University of South-Eastern Norway
Faculty of Health and Social Sciences

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Master's Thesis

Study program: MSc in Optometry and Visual Science

Spring 2020

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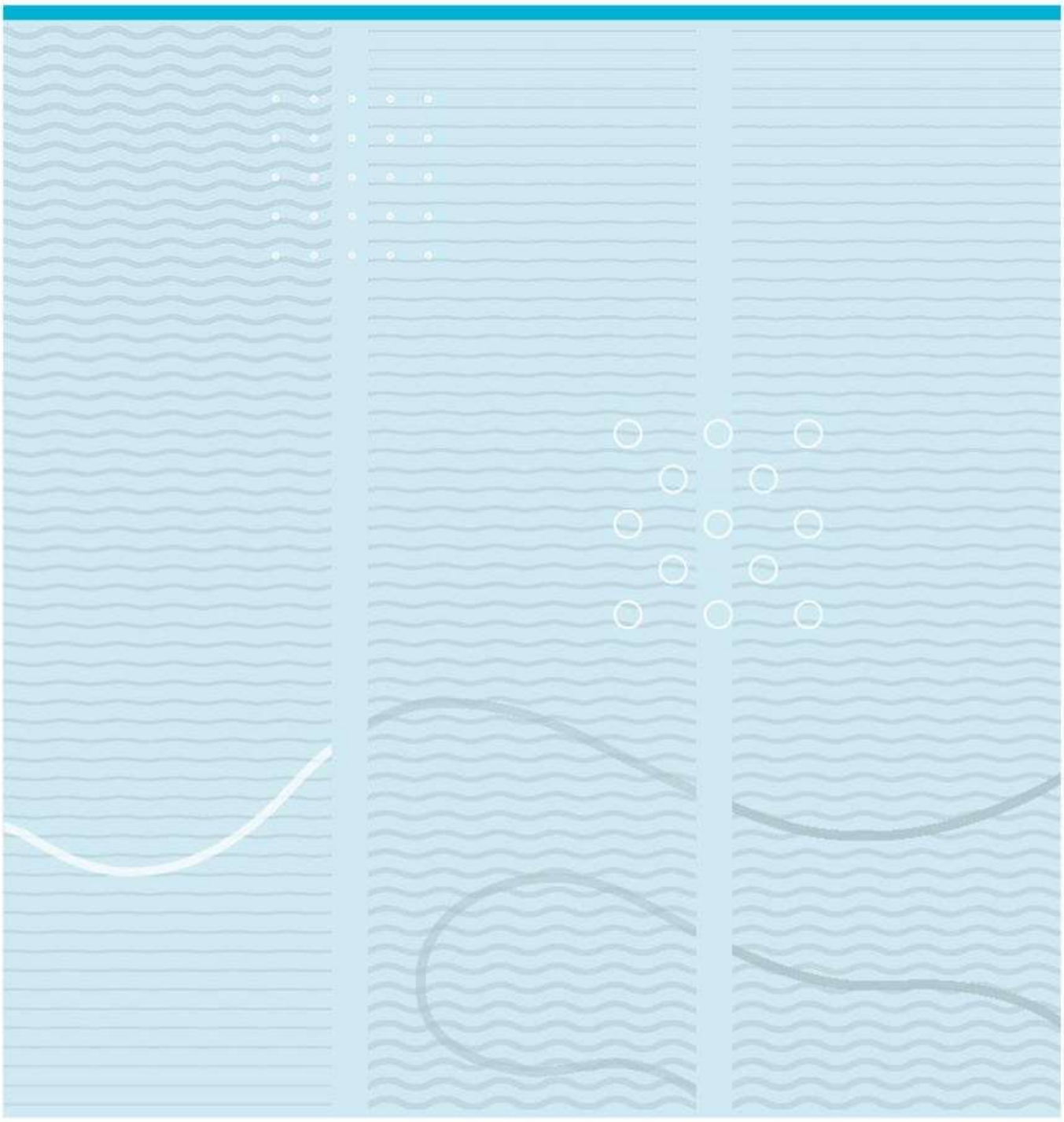
Dry Eye Disease, Dry Eye Signs and Symptoms, and Vision-related Quality of Life in people with Type 2 Diabetes Mellitus



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This thesis is worth 30 study points

Summary

Purpose

The aim of this study is to investigate dry eye disease (DED), dry eye signs and symptoms among people with type 2 diabetes mellitus (DM2), and the association between DED and dry eye signs and symptoms and Visual Quality of Life (VQoL).

Methods

This study has a cross-sectional design within the study population of people with DM2. The sample comprised people with DM2 recruited to the research project *Diabetes, Vision, and Ocular Health* at the University of South-Eastern Norway. In all, 89 participants underwent an eye examination with a dry eye work-up at the University of South-Eastern Norway during the period August 2018 to June 2019. Results are reported from the self-administered National Eye Institute Visual Function Questionnaire (NEI-VFQ-25), the Ocular Surface Disease Index (OSDI) questionnaire, and an extensive dry eye work-up according to the Tear Film and Ocular Surface Society (TFOS) Dry eye Workshop (DEWS) II report. DED was defined by an OSDI score ≥13 and the presence of a positive score for at least one of the homeostasis markers: tear film break-up time, osmolarity, or ocular surface staining. In addition, tear meniscus height, Schirmer test, and meibomian gland function were evaluated. Data were analyzed with frequency and summation tables and IBM SPSS Statistics 26 using standard statistical tests to assess group differences and associations. These included chi-square, Mann-Whitney U-test, Spearman's rho, and multivariate linear regression analysis. A p-value < 0.05 was considered significant. The study was approved by the Regional Committees for Medical Research Ethics (2018/804/REK sør-øst).

Results

The mean (sd) age of the participants was 65 (±10) years. The sample included 39 (44%) females and 50 (56%) males. Their mean duration for DM2 was 10 (±7) years. The mean (±sd) OSDI score for all participants was 8.0 (±10), and 24.9 (±10.1) and 4.2 (±3.9) for people with and without DED, respectively. In all, 16 (18%) were diagnosed with DED 95%CI [10.6, 27.5]. Most participants had at least one positive homeostasis marker:

ocular surface staining > 5; corneal spots > 9; conjunctival spots or lid margin staining > 2 mm and ≥ 25% width; positive osmolarity ≥ 308 mOsm/L in either eye; intraocular difference > 8 mOsm/L; or positive non-invasive tear breakup time (NIBUT) < 10 s. No correlations between dry eye symptoms and signs were observed. The overall mean (sd) composite NEI-VFQ-25 score was 87.43 (±10.37) and the ocular pain subscale score was 83.01 (±17.80). A Mann-Whitney test indicated that the overall composite NEI-VFQ-25 score was lower for those with DED (Mdn = 19.14) than for those without DED (Mdn = 45.0), (U =163, p < .001) and those with DED had more ocular pain (Mdn = 28.1) than those without (Mdn = 47.6), (U = 313, p = .004). In a linear regression model, adjusting age, gender, diabetes duration, and best corrected visual acuity at distance (BCVAD), DED was significantly correlated with the following NEI-VFQ-25 subscales: ocular pain, distance activities, social functioning, mental health, role difficulties, dependency, driving, and peripheral vision. In a multivariate linear regression model, adjusting for age, gender, diabetes duration and BCVA at distance, DED was an independent predictor only for the ocular pain score.

Conclusion

It was found that people with DM2 have a low prevalence of DED, but a substantial prevalence of clinical findings of DED. Symptoms and the clinical signs of DED are not associated. The correlation between DED and the composite score for NEI-VFQ-25 and the subscale score for ocular pain is fair and DED can be identified as an independent predictor of ocular pain. However, people with DM2 may have severe clinical surface damage without having symptoms. The OSDI questionnaire is not a reliable discriminative test for clinical findings of dry eye and ocular surface disease in people with DM2. Routine examination of the lids and ocular surface of people with DM2 is vital, as detection of ocular surface damage is important for early treatment and prevention of vision threatening complications.

Key words: diabetes mellitus type 2, dry eye disease, dry eye symptoms, OSDI, visual quality of life, ocular pain, NEI-VFQ-25

Contents

Foreword

I would like to thank my supervisor Vibeke Sundling for constructive feedback and invaluable help, motivation, and inspiration during the DVOH project and in writing this master's thesis. I would also like to thank Tove Lise Morisbakk and Ann Elisabeth Ystenæs for their constructive feedback and positive motivation during this project. My loving husband also deserves a great thank you for all his support and for help with programming the Visual Basic program to register the data in the project and for letting me spend so much time investigating this complex issue. Also, a great thank you to my parents for a lot of help during this period and to my children for their patience when I have been occupied collecting data and writing this thesis. And finally, I would like to thank my fellow students; Jenna Aaro, Jonas Luhr-Pettersen, Hanna Karoline Figenschau, Marina Rønning, and Aurora Bernt for collecting data together and developing discussions.

Rosendal, 28.04.2020
Siv Aaseth Sandvik

Abbreviations

ADDE	Aqueous Deficient Dry Eye
BCVA	Best corrected visual acuity
BCVAD	Best corrected visual acuity at distance
CL	Contact Lens
DED	Dry Eye Disease
DEQS	Dry Eye-related Quality of Life Score
DEWS	Dry Eye Workshop
DM	Diabetes Mellitus
DM1	Type 1 Diabetes Mellitus
DM2	Type 2 Diabetes Mellitus
DN	Diabetic Neuropathy
DR	Diabetic Retinopathy
DVOH	Diabetes Vision and Ocular Health
EDE	Evaporative Dry Eye
HRQoL	Health Related Quality of Life
LWE	Lid Wiper Epithelium
ME	Macular Edema
MMP-9	Matrix metalloproteinase - 9
NAD	Norwegian Association of Diabetes
NEI-VFQ-25	National Eye Institute Visual Function Questionnaire 25 Item
NIBUT	Non-invasive break up time
NIKBUT	Non-invasive Keratograph break up time
NPDR	Non proliferative diabetic retinopathy
OSDI	Ocular Surface Disease Index
PDR	Proliferative Diabetic Retinopathy
PN	Peripheral Neuropathy
QOL	Quality of Life
TBUT	Tear break up time
TFOS	Tear Film and Ocular Surface Society
TMH	Tear Meniscus Height
VA	Visual Acuity
VEGF	Vascular Endothelial Growth Factor
VQoL	Vision-related Quality of Life

1 Introduction

1.1 Dry Eye Disease

1.1.1 Prevalence

> 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, Nichols, et al., 2017).

The prevalence of Dry Eye Disease (DED) ranges from 5% to 50% in a normal population. It is a common symptomatic disease, with typical tear film instability and hyperosmolarity, and its consequences are increased ocular surface inflammation, damage, and neurosensory abnormalities. A higher prevalence of DED is reported among Asian populations, and the prevalence increases with increasing age. Females are known to have a higher risk of DED than males. Moderate-to-severe DED is associated with pain, limitations in performing daily tasks, reduced general health, and possible depression (Craig, Nelson, et al., 2017).

1.1.2 Anatomy, structure, and function of the tear film

The tear film is a protective and comforting layer of the ocular surface. It is the primary refracting surface when light enters the eye (Willcox et al., 2017). Tears are continuously distributed from the tear meniscus while blinking, and the tear film protects the surface from irritants, allergens, environmental extremes of dryness and temperature, potential pathogens, and pollutants. Reflex tears can help to wash irritating pollutants and pathogens away from the ocular surface effectively (Holland, Mannis, & Lee, 2013). A stable, 2–2.5 µm, preocular tear film is the hallmark of efficient ocular health. Lipids, proteins, mucins, and electrolytes are all substances important for the integrity of the tear film (Willcox et al., 2017). A three-layer model is the traditional presentation of the tear film: an outer lipid layer protects from evaporation;

underneath that is an aqueous layer, which is the largest part of the tear film; and then a mucin layer lies closest to the ocular surface to provide protection and lubrication of the cornea and conjunctiva. A newer, two-layer model describes the mucin/aqueous glycocalyx gel, which is the main part of the tear film volume and an outer lipid protective layer to avoid evaporation (Holland et al., 2013). Lipids are produced in the meibomian glands distributed in both the upper and lower eyelids, and the meibum they produce are essential for maintaining a healthy ocular surface and ensuring its integrity (Knop, et al., 2011).

The aqueous part of the tear film contains proteins, electrolytes, oxygen, and glucose, and has an average osmolarity of 300 mOsm/L. Matrix metalloproteinases (MMPs) are important for wound healing and reducing inflammation (Holland et al., 2013). MMP-9 is a particular protease that proteolyzes the tight junctions in the epithelium that lead to breakdown of the barrier of the epithelium (Bron et al., 2017). The aqueous volume is produced in the main and accessory lacrimal glands. Most of the non-reflex tears are produced in the Krause and Wolfring glands, which are the accessory lacrimal glands located in the palpebral conjunctiva of the upper eyelid (Holland et al., 2013). The main lacrimal gland is responsible for reflex tearing. Tear production is driven neurologically by a reflex loop linking the ocular surface, central nervous system stimulation, and the glands of the ocular surface (Holland et al., 2013).

The mucins in the tear film help to stabilize and spread tears by binding to the water using their high glycosylation (Willcox et al., 2017). The lacrimal gland and the conjunctival goblet cells both secrete mucin into the tear film and this protects the corneal epithelium from blinking forces, lowers the surface tension, and helps to maintain an optically smooth and uniform tear film (Holland et al., 2013). Below the tear film, on the corneal surface, the microvilli have filaments that interact with the mucin and support it forming a glycocalyx gel. The microvilli provide an anchor with a stabilizing and protective function for the cornea (Holland et al., 2013).

1.1.3 Pathophysiology of Dry Eye Disease

Several factors contribute to the pathophysiology of DED. The condition has two main subtypes: aqueous deficient dry eye (ADDE) and evaporative dry eye (EDE). These are not mutually exclusive but merge and act together where DED has a self-perpetuated nature and the pathological process is viewed as a vicious cycle (Craig, Nelson, et al., 2017). It is usual to examine the inter-reliant issues of this pathophysiology. Hyperosmolarity is a hallmark of DED, where both excessive evaporation (as a result of EDE) or reduced lacrimal secretion (caused by ADDE) lead to a hyperosmolarity state. Instability of the tear film (short break-up time) leads to drying and hyperosmolarity of the surface of the corneal epithelium. Thereafter, apoptosis, inflammation, and loss of the mucin-producing goblet cells occur. This process also involves osmotic, mechanical, and inflammatory stress, destruction of the goblet cells, and the defense system of the ocular surface will further damage the tear film. Risk factors include meibomian gland dysfunction (MGD), anterior blepharitis, contact lens (CL) wear, ocular allergy, preservatives, refractive surgery, and environmental factors such as low humidity, all of which may disrupt the tear homeostasis and initiate an entry point to the cycle of DED (Bron et al., 2017), as shown in Figure 1.

One of the most common causes of DED is MGD (Nichols et al., 2011). The International Workshop on MGD defined the condition as “a chronic and diffuse anomaly of Meibomian glands, commonly characterized by obstruction of the terminal duct and/or quantitative/qualitative changes in glandular secretion” (Nelson et al., 2011, p 1930). Challenges associated with MGD provide an entry point into the DED loop, as illustrated in Figure 1. With the absence of normal meibum, the lipid content reduces in the tear film and this lipid deficiency leads to increased evaporation, hyperosmolarity, and thereafter inflammation (Baudouin et al., 2016).

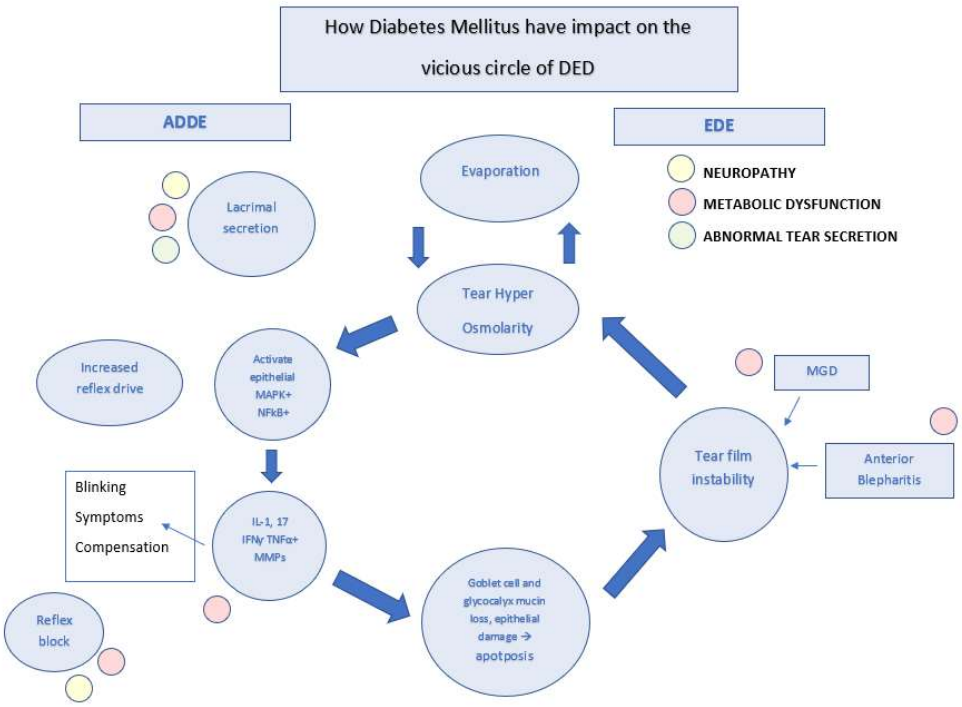


Figure 1: Impact of diabetes mellitus on the cycle of dry eye disease. Developed after the original vicious circle by Bron et al (2017).
Yellow, red, and green circles indicate that neuropathy, metabolic dysfunction, and abnormal tear secretion, respectively, have an impact on DED in people with diabetes mellitus.

1.1.4 Classifying and diagnostic methodology

The Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) ll report presents a classification scheme based on the earlier pathophysiology in which ADDE and EDE exist more as a continuum, where elements of each are considered in the diagnosis. In essence, a positive diagnosis of DED is based on both symptoms and signs, as shown in Figure 2. The main management goal for DED is to restore the homeostasis of the tear film (Craig, Nichols, et al., 2017). DED is a diagnosis of exclusion, whereby other ocular surface diseases are first excluded through triaging questions. The methodology starts with a symptom questionnaire, for example the Ocular Surface Disease Index (OSDI) questionnaire (Craig, Nichols, et al., 2017). For patients with a positive symptom score, a clinical diagnostic evaluation is recommended to establish

whether at least one positive homeostasis marker is present (Wolffsohn et al., 2017). The clinical diagnostic tests for the homeostasis markers are non-invasive break-up time (NIBUT), and osmolarity and ocular surface staining (Wolffsohn et al., 2017). Figure 2.

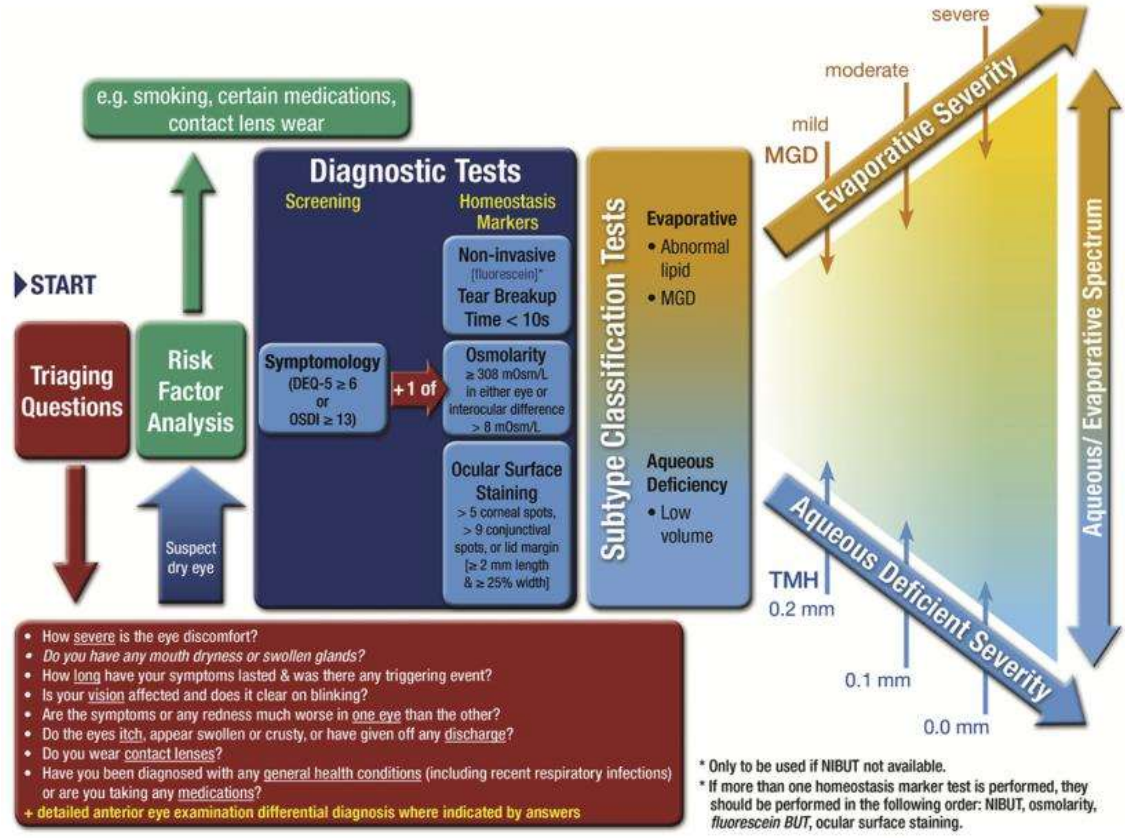


Figure 2: Dry eye disease diagnostic test battery. Obtained from (Craig, Nichols, et al., 2017).

According to the classification a patient can have DED with both symptoms and signs, be asymptomatic with signs and therefore be a pre-clinical state and predisposed to DED, or have a neurotrophic condition with reduced sensitivity (Figure 3). They can also have symptoms without signs. This is subclassified as neuropathic pain, and is not an ocular surface disease.

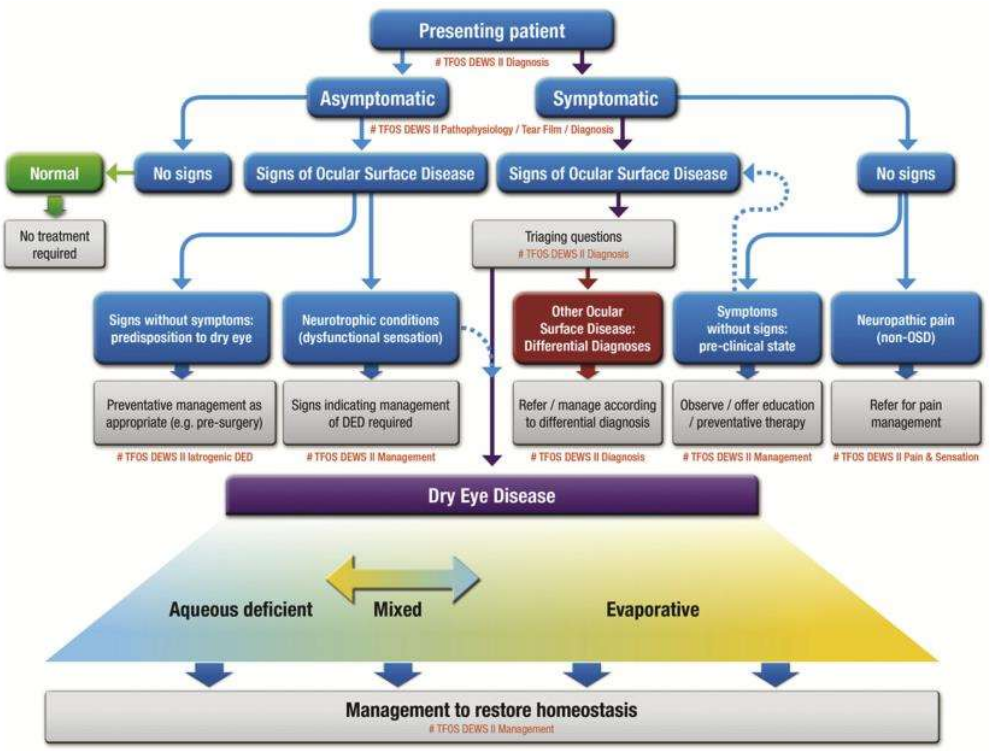


Figure 3: Classification of dry eye disease. Obtained from (Craig, Nichols, et al., 2017).

1.1.5 Risk factors

Risk factors for DED are identified in the DEWS ll report as consistent, probable, and inconclusive. Each group of risk factors is subdivided into non-modifiable and modifiable risks. For example, diabetes mellitus (DM) is a probable risk factor for DED. The following consistent risk factors are listed in the report: older age, female gender, Asian ethnicity, MGD, connective tissue disease, Sjögren syndrome, androgen deficiency, computer use, contact lens wear, hormone replacement therapy, hematopoietic stem cell transplantation, environmental factors such as pollution, low humidity, sick building syndrome, and medications, including antihistamines, antidepressants, anxiolytics, and isotretinoin (Stapleton et al., 2017).

