

TFOS European ambassador meeting: Unmet needs and future scientific and clinical solutions for ocular surface diseases

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SPECIAL ARTICLE**TFOS European Ambassador Meeting: Unmet Needs and Future Scientific and Clinical Solutions for Ocular Surface Diseases**

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Abstract. The mission of the Tear Film & Ocular Surface Society (TFOS) is to advance the research, literacy, and educational aspects of the scientific field of the tear film and ocular surface. Fundamental to fulfilling this mission is the TFOS Global Ambassador program. TFOS Ambassadors are dynamic and proactive experts, who help promote TFOS initiatives, such as presenting the conclusions and recommendations of the recent TFOS DEWS IITM, throughout the world. They also identify unmet needs, and propose future clinical and scientific solutions, for management of ocular surface diseases in their countries. This meeting report addresses such needs and solutions for 25 European countries, as detailed in the TFOS European Ambassador meeting in Rome, Italy, in September 2019.

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Abbreviations

AHCT	Allogenic hematopoietic stem cell transplantation
AM	Amniotic membrane
AMD	Age-related macular degeneration
ASO	Antisense oligonucleotide
COMET	Cultivated oral mucosal epithelial transplantation
DED	Dry eye disease
ECP	Eye care provider
EMA	European Medicines Agency
GVHD	Graft versus host disease
IT	Information technology
LASEK	Laser epithelial keratomileusis
LASIK	Laser-assisted in-situ keratomileusis
LSCD	Limbal stem cell deficiency
MGD	Meibomian gland dysfunction
NHS	National Health Service

OCP	Ocular cicatricial pemphigoid
oGVHD	Ocular graft versus host disease
OSD	Ocular surface disease
OSDI	Ocular Surface Disease Index
PED	Persistent epithelial defect
PRK	Photorefractive keratectomy
RK	Radial keratotomy
SLET	Simple limbal epithelial transplantation
TBUT	Tear film break-up time
TFOS DEWS™	TFOS Dry Eye WorkShop
TFOS DEWS II™	TFOS Dry Eye Workshop II
TFOS	The Tear Film & Ocular Surface Society
VKC	Vernal keratoconjunctivitis

INTRODUCTION

TFOS: Global Mission. Amy Gallant Sullivan, TFOS, Boston, MA, USA, and David A Sullivan, Schepens Eye Research Institute of Massachusetts Eye and Ear, and Department of Ophthalmology, Harvard Medical School, Boston, MA, USA

The Tear Film & Ocular Surface Society (TFOS; www.tearfilm.org), a 501(c)(3) non-profit organization, was created to advance the research, literacy, and educational aspects of the scientific field of the tear film and ocular surface. Since its incorporation in 2000, TFOS has launched numerous initiatives, including organization of multiple international conferences, symposia, and USA Congressional briefings; organization of international Workshops focused on dry eye disease ([DED] TFOS DEWS,™ TFOS DEWS II™), meibomian gland dysfunction (MGD), and contact lens discomfort; publication of the TFOS Workshop reports, the Initiating Innovation (i^2) series "white papers" (i.e., in-depth reviews of clinically relevant topics), and a 1,385-page book about the tear film and ocular surface in health and disease; sponsorship of the peer-reviewed journal *The Ocular Surface*, which it has helped grow into one of the highest ranked eye-related journals in the world; awarding of more than 250 Young Investigator Travel Awards for outstanding research; creation of global public awareness campaigns, networking events, vision lounges, and diagnostic and educational videos; organization of a Young Investigator Incubator focused on initiating innovation (in development); and most recently, creation of the TFOS Global Ambassador Program.

TFOS activities have also helped to promote increased international awareness of external eye diseases, enhance governmental funding for tear film and ocular surface research, stimulate the development of therapeutic drugs and diagnostic devices, and influence the design and conduct of clinical trials of novel treatments for ocular surface diseases (OSDs). TFOS reaches many hundreds of thousands of basic scientists, clinical researchers, industry representatives and patients throughout the world.

Imagination and innovation are key to the TFOS vision. TFOS is about making things happen. One such recent event was the TFOS organization of the TFOS European Ambassador meeting in Rome in September 2019. The participants of this meeting included most of the TFOS European Ambassadors, many of the TFOS Board of Directors (i.e., Jennifer P. Craig, José A.P. Gomes, Amy Gallant Sullivan, David A. Sullivan, Piera Versura, Mark D.P. Willcox, and James S. Wolffsohn), as well as attendees from around the world (Figure 1). Each TFOS Ambassador was asked to speak to the unmet needs, and possible clinical and scientific solutions, for the management of OSDs in his/her country in Europe. The report of this European meeting appears below. In the near future, TFOS aims to publish analogous reports from Africa, Asia, Latin America, North America and Oceania.

TFOS Global Ambassador Program: Clinical and Scientific Importance. Jennifer P. Craig, Department of Ophthalmology, The University of Auckland, New Zealand

TFOS has an overarching aim of helping the world to see better through its mission of advancing the research, literacy, and educational aspects of the scientific field of the tear film and ocular surface. The Society is unrelenting in its efforts to foster collaboration among scientists, clinicians, and industry professionals. TFOS considers its Global Ambassador Program fundamental to fulfilling its mission. Carefully chosen individuals are a vital link in identifying areas of unmet needs in different parts of the world, and enabling TFOS to seek and create solutions to address perceived shortfalls. These ambassadors are also crucial in promoting TFOS initiatives and membership throughout the world, and in ensuring dissemination of the learnings of TFOS to the clinicians and basic scientists, and ultimately to the affected members of the public, within their respective countries.

The TFOS DEWS II™ reports published in 2017 in *The Ocular Surface* journal have undoubtedly had a major impact within the scientific community. On the basis of the subsequent 2 years' citations in the peer-reviewed literature, eight of the ten TFOS DEWS II™ reports ranked among the top 1% of all published scientific papers, and two of the reports ranked among the top 0.1% of all papers published in the academic field of clinical medicine.

While justifiably proud of this achievement, TFOS recognizes that this global consensus report marks only the beginning in educating the world about OSD. Research indicates that clinicians prefer conferences and continuing education events over scientific articles as a means of staying abreast of the latest scientific evidence and informing patient management, so TFOS ambassadors play an important role in disseminating the key content of the reports at meetings around the world. To date, over 500 TFOS™ II presentations have been delivered across 6 continents by TFOS DEWS II™ authors and TFOS ambassadors, at major conferences, via virtual lectures, and at local clinical meetings (Figure 2).

It is the ambition of TFOS to have links with the ocular surface communities in every country in the world. Ambassadors represent a group of individuals whose actions demonstrate their passion for helping people with OSD. Often they are active in educating and disseminating knowledge, and/or they have the connections to enlist the help of others to do so. TFOS recognizes the value of involving those with local knowledge and the cultural awareness, sensitivity and literacy to help the Society achieve its aims. The program aims to stimulate interaction among existing ambassadors and members to help build a global community by providing a forum for sharing expertise and for empowering and inspiring others. TFOS tasks its ambassadors with encouraging new membership of basic scientists, academic clinicians, and industry representatives from a range of backgrounds, welcoming the diversity in disciplinary experiences and expertise that new members can bring to the field. TFOS ambassadors can also play an important role in educating and helping TFOS implement change for the benefit of affected patients by encouraging regulatory reform, facilitating innovation, and enabling greater access to diagnostic and therapeutic procedures.

Currently the ambassador team comprises 120 individuals, who are representatives of 76 countries. Within Europe, 34 ambassadors were invited to contribute to this meeting and to this report. Through the generous input and willingness of the attendees to share, insight into the current status of OSD and its management across Europe has been gathered, which we anticipate will help pave the way, through research and innovation, to improved OSD management.

WESTERN EUROPE

Austria. Jutta Horwath-Winter, Dry Eye Unit, Department of Ophthalmology, Medical University of Graz, Graz

The Republic of Austria comprises nine federal provinces with a total area of 83,879 km² and nearly 9 million inhabitants. The country has more than 1,000 ophthalmologists working in university eye

hospitals, ophthalmology departments, and private practice. Austria has many opticians, but only 45 optometrists.

OSD is among the most frequent reasons for patients to seek eye care. OSD etiology is known to be related especially to DED, MGD, blepharitis, and allergies, as well as infectious, inflammatory, and iatrogenic conditions.

Concrete epidemiologic data concerning OSD and DED in Austria are lacking. A survey of Austrian ophthalmologists was conducted in 2009 to evaluate the prevalence of DED and blepharitis.¹ A specially designed questionnaire was sent to 576 ophthalmologists, and 191 (33%) responded. The majority of the responding ophthalmologists suggested that approximately 20-50% of their patients suffered from DED, especially females over 40 years of age. They suggested that 5-20% of their patients had blepharitis, most commonly females over 40 years old.

Diagnostic methods according to the survey included the evaluation of medical history and symptoms. Lid margins and lid-parallel conjunctival folds were examined. Determination of tear film break-up time (TBUT) and tear meniscus height, Schirmer test, fluorescein and lissamine green staining, and lipid interferometry were rarely performed.

The responding ophthalmologists noted the need for improvements in the approach to diagnosis and management of patients with OSD. They requested additional educational programs on this topic and more specialized departments to which they could refer their challenging cases for a second opinion. They further asked for more options regarding artificial tear products and specific (e.g., anti-inflammatory) medications to be covered by the public health insurance.

In recent years, knowledge concerning OSD/DED has increased due to TFOS-sponsored workshops and their published reports. However, this advanced knowledge needs to be transferred from the OSD specialist to the general ophthalmologist. This goal could be achieved by special OSD/DED units.

Austria has corneal and refractive surgery units in the larger cities and five active DED units in Graz, Salzburg, Zell am See, Linz, and Vienna. The task of these special units is to properly diagnose and manage patients with complex DED, as well as those with severe OSD, such as Sjögren syndrome, ocular cicatricial pemphigoid (OCP), graft versus host disease (GVHD), Stevens-Johnson syndrome, and chemical or thermal injuries. They can also be valuable in sharing specialized clinical knowledge.

A committee for DED and OSD was founded last year by the Austrian Society of Ophthalmologists (ÖOG) to deal with the challenges in this field and to bring information to all federal provinces so as to achieve equal standards of diagnosis and therapeutic care. Transfer of knowledge can be facilitated by regular educational programs, such as lectures, talks, workshops, meetings in working groups, presentation of case reports, and job shadowing in specialized units. In recent years, education

regarding DED has been offered by the ÖOG, by university eye clinics, and by pharmaceutical companies.

Because a large selection of artificial tears is sold over the counter in Austrian pharmacies, pharmacists should be educated about their differences and uses, as well as about general knowledge, such as being advised not to sell vasoconstrictors.

Patients should also receive information directly. July 23 is World Sjögren Day. The first informative meeting for Austrian patients with Sjögren syndrome took place in Graz on the 23rd of July 2019. In the future, there will also be support groups, which would be helpful for these patients.

Austrian general ophthalmologists have very little time to perform sufficient diagnostic procedures and properly classify their DED patients. Few diagnostic methods for DED are reimbursed, for example, only the Schirmer test or the TBUT. Various new diagnostic tools, such as non-invasive TBUT or meibography, are not reimbursed.

Reimbursement of additional therapies for DED and OSD, such as unpreserved artificial tears, serum eye drops, nerve growth factor, or scleral lenses, should be established. New diagnostic tools, such as non-contact measurements, would save time but are also not reimbursed. Therefore, currently they are performed only for private patients or in refractive practices where patients pay a package price for the refractive procedure and more sophisticated and expensive therapeutic options, such as LipiFlow and intense pulsed light. Also, the funding of new technologies, such as limbal stem cell transplantation or gene therapy, need to be fully discussed and clarified.

In the future, European multi-center studies would be helpful to generate epidemiological data and diagnostic and therapeutic methods, medical devices, and drugs. This should be initiated by national and international platforms, such as European societies, or maybe TFOS. They should help to establish consistent guidelines and study endpoints to facilitate new approvals. Since OSD and especially DED have a significant negative impact on the population, the importance of these diseases, supported by European-based studies, should be made clear to decision-makers in public health care in order to establish understanding and to improve reimbursement for the benefit of patients.

Belgium. Peter Raus, Department of Ophthalmology/Eye Surgery, Free University of Brussels, Brussels, Belgium

Although Belgium is a very small country (population of 11.4 million), it is complex politically. It is divided into four relatively independent regions. Flanders is the biggest region, comprising about 60% of the population of Belgium. The language of Flanders is Flemish (very similar to Dutch). Wallonia

is the southern, primarily French-speaking region, which comprises about 30% of the population. The Brussels-Capital region has about 1.2 million inhabitants. There is also a small, German-speaking area in the east of Belgium (about 77,000 population). As a consequence, Belgium has six independent governments: the federal government; the Flemish government; the government of the French Community; the government of the German-speaking community; the Walloon Government; the government of the Brussels-capital Region. Every government has its own Minister responsible for some aspects of public health in their region: some items are regulated by the federal government and others regionally. This situation creates communication errors and problems relating to jurisdiction. Belgium is also 'ophthalmologically' divided, with two professional organizations of ophthalmology: the BOG (Belgisch oftalmologisch gezelschap) for the Flemish-speaking ophthalmologists and the SBO (Société Belge d'ophtalmologie) for the French-speaking colleagues.

In the general practice of ophthalmology, dry eye is frequently considered more as a symptom or a physiological condition than as a disease. For the majority of my Belgian colleagues, DED is synonymous with Sjögren syndrome, and patients with symptoms or complaints of dry eyes receive a prescription or a sample of artificial tears, usually a random sample of one of the drops the ophthalmologist has received from a pharmaceutical representative.

Most ophthalmologists are not even aware of the difference between aqueous deficiency and evaporative DED. Patients with symptoms of DED sometimes are considered to be troublesome patients who take a lot of time. There is no cure, only treatment for their complaints, and they frequently return to the ophthalmologist reporting that their treatments do not help. DED patients are taken seriously only when punctate keratitis is present or when the patient is seeking refractive surgery, the latter because refractive surgeons are aware that LASIK is an aggravating factor for DED. Some use a TearLab osmolarity test to document DED status and protect themselves medicolegally if a patient complains about dry eye after LASIK.

The proportion of patients with MGD and secondary evaporative dry eye is striking: up to 30-40% in all patients.² In addition to conventional DED treatment with eye drops, punctal plugs can be inserted to prevent the outflow of tears, especially in older patients. For severe cases of DED not responding to conventional treatments, transplantation of labial salivary glands to the tarsal conjunctiva can be considered. It is a technique originally described by Prof. Juan Murube (Madrid, Spain). Despite good results with this type of surgery, it still is considered controversial.

It is hoped that in the future, enhanced knowledge of DED and increased communication among ophthalmologists will contribute to better, individualized treatment of DED. At the same time, tears will play an increasingly important role in clinical investigations, containing invaluable information (biomarkers) for other ophthalmological and non-ophthalmological conditions. More studies must be

performed to evaluate tears as an alternative to blood analysis. Thanks to the sensitivity of modern top-down mass spectrometry, diagnosis and follow-up of several (also non-ophthalmological) diseases can be aided by such techniques in early or even pre-clinical stages.

France. Serge Doan, Ocular Surface Unit, Hôpital Bichat - Fondation A de Rothschild, Paris

France has a total population of 65 million and about 6,000 ophthalmologists. Only ophthalmologists are authorized to diagnose and treat DED.

Although France has no professional society dedicated to DED and OSD, Christophe Baudouin has, over a number of years, taken leadership of a group that shares this interest. There is also a society called The Group for Ocular Allergy, which is comprised of ophthalmologists and allergists.

Some French pharmaceutical companies have had longstanding interest in preservative-free treatments, making France a pioneer in this field. Laboratoires Théa Pharmaceuticals, which began as the Chibret Company, has manufactured preservative-free treatments, as well as various ocular surface devices and products for many years. Because of the strong link between this company and French ophthalmologists, many ophthalmologists now are very aware of the association of eye drop preservatives with DED. Another French company, *Horus*, is also involved in the manufacture of preservative-free and DED products.

French health care is provided by a universal health care system financed mainly by Social Security, the government-run national health insurance scheme. For example, artificial tears are paid for by Social Security at a rate of 70%, and the remaining portion can be reimbursed by a private insurance provider. If a medication is not reimbursed by Social Security, many patients will refuse to buy it. The factors that drive the reimbursement of a product are its level of proven efficacy (based on pivotal studies) and also the selling price demanded by the pharmaceutical company. French drug prices are among the lowest in the world. This creates a problem for companies marketing expensive sophisticated products. For instance, topical nerve growth factor eye drops have recently been approved by the European Medicines Agency (EMA), but they are not reimbursed and have not been launched in France because of their high price. Topical cyclosporine in single-dose cationic emulsion 0.1% eye drops have been approved by the EMA, but might not become reimbursed in France because the pivotal study did not reach the primary endpoint. If it doesn't become reimbursed, we may have to depend on pharmacies to supply home-made preparations of cyclosporine. The fact that availability of some excellent products is precluded by price is the basis for an unmet need in treatment of OSD. Table 1 shows a non-exhaustive list of treatments for OSD that are not reimbursed or not available in France.

