traditional signs and symptoms, specific differences are discernible. For example, there can be distinct differences between the type and chronicity of symptoms reported in each condition, symptoms are ameliorated on removal of the CL and differences in the natural history are observed. Contact lens wear impacts on normal ocular surface homeostasis [94], and while there may be overlap in clinical presentations, it is important to appreciate that CL wearers may have, or develop, concurrent DED.

4.6. Hematopoietic stem cell transplantation

Allogeneic hematopoietic stem cell transplantation is widely used as a potential curative treatment for hematologic malignancies. Despite improvement in outcomes, chronic Graft Versus Host Disease (GVHD) remains a life-threatening condition, involving various organs and tissues, including the ocular surface. The increased number of procedures performed and higher survival rates has led to a large number of patients with ocular morbidity. There are several good quality cross-sectional studies that have articulated the prevalence and presentation of DED related to ocular GVHD [95–102], confirming recipient sex mismatch, regimen intensity, history of viral infection and presence of skin, mouth and liver GVHD as associated risk factors. DED is the most common manifestation of ocular GVHD, resulting from lacrimal gland destruction from allogeneic T cells as well as from severe MGD [96], resulting in symptoms and a broad range of ocular surface manifestations. The poor accuracy of the Schirmer test used as the National Institutes of Health criteria for ocular GVHD has been criticized and is considered a limitation that must be addressed [101,103]. It is crucial to provide detailed screening and preventive strategies to avoid severe ocular discomfort as well as irreversible vision threatening complications.

4.7. Sjögren syndrome

Sjögren syndrome is a chronic autoimmune disorder characterized by exocrine gland dysfunction, which affects the salivary and lacrimal glands. Sjögren syndrome is associated predominantly with aqueous-deficient dry eye, although a higher rate of evaporative dry eye than in the non-Sjögren population has also been reported [104]. The prevalence of Sjögren syndrome is estimated to be in the order of 0.6% (0.19–1.39%) [105], although there is some variation in prevalence, based on the definition used. The incidence of physician diagnosed Sjögren syndrome in a white population in the US has been estimated at 3.9 per 100,000 per year, with a 14x higher rate in women than men [106]. Of 1208 participants in an international Sjögren syndrome registry, 85% reported symptoms of dry eye [61]. Of individuals with significant aqueous deficient dry eye, 10% are likely to have Sjögren syndrome [62]. In a US clinical study, 26% of patients with either aqueous tear deficiency or evaporative dry eye have an underlying rheumatic condition, including Sjögren syndrome [107].

4.8. Environmental exposures

Several environmental factors have been suggested to impact DED, such as air pollution, wind, low humidity and high altitude. There has been a limited number of case-control studies performed in selected populations (such as in India, Italy and Brazil) that compared metropolitan areas with rural areas and showed associations between DED and hazardous exposure [108–111]. However, despite these data, an important gap in knowledge about how environmental factors affect DED persists. Indeed, the understanding of the impact of pollution requires the challenging integration of location-based heath data and corresponding environmental data conditions.

Galor and colleagues demonstrated a higher risk of DED in metropolitan areas of the USA. Subjects with DED were identified by the International Classification of Disease (ICD-9) code 375.15. Spatial information was determined by assessing latitude and longitude coordinates of patients' zip codes, which were correlated with meteorological data, such as temperature, wind speed, relative humidity, visibility and atmospheric pressure from National Climatic Data Center and aerosol optical depth (a marker of air pollution) extracted from National Aeronautics and Space Administration, at each point location. This large population study comprised 606,708 subjects and demonstrated the risk of DED to be 13% higher in areas where the atmospheric pressure was one standard deviation higher (incidence rate ratio (IRR) 1.13x) and in areas with a higher level of aerosol optical depth (IRR 1.13x). In addition, higher humidity and wind speed (in the presence of air pollution) were inversely associated with the risk of DED (IRR 0.92x and IRR 0.93x) [112]. A large population based study conducted in Korea compared outdoor pollution measurements collected from national monitoring stations to DED based on symptoms or a prior clinical diagnosis, in 16,824 participants [113]. Higher ozone levels and lower humidity were significantly associated with DED.

Low humidity occupational exposure can also lead to DED, as shown in a study conducted with 352 clean room workers that work in a very low humidity of under 1% [114]. Symptoms and ocular signs were analysed during three annual examinations, and an increased prevalence of DED of 14.8% in the first year, 27.1% in the second year, and 32.8% in the third year was found.

4.9. Visual display use

Large cross-sectional studies have demonstrated a high prevalence of dry eye symptoms among visual display workers, predominantly young adults [8,60,115], It has been hypothesized that during visual display use, a diminished blink frequency rate and incomplete blinking contribute to accelerated tear evaporation, leading to tear film instability, mild epithelial damage and dry eye symptoms [116–119]. The use of visual displays has risen enormously, not only among workers but also in the general population, especially the young, due to the widespread use of home computers, tablets and mobile devices. In addition, a recent study found that in certain populations there is a pattern of very early and almost universal exposure to mobile media devices in young children aged 0–4 years [119]. There are limited well-controlled studies to understand the impact of tablet/mobile device usage on DED in young populations and this is clearly an area requiring further research.

4.10. Vitamin A deficiency/nutritional issues

Dietary vitamin A deficiency is recognized as a major health problem in certain parts of the world, such as the African continent, with children being more frequently affected. It is associated with a form of DED that contributes to corneal involvement, keratomalacia and preventable blindness [120]. Vitamin A deficiency also increases susceptibility to a range of illnesses and an increased risk of mortality. Worldwide vitamin A supplementation programs have significantly reduced illness, blindness and death [121–123]. In addition, similar presentations of DED may be related to other nutritional conditions, such as eating disorders (e.g. anorexia and bulimia), bariatric surgery, vegan diet, and malabsorption syndromes [124–127].

4.11. Dietary supplementation

Accumulated evidence over the past decade has shown a potential benefit of essential fatty acid (EFA) supplementation on dry eye. There is an increasing interest in the use of nutritional supplementation or dietary modification regarded EFAs on the prevention and treatment of dry eye, based on the understanding that a balance of omega-3/omega-6 is important to perform distinct and complementary functions. EFAs may play an important role in ocular surface heath and DED treatment. EFAs have been shown to display anti-inflammatory properties systemically, based on their effects on arachidonic acid metabolism, specifically the production of prostaglandins [128–130]. In the eye, EFAs enhance the lipid layer retarding tear evaporation and decrease apoptosis of lacrimal gland acini and epithelial cells, also contributing to improved tear secretion [131,132].

