. One has 17 years of dry eye practice experience, one has 10-15 years, and two have 5-10 years of experience.

The following six questions addressed dry eye practice setting. Half of them do dry eye assessments for everyone as a part of their routine eye examination. Two books 60 minutes for dry eye practice appointments, one for 40 minutes and one for 30 minutes. So, there is a 50% variation in appointment times. All four of them book an appointment for post-control. Three out of four do all procedures by themselves. In one practice, an optical assistant does all measurements with the dry eye analyzer in a separate room, except meibography, which an optometrist always does. Half of them have all equipment in the same examination room, and the other half has a separate room for a dry eye analyzer and other advanced technology devices. All the interviewees used advanced technology as a part of their dry eye assessment. The most common reason for utilizing advanced technology is patient education; second is monitoring and record keeping; third is getting objective measurements; fourth is identifying the actual cause of DED.

The following twelve questions addressed dry eye assessment (10 questions) and management (2 questions). Information is summarized in Table 10. Half of them use the DEQ-5 symptom questionnaire, one is using OSDI (adapted SPEED in routine eye examination), and one has developed her symptom questionnaire.

Ocular surface staining is always evaluated with fluorescein, and 50% use both fluorescein and lissamine green, one uses lissamine green rarely, and one is not using it at all. All the interviewees measured tear volume with a dry eye analyzer (Oculus Keratograph 5M, Myah, LipiView, or Idra). Only one also measures tear meniscus (TM) height and width with the slit lamp. All use the Schirmer test, and 75% sometimes use the PRT test if needed.

All use dry eye analyzer and slit lamp to assess tear film quality with NITBUT and FBUT, and one mentioned also tear break-up pattern evaluation. Only one said that FBUT is nowadays rarely used because of the advanced technology. A dry eye analyzer is used by 75% of interviewees to assess

tear film quality by measuring the LLT and 50% are using the slit lamp and specular reflection + diffuse filter to determine the color of the lipid layer. All evaluate the meibomian glands with the slit lamp and with meibography, and all evaluate blinking, 75% with a dry eye analyzer and 50% with the slit lamp. Judging by these, one considers blinking with the analyzer and the slit lamp. All evaluate LIPCOF and LWE.

Table 10. Assessment and management summary from specific aims 1-4. Table: Päivi Nokipii.

	AIM 1	AIM 2	AIM 3	AIM 4
ASSESSMENT With slit lamp	Own questionnaire Redness LIPCOF Lipid layer with specular reflection + diffuse filter FBUT Ocular surface staining - Fluorescein LWE Meibomian glands Blink/lid closure PRT or Schirmer test U-Tube (occasionally)	OSDI Redness LIPCOF TM height and width FBUT Ocular surface staining - Fluorescein - Lissamine green LWE Meibomian glands - Meibomian gland evaluator Schirmer test	Adapted SPEED, DEQ-5 Redness LIPCOF FBUT (rarely) Ocular surface staining - Fluorescein - Lissamine green LWE Meibomian glands Blink quality Conjunctivochalasis PRT or Schirmer test	DEQ-5 Redness LIPCOF Lipid layer with specular reflection + diffuse filter Telangiectasia FBUT Ocular surface staining - Fluorescein - Lissamine (rarely) LWE Tear break-up pattern Meibomian glands PRT or Schirmer (rarely)
OSMOLARITY	Yes, occasionally	Yes	No	Yes
INFLAMMATION	Yes, redness	Yes, redness + symptoms	Yes, MMP-9 + redness	Yes, redness
MANAGEMENT	Environmental issues Drinking water Omega-7 Omega-3s Lid hygiene Artificial tears Moisture retaining eyeglasses Warm compress Demodex treatment	Environmental issues Drinking water Omega-7 Omega-3s Diet Lid hygiene Wipes (Blephaclean, Blephademodex, Ocusoft demodex) Lubricants Punctal plugs Scleral lenses Demodex treatment Topical steroids	Environmental issues Drinking habits Omega-3s Smoking Blinking habits Lid hygiene Demodex treatment Artificial tears Moisture retaining eyeglasses Scleral lenses Soft bandage contact lenses Meibum expressor Punctal plugs	Environmental issues Drinking alcohol and coffee Blinking habits Omega-3s Lid hygiene Artificial tears Punctal plugs Warm compress Scleral lenses Topical steroids
ADVANCED TECHNOLOGY Why?	Oculus Keratograph 5M (TMH, NITBUT, meibography) BlephEX IPL (E>Eye) To monitor treatment outcomes and patient education	LipiView and Myah (TMH, NITBUT, LLT, blinking pattern, meibography) BlephEX LipiFlow + IPL IPL alone To identify the true cause of DED	Idra (TMH, NITBUT, LLT, blink rate, meibography) Masks Blephasteam BlephEX IPL (E>Eye) To track progress with objective measurements and patient education	Myah (TMH, NITBUT, LLT, blink rate, meibography) NuLids (mainly) or BlephEX IPL (Eye-Light) To make assessment more objective and produce accurate record and patient education