1.1.6 Dry eye symptoms and signs

Dryness and grittiness are the most frequent reported symptoms in people with DED (Nichols et al., 2002). The association between dry eye symptoms and signs in the general population is inconsistent, and an accurate diagnosis and classification can be

challenging due to the wide variation in symptoms and the heterogenous nature of the disease (Bartlett et al., 2015). As a multifactorial disease, there is no single test that can provide a diagnosis or aid in follow-up of the progression of the disease (or its treatment). Another challenging aspect is the change in severity of clinical signs that do not correlate to the patient's symptoms (Bartlett et al., 2015).

The NIBUT, osmolarity, and ocular surface staining clinical diagnostic tests evaluate different aspects of the tear film. The NIBUT test evaluates tear film stability by measuring the time between a complete blink until the first break appears. The NIBUT test is preferred instead of fluorescein break up time, because fluorescein is invasive and can affect the tear film stability. An automated non-invasive measurement is recommended. Tear film instability has been shown to cause a variation in osmolarity, and inter-eye variation in osmolarity is associated with the severity of DED. The instability in the tear film as a consequence of high evaporation rate, excessive inter-blink interval length, or environmental factors such as air condition or windy outdoor situations can lead to a hyperosmolarity of the tear film (Wolffsohn et al., 2017).

Osmolarity measurements have been suggested as the single test that is best correlated with dry eye severity and the most preferred test for dry eye classification and diagnosis (Wolffsohn et al., 2017). However, its variability has been noted (Bunya et al., 2015) and a recent study by Tashbayev et al. stated that tear osmolarity measured with a TearLab osmometer cannot be used as a key indicator of DED (Tashbayev et al., 2020).

Staining is the last of the clinical diagnostic tests, and is used to evaluate the damage to the ocular surface, cornea, conjunctiva, and eyelid margin. Sodium fluorescein dye is most commonly used. Staining occurs when viable cells are compromised due to disruption in integrity in the superficial cell tight junctions or defective glycocalyx. lissamine green dye is equally tolerated and stains epithelial cells if the cell membrane is damaged. A solution of fluorescein (2%) and lissamine green (1%) has been found to be optimal for assessment; however, this is not available for commercial use. Corneal and conjunctival staining have been shown to be informative markers in cases of severe DED, but less so for mild and moderate dry eye. The lid wiper is a small part of upper and lower eye lid margins. It is the most sensitive conjunctival

tissue and is rich in goblet cells (Wolffsohn et al., 2017). Staining in this part of the eye with fluorescein or lissamine green is referred to as lid wiper epitheliopathy (LWE) and is suggested to be related to increased friction while blinking. This condition occurs principally in people with DED (Korb et al., 2005).

1.2 Diabetes

1.2.1 Prevalence of diabetes

The World Health Organization Global Burden of Disease Study reports that in 2010, the global prevalence of DM2 was 220 million. This is predicted to increase to 366 million by 2030 (Barsegian et al., 2018). In Norway, the prevalence of DM2 in 2017 was 216 000 (Stene & Gulseth, 08.08.2017). DM2 is a serious chronic disease with a complex range of complications and treatment, and without an efficient prevention and control program its prevalence will continue to increase globally (Dehesh, Dehesh, & Gozashti, 2019). Studies have investigated the association between diabetic retinopathy (DR), proliferative diabetic retinopathy (PDR), macular edema (ME), and vision-related quality of life (VQoL) among people with DM (Granstrom et al., 2015; Hariprasad et al., 2008; Mazhar et al., 2011; Trento et al., 2017). However, little is known about how DED and ocular pain impact VQoL for people with DM2 (Yazdani-Ibn-Taz et al., 2019).

1.2.2 Diabetic neuropathy, reduced corneal sensitivity, and diabetic keratopathy

Hyperglycemia (high blood-sugar levels) affect the cornea in three main ways, causing defective corneal endothelial pump function, poor wound healing of the corneal epithelium, and abnormalities in the sub-basal nerve plexus (Barsegian et al., 2018).

People with DM2 and diabetic neuropathy (DN) can also experience peripheral neuropathy (PN), autonomic neuropathy, and other types of neuropathy (Kalteniece et al., 2020), and DN can lead to both decreased and increased corneal sensitivity

(Barsegian et al., 2018). The corneal nerves from the nasociliary branch of the trigeminal nerve play an important protective role for the cornea and under normal conditions corneal nerves contribute to the metabolism of the epithelial cells, cell adhesion, and wound healing in response to infection, trauma, and surgery (De Clerck et al., 2020). Patients with reduced corneal sensitivity due to hyperglycemia often present without dry eye symptoms and reduced reflex-induced lacrimal secretion and blink rate. This leads to increased evaporation and a risk of DED (Bikbova et al., 2018), as shown in Figure 1. Damage to the neurons and the collection of advanced glycation end products also activate inflammation, which in turn impacts the vicious cycle of DED and leads to oxidative stress, reduced neuronal health, and myelin creation (Barsegian et al., 2018). The main clinical sign for people with PN is reduced tear break-up time (TBUT) and basal tear secretion (measured with a Schirmer's test) and decreased corneal sensitivity.

People with painful diabetic corneal neuropathy report deep pain, itchiness, and cold pain as the most frequent symptoms (Kalteniece et al., 2020), and the reported symptoms (including photophobia, ocular irritation, and pain) are similar to symptoms of DED. However, these symptoms are not necessarily correlated with the severity of corneal neuropathy (Zhao et al., 2019). Corneal neuropathy is potentially vision threatening and is one of the pathological manifestations of diabetic keratopathy. The clinical manifestations of diabetic keratopathy are reduced corneal sensitivity, recurrent corneal erosions of the corneal epithelium, dry eye, and neurotrophic corneal ulceration. (Zhao et al., 2019).

1.2.3 Diabetes and Dry Eye Disease

As previously mentioned, diabetes is a risk factor for DED and studies indicate a DED prevalence of 15%–43% among people with diabetes. For patients with poor glycemic control, dry eye symptoms are more severe (Zhang et al., 2016). In most previous studies, the prevalence of DED has been shown to be higher among people with diabetes compared with a normal population (Yoo & Oh, 2019), and dry eye symptoms have been found to be more common and severe among people with DM2

compared with people who have type 1 diabetes mellitus (DM1) (Yazdani-Ibn-Taz et al., 2019). The association between duration of diabetes and dry eye is unclear (Lv et al., 2014). Hyperglycemia leads to microvascular damage and damage to the lacrimal gland, which results in insufficient tear production, tear loss, changed tear composition, and abnormal blinking (Han, Yang, & Hyon, 2019). DM has been associated with shorter TBUT, reduced Schirmer test value, reduced corneal sensitivity, increased tear osmolarity, and increased fluorescein and lissamine green staining (DeMill et al., 2016).

The literature reports that MGD is more frequent among people with DM compared to those without DM (Shamsheer & Arunachalam, 2015). A study by Lin et al. found that the meibomian gland morphology and dysfunction (meibography, lid margin abnormalities, and meibum expressibility) were worse among people with DM2 compared to a normal control group. Thus, they proposed that MGD is more severe among people with DM2 (Lin et al., 2017). This may be explained because insulin is essential for sebaceous gland activity and decreased insulin would lead to dysfunction. Moreover, hyperglycemia is toxic and causes progressive cell loss for the meibomian gland epithelial cells (Ding, Liu, & Sullivan, 2015). In addition, damage to the corneal nerves due to neuropathy has morphological and functional consequences and in terms of functionality, reduced corneal sensitivity leads to reduced blink rate, destabilization of the lipid layer, and faster evaporation. Reduced sensitivity also influences the control of the orbicularis and Riolan's muscle, which can be a reason for increased MGD. The inflammatory response is also a suggested contributor to obstructive MGD (Lin et al., 2017).

The challenge of inconsistency between symptoms and clinical findings in a normal population for DED has a number of influencing factors for people with DM2. Factors such as hyperglycemia and HbA1c have both been shown to be positively associated with dry eye symptoms (Sandra Johanna, Antonio, & Andres, 2019). Reduced corneal sensitivity adds to the evaluation requirements of the anterior segment in people with DM2 (Lv et al, 2014). Different studies have found that various clinical tests (such as the TBUT and Schirmer tests) have been more severe for people with diabetes (Lv et al., 2014). It is suggested that osmolarity is a more discriminative test for DED

than other tests for people with diabetes (Najafi et al., 2015); however, hyperosmolarity is associated with fewer symptoms among people with DM (Fuerst et al., 2014).

Based on the DEWS ll Classification scheme (Figure 3), people with DM can potentially be identified in all categories according to symptoms and signs and be classified with DED with symptoms and signs and they can be asymptomatic with signs because of reduced sensitivity. Both conditions need management to maintain a healthy ocular surface (Jones et al,. 2017). People with DM can also be symptomatic without signs because of neuropathic pain, which is not an ocular surface disease.

1.3 Vision-related Quality of Life

The National Eye Institute Visual Function Questionnaire (NEI-VFQ) is a generic questionnaire. The 51-item field test version was designed to capture the effect of vision on several health-related quality of life (HRQoL) dimensions (Mangione et al., 2001). In this study, the shorter 25-item version was used, the NEI-VFQ-25. This questionnaire has been widely used to assess patient experience relating to visual function and emotional well-being. The 25 items are divided in subscales, using a composite score and the following 12 subscale scores: general health, general vision, ocular pain, near activities, distance activities, vision-specific social functioning, mental health, role difficulties, dependency on others due to vision, driving, color vision, and peripheral vision. Focus is required on the ocular pain subscale score for people with DED. The questions behind the ocular pain item is “How much pain or discomfort have you had in and around your eyes (for example, burning, itching, or aching)?”, and “How much does pain or discomfort in or around your eyes, for example, burning, itching, or aching, keep you from doing what you’d like to be doing?”. This has been used as an assessment instrument for people with moderate-to-severe dry eye. However, use of the NEI-VFQ-25 as a utility assessment for DED is not conclusive (Guillemin et al., 2012).

The OSDI is a dry eye-specific questionnaire and it is reliable to discriminate between normal, mild to moderate and severe DED (Schiffman et al., 2000). Together with the NEI-VFQ-25, these questionnaires provide a comprehensive assessment of

VQoL. The disease-specific questionnaire tends to be more sensitive in terms of detecting vision-focused health-related impairments, whereas the generic questionnaire can be used for a broader range of visual and ocular disorders and provides a more holistic characterization of VQoL. OSDI and ocular pain have different questions regarding to pain and it seem as they assess different aspects of symptomology (Nichols et al., 2002) It is therefore recommended that both questionnaires should be used to get a more comprehensive evaluation of VQoL (Li et al., 2012; Mangione et al., 2001; Vitale et al., 2004).

In the literature there is little information about the association between the item in NEI-VFQ-25 and DED in people with DM2. One study found that DED is associated with reduced QoL among people with DM2, where QoL is evaluated with the Dry eye-related quality of Life scores (DEQS) (Yazdani-Ibn-Taz et al., 2019). A meta-analysis based on different questionnaire than the NEI-VFQ-25 by Jing et al (2018), found that diabetes is associated with worse quality of life. In a general population in China they found that dry eye symptoms is associated with a negative effect on the composite score of VQoL and the subscale scores of ocular pain and mental health (Le et al., 2012). Another study of younger people in the Beaver Dam Offspring Study comparing people with and without dry eye, they found that the participants with dry eye symptoms scored lower on all subscales, with the largest difference for the ocular pain subscale score (Paulsen et al., 2014).

2 Aims and Research Questions

The aim of this study was to investigate DED and dry eye signs and symptoms among people with DM2. Further, associations between DED, dry eye signs and symptoms, and VQoL were explored.

The underlying research aims were to investigate the following: the prevalence of DED among people with DM2; how DED affects VQoL among people with DM2; correlations between DED and items on the NEI-VFQ-25; and how OSDI correlates with diagnostic test items among people with DM2.

This study is important due to the lack of knowledge about how DED and dry eye signs and symptoms are associated with VQoL. Type 2 diabetes is a complex disease in which hyperglycemia leads to micro- and macrovascular changes that affect the cornea, eyelid, conjunctiva, and lacrimal gland. This has impact on the clinical diagnostic and subctype clinical tests of the tear film and anterior segment, and how people with DM2 report dry eye symptoms and ocular pain. In everyday practice, people with DM2 regularly visit optometrists. This study can add valuable information on how to avoid vision-threatening complications in the anterior part of the eye. Further knowledge about DED, dry eye signs and symptoms, and the association with VQoL is of great relevance for all Norwegian optometrists.

3 Methods

3.1 Study Design

The study utilized a descriptive cross-sectional design to investigate DED and dry eye signs and symptoms among people with DM2. The study did not seek to explore causality, but merely to describe associations between signs and symptoms of DED and VQoL sub-scores among people with DM2 with and without DED.

3.2 Study Subjects

3.2.1 Study population

The population for this study was men and women with DM2 over 18 years of age.

3.2.2 Study sample

The study sample comprised participants who had been examined as part of the research project "*Diabetes Vision and Ocular Health*" (DVOH) at the National Centre for Optics, Vision, and Eye Care at University of South-Eastern Norway in the period of August 2018 to June 2019. Anyone who did not have the ability to give informed consent was excluded.

3.2.3 Recruitment

Participants were recruited from the Norwegian Association of Diabetes (NAD), at public presentations held by local branches of NAD in Hokksund, Lier, Porsgrunn, and Ski, through information leaflets available at general practices in Kongsberg, and by information about the research project at University of South-Eastern Norway web and Facebook pages. Optometrists in the nearby counties of Vestfold, Telemark, and Viken (Buskerud) helped to inform patients with DM2 about the project.

3.2.4 Size and sample

The sample (N = 89) was a convenience sample from the baseline examinations of the DVOH project. A post hoc sample size analysis was conducted, based on the ratio

of DED and no DED patients in our study (16:73) and mean values the NEI-VFQ-25 subscale for ocular pain from previous research for: patients with dry eye symptoms (69.5 ± 18.7) (Nichols, Mitchell, & Zadnik, 2002) and patients without dry eye symptoms (90 ± 15) (Mangione et al, 2001), using a precision of 5% and a power of 80%. This indicated that sample size of 44 participants was required (8 with DED, 36 without DED). This requirement was fulfilled in this study.

3.2.5 Data collection

The participants received written information (Appendix 1) and a letter of consent (Appendix 2) prior to the examination day. Written information explained the purpose of the study, its design, and ethical considerations. Before starting the examination, participants were asked if they had questions about the study. Data was collected using two questionnaires: the NEI-VFQ-25 questionnaire (Appendix 3) and the OSDI questionnaire (Schiffman et al., 2000) (Appendix 4). In addition, an extensive dry eye examination was conducted according to the TFOS DEWS II report (Wolffsohn et al., 2017).

3.2.6 The National Eye Institute-Visual Function Questionnaire-25

The NEI-VFQ-25 is a validated, generic, non-disease-specific questionnaire with 25 item questions divided in three subsections measuring non-time-specific general health and vision (Mangione et al., 2001) and challenges with activities and vision problems (Grubbs et al., 2014). For this study, I used the Norwegian version, translated by RAND Health Care. To the best of my knowledge, the Norwegian translation has not been validated; however, Jelin et al. have demonstrated that the Norwegian translation has acceptable psychometric performance (Jelin et al., 2019). The questionnaire subscales include general health, general vision, ocular pain, difficulty with near vision activities and distance activities, limitations in social functioning due to vision, dependency on others due to vision, mental health symptoms due to vision, driving, limitations with peripheral vision, color vision, and ocular pain (Nichols et al., 2002). The overall composite score, ocular pain and driving was the subscales this master thesis had mainly evaluated, and general health was not included in the analysis. For all questions, the response value was converted to a scale (0–100) and then averaged to

create subscale scores (see Appendix 7). A score of 100 represents the best and 0 the worst possible score. (Mangione, 2000). The overall composite score was calculated as an average of the subscales except for general health.

3.2.7 Ocular Surface Disease Index

The OSDI is a validated disease-specific questionnaire (Schiffman et al., 2000) with 12 questions divided into three subscales: vision-related function, ocular symptoms, and environmental trigger factors. I used the validated Norwegian translated version for this study (Sundling, personal communication). Answers were provided to the questions based on the past week's experience, and the symptoms in each of the subgroups were rated in terms of frequency and intensity on a scale of 0–4 where 0 = "*non-of the time*"; 1 = "*some of the time*"; 2 = "*half of the time*"; 3 = "*most of the time*"; and 4 = "*all the time*" (Schiffman et al., 2000). Each subscale score was summarized into a total score, multiplied by 25 and divided by the total number of questions answered. (Grubbs et al., 2014). The total composite OSDI score represents the severity of dry eye symptoms, in a range of 0–100, where 0–12 is normal, 13–22 is mild, 23–32 is moderate, and 33+ is severe.

3.2.8 The dry eye examination and sequence of tests

To minimize disturbance of the tear film, the least invasive tests were performed first, with all the tests being performed in the following order: best corrected visual acuity (BCVA), tear meniscus height (TMH), non-invasive keratograph break up-time (NIKBUT), and tear osmolarity and slit lamp evaluation of the eyelids, conjunctiva, and cornea. Then, fluorescein and lissamine green was used for ocular surface staining evaluation, and finally evaluation of the meibomian glands was conducted to assess lid morphology, meibum expressibility, and quality.

3.2.9 Test procedure and technique

3.2.9.1 Best corrected visual acuity

Best corrected visual acuity (BCVA) was measured using a Bailey Lovie (LogMar) acuity chart. The viewing distance was 6 m with a mirror system and the LogMar visual

acuity was recorded using 0.02 accuracy. If the visual acuity was LogMAR ≥ 0.2 visual acuity with a pin hole was also noted.

3.2.9.2 Tear meniscus height

Tear meniscus height (TMH) was measured using a keratograph M5 (OCULUS, Optikergeräte, GmbH, Wetzlar, Germany). The patient was seated with their chin in the chinrest and the forehead towards the head rest, focusing into the device at the light in the center of the device. A picture was taken, and the height of the tear meniscus was measured, straight below the center of the pupil, at an even part of the central lower lid margin. The magnification tool was used to enhance detection of the margins. TMH < 0.2 mm in one eye was defined as a positive sub-classification finding of dry eye.

3.2.9.3 Non-invasive break up time

A keratograph M5 TF-scan was used to measure the NIBUT. The patient was seated in the same way as for the TMH measurements. Each participant was instructed to blink naturally twice and then to keep their eyes open as long as possible. The average of three measurements of the tear-break up time for each eye was recorded. If no break or blink was recognized before the film stopped (after 25 s), this was noted. If the measurement time was too short, the measurement was retaken until three valid measurements were achieved. A NIKBUT score of < 10 s in one eye was defined as an abnormal homeostasis marker.

3.2.9.4 Tear osmolarity

Tear osmolarity was measured with the TearLab osmolarity system. The instrument was temperature-stabilized and calibrated before use. Each participant was seated comfortably with their head slightly backward looking up. A sample of 50 nL from the tear meniscus was collected from the temporal inferior eyelid margin without touching the eyelids. One test card was used for each measurement, and the ID number on the test card was matched to the same ID number on the docking. The right eye was measured first, followed by the left. The result was noted in mOsm/L. An osmolarity score in one eye of ≥ 308 mOsm/L or an inter-eye difference of > 8 mOsm/L was defined as an abnormal homeostasis marker.

3.2.9.5 Ocular surface staining

Ocular surface staining was completed using fluorescein and lissamine green dye, in subsequent order, using a Takagi 700 GL slit lamp with 16× magnification. An Optitech fluorescein sodium 1 mg, ophthalmic impregnated paper strip was used. One drop of sterile saline was used to moisten the impregnated strip and any excess of saline was shaken off and dye instilled within the temporal lid with the patient gazing upward. The eyelid was carefully pulled downwards. The ocular surface staining was evaluated 1–3 min after instillation using a cobalt blue light and a yellow barrier filter in the slit lamp.

The Lissamine green (HUB Pharmaceuticals) impregnated paper strips were used to evaluate the ocular surface for cell membrane damage (Wolffsohn et al., 2017). One drop of saline was used to moisten the impregnated strip, which was then saturated for 5 s. Any excess of saline was shaken off and the dye instilled in the same way as the fluorescein. After 1–4 min, the staining was evaluated with white light, and the temporal conjunctiva evaluated while participants looked nasally and reversed.

The Oxford Grading Scale was used to estimate both fluorescein and lissamine green staining. The exposed cornea and conjunctiva were divided into three zones: nasal, temporal conjunctiva, and cornea. Each zone was graded 0–5, where 0 = absent; 1 = minimal; 2 = mild; 3 = moderate; 4 = marked; and 5 = severe (see Figure 4), and a total sum score of 0–15 was derived. A higher number denoted more severe staining. The number of punctuated erosions between each panel was 1 log unit from A to B, and 0.5 log unit between B, C, and D. (Bron et al., 2003). Grade l (panel B) was defined ≤ 10 spots. Transition between the Oxford Grading Scale and the Diagnostic Methodology in DEWS ll was used. This indicated an Oxford grade ≥ 1 represented positive corneal surface staining with punctuated erosions > 5 corneal spots and > 9 conjunctival spots as a positive homeostasis marker (Wolffsohn et al., 2017).

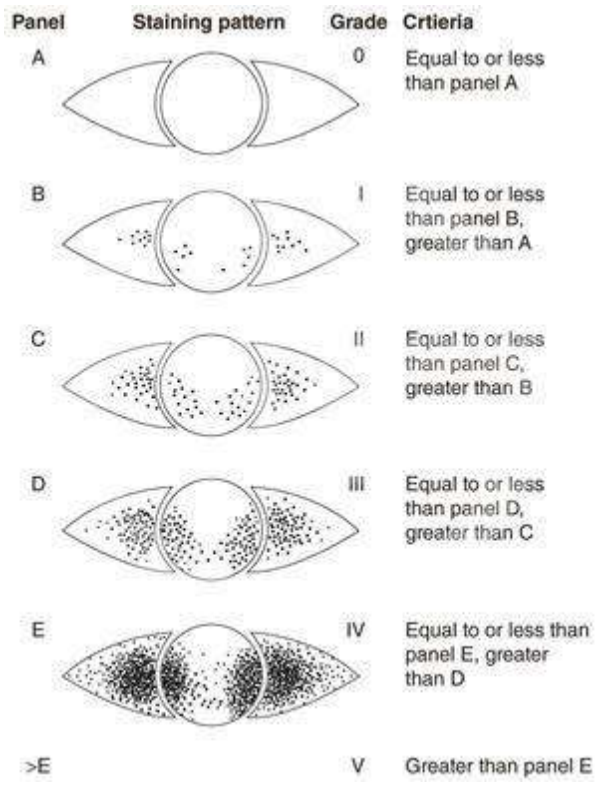


Figure 4: Oxford Grading Scale. Obtained from https://www.aao.org/detail/image.jpg?id=c712888e-5735-4e49-82ca-f1ea8760b4a1&t=635549488298130000 16.02.20 at 05:04 pm

The LWE was evaluated after lissamine green staining where the right eye was evaluated first. The upper eyelid was everted with a cotton tip (taking care to avoid contact with the lid wiper area). A slit lamp with white light and 16× magnification was used for evaluation. The horizontal length and sagittal height (width) of the lid wiper was evaluated, being careful not to include the Marx line (Korb et al., 2010). A result of LWE ≥ 2 mm length and ≥ 25% wide in one eye was defined as abnormal lid wiper epitheliopathy and was considered part of the ocular surface staining homeostasis marker according to the Diagnostic Methodology in DEWS ll (Wolffsohn et al., 2017).

In summary, a positive homeostasis marker of ocular surface staining was present if corneal or conjunctival staining was ≥ Oxford grade 1 and/or lid margin evaluation showed LWE ≥ 2 mm length and ≥ 25% wide in one eye.

3.2.9.6 Tear volume/Schirmer I test

The Schirmer strip was placed in an unanesthetized eye. At least 15 min passed between the fluorescein and lissamine green insertion and the Schirmer test evaluation. The test was performed in a dimly lit room. The patient looked up and the strip was placed in the conjunctival sac between the middle and the outer 1/3rd. A strip was inserted in the right eye first, then the stopwatch started; thereafter, another strip was inserted in the left eye. The strips were placed in the eyes for 5 min with the eyes closed and then removed from the right eye first. A measurement of < 10 mm was defined as a positive sub-classification finding of dry eye. If the eyes were wetted with > 10 mm reflex tears after few minutes, a note ("too many reflex tears") was made.

3.2.9.7 Meibomian gland dysfunction

Meibomian gland dysfunction was evaluated based on the expressibility and quality of the meibomian gland.

Meibomian gland expressibility was evaluated by first wiping the lid margin clean with the tip of a cotton bud and then squeezing the five central meibomian glands of the lower central eyelid with the tip. Expressibility was evaluated based on the glands releasing meibum on a scale of 0–3 and the highest score being used in the analysis. Scores were as follows: grade 0: 5 glands were expressible; grade 1: 3–4 glands were expressible; grade 2: 1–2 glands were expressible; and grade 3: no glands were expressible (Tomlinson et al., 2011).

Meibomian quality was evaluated at the same time as expressibility, squeezing the eight central meibomian glands in the lower eyelid. The pressure used was the same as a normal blink. The quality was graded for each gland on a scale of 0–3, as follows: grade 0 = clear fluid; grade 1 = cloudy fluid; grade 2 = cloudy particulate fluid; and grade 3 = toothpaste consistency (Tomlinson et al., 2011). The score for all eight glands were summed, and the total score (ranging 0–24) was given.