Well-designed and appropriately powered prospective, interventional trials have evaluated the role of EFA supplementation on dry eye signs and symptoms [133,134]. Recently, a multicenter 12-week intervention study comprising 1419 dry eye patients using oral omega 3 supplementation showed improvement in their symptoms and reported decreased use of lubricants [135]. Further evidence is outlined in the TFOS DEWS II Management and Therapy report [136].

It is important to note that the role of EFAs in the treatment of DED is still not completely understood and that there is also no consensus on the dose, composition and length of treatment [137]. Increased quality evidence on the usefulness of nutritional supplements is needed to enable eye care professionals to confidently outline specific treatment recommendations for using EFAs for DED.

4.12. Refractive surgery

Laser in Situ Keratomileusis (LASIK) is the most commonly performed vision correction surgery. However, signs and symptoms of DED can occur in both early and late postoperative periods. LASIK has been proposed to result in neuropathic dry eye [138], associated with sensory nerve damage, reducing lacrimal gland secretion and triggering neurogenic inflammation [139,140]. The risk of dry eye after LASIK is significantly associated with preoperative conditions, such as pre-existing tear dysfunction and long-term CL wear; Asian patients have a higher incidence of dry eye after LASIK (28%) compared to Caucasian patients (5%) [141]. Operative conditions may also contribute to DED after LASIK. The impact of factors such as flap hinge location (superior versus nasal) and flap width on the development of DED are not well defined, as recent studies report conflicting results [142,143]. Nevertheless, higher refractive corrections and deeper ablations are associated with decreased corneal sensitivity, increased postoperative dry eye symptoms, and chronic tear dysfunction [139,144].

4.13. Diabetes

The association between dry eye and diabetes mellitus is not significant in most population-based studies [10,21,25,102]. However, a population-based survey [145] analysing the comorbidities of dry eye and several case control studies [102,146–148] found a positive correlation with complicated disease. In two of these studies, dry eye was associated with neuropathy [148] and retinopathy classified according to the early treatment diabetic retinopathy study (ETDRS) criteria [147]. In a study conducted with 199 type 2 diabetic patients, the prevalence of DED was 54.3% and dry eye positively correlated with the duration of diabetes and the presence of retinopathy [146]. Another study compared symptoms and objective signs of DED in 104 children with type 1 diabetes compared to 104 age and sex-matched controls, where 15.4% of diabetic children complained of dry eye symptoms compared with 1.9% of the controls and 7.7% of diabetic children had dry eye signs compared with 1.0% of controls. [149].

In diabetics, it is possible that the signs of DED are a consequence of the reduction in corneal sensitivity and that impaired homeostasis can occur in this population. Thus, it is conceivable that in population studies that use self-reported symptoms as an outcome measure, that the prevalence of DED may be underestimated. In the Salnes Eye Study [7] an association was found with asymptomatic but not with symptomatic MGD. However, this was the only sign found to be associated with diabetes in this general population. The associations with TBUT, corneal and conjunctival staining and the Schirmer test were not significant, in contrast to the positive correlation found in the case control studies described above.

4.14. Affective and somatoform disorders

Recent studies have shown an association between DED and several affective disorders, with anxiety and depression the most frequently reported [69,12,25,26,70,150–152]. Whether these disorders precede or arise as a consequence of DED is not known, although these circumstances are not mutually exclusive. Irrespective of the nature of the association, there are a number of factors that can confound the results of these studies or the interpretation of risk factors. For example, the role of anxiolytics and antidepressants needs to be elucidated, as these medications can also be associated with DED [15,23,57,70]. Similarly, individuals with DED report lower self-perceived health [153], which could bias the results of the questionnaires used to evaluate mental health. Stress has been associated with both dry eye and mental health and could act as a trigger in some instances [11,12,26,102]. Psychological factors and the consequent altered immune response could increase the probability of DED associated with this disorder [154].

Several chronic pain syndromes such as chronic widespread pain syndrome, pelvic pain and irritable bowel syndrome have also been associated with DED, as has migraine [12,25,153,155,156], suggesting that these disorders could share etiopathogenic neuropathic mechanisms with DED. Although somatisation and increased pain sensitivity may impact on the frequency of reporting of symptoms of dry eye, the extent to which this impacts the prevalence of the disease remains to be elucidated.

4.15. Heritability and genetic risk factors

In addition to environmental risk factors, genetic susceptibility is likely to be important in the etiology of DED, but relatively little is known about the role of genes. DED has been shown to be moderately heritable in one female twin study in the United Kingdom [157], with heritability of approximately 30% for symptomatic dry eye and of 40% for a diagnosis of DED by an ECP. The remaining 60–70% of the variation of DED in the population was attributed to environmental factors. Like most common diseases, DED is complex or multifactorial, which means it is unlikely to have a simple Mendelian inheritance pattern controlled by a single gene locus [158].

Complex interactions between genes and the environment most likely play a role in making genes difficult to identify. Genome-wide association studies (GWAS) identify genetic variants by looking at millions of common single-nucleotide polymorphisms and have been highly successful in common eye diseases such as myopia, glaucoma and age-related macular degeneration [159]. To date, no

GWAS studies on DED have been published. Two large GWAS case-control studies on Sjögren syndrome have been performed [160,161], showing associations with immune-related genes, but not with genes encoding for salivary or lacrimal components, secretion machinery or neuronal proteins that innervate glands [162]. There have been several candidate gene studies in DED that examined a few selected polymorphisms in pre-specified genes of interest in clinic-based case-control studies. These studies suggested possible associations with pro-inflammatory cytokine genes [163], killer cell immunoglobulin-like receptor and human leukocyte antigen-C genes [164,165], the tachykinin receptor 1 gene [166] and brain-derived neurotrophic factor and vitamin D receptor genes [167]. However, it is important to note that none of these results were strong, they have not been (well) replicated in independent studies, and candidate gene studies are notorious for false positive results. Unravelling the interplay between genes and the environment in DED using hypothesis-free GWAS has the potential to identify new biological insights and therapeutic options and is highly encouraged by this subcommittee. It is important to note that sufficient statistical power using large sample sizes is critical to success in GWAS studies, especially in a poorly defined and multifactorial phenotype such as DED. International (gene-by-environment) GWAS collaborations using strict and similar disease definitions across cohorts are needed to obtain reliable results. A standardized, quantitative phenotype with a (near) normal distribution such as tear osmolarity may result in the highest power as per outcome measure, but large sample sizes and sufficient statistical power are most likely easier to obtain with a case-control setting using questionnaire-based disease definitions, such as the WHS questionnaire, particularly in populations that already have GWAS data available.