Early-generation lubricants are fully reimbursed, whereas the newer generation ones, for example, hyaluronic acid, Thealoz®, Optive®, Systane®, Cationorm®, Neovis®, etc., are only partially reimbursed. We do not have secretagogues for the stimulation of mucus secretion, such as diquafosol and rebamipide; this represents an important unmet need because we need drugs for treating unstable tears related to deficiency of the mucus layer.

There is also a need for other immune-modulating eye drops. The currently available topical cyclosporine emulsions have tolerability problems, and new formulations are needed for enhanced tolerability. *Lifitegrast* is not currently marketed in Europe. We don't have tacrolimus eye drops, which can be helpful for severe DED. We have autologous serum, but only as a hospital preparation and only in Paris. It cannot travel without refrigeration, so is available only to patients who live in the city where it is produced. To meet the needs of our patients, we need new preparation kits such as Endoret® to become more widely available

Another problem relates to scleral lenses. Some of them are reimbursed, and other brands, which have come on the market later, are not reimbursed. This is confusing for patients.

We are behind in the use of stem cell expansion and autologous stem cell grafting. There is only one study in France on cultivated oral mucosal epithelial transplantation (COMET). That monocentric study has stopped due to lack of funding, although the study showed good results. Holoclar®, made by an Italian company, uses autologous limbal stem cell expansion to treat ocular burns. It is approved in France, but it is not reimbursed and its cost would have to be covered by the hospital, which will not currently pay for such an expensive treatment.

My final points are in regard to unmet needs in the management of neuropathic pain and infection. We need topical treatments and more effective treatments for neuropathic pain. For infections, we have second-generation quinolones topically available, but not third- or fourth-generation quinolones.

To conclude, many treatments are available in France for treating OSD. However, issues relating to price and reimbursement limit the access to more expensive modern treatments.

Table 1: Availability of DED treatments in France

Treatments	Availability	Unmet needs	Solutions
Lubricants	Old generation reimbursed, new generation partially reimbursed	Need for mucous secretagogues, rebamipide, diquafosol	
Cyclosporine eye drops	Compounded preparation available in several hospitals	Cationic 0.1% emulsion unidose preparation available but not reimbursed. Issues with patient tolerability	Use aqueous cyclosporine to increase tolerability?
Other immunomodulating preparations		Topical lifitegrast and tacrolimus preparations not available	
Nerve growth factor eye drops		EMA-approved but too expensive	
Autologous serum	Hospital preparation in few sites only	Very complex logistics. Long delays for availability	Need for more availability, maybe via the way of preparation kits such as Endoret®
Scleral lenses	Only one brand reimbursed	Several other brands are available but not reimbursed	
Autologous stem cell expansions for limbal deficiency	Limbal stem cell expansion reimbursed only for ocular burns. Oral mucosa expansions available only through a clinical study	Very limited access	
Neuropathic pain	Systemic treatments available only	No topical treatments	
Infections	2 nd generation quinolones available	3 rd and 4 th generation quinolones eye drops	

		not available	
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Germany. Elisabeth M. Messmer, Department of Ophthalmology, Ludwig-Maximilians-University, Munich, Gerd Geerling, Department of Ophthalmology, University Hospital Duesseldorf, Duesseldorf, and Heiko Pult, Ophthalmic Research Group, Aston University, Birmingham, UK and School of Optometry and Vision Sciences, Cardiff University, Cardiff, UK and Dr Heiko Pult & Optometry and Vision Research, Weinheim, Germany

Germany has a total population of 83 million (2018), which is served by approximately 9,000 ophthalmologists (about 50% of them in hospital departments) and 12,000 optician shops. The diagnosis and treatment of eye diseases are – by law – limited to ophthalmologists. The general population is served by general ophthalmologists in individual or group practices. These ophthalmologists usually have basic ophthalmic equipment, and see both publicly and privately insured patients. Subspecialized dry eye clinics exist in some (predominantly university-based) but not all eye departments. The interest in and time for seeing patients with OSD is limited. The more highly educated opticians and optometrists are involved in contact lens dispensing. They are also aware of tear film abnormalities and sometimes recommend non-invasive and non-medical options to improve the tear film and/or refer patients to ophthalmologists.

Every German is obliged to have general public health insurance, but can alternatively obtain private health insurance if his/her income exceeds a defined level. Public or private health insurance companies cover the costs of basic diagnostic measures (but not, e. g., tear osmolarity or MMP-testing, tear film lipid assessment and/or meibography) and prescription “drugs,” but not tear substitutes (unless there is evidence of pemphigoid, facial nerve paralysis, or Sjögren syndrome). As a result, artificial tears or lacrimal plugs are purchased by patients without reimbursement. Although, at present, two large studies are assessing the prevalence of symptoms and signs of DED in a general population in Germany, the only published epidemiological data are from 1977 and suggest that 11.7% suffer from symptoms of dry eye.

It is likely that the current diagnostic recommendations for DED are not reflected in routine practice in Germany, since many doctors treating patients with DED lack at least some of the recommended and required diagnostic tools (e.g., a system to measure tear meniscus height or tear film osmolarity). Therefore, general ophthalmologists outside of subspecialized departments would benefit from a simplified diagnostic flow chart for the diagnosis of the disease. Advanced DED professionals, however, see the need for additional objective tests, especially biomarkers to diagnose inflammation and

differentiate this from other OSDs (allergies, etc.). The costs for such measures would likely have to be covered by the patient. Hence, reimbursement for diagnostics by German health insurance companies, including osmolarity measurement and evaluation of inflammatory markers, are unmet diagnostic needs.

The TFOS DEWS IITM report summarizes treatment options based on several severity levels of DED, but not on subtype. Grouping treatments in subtypes would help many practitioners to bring the diagnostic workflow together with the treatment recommendations of the TFOS DEWS IITM. In Germany, artificial tears, warm compresses, corticosteroids and cyclosporine 0.1%, topical NGF for neurotrophic keratopathy, and systemic tetracycline derivatives are available, but other options (such as topical acetylcysteine) are available only off-label and hence are rarely prescribed. In particular, in-office treatments, such as intense pulsed light treatment, low-level light therapy (LLLT) and meibomian gland expression, are not covered by health insurances. Unmet needs include the reimbursement of tear substitutes in general, the approval of further topical drugs in Europe such as lifitegrast, additional treatments for MGD, topical therapy addressing hormonal pathomechanisms or neuropathic pain, or mimicking nerve growth factor. These are unavailable, as is a service that provides access to autologous serum eye drops nationwide.

The list of unmet needs for a number of other conditions, e. g., natamycin eyedrops for keratomycosis, on-label topical cytotoxic medication for ocular surface neoplasia (such as mitomycin C or interferon for squamous cell carcinoma) is long, but beyond the scope of this discussion.

Beyond this— on a more global level — there is a need for prospective studies to provide sufficient evidence for the diagnostic workflow proposed by TFOS DEWS II, and to determine the sensitivity and specificity of tests for types of DED— aqueous deficient, evaporative, or a combination of both.

IRELAND. Conor Murphy, Department of Ophthalmology, Royal College of Surgeons in Ireland School of Medicine and Royal Victoria Eye and Ear Hospital, Dublin

Eye care in Ireland is delivered in both community and hospital settings by a combination of optometrists, orthoptists, medical ophthalmologists, ophthalmic surgeons, and an increasing number of specialist nurses. The greatest challenge we face across the health care sector is our ability to provide timely care in an appropriate setting. Long waiting lists hamper the delivery of care to patients with chronic OSDs like DED, and the current lack of suitable care pathways to ensure that patients are seen quickly means that patients with common chronic OSDs are inappropriately referred to senior hospital-based ophthalmic surgeons rather than to allied health professionals in the community. Recent changes in legislation have facilitated the greater involvement of optometrists in clinical care, and we have recently launched a new integrated model of community and hospital-based care to reduce waiting times for

patients. The implementation of clinical care plans that provide timely, safe, and effective care to patients with common ocular surface and external eye diseases is underway. Each member of the multidisciplinary team will see patients appropriate for their training and medical licensing, predominantly in the community setting, leaving highly trained specialist ophthalmologists to manage more complex diseases.

Regional variations in the quality of care provided for OSD arise from a lack of services in certain areas, which places increasing pressure on existing high quality services to compensate for this shortfall. Early diagnosis of keratoconus and treatment with corneal crosslinking is one of the highest priorities for any corneal service. The implementation of a nurse-led keratoconus diagnostic and crosslinking service in Dublin has been highly effective, but the delivery of similar service improvements elsewhere is hampered by severe shortages of nurses. A quality improvement plan using lean principles to implement a national care pathway for the early diagnosis and management of keratoconus is urgently required.

Patients with immune-mediated OSDs like Sjögren syndrome and GHVD frequently suffer unnecessarily because of delayed access to treatment, with significant regional variations in waiting times for assessment. Greater collaboration with medical specialists in rheumatology, hematology, and clinical immunology, supported by appropriate clinical care pathways, would expedite the delivery of effective care to this cohort of complex patients who often suffer adverse quality of life consequences from their disease. Improved patient education strategies and access to the full range of therapies would greatly alleviate patient distress.

The cost of new therapies is also a significant burden for many patients, as at least 60% of patients need to pay a significant portion of the cost of their prescriptions. In contrast, complex surgical interventions and human tissue product therapies for anterior segment disease, such as autologous and allogeneic serum drops and corneal, amniotic membrane (AM) and limbal stem cell transplantation, are readily available when clinically indicated.

In summary, the main challenges experienced in the delivery of an effective corneal and ocular surface service in Ireland relate to the operation of the health service, in particular regional variations in quality of care, timely implementation of appropriate multidisciplinary care pathways in community and hospital settings, and the prohibitive costs of novel therapies for some patients.

NETHERLANDS. Jelle Vehof, King's College, London, UK, and Departments of Ophthalmology and Epidemiology, University of Groningen, University Medical Center Groningen, Groningen

The Netherlands is located in Northwestern Europe and has a high population density (17 million inhabitants). Its mild maritime climate is a favorable environment for the ocular surface, with fungal infections being relatively rare and most corneal infections being associated with contact lens use.

Ocular trauma is relatively uncommon except on New Year's Eve, when consumer use of fireworks is allowed for 8 hours and results in major eye injuries. In recent years, 50-100 eyes had permanent damage from fireworks, and about 5 eyes per year had to be enucleated or eviscerated; the prevalence of ocular fireworks injuries exceeds all the war eye injuries of the Dutch Army. Public safety and medical organizations have been advocating for a complete ban on fireworks for decades, and recently the majority of the public has also favored a complete ban.

In the past two years, the oak processionary moth, which is thought to be migrating to cooler areas due to global climate change, has led to common ocular surface problems. In its caterpillar stage, it drops fine hairs, which become airborne and can enter the human eye. They usually cause a papillary rash with severe itch, but can also cause conjunctivitis. The hairs have tiny hooks, so they are difficult to remove, and they can migrate into the deeper layers of the eye. There are no evidence-based treatment protocols, but a 1-week regimen of chloramphenicol ointment usually appears effective. Surgical removal of the hairs may be required when the cornea is infiltrated. The oak processionary moth population is increasing rapidly in the Netherlands. The Government has not taken adequate measures to stop their outbreak, and such action represents an unmet need in eye care.

As in most Western countries, DED is the problem encountered most often in ophthalmology clinics. We recently performed a large (79,000 people) cross-sectional prevalence and risk-factor study in the Lifelines population-based cohort using the *Women's Health Study* dry eye questionnaire. As shown in Figure 3, the clinical diagnosis of DED increases with age, with a prevalence of around 20% in the elderly, more in women than in men. However, the graph at the left bottom corner shows a particularly high prevalence of symptomatic DED in the 20-30-year-old age group. In men, this age group had the highest prevalence of symptomatic DED. More studies are needed to look at the natural history of DED, treated and untreated, and the younger age groups should receive more attention in studies on DED. Contact lens use by the young, as well as use of electronic screens, likely contribute to the high prevalence of DED, but further investigations are needed. Younger patients are less likely than the elderly to use ocular lubricants.

We also looked at risk factors for DED (Figure 4). We investigated more than 100 comorbidities and found 48 to be independently associated with DED, including musculoskeletal, gastro-intestinal, ophthalmic, autoimmune, psychiatric, pain, functional, dermatological, and atopic disorders. Among the independent risk factors that were discovered or replicated from smaller studies, the highest risks were found for female sex, contact lens use, irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome,

keratoconus, osteoarthritis, connective tissue diseases, atherosclerosis, Graves' disease, autistic disorder, depression, 'burnout', Crohn's disease, sarcoid, lichen planus, rosacea, liver cirrhosis, sleep apnea, sinusitis, thyroid function, and air pollution (NO₂). One of the most interesting findings was the high prevalence of DED after ocular surgery. Essentially, every eye surgery was associated with a highly increased risk of DED, more than we anticipated. We should make ophthalmologists more aware of the DED that ocular surgery is causing. Also, more studies are needed into ways of preventing surgery-associated DED.

The only protective risk factor we found was hypertension, as defined by actual blood pressure measurement ---the higher the blood pressure, the lesser the DED. The pathways are unknown, but it is known that sympathetic and parasympathetic pathways can affect both lacrimation and blood pressure, and maybe sex hormones play a role. Interestingly, current smoking (for more than a year) was found to have a protective effect on DED, but smoking cessation after a year of smoking increased the odds of having DED. Perhaps smoking reduces the sensitivity of the eye, lessening symptoms, or, maybe smoking has some autoimmune advantages, which has been suggested in ulcerative colitis and Behçet's disease. In addition to the Lifelines cohort, we looked at the association between smoking and DED in the TwinsUK cohort in the UK and found similar (significant) odds ratios for smokers and ever-smokers as observed in the Lifelines cohort, indicating that the association we found is likely to be true.

The Dutch Corneal Society particularly stresses the need for proper multi-center placebo-controlled randomized clinical trials looking at the newer treatment options for DED. Level 1 evidence is generally needed to get reimbursement for these newer treatments. For instance, intense pulsed light therapy and lipid-containing drops and lid hygiene devices like thermal pulsation are not much used, because they are not reimbursed in the Netherlands.

There is a need for a greater role of optometrists in the diagnosis and treatment of DED. General practitioners usually prescribe artificial tears without investigating the ocular surface because they lack the skills and necessary equipment, and historically, patients who do not respond are referred to ophthalmologists. Compared to other countries in Europe, there is a relative shortage of ophthalmologists in the Netherlands, and the usual patient visit time of 5-10 minutes generally does not allow for adequate examination or diagnostic testing. Optometrists do have time for DED patients, and guidelines to enhance their ability to provide a substantial amount of care for patients with DED are being prepared.

Increasingly, the Netherlands is experiencing medication shortages, with ocular drugs particularly affected. In recent years there has been, usually short-term, unavailability of acyclovir ointment, fusidic acid, dexamethasone, and various artificial tears and gels. One reason for the shortages is the Dutch law on medicinal pricing and the so-called preference policy of health insurance companies, which allow only

the cheapest medications to be reimbursed. As a consequence, the Netherlands is an unattractive market for pharmaceutical companies.

SWITZERLAND. David Goldblum and Olivia E. O’Leary, Department of Ophthalmology, University Hospital Basel, University of Basel, Basel

Switzerland has a population of approximately 8.5 million people. Responsibilities in the Swiss health care system are divided among the federal, cantonal, and municipal levels of government. Each of the 26 cantons has its own constitution and is responsible for licensing providers, coordinating hospital services, and subsidizing institutions and individual premiums. The federal government regulates the financing of the system, which is effected through mandatory health insurance (MHI) and other social insurance. The municipalities are responsible mainly for long-term care and other social support services. Access to health care is relatively uniform across the Swiss population. Everybody has a free choice of doctors.

There are about 1000 ophthalmologists in Switzerland. The Swiss Ophthalmological Society includes a subgroup of dry eye specialists, which meets every year and is active in providing reports and journal articles. Only about 300 ophthalmologists perform surgeries. The other 700 are called conservative ophthalmologists, and they see a great many DED patients. There are no optometrists in Switzerland to share the burden.

As with most “Western” nations, the Swiss population is aging, creating the challenges associated with increasing health care costs. Ocular surface specialists face particular challenges, as age is a major risk factor for DED, pterygium, and bullous keratopathy after pseudophakia.

OSD is an umbrella term, which includes disorders such as DED, Sjögren syndrome, ocular (o) GVHD, keratoconus, ocular allergy, pterygium, and chemical injury. The lack of Swiss epidemiological studies makes it difficult to provide an accurate description of the current clinical situation, but, in general, the Swiss situation is probably similar to that in other areas of Western Europe.

The incidence of DED is increasing due not only to the aging population but also to increased use of digital technology. DED is recognized to be a progressive condition; more favorable clinical outcomes are likely achieved with earlier therapeutic intervention. However, timely diagnosis is hampered by lack of awareness of symptoms among the general population and a lack of reliable diagnostic tools available to clinicians. Furthermore, diagnosis, staging, and treatment of patients are complicated by the range of underlying conditions that can lead to ocular dryness. For example, the current reliance on artificial tears does nothing to address the underlying ocular surface inflammation that is present in many patients. However, without an objective and reliable means to “quantify” inflammation, it is difficult for

practitioners to prescribe an appropriate anti-inflammatory regimen. Therefore, arguably the greatest unmet needs in DED are the lack of availability of “in-office” or standardized laboratory testing capacity and, consequently, the inability to agree upon approved measurable endpoints for clinical trials of new therapies. Scientifically, this problem is being addressed by the ongoing search for reliable biomarkers for various forms of DED.