75% measure tear film osmolarity, and one explains the reason for not measuring to be invalid results. One is measuring osmolarity only occasionally because of the high cost of the tips.

All evaluate inflammation of the ocular surface by assessing the redness, but only one measures the MMP-9 inflammatory marker. Explanation of why measurement is not done seems congruent: redness is a good sign of inflammation. Everyone educates their customers/patients about their dry eyes by showing pictures of their eyes.

Dry eye management is titled as treatment in the questionnaire, but it is discussed as management in this thesis. Patient education, including discussion of environmental issues, diet, omega-3s, and drinking habits, is mentioned in all expert interviews. One said that 33% of her chair time is spent on patient education. 50% of the experts are sometimes recommending moisture retaining eyeglasses. Interestingly all are assessing blinking either with a dry eye analyzer or with the slit lamp, but only 50% are talking about blinking habits as a part of their dry eye management.

Scleral lenses are fitted in 75% of the private practices where experts are working, but only one of the experts is fitting them by himself. Due to a large amount of data, scleral lenses were excluded from the literature review. Still, based on the data from expert interviews, those are included in the dry eye practice model and soft bandage contact lenses.

75% of the experts insert punctal plugs as a part of ADDE management if there are no signs of inflammation. The one expert who doesn´t insert punctal plugs states that optometrists in Finland should be trained to insert punctal plugs and to do syringing. Considering the findings from the literature and the conclusions from the expert interviews, both confirm the decision to include punctal plugs and syringing in the future education program for optometrists in Finland. Punctal plugs and syringing are already included in the Master´s Degree in Health Care, Clinical Optometry education program, which started in Autumn 2020 at Oulu University of Applied Sciences in Finland. Akpek et al. (2019, p. 310) recommend punctal plugs after achieving tear homeostasis. If there is inflammation in the ocular surface, optometrists need co-operation with ophthalmologists in Finland before inserting punctal plugs regarding prescribing topical steroids. There was a congruent opinion that optometrists should be allowed to use therapeutics (e.g., topical steroids, cyclosporine A) as a part of DED management. According to Vehof et al. (2021, p. 92), dry eye symptoms are persistent in young adults. Combining that with the fact that the population is aging, we are dealing with a multitude of dry eye patients in the future. To meet these requirements, the role of optometrists as a part of dry eye management becomes inevitable. Based on these facts, this thesis supports the license for independent prescribing of mild topical steroids for optometrists as a part of dry eye management.

What comes to neuropathic pain in terms of assessment and management? When the customer is asymptomatic and has signs but no symptoms or vice versa, we need further research and advanced technology development to measure ocular surface sensation.

According to Fowler (2009, p. 45), sample estimates will be biased to the extent that those omitted differ from those included. Results are limited because the information from the selected experts in this survey study may vary from other experts in other countries. Sampling error exists because there were only four dry eye experts and educators from three different countries, Finland (n=1), Norway (n=1), and the UK (n=2) included, to participate in the interviews.

During the process, I started to see my ideas related to concepts in the published literature and used the literature to explain what I think, not just an imposed requirement (Harris 2020, p. 116). The dry eye practice model is developed by combining the literature data with the expert interviews' knowledge.