4.16. Summary and recommendations

This review has generated a broad summary of risk factors, categorized both based on whether factors are modifiable or non-modifiable and by the level of evidence in support of the association. However, these findings are still somewhat confounded by methodological differences between studies, the quality of studies in terms of the power to detect differences, differences in diagnostic criteria and study population differences. The review has highlighted the need for appropriately powered hypothesis driven studies, which address the major and important risk factors. Risk factors may vary with different diagnostic criteria but also may vary based on the health service provision in different jurisdictions. It may also be useful to consider population attributable-risk percentage to prioritize risk factors based on their impact.

The Committee concluded that there were limited studies to evaluate the impact of climate change, digital device use and dry eye in youth, and that it was important to distinguish dry eye from other symptomatic conditions, including allergic disease, infectious diseases, inflammatory conditions and other chronic ocular surface diseases.

5. Goal 3. to evaluate available data on the natural history of DED and disease morbidity

5.1. Natural history of DED

Despite the significant impact of DED in the community, there are limited published studies available which describe the natural history of treated or untreated DED. Bron and colleagues [168] proposed a theoretical model of progression based on the disease evolving through three stages 1) Initiation of DED, 2) Reflex compensation, and 3) Loss of the compensatory response. This model suggests that disease may worsen without intervention and that over time aqueous-deficient dry eye may show clinical signs of evaporative dry eye and *vice versa*. The disease may also plateau at a certain stage [168]. A counter view that not all DED is progressive is supported by a recent retrospective study based on resurveying 784 participants from the Women's and Physicians' Health Studies in the USA, who had previously reported a positive diagnosis of dry eye or severe dry eye symptoms [169]. This study determined the rate of, and risk factors for, an increase in dry eye discomfort, worsening vision related symptoms and greater social impact. Medical records were reviewed and a subset of participants also underwent clinical examination [169]. The average duration of DED was 10.5 years for men and 14.5 years for women. The most common perception of subjects was that there was no change in dryness symptoms (32% unchanged, 44% improved and 24% worsened), visual symptoms (52% unchanged, 19% improved and 29% worsened) or social impact (71% unchanged, 19% improved and 10% worsened) over time. The distribution of change in symptoms was not related to the type of treatment or its relative level of severity. Worsening of dryness symptoms was associated with a high monthly dollar spend for treatment, a history of severe symptoms and the use of systemic beta-blockers. A worsening of vision symptoms was also associated with a history of ocular surgery, depression and either MGD or blepharitis. A worsening of social impact was associated with older age, use of systemic beta-blockers and either MGD or blepharitis. Worsening symptoms was not related to the probability of corneal staining [169].

While recall bias in retrospective studies may confound symptom recall, these findings do support the view that DED characterized by severe dry eye symptoms at diagnosis, appears to progress irrespective of treatment. The lack of association between progression of symptoms and signs is not unexpected. Without reference to disease severity, a reduction in symptom reporting over time has been established in the Twins UK study, where 37% of subjects with symptomatic disease at baseline (using the Beaver Dam study criteria) did not report symptomatic disease when resurveyed two years later [25]. It is not clear whether these individuals were undergoing treatment or if this is representative of the waxing and waning course of the disease. A recent meta-analysis of the effects of topical 0.05% cyclosporine and artificial tears, vehicle control or no treatment on disease signs and symptoms confirmed the overall efficacy of treatment in reducing signs and symptoms, but there was heterogeneity between studies in severity and etiology of dry eye [170].

Prospective studies are needed to determine the clinical course of all severities of dry eye, prognostic factors in disease progression, and the role of treatment in reducing signs and symptoms. The subcommittee also recommends reviewing data from available placebo/vehicle and treatment groups in randomized double-masked controlled trials of sufficient duration to determine changes in prevalence over time. Other sources of information would include registry studies and claims data, although the type and quality of data may vary.

5.2. Morbidity of dry eye

Dry eye is common throughout the world and the prevalence increases with age. Given the aging of the population worldwide (Source Kevin Kinsella and Wan He, “An Aging World: 2008,” U.S. Census Bureau, International Population Reports, P95/09-1 [Washington, DC: U.S. Government Printing Office, 2009]) the overall morbidity of dry eye is important to consider to understand its full public health impact [12,56,171–173]. Dry eye represents the most common reason for seeking medical eye care and thus it represents a significant cost burden due to direct and indirect

health costs and reduced work productivity [54]. This section reviews the morbidity of DED with regard to both the social and economic burden and health-related quality of life (QoL).

5.2.1. Economic burden of dry eye

Since the initial TFOS DEWS epidemiology report [1], an increasing number of studies have quantified the costs incurred by healthcare systems in association with DED [174–184]. Many of the large cohort and population-based studies have calculated the estimated cost of DED treatment or work productivity losses. However, cost analyses cannot provide direct conclusions regarding effective resource allocation for particular treatments or strategies. Nevertheless, cost of illness analyses provide information about the patterns of resource use for a particular condition, thereby enabling a greater understanding of the framework within which decisions about resource allocation are made. Although the medical insurance fee and health care systems vary among countries, it has been consistently reported that DED significantly increases the utilization of healthcare resources.

DED affects tens of millions of individuals and carries significant socioeconomic implications, including the expenses associated with medications and physician visits and the effects on daily social and physical functioning. Furthermore, increased time spent on treatment and the avoidance of certain environments in the workplace that aggravate dry eye symptoms can lead to a decrease in workplace productivity.

The economic burden of DED can be attributed to direct medical care spending, the impact of loss of productivity, and impact on quality of life [179,181–186]. The total annual cost for the management of DED was estimated to be USD 3.84 billion in the United States [182], and USD 0.15 million in Singapore [180]. The annual total cost for 1000 patients with DED in Europe managed by ophthalmologists ranged from USD 0.27 million in France to USD 1.10 million in the United Kingdom [175]. The total

Table 4
The economic burden of dry eye disease.