I consulted with my colleagues from the dry eye working group and the Corneal Society regarding other unmet needs in our specialty area. The group noted the need for better understanding of ocular surface inflammation and inflammatory disease. We are aware of rheumatism and perforations, and we recognize them as systemic inflammatory disease. However, questions remain regarding why rheumatism manifests in the cornea and why perforation occurs. Similarly, we lack understanding of viral, especially herpetic, corneal disease - when and how infection originates, how re-infection and recidivism occur, and how they are best treated.

The number of all types of keratoplasty carried out in Switzerland is around 650 per year. The main indications for keratoplasty are Fuchs’ dystrophy, pseudophakic corneal decompensation, graft failure needing repeat keratoplasty, keratoconus, and corneal scarring. The demand for donor cornea material cannot be met domestically by available donors. Therefore, Switzerland is dependent on the import of corneas from foreign eye banks, mainly from the USA. Of the disorders requiring keratoplasty, Fuchs’ dystrophy has the greatest scope for new therapeutic interventions. In the future, there may be a role for biosynthetic artificial corneas or injection of ex vivo expanded endothelial cells as therapy to reduce the need for donor tissue. Furthermore, advances in the understanding of the pathogenesis of Fuchs’ dystrophy together with advances in antisense oligonucleotide (ASO) technology may allow the application of ASOs targeting mutant transcription factor-4 RNA repeats in a subset of Fuchs’ dystrophy patients.

In Switzerland, the average number of patients receiving allogeneic hematopoietic stem cell transplantation (AHCT) for benign and malignant hematological disorders has increased in the last 20 years. The increased long-term survival of AHCT recipients has resulted in an increased incidence of oGVHD. Like DED, oGVHD treatment and research is hampered by a lack of validated clinical biomarkers. The exact pathological mechanisms leading to initial ocular surface damage in oGVHD are unclear, and, therefore, it is difficult to pinpoint the onset of disease or to develop predictive biomarkers. Longitudinal analysis of AHCT patients before and after transplant may lead to identification of predictive biomarkers.

The University Hospital in Basel has a large stem cell transplantation service, where I have been fortunate to work with my hematology colleagues in the follow-up care of over 800 post-transplant patients. Approximately half of them develop at least some degree of oGVHD. Usually, the DED is mild

and can be treated with lubricants, but occasionally I see patients with perforations and severe bilateral disease. These patients represent a good model of DED/OSD insofar as we have detailed clinical histories and a relatively defined window for onset of disease. However, they are usually receiving various concurrent treatments for their systemic disease, and this introduces a number of confounding variables. The unmet clinical and scientific challenge is to find objective biomarkers that we can associate with the disease and that can be used as endpoints to monitor treatment success.

We conducted a prospective study to evaluate the potential of human tear proteins as biomarkers for oGVHD.³ In the proteomic profile of tears of oGVHD patients, a number of unique differentially expressed proteins were identified. Further studies with a higher number of participants are necessary to confirm these results and to evaluate the reliability of these expression patterns in longitudinal studies.

We are now evaluating transplant patients longitudinally, sampling tear proteins and monitoring clinical phenotype before the transplant, and monitoring the patients at follow-up visits every 3 months for up to 2 years. This will provide a comprehensive overview of proteomic and clinical changes that occur in the natural history of oGVHD.

UNITED KINGDOM. Sarah Farrant, Earlam and Christopher Optometrists and Contact Lens Specialists, Taunton

The UK health care situation can be considered in two entities; the well-known National Health Service (NHS) and the private sector.⁴ The UK has over 14,000 optometrists and 1500 ophthalmologists, servicing a population of roughly 65 million people. Both professions work within NHS primary care, hospitals, and private clinics. The NHS is, in some respects, a gold standard of care, with “equal access to all” at its heart. In reality, access to ophthalmology services in the UK varies depending on where you live, which hospital is near to you, and who the specialists are at that hospital.

The NHS time and budget constraints limit the care it can realistically offer to patients with non-sight threatening conditions, such as ocular allergy and DED. Most sight-threatening conditions are dealt with by ophthalmologists in NHS eye departments, but budgets and appointments are overstretched. Indeed, just recently the NHS launched a new recommendation to eliminate certain medications, including artificial tears used for DED management, from its formulary. The NHS in its current form does not have the capacity or budget to meet the needs of patients with dry eye on the more minor end of the DED spectrum, and so generally NHS care is provided only for the more severe cases.

As in many countries, there are significant health care inequalities and unmet needs in deprived areas of the UK, where patients are also less inclined to seek help. Privately, optometrists and some

specialist ophthalmologists offer DED services and clinics around the country. Such centers are growing, in part thanks to TFOS™ and TFOS DEWS II™ and the wave of interest they have created.

The primary unmet needs in eye care in the UK could be considered a numbers game, with the more prevalent conditions, such as DED, being the most common and the least well managed. Solutions in the shorter term ultimately lie in utilizing the current resources, as NHS budget constraints do not allow for expansion. Given the number of optometrists in the UK, better education and training of this workforce could fulfill this unmet need in a primary care setting within the existing infrastructure. The main limiting factors to this are funding to cover the chair time of patients that would be seen, particularly because the NHS has created a culture of free health care. A number of primary care commissioners (people who finance the NHS) are now allocating NHS resources to optometry clinics, where optometrists are trained to deal with acute eye problems, and this also requires re-educating members of the public about where to gain access to care for OSD. Longer-term developments are already evolving with the advent of independent prescribing privileges for optometrists, allowing a greater range of presenting conditions to be managed in the community. When referral to ophthalmology is required, there is often a problem with receiving feedback from secondary care to primary care, which hinders professional development and continuity of patient care.

Communication among optometrists, ophthalmologists, and general practitioners is inadequate. Electronic networking to achieve better data-sharing is vital for eye care management. We also need to address the psychology of DED. There should be psychologists who are knowledgeable about the pain and disability that affect such patients and can help them cope with their disease.

Brexit is a significant current concern, with potential problems for pharmaceutical supplies and diminished ability to recruit NHS clinical staff. The problems are particularly worrisome given that the UK has an aging population, which will require long-term planning and funding of an adequately trained workforce to meet the increasing demand for medical care.

Highlights of the Panel Discussion: Western Europe

Moderator. It was noted that smoking had a protective effect on DED. This is in contrast to other reports and to epidemiology evaluation of the TFOS DEWS II™ report.

Jelle Vehof. About 2 years ago, a review on the effects of smoking on the anterior segment of the eye found that smoking had detrimental effects on most diseases, but for DED the data were not conclusive. There was actually little evidence that smoking increased DED and, rather, it seemed to provide a

protective effect. Clinical studies have shown evidence that the tear film is not as good in smokers, but a small study also found that ocular surface sensitivity is reduced. So, it might be that reduced sensitivity reduces symptomatology and, hence, fewer DED diagnoses based on questionnaire responses. We replicated our findings of the Lifelines cohort in the TwinsUK cohort, and also in this cohort the protective effect reversed after smoking cessation. The number of participants in our studies is significantly higher than in all other studies combined. We were also surprised by these findings.

Moderator. In Western Europe, is there any type of initiative by the health system to look for ocular allergy? Or, is it not a big problem?

Moderator. We are probably not taking care of patients with allergy as we should and not giving the condition enough attention. Allergy and immunology of the ocular surface are areas that would benefit from the interest of TFOS.

Moderator. May I ask a question about biomarkers? Do you really think we're going to get to the stage where we can differentiate between all the different possibilities leading to ocular surface symptoms? For example, allergy versus DED, or infections, or... is that possible, do you think?

Peter Raus. I believe that the technique of top-down proteomics, with its ability to identify proteoforms, will significantly help with such differential diagnoses in the future.

David Goldblum. I absolutely agree with Peter.

SOUTHERN EUROPE

CYPRUS. Erol Dülger, Department of Ophthalmology Near East University Hospital, and VIP Health Clinic Nicosia

Cyprus is the third largest Mediterranean island. Located in the East Mediterranean, it has a subtropical climate, with mostly sunny weather. Race and ethnicity of the population include Cypriot Greeks, Cypriot Turks, Cypriot Maronites, and Cypriot Brits, as well as immigrants from other countries (especially Greece, Turkey, Russia, and South Asian countries). The population is about 1.2 million and is increasing rapidly. The official languages of Cyprus are Greek and Turkish.

Cyprus has a multi-payer health care system that consists of a public and a private sector. The public sector is funded by payroll, earnings taxes, and employer contributions. The public sector health care provides social insurance for the employed, self-employed, and several types of civil servant. Access to basic health care and ophthalmologists is easy, because Cyprus is a small country and government and private hospitals and clinics always accept patients.

Despite the small population of Cyprus, a variety of OSDs are seen. Unmet needs for delivering eye care are a result of economic, political, and institutional limitations, as well as language barriers. Cyprus has 82 ophthalmologists and 45 optometrists, none with expertise in OSD. We do not have culture laboratories or means to objectively evaluate tears. We do not have an eye bank. Although corneal and stem cell tissues are not available, AM implantation can be used to treat severe corneal epithelial defects. Challenging cases are usually referred to centers in Greece or Turkey.

Most of the patients seen in our practice have myopic refractive disorders, keratoconus, contact lens side effects, and allergies. Allergies are common because of the warm climate and abundant flora. Allergies such as contact dermatitis and conjunctivitis are treated with topical and, if needed, oral medications. Immunotherapy is not available in Cyprus, so patients needing such therapy are transferred to other countries.

We see patients with DED and MGD, as well as dry eye associated with LASIK, PRK, contact lens wear, autoimmune disease, GVHD, medications, and other factors. DED is treated clinically without objective evaluation. Because Cyprus has a dynamic population, with many visitors from Europe and Asia, and many people are in close contact, diseases such as adenoviral conjunctivitis are transmitted rapidly. Microbial keratitis and pterygium are also commonly seen.

The major refractive disorder is myopia, and this is treated with eyeglasses or contact lenses. Contact lens solutions can lead to DED and allergic conjunctivitis, and bacterial or Acanthamoeba keratitis can result from contact lens misuse. Interestingly, we don't see fungal keratitis.

Keratoconus is very common in Cyprus, but we do not know why. It is often diagnosed during the examination of patients seeking refractive surgery. We use crosslinking therapy, hard contact lenses, or hybrid lenses for treatment. Patients who need Intacs or keratoplasty are usually sent to Turkey or Greece. Patients with conjunctival melanoma and other benign and malignant eyelid tumors are treated in Cyprus.

To better meet the needs of patients with OSD, we need specialized training, such as exchange programs and fellowships. We need modern equipment and supplies and specialized laboratories. We need better communication networks to obtain relevant epidemiologic data and to discuss challenging cases. We have only one national ophthalmology meeting a year in Cyprus, and we usually go abroad to improve our knowledge. We need regular seminars and case presentations locally, as well experienced ocular surface specialists to consult when needed.

GREECE. Georgios Kontadakis, Institute of Vision and Optics, University of Crete, and Department of Ophthalmology, University Hospital of Heraklion, Heraklion

Greece, with a population of around 11 million people, has more than 2000 ophthalmologists, 45% of whom practice in Athens. This amounts to 178 ophthalmologists per million of the population, which, according to a survey performed by the International Council of Ophthalmology a few years ago, places Greece first worldwide in the number of ophthalmologists per head of population. Ophthalmologists are working both in public and private sectors. Greece has only a small number of optometrists, most of whom work in clinics assisting an ophthalmologist and do not perform clinical evaluation of patients independently.

Greece has a unique landscape that features 227 inhabited islands and a mainland that is 80% mountainous. In many areas, people have very poor access to tertiary health care. As a consequence, ophthalmologic care is provided mainly by general ophthalmologists, and few cases are referred to specialized centers. For example, on the island of Karpathos, which has almost 7000 permanent residents, until 2 years ago there was no ophthalmologist, and visiting ophthalmologists reviewed patients sporadically; thus, patients with urgent needs were obliged to travel to the neighboring islands of Rhodes or Crete.

Many general ophthalmologists are not familiar with specifics in diagnosis and management of OSD. In addition, patients with disorders that are not considered to be vision-threatening or do not present with intense symptoms, as in the case of many OSDs, are not referred to an ocular surface specialist and

often go underdiagnosed and undertreated. Referral to a tertiary center is less likely for corneal disorders and OSDs that do not need surgical management.

Another significant issue is the lack of modern equipment for the diagnosis and management of OSD in public hospitals, mostly due to financial limitations. Private centers are somewhat better equipped, but more in the area of refractive surgery than in management of OSD.

Patients with OSD may need systemic medication, as in the case of OCP. In such cases, systemic treatment is often deferred, as ophthalmology training in Greece does not include a general medicine rotation. Therefore, many ophthalmologists are not familiar with systemic administration of medication, and patients who are not referred to a specialist are deprived of essential treatment. Unfortunately, collaboration with other specialists, e.g., rheumatologists, is also lacking, perhaps due to lack of awareness.

Environmental factors that affect OSD include the Mediterranean climate, with warm, dry summers and sunshine throughout the year (4 hours/day in winter to 12 hours/day in summer). As a result, Greece has a high incidence of OSD related to sun exposure and to the extensive use of air-conditioning in both work and home environments. There is a high concentration of dust in the atmosphere because of the dryness, which causes ocular irritation and allergic reactions, especially with wind-borne dust coming from Africa.

In addition to DED and allergic conjunctivitis, MGD and keratoconus are also common, the latter perhaps related to genetic predisposition or eye rubbing secondary to allergic conjunctivitis. Pterygium associated with sun exposure is also common. Since Greece does not have a systematic registry of cases of OSD, our observations are based only on empirical data. No case studies have been performed.

There is only one hospital in Athens that is considered to be a tertiary center for referral of patients with OSD and that maintains a registry of those cases. However, as noted previously, DED, MGD, and allergic conjunctivitis are often not referred to a specialist center. Despite this, MGD represents the vast majority of the cases referred to the Athens ocular surface center. Other disorders frequently referred to the center include pterygium, Sjögren syndrome, conjunctivochalasis, and OCP. Demodex infestation is often present among patients with MGD.

Greece has no eye bank for the preparation of corneal grafts and AMs, so these tissues must be imported from eye banks abroad. Interestingly, many transplantations in Greece are performed when American transplant surgeons are attending the American Academy of Ophthalmology meeting, as eye bank tissues are more available at that time. Corneal grafts can be harvested from donors in Greece, but, while the general health of the donor is verified, no quality testing is performed on the graft. In addition, precut grafts cannot be prepared. It is calculated that, based on the population, approximately 1500 graft procedures are needed per year in Greece, but only about 300 are performed.

Efforts are being made to better meet the needs for management of OSD in Greece. Greece's economy is expected to improve, so we expect health financing to increase. This should allow for the purchase of modern equipment for diagnosis of OSD in the public hospitals. The fact that most OSD is in the hands of general ophthalmologists will not be easily changed. We have created the Hellenic Ocular Surface and Dry Eye Society to increase awareness of modern diagnosis and management among general ophthalmologists. This society will establish a registry of OSD and gather statistics on its epidemiology. A primary goal of this society is to familiarize Greek ophthalmologists with activities and guidelines of TFOS. The Greek society will have its first meeting in November 2019.

ITALY. Stefano Barabino, Ocular Surface Center and Department of Ophthalmology, Sacco Hospital, Milan University, Milan, and Edoardo Villani, Department of Ophthalmology, University of Milan & Ocular Surface Service, San Giuseppe Hospital Eye Clinic, Milan

In recent years, Italian ophthalmologists have shown a growing awareness of the importance of the ocular surface morpho-functional unit. Regarding management of OSDs, the most severe conditions are usually referred to second-level specialized centers, whereas patients with mild-moderate forms are often managed by general ophthalmologists or, sometimes, by general practitioners. We have particular concerns about the management of acute conjunctivitis, eyelid margin disorders, and DED.

Regarding acute conjunctivitis, our major concerns relate to the abuse of broad-spectrum topical antibiotics. These drugs, often prescribed by ophthalmologists, but also by general practitioners and emergency room doctors, are commonly used unnecessarily not only in cases of viral, allergic or non-specific conjunctivitis, but also as prophylaxis in patients undergoing ophthalmic surgical procedures.

About eyelid margin disorders, we feel that a major problem relates to lack of awareness of the very different pathophysiologic mechanisms leading to these diseases. Specifically, most general ophthalmologists fail to discriminate between MGD and inflammatory conditions, missing the opportunity to provide a treatment tailored to the patient.