One problem with applying the same recommendations in Finland is that the legislation prohibits the use of topical administered therapeutic drugs for optometrists in terms of management.

6.1 Dry Eye Practice Model in Finland

The first version of the dry eye practice model (Figure 9) was developed before the expert interviews. The model was based on a complex model of an activity system (Figure 8) (Engeström, Miettinen, and Punamäki, 1999, p. 31); the information from the report of the TFOS DEWS II Diagnostic Methodology subcommittee (Wolffsohn et al. 2017, pp. 539–574) and AAOs Dry Eye Syndrome Preferred Practice Pattern (Akpek et al. 2018, pp. 286–334) which mainly follows the DEWS II report.

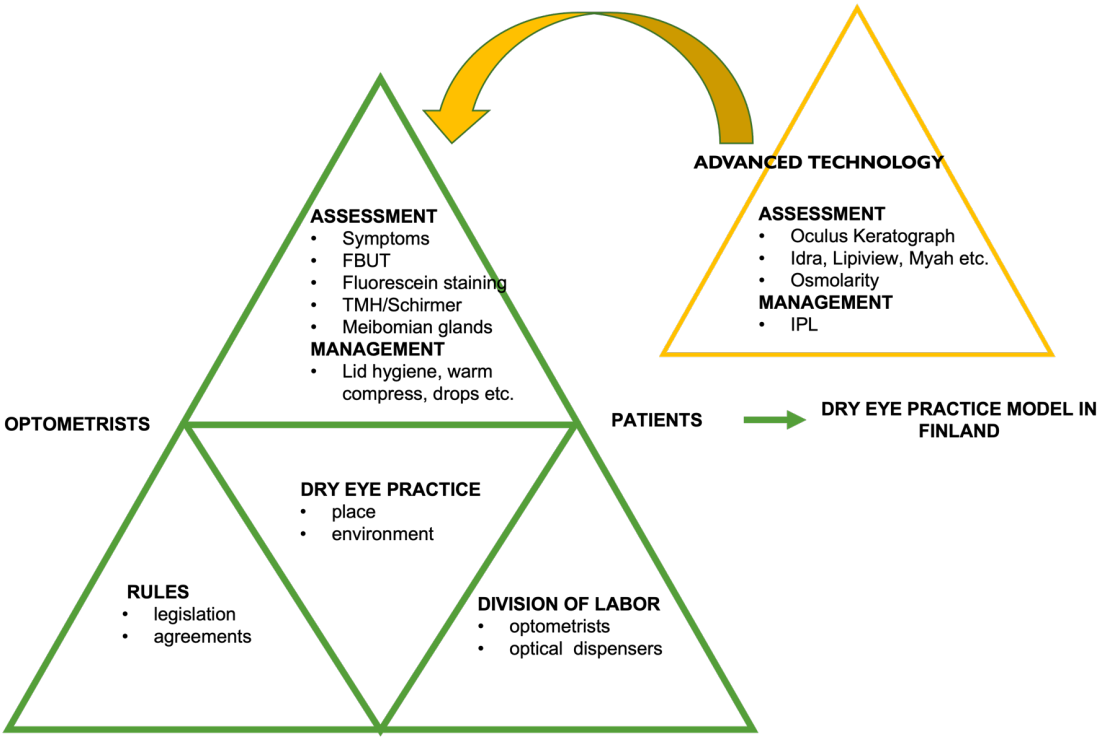


Figure 9. The first version of the dry eye practice model. Picture: Päivi Nokipii.

The first part of the dry eye practice model was developed after expert interviews and was based on the first version of the model, literature review, and expert interviews. Figure 10 illustrates the roles of the subject (optometrist) and object (patient/client) at different management levels. The optometrist's role is dominant in Level 3, and the role of the customer is dominant in Level 1. Screening and risk factor analysis are not detailed in this model because the content is like the DED diagnostic test battery and can be found in the DEWS II Diagnostic Methodology report (Wolffsohn et al. 2017, p. 561).