MGD was defined by treatment stage 2 MGD, based on the MGD report: meibum expressibility grade 1 and higher, and meibum quality score ≥ 4 (Tomlinson et al., 2011).

3.2.9.8 Dry Eye Disease

The Dews ll Diagnostic Methodology scheme was used to diagnose DED. A diagnosis was made if OSDI ≥ 13 and at least one positive or abnormal homeostasis marker was present in one eye: NIKBUT < 10 s or osmolarity score ≥ 308 mOsm/L or inter-eye difference > 8 mOsm/L or positive ocular surface staining punctuate erosions > 5 corneal spots, > 9 conjunctival spot, or lid margin staining ≥ 2 mm length and ≥ 25% wide (Wolffsohn et al., 2017).

3.3 Data Entry and Verification

The test results were noted by hand in the registration booklet (Appendix 5). Thereafter, the data and questionnaire responses were registered in Excel using a Visual Basic entering program. The data were controlled by visual inspection with regards to missing data and outliers. Punching errors were not checked; however, the data was examined for missing values.

3.4 Data Analysis

Data were analyzed using Excel and IBM SPSS Statistics version 26. New variables were calculated in Excel and SPSS. DED was defined according to the DEWS II report (Wolffsohn et al., 2017) and the OSDI score, and NEI-VFQ-25 scores were calculated according to the manuals (Appendix 6, also see Mangione, 2000). Frequency and summation tables were used to present the data, which were not normally distributed. Mann Whitney U test and Chi-square and Fischers' exact tests were used to compare groups. The strength of associations was evaluated with Spearman bivariate correlation analysis. A correlation of 0–0.25 indicated little or no relationship, correlation of 0.25–0.50 is considered a fair degree of relationship, 0.50–0.75 is moderate-to-good, and correlation greater than 0.75 is considered very good-to-excellent (Dawson & Trapp,

2004, p. 48). A multivariate linear regression analysis was applied to adjust for age, gender, diabetes duration, and best corrected visual acuity at distance (BCVAD) in the analysis of associations.

3.5 Ethical Considerations

The research was carried out in accordance with the guidelines in the Declaration of Helsinki (Code of Ethics of the World Medical Association) and the study was approved by the Regional Committee for Medical Research Ethics for the Southern Norway Regional Health Authority (REK), (2018/804/REK sør-øst) (Appendix 8). The participants received written information and gave informed consent before the examination. The participants could ask questions and leave the study or withdraw their consent at any time if they wanted without explanation. None of the examinations were associated with risk or danger. When needed, the participant was recommended to follow up and seek advice based on the findings for DED, and a referral to ophthalmologists if required. The participants also received a full eye examination including evaluation of visual function, the lens, and posterior as part of the DVOH study. All information was treated confidentially. The data used for statistical analysis did not contain personal sensitive information. The participants were given an ID number and the list with the identification key was kept separately from the collected data. The identification key will be deleted when the project is ended.

4 Results

In total, examinations were conducted with 89 participants with DM2, of whom 39 (44%) were female and 50 (56%) were male. The mean age (sd) was 65 (±10) years, with a range of 37–82 years. The mean duration of diabetes was 10 (±7) years, with a range of 0–36 years. Further, 16 (18%, 95% CI [10.6, 27.5]) had DED, of whom 8 (50%) were female. The mean (sd) BCVAD was logMAR -0.09 (±0.13) (equivalent to Snellen VA 1.25+). Five participants were CL users, and none of them had DED. There was no statistically significant difference in age, gender, diabetes duration, or BCVAD between participants with and without DED.

4.1 Dry Eye Symptoms

The mean (sd) OSDI score for all participants was 8 (±10); whilst for participants with and without DED the scores were 25 (±10) and 4 (± 4), respectively. In total, 16 (18%) reported dry eye symptoms (OSDI score ≥ 13). All had DED, of whom 10 (63%) had mild, 2 (13%) had moderate, and 4 (25%) had severe dry eye symptoms.

There was no significant difference in severity of dry eye symptoms between females (Mdn = 47) and male (Mdn = 43), U = 863 (p = .433). A Mann-Whitney test indicated that females scored higher (Mdn = 54) than men (Mdn = 40), U = 625, p < .001) on the subscale environmental trigger. There was no correlation between OSDI score and age, diabetes duration, or BCVA at distance.

4.2 Dry Eye Signs

The majority of participants (*n* = 85, 95%), had at least one positive homeostasis marker for DED, as shown in Table 1 Participants with DED had more staining, more inter-eye variability and increased osmolarity, but less frequently reduced NIKBUT than participants without DED. However, there was no statistically significant difference in frequency of positive homeostasis markers between participants with and without DED.

There was no correlation between the dry eye symptoms (OSDI ≥ 13) and signs (staining, osmolarity ≥ 308 mOsm/L, NIKBUT < 10 sec, Schirmer test < 10 mm or TMH < 0.2 mm). There was a positive correlation between having at least one positive homeostasis marker present and participant age (r_s = - 0.223, p = 0.036). There was no correlation between having at least one positive homeostasis marker present and gender, diabetes duration, or BCVAD. Staining had a weak negative correlation with age (r_s = -.216, p = 0,043) and diabetes duration (r_s = -0.252, p < 0.017). However, when adjusting for CL wear in a multivariate linear regression, the correlation between age, diabetes duration, and staining was no longer significant. There was no statistically significant correlation between NIKBUT and osmolarity with age, gender and diabetes duration. There was a weak negative correlation between NIKBUT and BCVAD (r_s = -0.290, p < 0.007).

In total, 22 (25%) participants had three positive homeostasis markers, of whom 82% did not have dry eye symptoms (OSDI score ≥ 13); therefore, they did not meet the DED diagnostic criteria defined by the TFOS DEWS ll report.

With regard to dry eye subtype classification signs, 31 (35%) had MGD and participants with DED had more frequent signs of MGD than those without DED (56% versus 30% (X^2 (1, N = 86) = 3.951, p = .047)). However, the correlation between MGD and DED was little (r_s = 0.214, p = 0.048). There was no correlation between DED and any of the other clinical tests: staining, osmolarity, NIKBUT, TMH, and Schirmer. Moreover, there was no correlation between MGD or TMH and age, gender, diabetes duration, or BCVAD.

Table 1: Clinical findings for dry eye signs in participants with and without DED, n (%).

Clinical findings	All (n = 89)	DED (n = 16)	No DED (=71) [e]
Positive marker[a,d]	85 (96)	16 (100)	68 (96)
Staining[d]	66 (74)	13 (81)	51 (72)
Osmolarity[d]	50 (56)	10 (63)	39 (55)
NIKBUT[d]	47 (53)	6 (38)	41 (58)
MGD ≥ 2 [b,d,*]	31 (35)	9 (56)	21 (30)[d]
TMH < 0.2 mm[c]	12 (14)	2 (13)	8 (11)[f]
Schirmer < 10 mm[f]	57 (64)	10 (63)	46 (65)

Abbreviations: DED; Dry Eye Disease, OSDI; Ocular Surface Disease Index, NIKBUT; Non-Invasive Keratograph Break Up Time, MGD; Meibomian Gland Dysfunction, TMH; Tear Meniscus Height. [a] Positive marker: positive findings of one or more homeostasis markers; Staining (LWE ≥ 2 mm in length and ≥ 25% width or > 5 corneal spots or > 9 conjunctival spots), Osmolarity ≥ 308 mOsm/L in one eye or intraocular difference > 8 mOsm/L or NIKBUT < 10 sec. [b] Meibum quality ≥ grade 4 and expressibility ≥ grade 1. [c] TMH < 0,2 mm, Missing data for [d] 1, [e] 2 and [f] 3 participants. *Statistically significant different mean DED vs no-DED Mann Whitney U test p < 0,05.

4.3 Vision-related Quality of Life

The mean (sd) NEI-VFQ-25 composite score was 87 (± 10). The mean (sd) of the subscales ocular pain and driving were 83 (±18) and 87 (±18), respectively. Participants with DED had scores that were statistically significantly lower for all subgroups except

near activities and color vision (Mann-Whitney U test, $p < 0.05$), as shown in Table 2. In a multivariate linear regression model, adjusting for age, gender, diabetes duration, and BCVAD, participants with DED scored statistically significantly lower for all subgroups except for general vision, near activities, and color vision.

Table 2: Mean (sd) NEI-VFQ-25 subscale scores for participants with and without DED.

	All (n = 89)	DED (n = 16)	No DED (n = 71)
General Vision*	76 (13)	68 (14)	77 (12)
Ocular Pain**+	83 (18)	68 (25)	86 (14)
Near Activities	82 (16)	73 (22)	83 (14)
Distance Activities**+	84 (14)	74 (18)	86 (12)
Social Functioning*+	94 (12)	85 (20)	96 (8)
Mental Health***+	87 (11)	74 (19)	90 (6)
Role difficulties***+	81 (18)	64 (20)	85 (16)
Dependency**+	97 (11)	88 (22)	99 (5)
Driving*+,a	87 (18)	73 (33)	90 (11)
Color Vision	96 (11)	91 (18)	97 (8)
Peripheral Vision*+	88 (17)	78 (24)	90 (15)
Composite score***,a,b	87 (10)	76 (16)	90 (7)

Abbreviations: NEI VFQ-25; National Eye Institute Visual Function Questionnaire-25, DM2; Diabetes mellitus type 2, DED; Dry Eye Disease, SD; Standard deviation. Statistically significant different between participants with and without DED Mann Whitney U test *p < 0.05, **p < 0.01 and *** p < 0.001. +Statistically significant correlation with DED when adjusted for age, gender, diabetes duration and best corrected visual acuity. [a] Missing data for 7 participants. [b] Missing data for 2 in DED and 5 in no-DED

There was a fair correlation between DED and the composite score and the ocular pain subscale score, and a little correlation with the driving subscale score. Table 3 shows the correlation between VQoL and DED, OSDI score, and having at least one positive homeostasis marker present.

Table 3: Correlation between NEI-VFQ-25 subscale scores and DED and OSDI score

	DED	OSDI score	One or more positive homeostasis markers
General Vision	-0.259*	-0.310**	-0.077
Ocular Pain	-0.314**	-0.416***	-0.148
Near Activities	-0.182	-0.408***	-0.117
Distance Activities	-0.277**	-0.391***	-0.013
Social Functioning	-0.240*	-0.277**	-0.005
Mental Health	-0.466***	-0.565***	-0.147
Role difficulties	-0.399***	-0.458***	-0.097
Dependency	-0.367***	-0.315**	-0.071
Driving[a]	-0.234*	-0.333**	0.017
Color Vision	-0.151	-0.055	-0.078
Peripheral Vision	-0.229*	-0.290**	0.093
Composite score	-0.426***	-0.614***	-0.070

Abbreviations: NEI VFQ-25; National Eye Institute Visual Function Questionnaire-25, DED; Dry Eye Disease, OSDI; Ocular Surface Disease Index. Statistically significant correlation *p < 0.05, ** p < 0.01 and *** p < 0.001. [a] Missing data for 7 participants.

A multiple linear regression was calculated to predict ocular pain and driving subscale scores based on age, gender, diabetes duration, BCVAD and DED, as shown in Table 4. A significant regression equation was found for ocular pain ($F(5,78) = 3.248$; $p = .010$), with an R^2 of .172. Participants' predicted ocular pain score was equal to 90.9 – 20.1 (DED) where DED is coded as 0 = no DED, 1 = DED. Participants ocular pain score decreased 20.1 points when DED was positive. DED was the only significant predictor for the ocular pain score. A significant regression equation was also found for driving ($F(5,71) = 6.367$; $p < .001$), with an R^2 of .310. Participants' predicted driving score was equal to 82.5–54.9 (BCVAD) -11.9 (DED) where BCVAD is measured in log unit and DED is coded as 0 = no DED, 1 = DED. Participants' driving score decreased 54.9 points for each log unit of decrease in BCVAD and 11.9 when DED was positive. Both BCVAD and DED were significant predictors for the driving subscale score.

Table 4: Bivariate and multivariate linear regression summary for DED prediction NEI-VFQ score.

	Unadjusted parameter estimate[a]			Adjusted parameter estimate[b]		
	B	SE B	P	B	SE B	p
General Vision	-9.7	3.4	0.006	-6.7	3.6	0.070
Ocular Pain***	-18.3	4.6	0.000	-20.1	5.2	0.000
Near Activities	-9.9	4.4	0.028	-7.7	4.8	0.113
Distance Activities*	-11.9	3.7	0.002	-8.5	3.9	0.034
Social functioning*	-10.4	3.1	0.001	-7.0	3.4	0.040
Mental Health***	-15.5	2.8	0.000	-12.1	2.6	0.000
Role Difficulties***	-20.8	4.6	0.000	-21.8	5.1	0.000
Dependency**	-11.3	2.8	0.000	-8.9	2.8	0.002
Driving*	-16.5	5.0	0.001	-11.9	5.2	0.026
Color Vision	-6.2	3.0	0.039	-2.5	3.1	0.431
Peripheral Vision*	-12.4	4.7	0.009	-11.4	5.0	0.025
Composite score***	-13.7	2.7	0.000	-11.6	2.8	0.000

[a]A bivariate linear regression model for prediction of NEI-VFQ score based on DED

[b]A multivariate linear regression model for prediction of NEI-VFQ score based on DED, BCVA, age, gender and diabetes duration. Statistically significant correlation *$p < 0.05$, ** $p < 0.01$ and *** $p < 0.001$

5 Discussion

To the best of my knowledge this study is the first to evaluate DED among people with DM2 based on the diagnostic methodology from the TFOS DEWS II report.

5.1 Prevalence

The prevalence of DED found in this study (18%) is in the lower range described previously among people with DM2. Previous studies have reported a prevalence among people with diabetes, ranging from 15%–55% (De Freitas et al., 2020; Ma et al., 2018; Olaniyan et al., 2019; Yazdani-Ibn-Taz et al., 2019; Zhang et al., 2016; Zou et al., 2018).

Comparing the prevalence among people with DM2 here to other studies using the same diagnostic criteria for dry eye symptoms (OSDI ≥13), (Olaniyan et al., 2019; Yazdani-Ibn-Taz et al., 2019), this study demonstrated the lowest prevalence. The highest prevalence (55%) was found in the Glasgow study, in which participants were younger with a longer duration of diabetes. Two Chinese studies, (Ma et al., 2018; Zou et al., 2018) demonstrate similar prevalence as in this study, at 17.5% and 20%, respectively. However, the diagnostic criteria applied in these studies were different. Zou et al. used different symptom evaluation and diagnostic tests, and Ma et al. used stricter NIKBUT criteria (NIKBUT ≤ 5 s). Because of the high frequency of positive homeostasis markers in the current study, a stricter NIKBUT criteria would probably have had little impact on prevalence. It should also be noted that the participants in the study by Ma were also older and had diabetes for a longer time than participants in this study.

No difference in frequency of DED between gender was observed in this study. This is supported by other studies including people with diabetes (Fuerst et al., 2014; Kaiserman et al., 2005; Manaviat et al., 2008; Olaniyan et al., 2019). It is suggested that the difference in DED between genders found in a normal population (where DED is more frequent in females) (Schaumberg et al., 2013; Sullivan et al., 2017) is neutralized among the diabetes population due to late complications of the diabetic disease (Olaniyan et al., 2019).

No association was found in this study between DED and duration of diabetes. This is supported by the work of Yazdani et al (2019). and Olaniyan et al. (2019), both having used the same diagnostic criteria for dry eye symptoms (OSDI). In contrast, a study by Manaviat found a significant association between the duration of diabetes and DED (Manaviat et al., 2008); however, they used less strict clinical diagnostic criteria (TBUT < 15 s or Schirmer < 15mm in 5 min) and the prevalence of DED was based on clinical signs and not symptoms. The DED diagnostics in this study (compared with the current study) may have overestimated the prevalence of DED. This will influence the association between DED and duration of diabetes. Manaviat et al. did not state whether there was a positive or negative association between DED and diabetes duration.

In this study, DED is diagnosed based using the DEWS ll Diagnostic Methodology. Dry eye symptoms (OSDI score ≥ 13) provide the first indicator for diagnosing DED and a positive symptom score is the trigger for a more detailed ocular surface examination for dry eye clinical signs (Craig, Nelson, et al., 2017).

5.2 Dry Eye Symptoms

Mild symptoms were the most frequent reported grade of dry eye symptoms in the current study. This is supported by findings in the study by Yazdani-Ibn-Taz et al. (2019), in another DM2 population. The frequency of dry eye symptoms (OSDI ≥ 13) in the current study corresponds with findings from a study of people with DM2 in Iran (Najafi et al., 2013) and Nigeria (Olaniyan et al., 2019), but is lower than in the study from Glasgow (Yazdani-Ibn-Taz et al., 2019). Here, no association was found between dry eye symptoms and age, gender, or duration of diabetes. This supports the findings from previous studies with respect to age and duration of diabetes (Olaniyan et al., 2019; Yazdani-Ibn-Taz et al., 2019). The low prevalence of dry eye symptoms in the current study may reflect reduced corneal sensitivity as a late complication of diabetes (De Clerck et al., 2020). Hyperglycemia can cause damage in the peripheral nerves and decrease corneal sensitivity. Decreased sensitivity is related to the severity of diabetes

(Yoo & Oh, 2019) and with PN (Hom & De Land, 2006). It is known from previous studies that corneal sensitivity among people with diabetes is lower than in a normal population (Lv et al., 2014). Here, all participants with dry eye symptoms had dry eye findings, and the majority of those with dry eye signs did not have dry eye symptoms.

These findings are supported by DeMill et al., who discovered many signs and few symptoms of dry eye disease among people with DM and peripheral neuropathy. They also observed a non-statistically significant decrease in dry eye symptoms among people with severe peripheral neuropathy compared to those with mild or no peripheral neuropathy (DeMill et al., 2016). Since peripheral neuropathy is the most common complication associated with diabetes affecting 50% of those with diabetes (Pasnoor et al., 2013), it is likely that some participants in the current study may have peripheral neuropathy. However, the association between peripheral neuropathy and dry eye symptoms is not clear (DeMill et al., 2016).

People with peripheral neuropathy have more severe dry eye than those without peripheral neuropathy (Yoo & Oh, 2019). Unfortunately, this study did not assess corneal sensitivity and it was not possible to assess the relationship between dry eye symptoms and corneal sensitivity. Nevertheless, this illustrates a challenge of diagnosing dry eye among people with diabetes. Najafi et al. state that OSDI is not a good screening test for DED among people with diabetes due to its low diagnostic sensitivity (Najafi et al., 2015). DEWS ll stated that DED may be underestimated among people with DM, when self-reported symptoms are used as outcome variable (Stapleton et al., 2017). In cases were the patient has a negative symptom score (OSDI < 13) and positive findings of homeostasis markers, patients will not be diagnosed with DED. However, it is recommended to consider dry eye management for these patients (Craig, Nichols, et al., 2017).

5.3 Dry Eye Signs

Some studies of the diabetes population have only used clinical examination as the diagnostic criteria for DED (De Freitas et al., 2020; Najafi et al., 2015). Further, Stapleton et al. state that in a normal population, diagnosis based on only clinical findings gives a higher and more variable prevalence of DED because of poor repeatability of the tests, variation in measurement techniques, different cut-off values,

and differences in population characteristics (Stapleton et al., 2017). In a DM2 population, because of low diagnostic sensitivity symptom assessment, the same generalizations may not be valid. Using the same clinical criteria as diagnostic cut-off as used by Najafi (osmolarity ≥ 308 mOsm/L) or De Freitas (Schirmer I ≤ 10 mm one eye), the prevalence of DED in the current study would be higher than when considering OSDI as the first diagnostic step. Using osmolarity as a diagnostic criteria, the prevalence in the current study and the study by Najafi would be 56% versus 27.7%, respectively.

This study also considered inter-eye variability in osmolarity of > 8 mOsm/L as a diagnostic criterion and may therefore include more participants compared to the study of Najafi. However, inter-eye variability is stated to be greater among people with DED compared to those without (Wolffsohn et al., 2017), supporting the higher frequency in this study. Moreover, using the same diagnostic criteria as De Freitas (Schirmer I ≤ 10 mm one eye), the prevalence in our study would be 64% versus 38.3%, respectively. Age may also explain the higher frequency of dry eye signs in this study compared to the studies by Najafi and De Freitas, since the participants in these studies were younger. The current study found a positive correlation between age and the manifestation of one or more positive clinical homeostasis markers; it is the case that the frequency of clinical signs among a normal population increase with increasing age (Craig, Nelson, et al., 2017). Duration of diabetes was similar for all studies. However, other diabetes-related differences (such as HbA1c level, the severity of diabetes, and hyperglycemia) may also explain the differences (Ma et al., 2018; Yoo & Oh, 2019).

In this study, almost all participants had one (or more) positive homeostasis marker (osmolarity, NIBUT, and staining) or other signs of DED (Schirmer, TMH, and MGD). Ocular surface damage (staining) was the most frequent clinical finding and thereafter reduced tear volume, measured by Schirmer test (< 10 mm), and an increased tear osmolarity or difference in osmolarity between the two eyes (≥ 308 mOsm/L or an inter-eye difference > 8 mOsm/L). Clinical signs in dry eye often underestimate the severity of the condition (Guillemin et al., 2012). It would appear for people with diabetes this is not true. Because of changes in the cornea's morphological, physiological, metabolic, and clinical state, people with DM have greater risk of corneal

abnormalities (such as superficial punctuate keratitis and recurrent corneal erosions) than the normal population. They also demonstrate slower and delayed corneal wound healing (Misra, Braatvedt, & Patel, 2016). To some extent, this may explain the high frequency of corneal staining observed in this study, which is supported by a study of Sandra Johanna et al., who found that lissamine green staining was significantly higher among those with DM2 compared to a healthy control group. Compared to a normal population with DED, the prevalence of corneal staining with fluorescein in this study was higher than in people with mild-to-severe dry eye disease (Wang et al., 2019).

Compared to a large cohort study conducted in Norway, where Schirmer I was found to be a good discriminator of dry eye severity among people with DED (Yazdani et al., 2018), a higher frequency of positive Schirmer l was found in this study. This can be explained by the impact DM2 has on the lacrimal gland (Han et al., 2019). People with DM have reduced tear secretion (Misra et al., 2016; Yoo & Oh, 2019) and thereafter reduced tear volume, measured by TMH. Hyperglycemia leads to histological changes in the lacrimal gland (Zou et al., 2018) because of microvascular damage. The lacrimal innervation reduces as a consequence of neuropathy and this gives reduced trophic support to lacrimal tissue and reduced reflex tearing (Bron et al., 2017).

Tear film instability and shorter tear film rupture time is common among people with diabetes (Yu et al., 2019). Hyperglycemia causes goblet cell loss, conjunctival squamous metaplasia, and reduced mucin secretion, as well as affecting the meibomian glands and secretion of meibum, all of which lead to change in tear evaporation, hyperosmolarity, and ocular surface inflammation (Yoo & Oh, 2019). This may explain the high frequency of positive osmolarity measurements in this study. Moreover, osmolarity measurement has been suggested as a suitable test for detecting DED in people with DM2 because it has a higher diagnostic value than other tests (Najafi et al., 2015). However, it has recently been stated that for a normal population osmolarity cannot be used as a key indicator of DED (Tashbayev et al., 2020).

The prevalence of MGD in our study was 35%. In a normal Caucasian population, the prevalence of MGD varies widely from 3.5% to 19.9% (Schaumberg et al., 2011).

Few studies have investigated MGD among people with DM2; however, the reported prevalence varies greatly, ranging from 11% to 75.6% (Hom & De Land, 2006; Sandra Johanna et al., 2019; Shamsheer & Arunachalam, 2015). The prevalence in the current study lies in the middle of this range. Differences may be because of different diagnostic criteria, recruitment criteria, age, and duration of diabetes, as longer duration indicates an increase in meibomian gland drop-out (Nichols et al., 2011; Sandra Johanna et al., 2019; Schaumberg et al., 2011; Yu et al., 2019). The study with the lowest prevalence recruited only symptomatic people, and in the knowledge that the double of those with MGD is asymptomatic this prevalence is probably underestimated.

In this study, many of those without DED had MGD. MGD is a risk factor for DED (Stapleton et al., 2017); moreover, in this study MGD was the only clinically objective evaluation that was significantly different when comparing those with and without DED. The positive correlation between DED and MGD was little. More than half the participants with DED had MGD, and nearly a third of those without DED had MGD. The impact of MGD on the tear film may contribute to the high frequency of staining, reduced NIKBUT, and increased osmolarity found in this study, because lipid deficiency leads to excessive evaporation of the tear film. For people with DM2, reduced insulin and hyperglycemia leads to dysfunction of the sebaceous glands and reduces the quality of the meibum (Ding et al., 2015), which may explain the higher frequency of MGD among people with DM2 compared with the general population.