DED is very common in Italy. The most commonly used tests to diagnose the disease and the current therapeutic approach have recently been surveyed. A questionnaire designed by the Italian Society of Dacryology and Ocular Surface (SIDSO) was submitted to about 300 ophthalmologists attending the Congress of the Italian Ophthalmology Society in 2016. It consisted of a list of multiple choice questions concerning the management of DED, in particular, the risk factors, symptoms, patients' quality of life, diagnostic procedures used, and therapeutic management. A total of 191 ophthalmologists responded.⁵

The first question asked the ophthalmologist to indicate the symptoms most commonly described by patients (Figure 5). Foreign body sensation and dryness and burning were the most commonly reported. This is similar to the questionnaire responses of ophthalmologists in other European countries collected by a survey of the European Society of Cataract and Refractive Surgery (ESCRS). This consistency is interesting, because in Europe, we would expect differences from country to country because of cultural differences and because of the translation from English to the local languages. Interestingly, after cataract surgery, the most commonly reported symptom was foreign body sensation. Dry eye after surgery is similar to other forms of DED, but it is actually very specific, and its detailed discussion is beyond the scope of this review. Asked if they saw a correlation between DED symptoms and depression or anxiety, most of the respondents said yes. However, we don't know whether the depression or DED comes first. The most commonly used diagnostic tests are the TBUT and the Schirmer test (Figure 6). When DED first became recognized in Italy, it was associated with Sjögren syndrome, so DED was attributed to a lack of tears. Therefore, the Schirmer test is common in Italy. Fluorescein staining and TBUT measurements were also commonly used. Use of TBUT in the Italian survey was similar to that reported by ophthalmologists in other European countries.

Questions remain regarding how to diagnose ocular surface inflammation, not only in DED but in all OSDs. If the diagnosis is based on conjunctival hyperemia, a lot of patients with DED may be missed. There is disagreement among ophthalmologists about the association of inflammation and DED. We do not have an efficient method of diagnosing ocular surface inflammation. Ophthalmologists in Italy have an average time of 15 minutes per patient visit, so the method must be fast and easy to use.

As shown by the questionnaire results, Italian ophthalmologists do not have a standard protocol for the treatment of DED. They prescribe artificial tears, and with recent awareness of inflammation, they are interested in treating that also. They reported using topical corticosteroids (62%), tetracyclines (20%), omega 3 fatty acid (10%), and topical cyclosporine (6%). Topical cyclosporine is not reimbursed, which may account for its limited use. A compounded formulation of cyclosporine can be obtained, but the patient must be referred to a hospital-based specialist, and the hospital has to be authorized to prepare the formulation. Another problem for DED patients in Italy is that artificial tears are not reimbursed, and many of them have no clinical or pre-clinical data. Fortunately, beginning in 2020, a new European law will require thorough pre-clinical and clinical data for a medical device to be put on the market.

In addition to the problems of sourcing medications, a patient may have to wait 6 months or more to see a DED specialist. A general practitioner must refer the patient to a general ophthalmologist, who then refers the patient to the specialist.

Another problem for DED patients is the internet dissemination of "fake news." A web search for *dry eye* or *dry eye specialist* may lead the patient to sites of people fraudulently claiming to be

specialists. Such charlatans may, for example, propose a laser treatment, which will not work and may represent great cost (and disappointment) to the patient. SIDSO now has a web page to provide correct information to patients.

In terms of treatment, we are working with some companies on new solutions. The first one is a combination of hyaluronic acid plus a very low percentage of hydrocortisone; a recently published paper demonstrates its anti-inflammatory effect in an animal model of DED.⁶ We are also working on developing a type of tear substitute that modulates epithelial cells and supports their metabolism.⁷

Regarding the clinical management of DED, two more issues are worth mentioning. First, we know that topical immunomodulators can play a major role in the chronic management of several severe forms of DED, but, at present, only one product is on the market in Italy. It is very expensive, and it cannot be prescribed under the current NHS. The second issue relates to high-tech treatments for MGD, eyelid margin disorders, and DED, including the novel instruments for intense pulsed light therapy. These new technologies have intriguing rationale and interesting preliminary data; however, their exact mechanisms of action in different types of patients are not yet fully understood. Our main concern is related to the scarcity of these technologies in university and research centers relative to their concomitant widespread promotion among private practitioners.

Last but not least, we made an interesting observation about blinking patterns and dry eye. It is generally accepted that an unblinking eye in up-gaze position will develop dry eye. However, we demonstrated that professional Grand Prix motorcycle drivers can go up to 10 minutes without blinking when assuming the driving position, even if they are not actually driving, without developing dry eye. They do not have symptoms or changes in the tear meniscus, there is no inflammation, and there is a decrease of osmolarity. These findings, which we presented at The Association for Research in Vision and Ophthalmology meeting in 2019, are interesting in terms of research and trying to better understand the role of corneal sensitivity and the role of the central nervous system.⁸

PORTUGAL. José Salgado Borges, Department of Ophthalmology, Private Hospital of Boa Nova & Prof. J. Salgado-Borges Clinic, Perafita, and José Manuel González- Méijome, Optometry and Vision Science, and CEORLab - Center of Physics, University of Minho, Braga

Portugal has 10.5 million inhabitants, most living near the coast. The mean age is 44.2 years, with more people over 65 years old than under 14 years old.

Portugal has 1000 ophthalmologists and 1800 optometrists with a higher education degree, which together comprise the main eye care practitioner (ECP) workforce. According to the process of the NHS,

patients with ocular problems should first go to a general practitioner (GP) and after that to the hospital, where they can be seen by an ophthalmologist. Alternatively, they go to optical facilities, where most of the optometrists work, and/or consult an ophthalmologist in private practice.

The NHS lacks the capability to respond to the long waiting lists of patients, and socio-economic constraints prevent easy access to private medical care. The Portuguese population has a low level of awareness of DED, and general practitioners have little knowledge in this area, so for the DED patient to reach a dry eye specialist typically involves a long and convoluted process.

The incidence and prevalence of DED in Portugal is currently unknown. With an aging population, polypharmacy, increased artificial indoor environments (often involving prolonged video-display terminal use), increased use of contact lenses, and ocular surgical procedures, DED is expected to increase over the next few years. Today the diagnosis is usually made by ECPs, assisted by other allied ophthalmic personnel, such as orthoptists, based on self-reported symptoms and ocular surface signs (such as corneal staining and short TBUT values). Recently, a limited number of ECPs have reinforced their diagnostic capability with the use of advanced ocular imaging, tear osmolarity, and other techniques. The routine use of questionnaires such as the Ocular Surface Disease Index (OSDI) or Dry Eye Questionnaire (DEQ) is rare. Differentiation between aqueous deficient and lipid deficient DED is still a challenge for many ECPs. During the past 2 years, we have participated in various local and international meetings demonstrating the importance of identifying the pathogenesis of DED and the new diagnostic tools.

The first step in treatment of DED is the prescription of artificial tear supplements. This is a well-developed option in Portugal, with several companies intensively promoting the use of specific solutions for each type of tear deficiency potentially related to DED (aqueous deficient versus lipid deficient); these treatments are usually prescribed by both ophthalmologists and optometrists. However, because of the limitations in differentiating the underlying pathogenesis of the DED, the solution prescribed for individual patients may not be appropriate. Treatments involving eyelid cleansing and warming of the meibomian oils are also advised by ECPs. More severe DED is treated by ophthalmologists specialized in anterior segment disease and involves anti-inflammatory drugs, such as corticosteroids or cyclosporine. New treatments have been introduced recently in Portugal, such as Plasma Rich in Growth Factors (PRGF/ENDORET) and Intense Ultra-Regulated Pulsed Light (IURPL).

In the short term, based on the available knowledge, ECPs should adopt standardized clinical routines to more accurately detect and differentiate the types of DED, grade them, and provide adequate treatment accordingly. Improvement of DED with most existing treatments takes a long time to be noticed by the patient, and ECPs should be trained in effective communication to increase patient compliance with the treatment over time. This management approach should involve an interdisciplinary relationship

between primary ECPs, medical specialists such as dermatologists and rheumatologists, and ocular surface specialists to monitor changes in levels of severity of DED and adjust the treatment. In our opinion, eye clinics should incorporate Integrated Centers of Dry Eye, similar to those that are established for cataract, refractive surgery, and glaucoma.

Current research in DED in Portugal includes the evaluation of DED in contact lens wearers, the impact of ophthalmic surgery, and the molecular basis of DED, using advanced methodologies, such as molecular biology, objective analysis of image quality metrics, subjective and psychometric questionnaires to quantify the presence and severity of DED. In the future, there must be a greater effort to gather epidemiological data on the incidence, prevalence, and socioeconomic impact of the disease. More effective and specific diagnostic tools and more effective and safe treatments should be made available to assist practitioners.

It is important to increase knowledge of DED by participating in meetings with small groups of ophthalmologists, optometrists, and technicians, regionally, as well as in large meetings and symposia nationally and internationally. It is necessary to enhance knowledge about DED not only for our colleagues but also for patients and the public to allow them to recognize their symptoms and seek appropriate care. As Portuguese ECPs, we have the privilege of communicating information to physicians and ECPs in other countries also, for example, African nations that do not have easy access to the type of information that is disseminated by TFOS. It is important to develop easily accessible eye care units where patients and DED care providers can obtain information.

SPAIN. Jose M. Benitez-del-Castillo, Complutense University of Madrid and Hospital Clinico San Carlos, Madrid, Spain

Spain has a population of 47 million people and is divided into 17 autonomous regions. Medical treatment opportunities are not necessarily equal among regions. Spain has two different approaches to health care, two different health care providers. The public system is universal and free (even for illegal immigrants). Private health insurance, which can be purchased, is the other option. The public system prioritizes more “important” problems, which do not include DED. There are many patients on long waiting lists. Doctors are well-trained, but are more interested in cataracts, Descemet's stripping automated endothelial keratoplasty, Descemet's membrane endothelial keratoplasty, and difficult glaucoma and retinal detachment cases than in DED. Cataract surgery with premium intraocular lenses and refractive surgery are not available at public hospitals, and these procedures are performed in private clinics. Therefore, the dry eye commonly associated with such surgeries, as well as MGD, are generally

diagnosed and treated in private clinics. Private offices are equipped with osmometry, interferometry, meibography, intense pulsed light therapy, and thermal devices.

The public system lacks the time and sophisticated instrumentation to diagnose and treat DED. Even more important, there is not time for discussion about the chronic nature of the disease and how to correctly use the various therapeutic options. Seven years ago, tear substitutes were covered by the public system (most of them free), but today, only patients with Sjögren syndrome have access to artificial tears, usually old ones that contain preservatives. In Spain the majority of tear substitutes and anti-glaucoma drops are preservative-free. There are two ways to obtain topical cyclosporine. It can be purchased in any pharmacy for €117, or it can be obtained free after an appointment with a general practitioner, followed by an appointment with a public hospital eye doctor, who may decide to issue a prescription (some ophthalmologists still think cyclosporine is poisonous and are reluctant to prescribe it). With a prescription, cyclosporine can be obtained at the hospital pharmacy, but only a 1-month supply, so ongoing treatment entails a tedious monthly trip to the pharmacy.

There are also unmet or poorly met needs in the management of other OSDs. Regarding limbal stem cell deficiency (LSCD), because the European law is under revision, the ex vivo expansion of allogenic stem cells for transplant is illegal, and the only approved therapy costs more than €100,000. The influx of immigrants from South America, with its dry climate and UV exposure, has resulted in a high prevalence of pterygium. Spain lacks commercial medications to treat *Acanthamoeba*, the incidence of which is increasing due to contact lens use and orthokeratology, and fungal keratitis, which remains uncommon. When such drugs are needed, we must rely on a compounding pharmacy or request the drugs from the Foreign Drug Department.

In summary, with respect to diagnosis and management of OSD in Spain, we need to have a better understanding of DED and MGD and improved access to effective medications, better and cheaper LSCD treatments (some keratoprotheses have no CE mark), and rapid access to anti-amoebic and anti-fungal drugs.

TURKEY. Afsun Şahin, Department of Ophthalmology, Koç University Medical School, Istanbul, and Ömür Uçakhan Gündüz, Cornea and Contact Lens Service & Department of Ophthalmology, Ankara University Medical School, Ankara

A new era for modern Turkey began with the 1923 foundation of the Turkish Republic, which arose from the remains of the Ottoman Empire. At that time, the population was about 13 million, and there were only 1,078 physicians in the entire country in 1928 when the Turkish Society of Ophthalmology was established. Today, with a population of over 80 million, Turkey has over 150,000

physicians, and some 5000 ophthalmologists are currently providing eye care in 81 cities. Despite new legislation and measures taken by the government in the last decade, there are still significant variations in access to health care, particularly among the 4 million refugees, who pose a great challenge for Turkey.

Although under-reported, corneal/ocular surface disorders such as microbial keratitis and corneal trauma (including chemical injuries) continue to be significant causes of visual impairment in Turkey, leading to an estimated one million new cases of unilateral/bilateral blindness each year. Herpes simplex and fungal keratitis are particularly common and challenging. With an increasing number of refugees, previously eradicated ocular surface infections such as trachoma and chickenpox have also increased in prevalence, and more keratoconjunctivitis due to chickenpox is being encountered in children. Conjunctivitis in children and newborns is common.

Other significant ocular surface problems in Turkey are DED and allergy. Although the prevalence is unknown, DED is being diagnosed at all ages, including the teenage and younger populations, particularly because of pollution and heavy use of smart phones and tablets. With the increasing digital device use, myopia is also on the rise in children. As Turkey is a Mediterranean country, other common conditions encountered are keratoconus, UV-driven inflammatory/degenerative conditions such as pterygium/pinguecula, and vernal keratoconjunctivitis.

Turkey has a small number of cornea specialists, and in rural areas the access to health care facilities is limited. The patient load per doctor in State hospitals is excessive, with an ophthalmologist seeing more than 50 patients in a working day, even up to 80 patients in some communities. This often precludes the proper diagnosis of DED and other ocular surface diseases.

There are more than 20 corneal eye banks in Turkey, but a number of obstacles interfere with the acquisition of corneal grafts from cadavers. Some religious concerns prevent organ donation, and legal regulations are still in effect. Organ donation awareness is low among less educated people. Harvesting grafts is further limited by the expense of the procedure.

The Turkish Ophthalmology Society needs to be in close collaboration with the Ministry of Health to develop new policies. Unfortunately, political considerations make this difficult. We need to create tertiary referral centers that are specialized in cornea and OSDs, and increase the number of cornea specialists. Ophthalmology residency education among teaching hospitals is not standardized. In some communities, the residents receive adequate education about DED, but not in others. The time allotted for ophthalmologists to see their patients needs to be increased, but because of health care provider regulations, this is not currently possible. We need to increase the awareness of DED and OSDs, especially by young ophthalmologists, who are more focused on cataract surgery. We need to establish standardized cornea fellowship programs throughout Turkey and recruit talented young ophthalmologists to pursue specialized training in OSD.

VATICAN CITY. Stefano Bonini, Department of Ophthalmology, University of Rome Campus BioMedico, Rome

The Vatican City is an independent city-state enclaved within Rome, Italy. With an area of 44 hectares (110 acres) and a population of about 1,000, it is the smallest sovereign state in the world by both area and population. I work at the University in Rome, but for more than 12 years have served as an ophthalmologist at the Vatican City. My comments here refer to both Rome and the Vatican City, because the health care systems work similarly, although a little better in the Vatican City.

We may fail to meet the needs of our patients with DED because of the need to make a clear and quick diagnosis. We generally see the patient and make notations based on visual function and intraocular pressure, but we do not provide a meaningful explanation of what disease may be present, whether it is chronic or acute, what visual function to expect in the future, how much the therapy may cost, and what is and is not covered by the NHS.

As defined in the TFOS DEWS IITM report, DED is a multifactorial disease. Many clinical entities are involved, and one clinical finding may not be comparable to another. Different aspects of the disease may need different treatments, and this creates major problems in conducting clinical trials. One reason we do not have cyclosporine in Europe is because of the failure of all the studies presented to the European Medicines Agency. Studies probably have a bias in the selection of patients, and all types of DED are included together. For purposes of both patient care and clinical studies, the factors underlying individual cases of DED must be identified through diagnostic tests, clarifying whether the DED is evaporative or due to another condition. The patient should be aware that, as demonstrated by clinical trials, all artificial tears do not have the same efficacy, and the ophthalmologist should advise patients of the appropriate choices.

One reason for clinicians to differentiate between the severity levels and conditions underlying DED is to provide the NHS with data. There is a law in Italy (N 648) under which a drug that is not available in Italy can be obtained from another country and have its cost covered by the NHS if the patient's condition requires the medication. A few years ago, my request that cyclosporine be provided for treatment of DED was at first granted by the Ministry of Health. However, when they realized that the indication of cyclosporine for all forms of DED (as in FDA approval) could cost the government millions of Euros, they declined to cover it. This is why we should separate different clinical entities involved in DED and be able to estimate the number of patients who are likely to need the imported drug. I hope that Restasis and other approved cyclosporine formulations will be available in Italy in the future. The costs of

importing such drugs in Vatican City are high, e.g., ranging from €150 to €250 for long-established products to €700 for the new products, such as Liftegrast.

The various types of ocular allergies also need to be differentiated, such as mild versus more severe seasonal allergy, mild versus severe vernal keratoconjunctivitis (VKC), and atopic keratoconjunctivitis, among others. The severe forms may require aggressive treatment. My colleagues and I have proposed a staging approach to treatment of VKC, according to severity of signs and symptoms.⁹ Such a staging approach should be considered by the NHS in its decisions regarding the drugs covered for various levels of severity.

Because inflammation can evolve into severe, long-term conditions, e.g., conjunctival cicatrization, it should be prevented and treated aggressively with appropriate treatments. In monitoring patients with DED, we should consider that the severity of the disease may change from one day to another and be prepared to adapt therapy accordingly.