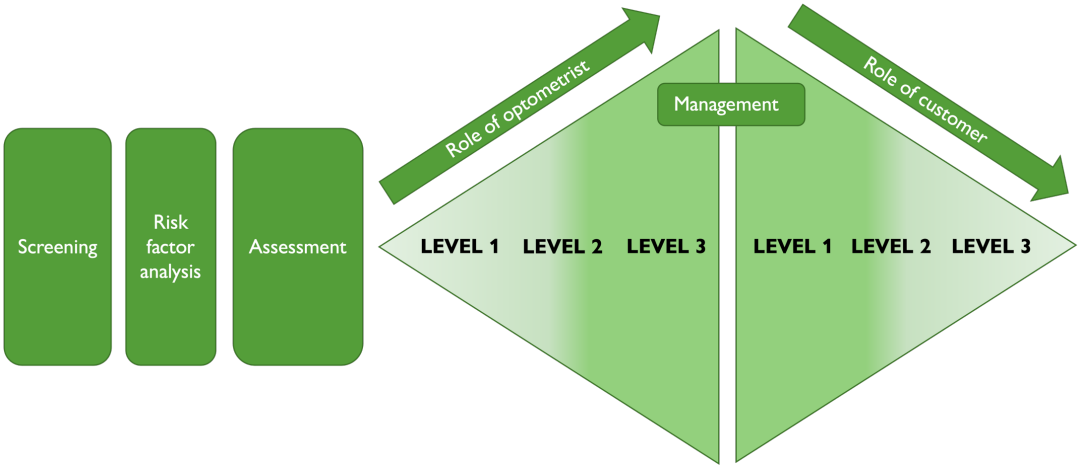
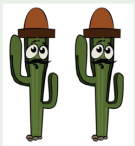
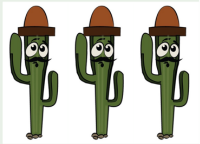


Figure 10. Dry eye practice model part 1 in Finland illustrates the roles between subject and object (subject=optometrist and object=customer). Picture: Päivi Nokipii.

The second part of the dry eye practice model includes more detailed content concerning different assessments and management in levels 1-3. It is seen in Table 11 in which assessment and management are categorized into three different levels depending on how advanced level (1-3) dry eye assessment and management has been taken. Also, the roles of the optometrist and the customer are more detailed.

Table 11. Table format of dry eye practice model in Finland. Table: Päivi Nokipii.

	Optometrist		**Customer**	
LEVEL 1	**Assessment**	**Management**	**Assessment**	**Management**
	Fluorescein staining FTBUT TMH LIPCOF Lids (+LWE) Meibomian glands Demodex	Education • Environment • Blink rate • Diet • Medication	DEQ-5, OSDI or SPEED	Ocular lubricants Blinking Drink water Less coffee, alcohol Omega-3s Lid hygiene Warm compress Demodex wipes
LEVEL 2	+	+		+
	NITBUT (Tearscope) SMTube/ PRT test Schirmer (if SS suspect) Osmolarity	Punctal plugs (if competency) Therapeutic CL* • Soft bandage • Scleral		Ocular lubricants (over-night) Regular follow-up
LEVEL 3	+	+		+
	Dry eye analyzer • NITBUT • TMH • LLT • Blinking • Meibography	BlephEX IPL+MGX for MGD		Regular in-office visits of • BlephEX • IPL+MGX for MGD

*Not included in this thesis.

Level 1 assessment is an introductory level where the only required equipment is a slit lamp combined with fluorescein strips and saline. In level 1, the role of the customer is dominant considering the management, which needs a good management plan to maintain compliance.

Level 2 assessment adds a little boost to level 1 with simple equipment like Tearscope to evaluate NITBUT, strips to evaluate ADDE by measuring tear film volume and osmolarity. Management in level 2 needs specialized training from optometrists to fit therapeutic contact lenses (soft bandage and scleral) and to insert punctal plugs. A license to use diagnostic drugs is also required at the intermediate level because there is a need for topical anesthetics. Intermediate level 2 has the exact requirements from the customer as in basic level 1, added with overnight ocular lubricants.
Level 3 is the advanced level which means adding advanced technology to dry eye practice in assessment and management. The responsibility of the customer is highly reduced concerning the management. When dry eye practice is advanced with BlephEX and IPL with MGX for MGD, there

is no need for lid hygiene and warm compress treatment at home. Another benefit of taking dry eye practice at an advanced level is saving optometrists' time because an optical assistant can perform all procedures with a dry eye analyzer if they are competent.