Authors	Methods	Study Population	Years Studied	Cost Analysis
United States				
Fiscella 2008 [183]	Retrospective administrative claims analysis	23,821 of dry eye patients treated with cyclosporine or punctal plugs	2004–2005	• The total health plan for topical cyclosporine, US$3.05 million (mean cost $336/patient). • Total health plan costs for punctal plugs procedures, $3.28 million (mean cost $375/patient).
Wlodarczyk 2009 [184]	Meta-analysis, literature review and economic model for dry eye	Cohort of dry eye patients from two clinical trials (n = 147) treated with either Systane® or Refresh Tears®	2006	• Systane® cost on average US$57.79/year more than Refresh Tears® • Assigning a quality-adjusted life year (QALY) gain of 0.03 to responders results in an incremental cost per QALY gain of US$5837.
Brown 2009 [174]	Multicenter, randomized, clinical trials	877 of dry eye (270 had Sjögren syndrome)	2007	• The societal perspective incremental cost-utility ratio (CUR) for cyclosporine over vehicle therapy is $34,953 per QALY and the societal perspective average CUR is $11,199 per QALY. The third-party-insurer incremental CUR is $37,179 per QALY, while the third-party-insurer perspective average CUR is $34,343 per QALY.
Patel 2011 [178]	Online survey	9034 of dry eye panel	2009	• Approximately 31% of severe DED patients, 40–60% loss in productivity while working; 15% experienced 70–100% loss.
Yu 2011 [182]	Survey	2171 of DED	2008	• From payer's perspective: US $783/person, US $3.84 billion/year • From a societal perspective: US$11,302/person, US$55.4 billion/year
Galor 2012 [176]	Survey	147 of nationally representative subsample of US population using topical cyclosporine and/or Blephamide®	2001–2006	• Mean expenditure per patient per year being US$55 in 2001–2002 (n = 29), US$137 in 2003–2004 (n = 32), and $299 in 2005–2006.
Japan				
Yamada 2012 [181]	Online survey	396 aged ≥20 years	2012	• Cost of work productivity loss, US$ 799/person in definite DED, US$ 58/person in marginal DED, and US$ 1036/person in self-reported DED.
Mizuno 2012 [177]	Estimated annual direct costs from outpatient medical records and survey	118 of prospective cohort dry eye	2008	• Drug cost was US$323 ± 219/year; Clinical cost US$165 ± 101/year; Total direct costs including punctal plug treatment US$530 ± 384/year
Uchino 2014 [179]	Survey	672 office workers	2013	• The estimated cost of annual work productivity losses: US$6160/person in the definite DED group; US$2444/person in the probable DED group.
Singapore				
Waduthantri 2012 [180]	Retrospective chart review	54,052 patients; 132,758 patients' episode (PE).	2008–2009	• US$1,509,372.20/year in 2008; • US $1,520,797.8/year in 2009. • US $22.11/PE in 2008; US $23.59/PE in 2009.
France, Germany, Italy, Spain, Sweden, and the United Kingdom				
Clegg 2006 [175]	Systemic literature review and interviews	Model cohort 1000 dry eye patients	2003–2004	• Annual burden of UK (~US $1100/person), Spain (~US $800/person), Italy (~US $600/person), Germany (~US $500/per son), Sweden (~US $400/person), and France (~US $300/person).

annual health plan cost per patient was estimated as USD 323 in Japan, and USD 375 in United States [183]. Annual productivity loss per patient associated with definite DED was estimated to be USD 6160 in Japan [179] and the annual cost of DED from a societal perspective, was USD 11,302 in the United States [182]. Measurement of the treatment cost of DED is challenging because the treatment options and health insurance service vary by country. The treatment utilization includes prescription medication, punctal plugs, and surgical management [182]. Fiscella and colleagues reported the mean treatment cost per patient at USD 336 for topical cyclosporine and USD 375 for punctal plugs [183]. Mizuno et al in 2012 estimated the total annual cost of prescription drug per patient to be USD 323 and the cost of punctal plugs per patient to be USD 42 [177].

Table 4 summarizes the healthcare costs by region [174–184]. A recent systematic literature review has confirmed that the largest proportion of costs are attributed to indirect costs due to reduced productivity at work [187].

While cost analyses cannot recommend resource allocation for particular treatments or strategies, cost of illness analyses provide information about the patterns of resource use for a particular condition, thereby enabling a greater understanding of the framework within which decisions about resource allocation are made. Although the medical insurance fee and health care systems vary among countries, it is widely accepted that DED significantly increases the utilization of healthcare resources. Cost savings through improved QoL, improved productivity and reduction in healthcare utilization costs associated with effective disease treatment should also be modelled in future studies.

5.2.2. Quality of life (QoL) questionnaires

The currently validated dry eye specific questionnaires, the OSDI and the Impact of Dry Eye on Everyday Life (IDEEL) are frequently used to measure disease severity (Table 5) [12,24,26,185,188–193].

The OSDI is a DED-specific instrument that includes 12 questions assessing the frequency of dry eye symptoms and their effects on vision-related function. The 12 OSDI questions form three different subscales, namely ocular symptoms, vision-related functions and limitations, and environmental triggers on which to evaluate symptoms during a 1-week recall period. Each answer is scored on the basis of symptom frequency using a 5-point scale where 0 indicates no problem and 4 indicates a significant problem. However, the OSDI has some limitations in that it does not assess the psychological and social aspects of DED, therefore, it is not widely used to evaluate the more holistic effects of DED on QoL.

The IDEEL, which is a 57-item questionnaire, comprises three modules: dry eye symptom bothersomeness; impact on daily life (including daily activities, emotional impact, and impact on work) and treatment satisfaction (both effectiveness and treatment-related bother/inconvenience). There are two items related to visual disturbance that assess the extent to which the patient is affected by blurry vision and sensitivity to light, glare, and wind. The strength of the IDEEL is that it covers all relevant domains of DED and it also distinguishes the severity of DED, however, it is not frequently used in routine clinical practice because of a long duration of testing (typically taking over 30 min).

Perhaps the most widely used questionnaires pertaining to general health and general eye health include the Short Form-36 (SF-36) and the 25-item National Eye Institute's Visual Function Questionnaire (NEI VFQ-25), respectively. The SF-36 is used as a measure of the general health status of an individual. It includes 36 items under the following subscales: Physical Functioning, Role-Physical (role limitations due to physical problems), Bodily Pain, General Health Perceptions, Vitality, Social Functioning, Role-Emotional (role limitations due to emotional problems), and Mental Health [194]. A 4-week recall period is used for all these subscales, except Physical Functioning and General Health, which reflect the health of the patient at the time of questionnaire completion. The NEI-VFQ-25 assesses the effects of various eye diseases on QoL [195]. The ocular pain subscale of the NEI-VFQ-25 shows the strongest overall correlation with the OSDI in individuals with Sjögren syndrome [196], leading some researchers to suggest that patients with low ocular pain scores (where a higher score reflects better function) in NEI-VFQ-25 should undergo further testing for dry eye. However, with regard to the assessment of QoL in patients with dry eye, the NEI-VFQ-25 is limited because it is not disease-specific and needs further validity and reliability testing in a dry eye cohort, lacks a specified recall period, and requires 10 min for completion. In some instances, a 14-item appendix can be administered to subjects to enhance the reliability of the various subscales. The NEI-VFQ comprises 39 questions with the following 12 domains or subscales: (1) general health, (2) general vision, (3) ocular pain, (4) difficulty with short distance vision activities, (5) difficulty with long distance vision activities, (6) vision-related limitations in social functioning, (7) mental health symptoms related to vision, (8) vision-related role difficulties, (9) vision-related dependency, (10) vision-related driving difficulties, (11) limitations with color vision, and (12) limitations with peripheral vision. The scores range from 0 to 100, with higher scores indicating better function.