5.4 Visual-related Quality of Life

To the best of my knowledge, this is the first study to report on VQoL among people with DED and DM2, based on the new DEWS ll criteria for DED and the NEI-VFQ-25 questionnaire. The study found evidence that DED has a negative impact on VQoL. People with DED scored significantly lower than people without DED on the VQoL composite score. This finding corresponds with a previous study in which people with diabetes were assessed using the DEQS to evaluate quality of life (Yazdani-Ibn-Taz et al., 2019). The findings here are also similar to studies among a general population with and

without DED using the same NEI-VFQ-25 questionnaire (Le et al., 2014; Li et al., 2012; Paulsen et al., 2014).

5.4.1 Ocular pain

This study reported an ocular pain subscale score that was at the same level as people with Sjögrens syndrome DED (Vitale et al., 2004). Compared to the ocular pain score in a general population with DED and to a general diabetes population, it would appear people with DM2 and DED experience more ocular pain than both these populations (Granstrom et al., 2015; Hariprasad et al., 2008; Le, et al. 2012; Trento, Passera et al., 2013 Trento, Durando et al., 2017). It would also appear that people with DM have more ocular pain than the general population (Mangione et al., 2001). This is supported by a previous study using a different VQoL questionnaire comparing people with diabetes with a healthy non-diabetic control group (Benbow et al., 1998).

Ocular pain is one of the subscales most affected by DED (> 20 points) and DED was an independent predictor for ocular pain score. The correlation between ocular pain and DED is therefore considered reasonable. However, DED only explains a small part of the variation in ocular pain, so there are other factors to consider regarding ocular pain among this population.

Corneal neuropathy has similar symptoms to DED, and this could be an attributor to the ocular pain score (Barsegian et al., 2018; Zhao et al., 2019). Ocular pain is also associated with systemic pain and people with higher systemic pain have an increased risk of ocular pain (Yamanishi et al., 2019). The most frequent reported pain among people with painful diabetic retinopathy was “deep pain” (Kalteniece et al., 2020). Neurosensory dysfunction is a feature of DED that has been suggested to explain (in part) the lack of association between symptoms and signs (Belmonte et al., 2017). This can help explain why people with DM2 reported more ocular pain than the general population and can also explain why people with DM2 and DED reported ocular pain in the lower range compared to a general population with DED (Le et al., 2012).

5.4.2 Driving and daily living

Driving and peripheral vision are important aspects of daily living and this study shows that DED had a negative impact on these subscales. The driving score was reported lower than Chinese people with DED (Li et al., 2012) and at the same level as people with DM2 about to undergo anti vascular endothelial growth factor (VEGF) treatment for ME (Granstrom et al., 2015). Since these participants had worse visual acuity but rated their challenges with driving at the same level as the participants in the current study, the score cannot be explained by visual acuity alone. A study by Sandlin et al. among a population of adults aged over 70 years, found that impairment in contrast sensitivity impacted on driving exposure, in contrast to visual acuity (Sandlin et al., 2013). For people with DED, contrast sensitivity has been shown to be disturbed (Bron et al., 2017) so it is likely to believe that in addition to DED and BCVAD, contrast sensitivity also can have impact on the driving score. There is also found that factors related to the level of metabolic control has shown to decrease driving ability (Trento et al., 2017).

It is likely that the DEWS diagnostic methodology (based on the OSDI questionnaire) underestimates the prevalence of DED among people with DM2, and therefore the frequency and severity of DED is higher. As a consequence, the degradation of optical quality related to DED is associated with visual impairments during driving (Deschamps et al., 2013).

Peripheral vision is also important for driving and this study found a decrease in peripheral vision for those with DED. However, they still had a high score, which is in accordance with previous studies of people with DM1 where peripheral vision was among those subscales with the highest score (together with color vision) (Hirai et al., 2011). Compared to a normal population, a lower peripheral vision score was found (Mangione et al., 2001). One explanation for this could be that some participants may have been treated by pan-retinal photocoagulation (Filek et al., 2017). Losing the ability to drive have been shown to be associated with a range of negative effects, such as reduced quality of life and reduced wellbeing (Musselwhite & Shergold, 2013). It is

important to be aware that DED also has an impact on driving in people with DM2. DED was not the only significant predictor for this subscale, as BCVA also had impact.

5.4.3 Duration of diabetes and age

In this study it was found that diabetes duration had impact on the overall composite VQoL score. This finding is supported by the work of Klein et al. (2001) and a systematic review by Jing et al. (2018). DED was also a significant predictor for role difficulties. Role difficulties refers to challenges in performing daily tasks, limits on what can be performed, and endurance of daily tasks as a consequence of vision problems (Mangione et al., 2001). Based on the age of our participants, it is likely that age-related factors (such as cataract with reduced contrast sensitivity, retinopathy, age-related macular degeneration, and glaucoma) are likely to have an impact on quality of life. Evaluating this issue was beyond the scope of this master's thesis, and by controlling for BCVAD it was possible to adjust for the impact of vision-related confounding factors indirectly. Factors related to the subscales mental health, role difficulties, and dependency are more complex and need further investigation in future studies.

5.5 Strengths and Weaknesses of the Study

5.5.1 Strengths of the study

One strength of this study is the use of the new DEWS ll Diagnostic Methodology, with DED diagnosis being based on evaluation of both symptoms and signs (Yazdani et al., 2019). All homeostasis markers were evaluated as well as commonly used dry eye tests such as Schirmer l, TMH, and MGD. All clinical evaluations were conducted in the same environment and with the same instruments with the least invasive test first.

Another strength of this study is the use of both a generic and a disease-specific questionnaire, enabling use of strengths from the theoretically more sensitive disease-specific instrument together with additional aspects of the systemic disease being captured by the generic instrument. Therefore, a broader aspect of the health-related quality of life was attained (Li et al., 2012; Vitale et al., 2004). Furthermore, there is no

difference between the two groups (those with and those without DED) according to age, gender, diabetes duration, or BCVA at distance. This neutralizes the possible impact these factors may have on the results. A post hoc sample size analysis based on the ratio of DED and no-DED patients in our study (16:73) showed that the sample size requirements for detecting a difference of 20 points for the NEI-VFQ-25 score had been met.

5.5.2 Limitations of the study

This study has limitations that need to be considered when interpreting the results. The sample was not controlled for other diseases that can impact on DED, such as connective tissue diseases, Sjögrens syndrome, allergy, androgen deficiency, pterygium, smoking, alcohol, and medications with dry eye adverse effect.

Data was gathered by multiple investigators; therefore, there is a possibility that intra-observer bias may have been introduced to the results. This is also possible for differences in grading and evaluation of subjective measurements. To minimize the possible impact, a detailed written protocol was developed in advance of the data collection to ensure that investigators followed the same procedure, and used the same grading tool, equipment, and patient instructions.

It is also possible that some participants had allergies for which they used antihistamines, which could influence the results. Moreover, participants using eyedrops or with known predisposing rheumatism, dryness according to Sjögrens syndrome, smoking, and systemic diseases as hypertension, high cholesterol, and vascular diseases were not excluded from the study.

Another limitation is that diabetic retinopathy and cataract was not evaluated. Studies have shown that people with late diabetes complications such as diabetic retinopathy are more likely to have DED (Stapleton et al., 2017) and people with proliferative retinopathy have reduced corneal sensitivity compared to those without retinopathy (Lv et al., 2014). Posterior cortical and posterior subcapsular cataract, neovascular glaucoma, and age-related macular degeneration is also more common among the diabetes population (Khan et al., 2017). Cataracts are shown to have little effect on NEI-VFQ-25 among people with long-term diabetes (Klein et al., 2001),

whereas exudative age-related macular degeneration are shown to have an impact on VQoL subscales (Inan et al., 2019). By controlling for BCVA at distance in the model, I indirectly controlled for the impact of cataracts, age-related macular degeneration and retinopathy. I could have adjusted for habitual visual acuity at distance and the results would be more accurate based on the situation they answered the NEI-VFQ-25 questionnaire for. This only have a small impact on the results and is therefore not been changed in the thesis.

Only Caucasian people were investigated, and the mean age was high. No adjustment for comorbidities, such as high blood pressure, high cholesterol, arteritis, rheumatism, hearing issues, educational level, occupation, and lifestyle factors such as outdoor exposure, dietary practice, physical health, BMI, smoking, time in front of visual display units, and contact lens use was made. All these are comorbidities and potential confounders of the outcome.

The number of punching errors should also have been checked; however, to avoid punching errors we tried to punch data with precision into Excel using a Visual Basic punching tool.

This study was a descriptive cross-sectional design and the results can provide information about associations between variables at one specific time; however, it cannot explain causality. The study also used convenience sampling, whereas a case control study controlling for age, gender, diabetes duration, and bcva at distance would have yielded stronger evidence.

5.6 Future Studies and Practical Advice

It would be interesting to see a future study with a larger sample size to gain better statistical power and a case control study with two matched groups for age, gender, diabetes duration, HbA1c level, and retinopathy. This would enable better understanding of the association, exposure, and cause and effect. A study investigating the late complications of diabetic neuropathy with in vivo confocal microscopy with

corneal sensitivity would provide additional information on this population and also about the association between corneal sensitivity, duration of diabetes, and clinical signs. Biomarker tests may be developed in the future that are more precise and efficient as diagnostic tool to diagnose or screen people with DM who need further anterior segment evaluation to avoid vision-threatening corneal complications due to DED.

6 Conclusion

In this study, it was found that people with DM2 have a low prevalence of DED, but substantial prevalence of clinical findings of DED. Symptoms and clinical signs of DED are not associated. The correlation between DED and the composite score for NEI-VFQ-25 and the subscale score for ocular pain is fair, and DED can be considered an independent predictor for ocular pain. However, people with DM2 may have severe clinical surface damage without having symptoms. The OSDI questionnaire is not a strong discriminative test for clinical findings of dry eye and ocular surface disease in people with DM2. Routine examination of the lids and ocular surface among people with DM2 is vital, as detection of ocular surface damage is important for early treatment and prevention of vision threatening complications.

7 References

Barsegian, A., Lee, J., Salifu, M. O., & McFarlane, S. I. (2018). Corneal Neuropathy: An Underrated Manifestation of Diabetes Mellitus. *Journal of Clinical Endocrinology and Diabetes, 2*(1).

Bartlett, J. D., Keith, M. S., Sudharshan, L., & Snedecor, S. J. (2015). Associations between signs and symptoms of dry eye disease: a systematic review. *Clinical Ophthalmology, 9*, 1719-1730. doi:10.2147/OPTH.S89700

Baudouin, C., Messmer, E. M., Aragona, P., Geerling, G., Akova, Y. A., Benitez-del-Castillo, J., . . . Labetoulle, M. (2016). Revisiting the vicious circle of dry eye disease: a focus on the pathophysiology of meibomian gland dysfunction. *The British Journal of Ophthalmology, 100*(3), 300-306. doi:10.1136/bjophthalmol-2015-307415

Belmonte, C., Nichols, J. J., Cox, S. M., Brock, J. A., Begley, C. G., Bereiter, D. A., . . . Wolffsohn, J. S. (2017). TFOS DEWS II pain and sensation report. *The Ocular Surface, 15*(3), 404-437. doi:10.1016/j.jtos.2017.05.002

Benbow, S. J., Wallymahmed, M. E., & MacFarlane, I. A. (1998). Diabetic peripheral neuropathy and quality of life. *Qjm: Monthly journal of the Association of Physicians, 91*(11), 733-737. doi:10.1093/qjmed/91.11.733

Bikbova, G., Oshitari, T., Baba, T., Bikbov, M., & Yamamoto, S. (2018). Diabetic corneal neuropathy: clinical perspectives. *Clinical Ophthalmology, 12*, 981-987. doi:10.2147/opth.S145266

Bron, A. J., de Paiva, C. S., Chauhan, S. K., Bonini, S., Gabison, E. E., Jain, S., . . . Sullivan, D. A. (2017). TFOS DEWS II pathophysiology report. *The Ocular Surface, 15*(3), 438-510. doi:10.1016/j.jtos.2017.05.011

Bron, A. J., Evans, V. E., & Smith, J. A. (2003). Grading of corneal and conjunctival staining in the context of other dry eye tests. *Cornea, 22*(7), 640-650. doi:10.1097/00003226-200310000-00008

Bunya, V. Y., Fuerst, N. M., Pistilli, M., McCabe, B. E., Salvo, R., Macchi, I., . . . Massaro-Giordano, M. (2015). Variability of Tear Osmolarity in Patients With Dry Eye. *JAMA Ophthalmology, 133*(6), 662-667. doi:10.1001/jamaophthalmol.2015.0429

Craig, J. P., Nelson, J. D., Azar, D. T., Belmonte, C., Bron, A. J., Chauhan, S. K., . . . Sullivan, D. A. (2017). TFOS DEWS II Report Executive Summary. *The Ocular Surface, 15*(4), 802-812. doi:10.1016/j.jtos.2017.08.003. (Accession No. 28797892)

Craig, J. P., Nichols, K. K., Akpek, E. K., Caffery, B., Dua, H. S., Joo, C. K., . . . Stapleton, F. (2017). TFOS DEWS II Definition and Classification Report. *The Ocular Surface, 15*(3), 276-283. doi:10.1016/j.jtos.2017.05.008

Dawson, B., & Trapp, R. G. (2004). *Basic & clinical biostatistics* (4th ed. ed.). New York: Lange Medical Books/McGraw-Hill.

De Clerck, E. E. B., Schouten, J., Berendschot, T., Koolschijn, R. S., Nuijts, R., Schram, M. T., . . . Webers, C. A. B. (2020). Reduced corneal nerve fibre length in prediabetes and type 2 diabetes: The Maastricht Study. *Acta Ophthalmologica*. doi:10.1111/aos.14359

De Freitas, G. R., Ferraz, G. A. M., Gehlen, M., & Skare, T. L. (2020). Dry eyes in patients with diabetes mellitus. *Primary Care Diabetes*. doi:10.1016/j.pcd.2020.01.011

Dehesh, T., Dehesh, P., & Gozashti, M. H. (2019). Metabolic factors that affect health-related quality of life in type 2 diabetes patients: a multivariate regression analysis. *Diabetes Metabolic Syndrome and Obesity: targets and therapy, 12*, 1181-1188. doi:10.2147/dmso.S208689

DeMill, D. L., Hussain, M., Pop-Busui, R., & Shtein, R. M. (2016). Ocular surface disease in patients with diabetic peripheral neuropathy. *The British Journal of Ophthalmology, 100*(7), 924-928. doi:10.1136/bjophthalmol-2015-307369

Deschamps, N., Ricaud, X., Rabut, G., Labbe, A., Baudouin, C., & Denoyer, A. (2013). The impact of dry eye disease on visual performance while driving. *American Journal of Ophthalmology, 156*(1), 184-189.e183. doi:10.1016/j.ajo.2013.02.019

Ding, J., Liu, Y., & Sullivan, D. A. (2015). Effects of Insulin and High Glucose on Human Meibomian Gland Epithelial Cells. *Investigative Ophthalmology and Visual Science, 56*(13), 7814-7820. doi:10.1167/iovs.15-18049

Filek, R., Hooper, P., Sheidow, T., Gonder, J., Varma, D. K., Heckler, L., . . . Hutnik, C. M. L. (2017). Structural and functional changes to the retina and optic nerve following panretinal photocoagulation over a 2-year time period. *Eye (London, England), 31*(8), 1237-1244. doi:10.1038/eye.2017.66

Fuerst, N., Langelier, N., Massaro-Giordano, M., Pistilli, M., Stasi, K., Burns, C., . . . Bunya, V. Y. (2014). Tear osmolarity and dry eye symptoms in diabetics. *Clinical Ophthalmology, 8*, 507-515. doi:10.2147/opth.s51514

Granstrom, T., Forsman, H., Leksell, J., Jani, S., Raghib, A. M., & Granstam, E. (2015). Visual functioning and health-related quality of life in diabetic patients about to undergo anti-vascular endothelial growth factor treatment for sight-threatening macular edema. *Journal of Diabetes and its Complications, 29*(8), 1183-1190. doi:10.1016/j.jdiacomp.2015.07.026

Grubbs, J. R., Jr., Tolleson-Rinehart, S., Huynh, K., & Davis, R. M. (2014). A review of quality of life measures in dry eye questionnaires. *Cornea, 33*(2), 215-218. doi:10.1097/ico.0000000000000038

Guillemin, I., Begley, C., Chalmers, R., Baudouin, C., & Arnould, B. (2012). Appraisal of patient-reported outcome instruments available for randomized clinical trials in dry eye: revisiting the standards. *The Ocular Surface, 10*(2), 84-99. doi:10.1016/j.jtos.2012.01.007

Han, S. B., Yang, H. K., & Hyon, J. Y. (2019). Influence of diabetes mellitus on anterior segment of the eye. *Clinical Interventions in Aging, 14*, 53-63. doi:10.2147/cia.S190713

Hariprasad, S. M., Mieler, W. F., Grassi, M., Green, J. L., Jager, R. D., & Miller, L. (2008). Vision-related quality of life in patients with diabetic macular oedema. *The British Journal of Ophthalmology, 92*(1), 89-92. doi:10.1136/bjo.2007.122416

Hirai, F. E., Tielsch, J. M., Klein, B. E., & Klein, R. (2011). Ten-year change in vision-related quality of life in type 1 diabetes: Wisconsin epidemiologic study of diabetic retinopathy. *Ophthalmology, 118*(2), 353-358. doi:10.1016/j.ophtha.2010.06.022

Holland, E. J., Mannis, M. J., & Lee, W. B. (2013). *Ocular surface disease: cornea, conjunctiva and tear film*. London: Elsevier Saunders.

Hom, M., & De Land, P. (2006). Self-reported dry eyes and diabetic history. *Optometry, 77*(11), 554-558. doi:10.1016/j.påtom.2006.08.002

Inan, S., Cetinkaya, E., Duman, R., Dogan, I., & Inan, U. Ü. (2019). Quality of life among patients with age-related severe macular degeneration assessed using the NEI-VFQ, HADS-A, HADS-D and SF-36 tests. A cross-sectional study. *Sao Paulo Medical Journal, 137*(1), 25-32. doi:10.1590/1516-3180.2018.0195071218

Jelin, E., Wisloff, T., Moe, M. C., & Heiberg, T. (2019). Psychometric properties of the National Eye Institute Visual Function Questionnaire (NEI-VFQ 25) in a Norwegian population of patients with neovascular age-related macular degeneration compared to a control population. *Health and Quality of Life Outcomes, 17*(1), 140. doi:10.1186/s12955-019-1203-0

Jing, X., Chen, J., Dong, Y., Han, D., Zhao, H., Wang, X., . . . Ma, J. (2018). Related factors of quality of life of type 2 diabetes patients: a systematic review and meta-analysis. *Health and Quality of Life Outcomes, 16*(1), 189. doi:10.1186/s12955-018-1021-9

Jones, L., Downie, L. E., Korb, D., Benitez-del-Castillo, J. M., Dana, R., Deng, S. X., . . . Craig, J. P. (2017). TFOS DEWS II Management and Therapy Report. *The Ocular Surface, 15*(3), 575-628. doi:https://doi.org/10.1016/j.jtos.2017.05.006

Kaiserman, I., Kaiserman, N., Nakar, S., & Vinker, S. (2005). Dry eye in diabetic patients. *American Journal of Ophthalmology, 139*(3), 498-503. doi:10.1016/j.ajo.2004.10.022

Kalteniece, A., Ferdousi, M., Azmi, S., Mubita, W. M., Marshall, A., Lauria, G., . . . Malik, R. A. (2020). Corneal confocal microscopy detects small nerve fibre damage in patients with painful diabetic neuropathy. *Scientific Repors, 10*(1), 3371. doi:10.1038/s41598-020-60422-7

Khan, A., Petropoulos, I. N., Ponirakis, G., & Malik, R. A. (2017). Visual complications in diabetes mellitus: beyond retinopathy. *Diabetic Medicine: a journal of the British Diabetic Association, 34*(4), 478-484. doi:10.1111/dme.13296

Klein, R., Moss, S. E., Klein, B. E., Gutierrez, P., & Mangione, C. M. (2001). The NEI-VFQ-25 in people with long-term type 1 diabetes mellitus: the Wisconsin Epidemiologic Study of Diabetic Retinopathy. *Archives of Ophthalmology, 119*(5), 733-740. doi:10.1001/archopht.119.5.733

Knop, E., Knop, N., Millar, T., Obata, H., & Sullivan, D. A. (2011). The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. *Investigative Ophthalmology & Visual Science, 52*(4), 1938-1978. doi:10.1167/iovs.10-6997c

Korb, D. R., Herman, J. P., Blackie, C. A., Scaffidi, R. C., Greiner, J. V., Exford, J. M., & Finnemore, V. M. (2010). Prevalence of lid wiper epitheliopathy in subjects with dry eye signs and symptoms. *Cornea, 29*(4), 377-383. doi:10.1097/ICO.0b013e3181ba0cb2

Korb, D. R., Herman, J. P., Greiner, J. V., Scaffidi, R. C., Finnemore, V. M., Exford, J. M., . . . Douglass, T. (2005). Lid wiper epitheliopathy and dry eye symptoms. *Eye Contact Lens, 31*(1), 2-8. doi:10.1097/01.icl.0000140910.03095.fa

Le, Q., Ge, L., Li, M., Wu, L., Xu, J., Hong, J., & Gong, L. (2014). Comparison on the vision-related quality of life between outpatients and general population with dry eye syndrome. *Acta Ophthalmology, 92*(2), e124-132. doi:10.1111/aos.12204

Le, Q., Zhou, X., Ge, L., Wu, L., Hong, J., & Xu, J. (2012). Impact of dry eye syndrome on vision-related quality of life in a non-clinic-based general population. *BMC Ophthalmology, 12*, 22. doi:10.1186/1471-2415-12-22

Li, M., Gong, L., Chapin, W. J., & Zhu, M. (2012). Assessment of vision-related quality of life in dry eye patients. *Investigative Ophthalmology & Visual Science, 53*(9), 5722-5727. doi:10.1167/iovs.11-9094

Lin, X., Xu, B., Zheng, Y., Coursey, T. G., Zhao, Y., Li, J., . . . Zhao, Y. E. (2017). Meibomian Gland Dysfunction in Type 2 Diabetic Patients. *Journal of Ophthalmology, 2017*, 3047867. doi:10.1155/2017/3047867

Lv, H., Li, A., Zhang, X., Xu, M., Qiao, Y., Zhang, J., & Yu, L. (2014). Meta-analysis and review on the changes of tear function and corneal sensitivity in diabetic patients. *Acta Ophthalmologica, 92*(2), e96-e104. doi:10.1111/aos.12063

Ma, A., Mak, M. S., Shih, K. C., Tsui, C. K., Cheung, R. K., Lee, S. H., . . . Tong, L. (2018). Association of long-term glycaemic control on tear break-up times and dry eye symptoms in Chinese patients with type 2 diabetes. *Clinical & Experimental Ophthalmology, 46*(6), 608-615. doi:10.1111/ceo.13146

Manaviat, M. R., Rashidi, M., Afkhami-Ardekani, M., & Shoja, M. R. (2008). Prevalence of dry eye syndrome and diabetic retinopathy in type 2 diabetic patients. *BMC Ophthalmology, 8*, 10. doi:10.1186/1471-2415-8-10

Mangione, C. M. (2000). NEI VFQ-25 Scoring Alborithm - August 2000 (manual). Retrieved from https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=6&ved=2ahUKEwimsPLxju3oAhU0xMQBHc-PDeAQFjAFegQIBRAB&url=http%3A%2F%2Fretina-amd.org%2Fwp-content%2Fuploads%2F2017%2F10%2FNEI-VFQ-25-SCORING-ALGORITHM-2000.pdf&usg=AOvVaw1uMOqVmGPm2SkPSnWnz8mp

Mangione, C. M., Lee, P. P., Gutierrez, P. R., Spritzer, K., Berry, S., & Hays, R. D. (2001). Development of the 25-item National Eye Institute Visual Function Questionnaire. *Archives of Ophthalmology, 119*(7), 1050-1058. doi:10.1001/archopht.119.7.1050

Mazhar, K., Varma, R., Choudhury, F., McKean-Cowdin, R., Shtir, C. J., & Azen, S. P. (2011). Severity of diabetic retinopathy and health-related quality of life: the Los Angeles Latino Eye Study. *Ophthalmology, 118*(4), 649-655. doi:10.1016/j.ophtha.2010.08.003

Misra, S. L., Braatvedt, G. D., & Patel, D. V. (2016). Impact of diabetes mellitus on the ocular surface: a review. *Clinical & Experimental Ophthalmology, 44*(4), 278-288. doi:10.1111/ceo.12690

Musselwhite, C. B. A., & Shergold, I. (2013). Examining the process of driving cessation in later life. *European Journal of Ageing, 10*(2), 89-100. doi:10.1007/s10433-012-0252-6

Najafi, L., Malek, M., Valojerdi, A. E., Aghili, R., Khamseh, M. E., Fallah, A. E., . . . Behrouz, M. J. (2013). Dry eye and its correlation to diabetes microvascular complications in people with type 2 diabetes mellitus. *Journal of Diabetes and its Complications, 27*(5), 459-462. doi:10.1016/j.jdiacomp.2013.04.006

Najafi, L., Malek, M., Valojerdi, A. E., Khamseh, M. E., & Aghaei, H. (2015). Dry eye disease in type 2 diabetes mellitus; comparison of the tear osmolarity test with other common diagnostic tests: a diagnostic accuracy study using STARD standard. *Journal of Diabetes and Metababolic Disorders, 14*, 39. doi:10.1186/s40200-015-0157-y

Nelson, J. D., Shimazaki, J., Benitez-del-Castillo, J. M., Craig, J. P., McCulley, J. P., Den, S., & Foulks, G. N. (2011). The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee. *Investigative Ophthalmology & Visual Science, 52*(4), 1930-1937. doi:10.1167/iovs.10-6997b

Nichols, K. K., Foulks, G. N., Bron, A. J., Glasgow, B. J., Dogru, M., Tsubota, K., . . . Sullivan, D. A. (2011). The international workshop on meibomian gland dysfunction: executive summary. *Investigative Ophthalmology & Visual Science, 52*(4), 1922-1929. doi:10.1167/iovs.10-6997a

Nichols, K. K., Mitchell, G. L., & Zadnik, K. (2002). Performance and repeatability of the NEI-VFQ-25 in patients with dry eye. *Cornea, 21*(6), 578-583.