Addressing corneal infection, we have effective antibiotic and anti-inflammatory agents to treat these conditions, many of them covered by the NHS. However, there are many conditions, mainly rare ones, for which we do not have treatments. For instance, we do not have a specific therapy for fungal ulcers or *Acanthamoeba* keratitis. We should follow these patients and try to keep them informed about their status and prognosis, including the expected course of disease, effect on vision, and possible need for surgery, for example. Costs of treatments are also a consideration. Some specific products are available in France and the UK, and we can obtain them through the Vatican City. This is not the case for the Italian NHS.

In summary, OSDs seen in the Vatican City are similar to those seen in other European countries, and these probably represent 70% of all the patients attending our ambulatory unit. For the purpose of patient information and a closer collaboration with the NHS, it is important to differentiate between various forms of DED, for example, Sjögren syndrome. In these patients, we must consider that not only the eye is involved but that they have other problems requiring additional treatments and expenses. These patients may also benefit from psychological counselling.

The TFOS DEWS IITM report provides valuable information for ophthalmologists in Italy and across Europe, and I suggest that we draw from this report to provide practical summaries in multiple languages to aid DED patients in better understanding their conditions.

Highlights of the Panel Discussion: Southern Europe

Moderator. Some southern European countries, especially islands, have high levels of UV light. This is associated with pterygium and other diseases of the ocular surface. Perhaps Drs. Dülger and Kontadakis could comment on the prevalence of pterygium in Cyprus and Greece and on its management. Do you have access to fibrin glue to facilitate surgery? What other peripheral diseases of the conjunctiva do you see, for instance, dysplastic disease or tumors of the conjunctiva?

Erol Dülger. Allergy is very common in Cyprus. We usually treat it with topical medications and suggestions of lifestyle changes. Rarely, we send patients to Greece and Turkey for immunotherapy injections.

Georgios Kontadakis. Pterygium is common in Greece. It sometimes does not require treatment, and patients may not seek treatment until it affects their vision. Then it is usually treated in public hospitals, where the surgeon's time is very limited, and the procedure consists of just surgical section without autologous graft or fibrin glue. The treatment is not always effective in such cases.

Audience question. I was very surprised to learn that in Cyprus you do not attempt to treat certain conditions, but rather send patients to Turkey or Greece for treatment. As we have heard from other speakers today, relatively few ophthalmologists in Greece and Turkey are trained in ocular surface and external eye disease. So, how do the patients obtain specialized care in those countries? How could Cyprus establish treatment programs of their own so that it is not necessary to send patients to other countries?

Erol Dülger. It is a very small number of patients whose cases are too challenging to be treated in Cyprus. When such treatment is needed, we make arrangements with a colleague, and usually the government pays travel expenses.

Stefano Barabino. In Italy we have many patients with pterygium among the large population of immigrants from Central America. It occurs also in native Italians but with less frequency.

Moderator. I would like to stress the importance of collecting data in the specialized centers. Dr. Barabino, you mentioned that data were collected from clinicians at the Italian Society of Ophthalmology meeting. Participation was voluntary and about 25% responded.

Stefano Barabino. We learned that the responding ophthalmologists were, at least, treating DED with artificial tears. However, there was some confusion about exactly what protocols were followed. Patients come to me with a bagful of different artificial tears that haven't helped, which have been prescribed by multiple ophthalmologists. Now that dry eye is recognized as a disease of the ocular surface and we know that inflammation plays a role, ophthalmologists are beginning to prescribe steroids. Further discussion is needed about kinds of steroids and specific uses, but, at least, ophthalmologists are familiar with this approach.

Moderator. Having a standard algorithm for diagnosing and treating DED, and informing the patients, would help to save time and provide good care to the patient.

Moderator. On the topic of dry eye after surgery, do different types of ocular surgery produce different degrees of dry eye?

Stefano Barabino. This is a very interesting question. Here, we are talking about surgery, but not, for example, about intravitreal injections, which are often performed. Intravitreal injections induce ocular surface changes, as I think all the clinical procedures involving the ocular surface can do. The kinds of dry eye induced by various procedures differ, but we do not have sufficient information about this. I think that dry eye after cataract is different from dry eye after refractive surgery, or after vitreoretinal surgery, or after glaucoma surgery. It has been reported recently that 77% of patients complain of dry eye symptoms after glaucoma surgery, although the mechanism is certainly different from other ocular surgeries. We simplify the problem and give the patient artificial tears, but we should look more deeply into the mechanisms of post-surgical changes.

Moderator. It was pointed out in the TFOS DEWS IITM report that about 75% of the literature on post-surgical dry eye relates to refractive surgery, especially LASIK. Maybe we should focus on the need for a screen for dry eye before any ocular surgery to learn more about the features of dry eye associated with different procedures.

Enesa Begovic. I just want to emphasize a point made by Dr. Barabino. There is a clinical entity that we may call *dry eye-like disease*. Unlike DED, it occurs after cataract and other ocular procedures, and it is reversible. We prescribe artificial tears for that clinical condition, and it is cured. However, DED is a chronic disease, and it is diagnosed very rarely.

Stefano Barabino. I agree, and Dr. Bonini made this point also. We can mean many different things when we refer to dry eye. In clinical trials for “dry eye” medications, it very important that the reviewing agencies are clear on what we mean by dry eye.

Enesa Begovic. It would be a good idea to call post-surgical dry eye “dry eye-like disease,” and to adopt it as a diagnostic term. The patients will know then that it is not a chronic disease, that it can be treated with eye drops, and that it is reversible.

Moderator. I have a question for Drs. Salgado, Barabino, and Sahin about the changes that Europe is facing with the influx of refugees and the stress on the medical systems. Can you comment on increased prevalence of certain diseases, e.g., pterygium, allergy, keratoconus?

José Salgado Borges. Portugal previously had an influx of immigrants from Africa, so we have experience in dealing with difficult cases within our health care system. Portugal is currently not receiving as many refugees as other countries, and we can accommodate those patients in our system.

Afsun Şahin. Turkey is the country with the largest number of refugees in the world, and we have spent more than 40 billion dollars, in the last 5 years, for their health care and other life expenses. The prevalence of pterygium is greatly increased. I invite my colleague, Doctor Ömür, to provide more information about this.

Ömür Uçakhan Gündüz. Pterygium is only one of the conditions arriving with the refugees. They have many contagious infections, including trachoma, herpes, adenoviral infections, neonatal conjunctivitis, and chickenpox. We see chickenpox in Turkish children, even those who have been vaccinated, and we see more chickenpox-induced keratitis and keratoconjunctivitis than we have ever seen before. So, the health care system is very stressed. It is difficult for the institutions, the practitioners, and the patients. The government pays completely for the health care and medications of refugees, more so than for Turkish citizens, and this can create resentment.

Moderator. Dr. Barabino, you have noted that all surgical manipulation causes dry eye. As a surgeon, what steps do you take to prevent dry eye?

Stefano Barabino . I'm not saying that ocular surgery induces dry eye, rather that ocular surgery induces changes of the ocular surface, which can be dry eye-like. As Dr. Gomes said, it is important to evaluate the patient before surgery. In Italy, some surgeons dedicated to cataract surgery may perform 20 surgeries a day without seeing the patients before surgery. The surgeon should evaluate the patient's ocular surface situation before doing the surgery and treat any conditions that might predispose to ocular surface problems before scheduling the surgery.

Translator for a Russian TFOS Ambassador. In my training program in Russia, patients are examined before surgeries and if they don't have a clinically healthy ocular surface, surgery is not allowed. However, a surgeon doing 20 cataract surgeries a day has a monetary interest that could make ocular surface health a lesser priority.

Stefano Barabino. There can be a monetary value in assuring that the ocular surface is healthy before surgery. Considering the high cost of the primary IOL and cost of cataract surgery, it makes sense to detect and correct any ocular surface problems, such as an unstable tear film, in advance rather than risk a poor surgical outcome. Some surgeons have begun to realize this and seek collaboration of an ocular surface specialist.

Central & Eastern Europe

BOSNIA AND HERZEGOVINA. Enesa Begovic, Huda Hajjir Karcic, Suvad Karcic , and Alma Cerim. Private Health Institution Polyclinic "Eye" Dr Karcic, Sarajevo, Bosnia and Herzegovina

Bosnia and Herzegovina (BiH) is a sovereign country located in southeast Europe in the western part of the Balkans. The total population is 3.5 million, and population growth is negative.

Based on the Dayton Peace Agreement of 1995, BiH consists of two entities: The Federation of Bosnia and Herzegovina (FBiH) and Republic of Srpska (RS). Another entity, the Brcko District, was later created as a condominium of FBiH and RS. The health care system is not unified in FBiH and RS. While in the Republic of Srpska it is centralized, with Banja Luka as the capital and administrative center, in the FBiH it is decentralized, and it is divided into 10 cantons. Each canton has its own government with its own Ministry of Health. So, in a country with only 3.5 million people, we have 13 Ministries of Health. A public insurance foundation provides everyone with a basic health care package regardless of income. There is no alternative to public insurance, such as private insurance, so people who choose private clinics pay the full amount for the services. People may pay additional health care insurance voluntarily for a higher level of health care services, but public insurance is mandatory.

BiH faces a difficult task in dealing with emigration. People move to more developed countries (Scandinavia and Western Europe) in search of better opportunities. It is estimated that more than 300 doctors leave BiH annually. BiH is not yet a member of the European Union.

We have only about 200 ophthalmologists in BiH, including residents. Only 62 ophthalmologists live in the FBiH, while the majority of them are in capital cities. So, the less developed cantons have one or two ophthalmologists, each of whom commonly examines more than 40 patients per day. There are no optometry training programs.

There are five clinical university centers in BiH, where eye clinics are organized very similarly. They have trauma, pediatric, and anterior and posterior segment departments. There are no independent corneal and ocular disease units, and patients with OSD and DED are directed to the anterior segment department. The anterior segment department is busy with cataract surgery and glaucoma patients, and there is little time for doctors to spend with patients with OSD and DED.

In daily practice, assessment of DED and OSD is based on questionnaires and simple clinical tests, such as biomicroscopy, Schirmer test, and tear film evaluation. Some private clinics can assess the ocular surface with anterior optical coherence tomography or corneal topography, but tests such as tear film osmolarity, impression cytology, thermography, confocal microscopy, meibography, and interferometry are not a part of routine examination. Although there are doctors and teams trained abroad for corneal transplantation, because of legislative issues, a corneal tissue bank is not yet established. Patients who need corneal transplantation surgery are directed to clinics in neighboring or other European countries.

During the last 15 years, more attention has been paid to DED and OSD in our national and international congresses and meetings. In 2007, a master's thesis on the topic of tear film quality

assessment in patients with diabetes mellitus was defended. In June 2017, a multi-center study was initiated on cyclosporine efficiency in medium-severe forms of DED in menopausal women. Three centers in BiH are involved in the study, which is currently in its final phase.

In practice, the DED diagnosis is established in only 1-3% of examined patients, while around 30% of the total gets a prescription for artificial tears in the form of solutions or gels. We use topical corticosteroids with an antibiotic when necessary. We advise and educate patients about altering environmental factors that may cause DED symptoms. Patients who receive prescriptions for artificial tears are those with dry eye symptoms associated with other conditions, for example, glaucoma patients on topical anti-glaucoma therapy, patients who have undergone cataract or refractive surgery. In the latter case, if complaints are prolonged, lacrimal punctal plugs may be inserted temporarily. If necessary, we apply soft bandage contact lenses and scleral rigid lenses. We prepare autologous serum in our clinic. AM graft and tarsorrhaphy are reserved for the most severe cases. We do not have medicines such as topical secretagogues, immunomodulatory drugs, or cyclosporine, and we do not have experience in salivary gland transplantation.

Legislative procedures for the registration of a single medicine takes about 1 year, and the license expires after 1 or 2 years. We have 34 medications registered now for DED, and all of them are artificial tears. Medicines, such as cyclosporine, topical fungicides and anti-microbes against *Acanthamoeba*, are not available in our country. Topical acyclovir is manufactured in one pharmacy near the capital.

The TFOS DEWS IITM report has been presented to ophthalmologists in BiH and to the general public via electronic and printed media and TV programs. It is not possible to completely implement the recommendations for the management of OSDs, due to the reasons stated above.

In conclusion, there is no established protocol for management of DED in BiH. We recommend the organization of workshops with the professionals involved in DED management to improve collaboration with other specialists, such as immunologists and rheumatologists. We should also simplify the procedures for registering medicines and procuring state-of-the-art equipment.

BULGARIA. Christina N. Grupcheva. Department of Ophthalmology and Visual Sciences, Medical University of Varna, Varna.

Bulgaria is a relatively small country with a population of approximately 7.5 million; however, it is endemic for corneal dystrophies. Worldwide, 1 in 10,000 people have corneal dystrophies, while in Bulgaria 1 in 3,000 are affected, especially in the northern part of the country. Unfortunately, most of these dystrophies are associated with recurrent erosion syndrome and significant disturbances of visual,

perceptual, and cosmetic comfort. In all those conditions, *in vivo* confocal microscopy demonstrates changes in the basement membrane over time, with significant scarring at the level of Bowman's membrane.

Although many families have phenotypic presentations with characteristic clinical signs and symptoms, genetic testing in Bulgaria is very limited, bordering on impossible. The socioeconomic status of these patients is relatively low, but they are expected to cover the cost of genetic evaluation, as the health insurance system does not cover such testing. We did some genetic testing, which revealed transforming growth factor- β -induced protein positivity. The inability to routinely perform genetic testing on patients with corneal dystrophy represents an important unmet need.

Currently, patients with corneal dystrophy complications of the anterior ocular surface are managed by lubricants, utilization of therapeutic lenses, AM transplantation, and limited application of translational products such as cultured limbal stem cells.¹⁰ This represents another unmet need, as the development of products based on cell cultures is facing numerous regulatory problems and financial constraints. Nevertheless, we have a registry of patients with chronic ocular surface problems, and we provide them with tailor-made solutions that best fit their lifestyle and needs.¹¹

Another challenge related to corneal dystrophies is keratoconus, again a very common reason for astigmatism in the Bulgarian population. In general, the diagnosis of keratoconus is relatively timely, but the optical management is associated with some cost- and availability-related difficulties. There is no contemporary, comprehensive contact lens-producing laboratory in Bulgaria, and patients are fitted with lenses produced in other EU countries, mostly in the UK. The anticipated Brexit will most probably affect the availability and timely fitting of contact lenses to patients with keratoconus in the near future, presenting an impediment to the provision of a quality of vision and life upon which around 80% of these patients rely.

Keratoconus is also associated with ocular surface pathology. The corneal nerves, as seen with *in vivo* corneal microscopy, are very prominent, producing marked eye sensitivity. Ocular surface management requires application of lubricants and control of inflammation. Investigations are needed to better understand the reasons for the ocular surface pathology.

In Bulgaria there is a good system for referral of corneal trauma and burns, such that they usually reach the tertiary hospital, where the subsequent surgery and follow-up are state-of-the-art, within 2-3 hours. In general, recently we have observed less industrial and more home-related trauma. Considering that East Bulgaria is coastal, and one-fifth of Bulgaria comprises skiing resorts, we must mention that UV ocular surface trauma is a common observation in everyday ophthalmology practice. Recently, interesting research has been dedicated to UV-related trauma and possible long-term consequences for the anterior ocular surface.^{12,13} Unfortunately, public awareness regarding UV damage to the anterior eye is at a very

low level (proven by a number of surveys), and another unmet need is to expand the general knowledge of the public about the benefits of UV protection.

Another negative condition remotely related to trauma is polypragmasia, which can be iatrogenic or, less commonly, patient-driven. This is the most common cause of LSCD, especially in patients on multiple anti-glaucoma medications. Again, being a small country, Bulgaria experiences difficulties in registering a broad portfolio of eye drops. The number of non-preserved formulations is very limited. This is a significant unmet need, especially in regard to drops crucial for the treatment of severe OSD, such as cyclosporine, dexamethasone, and antibiotics.¹⁴ This problem might be solved with some regulatory advancements facilitating the registration process of ophthalmic preparations and also increasing the interest of the related industry.

Recurrent corneal erosions and trauma and burns may require AM transplantation. In 2005, we established an AM bank, and since then, we have performed more than 2,000 AM transplants. In some patients, we have performed multiple transplants with good results. Patients report reduced pain on the day after the procedure, the visual acuity increases in up to 55% of our patients, and more than 2/3 of operated patients report an improved quality of life.

We have created a preserved AM product, which is called ALOAM (allogenic AM). It is prepared according to standard approved procedures and is registered for use in Bulgaria. We have also created a third eye bank in Bulgaria, which supplies corneal tissue as well as AM. Previously, with two eye banks, the waiting time for corneal transplantation was 3 years. The new eye bank is expected to reduce the waiting time to a year and a half, although our goal is to reduce it even further.

Lastly, one of the biggest challenges in regard to diagnosis and proper management of the anterior ocular surface is professional development. In Bulgaria, before the year 2000, the only eye care profession was ophthalmology and the role of opticians was exclusively technical (making spectacles). Over the past 10 years, two related specialties have been successfully developed: a bachelor's degree program in medical optics and a master's degree program in optometry. These eye care practitioners have a structured curriculum of activities that have increased significantly the portfolio of eye care in Bulgaria. Collaboration between specially trained staff and ophthalmologists have led to better and more efficient ophthalmology practices, including specific DED-related clinics and special therapeutic procedures. Bulgaria still needs to implement a number of established practices from countries with established expertise in the field.