5.2.3. Effects of dry eye on quality of life

The available evidence suggests that DED has an adverse effect on overall QoL. It causes pain and irritation and affects ocular and general health and well-being, the perception of visual function, and visual performance [12,24,26,185,188–193,197,198]. The development of methods to assess DED patients in detail enables clinicians to understand the magnitude of the effects of DED on QoL. Some available measurement tools are specific to DED or vision, some are generic, and some focus on work productivity or anxiety/depression. Pain associated with DED can have psychological and physical impacts, while blurred vision may impose restrictions in daily life activities such as reading, driving, watching television, and operating smartphones. Moreover, the cost of DED treatment and the chronicity/intractability of DED symptoms affect the social life of an individual. Collectively, all these factors affect QoL and have an impact on public health.

Utility assessments suggest that patients with mild and severe DED experience a reduction in QoL at a level similar to that experienced by patients with mild psoriasis and moderate-to-severe angina, respectively [199]. In everyday activities, such as driving, reading, carrying out professional work, using a computer, and watching television, individuals with DED are three times more likely, than those without DED, to report difficulties [200].

5.2.4. Impact of dry eye on quality of vision

The precorneal tear film has an important optical function. Tear film instability and corneal surface irregularities due to epithelial desiccation, resulting in changes in optical quality, can be visualized and quantified using a range of techniques [200–202]. In the majority of patients with DED, the visual acuity is normal according to standard measurements, however, instability of the tear film introduces higher-order aberrations that result in a decrease in visual quality. Early studies investigated optical fluctuations using the double-pass method to assess changes in the modulation transfer function after blinking [202]. Others involved the continuous acquisition of corneal topography or videokeratoscopy images to show that fluctuations in the tear film cause increased irregular astigmatism [201]. Patients with DED often report vision-related

Table 5
Health-related Quality of Life and dry eye.

Authors	Country	Instruments	Subjects	Analysis
Mertzanis 2005 [188]	United States	IDEEL, SF-36	32 with SS, 130 with non-SS KCS, 48 controls	- Non-SS KCS patients had lower Role-Physical (effect size [ES] = -0.07), Bodily Pain (ES = −0.08), and Vitality (ES = −0.11) scores. - All SF-36 scale scores except Mental Health (ES = 0.12) were lower in the SS group than the adjusted norm. - Mild patients consistently had lower Role-Physical and Bodily Pain scores than the norm, suggesting impact on daily roles (ES < 0.2). - The group with severe disease scored lower than the norm across all domains (ES range: −0.14 to −0.91) except Role-Emotional (ES = 0.13) and Mental Health (ES = 0.23).
Rajagopalan 2005 [189]	United States	SF-36,EQ-5D, IDEEL	130 with non-SS KCS, 32 with SS, 48 controls	- Significant differences between severity levels were found with most SF-36 scales (P < 0.05), all EQ-5D scales (P < 0.05), and all IDEEL scales (P < 0.0001), except for Treatment Satisfaction. - IDEEL scales consistently outperformed the generic QoL measures regardless of the severity criterion used. Most SF-36 scales outperformed the EQ-5D QoL scale, but the EQ-5D visual analog scale outperformed the SF-36 scales, except for General Health Perceptions.
Paulsen 2014 [24]	United States	NEI-VFQ 25, SF-36	The Beaver Dam Offspring Study (BOSS) (2005–2008), participants (N = 3285), aged 21–84 years	- Dry eye was also associated with lower scores on the Medical Outcomes Study Short Form 36 (β = −3.9, P < 0.0001) as well as on the National Eye Institute 25-Item Visual Function Questionnaire (NEI VFQ-25) (β = −3.4, P < 0.0001) when controlling for age, sex, and comorbid conditions.
Abetz 2011 [185]	United States, Canada	IDEEL, SF-36, EQ-5D	The focus groups had 6 to 10 participants in each; the total population consisted of 45 patients: 30 with non-SS KCS and 15 with SS.	- Significantly different (p < 0.0001) mean scores were observed between different levels of severity in all the IDEEL dimensions except Satisfaction with Treatment Effectiveness. - For the SF-36, significant differences between the various severity levels were noted in the Physical Component Scale scores across the 3 different severity criteria. - In observing the EQ-5D results, significant differences in mean dimension scores at the varying severity levels were also consistently noted across all criterion measures.
Hackett 2012 [190]	United Kingdom	Improved Health Assessment Questionnaire	69 subjects with SS from specialist clinical service. 69 age and sex matched controls. Functional ability assessed	- Significantly poorer functional ability in SS compared with controls across all domains; Functional impairment specifically associated in univariate analysis with physical fatigue, pain, depression, symptom burden, disease activity, quality of life, dryness, daytime somnolence, anxiety score and circulating C-reactive protein level.
Buchholz 2006 [191]	United Kingdom	NEI VFQ-25. OSDI	Dry eye disease (N = 44) of whom had mild/moderate disease (N = 24) and severe disease (N = 20).	- There was a statistically significant difference between the mean VFQ-25 score for patients who rated themselves as mild or moderate (78.1, N = 24) and for those who rated themselves as severe (64.5, N = 20 [p-value = 0.005]) - OSDI scores strongly correlated to VFQ-25 scores (Pearson correlation coefficient: −0.7495, p-value<0.0001)
Na 2015 [26]	South Korea	EQ-5D, EQ VAS	Korea National Health and Nutrition Examination Survey (KNHANES)(2010–2011), (N = 3285), women aged over 19 years	- Significant different (p < 0.05) value of pain/discomfort (EQ_4), and anxiety/depression (EQ_5) in both clinically diagnosed DED and symptoms of DED compare to normal controls.
Ahn 2014 [12]	South Korea	EQ-5D, EQ-VAS	Korea National Health and Nutrition Examination Survey (KNHANES)(2010–2011), (N = 11,666), aged 19–95.	- Means of pain, discomfort/anxiety, depression dimensions, and EQ-VAS in the EQ-5D were significantly higher in the group diagnosed with DES than in the normal group (all P < 0.01)
Belenguer 2005 [192]	Spain	SF-36	110 patients (105 women and 5 men, mean age of 56 years) with primary SS	- Comparison between patients with primary SS and the control population showed lower scores in SS in all SF-36 scales (p < 0.001)
Mizuno 2010 [193]	Japan	VFQ-25, SF8	158 with DED (30 with SS, 128 with non-SS)	- Some patients recorded extremely low VFQ-25 scores - VFQ-25 and SF-8 scores were not significantly different between the SS and non-SS patients.

difficulties during daily activities, resulting in a decreased QoL and these changes are often related to depression and anxiety [203].