Considering the poor compliance to care instructions found in the literature and the expert interviews, a management plan was developed in the third part of the dry eye practice model. The management plan (Figure 11) is based on individual needs by ticking the box next to the option relevant to a particular individual.

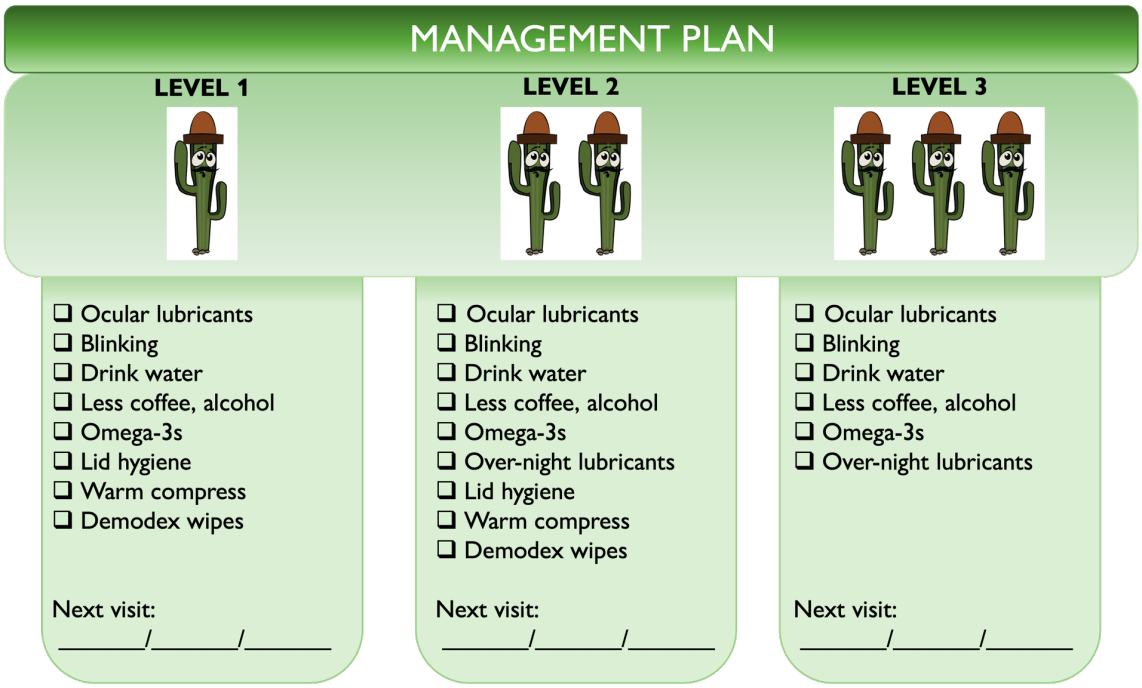


Figure 11. Management plan for dry eye. Picture: Päivi Nokipii.

A further research proposal is to develop written instructions for the customer concerning Level 1 and Level 2 lid hygiene and warm compress management.

Another future research proposal is to develop a standard in cooperation with the Finnish Standards Association SFS for dry eye assessment and management to ensure equal quality dry eye practice for all customers. That requires a multi-professional standardization group with a minimum of six members, including members from the field of dry eye, representing companies and other organizations. A national standard may eventually become an international standard. (SFS 2022).