GEORGIA. Nino Karanadze, Department of Eye Diseases, Tbilisi State Medical University, Tbilisi

Georgia is a country in the Caucasus region of Eurasia, located at the crossroads of Western Asia and Eastern Europe. It includes two autonomous republics and nine regions. Georgia's population is estimated to be 4 million, with 1.1 million located in its capital city, Tbilisi. There are 585 ophthalmologists in Georgia, most of whom are members of the Georgian Ophthalmological Society, which was established in 2000. The Society maintains close relationships with TFOS and other international ophthalmology societies.

DED and OSD are serious problems in our country. The most commonly seen OSDs in Georgia are consistent with those seen in other European countries. There is a particularly high incidence of keratoconus in the mountainous and Black Sea areas of the Adjara region. Intensive use of computers, tablets and mobile phones appears to have increased the incidence of DED in children. Frequent misdiagnosis and inadequate treatment of DED in children and young people represents a serious unmet need.

Regarding management of OSD, we use AM transplantation in patients with severe DED. Lacrimal plugs have been used before and after keratoplasty to reduce the risk of postoperative DED in patients with keratoconus, and similarly have been applied in LASIK patients one month prior to surgery.

We are grateful to the pharmaceutical companies, notably Santen, Alcon, and Impexfarm, who regularly provide workshops, webinars, and conferences to inform us about new approaches and products (eye drops, dietary supplements) for the management of DED. Santen devised a very effective educational game for use in roundtable meetings. It is called "What? Where? When? About Current Issues in Dry Eye." On video, dry eye specialists pose questions to be answered by groups of participants. This format generates interesting and enjoyable discussions on the pathology of OSD and DED.

In Tbilisi State Medical University, red eye syndrome is included in the curriculum to make students aware of DED and ocular surface pathology. However, the brief exposure to the topic is not adequate, as it is only a 10-day course. The students become primary care doctors and remember little of the teaching about ophthalmology. Further education is required.

Unmet needs for management of OSD and DED include early detection and treatment to avoid complications. Because family physicians are responsible for the initial evaluation and diagnosis of such patients, they need to receive education in this area. Patient education is also crucial. The DED questionnaire recommendation provided by the TFOS DEWS IITM report is very valuable. We have translated it and will distribute it to ophthalmologists for use with their patients.

Importantly, educational efforts in the care of OSD must reach the eye doctors in the rural, so-called border villages of the Russian-occupied areas, and high mountain areas, as it is difficult for doctors in those locations to go to the capital to attend workshops. Therefore, it is crucial to create and distribute written educational materials.

Although many kinds of eye drops for DED are available in Georgia, we do not have cyclosporine. This significantly inhibits the more complex treatment of DED. Because Georgia is a small country, pharmaceutical companies have had limited interest in establishing distribution of specialized medications there. Similarly, diagnostic technology for DED is not implemented in Georgia, and doctors manage the disease based only on clinical signs and patients' reported symptoms.

As an area of specialty, OSD is less attractive to ophthalmologists than cataract surgery, vitreoretinal surgery, and other surgeries. Advances in knowledge of OSD pathology and availability of modern diagnostic and treatment modalities will enhance interest in this specialty and lead to better care of patients affected by DED and other OSDs.

We would like to create a Georgian Ocular Surface Society to address the issues discussed in this presentation. A main focus of this society's work will be to implement the directives of TFOS, and we would greatly welcome the organization of a TFOS Conference in Georgia for Caucasus countries.

POLAND. Zbigniew Zagórski, Department of Ophthalmology, Lublin Medical University, Lublin, and Malgorzata Mrugacz, Department of Ophthalmology and Eye Rehabilitation, Medical University of Bialystok, Bialystok

During the Second World War, Poland lost 6 million of its citizens, including 3 million people of Jewish origin. Many of the victims were physicians. After the war, Poland did not regain its sovereignty, which was lost in 1939 under German and Soviet occupation. Until 1989, it was dependent on the Soviet Union and was governed by the communist party in an authoritarian system. This resulted in an inefficient economic system and underdevelopment of the health care system.

After regaining independence in 1989, a slow process of improving medical care began. It was a challenging process, because Polish specialists, including ophthalmologists, had had very limited contacts with colleagues in Western countries, and the financial means were insufficient to quickly modernize hospital equipment and train personnel. In 1992, only about 100 cataract phacoemulsifications were performed, the rest being either intra- or extracapsular, and the cataract surgery ratio in Poland was one of the lowest in Europe (1700 surgeries per million citizens in 1996).

Progress was facilitated through increasing cooperation with Western ophthalmologists in several university eye hospitals. One of those was the University Eye Hospital in Lublin, which I (ZZ) chaired from 1991 till 2006. I could take advantage of my contacts with German ophthalmologists, as I spent over two years in Erlangen as a Humboldt fellow. Also, as a member of the American Academy of

Ophthalmology, I was able to enlist the help of several AAO volunteers to introduce newer procedures to the country and to teach their colleagues in Poland at numerous courses and conferences.

In 1994 we organized the first cornea bank in Poland and performed the first limbal transplant. The number of keratoplasty procedures was steadily increasing, and soon other eye banks were opened in Warsaw and Katowice. Currently, about 1,000 keratoplasty procedures, including lamellar procedures, are performed each year in Poland, most in Katowice, Warsaw, and Lublin; however, there is a need for many more.

The diagnosis and treatment of OSD have been slowly introduced. One stimulus for this was the European Cornea Conference organized near Lublin in 1995, which was attended by leading specialists from all over Europe. In the same year, Jack Kanski's classic ophthalmology manual, *Clinical Ophthalmology*, was translated into Polish under my (ZZ) editorship. The first AM transplants were performed in Lublin in 1997, and in 2000 we organized an international conference on AM as a Regional Symposium of the International Ocular Surface Society.

Although more and more ophthalmologists in Poland in those years became aware of ocular surface problems, including DED, during that time, most cases were treated with antibiotics and steroids. The main challenges in Polish ophthalmology were still cataract, glaucoma, and vitreoretinal surgery. In some centers, like Katowice, Warsaw, and Lublin, interest in modern advances in managing OSD was increasing, and the procedures were improving. In 2008, the manual *Diseases of the Cornea, Sclera and Ocular Surface* was published in Polish. It was written by leading international and Polish experts and edited by Z. Zagórski, G. Naumann and P. Watson.

Successively, several foreign and Polish companies became engaged in supplying treatment modalities, equipment, and pharmaceuticals, at the same time organizing courses and educating physicians. One of the first, and most proactive, was Laboratoires Théa, which also arranged the Polish translation of the TFOS-MGD Workshop summary. Because the proper diagnosis of OSD and DED requires time which is not available in busy practices, we organized the first Dry Eye Clinic in Kraków in 2013. The clinic is equipped with an Oculus Keratograph 5M, Maskin MG probes, Blephex, MIBOflo, and intense pulsed light. Some of these methods are available in several other clinics in Poland. The increasing number of cataract and refractive surgeries provides a stimulus to seriously address ocular surface problems, as neglected dry eye is the main factor in patient dissatisfaction after even uncomplicated surgery.

Increasingly, Polish hospitals are conducting and publishing clinical and basic research studies, including multinational surveys of MGD seen in general ophthalmological practice involving over 6000 patients in nine countries, including Poland, Germany, and Spain.

Although there has been much progress in the management of OSD and DED in Poland in recent years, we recognize a number of unmet needs. We lack the newest medications for topical anti-inflammatory therapy. We have 25 centers that can perform keratoplasty, but only five of them do more than 100 procedures per year. DED treatments are generally not reimbursed by the insurance system. Scleral lenses are rarely available in Poland, and many severe OSDs are undertreated. Keratoprosthesis surgery is not accessible for most patients in Poland.

Because many patients suffer from neuropathic pain in the absence of clinical signs, ophthalmologists should be aware of the proper diagnosis and treatment of pain of corneal or central origin.

In addition to addressing the unmet needs mentioned above, pediatric and adolescent patients should be evaluated for DED, and patients with aqueous-deficient DED should be referred for blood analysis to test for Sjögren syndrome biomarkers. Educational efforts to enhance the knowledge of physicians and patients about OSD and DED should continue. Colleagues interested in the ocular surface should be encouraged to join and become active in TFOS.

REPUBLIC OF MOLDOVA. Valeriu Cușnir, Valeriu Cușnir Jr., Nina Bulat, Vitalie Cușnir and Vitalie Procopciuc, Department of Ophthalmology and Optometry, S Nicolae Testemițanu State University of Medicine and Pharmacy, Chișinău

The Republic of Moldova is a state in Eastern Europe with an area of approximately 33,000 km² and a population of about 3 million people. In the last 20 years, both the country's population and its birth rate have significantly decreased. As a result of the aging of the population and the low birth rates, the age distribution of the general population has changed. About 20% of the population is elderly.

Many people work in the fields. Recently, however, there has been rapid development of information technologies (IT), with the training of specialists (IT engineers, programmers, etc.). Large corporations in Europe and the USA often employ local inhabitants.

Moldova has an increasing incidence of OSDs, due variously to the increased use of electronic devices, the treatment of ocular pathologies (including glaucoma) with solutions containing preservatives, and the lack of screening methods for ocular surface pathologies. In our recent study of DED symptoms among Moldovan citizens, we found an increased prevalence even in young, working people. In fact, 70% of people who came to us to be evaluated reported DED symptoms, which we attributed to high employment in the IT industry, with consequent changes of lifestyle and long working periods on the computer.

Diseases of the eye and ocular adnexa represent about 4% of the total number of diseases among adults in Moldova. In the prevalence ranking of eye diseases that led to disability in adults in 2017, the highest rate was attributed to glaucoma (25.4%), followed by ocular trauma of the eyeball and degenerative myopia (17%). Cataract surgery accounted for about one-third of patients hospitalized due to ocular diseases, and more than 50% of the surgical interventions in ophthalmology are cataract surgeries. Even so, the number of cataract surgeries performed is far lower than that needed, with demand for about six times as many should be done. Unfortunately, the infrastructure and government financing are inadequate to allow more cataract surgeries to be performed. In addition to cataract, the prevalence of diabetes is also increasing with the aging population.

As eye diseases increase, there is an acute insufficiency of specialists. We have only 1 ophthalmologist, on average, per 10,000 inhabitants, although the distribution is not even. The capital city of Chişinău has 1 ophthalmologist per 6,500 people, and the rest of the country has 1 per 15,000 people. We currently have no optometrists or opticians, although an initial cohort of opticians are due to graduate in 2 years.

Although ocular surface pathologies represent a large portion of eye diseases in Moldova, with complaints of DED symptoms being one of the most common reasons that a patient presents to the ophthalmologist, DED signs are frequently under-appreciated and under-diagnosed by clinicians. Raising awareness about DED for both clinicians and patients is an important goal for the future. Morbidity analysis is necessary to determine the frequency and impact of the disease and the risk factors for the population.

We do not have a questionnaire that allows a quick and efficient assessment of the severity of DED symptoms. In our studies, for the subjective assessment of the severity of DED we have used the OSDI questionnaire, because it is shorter and less tedious than the others. A perceived disadvantage of this questionnaire is the focus on frequency of symptoms; often patients are uncertain or they forget this aspect of their history and will invent something in order to comply with the doctor's request. One of our challenges for the future is to establish a questionnaire with better reliability, validity, and specificity for all factors that would allow a rapid and efficient assessment of the severity of DED symptoms.

Diagnosing the pathology of DED requires increased time and attention from clinicians. In polyclinics, doctors see 50 patients per day. It is not a quality visit, and documentation is inadequate.

In our study, which included 444 individuals, in many cases we found a discrepancy between the intensity of symptoms and the presence of clinical signs. Of the 318 patients diagnosed with DED symptoms, 23% had tear secretion greater than 15 mm, while 30% exhibited lacrimal hyosecretion without DED symptoms. To address such lack of correlation between signs and symptoms, a more detailed diagnosis is needed—e.g., measurement of TBUT, staining with fluorescein, the Schirmer test.

These tests unfortunately cannot be performed in any ophthalmology office in our country. We have only one private clinic that specializes in DED. It cannot perform all the tests, and there are limits to the amount of work that can be done. Likewise, we do not have the tools necessary to determine other important factors in diagnosis, such as biomarkers of inflammation and apoptosis, or tear osmolarity.

Although multiple therapeutic approaches are currently known, in many cases, treatment of DED is a real challenge for Moldovan clinicians, at least in part due to the lack of some medications (for example, cyclosporine eye drops, other preservative-free eye drops, etc.), which are often critical. Tear substitutes, especially new-generation products, such as those that are more specific, more efficient, and without preservatives, are not covered by Moldova's mandatory insurance or by the only insurance company for medical aid. Usually, patients will buy only the cheapest tear substitute, and this is not the best one. In our experience, even when appropriate treatment is proposed to patients with DED, few take advantage of this, and even fewer return for further checkups unless signs and symptoms are severe. This highlights the low level of awareness about DED among the population of our country.

One category of patients with DED that we observe is that associated with anti-glaucoma treatment containing preservatives. These patients receive little explanation about why they have red eyes after instilling their drops, and they have no additional treatment prescriptions to treat their DED symptoms. One of our tasks for the future is to raise awareness of the effects of anti-glaucoma medications on DED to encourage better identification and treatment.

One way to address the rising threat of DED would be to implement screening programs aimed at professional groups that are at high risk of developing this disorder. This measure would require education, under standardized programs, of ophthalmologists and family doctors to allow them to identify and manage DED.

ROMANIA. Adriana Stanila and Dan Mircea Stanila, Ofta Total Clinic, Faculty of Medicine, University of Lucian Blaga, Ocular Surface Research Center, Sibiu

Romania has numerous unmet needs for the management of OSDs. We do not have a tissue bank, and we cannot perform AM or corneal transplantation. We lack ophthalmological skill, social and cultural education, and health education.

OSDs that lead to PED comprise more than 35 etiologies. Too often, they are not detected early, are ignored, or are treated incorrectly and sometimes harmfully. For example, one patient with DED instilled 13 different types of eye drops prescribed by several ophthalmologists within a 30-day period. Cases such as bilateral neurotrophic keratopathy with descemetocoele or a complex Mooren's ulcer that

has perforated may be referred to specialized centers too late. On the other hand, erroneous diagnoses, such as DED with severe epitheliopathy, may be treated with anterior corneal transplantation, having been confused with corneal dystrophy.

Most ophthalmology residents want to specialize in surgery, especially cataract, and their training in ocular surface pathology is insufficient. The ophthalmologist with inadequate training in OSD may inappropriately prescribe use of eye drops for use on the ocular surface which, in the presence of PEDs, can aggravate the symptoms.

The social and cultural education of patients in certain areas, especially in more peripheral, rural areas of the country, is limited due to the lack of schooling and limited access to information (radio, TV, telephone, computer). Often, good health is taken for granted, and patients presume that their ailments will heal on their own. They may delay going to the specialist until the disease is at an advanced stage.

In Romania, there are no national programs for the prevention and early detection of OSD. In the absence of a tissue bank, complications of PEDs with deep ulcers cannot be protectively treated except with an eye patch or therapeutic contact lens. Health education relating to ocular surface pathology needs to be publicized on all social networks. Multiple disorders of the ocular surface can degenerate into PED, which can lead to the functional and anatomic loss of the eye. Treatment of PEDs can fail due to lack of medical information and culture.

The unmet needs in management of PED must be addressed by the establishment of tissue and organ banks, training of residents in high-ranking university centers, introducing an ocular surface module to training programs, conducting symposia and roundtable discussions with family doctors presenting ocular surface pathology, and enhancing health education of the population through social networks.

RUSSIA. Vladimir Brzheskiy, Department of Ophthalmology, St. Petersburg State Pediatric Medical University, St. Petersburg, and Sergey Golubev, Department of Ophthalmology, National Pirogov Medical and Surgical Centre, Moscow

We estimate that the prevalence of DED in Russia is now 14-16% among the adult population, although as yet there is no official registry of this pathology. According to our data, DED can be detected in almost every second patient who makes an initial visit to an ophthalmologist, regardless of the purpose of the visit (for example, for the selection of glasses, for the measurement of intraocular pressure, or for cataract assessment). As in other European countries, the increased prevalence of corneal and conjunctival xerosis has been mainly attributed to the increased use of computers, damage to the ocular

surface by regular use of eye drops with preservatives, the wearing of contact lenses (including those made from the most modern material and modern design), as a side effect following keratorefractive surgery (LASIK, LASEK, and PRK).

The lack of timely diagnosis of DED in Russia relates to a lack of knowledge among outpatient doctors about the features of this pathology, as well as the lack of adequate diagnostic equipment and supplies, such as solutions (or diagnostic strips) of lissamine green (or rose Bengal), as well as fluorescein stain.

In Russia today, there are 45 registered artificial tear preparations that supplement the main layers of the tear film, including two lipid-containing supplements. Timely diagnosis of MGD is especially important, as it requires not only prescription of artificial tear preparations containing lipids, but also a combination of therapeutic measures aimed at correcting the deficiency of the lipid component of the tear film.