Olaniyan, S. I., Fasina, O., Bekibele, C. O., & Ogundipe, A. O. (2019). Relationship between dry eye and glycosylated haemoglobin among diabetics in Ibadan, Nigeria. *The Pan African Medical Journal, 33*, 14. doi:10.11604/pamj.2019.33.14.14074

Pasnoor, M., Dimachkie, M. M., Kluding, P., & Barohn, R. J. (2013). Diabetic neuropathy part 1: overview and symmetric phenotypes. *Neurologic Clinics, 31*(2), 425-445. doi:10.1016/j.ncl.2013.02.004

Paulsen, A. J., Cruickshanks, K. J., Fischer, M. E., Huang, G. H., Klein, B. E., Klein, R., & Dalton, D. S. (2014). Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. *American Journal of Ophthalmology, 157*(4), 799-806. doi:10.1016/j.ajo.2013.12.023

Sandlin, D., McGwin, G., Jr., & Owsley, C. (2014). Association between vision impairment and driving exposure in older adults aged 70 years and over: a population-based examination. *Acta Ophthalmologica, 92*(3), e207-212. doi:10.1111/aos.12050

Sandra Johanna, G. P., Antonio, L. A., & Andres, G. S. (2019). Correlation between type 2 diabetes, dry eye and Meibomian glands dysfunction. *Journal of Optometry, 12*(4), 256-262. doi:10.1016/j.optom.2019.02.003

Schaumberg, D. A., Nichols, J. J., Papas, E. B., Tong, L., Uchino, M., & Nichols, K. K. (2011). The international workshop on meibomian gland dysfunction: report of the subcommittee on the epidemiology of, and associated risk factors for, MGD. *Investigative Ophthalmology & Visual Science, 52*(4), 1994-2005. doi:10.1167/iovs.10-6997e

Schaumberg, D. A., Uchino, M., Christen, W. G., Semba, R. D., Buring, J. E., & Li, J. Z. (2013). Patient reported differences in dry eye disease between men and women: impact, management, and patient satisfaction. *PLoS One, 8*(9), e76121. doi:10.1371/journal.pone.0076121

Schiffman, R. M., Christianson, M. D., Jacobsen, G., Hirsch, J. D., & Reis, B. L. (2000). Reliability and validity of the Ocular Surface Disease Index. *Archives of Ophthalmology, 118*(5), 615-621.

Shamsheer, R. P., & Arunachalam, C. (2015). A Clinical Study of Meibomian Gland Dysfunction in Patients with Diabetes. *Middle East African Journal of Ophthalmology, 22*(4), 462-466. doi:10.4103/0974-9233.167827

Stapleton, F., Alves, M., Bunya, V. Y., Jalbert, I., Lekhanont, K., Malet, F., . . . Jones, L. (2017). TFOS DEWS II Epidemiology Report. *The Ocular Surface, 15*(3), 334-365. doi:10.1016/j.jtos.2017.05.003

Stene, L. C. S., H., Gulseth, H. L. (08.08.2017). Diabetes in Norway. Retrieved from https://www.fhi.no/en/op/hin/health-disease/diabetes-in-norway---public-health-/

Sullivan, D. A., Rocha, E. M., Aragona, P., Clayton, J. A., Ding, J., Golebiowski, B., . . . Willcox, M. D. P. (2017). TFOS DEWS II Sex, Gender, and Hormones Report. *The Ocular Surface, 15*(3), 284-333. doi:10.1016/j.jtos.2017.04.001

Tashbayev, B., Utheim, T. P., Utheim, O. A., Raeder, S., Jensen, J. L., Yazdani, M., . . . Chen, X. (2020). Utility of Tear Osmolarity Measurement in Diagnosis of Dry Eye Disease. *Scientific Reports, 10*(1), 5542. doi:10.1038/s41598-020-62583-x

Tomlinson, A., Bron, A. J., Korb, D. R., Amano, S., Paugh, J. R., Pearce, E. I., . . . Dogru, M. (2011). The international workshop on meibomian gland dysfunction: report of the diagnosis subcommittee. *Investigative Ophthalmology & Visual Science, 52*(4), 2006-2049. doi:10.1167/iovs.10-6997f

Trento, M., Durando, O., Lavecchia, S., Charrier, L., Cavallo, F., Costa, M. A., . . . Porta, M. (2017). Vision related quality of life in patients with type 2 diabetes in the EUROCONDOR trial. *Endocrine, 57*(1), 83-88. doi:10.1007/s12020-016-1097-0

Trento, M., Passera, P., Trevisan, M., Schellino, F., Sitia, E., Albani, S., . . . Porta, M. (2013). Quality of life, impaired vision and social role in people with diabetes: a multicenter observational study. *Acta Diabetologica, 50*(6), 873-877. doi:10.1007/s00592-013-0470-1

Vitale, S., Goodman, L. A., Reed, G. F., & Smith, J. A. (2004). Comparison of the NEI-VFQ and OSDI questionnaires in patients with Sjogren's syndrome-related dry eye. *Health and Quality of Life Outcomes, 2*, 44. doi:10.1186/1477-7525-2-44

Wang, M. T. M., Dean, S. J., Xue, A. L., & Craig, J. P. (2019). Comparative performance of lid wiper epitheliopathy and corneal staining in detecting dry eye disease. *Clinical & Experimental Ophthalmology, 47*(4), 546-548. doi:10.1111/ceo.13415

Willcox, M. D. P., Argüeso, P., Georgiev, G. A., Holopainen, J. M., Laurie, G. W., Millar, T. J., . . . Jones, L. (2017). TFOS DEWS II Tear Film Report. *The Ocular Surface, 15*(3), 366-403. doi:https://doi.org/10.1016/j.jtos.2017.03.006

Wolffsohn, J. S., Arita, R., Chalmers, R., Djalilian, A., Dogru, M., Dumbleton, K., . . . Craig, J. P. (2017). TFOS DEWS II Diagnostic Methodology report. *The Ocular Surface, 15*(3), 539-574. doi:10.1016/j.jtos.2017.05.001

Yamanishi, R., Uchino, M., Kawashima, M., Dogru, M., Matsuguma, S., & Tsubota, K. (2019). Analysis of the association between the severity of ocular and systemic pain. *The Ocular Surface, 17*(3), 434-439. doi:10.1016/j.jtos.2019.05.008

Yazdani-Ibn-Taz, M. K., Han, M. M., Jonuscheit, S., Collier, A., Nally, J. E., & Hagan, S. (2019). Patient-reported severity of dry eye and quality of life in diabetes. *Clinical Ophthalmology, 13*, 217-224. doi:10.2147/opth.S184173

Yazdani, M., Chen, X., Tashbayev, B., Utheim, O. A., Raeder, S., Hua, Y., . . . Utheim, T. P. (2019). Evaluation of the Ocular Surface Disease Index Questionnaire as a Discriminative Test for Clinical Findings in Dry Eye Disease Patients. *Current Eye Research, 44*(9), 941-947. doi:10.1080/02713683.2019.1604972

Yazdani, M., Chen, X., Tashbayev, B., Utheim, O. A., Raeder, S., Lagali, N., . . . Utheim, T. P. (2018). Tear Production Levels and Dry Eye Disease Severity in a Large Norwegian Cohort. *Current Eye Research, 43*(12), 1465-1470. doi:10.1080/02713683.2018.1514055

Yoo, T. K., & Oh, E. (2019). Diabetes mellitus is associated with dry eye syndrome: a meta-analysis. *International Ophthalmology, 39*(11), 2611-2620. doi:10.1007/s10792-019-01110-y

Yu, T., Han, X.-G., Gao, Y., Song, A.-P., & Dang, G.-F. (2019). Morphological and cytological changes of meibomian glands in patients with type 2 diabetes mellitus. *International Journal of Opthalmology, 9*(12), 1740-1744. doi:10.18240/ijo.2016.12.06

Zhang, X., Zhao, L., Deng, S., Sun, X., & Wang, N. (2016). Dry Eye Syndrome in Patients with Diabetes Mellitus: Prevalence, Etiology, and Clinical Characteristics. *Journal of Ophthalmology, 2016*, 8201053. doi:10.1155/2016/8201053

Zhao, H., He, Y., Ren, Y. R., & Chen, B. H. (2019). Corneal alteration and pathogenesis in diabetes mellitus. *International Journal of Ophthalmology, 12*(12), 1939-1950. doi:10.18240/ijo.2019.12.17

Zou, X., Lu, L., Xu, Y., Zhu, J., He, J., Zhang, B., & Zou, H. (2018). Prevalence and clinical characteristics of dry eye disease in community-based type 2 diabetic patients: the Beixinjing eye study. *BMC Ophthalmology, 18*(1), 117. doi:10.1186/s12886-018-0781-7

List of tables and charts

Appendixes

Appendix 1:	*Written information form*
Appendix 2:	*Informed consent form*
Appendix 3:	*National Eye Institute Visual Function Questionnaire-25 (NEI-VFQ-25)*
Appendix 4:	*Ocular Surface Disease Index*
Appendix 5:	*Data registration booklet*
Appendix 6:	*OSDI manual*
Appendix 7:	*NEI-VFQ-25 manual*
Appendix 8:	*Letter of reply from Regional Committee for Medical Research Ethics for the Southern Norway Regional Health Authority (REK)*

FORESPØRSEL OM DELTAKELSE I FORSKNINGSPROSJEKTET

Diabetes, syn og øyehelse

Dette er et spørsmål til deg om å delta i ett forskningsprosjekt hvor formålet med prosjektet er undersøke hvordan synsfunksjon, øyehelse og livskvalitet påvirkes hos personer som har type 2 diabetes, og vurdere hvilke undersøkelsesmetoder som er mest effektive for å avdekke syn- og øyeproblemer hos optiker. Resultatene fra prosjektet forventes å gi et vesentlig bidrag til å gjøre optikere i bedre stand til å avdekke syn- og øyeproblemer og håndtere disse målrettet og effektivt, og redusere antallet henvisninger til øyelege.

Du forespørres om å delta fordi du har diabetes type 2 og har blitt invitert gjennom Nasjonalt senter for optikk, syn og øyehelse (NOSØ), Diabetesforbundets lokallag i Buskerud, Telemark og Vestfold, eller gjennom optikere i disse fylkene. Forskningsprosjektet og alle undersøkelser gjennomføres ved NOSØ, Institutt for optometri, radiografi og lysdesign, Fakultet for helse og sosialvitenskap, Høgskolen i Sørøst-Norge, avdeling Kongsberg.

HVA INNEBÆRER PROSJEKTET?

Ved deltakelse i prosjektet vil du bli bedt om å fylle ut spørreskjemaer som avdekker syn- og øyesymptomer og din oppfattelse av livskvalitet knyttet opp mot syn. Du vil gjennomgå undersøkelser som er etter Norges Optikerforbund's retningslinjer. Dette innebærer blant annet: innledende samtale og spørsmål, måling av synsevne, utmåling av eventuelle synsfeil på avstand, samt mikroskopiundersøkelse av fremre og bakre del av øynene. Det vil bli målt øyetrykk, samt at netthinnen din blir avbildet med forskjellige instrumenter. Noen målinger krever at vi drypper med pupilleutvidende dråper. Undersøkelsene som inngår i prosjektet er fordelt over tre besøk, og tidsforbruket vil være ca. 2 timer for hvert besøk. Vi vil også be deg om å komme tilbake til oppfølgende undersøkelse etter 1, 5 og 10 år.

I prosjektet vil vi innhente og registrere opplysninger om deg. Dette er opplysninger som kjønn, alder og resultater fra spørreskjemaer og kliniske tester. Dine opplysninger og resultater vil under prosjektperioden være knyttet til en navneliste gjennom en kode. Kodenøkkelen slettes når datainnsamlingen er avsluttet. Opplysningene som lagres vil i etterkant ikke kunne knyttes til din person.

MULIGE FORDELER OG ULEMPER

Som deltaker i prosjektet får du gjennomført en grundig syn- og øyeundersøkelse. Undersøkelsen inkluderer undersøkelse av tårefilmen, det ytre øyet og netthinnen, og undersøkelser av hvor godt du ser. Det vil bli gitt veiledning og råd som kan gi deg best mulig syn og lindre eventuelle plager for eksempel hvis du har tørre øyne. Dersom det oppdages noen unormale funn, vil vi følge opp dette og sørge for at du får informasjon og eventuell henvisning til øyelege eller lege.

Det er ikke knyttet risiko, betydelig ubehag eller bivirkninger til noen av undersøkelsene. Det vil være nødvendig å bruke øyedråper (Tropikamid 0,5% minims) for å utvide pupillene. Dette kan av noen oppleves litt

ubehagelig da dråpene kan svi noe, og at man blir mer lysømfintlig i etterkant. Effekten av øyedråpene vil avta gradvis og opphører helt etter noen timer. Du bør ikke kjøre bil før synet er normalisert.

Det er gratis å delta i prosjektet.

FRIVILLIG DELTAKELSE OG MULIGHET FOR Å TREKKE SITT SAMTYKKE

Det er frivillig å delta i prosjektet. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke. Dette vil ikke få konsekvenser for din videre behandling ved NOSØ. Dersom du trekker deg fra prosjektet, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner. Dersom du senere ønsker å trekke deg eller har spørsmål til prosjektet, kan du kontakte førsteamanuensis Tove Lise Morisbakk (tlf 31 00 97 55, tovelm@usn.no) eller førsteamanuensis Vibeke Sundling (tlf 31 00 89 55, vibeke.sundling@usn.no).

HVA SKJER MED INFORMASJONEN OM DEG?

Informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Du har rett til innsyn i hvilke opplysninger som er registrert om deg og rett til å få korrigert eventuelle feil i de opplysningene som er registrert.

Alle opplysningene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger gjennom en navneliste.

Prosjektleder, førsteamanuensis Vibeke Sundling, Institutt for optometri, radiografi og lysdesign, Fakultet for helse og sosialvitenskap, Høgskolen i Sørøst-Norge ved Nasjonalt Senter for optikk syn og øyehelse har ansvar for den daglige driften av forskningsprosjektet og at opplysninger om deg blir behandlet på en sikker måte. Informasjon om deg vil bli anonymisert eller slettet senest fem år etter prosjektslutt. Prosjektleder kan kontaktes på tlf: 924 24 360 eller vibeke.sundling@usn.no .

FORSIKRING

Pasientskadeloven.

GODKJENNING

Prosjektet er godkjent av Regional komite for medisinsk og helsefaglig forskningsetikk, (2018/804).

Diabetes, syn og øyehelse

SAMTYKKE TIL DELTAKELSE I PROSJEKTET

JEG ER VILLIG TIL Å DELTA I PROSJEKTET

Sted og dato

Deltakers signatur

Deltakers navn med trykte bokstaver

Jeg bekrefter å ha gitt informasjon om prosjektet

Sted og dato

Signatur

PB/SA

National Eye Institute
Spørreskjema om synsfunksjon - 25
(VFQ-25)

(FOR EGENUTFYLLING)

Februar 1997

Dette er et spørreskjema med utsagn om problemer du har med synet ditt, eller følelser du har omkring dette. Etter hvert spørsmål ber vi deg velge det svaret som best beskriver din egen situasjon.

Vennligst svar på alle spørsmålene som om du hadde på deg dine briller eller kontaktlinser (hvis du bruker noe av dette).

Vennligst ta den tiden du trenger for å svare på hvert spørsmål. Alle svar behandles konfidensielt. For at denne spørreundersøkelsen skal øke vår kunnskap om synsproblemer og hvorledes disse problemene påvirker din livskvalitet, må svarene være så presise som mulig. Husk at dersom du bruker briller eller kontaktlinser, så vennligst svar på alle spørsmålene som om du hadde dem på deg.

VEILEDNING:

1. I det store og hele vil vi helst at folk forsøker å fylle ut disse skjemaene på egenhånd. Dersom du merker at du trenger hjelp, så vennligst ikke nøl med å henvende deg til prosjektmedarbeiderne, som vil gi deg assistanse.

2. Vennligst svar på alle spørsmålene (unntatt de spørsmålene du blir bedt om å hoppe over, fordi det/de neste spørsmål(ene) ikke angår deg).

3. Svar på spørsmålene ved å sette en ring rundt tallet for det svaret som passer.

4. Hvis du er usikker på hvilket svar du skal velge, vennligst velg det svaret som passer best, og sett en kommentar i venstre marg.

5. Vennligst fyll ut skjemaet før du går herfra og gi det til en av prosjektmedarbeiderne. Ta ikke med skjemaet hjem.

6. Hvis du har noen spørsmål, må du gjerne spørre en av prosjektmedarbeiderne, og de vil med glede hjelpe deg.

KONFIDENSIELLE OPPLYSNINGER:

Alle opplysninger som kunne tillate identifisering av en person som har fyit ut dette skjemaet, skal anses som strengt konfidensielle. Slike opplysninger vil bare bli brukt til denne undersøkelsens formål, og vil ikke være tilgjengelige for innsyn eller bruk til andre formål uten forhåndssamtykke, unntatt dersom loven krever det.

Spørreskjema om synsfunksjon - 25

DEL 1 - HELSE OG SYN GENERELT

1. **Stort sett, vil du si at din helse alt i alt er:**

(Sett ring rundt ett tall)

Utmerket	1
Meget god	2
God	3
Nokså god	4
Dårlig	5

2. **Vil du si at synet ditt på det nåværende tidspunkt, når du bruker begge øynene (med briller eller kontaktlinser hvis du bruker det), er utmerket, godt, nokså godt, dårlig eller meget dårlig, eller er du helt blind?**

(Sett ring rundt ett tall)

Utmerket	1
Godt	2
Nokså godt	3
Dårlig	4
Meget dårlig	5
Helt blind	6

3. **Hvor ofte bekymrer du deg om synet ditt?**

(Sett ring rundt ett tall)

Aldri	1
Sjelden	2
Iblant	3
Ofte	4
Alltid	5

4. **Hvor mye smerte eller ubehag har du hatt i eller rundt øynene (for eksempel at det brenner, klør eller gjør vondt)?**

(Sett ring rundt ett tall)

Ingen/ikke noe	1
Mild(t)	2
Moderat	3
Sterk(t)	4
Meget sterk(t)	5

DEL 2 - VANSKER MED GJØREMÅL

De neste spørsmålene dreier seg om hvor store vansker, om noen, du har med å utføre visse gjøremål når du bruker briller eller kontaktlinser, dersom du bruker briller eller kontaktlinser til slike gjøremål.

5. **Hvor store vansker har du med å lese vanlig skrift i en avis?**

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	1
Små vansker	2
Moderate vansker	3
Svært store vansker	4
Har sluttet å gjøre dette pga. synet	5
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	6

6. Hvor store vansker har du med å drive med arbeid eller hobbyer som krever at du må se godt på kort avstand, slik som matlaging, søm, småreparasjoner i hjemmet eller bruk av håndholdt verktøy?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	1
Små vansker	2
Moderate vansker	3
Svært store vansker	4
Har sluttet å gjøre dette pga. synet	5
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	6

7. Hvor store vansker har du, på grunn av synet ditt, med å finne noe på en overfylt hylle?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	1
Små vansker	2
Moderate vansker	3
Svært store vansker	4
Har sluttet å gjøre dette pga. synet	5
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	6

8. Hvor store vansker har du med å lese veiskilt eller navnet på butikker?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	1
Små vansker	2
Moderate vansker	3
Svært store vansker	4
Har sluttet å gjøre dette pga. synet	5
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	6

9. Hvor store vansker har du, på grunn av synet ditt, med å gå ned trinn, trapper eller fortauskanter i svak belysning eller når det er mørkt?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	1
Små vansker	2
Moderate vansker	3
Svært store vansker	4
Har sluttet å gjøre dette pga. synet	5
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	6

10. Hvor store vansker har du, på grunn av synet ditt, med å legge merke til gjenstander som er til siden for deg når du er ute og går?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	1
Små vansker	2
Moderate vansker	3
Svært store vansker	4
Har sluttet å gjøre dette pga. synet	5
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	6

11. Hvor store vansker har du, på grunn av synet ditt, med å se hvordan folk reagerer på ting du sier?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	1
Små vansker	2
Moderate vansker	3
Svært store vansker	4
Har sluttet å gjøre dette pga. synet	5
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	6

12. Hvor store vansker har du, på grunn av synet ditt, med <u>å velge og sette sammen dine egne klær</u>?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	1
Små vansker	2
Moderate vansker	3
Svært store vansker	4
Har sluttet å gjøre dette pga. synet	5
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	6

13. Hvor store vansker har du, på grunn av synet ditt, med <u>å være sammen med mennesker hjemme hos folk, i selskaper eller på restauranter</u>?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	1
Små vansker	2
Moderate vansker	3
Svært store vansker	4
Har sluttet å gjøre dette pga. synet	5
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	6

14. Hvor store vansker har du, på grunn av synet ditt, med <u>å gå på forestillinger/oppvisninger, i teater eller på sportsbegivenheter</u>?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	1
Små vansker	2
Moderate vansker	3
Svært store vansker	4
Har sluttet å gjøre dette pga. synet	5

Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette..... 6

15. Kjører du selv bil for tiden, i alle fall en gang iblant?

(Sett ring rundt ett tall)

Ja..... 1 *Gå til spm. 15c*

Nei 2

15a. HVIS NEI: Har du aldri kjørt bil, eller har du sluttet med å kjøre?

(Sett ring rundt ett tall)

Har aldri kjørt.... 1 *Gå til del 3, spm. 17*

Har sluttet 2

15b. HVIS DU HAR SLUTTET Å KJØRE: Sluttet du først og fremst på grunn av synet, først og fremst av andre grunner, eller både på grunn av synet og av andre grunner?

(Sett ring rundt ett tall)

Først og fremst synet ..... 1 *Gå til del 3, spm. 17*

Først og fremst andre grunner .... 2 *Gå til del 3, spm. 17*

Både synet og andre grunner ..... 3 *Gå til del 3, spm. 17*

15c. HVIS DU KJØRER SELV FOR TIDEN: Hvor store vansker har du med å kjøre på dagtid på kjente steder?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt 1

Små vansker 2

Moderate vansker 3

Svært store vansker 4

16. Hvor store vansker har du med å kjøre når det er mørkt?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt 1
Små vansker 2
Moderate vansker 3
Svært store vansker 4
Har sluttet å gjøre dette pga. synet 5
Har sluttet å gjøre dette av andre grunner, eller
er ikke interessert i å gjøre dette..... 6

16a. Hvor store vansker har du med å kjøre under vanskelige forhold, slik som i rushtiden, på motorveien, i bytrafikk eller i dårlig vær?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt 1
Små vansker 2
Moderate vansker 3
Svært store vansker 4
Har sluttet å gjøre dette pga. synet 5
Har sluttet å gjøre dette av andre grunner, eller
er ikke interessert i å gjøre dette..... 6

DEL 3 - KONSEKVENSER AV SYNSPROBLEMER

De neste spørsmålene dreier seg om hvorledes ting som du gjør kan bli påvirket av synet ditt. For hvert spørsmål ber vi deg sette en ring rundt det tallet som viser om utsagnet stemmer for deg alltid, ofte, iblant, sjelden eller aldri.

	(Sett ring rundt ett tall på hver linje) Alltid	Ofte	Iblant	Sjelden	Aldri
17. Får du utrettet mindre enn det du kunne ønske på grunn av synet?	1	2	3	4	5
18. Er det begrenset hvor lenge du kan arbeide eller drive med andre gjøremål på grunn av synet?	1	2	3	4	5
19. Hvor mye hindrer smerte eller ubehag i eller rundt øynene (for eksempel at det brenner, klør eller gjør vondt) deg i å drive med det du har lyst til å drive med?	1	2	3	4	5

For hvert av de følgende utsagnene ber vi deg sette en ring rundt det tallet som viser om utsagnet gjelder for deg i meget stor grad, i stor grad, i liten grad eller overhodet ikke, eller om du er usikker.