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EXPERT INTERVIEW FORM APPENDIX 1

BACKGROUND INFORMATION (4 questions)

1. Education
    a. Optometrist
    b. Optician

2. Work setting
    a. Private practice
    b. Hospital setting
    c. Optical store
    d. Other

3. How long have you been working after graduation?
    a. 1-5 years
    b. 5-10 years
    c. 10-15 years
    d. 15-20 years
    e. Over 20 years

4. How long have you been doing dry eye practice?
    a. 1-5 years
    b. 5-10 years
    c. 10-15 years
    d. 15-20 years
    e. Over 20 years

DRY EYE PRACTICE SETTING (6 questions)

5. Do you do dry eye assessments for everyone as a part of your routine eye examination?
    a. Yes
    b. No
6. How long appointments do you book for an eye examination or dry eye workup?
    a. 30 minutes
    b. 45 minutes
    c. 60 minutes
    d. 90 minutes
    e. Other

7. Do you book an appointment for the post control?
    a. Yes
    b. No

8. Do you do all procedures by yourself?
    a. Yes
    b. No
    c. If not, who is doing and what parts of the dry eye examination?

9. Do you have all equipment in the same room?
    a. Yes
    b. No

10. Do you use advanced technology like Idra or Oculus Keratograph 5M in your routine dry eye examination?
    a. Yes
        i. Why?
    b. No
        i. Why not?

DRY EYE ASSESSMENT (10 questions)

11. Which symptom questionnaire do you use?
    a. Ocular Surface Disease Index (OSDI)
    b. Dry Eye Questionnaire (DEQ)
    c. Impact of Dry Eye on Everyday Life (IDEEL)
    d. National Eye Institute-Visual Function Questionnaire (NEI-VFQ)
    e. Dry Eye-Related Quality-of-Life Score Questionnaire (DEQS)
    f. Subjective Evaluation of Symptom of Dryness (SESoD)
    g. Standard Patient Evaluation of Eye Dryness (SPEED)
    h. None

12. How do you evaluate ocular surface staining?
    a. Fluorescein
    b. Lissamine green
    c. Rose Bengal

13. How do you measure tear volume?
    a. Tear meniscus height (TMH)
        i. With slit lamp
        ii. With advanced technology meniscometry (Strip meniscometry)
        iii. With anterior segment OCT
    b. Schirmer test
    c. Phenol Red Thread test
        1. Why the selected tests?

14. How do you measure tear film quality?
    a. With advanced technology like Idra
    b. NITBUT
    c. FBUT
    d. Slit lamp (specular reflection + diffuse filter)

15. Do you assess MGD?
    a. Yes
        i. Meibography
        ii. Interferometry
        iii. Lipid thickness
        iv. Slit lamp (duct observation and expressibility)
        v. Other
    b. No

16. Do you measure tear film osmolarity?
    a. Yes
        i. Why?
    b. No
        i. Why not?

17. Do you evaluate blink/lid closure?
    a. Yes
    b. No

18. How do you evaluate inflammation of the ocular surface?
    a. Ocular/conjunctival redness
    b. Matrix metalloproteinases (MMPs)
    c. Cytokines and chemokines
    d. Ocular surface immune markers
    e. I don´t evaluate inflammation

19. Do you evaluate the following?
    a. LWE
    b. LIPCOF
    c. Ocular surface temperature (Thermography)
    d. Tear evaporation rate (Evaporimetry)

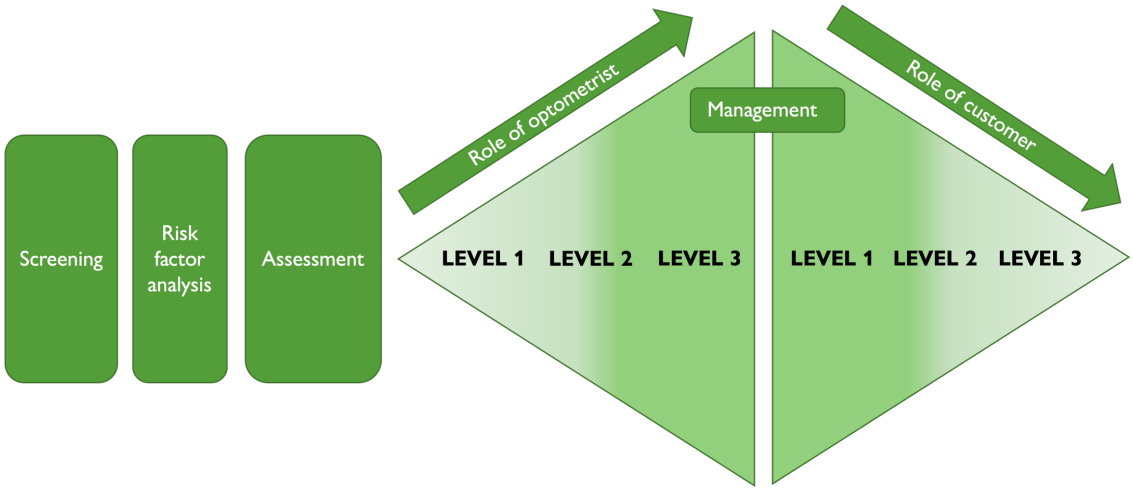
20. Do you educate the customer about their dry eye by showing pictures of their eyes?
    a. Yes
    b. No