We have been actively involved in educational projects on DED in Russia and in the Union of Independent States countries for over 10 years. Despite this, many doctors and patients remain insufficiently aware of modern methods of diagnosing this disease, and this represents an important unmet need in the management of DED. Adequate treatment methods are also lacking: lacrimal punctal occlusion, immunosuppressive agents (such as cyclosporine and tacrolimus), as well as targeted anti-inflammatory and other therapies (such as secretagogues)

There is also a need in clinical practice for preservative-free eye drops, including non-preserved corticosteroid drops. Recognition that DED affects children as well as adults is important, as is the identification of appropriate drugs for successfully treating pediatric DED.

Highlights of the Panel Discussion: Central and Eastern Europe

Moderator. The high prevalence of corneal dystrophies in Bulgaria is interesting. Dr. Grupcheva, can you tell us more about this?

Christina Grupcheva. The high prevalence tends to be localized to families in rural areas. They are generally large families, sometimes with multiple wives and several generations. With each generation, the presentation of the phenotype tends to present earlier. There are children younger than 5 years already suffering from recurrent erosion syndrome. Unfortunately, we do not have sufficient funding to perform genetic analysis on all of them. It is definitely an autosomal dominant disease, and there are many siblings suffering from the same dystrophy. We would be very interested in collaborating with other groups to study these families.

Audience question. In Russia, are certain OSDs more prevalent in Siberia than in Western Russia?

Vladimir Brzheskiy. As the Russian Federation is a very big country, there are regional differences in types of DED. For example, in the South where the climate is dry, it tends to be more severe than, for example, in the North, in Siberia. In ocular diseases other than DED, there is no difference.

Moderator. Many radial keratotomy (RK) surgeries have been performed in Russia. Do you see an association between OSD, DED, and RK?

Vladimir Brzheskiy. OSD can be a life-long problem for RK patients. There is epithelial hyperplasia at the incision lines, affecting tear break-up time and causing discomfort.

Moderator. Dr. Grupcheva, you mentioned that in keratoconus the nerves are near the surface. Is that why it becomes symptomatic?

Christina Grupcheva. At the thinnest point, there is epithelial damage, which leads to epithelial ingrowth into the Bowman's membrane. At this thin and high point in keratoconus, the tear break-up time is fast, and staining can remain for as long as 2 hours. Patients complain of discomfort, and they cannot be fitted with contact lenses. Scleral lenses sometimes provide relief, but some patients require surgical intervention.

Moderator. Scleral lenses are not commonly available in opticians' shops in Europe, except in the UK.

Christina Grupcheva. In Bulgaria, scleral lenses are considered to be medical devices, which do not have to be registered. We can import them from the UK or Greece. The UK lenses provide more flexible options, including exchanging lenses, if necessary.

Moderator. Do keratoconus patients have high rates of allergy?

Christina Grupcheva. They have a very high rate of allergy and, also, of some genetic problems, such as Down syndrome. It is difficult to manage patients with cognitive or behavioral (such as autism) problems, as they are in often day-care programs that are not well equipped to participate in management regimens.

Moderator. Dr. Cuşnir, your data showed that 12.5% of eye problems are related to eyelid disorders and only 4% to corneal diseases. It seems 12.5% is very high. Can you comment on this? What are the more prevalent eyelid disorders?

Valeriu Cuşnir. Blepharitis is one. When it is severe, we hospitalize the patient, as there is a high rate of complications.

Moderator. Is dry eye common after cataract surgery?

Valeriu Cuşnir. The level of complaints depends on how the clinician communicates with the patient. If the patient is reassured that dry eye for 2-3 months after surgery is normal, the patient is less likely to seek treatment.

Audience question. Dr Karanadze, could you comment further about some of the most prevalent OSDs in Georgia?

Nino Karanadze. In Georgia, one of the OSDs we see is corneal dystrophy. Since 2008, we have performed corneal transplants with corneas that we get from the United States. We have an AM transplantation bank and are now creating an eye bank. We commonly see DED and allergic conjunctivitis in children. When antibiotics are indicated, Phage therapy, which uses lytic bacteriophages, may be an alternative to traditional antibiotic therapy. There is great interest in Phage therapy in Georgia. We have the Phage Therapy Institute, which is one of the best in the world. In Russia, Georgia, and other post-Soviet countries, Phage therapy is used in clinical practice. We have had good results, but more needs to be learned about how it works.

Moderator. Doctor Zagórski, your study showed a very high prevalence of OSD, about 60%.

Zbigniew Zagoórski. That is because our patient group was comprised of patients visiting an ophthalmologist, not the general population. On another topic, as a cataract surgeon, I would like to share a useful observation mentioned at a recent meeting. It was noted that the origins of neuropathic pain following cataract surgery can be local or central. To help distinguish between them, we can instill anesthetic. If the pain disappears, it is local and can be treated with nerve growth factor or platelet-rich autologous plasma. If the origin is central, the patient is referred to the pain clinic.

Northern Europe

FINLAND. Niko Setälä, Department of Ophthalmology, Central Finland Central Hospital, Jyväskylä

Finland is situated in the Northeastern corner of Europe. It is about the size of Germany, and it has a population of 5.5 million people, most of whom live in the west and south of Finland.

Finland has a cold and very dry winter, lasting 6-9 months. Heating in home and office settings significantly enhances the environmental stress to the ocular surface. The short summers with endless daylight give rise to abundant flowering of nature, producing a short and intense allergy season. The frequent use of saunas with temperatures up to 100 degrees Celsius and the sauna's dry air (not damp, as many believe) present a huge stress to the ocular surface. Because of rapid migration to urban areas in the 1960s and 1970s, housing was built quickly and poorly, and indoor air quality is poor, especially with regard to dampness and mold. Finland has the world's highest percentage of aging people, which is accompanied by increases in eye disorders. All of these factors contribute to a high prevalence of OSD in Finland.

Health care in Finland consists of a highly decentralized three-level publicly funded health care system and a smaller private sector. The municipalities (local governments) are responsible for providing health care to their residents. Finland is divided into 20 different health care districts. Each hospital has community-paid doctors, but the hospitals are understaffed, as most of the doctors prefer to work in the private sector. In some areas, a patient must travel several hundred kilometers to see an ophthalmologist. Finland has 480 ophthalmologists and 120 ophthalmology residents. There are 1800 opticians, who 2 years ago renamed themselves "optometrists." Their role has been controversial in terms of the tests and procedures they are perceived to be qualified to perform.

Patients may turn first to the internet to seek information about their DED symptoms, and there they may find misinformation and, worse, bogus remedies. They may then consult the pharmacist for help. Unfortunately, pharmacists are not able to provide good advice about which eye drop to use and how to use it. Even if they are well informed about products, they do not know the specific cause of the patient's problem.

When the patient sees an ophthalmologist, it is for a 15-minute appointment, which is inadequate for a thorough examination. Moreover, most ophthalmologists lack the tools to perform the procedures needed to specifically diagnose DED.

None of the clinics is specialized solely in OSDs, and, therefore, the introduction of the latest technologies is delayed. The expense of private sector medical care and limited reimbursement restricts

the use of services and medication, especially novel anti-inflammatory therapies. There is a need to develop simple algorithms or methods to determine which subgroups of patients respond best to the various medications.

Finnish ophthalmologists have a good awareness of OSDs, and a Nordic guideline for DED is available. Yet, there are perceived pitfalls in the diagnostic tests used as the gold standard today, and a more standardized approach is needed. The discordance between signs and symptoms complicates optimal diagnosis and treatment. Also, both professionals and patients often forget about the chronic nature of OSD. Too often, the patient expects a medication to “cure” their OSD within a given time-frame and returns to the ophthalmologist later, complaining that the condition has recurred.

Finland’s Helsinki Eye Lab was established by the late Professor Juha Holopainen, who unfortunately passed away 3 years ago. A group of researchers and PhD students are continuing his investigative work on dry eye. Our group has two main investigative arms to explore the pathogenesis of DED. We use bioinformatics, whereby with supercomputers we can observe molecule-by-molecule the behavior of tear lipid layer components. Our second focus is to use the Langmuir film balance to elucidate diesters and fatty acids and their contribution to the restriction of tear evaporation.

ICELAND. Gunnar Már Zoega, Sjónlag Eye Center and Department of Ophthalmology, Landspítali, Reykjavik

Iceland is an island in the north Atlantic, almost the size (103.000 km²) of England but with a population of just 360,000. The climate is more temperate than might be expected given its subarctic latitude, thanks to the Gulf Stream. The occasional volcanic eruption causes challenges with volcanic ash and air pollution.

Most of the population lives in urban areas on the southwest part of the island. The remainder are scattered around the coastal areas in small towns and communities. More than two million tourists from all over the world visit Iceland each year, making otherwise unusual medical problems more prevalent, for example, antibiotic-resistant bacterial keratitis or fungal infections.

The Icelandic health care system is state-funded with some co-payment by the user. The official goal of the system is to provide the best possible health care to all inhabitants. The small island population creates challenges for health care providers, especially with regard to low-prevalence diseases, and access to specialized health care is more limited for those living in the rural areas. There are 39 ophthalmologists practicing in Iceland. There is one university hospital clinic at which nearly all of the subspecialties in ophthalmology are represented, and where research and teaching are conducted in addition to patient care.

With regard to ocular surface health in Iceland, DED certainly is a significant challenge, both with regard to aqueous deficient dry eye and MGD, which is very common. Most of the treatment options laid out in the TFOS DEWS IITM report are available, although the patient has to pay out-of-pocket for some of them. Another challenge is the lack of, or difficulty in getting, various eye drops or ointments. This is due to the small market in Iceland and applies to both over-the-counter eye drops and prescription ophthalmic medicines. Also, there can be challenges in providing information on available diagnostic and treatment options to health care providers as well as to the general public, especially in the rural areas.

Corneal infections are predominantly bacterial, secondary to contact lens use, although the occasional Acanthamoeba infection is seen. Fungal infections are extremely rare and present almost exclusively in people travelling from warmer climates.

A good and longstanding collaboration with Miracles in Sight, North Carolina, USA, makes corneal transplantation possible. About 20-30 corneal transplantations are performed every year, including Descemet membrane endothelial keratoplasty, Descemet stripping automated endothelial keratoplasty, and penetrating keratoplasty. Fuchs' endothelial dystrophy is the most common indication for endothelial keratoplasty and macular corneal dystrophy for penetrating keratoplasty.

The small number of inhabitants and the large size of Iceland present the biggest challenge in the management of OSDs. There are opportunities to further the education of physicians, including ophthalmologist, optometrist and nurses in the field of DED. Collaboration with major university hospitals, in Europe and the USA, for management of rare cases has been successful and must be continued. Another important challenge is the limited access to specialized health care for those living far away from the capital, where most of the services are located.

NORWAY. Tor Paaske Utheim, Norwegian Dry Eye Clinic, Institute of Eye Health & University of Oslo, Oslo

Norway has a population of about 5 million. It has almost 500 ophthalmologists and about 1500 opticians.

Most of the eye research in Norway over the past 50 years has been focused on the cornea. In 1971, Norwegian scientists Davanger and Evensen identified cells in the periphery of the cornea, which were later termed limbal stem cells. This opened up a whole new field of research and, later, treatment. In 1997, Pellegrini and her Italian collaborators demonstrated for the first time the ability to use cultured cells to treat LSCD, a painful disease that can result in decreased vision or blindness.¹⁵ The disease can be caused by infections, autoimmune diseases, chemical burns, and UV radiation.

Severe LSCD in Norway is rare, but mild forms are more frequently encountered. Treatment available today for severe forms is limited to ex vivo expansion of epithelial cells, a procedure that was first performed in the Nordic region (Oslo) in 2007 using limbal cells. Several years later, oral mucosal cells were used to enable treatment of bilateral LSCD without the need for immunosuppression.¹⁶ Only minimal biopsies (1-9 mm²) are required for these transplantations. The challenge, however, with both these methods is the complexity of the procedure, which relies on access to a laboratory for cell culture. This involves high costs and regulatory challenges.

One solution to these challenges is centralization of the culture units and use of storage and transportation technology developed over the past 12 years. Another alternative is to take advantage of a new simplified technique termed *simple limbal epithelial transplantation* (SLET), first presented by Sangwan and his colleagues in India in 2012. Advantages of SLET include direct transfer to the injured eye of a minimal amount of tissue harvested from the healthy eye, which precludes the need for laboratory-cultured cells. This means that harvest and transplantation can be done within a single operation. Success so far using SLET is comparable to that of ex vivo expansion of limbal epithelial cells with 276 of 339 (81.4%) of operations resulting in restoration of the corneal epithelium and improvement in visual acuity in 228 of 314 (72.6%) cases reported.¹⁷

To my knowledge, SLET has never been performed in Norway. Intriguingly, SLET can be further developed for treatment of both unilateral and bilateral LSCD by replacing limbal cells with an alternative autologous cell source. Simple oral mucosal epithelial transplantation may prove to be a viable approach in the future, although no clinical reports have been presented so far. As epidermal cells have also proven highly effective in treating LSCD in animal models and the epidermis (skin) provides an almost unlimited source of these cells, a technique that may come to be called *simple epidermal epithelial transplantation* may also be developed in the future.

Since Henrik Sjögren in Sweden defended his thesis on keratoconjunctivitis sicca in 1933, most Norwegians have, to my understanding, considered DED (first formally defined in 1995) as primarily a result of inadequate production of aqueous tears. Unfortunately, the negative effect of increased evaporation and the contribution of inflammation have been largely ignored. Data from the Norwegian Dry Eye Clinic based on thousands of consultations demonstrate that about 90% of our patients suffer from MGD. However, the majority of the patients who were treated for DED prior to their first consultation at the Norwegian Dry Eye Clinic had only been given aqueous-based tear substitutes. Very few had received or even heard of the possibility of eyelid cleaning and/or warming, and even fewer had been presented with the opportunity for treatment with anti-inflammatory medication.

Although Norway is an affluent country with a well-developed health care system, diagnosis and treatment of DED has until recently received little attention. With an increasingly broad range of

treatment options and improved documentation of their effectiveness, I believe that the main challenge in the ocular surface field in Norway today is to increase ophthalmologists' awareness of how DED can be diagnosed and treated. The risk of entering a vicious cycle of recurring disease is under-appreciated, and the need to treat DED should be considered urgent. The correct course of treatment is of crucial importance.

In 2012, the first private clinic devoted to research on DED was established in Norway, and in 2018 the first discussions took place regarding the merging of resources from public and private institutions in Norway to form a health innovation consortium on DED. A dry eye consortium in Norway is thought to be a good platform to apply for external funding and contribute to the body of knowledge. Moreover, it is likely to substantially increase the awareness of DED. Research, innovation and education will be the main activities in the planned Norwegian consortium.

In summary, for cases of unilateral LSCD, SLET should be considered and further developed. For cases of bilateral LSCD, cultured non-limbal cells using storage technology is a good option. However, in the future, we may see cultured oral mucosal epithelial cell transplantation and cultured epidermal cell transplantation used more and more.

Regarding DED, there is a need for more attention, information, and education in this area. There is also a need for more collaboration between opticians, optometrists, general practitioners, and ophthalmologists in Norway.

SWEDEN. Fredrik Källmark, Källmark Dry Eye Clinics, Stockholm

In Sweden there are currently fewer than 600 active ophthalmologists caring for about 10 million people. The level of recruitment of new ophthalmologists is low and with the expected retirement rate of practicing ophthalmologists, it will become increasingly difficult to meet the needs in all areas of eye care, but especially in the area of OSD.

Ophthalmic interest has been strongly weighted toward the posterior segment, including glaucoma, age-related macular degeneration (AMD), and diabetic retinopathy. Even in these areas, the lack of resources in terms of money and staff make waiting time for examination or treatment unacceptable, sometimes up to one or two years after first diagnosis. Given such limitations in care for even the high-interest entities, it is clear that the treatment of diseases of the anterior segment receives very little attention. Routinely, the typical treatment for OSD is antibiotics, whether needed or not. The tight time schedule in a typical eye clinic allows no room for an in-depth medical history or examination, and follow-up is rare or never.

Making the situation even worse for DED patients is the fact that dry eye conditions are not regarded as a disease, and the subject of dry eye is taught at medical schools only briefly and in the context of Sjögren syndrome. Although Sjögren syndrome has an International Statistical Classification of Diseases and Related Health Problems (ICD)-10 code, which is mandatory for reimbursement, DED per se has no code. Limited ICD-10 codes, e.g., H04.121-129 or 375.15, exist internationally but are not used in Sweden. No statistics are available on the number of people suffering from DED or the resulting sick leave it causes, so DED does not exist in the view of the public health authority and NHS. Tools for diagnosis are limited to the Schirmer test and, other than antibiotics, virtually no treatments are provided. Long waiting times and higher priorities often force ophthalmologists to refer patients to general practitioners, who, of course, know even less about DED and thus tell the patient that nothing can be done to help.

I currently run the only two DED clinics in Sweden, and we see approximately 7000 patients per year. We maintain a holistic view of patient care. We have our own laboratory, and we also have close collaboration with our ophthalmic subspecialists, for example, eyelid surgeons, and also with dermatologists, rheumatologists, and dentists. Recognizing that inflammation can contribute to DED, we address it as a systemic process affecting not only the eye. We also have a psychologist who provides an additional dimension of care. Many more DED clinics are needed.