(Sett ring rundt ett tall på hver linje)

	I meget stor grad	I stor grad	Usikker	I liten grad	Over-hodet ikke
20. På grunn av synet holder jeg meg hjemme mesteparten av tiden	1	2	3	4	5
21. På grunn av synet føler jeg meg oppgitt og frustrert mye av tiden	1	2	3	4	5
22. På grunn av synet har jeg mye mindre kontroll over det jeg gjør	1	2	3	4	5
23. På grunn av synet må jeg stole alt for mye på det andre folk forteller meg.....	1	2	3	4	5
24. På grunn av synet trenger jeg mye hjelp fra andre.....	1	2	3	4	5
25. På grunn av synet bekymrer jeg meg for å gjøre ting som vil være pinlig for meg selv eller andre.....	1	2	3	4	5

Ocular surface disease index (OSDI©)[2]

Be pasienten svare på følgende 12 spørsmål ved å sette en sirkel rundt tallet i den boksen som passer best for hvert svar. Kryss deretter av i rubrikkene A, B, C, D og E etter gitt instruksjon ved siden av rubrikken.

Har du opplevd noen av de følgende symptomene i løpet av forrige uke?	Hele tiden	Det meste av tiden	Halv-parten av tiden	Noe av tiden	Ikke noe av tiden
1. Øyne som er sensitive for lys?	4	3	2	1	0
2. Sandfølelse i øynene?	4	3	2	1	0
3. Smertefulle eller såre øyne?	4	3	2	1	0
4. Tåkesyn?	4	3	2	1	0
5. Dårlig syn?	4	3	2	1	0

Delsum for svarene 1 til 5 (A)

Har øyeproblemene dine begrenset deg i å utføre noe av det følgende i løpet av forrige uke?	Hele tiden	Det meste av tiden	Halv-parten av tiden	Noe av tiden	Ikke noe av tiden	IA Ikke aktuelt
6. Lesing?	4	3	2	1	0	IA
7. Kjøring om kvelden?	4	3	2	1	0	IA
8. Skjermarbeid?	4	3	2	1	0	IA
9. Se på TV?	4	3	2	1	0	IA

Delsum for svarene 6 til 9 (B)

Har du følt ubehag i øynene dine i noen av følgende situasjoner i løpet av forrige uke?	Hele tiden	Det meste av tiden	Halv-parten av tiden	Noe av tiden	Ikke noe av tiden	IA Ikke aktuelt
10. I vind	4	3	2	1	0	IA
11. På steder eller områder med lav luftfuktighet (veldig tørt)	4	3	2	1	0	IA
12. På steder hvor klimaanlegg er i bruk	4	3	2	1	0	IA

Delsum for svarene 10 til 12 (C)

Legg sammen delsummene A, B og C for å få D
(D = summen av alle besvarte spørsmål) (D)

Antall besvarte spørsmål
(Ikke regn med spørsmål besvart med IA) (E)

Vennligst snu spørreskjemaet for å beregne pasientens endelige OSDI© poengsum.

DIABETES, VISION AND OCULAR HEALTH

Name:

Date of birth:

Phone-number:

Mail address:

Date for examination 1:
Date for examination 2:
Date for examination 3:
Date for examination 4:

Date:

Signature:

PB/SA

National Eye Institute
Spørreskjema om synsfunksjon - 25
(VFQ-25)

(FOR EGENUTFYLLING)

Februar 1997

Dette er et spørreskjema med utsagn om problemer du har med synet ditt, eller følelser du har omkring dette. Etter hvert spørsmål ber vi deg velge det svaret som best beskriver din egen situasjon.

Vennligst svar på alle spørsmålene som om du hadde på deg dine briller eller kontaktlinser (hvis du bruker noe av dette).

Vennligst ta den tiden du trenger for å svare på hvert spørsmål. Alle svar behandles konfidensielt. For at denne spørreundersøkelsen skal øke vår kunnskap om synsproblemer og hvorledes disse problemene påvirker din livskvalitet, må svarene være så presise som mulig. Husk at dersom du bruker briller eller kontaktlinser, så vennligst svar på alle spørsmålene som om du hadde dem på deg.

VEILEDNING:

1. I det store og hele vil vi helst at folk forsøker å fylle ut disse skjemaene på egenhånd. Dersom du merker at du trenger hjelp, så vennligst ikke nøl med å henvende deg til prosjektmedarbeiderne, som vil gi deg assistanse.

2. Vennligst svar på alle spørsmålene (unntatt de spørsmålene du blir bedt om å hoppe over, fordi det/de neste spørsmål(ene) ikke angår deg).

3. Svar på spørsmålene ved å sette en ring rundt tallet for det svaret som passer.

4. Hvis du er usikker på hvilket svar du skal velge, vennligst velg det svaret som passer best, og sett en kommentar i venstre marg.

5. Vennligst fyll ut skjemaet før du går herfra og gi det til en av prosjektmedarbeiderne. Ta ikke med skjemaet hjem.

6. Hvis du har noen spørsmål, må du gjerne spørre en av prosjektmedarbeiderne, og de vil med glede hjelpe deg.

KONFIDENSIELLE OPPLYSNINGER:

Alle opplysninger som kunne tillate identifisering av en person som har fylt ut dette skjemaet, skal anses som strengt konfidensielle. Slike opplysninger vil bare bli brukt til denne undersøkelsens formål, og vil ikke være tilgjengelige for innsyn eller bruk til andre formål uten forhåndssamtykke, unntatt dersom loven krever det.

Spørreskjema om synsfunksjon - 25

DEL 1 - HELSE OG SYN GENERELT

1. Stort sett, vil du si at din helse alt i alt er:

(Sett ring rundt ett tall)

Utmerket 1
Meget god 2
God 3
Nokså god 4
Dårlig 5

2. Vil du si at synet ditt på det nåværende tidspunkt, når du bruker begge øynene (med briller eller kontaktlinser hvis du bruker det), er utmerket, godt, nokså godt, dårlig eller meget dårlig, eller er du helt blind?

(Sett ring rundt ett tall)

Utmerket 1
Godt 2
Nokså godt 3
Dårlig 4
Meget dårlig 5
Helt blind 6

3. Hvor ofte bekymrer du deg om synet ditt?

(Sett ring rundt ett tall)

Aldri	**1**
Sjelden	**2**
Iblant	**3**
Ofte	**4**
Alltid	**5**

4. Hvor mye smerte eller ubehag har du hatt i eller rundt øynene (for eksempel at det brenner, klør eller gjør vondt)?

(Sett ring rundt ett tall)

Ingen/ikke noe	**1**
Mild(t)	**2**
Moderat	**3**
Sterk(t)	**4**
Meget sterk(t)	**5**

DEL 2 - VANSKER MED GJØREMÅL

De neste spørsmålene dreier seg om hvor store vansker, om noen, du har med å utføre visse gjøremål når du bruker briller eller kontaktlinser, dersom du bruker briller eller kontaktlinser til slike gjøremål.

5. Hvor store vansker har du med å lese vanlig skrift i en avis?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	**1**
Små vansker	**2**
Moderate vansker	**3**
Svært store vansker	**4**
Har sluttet å gjøre dette pga. synet	**5**
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	**6**

6. Hvor store vansker har du med å drive med arbeid eller hobbyer som krever at du må se godt på kort avstand, slik som matlaging, søm, småreparasjoner i hjemmet eller bruk av håndholdt verktøy?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	**1**
Små vansker	**2**
Moderate vansker	**3**
Svært store vansker	**4**
Har sluttet å gjøre dette pga. synet	**5**
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	**6**

7. Hvor store vansker har du, på grunn av synet ditt, med å finne noe på en overfylt hylle?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	**1**
Små vansker	**2**
Moderate vansker	**3**
Svært store vansker	**4**
Har sluttet å gjøre dette pga. synet	**5**
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	**6**

8. Hvor store vansker har du med å lese veiskilt eller navnet på butikker?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	**1**
Små vansker	**2**
Moderate vansker	**3**
Svært store vansker	**4**
Har sluttet å gjøre dette pga. synet	**5**
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	**6**

9. Hvor store vansker har du, på grunn av synet ditt, med å gå ned trinn, trapper eller fortauskanter i svak belysning eller når det er mørkt?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	**1**
Små vansker	**2**
Moderate vansker	**3**
Svært store vansker	**4**
Har sluttet å gjøre dette pga. synet	**5**
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	**6**

10. Hvor store vansker har du, på grunn av synet ditt, med å legge merke til gjenstander som er til siden for deg når du er ute og går?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	**1**
Små vansker	**2**
Moderate vansker	**3**
Svært store vansker	**4**
Har sluttet å gjøre dette pga. synet	**5**
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	**6**

11. Hvor store vansker har du, på grunn av synet ditt, med å se hvordan folk reagerer på ting du sier?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	**1**
Små vansker	**2**
Moderate vansker	**3**
Svært store vansker	**4**
Har sluttet å gjøre dette pga. synet	**5**
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	**6**

12. Hvor store vansker har du, på grunn av synet ditt, med <u>å velge og sette sammen dine egne klær</u>?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	**1**
Små vansker	**2**
Moderate vansker	**3**
Svært store vansker	**4**
Har sluttet å gjøre dette pga. synet	**5**
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	**6**

13. Hvor store vansker har du, på grunn av synet ditt, med <u>å være sammen med mennesker hjemme hos folk, i selskaper eller på restauranter</u>?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	**1**
Små vansker	**2**
Moderate vansker	**3**
Svært store vansker	**4**
Har sluttet å gjøre dette pga. synet	**5**
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette	**6**

14. Hvor store vansker har du, på grunn av synet ditt, med <u>å gå på forestillinger/oppvisninger, i teater eller på sportsbegivenheter</u>?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt	**1**
Små vansker	**2**
Moderate vansker	**3**
Svært store vansker	**4**
Har sluttet å gjøre dette pga. synet	**5**

Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette..... 6

15. Kjører du selv bil for tiden, i alle fall en gang iblant?

(Sett ring rundt ett tall)

Ja..... 1 ***Gå til spm. 15c***

Nei 2

15a. HVIS NEI: Har du aldri kjørt bil, eller har du sluttet med å kjøre?

(Sett ring rundt ett tall)

Har aldri kjørt.... 1 ***Gå til del 3, spm. 17***

Har sluttet 2

15b. HVIS DU HAR SLUTTET Å KJØRE: Sluttet du først og fremst på grunn av synet, først og fremst av andre grunner, eller både på grunn av synet og av andre grunner?

(Sett ring rundt ett tall)

Først og fremst synet ..... 1 ***Gå til del 3, spm. 17***

Først og fremst andre grunner .... 2 ***Gå til del 3, spm. 17***

Både synet og andre grunner ..... 3 ***Gå til del 3, spm. 17***

15c. HVIS DU KJØRER SELV FOR TIDEN: Hvor store vansker har du med å kjøre på dagtid på kjente steder?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt 1
Små vansker 2
Moderate vansker 3
Svært store vansker 4

16. Hvor store vansker har du med <u>å kjøre når det er mørkt</u>?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt 1
Små vansker 2
Moderate vansker 3
Svært store vansker 4
Har sluttet å gjøre dette pga. synet 5
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette……... 6

16a. Hvor store vansker har du med <u>å kjøre under vanskelige forhold, slik som i rushtiden, på motorveien, i bytrafikk eller i dårlig vær</u>?

(Sett ring rundt ett tall)

Ingen vansker i det hele tatt 1
Små vansker 2
Moderate vansker 3
Svært store vansker 4
Har sluttet å gjøre dette pga. synet 5
Har sluttet å gjøre dette av andre grunner, eller er ikke interessert i å gjøre dette……... 6

DEL 3 - KONSEKVENSER AV SYNSPROBLEMER

De neste spørsmålene dreier seg om hvorledes ting som du gjør kan bli påvirket av synet ditt. For hvert spørsmål ber vi deg sette en ring rundt det tallet som viser om utsagnet stemmer for deg alltid, ofte, iblant, sjelden eller aldri.

	(Sett ring rundt ett tall på hver linje)				
	Alltid	**Ofte**	**Iblant**	**Sjelden**	**Aldri**
17. Får du utrettet mindre enn det du kunne ønske på grunn av synet?	**1**	**2**	**3**	**4**	**5**
18. Er det begrenset hvor lenge du kan arbeide eller drive med andre gjøremål på grunn av synet?	**1**	**2**	**3**	**4**	**5**
19. Hvor mye hindrer smerte eller ubehag i eller rundt øynene (for eksempel at det brenner, klør eller gjør vondt) deg i å drive med det du har lyst til å drive med?	**1**	**2**	**3**	**4**	**5**

For hvert av de følgende utsagnene ber vi deg sette en ring rundt det tallet som viser om utsagnet gjelder for deg i meget stor grad, i stor grad, i liten grad eller overhodet ikke, eller om du er usikker.

(Sett ring rundt ett tall på hver linje)

	I meget stor grad	I stor grad	Usikker	I liten grad	Over-hodet ikke
20. På grunn av synet holder jeg meg hjemme mesteparten av tiden	1	2	3	4	5
21. På grunn av synet føler jeg meg oppgitt og frustrert mye av tiden	1	2	3	4	5
22. På grunn av synet har jeg mye mindre kontroll over det jeg gjør	1	2	3	4	5
23. På grunn av synet må jeg stole alt for mye på det andre folk forteller meg.....	1	2	3	4	5
24. På grunn av synet trenger jeg mye hjelp fra andre.....	1	2	3	4	5
25. På grunn av synet bekymrer jeg meg for å gjøre ting som vil være pinlig for meg selv eller andre.....	1	2	3	4	5

Ocular surface disease index (OSDI©)[2]

Be pasienten svare på følgende 12 spørsmål ved å sette en sirkel rundt tallet i den boksen som passer best for hvert svar. Kryss deretter av i rubrikkene A, B, C, D og E etter gitt instruksjon ved siden av rubrikken.

Har du opplevd noen av de følgende symptomene *i løpet av forrige uke?*	**Hele tiden**	**Det meste av tiden**	**Halv-parten av tiden**	**Noe av tiden**	**Ikke noe av tiden**
1. Øyne som er sensitive for lys?	4	3	2	1	0
2. Sandfølelse i øynene?	4	3	2	1	0
3. Smertefulle eller såre øyne?	4	3	2	1	0
4. Tåkesyn?	4	3	2	1	0
5. Dårlig syn?	4	3	2	1	0

Delsum for svarene 1 til 5 **(A)**

Har øyeproblemene dine begrenset deg i å utføre noe av det følgende *i løpet av forrige uke?*	**Hele tiden**	**Det meste av tiden**	**Halv-parten av tiden**	**Noe av tiden**	**Ikke noe av tiden**	**IA Ikke aktuelt**
6. Lesing?	4	3	2	1	0	IA
7. Kjøring om kvelden?	4	3	2	1	0	IA
8. Skjermarbeid?	4	3	2	1	0	IA
9. Se på TV?	4	3	2	1	0	IA

Delsum for svarene 6 til 9 **(B)**

Har du følt ubehag i øynene dine i noen av følgende situasjoner *i løpet av forrige uke?*	**Hele tiden**	**Det meste av tiden**	**Halv-parten av tiden**	**Noe av tiden**	**Ikke noe av tiden**	**IA Ikke aktuelt**
10. I vind	4	3	2	1	0	IA
11. På steder eller områder med lav luftfuktighet (veldig tørt)	4	3	2	1	0	IA
12. På steder hvor klimaanlegg er i bruk	4	3	2	1	0	IA

Delsum for svarene 10 til 12 **(C)**

Legg sammen delsummene A, B og C for å få D
(D = summen av alle besvarte spørsmål) **(D)**

Antall besvarte spørsmål
(Ikke regn med spørsmål besvart med IA) **(E)**

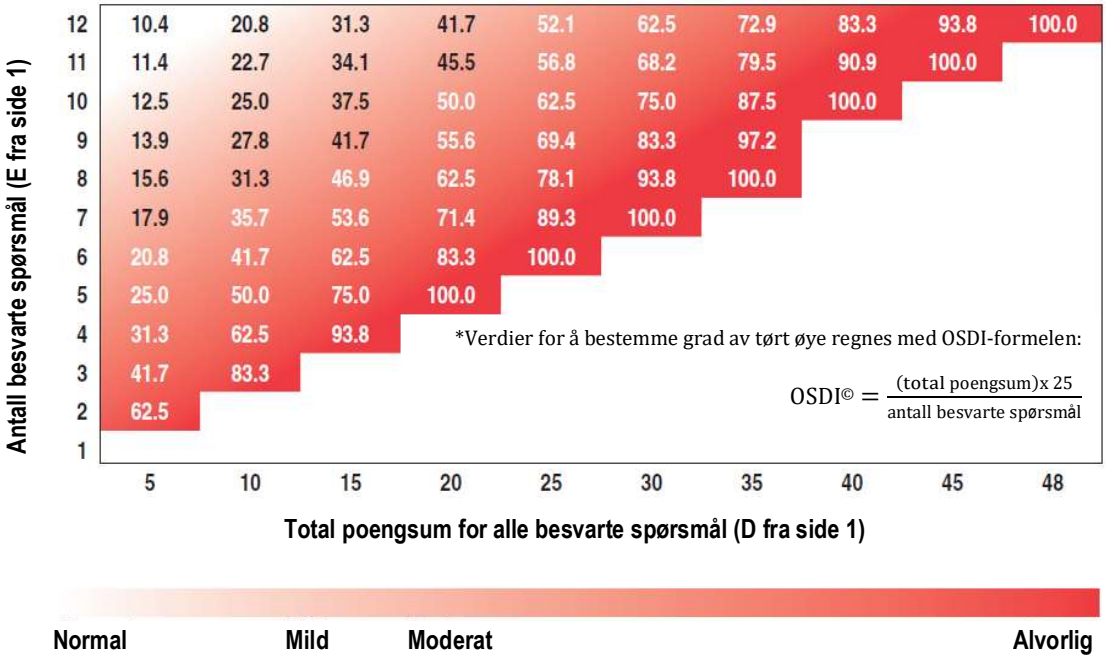
Vennligst snu spørreskjemaet for å beregne pasientens endelige OSDI© poengsum.

EVALUERING AV OSDI©[1]

OSDI© vurderes på en skala fra 0 til 100. Høyere poengsum representerer alvorligere grad av tørt øye. Indeksen viser sensitivitet og spesifisitet i å skille mellom normale personer og personer med tørre øyne. OSDI© er et sterkt og pålitelig verktøy for å måle tørt øye (normal, mild til moderat og alvorlig) og effekten på synsfunksjonen.

VURDERING AV PASIENTENS TØRRE ØYNE [1, 2]

Bruk svarene D og E fra side 1 for å sammenligne poengsummene fra alle besvarte spørsmål (D) og antall besvarte spørsmål (E) med diagrammet nedenfor*. Finn ut hvor din pasients poengsum ligger. Sammenlign rødheten med skalaen nedenfor for å bestemme om din pasients poengsum indikerer normale, milde, moderate eller alvorlig tørre øyne.



*Verdier for å bestemme grad av tørt øye regnes med OSDI-formelen:

$$\text{OSDI©} = \frac{(\text{total poengsum}) \times 25}{\text{antall besvarte spørsmål}}$$

Pasientens navn:_____Dato:_____

Hvor lenge har pasienten opplevd symptomer på tørre øyne? _____

Øyehelsepersonellets kommentarer:

_____

_____

_____

_____

1. Lagrede data, Allergan Inc.
2. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Disease Index. Arch Ophthalmol. 2000; 118:615-621

Oversatt til norsk ved IORL, HSN av Ann Elisabeth Ystenæs, Vibeke Sundling, Jan Richard Bruenech
07-07-2017

SPØRRESKJEMA (etter McMonnies questionnaire for tørre øyne) **v1987**

Spørreskjemaet er egnet til å screen for tørre øyne

Besvar spørreskjemaet ved å kryss av for de svaralternativene som er mest passende for deg.

	Mann	Under 25 år ☐	**0**	**Kvinne**	Under 25 år ☐	0	
		25 – 45 år ☐	**1**		25 – 45 år ☐	3	
		Over 45 år ☐	**2**		Over 45 år ☐	6	
	Hva slags kontaktlinser bruker du?			Ingen kontaktlinser ☐			
				Harde kontaktlinser ☐			
				Myke kontaktlinser ☐			
1	**Har du noen gang fått foreskrevet øyedråper eller annen behandling for tørre øyne?**			Ja ☐		2	
				Nei ☐		0	
				Usikker ☐		1	
2	**Opplever du noen gang følgende symptomer på tørre øyne?**			Sårhet ☐		1	
				Kløe ☐		1	
				Tørrhet ☐		1	
				Sandfølelse ☐		1	
				Svie ☐		1	
3	**Hvor ofte opplever du disse symptomene?**			Aldri ☐		0	
				Noen ganger ☐		1	
				Ofte ☐		2	
				Konstant ☐		3	
4	**Opplever du at øynene dine er spesielt sensitive mot sigarettrøyk, forurensning, luft fra klima- eller sentralvarmeanlegg?**			Ja ☐		2	
				Nei ☐		0	
				Noen ganger ☐		1	
5	**Blir øynene dine lett røde og irriterte når du svømmer i klorvann?**			Ja ☐		2	
				Nei ☐		0	
				Noen ganger ☐		1	
6	**Blir øynene dine tørre og irriterte dagen etter at du har drukket alkohol?**			Ja ☐		2	
				Nei ☐		0	
				Noen ganger ☐		1	
7	**Bruker du? (Kryss av for de medisinene som er aktuelle for deg)**			Antihistamintabletter ☐		1	
				Antihistamin øyedråper ☐		1	
				Vanndrivende medikamenter ☐		1	
				Sovetabletter ☐		1	
				Beroligende medikamenter ☐		1	
				P-piller ☐		1	
				Medikamenter mot magesår ☐		1	
				Medikamenter mot fordøyelsesproblemer ☐		1	
				Medikamenter mot høyt blodtrykk ☐		1	
				Andre medikamenter ☐		1	
8	**Har du revmatisme?**			Ja ☐		2	
				Nei ☐		0	
				Usikker ☐		1	
9	**Opplever du tørrhet i nese, munn, hals, bryst eller vagina?**			Aldri ☐		0	
				Noen ganger ☐		1	
				Ofte ☐		2	
				Konstant ☐		3	
10	**Har du problemer med stoffskiftet?**			Ja ☐		2	
				Nei ☐		0	
				Usikker ☐		1	
11	**Sover du med øynene delvis åpne?**			Ja ☐		2	
				Nei ☐		0	
				Usikker ☐		1	
12	**Er du irritert i øynene når du våkner?**			Ja ☐		2	
				Nei ☐		0	
				Usikker ☐		1	

SUM

ID-Number: _____

DIABETES, VISION AND OCULAR HEALTH

1 Patient history

1.1	Gender	☐ Female ☐ Male		
1.2	Year of birth	19		
1.3	Symptoms	☐ Blurred vision ☐ Variable vision ☐ Floaters ☐ Parts of the visual field is missing ☐ Double vision ☐ Metamorphopsia ☐ Photophobia		
1.4	Do symptoms disappear with glasses or contact lenses?	☐ Yes, ☐ No		
1.5	Vision aids:	☐ Spectacles for distance ☐ Reading glasses / computer/VDU glasses ☐ Bifocal / progressive glasses ☐ Contact lenses ☐ Low vision aid		
1.6	Regular vision examination	☐ Yes ☐ No	☐ Optometrist ☐ Ophthalmologist	/12
1.7	Regular eye examination	☐ Yes ☐ No	☐ Optometrist ☐ Ophthalmologist	/12
1.8	Ocular health	Own: ☐ Diabetes retinopathy ☐ Other retinopathy ☐ AMD ☐ Glaucoma ☐ Cataract ☐ Other ☐ Surgery; when:	Family: ☐ Diabetes retinopathy ☐ Other retinopathy ☐ AMD ☐ Glaucoma ☐ Cataract ☐ Other	
1.9	Diabetes type 2 duration:	_____ years		
1.10	Glucose level	_____ Mmol/l (%)		
1.11	Treatment of diabetes	☐ Lifestyle intervention	☐ Oral medication	☐ Insulin
1.12	Diabetes in the family	☐ Yes ☐ No		
1.13a	Hypertension	☐ Yes ☐ No		
1.13b	Vascular disease, incl stroke	☐ Yes ☐ No		
1.14	Blood pressure	☐ Low ☐ Normal ☐ High ☐ Not sure	_____ / _____ mmHg	
1.15	Cholesterol	☐ Low ☐ Normal ☐ High ☐ Not sure	LDL /HDL _____ / _____.	
1.16	Smoking	☐ Yes ☐ No		
1.17	Allergy	☐ Yes ☐ No		

ID-Number: _____

2 Visual function

2.0 Pd:

		OD	OS	OU
2.1	Habitual correction ☐Contact Lens	/ x Δ	/ x Δ	
2.2	Habitual visual acuity (logMAR)			
2.3a	Autorefractor			
2.3b	Pachymetry			
2.4	Subjective refraction	/ x Δ	/ x Δ	
2.5	Best corrected visual acuity (logMAR)			
2.6	Visual acuity with pinhole (logMAR ≤ 0.2)			
2.7	Near add at 40 cm			
2.8	Near visual acuity at 40 cm			

2.9 Cover test

Distance	Near
☐ Ortho	☐ Ortho
☐ ExoP ☐ ExoT	☐ ExoP ☐ ExoT
☐ EsoP ☐ EsoT	☐ EsoP ☐ EsoT
☐ HyperP ☐ HyperT	☐ HyperP ☐ HyperT

Comments:

2.10 Color vision – HRR at 66 cm

OD	OS
☐ Normal	☐ Normal
☐ Deficiency	☐ Deficiency

2.11 Amsler at 30 cm

OD	OS
☐ Normal	☐ Normal
☐ Metamorphopsia	☐ Metamorphopsia
☐ Visual field loss	☐ Visual field loss

2.12 Contrast sensitivity MARS at 50 cm

OD	OS

2.14 Pupillary responses
☐ Normal
☐ Abnormal

2.13 Motility
☐ Normal
☐ Abnormal

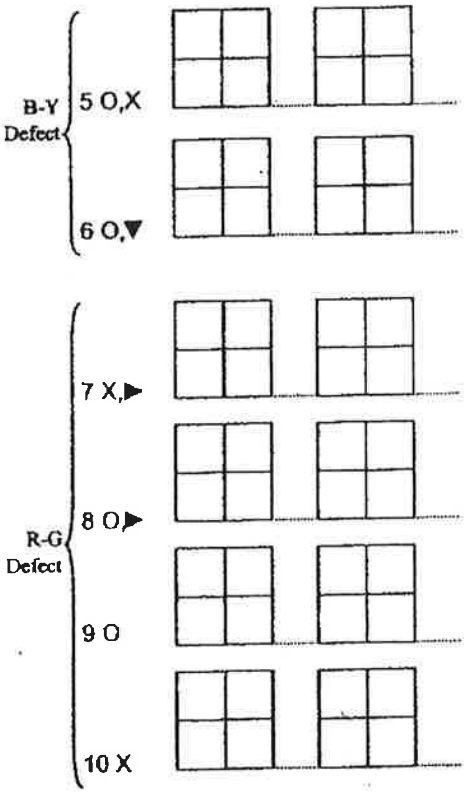
*** Remember to check blink rate before switching room!**

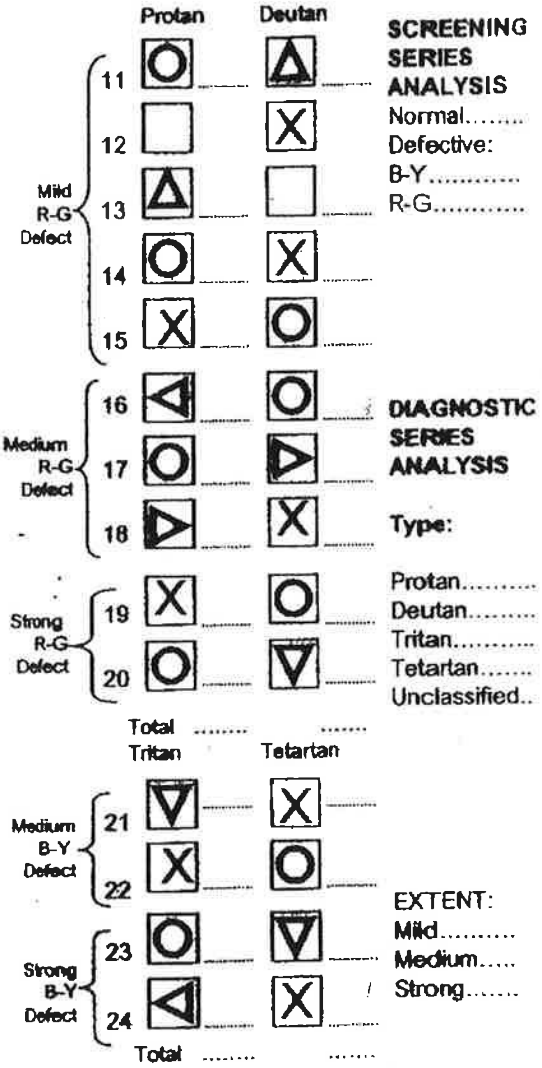
H R R PSEUDOISOCHROMATIC PLATES

NAME..... **DATE**..... **EXAMINER**.....