There are two categories of vision-related QoL instruments. Generic instruments are designed for a broad spectrum of visual disorders and ocular diseases, while disease-specific instruments are designed and validated for a specific ocular disorder [196]. Generic instruments provide broader and more general vision-related information, whereas disease-specific instruments provide more sensitive results on vision-related QoL. Most studies assessing the vision-related QoL of patients with DED used both generic (e.g. NEI-VFQ-25) and disease-specific instruments (e.g. the vision-related functions and limitations subscale of the OSDI) [200–205].

5.2.5. Impact of dry eye on mental health

The effects of DED associated with Sjögren syndrome on mental health status have been widely reported, although the impact on DED more broadly has not been evaluated. Patients with Sjögren syndrome experience significant symptoms of fatigue, autonomic dysfunction, and excessive sleepiness in addition to sicca-related symptoms. The overall impact of these symptoms on the functional ability of individuals is considered to have a significant

negative impact on psychological well-being [190,197,206,207]. Because most previous studies on autoimmune-related DED did not assess the burden of dry eye separately from that of other systemic symptoms and signs of Sjögren syndrome, there is limited information of the impact of DED. Hackett and colleagues reported that patients with primary Sjögren syndrome experienced greater functional impairment than controls (Improved HAQ total scores: mean ± SD 24 ± 25 for primary SS versus 9 ± 19 for controls; $p = 0.0002$) across all domains of activity, including physical fatigue, pain, depression, total symptom burden, systemic disease activity, quality of life, dryness, daytime somnolence, anxiety score, and C-reactive protein (CRP) level [190]. Patients with primary Sjögren syndrome showed similar scores compared with those with systemic lupus erythematosus, using the Zung Self-rating Anxiety/Depression Scales [208].

Recently, population-based studies indicated a relationship between depression/anxiety and DED [25,70,150,151,209–211]. Ocular pain and discomfort without a definitely impaired tear film may also be associated with depression, anxiety, and psychological stress [186,200,201,203,205,212,213]. DED affects vision quality through tear-related changes in aberrations, and an impaired visual performance can likewise lead to depression and impaired QoL. An awareness of such associations between dry eye symptoms and depression is important for ECP, who may serve as the starting point for medical care. Although the precise mechanisms underlying the effects of DED on mental health remain unclear, one possible explanation is that DED results in neuropathic disease, resulting in chronic pain and negatively affecting the patient's QoL, function, and daily activities and work, eventually leading to depression and/or anxiety. A further consideration is the use of medications for these conditions which may increase the risk of dry eye.

5.2.6. New methods for measurement of dry eye related QoL

Because there is no “gold standard” diagnostic test for DED, a combination of signs and symptoms is commonly used as diagnostic criteria. Most methods for assessing dry eye-related QoL are time consuming, and their ability to quantify changes in symptoms is limited. Therefore, the development of a simple, reproducible, reliable, and quantitative instrument is critical for the diagnosis, treatment, and follow-up of DED patients.

A short questionnaire based on a visual analog scale (VAS) to quantify the frequency and severity of dry eye symptoms has been developed. This is known as the Symptom Assessment in Dry Eye (SANDE) questionnaire [214], which comprises two questions assessing the frequency and severity of dry eye symptoms. Each of these two items is assessed using a 100-mm VAS and scored from 0 to 100. The total SANDE score is calculated as the square root of the product of the two scores and ranges from 0 to 100, with higher scores indicating greater disability [214]. The SANDE questionnaire has been validated against the OSDI instrument in a clinic population and the SANDE scores have shown negligible differences from OSDI scores [215], suggesting that the SANDE may be used in clinical practice as a short, quick, and reliable measure of disease symptoms.

In 2013, the Dry Eye-Related Quality-of-Life Score (DEQS) questionnaire was developed and validated in Japan [216]. The diagnostic criteria conformed to those defined by the Japanese Dry Eye Society in 2006. The questionnaire comprises 15 items under an Overall Summary scale and two multi-item subscales, namely Impact on Daily Life and Bothersome Ocular Symptoms. When the results were compared with those of the SF-8 and NEI-VFQ-25, the DEQS questionnaire was valid and reliable for evaluating the multifaceted effects of DED on the daily lives of patients, including their mental health [216]. This suggests that this instrument may be used in routine clinical practice, although the questionnaire is time consuming and the generalizability to other populations has not been reported.

5.2.7. Future research directions

With the development of electronic devices and transmission technology, monitoring symptoms and the burden of disease in individuals with DED is changing rapidly compared with existing measurement tools. Smartphone based applications, such as electronic diaries or electronic data capture systems may be used to translate and validate the prevalence of disease effect of chronicity and treatment and the effect of DED on quality of life.

6. Goal 4: review of instruments and their use/applicability in epidemiological research

Although clinical tests have shown a wide variability in their ability to detect many cases of DED [40,217,218], conducting a battery of tests could provide information on risk factors in the absence of symptoms, as recent research has suggested [7,21,56]. Evaporimetry and interferometry and other investigational techniques may be useful and specific diagnostic tools, but they lack standardization and are not yet applicable to epidemiological research.

Symptoms alone or in combination with signs are present in many definitions of dry eye used in published epidemiological studies. Since the initial TFOS DEWS report, MGD or evaporative dry eye has been identified as the most common cause of dry eye [2–5] and MGD is more frequently asymptomatic than symptomatic [7], which perhaps challenges the use of current symptoms instruments. The definition of dry eye in the current workshop includes both signs and symptoms, although symptoms or signs may be absent in a single subject where there is a disturbance or a lack of tear film homeostasis. There has been increasing focus on non-obvious disease, characterized by signs in the absence of symptoms [7,237]. The report of the TFOS DEWS II Diagnostic Methodology subcommittee [40] has described a battery of tests suitable to diagnose and monitor dry eye and the grading of disease severity includes both signs and symptoms. While the relationship between signs and symptoms may be absent in early or mild disease, the assessment of both symptoms and signs is clearly important in grading disease severity, understanding the natural history and in monitoring response to treatment.