DRY EYE TREATMENT (2 questions)

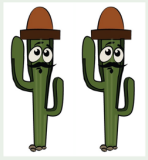
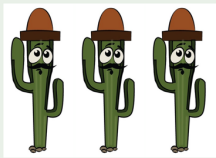
21. How do you treat dry eyes?
    a. Add moisture to the air with a cool mist humidifier
    b. Drinking water to stay hydrated
    c. Omega-3 / Omega-7 supplements
    d. Lid hygiene
    e. Artificial tears
    f. Moisture retaining eyeglasses
    g. Scleral lenses
    h. Corticosteroid eye drops
    i. Punctal plugs
    j. Other
        i. What? Cyclosporine A etc.

22. How do you treat MGD?
    a. Warm compress
    b. Expression with spatula
        i. Interval
    c. BlephEX
        i. Interval
        ii. Results
    d. IPL
        i. Interval
        ii. Results
23. What is your opinion, should optometrists be allowed to use therapeutics (i.e., topical corticosteroids, cyclosporine A) to be able to treat dry eye disease?
    a. Yes
    b. No
24. Is there something that you want to add considering your dry eye practice, that I forgot to ask?

PART 1



PART 2

	Optometrist		Customer	
LEVEL 1	**Assessment**	**Management**	**Assessment**	**Management**
	Fluorescein staining FTBUT TMH LIPCOF Lids (+LWE) Meibomian glands Demodex	Education • Environment • Blink rate • Diet • Medication	DEQ-5, OSDI or SPEED	Ocular lubricants Blinking Drink water Less coffee, alcohol Omega-3s Lid hygiene Warm compress Demodex wipes
LEVEL 2	**+**	**+**		**+**
	NITBUT (Tearscope) SMTube/ PRT test Schirmer (if SS suspect) Osmolarity	Punctal plugs (if competency) Therapeutic CL* • Soft bandage • Scleral		Ocular lubricants (over-night) Regular follow-up
LEVEL 3	**+**	**+**		**+**
	Dry eye analyzer • NITBUT • TMH • LLT • Blinking • Meibography	BlephEX IPL+MGX for MGD		Regular in-office visits of • BlephEX • IPL+MGX for MGD

*Not included in this thesis.

PART 3

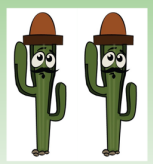
MANAGEMENT PLAN

LEVEL 1

- ❑ Ocular lubricants
- ❑ Blinking
- ❑ Drink water
- ❑ Less coffee, alcohol
- ❑ Omega-3s
- ❑ Lid hygiene
- ❑ Warm compress
- ❑ Demodex wipes

Next visit:
_____/_____/_____

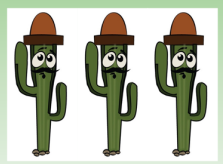
LEVEL 2



- ❑ Ocular lubricants
- ❑ Blinking
- ❑ Drink water
- ❑ Less coffee, alcohol
- ❑ Omega-3s
- ❑ Over-night lubricants
- ❑ Lid hygiene
- ❑ Warm compress
- ❑ Demodex wipes

Next visit:
_____/_____/_____

LEVEL 3



- ❑ Ocular lubricants
- ❑ Blinking
- ❑ Drink water
- ❑ Less coffee, alcohol
- ❑ Omega-3s
- ❑ Over-night lubricants

Next visit:
_____/_____/_____