1-4 DEMONSTRATION SERIES
Four plates. Do NOT score.

SCREENING SERIES





SCREENING SERIES ANALYSIS
Normal.....
Defective:
B-Y.....
R-G.....

DIAGNOSTIC SERIES ANALYSIS

Type:
Protan.....
Deutan.....
Tritan.....
Tetartan.....
Unclassified..

EXTENT:
Mild.....
Medium.....
Strong.....

1021 South Rogers Circle Suite 6 Boca Raton, FL 33487

Laminated Version P/N 4458

The Mars Letter Contrast Sensitivity Test

Score Sheet

Patient _____ Administered by _____

Date _____ Correction _____ Test distance _____

Comments _____

Quick Instructions: Instruct patient to read letters left to right for each line, from top to bottom of the chart. Mark misses with an "X." Stop test on 2 consecutive misses.

Important: Allow *only* the letters C D H K N O R S V Z as responses.

FORM 1

Left eye ☐ Right eye ☐ Binocular ☐

C ☐ 0.04	H ☐ 0.08	V ☐ 0.12	O ☐ 0.16	S ☐ 0.20	N ☐ 0.24
D ☐ 0.28	S ☐ 0.32	Z ☐ 0.36	N ☐ 0.40	R ☐ 0.44	K ☐ 0.48
N ☐ 0.52	D ☐ 0.56	R ☐ 0.60	H ☐ 0.64	V ☐ 0.68	Z ☐ 0.72
C ☐ 0.76	S ☐ 0.80	O ☐ 0.84	N ☐ 0.88	K ☐ 0.92	H ☐ 0.96
K ☐ 1.00	N ☐ 1.04	V ☐ 1.08	D ☐ 1.12	S ☐ 1.16	R ☐ 1.20
Z ☐ 1.24	R ☐ 1.28	D ☐ 1.32	K ☐ 1.36	H ☐ 1.40	O ☐ 1.44
H ☐ 1.48	Z ☐ 1.52	C ☐ 1.56	V ☐ 1.60	R ☐ 1.64	K ☐ 1.68
S ☐ 1.72	C ☐ 1.76	Z ☐ 1.80	D ☐ 1.84	V ☐ 1.88	O ☐ 1.92

Value of final correct letter: _____

Number of misses prior to stopping _____X 0.04 = _____

Subtract

log Contrast Sensitivity _____

FORM 2

Left eye ☐ Right eye ☐ Binocular ☐

K ☐ 0.04	S ☐ 0.08	H ☐ 0.12	O ☐ 0.16	N ☐ 0.20	C ☐ 0.24
Z ☐ 0.28	D ☐ 0.32	C ☐ 0.36	R ☐ 0.40	V ☐ 0.44	O ☐ 0.48
C ☐ 0.52	K ☐ 0.56	O ☐ 0.60	N ☐ 0.64	R ☐ 0.68	S ☐ 0.72
N ☐ 0.76	S ☐ 0.80	Z ☐ 0.84	K ☐ 0.88	H ☐ 0.92	D ☐ 0.96
H ☐ 1.00	N ☐ 1.04	C ☐ 1.08	O ☐ 1.12	R ☐ 1.16	Z ☐ 1.20
V ☐ 1.24	K ☐ 1.28	S ☐ 1.32	N ☐ 1.36	D ☐ 1.40	R ☐ 1.44
K ☐ 1.48	R ☐ 1.52	V ☐ 1.56	Z ☐ 1.60	O ☐ 1.64	S ☐ 1.68
V ☐ 1.72	Z ☐ 1.76	C ☐ 1.80	D ☐ 1.84	V ☐ 1.88	H ☐ 1.92

Value of final correct letter: _____

Number of misses prior to stopping _____X 0.04 = _____

Subtract

log Contrast Sensitivity _____

FORM 3

Left eye ☐ Right eye ☐ Binocular ☐

H ☐ 0.04	R ☐ 0.08	Z ☐ 0.12	V ☐ 0.16	C ☐ 0.20	N ☐ 0.24
S ☐ 0.28	O ☐ 0.32	K ☐ 0.36	D ☐ 0.40	R ☐ 0.44	S ☐ 0.48
K ☐ 0.52	D ☐ 0.56	C ☐ 0.60	V ☐ 0.64	O ☐ 0.68	H ☐ 0.72
N ☐ 0.76	S ☐ 0.80	O ☐ 0.84	Z ☐ 0.88	C ☐ 0.92	D ☐ 0.96
R ☐ 1.00	H ☐ 1.04	N ☐ 1.08	K ☐ 1.12	Z ☐ 1.16	O ☐ 1.20
C ☐ 1.24	R ☐ 1.28	S ☐ 1.32	V ☐ 1.36	K ☐ 1.40	N ☐ 1.44
S ☐ 1.48	K ☐ 1.52	R ☐ 1.56	N ☐ 1.60	H ☐ 1.64	D ☐ 1.68
C ☐ 1.72	V ☐ 1.76	H ☐ 1.80	D ☐ 1.84	O ☐ 1.88	Z ☐ 1.92

Value of final correct letter: _____

Number of misses prior to stopping _____X 0.04 = _____

Subtract

log Contrast Sensitivity _____

mars perceptrix

ID-Number:

3 Ocular health

Have you used eye drops today? ☐ No ☐ Yes, type and time:

OD					OS			
/min.				3.1a Blink rate	/min.			
60/.....= .....sec.				3.1b Inter blink interval 60/ blinks per minute	60/.....=.....sec.			
				KERATOGRAPH K5 3.2a Tear meniscus height				
……. mm					…… mm			
Sec.	Sec.	Sec.	Mean	3.2b Non-invasive Keratograph Break-up Time	Sec.	Sec.	Sec.	Mean
Temporal:		Nasal:		3.2c Bubar redness	Nasal:		Temporal:	
Temporal:		Nasal:		3.2d Limbal redness	Nasal:		Temporal:	
☐ Yes ☐ No				3.2e. Lipid Layer Thickness Video sequence 20 sec	☐ Yes ☐ No			
mOsm/L				3.3. Tear osmolarity	mOsm/L			
☐ Exophtalmos ☐ Enophtalmos				3.4a Position	☐ Exophtalmos ☐ Enophtalmos			
☐ Yes ☐ No				3.4b Eye movemnets Free in all directions	☐ Yes ☐ No			
☐ Blepharitis (Efron grade ≥ 2) ☐ Collarets ☐ Telangiectasia ☐ Ectropion ☐ Entropion ☐ Trichiasis ☐ Eye lid tumor				3.4c Eye lids	☐ Blepharitis (Efron grade ≥ 2) ☐ Collarets ☐ Telangiectasia ☐ Ectropion ☐ Entropion ☐ Trichiasis ☐ Eye lid tumor			
				3.4d Conjuctiva				
☐ Scar ☐ Infiltrates ☐ Pigmentation ☐ Other				3.4e Cornea	☐ Scar ☐ Infiltrates ☐ Pigmentation ☐ Other			
				3.5 Van Herrick				
Sec.	Sec.	Sec.	Mean	3.6 Fluorescein break-up time	Sec.	Sec.	Sec.	Mean
Grade Temp.	Grade Corneal	Grade Nasal	Total	3.7a Ocular surface fluorescein staining (Oxford grading)	Grade Nasal	Grade Corneal	Grade Temp.	Total
Grade Temp. …….	Grade Corneal ……..	Grade Nasal …….	Total ……	3.7b Ocular surface lissamine green staining (Oxford grading)	Grade Nasal …….	Grade Corneal ……..	Grade Temp. …….	Total ……
☐ ≥ 2 mm ☐ ≥ 25%				3.8 Lid wiper epitheliopathy	☐ ≥ 2 mm ☐ ≥ 25%			
				3.9 Intra ocular pressure (I-care)				

ID-Number:

3 Ocular health

<table>
<tr><th colspan="4">OD</th><th></th><th colspan="4">OS</th></tr>
<tr><td colspan="4">…… mm /5 min.</td><td>3.10 Schirmer 1 Test
15 minutes after ocular staining</td><td colspan="4">…… mm/5 min.</td></tr>
<tr><td colspan="8">* Remember to clean lid margin!</td></tr>
<tr><td colspan="4">☐ Meibomian glands in line
☐ Even lid margin:
Other:</td><td>3.11a Eye lid examination
Morphological features</td><td colspan="4">☐ Meibomian glands in line
☐ Even lid margin:
Other:</td></tr>
<tr><td colspan="3">No. of expressible glands OD
……...</td><td>Grade

……..</td><td>3.11b Meibum expressibility
(Central 5 glands)</td><td colspan="3">No. of expressible glands OS

……..</td><td>Grade

……..</td></tr>
<tr><td colspan="3">…. glands x 0 =
…. glands x 1 =
…. glands x 2 =
…. glands x 3 =</td><td>Total score</td><td>3.11c Meibum quality
(central 8 glands)
Clear fluid= 0
Cloudy fluid= 1
Cloudy particulate fluid = 2
Like toothpaste = 3</td><td colspan="3">…. glands x 0 =
…. glands x 1 =
…. glands x 2 =
…. glands x 3 =</td><td>Total score</td></tr>
<tr><td>Upper lid:</td><td colspan="2">Lower lid:</td><td>Total</td><td>3.12 Meibography
Meibomian gland drop-out Upper and lower lid according to scale</td><td>Upper lid:</td><td colspan="2">Lower lid:</td><td>Total</td></tr>
<tr><td colspan="4"></td><td>3.13 Corneal senstivity (Cochet-Bonnet)*</td><td colspan="4"></td></tr>
<tr><td>NCC</td><td>NCO</td><td>CC</td><td>PCC</td><td rowspan="2">3.14 Crystalline lens transparency
(LOCS III grading)**</td><td>NCC</td><td>NCO</td><td>CC</td><td>PCC</td></tr>
<tr><td colspan="2">☐
Pseudophakia</td><td colspan="2">☐
PCO</td><td colspan="2">☐
Pseudophakia</td><td colspan="2">☐
PCO</td></tr>
<tr><td colspan="4"></td><td>3.15 Pupille size after dilation</td><td colspan="4"></td></tr>
</table>

**NCC – Nuclear cataract colour; NCO – Nucelar cataract opacity; CC – Cortical cataract; PCC – Posterior capsular cataract; PCO – Posterior capsular opacity

*** Dilate after measuring corneal sensitivity. Check dilation after 10 minutes**

Comments:

ID-Number: _____

3 Ocular health

3.16a	OCT (Cirrus)	OD ☐ Macular Cube ☐ HD 1 line 100x EDI ☐ HD Raster 5 lines EDI ☐ HD Radial (Optic disc) ☐ Optic Disc Cube	OS ☐ Macular Cube ☐ HD 1 line 100x EDI ☐ HD Raster 5 lines EDI ☐ HD Radial (Optic disc) ☐ Optic Disc Cube
3.16b	Check pupille size and eyelid position	☐ Ok	☐ Ok
3.17	Retinal photography (Optomap)	OD ☐ Normal x 2 ☐ AF	OS ☐ Normal x 2 ☐ AF
3.18	Retinal photography (KOWA)	OD ☐ Normal - disc ☐ Normal - macula ☐ Stereo disc	OS ☐ Normal - disc ☐ Normal - macula ☐ Stereo disc

*** Remember to check the crystalline lens!**

3.19	Perimetry - Octopus	OD ☐ Normal ☐ Visual field loss	OS ☐ Normal ☐ Visual field loss

Retinal Assessment

3.20	Evaluation retina	OD ☐ Normal ☐ Abnormal	OS ☐ Normal ☐ Abnorma
3.21	Grading diabetes retinopathy	OD ☐ No ☐ Mild NPDR ☐ Moderat NPDR ☐ Severe NPDR ☐ PDR ☐ Macular edema	OS ☐ No ☐ Mild NPDR ☐ Moderat NPDR ☐ Severe NPDR ☐ PDR ☐ Macular edema

3.22 Comments:

4 Management of participants

4.1	Prescription provided	☐ Yes ☐ No	
4.2	Further managment	☐ Yes ☐ No	☐ Full eye examination ☐ Dry eye ☐ Referral ☐ Emergency
4.3	Reason for further managment		☐ Symptoms ☐ Visual acuity ☐ Binocular vision ☐ Visual fields ☐ Colour vision ☐ Intraocular pressure ☐ Anterior segment / dry eye ☐ Cataract ☐ Retinopathy ☐ Maculopathy ☐ Glaucoma ☐ Other

5 Comments:

Date:

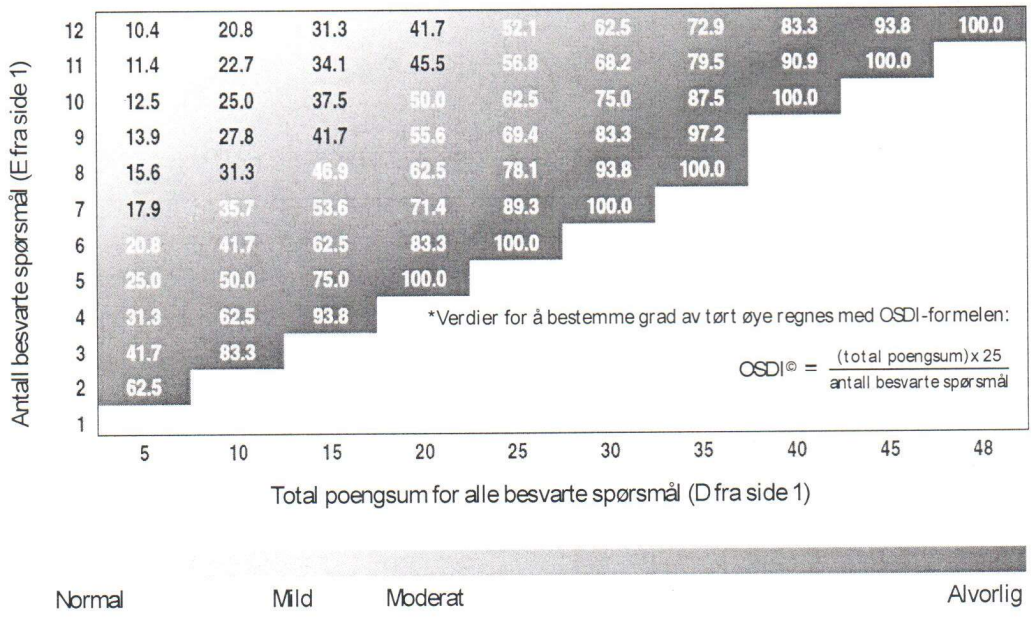
Signature:

EVALUERING AV OSDI© [1]

OSDI© vurderes på en skala fra 0 til 100. Høyere poengsum representerer alvorligere grad av tørt øye. Indeksen viser sensitivitet og spesifisitet i å skille mellom normale personer og personer med tørre øyne. OSDI© er et sterkt og pålitelig verktøy for å måle tørt øye (normal, mild til moderat og alvorlig) og effekten på synsfunksjonen.

VURDERING AV PASIENTENS TØRRE ØYNE [1, 2]

Bruk svarene D og E fra side 1 for å sammenligne poengsummene fra alle besvarte spørsmål (D) og antall besvarte spørsmål (E) med diagrammet nedenfor*. Finn ut hvor din pasients poengsum ligger. Sammenlign rødheten med skalaen nedenfor for å bestemme om din pasients poengsum indikerer normale, milde, moderate eller alvorlig tørre øyne.



Pasientens navn:_____ Dato:_____

Hvor lenge har pasienten opplevd symptomer på tørre øyne?_____

Øyehelsepersonellets kommentarer:

_____

_____

_____

_____

1. Lagrede data, Allergan Inc.
2. Schiffman RM, Christianson MD, Jacobsen G, Hirsch JD, Reis BL. Reliability and validity of the Ocular Disease Index. Arch Ophthalmol. 2000; 118:615-621

Oversatt til norsk ved IORL, HSN av Ann Elisabeth Ystenæs, Vibeke Sundling, Jan Richard Bruenech
07-07-2017

Version 2000

The National Eye Institute 25-Item Visual Function Questionnaire (VFQ-25)

Version 2000

This final version of the VFQ-25 differs from the previous version in that it includes an extra driving item from the appendix of supplementary questions as part of the base set of items. Also, the revised scoring algorithm excludes the single-item general health rating question from the calculation of the vision-targeted composite score. Because of these 2 changes, the base set of items actually includes 26 questions, however, only 25 are vision-targeted and included in the composite score. Please see the "Frequently Asked Questions" or FAQ section for additional clarifications of these changes.

Background

The National Eye Institute (NEI) sponsored the development of the VFQ-25 with the goal of creating a survey that would measure the dimensions of self-reported vision-targeted health status that are most important for persons who have chronic eye diseases. Because of this goal, the survey measures the influence of visual disability and visual symptoms on generic health domains such as emotional well-being and social functioning, in addition to task-oriented domains related to daily visual functioning. Questions included in the VFQ-25 represent the content identified during a series of condition-specific focus groups with patients who had age-related cataracts, glaucoma, age-related macular degeneration, diabetic retinopathy, or CMV retinitis. [1]

The VFQ-25 is the product of an item-reduction analysis of the longer field test version of the survey called the 51-item National Eye Institute Vision Function Questionnaire (NEI-VFQ).[2] The longer version contains 51 questions which represent 13 different sub-scales. The NEI-VFQ Field Test Study collected the data needed to examine the reliability and validity of the survey across all of the above-mentioned ocular diseases. Also, reliability and validity was assessed in a heterogeneous group of patients with low vision from any cause and a group of age-matched persons with normal vision. A published report describes the psychometric properties of the longer field test version of the survey. [3] Additional a number of clinical studies have used either the 51 or the 25-item version of the NEI-VFQ across a number of chronic ocular conditions. [4-8] Despite the success of the longer field test version and its continued use, to enhance feasibility a short-form version was planned since the earliest developmental phase.

The VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. The VFQ-25 also includes an appendix of additional items from the 51-item version that researchers can use to expand the scales up to 39 total items. All items in the VFQ-25 are from the 51-item field test version; no new items were developed for use in the VFQ-25. Unless otherwise specified, the remainder of this document will use the term VFQ-25 to refer to the base set of items.

The VFQ-25 takes approximately 10 minutes on average to administer in the interviewer format. There is also a self-administered version of the survey, however, psychometric testing of the self-administered version has not been done. The VFQ-25 generates the following vision-targeted sub-scales: global vision rating (1), difficulty with near vision activities (3), difficulty with distance vision activities (3), limitations in social functioning due to vision (2), role limitations due to vision (2), dependency on others due to vision (3), mental health symptoms due to vision (4), driving difficulties (3), limitations with peripheral

(1) and color vision (1), and ocular pain (2). Additionally, the VFQ-25 contains the single general health rating question which has been shown to be a robust predictor of future health and mortality in population-based studies. Please see the FAQ section for more information about the general health rating question.

Development of the NEI VFQ-25

The guiding principles for the selection of the short-form items included: 1) low item-level missing data rates; 2) normal distribution of response choices; and 3) retention of items that explained the greatest proportion of variance in the 51-item sub-scales. The items retained in the VFQ-25 and the optional items (provided in the appendix to the survey) are listed on Table 1. A report describing the performance of the VFQ-25 relative to the Field Test version is currently under review.[2] The reliability and validity of the VFQ-25 is similar to that observed for the 51-item version of the survey. On average, each VFQ-25 sub-scale predicts 92% of the variance in the corresponding 51-item sub-scale score.

Optional Items

Appendix 1 consists of additional questions that users may add to a specific sub-scale. Inclusion of these may be helpful if a particular sub-scale represents the primary domain of vision-targeted HRQOL that is felt to be most important for the condition under study. For example, if a user is testing a new treatment for macular degeneration, by adding near vision questions A3, A4, and A5 to VFQ-25 questions 5, 6, and 7, the investigator would have a six-item near vision scale rather than a three-item scale. The addition of these items would enhance the reliability of the near vision sub-scale and is likely to improve the responsiveness of the sub-scale to the intervention over time (Table 6). If items from the appendix are used, the VFQ-25 developers would encourage users to incorporate all optional items for a given sub-scale. This strategy will enhance the comparability of results across studies.

Scoring

Scoring VFQ-25 with or without optional items is a two-step process:

- First, original numeric values from the survey are re-coded following the scoring rules outlined in Table 2. All items are scored so that a high score represents better functioning. Each item is then converted to a 0 to 100 scale so that the lowest and highest possible scores are set at 0 and 100 points, respectively. In this format scores represent the achieved percentage of the total possible score, e.g. a score of 50 represents 50% of the highest possible score.

- In step 2, items within each sub-scale are averaged together to create the 12 sub-scale scores. Table 3 indicates which items contribute to each specific sub-scale. Items that are left blank (missing data) are not taken into account when calculating the scale scores. Sub-scales with at least one item answered can be used to generate a sub-scale score. Hence, scores represent the average for all items in the sub-scale that the respondent answered.

Composite Score Calculation

To calculate an overall composite score for the VFQ-25, simply average the vision-targeted sub-scale scores, excluding the general health rating question. By averaging the sub-scale scores rather than the individual items we have given equal weight to each sub-scale, whereas averaging the items would give more weight to scales with more items.