In 2007, the initial TFOS DEWS report summarized the available instruments for DED [1]. In the previous report, the focus was on questionnaires that had been used in randomized clinical trials or epidemiologic studies [1]. This report will similarly focus on those instruments used in epidemiological studies in disease ascertainment or determination of severity.

We searched PubMed using the terms ‘dry eye’ and ‘questionnaire’ and we limited the language to ‘English’ and the use as ‘human’. We also reviewed existing data regarding validation and utility of each questionnaire. In the present report, we discuss seventeen questionnaires. The first twelve questionnaires have been validated using various methods, while the last five questionnaires have not yet been validated.

The twelve validated questionnaires are reviewed below and are summarized in Table 6. The first five questionnaires (OSDI, IDEEL, NEI-VFQ, SANDE, and DEQS) are described in the quality of life section above, and the remainder are described below.

1) Ocular Surface Disease Index (OSDI) [219].
2) Impact of Dry Eye on Everyday Life (IDEEL) [189].

Table 6
Summary of questionnaires.

Number	Instrument Title	Description	Category	Number items	Domains sampled	Recall frequency	Utility
1	McMonnies	Key questions in a dry eye history	Symptoms and risk factors	15	1) Symptoms; 2) Environment; 3) Review of systems	Not specified	Clinical studies
2	OSDI	The Ocular Surface Disease Index	Symptoms and HRQL	12		1 week	Clinical studies
3	IDEEL	Impact of Dry Eye on Everyday Life	Symptoms and HRQL	57	1) Daily Activities 2) Treatment Satisfaction 3) Symptom Bother	2 weeks	Epidemiological and clinical studies
4	WHS	Women's health study questionnaire	Symptoms	3	1) Ocular symptoms 2) History of DED	Not specified	Epidemiological studies
5	DEQ	Dry Eye Questionnaire	Symptoms and bothersomeness	21	1) Prevalence 2) frequency, diurnal severity and intrusiveness	Not specified	Epidemiological and clinical studies
6	UNC DEMS	North Carolina Dry Eye Management Scale	HRQL	1	Symptom bothersomeness	1 week	Clinical studies
7	SPEED	Standard Patient Evaluation of Eye Dryness	Symptoms	4	Symptoms (type, frequency, severity)	3 months	Epidemiological studies, clinical practice
8	SESoD	Subjective Evaluation of Symptom of Dryness	Symptoms	3	Symptoms	Not specified	Clinical practice
9	DEQS	Dry Eye-Related Quality-of-Life Score Questionnaire	Symptoms and HRQL	15	Symptoms (frequency and severity)	1 week	Clinical practice
10	SANDE	Symptom Assessment in Dry Eye	Symptoms	2 (visual analog scale)	Symptoms (frequency and severity)	Not specified	Clinical practice
11	DEEP	Dry Eye Epidemiology Projects	Symptoms	19	Symptoms (frequency)	Not specified	Screening
12	NEI-VFQ	National Eye Institute Visual Function Questionnaire	Visual functioning; HRQL	25	Symptoms (frequency and severity), impact	Not specified	Clinical research[a]
13	CANDEES	Canadian Dry Eye Epidemiology Study Questionnaire	Symptoms	13	Symptoms severity, risk factors	Not specified	Prevalence study
14	SEE	Salisbury Eye Evaluation	Symptoms	6	Symptoms (frequency)	Not specified	Prevalence study
15	Melbourne VIP	Melbourne Visual Impairment Project	Symptoms	6	Symptoms (severity)	Not specified	Epidemiological studies
16	Bjerrum questionnaire		Symptoms	14	Symptoms	Not specified	Clinical practice
17	Japanese dry eye awareness study		Symptoms	30	Symptoms	Not specified	Prevalence study; clinical practice (self-diagnosis)

HRQL = Health related quality of life.
[a] Useful for group-level comparisons of vision-targeted, health-related QoL.

3) National Eye Institute-Visual Function Questionnaire (NEI-VFQ) [220].
4) Symptom Assessment in Dry Eye [214,221,222].
5) Dry Eye-Related Quality-of-Life Score Questionnaire (DEQS) [216].
6) McMonnies Dry Eye Questionnaire [223,224].
7) Women's Health Study Questionnaire [53].
8) Dry Eye Questionnaire (DEQ) [225].
9) North Carolina Dry Eye Management Scale (UNC DEMS) [226].
10) Subjective Evaluation of Symptom of Dryness (SESoD) [227].
11) Standard Patient Evaluation of Eye Dryness (SPEED) [228].
12) Dry Eye Epidemiology Project Questionnaire (DEEP) [222].
13) Canada Dry Eye Epidemiology Study (CANDEES) [229].
14) Salisbury eye evaluation [230].
15) Melbourne visual impairment project [52].
16) Bjerrum questionnaire [231].
17) Japanese dry eye awareness study [232].

6.1. McMonnies Dry Eye Questionnaire

The McMonnies Dry Eye Questionnaire consists of 12 items, of which most are dichotomous (yes/no) [223]. This questionnaire has been used for dry eye screening in dry eye clinic populations [25,27]. Items include age, sex, contact lens wear, previous diagnosis of dry eye, and triggers (environment, swimming, alcohol). It also assesses the frequency of symptoms dryness, grittiness, soreness, redness, tiredness (never, sometimes, often, constantly), and medications used (arthritis, dry mouth, thyroid status) [224].

6.2. Women's Health Study (WHS) questionnaire

The WHS questionnaire has been used widely in population based studies of dry eye (Table 1). It consists of the following 3 items:

1) Previous diagnosis of dry eye from clinician? (yes or no).
2) How often eyes feel dry (not wet enough)? (constantly, often, sometimes, or never)
3) How often eyes feel irritated? (constantly, often, sometimes, or never)

An individual is considered positive for dry eye with reported rates of disease based on symptoms of dryness and irritation at least often and/or a physician's diagnosis of dry eye, as reported by the participant. The WHS has been reported to have similar sensitivity and specificity as a 16 item instrument [233], comprising symptoms including: sandy or gritty, burning or stinging pain, itching, light sensitivity, blurry vision, tiredness, soreness, scratchiness, redness, stickiness, achy feeling watery eyes and swollen eyelids. In addition, it has been validated against a standardized clinical exam [53].