Table 1. Item Number Translation from the 51-Item Field Test Version to the VFQ 25

S = retained in the VFQ-25, A = retained in the appendix should be used for the VFQ-39,

--- = deleted from the VFQ-25 & VFQ-39

Field Test Version Ques.#	Sub-scale	Status	VFQ-25 Ques. #	Field Test Version Ques.#	Sub-scale	Status	VFQ-25 Ques. #
1	general health	S	1	29	social fx	---	---
2	general health	A	A1	30	social fx	A	A9
3	general vision	S	2	31	social fx	S	13
4	expectations	---	---	32	distance vision	A	A8
5	well-being/ distress	S	3	33	distance vision	A	A7
6	well-being/ distress	---	---	34	distance vision	S	14
7	ocular pain	S	19	35	driving (filter item)	S	15
8	expectations	---	---	35a	driving (filter item)	S	15a
9	expectations	---	---	35b	driving (filter item)	S	15b
10	expectations	---	---	35c	driving	S	15c
11	well-being/ distress	S	25	36	driving	---	---
12	ocular pain	S	4	37	driving	S	16
13	well-being/ distress	---	---	38	driving	S	16a *
14	general vision	A	A2	39a	role limitations	S	17
15	near vision	S	5	39b	role limitations	A	A11a
16	near vision	A	A3	39c	well-being/ distress	---	---
17	near vision	S	6	39d	role limitations	---	---
18	near vision	---	---	39e	role limitations	A	A11b
19	near vision	S	7	39f	role limitations	S	18
20	distance vision	S	8	40	well-being/ distress	A	A12
21	distance vision	---	---	41	dependency	S	20
22	distance vision	S	9	42	well-being/ distress	S	21
23	peripheral vision	S	10	43	well-being/ distress	S	22
24	distance vision	A	A6	44	dependency	---	---
25	social fx	S	11	45	dependency	A	A13
26	near vision	A	A4	46	dependency	S	23
27	color vision	S	12	47	dependency	S	24
28	near vision	A	A5				

* VFQ-25 item 16a was listed in previous versions as part of the appendix of supplemental items (#A10).

Table 2. Scoring Key: Recoding of Items

Item Numbers	Change original response category [a]	To recoded value of:
1,3,4,15c[b]	1	100
	2	75
	3	50
	4	25
	5	0
2	1	100
	2	80
	3	60
	4	40
	5	20
	6	0
5,6,7,8,9,10,11,12,13,14,16,16a A3,A4,A5,A6,A7,A8,A9[c]	1	100
	2	75
	3	50
	4	25
	5	0
	6	*
17,18,19,20,21,22,23,24,25, A11a,A11b,A12,A13	1	0
	2	25
	3	50
	4	75
	5	100
A1,A2	0	0
	to	to
	10	100

[a] Precoded response choices as printed in the questionnaire.

[b] Item 15c has four-response levels, but is expanded to a five-levels using item 15b.
Note: If 15b=1, then 15c should be recoded to "0"
If 15b=2, then 15c should be recoded to missing.
If 15b=3, then 15c should be recoded to missing.

[c] "A" before the item number indicates that this item is an optional item from the Appendix. If optional items are used, the NEI-VFQ developers encourage users to use <u>all</u> items for a given sub-scale. This will greatly enhance the comparability of sub-scale scores across studies.

* Response choice "6" indicates that the person does not perform the activity because of non-vision related problems. If this choice is selected, the item is coded as "missing."

Table 3. Step 2: Averaging of Items to Generate VFQ-25 Sub-Scales

Scale	Number of items	Items to be averaged (after recoding per Table 2)
General Health	1	1
General Vision	1	2
Ocular Pain	2	4, 19
Near Activities	3	5, 6, 7
Distance Activities	3	8, 9, 14
Vision Specific:		
Social Functioning	2	11, 13
Mental Health	4	3, 21, 22, 25
Role Difficulties	2	17, 18
Dependency	3	20, 23, 24
Driving	3	15c, 16, 16a
Color Vision	1	12
Peripheral Vision	1	10

Table 4. Step 2: Averaging of Items to Generate VFQ-39 Sub-Scales (VFQ-25 + Optional Items)

Scale	Number of items	Items to be averaged (after recoding per Table 2)
General Health	2	1, A1
General Vision	2	2, A2
Ocular Pain	2	4, 19
Near Activities	6	5, 6, 7, A3, A4, A5
Distance Activities	6	8, 9, 14, A6, A7, A8
Vision Specific:		
Social Functioning	3	11, 13, A9
Mental Health	5	3, 21, 22, 25, A12
Role Difficulties	4	17, 18, A11a, A11b
Dependency	4	20, 23, 24, A13
Driving	3	15c, 16, 16a
Color Vision	1	12
Peripheral Vision	1	10

Figure 1. Example of VFQ-25 Scoring Algorithm for Near Activities Sub-Scale

5. How much difficulty do you have <u>reading ordinary print in newspapers</u>? Would you say you have:

No difficulty at all..... 1
A little difficulty 2
Moderate difficulty 3
Extreme difficulty .....**(4)**
Stopped doing this because of your eyesight 5
Stopped doing this for other reasons or not
interested in doing this..... 6

6. How much difficulty do you have doing work or hobbies that require you to see well up close, such as cooking, sewing, fixing . . . ? Would you say you have:

No difficulty at all.....**(1)**
A little difficulty 2
Moderate difficulty 3
Extreme difficulty 4
Stopped doing this because of your eyesight 5
Stopped doing this for other reasons or not
interested in doing this..... 6

7. Because of your eyesight, how much difficulty do you have finding something on a crowded shelf? Would you say you have:

No difficulty at all..... 1
A little difficulty 2
Moderate difficulty 3
Extreme difficulty .....**(4)**
Stopped doing this because of your eyesight 5
Stopped doing this for other reasons or not
interested in doing this..... 6

Scoring example - Figure 1

Items 5, 6, and 7 are used to generate the near activities sub-scale score (Table 3). Each of the items has 6 response choices. Response choice 6 indicates that the respondent does not perform the activity because of reasons that are unrelated to vision. If a respondent selects this choice, the answer is treated as missing and an average of the remaining items is calculated. Response choice 5 indicates that an activity is so difficult that the participant no longer performs the activity. This extremely poor near vision response choice is recoded to "0" points before taking an average of all three items. To score all items in the same direction, Table 2 shows that responses 1 through 5 for items 5, 6, and 7 should be recoded to values of 100, 75, 50, 25, and 0 respectively. If the respondent is missing one of the items, the person's score will be equal to the average of the two non-missing items.

Formula:

$$\text{Mean} = \frac{\text{(Score for each item with a non-missing answer)}}{\text{Total number of items with non-missing answers}}$$

Example:

$$\text{With responses converted:} = \frac{(25 + 100 + 25)}{3} = 50$$

Note: 100 = Best, 0 = Worst possible score.

Psychometric properties of VFQ-25 sub-scales

Psychometric data for VFQ-25 reported in the earlier pre-publication version of the scoring manual have been updated and submitted for peer-reviewed publication.[2] The values reported in this document are identical to those reported in the future publication and should be used when citing the performance characteristics of the VFQ-25.

Statistical Power Calculations

Tables 8, 9, and 10 are provided to estimate statistical power when using the VFQ-25 and VFQ-39. These tables estimate the number of subjects needed per group to attain 80% power (alpha = 0.05, two-tailed) depending on the anticipated difference in scores between groups. Table 8 contains power calculations for changes over time between two experimental (i.e. randomized) groups using a repeated-measures design. For example, if one were interested in being able to detect a 5-point difference for the VFQ-25 General Vision sub-scale, one would need 271 subjects per group. Table 9 shows power calculations for two experimental groups using a single, post-intervention measurement design. Such a design is not as precise as a design that uses a baseline and post-intervention measurement points (i.e., more subjects are needed per group to detect the same difference). Table 10 provides corresponding sample size information for a non-experimental (i.e. non-randomized) repeated-measures design where subjects self-select into the two groups. One sees that the number of subjects needed per group is more than that needed for a randomized experiment (Table 8) and less than the number needed for a randomized, post-intervention-only measurement design (Table 9).

Table 8. Sample sizes needed per group to detect differences in *change over time* between two experimental groups for the VFQ-25, repeated measures design

		Number of Points Difference			
Scale Name	SD	2	5	10	20
VFQ-25:					
General Health	26.00	1696	271	68	17
General Vision	21.00	1106	177	44	11
Ocular Pain	17.00	725	116	29	7
Near Activities	29.00	2110	338	84	21
Distance Activities	29.00	2110	338	84	21
Social Functioning	27.00	1829	293	73	18
Mental Health	27.00	1829	293	73	18
Role Difficulties	29.00	2110	338	84	21
Dependency	28.00	1967	315	79	20
Driving	35.00	3073	492	123	31
Color Vision	23.00	1327	212	53	13
Peripheral Vision	27.00	1829	293	73	18
VFQ-25 Composite	20.00	1004	161	40	10
VFQ-39:					
General Health	21.00	1106	177	44	11
General Vision	19.00	906	145	36	9
Ocular Pain	17.00	725	116	29	7
Near Activities	28.00	1967	315	79	20
Distance Activities	26.00	1696	271	68	17
Social Functioning	25.00	1568	251	63	16
Mental Health	26.00	1696	271	68	17
Role Difficulties	28.00	1967	315	79	20
Dependency	27.00	1829	293	73	18
Driving	35.00	3073	492	123	31
Color Vision	23.00	1327	212	53	13
Peripheral Vision	27.00	1829	293	73	18
VFQ-39 Composite	21.00	1106	177	44	11

Note: Scales are all scored on 0-100 possible range. Estimates assume alpha = 0.05, two-tailed t-test, power = 80%, and an inter-temporal correlation between scores of 0.60.

Table 9. Sample sizes needed per group to detect differences between two experimental groups for the VFQ-25, *post-intervention measures only.*

		Number of Points Difference			
Scale Name	SD	2	5	10	20
VFQ-25:					
General Health	26.00	2650	424	106	26
General Vision	21.00	1729	277	69	17
Ocular Pain	17.00	1133	181	45	11
Near Activities	29.00	3297	527	132	33
Distance Activities	29.00	3297	527	132	33
Social Functioning	27.00	2858	457	114	29
Mental Health	27.00	2858	457	114	29
Role Difficulties	29.00	3297	527	132	33
Dependency	28.00	3073	492	123	31
Driving	35.00	4802	768	192	48
Color Vision	23.00	2074	332	83	21
Peripheral Vision	27.00	2858	457	114	29
VFQ-25 Composite	20.00	1568	251	63	16
VFQ-39:					
General Health	21.00	1729	277	69	17
General Vision	19.00	1415	226	57	14
Ocular Pain	17.00	1133	181	45	11
Near Activities	28.00	3073	492	123	31
Distance Activities	26.00	2650	424	106	26
Social Functioning	25.00	2450	392	98	25
Mental Health	26.00	2650	424	106	26
Role Difficulties	28.00	3073	492	123	31
Dependency	27.00	2858	457	114	29
Driving	35.00	4802	768	192	48
Color Vision	23.00	2074	332	83	21
Peripheral Vision	27.00	2858	457	114	29
VFQ-39 Composite	21.00	1729	277	69	17

Note: Scales are all scored on 0-100 possible range. Estimates assume alpha = 0.05, two-tailed t-test, and power = 80%.

Table 10. Sample sizes needed per group to detect differences between two *self-selected groups* for the VFQ-25, repeated measures design

		Number of Points Difference			
Scale Name	SD	2	5	10	20
VFQ-25:					
General Health	26.00	2120	339	85	21
General Vision	21.00	1383	221	55	14
Ocular Pain	17.00	906	145	36	9
Near Activities	29.00	2637	422	105	26
Distance Activities	29.00	2637	422	105	26
Social Functioning	27.00	2286	366	91	23
Mental Health	27.00	2286	366	91	23
Role Difficulties	29.00	2637	422	105	26
Dependency	28.00	2459	393	98	25
Driving	35.00	3842	615	154	38
Color Vision	23.00	1659	265	66	17
Peripheral Vision	27.00	2286	366	91	23
VFQ-25 Composite	20.00	1254	201	50	13
VFQ-39:					
General Health	21.00	1383	221	55	14
General Vision	19.00	1132	181	45	11
Ocular Pain	17.00	906	145	36	9
Near Activities	28.00	2459	393	98	25
Distance Activities	26.00	2120	339	85	21
Social Functioning	25.00	1960	314	78	20
Mental Health	26.00	2120	339	85	21
Role Difficulties	28.00	2459	393	98	25
Dependency	27.00	2286	366	91	23
Driving	35.00	3842	615	154	38
Color Vision	23.00	1659	265	66	17
Peripheral	27.00	2286	366	91	23
VFQ-39 Composite	21.00	1383	221	55	14

Note: Scales are all scored on 0-100 possible range.Estimates assume alpha = 0.05, two-tailed t-test, power = 80%, and an inter-temporal correlation between scores of 0.60.

Frequently Asked Questions (FAQ)

Q. *What kind of permissions are required to use the VFQ-25 in a research study?*

The VFQ-25 is a public document available without charge for all researchers to use provided they identify the measure as such in all publications and cite the appropriate developmental papers. Users do not need to notify the developers or the NEI that they intend to use the measure. However, there are some specific permissions for using the VFQ-25 that are detailed on the cover page of the questionnaire itself. These include acknowledging in all publications that the VFQ-25 was developed by RAND and funded by the NEI, and that any changes made to the measure for your particular study will be identified as such.

Q. *Can I change the format of the VFQ-25 to suit my study?*

Any change to the wording or order of the items would constitute a change to the measure and should be specified as such in any published papers. Other than this, it is expected that researchers may need to change the format or appearance of items to suit their purposes.

As of August 2000, to our knowledge no studies have reported on the effect of item order on responses to VFQ-25 or other similar vision-targeted surveys. That is, whether responses change depending where particular items appear in the questionnaire. However, to ensure the comparability of scores across studies, it is our position that the order of items should not be changed.

Q. Has the VFQ-25 been translated into any other languages?

As of August 2000, the developers are aware of translation into approximately 9 languages. For the cost of distribution, a Spanish language version for Mexican-American populations is available from the UCLA and RAND based developers. The developers will provide researchers with the names of other persons to contact for other language translations. Should researchers wish to translate the VFQ-25, the same permissions apply, with the additional requirement that all publications specify responsibility for the translation along with instructions for obtaining a copy of the translated version.

Q. Do you have any additional normative information for specific populations?

The developers currently are not conducting studies for the express purpose of further investigating the psychometric properties of the VFQ-25 or producing normative data. However, many researchers are currently using the VFQ-25 as an endpoint or outcome in a number of health services and clinical studies. It is likely that as these studies are completed, results that are relevant to better understanding the performance of the VFQ-25 will accompany the main results of each study. The developers and staff at the NEI are aware of other researchers who are collecting condition-specific normative data on population-based samples with the VFQ-25 and when possible will provide contact information for these investigators to new users.

Q. How relevant is the normative data provided in the scoring manual to my sample?

The means, standard deviations, and statistical power values shown in this document were estimated using cross-sectional data from the Field Test Study. Participants recruited for the Field Test were not randomly sampled, but rather were identified for enrollment based on clinical criteria biased towards persons with moderate to severe forms of each target disease. Further, because it was our desire to enroll a broad spectrum of patients based on disease severity, we did not take into consideration treatment status. Please see references #3 for a full description of the NEI-VFQ field test study sample.

Q. Why is a single-item general health item included in the VFQ-25?

During the developmental phase of the NEI-VFQ, vision-targeted health-related quality of life (HRQOL) was a relatively new concept. For this reason, we included this question to insure that researchers had a minimal amount of information about a person's general health status to use as a benchmark against other published samples or cohorts.

This general health rating question has been widely used in studies and is a robust predictor of future health and mortality. However, to fully measure generic HRQOL, many quality of life measurement experts recommend including a separate generic measure of HRQOL such as the SF-36 or SF-12.[9] In such a situation the single-item VFQ-25 general health rating question is not needed because the identical question is asked as part of these surveys.[10, 11]

Q. Should we be looking at the sub-scales or the composite score?

The VFQ-25 sub-scales are grouped by theme or domain. So, for example, items having to do with near vision are differentiated from items having to do with other vision activities like distance vision or ocular pain. This does not mean that the items are not highly correlated or that they are psychometrically distinct. What it does mean is that researchers should beforehand carefully consider which vision-specific domains are most likely to be influenced by a particular disease and/or treatment and then focus on the results from those sub-scales to support their findings.

The composite score is best used in situations where an overall measure of vision-targeted health related quality of life is desired. For example, in studies where it is not clear what the specific impact of ocular disease or a new treatment might be. Also, in situations where differences can be hypothesized between groups beforehand across multiple sub-scales but the overall sample size of the study is relatively small, because it is likely that the error term for the composite score is likely to be smaller than for any given sub-scale, it may be more efficient to represent these differences as a single score.

Q. What benefit is there to using the VFQ-25 over a measure more specific to a particular disease, like the Activity of Daily Vision Scale (ADVS)[10] for persons with age-related cataracts?

The VFQ-25 contains items that are very similar to items found in other vision-targeted measure like the ADVS that are more task oriented. However, whereas the ADVS was designed specifically to assess a set of activities most relevant to patients undergoing cataract surgery, the VFQ-25 expands the range of activities to measure the impact of ocular disease on broader domains of health such as social and emotional well-being. Serious ocular diseases that lead to irreversible loss of vision are likely to impact dimensions of a person's life beyond simple tasks such as driving or reading the newspaper, and similarly, by preserving vision, many successful interventions also will impact persons' lives at this more global level. Especially in these situations, use of the VFQ-25 should be considered.

Q. Why does the response to item 15b, "stopped driving due to vision <u>and</u> other reasons", generate a missing score for the subsequent driving items?

Driving items 15, 15a, and 15b are filter questions designed to specify whether a person has ever driven a car, and if so, whether they are currently driving or if they have stopped. If people have never driven a car, then, of course, their answers should be set to missing for all driving items. Similarly, this also applies to people who have stopped driving for other reasons not due to vision. However, in the course of pilot testing the field test participants wanted this additional mixed response option. It was our decision that although persons did indeed report not driving due to vision, it was not clear how much of a role the "other" reason also played in this decision. Therefore, we set

the scoring criteria for this response to be missing for all subsequent driving items to be absolutely sure that all driving responses reflected only problems with vision. Should researchers wish to change this response option to allow persons to answer subsequent driving items (currently there is a skip to item #17), this change should be noted in subsequent publications.

References

1. Mangione CM, Berry S, Lee PP, et al. Identifying the content area for the National Eye Institute Vision Function Questionnaire (NEI-VFQ): Results from focus groups with visually impaired persons. *Arch Ophthalmol.* 1998;116:227-238.

2. Mangione CM, Lee PP, Gutierrez PR, et al. Development of the 25-item National Eye Institute Visual Function Questionnaire (VFQ-25). Submitted 1999.

3. Mangione CM, Lee PP, Pitts J, et al. Psychometric properties of the National Eye Institute Visual Function Questionnaire, the NEI-VFQ. *Arch Ophthalmol.* 1998;116:1496-1504

4. Gutierrez P, Wilson MR, Johnson C, Gordon M, Cioffi GA, Ritch R; Sherwood M, Meng K, Mangione CM. Influence of glaucomatous visual field loss on health-related quality of life. *Arch Ophthalmol.* 1997;115:777-84.

5. Parrish RK 2nd, Gedde SJ, Scott IU, Feuer WJ, Schiffman JC, Mangione CM, Montenegro-Piniella A. Visual function and quality of life among patients with glaucoma. *Arch Ophthalmol.* 1997;115:1447-55

6. Quality of life assessment in the collaborative ocular melanoma study: design and methods. COMS-QOLS Report No. 1. COMS Quality of Life Study Group. *Ophthal. Epidemiology.* 1999;6:5-17.

7. Scott IU, Smiddy WE, Schiffman J, Feuer WJ, Pappas CJ. Quality of life of low-vision patients and the impact of low-vision services. *Amer. J. Ophthalmol.* 1999;128:54-62.

8. Cole SR, Beck RW, Moke PS, Gal RL, Long DT. The National Eye Institute Visual Function Questionnaire: experience of the ONTT. Optic Neuritis Treatment Trial. *Invest Ophthalmol Vis Sci* 2000;41:1017-21.

9. Mangione CM, Lee PP, Hays RD. Measurement of visual functioning and health-related quality of life in eye disease and cataract surgery. In B. Spilker (ed.), Quality of Life and Pharmacoeconomics in clinical trials, 2nd edition. New York: Raven Press 1996:1045-1051.

10. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-item Health Survey 1.0. *Health Econ* 1993;2:217-227.

11. Ware J Jr, Kosinski M, Keller SD 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220-33A.

Attachments include:

NEI VFQ-25 (IA = Interviewer-Administered format)
(SA = Self-Administered format)

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Henriette Snilsberg	22845531	29.05.2018	2018/804/REK sør-øst B
			Deres dato:	**Deres referanse:**
			20.03.2018	

Vår referanse må oppgis ved alle henvendelser

Vibeke Sundling
Høgskolen i Sørøst-Norge

2018/804 Diabetes, syn og øyehelse

Forskningsansvarlig: Høgskolen i Sørøst-Norge
Prosjektleder: Vibeke Sundling

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK sør-øst) i møtet 24.04.2018. Vurderingen er gjort med hjemmel i helseforskningsloven (hfl.) § 10.

Prosjektomtale
Formålet med prosjektet er undersøke hvordan synsfunksjon, øyehelse og livskvalitet påvirkes hos personer som har type 2 diabetes, og vurdere hvilke undersøkelsesmetoder som er mest effektive for å avdekke syn- og øyeproblemer hos optiker. Prosjektet har et tverrsnitt design. Deltagerne vil bli rekruttert gjennom Nasjonalt senter for optikk, syn og øyehelse (NOSØ), Diabetesforbundet og optikere. Målet er å rekruttere 400 personer til studien. Det vil bli utført synsfunksjonsmålinger, strukturmålinger av øyets bakre segment, klinisk undersøkelse av øyets fremre strukturer, og standardiserte og validerte spørreundersøkelser som avdekker syn- og øyesymptomer og livskvalitet knyttet opp mot syn. Alle undersøkelser vil foregå ved NOSØ og utføres av optiker eller øyelege. Resultatene fra prosjektet forventes å gi et vesentlig bidrag til å gjøre optikere i bedre stand til å avdekke syn- og øyeproblemer og håndtere disse målrettet og effektivt, og redusere antallet henvisninger til øyelege.

Komiteens vurdering
I dette forskningsprosjektet vil man undersøke hvordan synsfunksjon, øyehelse og livskvalitet påvirkes hos personer som har type 2 diabetes, og vurdere hvilke undersøkelsesmetoder som er mest effektive for å avdekke syn- og øyeproblemer hos optiker. Studien planlegger å inkludere 400 deltakere. Deltagerne vil bli rekruttert gjennom Nasjonalt senter for optikk, syn og øyehelse (NOSØ), Diabetesforbundet og optikere og vil være personer over 18 år som har type 2 diabetes. Deltagere vil bli rekruttert til prosjektet i perioden 2018-2020 og bli fulgt opp etter 1 år, 5 år, og 10 år, slik at prosjektperioden vil vare frem til 2030.

Helseopplysninger om synsfunksjon vil registreres, og det er det skrevet inn i søknaden at det skal samles inn nytt humant biologisk materiale i studien: kroppsvæske, hår og negler fra deltakerne. Dette er ikke videre omtalt i prosjektbeskrivelsen eller i andre saksdokumenter. Komiteen antar at dette derfor er krysset av feil i skjemaet, og forutsetter dette. Dersom dette ikke stemmer, ber komiteen å få begrunnelse for at dette skal samles inn, samt at det må inn i informasjons- og samtykkeskrivet.

Det er en samtykkebasert studie. Komiteen forstår det som at deltakelse på enkelte av undersøkelsene har den konsekvens at man ikke kan kjøre bil rett etter avsluttet undersøkelse, og ber om at deltakerne informeres om dette i informasjons- og samtykkeskrivet på forhånd.

Komiteen mener det vil være nyttig at prosjektet gjennomføres. Komiteen godkjenner prosjektet slik det nå foreligger på følgende vilkår:

- informasjons- og samtykkeskrivet må ha med informasjon om at man ikke kan kjøre bil etter undersøkelsen

Revidert skriv må sendes til komiteen til orientering.

Vedtak
Med hjemmel i helseforskningsloven § 9 jf. 33 godkjenner komiteen at prosjektet gjennomføres under forutsetning av at ovennevnte vilkår oppfylles.

I tillegg til vilkår som fremgår av dette vedtaket, er godkjenningen gitt under forutsetning av at prosjektet gjennomføres slik det er beskrevet i søknad og protokoll, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Tillatelsen gjelder til 30.06.2030 Av dokumentasjonshensyn skal opplysningene likevel bevares inntil 30.06.2035. Forskningsfilen skal oppbevares atskilt i en nøkkel- og en opplysningsfil. Opplysningene skal deretter slettes eller anonymiseres, senest innen et halvt år fra denne dato.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for «*Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helse og omsorgssektoren*».

Sluttmelding og søknad om prosjektendring
Dersom det skal gjøres vesentlige endringer i prosjektet i forhold til de opplysninger som er gitt i søknaden, må prosjektleder sende endringsmelding til REK.

Prosjektet skal sende sluttmelding på eget skjema, senest et halvt år etter prosjektslutt.

Klageadgang
REKs vedtak kan påklages, jf. forvaltningslovens § 28 flg. Eventuell klage sendes til REK sør-øst B. Klagefristen er tre uker fra du mottar dette brevet. Dersom vedtaket opprettholdes av REK sør-øst B, sendes klagen videre til Den nasjonale forskningsetiske komité for medisin og helsefag for endelig vurdering.

Komiteens avgjørelse var enstemmig.

Med vennlig hilsen

Ragnhild Emblem
Prof. dr. med
Leder REK sør-øst B

Henriette Snilsberg
komitésekretær

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