6.3. Dry eye questionnaire (DEQ)

The DEQ has 21 items and includes questions about contact lens wear, age, and sex. It includes categorical scales of prevalence, frequency, diurnal severity and intrusiveness of symptoms in a typical day over a one-week recall period. It also assesses the frequency (never, infrequent, frequent, constantly) and intensity (from 0; none to 5; very intense) of the following symptoms of comfort, dryness, blurry vision, soreness and irritation, grittiness and scratchiness, burning and stinging, foreign body sensation, light sensitivity, and itching. The DEQ also includes questions regarding the time of day of worsening, the effect on daily living activities, medications, allergies, dry mouth, nose, or vagina, treatments, and patient global assessment [234]. The short version of DEQ comprising 5 questions only (DEQ-5) is sensitive to disease severity [235] and is one of two instruments recommended by the TFOS DEWS II diagnostic methodology report [40].

6.4. North Carolina Dry Eye Management Scale (UNC DEMS)

The UNC DEMS has 1 item, which asks about the severity of dry eye symptoms (pain, burning, tearing, grittiness, feeling like something is in your eye, and sensitivity to light), and how symptoms affect daily life. The answer uses a 10-point scale over a one week of recall period. It has been validated using dry eye patients and non-dry eye patients, and appears to be highly correlated with the longer OSDI [226].

6.5. Subjective Evaluation of Symptom of Dryness (SESoD)

The SESoD consists of a three-item questionnaire to evaluate a patient's perception of ocular discomfort related to dryness for the purpose of clinical practice. Key questions are frequency of symptoms [31], the presence of discomfort [32], and interference with activity. The SESoD assesses dry eye using a 5-point scale where 0 = no dryness to 4 = severe dryness. This questionnaire has been validated against the SPEED, OSDI, DEQ, and McMonnies Dry Eye History questionnaires [227].

6.6. Standard Patient Evaluation of Eye Dryness (SPEED)

The SPEED questionnaire is a four-question survey to assess the frequency and severity of patient dry eye symptoms. Specifically, it monitors diurnal and longer-term symptom changes over the course of three months. The SPEED questionnaire has been shown to exhibit good validity, unidimensionality, objectivity and consistency when compared with the DEQ, McMonnies questionnaire, OSDI and SESoD questionnaires [236].

6.7. Dry Eye Epidemiology Project (DEEP)

The DEEP questionnaire consists of 19 questions and is used, as a phone interview-screening questionnaire, to screen for DED. The resulting sensitivity/specificity values are reasonably high (60%/94%). It surveys the use of eye washes, compresses, drops, frequency of symptoms such as itchy, sore, dry, scratchy, gritty, burning, irritated, watering, photophobia, red, sticky, achy (never, sometimes, often, constantly). In addition, it surveys the presence of dry mouth, ocular allergies, the frequency of contact lens wear and whether a physician has made a diagnosis of dry eye [222].

6.8. Summary/recommendations - utility for patients/patient acceptance

Although there are many questionnaires to evaluate DED, more research is required to better reflect symptom reporting in dry eye and define normative data and clinically significant changes. The symptoms that patients frequently report are missing from many questionnaires – e.g. photophobia; menthol (cold sensation); burning, which needs to be addressed in questionnaire development. Further evidence is needed to identify the best methods for self-monitoring or in communicating with practitioners, and methods of capture of symptoms including electronic data capture/electronic diaries.

7. Conclusions and recommendations

This report has considered the epidemiology of DED based on diagnostic criteria, including symptoms and/or signs, and one that based on a prior diagnosis of DED made by an ECP. While disease definitions vary between studies, the prevalence of disease increases with age and females are more frequently affected, with the exception of MGD where sex effects are more equivocal. Limited studies have been carried out in youth and there remains a need for studies in populations below 40 years of age. Prevalence appears to be higher in Asian than in Caucasian populations, although studies have not been conducted in major geographic regions. However, it does appear from scientific abstracts presented since September 2015 that studies are/have been carried out in some of these regions identified. Geographical mapping approaches will facilitate future exploration of the impact of climate, socioeconomic and environmental factors on dry eye. There are limited studies of both disease incidence and the natural history of treated and untreated disease, both of which remain future needs for this field.

While modifiable and non-modifiable risk factors have been summarized, the report has identified a need for appropriately powered hypothesis driven studies, which address the major and important risk factors and emerging factors such as associations with other conditions, youth, screen use, air quality, climate change and environmental factors. Overlap of dry eye with (or misdiagnosis of) other chronic ocular surface conditions including allergy has confounded study of their contribution to, or as risk factors for, dry eye. A better appreciation of the contribution of allergic or inflammatory disease to dry eye would advance this field.

The economic burden of DED is considerable, particularly related to indirect costs such as those attributed to loss of productivity and impact on QoL. Future studies should also consider cost savings associated with treatment. The wide-ranging impact of dry eye on QoL has been summarized and the limitations of many existing instruments are recognized, particularly in sensitivity to detect changes in symptoms. Future exploration of the impact of dry eye on quality of life may be facilitated by real time smartphone-based electronic data capture approaches.

Instruments used in epidemiological studies in disease ascertainment or determination of severity were reviewed. Future questionnaire design and development should focus on defining normative data and ensuring sufficient sensitivity to detect clinically significant changes in both the natural history of disease and in response to treatment, and on determining recommendations for patients for self-monitoring and in communicating with practitioners. Improved public and practitioner awareness will result in both eye and general health improvement.

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Appendix I. Questionnaires not yet validated

Canada Dry Eye Epidemiology Study (CANDEES)

CANDEES is a 13-item questionnaire. The assessment of frequency and intensity of symptoms are combined, with patients asked to rate each using the following categories: occasional and mild, occasional and moderate, constant and mild, constant and moderate, and severe. This questionnaire also evaluates medications, time of day, allergies, dry mouth, and itchy/swollen/red eyelids [229].

Salisbury eye evaluation

The Salisbury eye evaluation is a standardized 6-item questionnaire that assesses the frequency of symptoms and 3 signs (Answers: Rarely, Sometimes, Often, All of the time). This questionnaire has been used for a self-reported population-based prevalence survey in the elderly for clinical and subjective evidence of dry eye [230].

Melbourne visual impairment project

The questionnaire used in the Melbourne visual impairment project assesses self-reported dry eye symptoms elicited by an interviewer-administered questionnaire [52].

Bjerrum questionnaire

The Bjerrum questionnaire is a three-part questionnaire, which includes an ocular part with fourteen questions. It has been used to evaluate QoL due to Sjögren syndrome dry eye, diagnosis of dry eye, and the epidemiology of Sjögren syndrome [231].

Japanese dry eye awareness study

This questionnaire consists of thirty questions relating to symptoms and knowledge of dry eye. It has been used for a population-based, self-diagnosis study to assess public awareness and symptoms of dry eye [232].

Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jtos.2017.05.003.

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