A number of approaches should be taken to meet the challenges and unmet needs for the treatment of OSDs in Sweden. DED must be formally recognized as a medical condition. We must inspire more medical students to choose ophthalmology as a specialty, not only to replace retiring ophthalmologists but to increase the number in practice. We need greater collaboration with optometrists. In Sweden today, optometrists are well educated and qualified to screen for glaucoma, diabetes, and AMD, and to diagnose and treat ocular surface pathologies, including allergy, conjunctivitis and blepharitis. To relieve the burden on ophthalmologists, optometrists must be allowed to be primary health care providers, as they are, for instance, in the United Kingdom.

We should make specialized diagnostic methodology more widely available to better evaluate MMP-9 levels, osmolarity, tear volume, lipid layer thickness, meibography, lid wiper epitheliopathy, etc. Likewise, a variety of treatment options should be available to appropriately treat specifically diagnosed conditions.

Furthermore, a supplemented and broader education in DED must be introduced to resident and intern physicians, optometrists and nurses, all of whom interact with patients on a daily basis. Such education should be provided to other groups of physicians as well, e.g., dermatologists, gynecologists, rheumatologists, and dentists, in order to establish interprofessional and interdisciplinary collaboration to benefit the patient.

Interprofessional education is a necessary investment to meet the need for multifaceted care. With a changing health care panorama and an aging population, future health care will become increasingly integrated with other activities both within the municipality and in the local community. This places increasing demands on the co-operative capacity and interprofessional skills of health care professionals.

Highlights of the Panel Discussion: Northern Europe

Moderator. Dr. Källmark, how do you evaluate patients with Sjögren syndrome?

Fredrik Källmark. Rose Bengal, TBUT, and the Schirmer test can be used in the diagnosis of Sjögren syndrome, but we don't use rose Bengal in our clinic. Most of the patients who come to us with a diagnosis of Sjögren syndrome do not actually have it. They have been diagnosed only by the Schirmer test and have not been to the rheumatologist or the dentist, and they have not had blood tests.

Moderator. Usually with a Sjögren syndrome patient, the rheumatologist refers the patient to the ophthalmologist and requests a Schirmer test. I do the Schirmer test, but I also evaluate the ocular surface and send a report to the rheumatologist. Diagnosis of Sjögren syndrome needs to be a collaborative effort of both specialists.

Moderator. Dr. Utheim, can you comment on induced pluripotent stem cells in the treatment of bilateral LSCD?

Tor Paaske Utheim. There are nine different cell sources of cells for transplant. Interestingly, most of these cell sources work equally well, so we should choose the one that is most easily available and most extensively documented. This narrows it down to three non-limbal cell sources: conjunctival, oral, and epidermal. Induced pluripotent stem cells may give rise to tumors, and it's also a very complicated technology.

Audience question. Some of our patients want to go to a foreign country for treatment of LSCD. Can we send them to Norway?

Tor Paaske Utheim. In Norway we have some experience, about 20 operations, but the Italian group, led by Graziella Pellegrini and Paolo Rama, and also Virender Sangwan in India, have much more experience. I would recommend SLET as the procedure of choice rather than ex vivo expansion of limbal epithelial cells, although I do not do SLET myself.

Moderator. Dr. Källmark mentioned establishing clinics to provide a multidisciplinary approach to doing more prevalence studies on DED. What about expanding the approach to patients? In Brazil, we have a DED association just for patients, which is focused on providing information for the population in a very simple way, but also providing access to expensive medications and psychological support to poor people

with DED. Do other countries have this kind of approach? I think it is very helpful for the patient to feel supported and also for the doctors to feel they are doing something good for patients, especially those with severe DED that badly affects their quality of life.

Fredrik Källmark. We don't have a DED organization for patients in Sweden, but I agree that it is an excellent idea. Patients have told me they thought they were the only one suffering from DED, and they are reassured to learn that their problem is shared by over a million people in Sweden. Organizations to provide information and services for patients with DED are very important.

Moderator. TFOS is active in increasing public awareness by providing the helpful summary for patients.

Moderator. I think that establishing organizations for patients is something TFOS should encourage and support. Involving psychologists in such centers is a very good idea.

Audience comment. I completely agree. Our center has a nutritionist as well as a psychologist. They are valuable members of the management team.

Synopsis

Summary of Country Differences in Eyecare Professionals, Scope of Practice and Access to

Treatment. James S. Wolffsohn, Ophthalmic Research Group, Aston University, Birmingham, United Kingdom

Delivery of eye care in Europe is affected by a number of demographic factors, including sex and age distribution of the population, population density, socioeconomic conditions, willingness and ability to access health (including coverage of health care costs). Similarly, many factors affect the ability of practitioners to diagnose and manage OSD. As shown in Table 2, the number of ophthalmologists per population varies from country to country; in general, eye care is less available in rural areas than in cities. A small number of ophthalmologists specialize in anterior eye disease, and, of those, most are more interested in surgery (cataract, refractive procedures) than in OSD. Proper diagnosis of OSD, MGD, and DED are hampered not only by the limited knowledge and interest, and the high workload of most practitioners, but by the lack of diagnostic tools and methodology. A patient may have to wait months or years to see an ophthalmologist, and then the visit may be very brief (15 minutes). The resulting diagnoses end up non-specific with regard to cause, and, even if the cause is determined, appropriate medications may be unavailable.

Few hospitals and clinics have specialized OSD units, and DED is not generally recognized as a disease entity. Many facilities are inadequately financed, and the low drug prices set by governments may provide little incentive for manufacturers to supply drugs. Table 2 summarizes some of the factors affecting eye care delivery in European countries.

The main unmet need for eye care across Europe relates to the high demand for care, with the roles and utilization of allied health professionals varying between countries. Since OSD, and specifically DED, is generally considered to be a chronic condition, its management is not well covered by public health care services, but most patients feel they should not have to pay privately. Epidemiologic data on eye diseases are lacking, making it impossible to assess actual prevalence, characteristics, and outcomes of DED. More information is needed on the apparent rise in DED in young people and the consequences of unmanaged OSD associated with eye surgery – how it should best be managed. There is a perceived need for multi-center, placebo-controlled randomized clinical trials, and the development of biomarkers, such as for predicting GHVD. Better education of practitioners and patients is essential. In Southern Europe, allergic eye disease and pterygia are significant problems. Migration and travel are leading to more frequent presentations of different manifestations of OSD. There is a lack of eye banks, resulting in the need for some countries to import tissues from other countries. Financial limitations have also made service delivery more challenging. In central and Eastern Europe, there has been a loss of population and expertise. This, combined with a lack of equipment, causes delays in timely diagnosis. Additional unmet needs relate to eye trauma and corneal dystrophies, including keratoconus. In Northern Europe, DED is generally not recognized as a medical condition, and adequate statistics are lacking. There is generally low interest in OSD, despite the environmental triggers such as saunas, cold dry air, and poor inside air quality. Social media information can often be misleading and pharmacies often offer suboptimal recommendations for management without an appropriate patient work-up.

INSTRUCTION TO COMPOSITOR: Please widen columns and set table horizontally on pageTable 2: Eye Care Availability by Country¹⁸

Country	Population	Ophthalmologists		Optometrists / Opticians			Patient Advocacy Groups	Other
		Number	Percentage specializing in ocular surface disease management	Number	Percentage specializing in ocular surface disease management	Diagnostics & Therapeutics Rights		
AUSTRIA	8.8m	1,103	10%	45/1,105	CL fitting only	No diagnostics and therapeutic prescribing rights	Sjögren group started 2019	
BELGIUM	11.3m	1,100		400/3,500		No		
BOSNIA and HERZEGOVINA	3.8m	212	28%	None				No corneal bank, antivirals, anti-fungals, cyclosporine
BULGARIA	7.2m	862	35%	150/2,200		No		
CYPRUS	1.2m	82		45/252		No		
DENMARK	5.6m	450		1,800/200		No		
FINLAND	5.5m	480		1,483/0		No		Specialized nurses can prescribe antibiotics
FRANCE	64.4m	5,927	<10%	3,000/34,370		No	Association Française du Gougerot Sjögren	No well tolerated cyclosporine

GEORGIA	4.0m	585	30%	None/ <i>None</i>			None	No Cyclosporin e
GERMANY	83m	9,000		/12,000				
GREECE	11.0m	2,237		2,000/ <i>1,000</i>		No		
IRELAND	4.8m	200	10%	700/150		Some	None	
ICELAND	0.3m	39						
ITALY	59.8m	7,000	5%	2,500/16,00 <i>0</i>	0.5%	No		
NETHERLANDS	16.9m	637	10%	1,186/ <i>4,180</i>		Diagnostics	National Society of Sjogren patients	-
NORWAY	5.2m	440	25	1,500/ <i>None</i>	30	Diagnostics		
POLAND	38.6m	4,565	All	1,700/ <i>5,000</i>		No	None	
PORTUGAL	10.4m	1,100	3%	1,700/2,500	2%	No		
REPUBLIC MOLDOVA	4.1m	250	2%	None currently				No soft steroids or antivirals
ROMANIA	19.5m	1,200		1,000/400		Diagnostics practiced		
RUSSIA	143.5m	13,700		3,800/-		Diagnostics		
SPAIN	46.4m	4,000	5%	8,000/-		No	Asociació n Española de Síndrome de Sjögren Asociació n	
SWEDEN	9.8m	600		2,000/ <i>None</i>		Diagnostics		
SWITZERLAND	8.3m	830	2%	1,000/2,700				
TURKEY	78.7m	4,000	3%	-//4,200		No	None	No lissamine
UNITED	64.7m	1,500	10%	15,034/		Some	British Sjögren	

KINGDOM				6,612			syndrome associatio n	
VATICAN CITY	0.0008m	5	40%	None			None	

Table based on ECCO Blue Book 2017¹⁹ and IAPB Vision Atlas (May, 2019 [atlas.iapb.org]). None of Europe has access to diquafosol and mucosta (rebamipide), and Lifitegrast is apparently available only in Georgia (despite a lack of diagnostic tests/instruments)

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Legends:

Figure 1. Participants in the TFOS European Ambassador Meeting: Unmet Needs & Future Scientific & Clinical Solutions for OSDs, Rome, Italy, September 21, 2019.

Figure 2. Through August 2019 over 500 TFOSTM II presentations have been delivered across 6 continents by TFOS DEWS IITM authors and TFOS Ambassadors, at major conferences, via virtual lectures, and at local clinical meetings.

Figure 3: Prevalence of dry eye stratified by age and sex (women pink, men blue) in the Netherlands (Lifelines cohort study, n=79,866). (a) dry eye as defined by the Women's Health Study (WHS) questionnaire (either a clinical diagnosis of dry eye and/or symptoms of both dryness and irritation of the eyes 'often' or 'constantly' (b) diagnosis of dry eye by a clinician; (c) symptomatic dry eye (defined as 'often' or 'constantly' symptoms of dryness of the eyes); (d) current use of ocular lubricants for dry eye. Error bars indicate 95% confidence interval.

Figure 4: Odds ratios of comorbidities and traits independently associated with dry eye (Lifelines cohort study in the Netherlands, n=79,866). All 48 comorbidities/traits in figures above were independently associated with dry eye in a stepwise multivariable logistic regression analysis, starting with 120 comorbidities/traits and age, sex and BMI. 95% confidence intervals of odds ratios are depicted by the lines. OHT = ocular hypertension; RSI = repetitive strain injury; SLE = systemic lupus erythematosus.

Figure 5. Most common symptoms reported by patients to Italian ophthalmologists. Data were obtained through the use of a dry eye disease questionnaire, and originally reported in an article by Stefano Barabino in the June 2018 issue of the *Italian Review of Ophthalmology*.

Figure 6. Diagnostic tests used by Italian ophthalmologists for the diagnosis of dry eye disease. Data were obtained with a dry eye disease questionnaire, and originally reported in an article by Stefano Barabino in the June 2018 issue of the *Italian Review of Ophthalmology*.

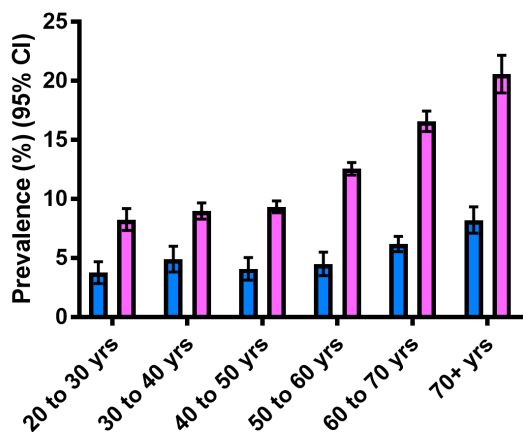


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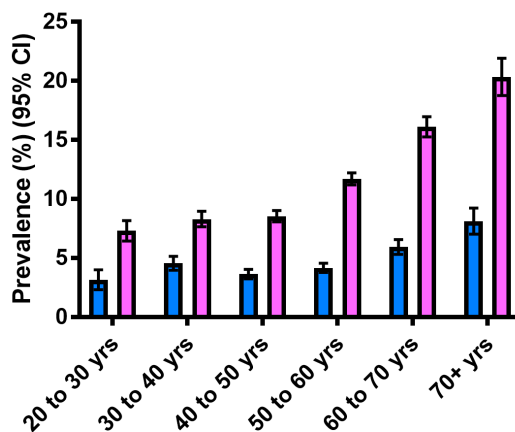


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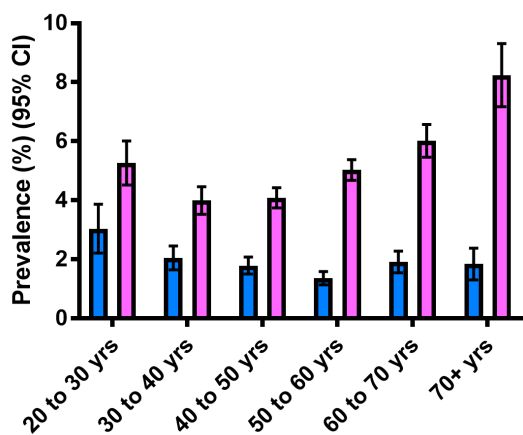
a. Dry eye (WHS definition)



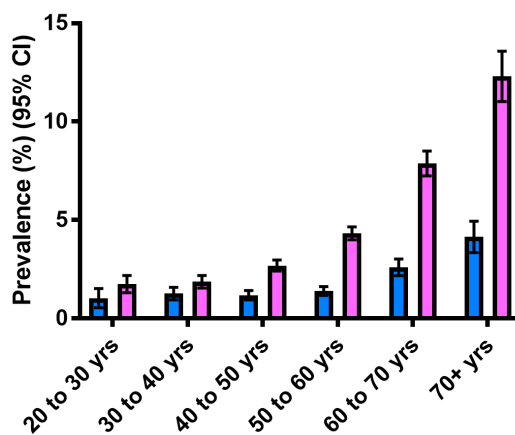
b. Diagnosis of dry eye by a clinician



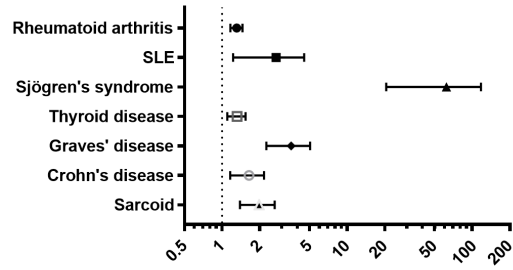
c. At least 'often' symptoms of dryness of the eyes



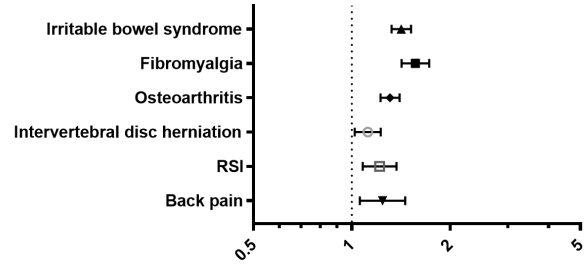
d. Current use of ocular lubricants



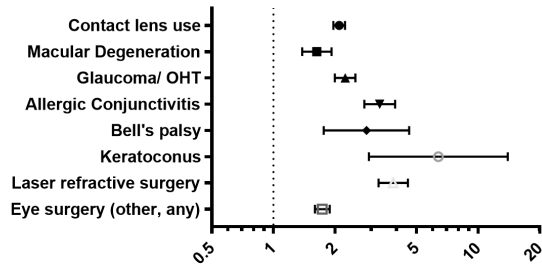
Autoimmune disorders



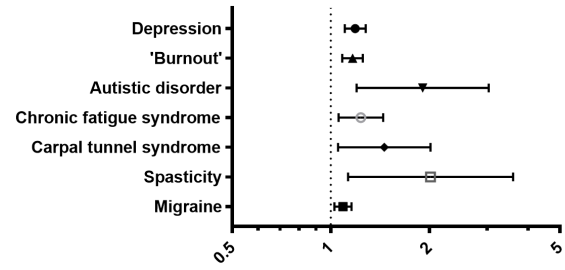
Pain disorders



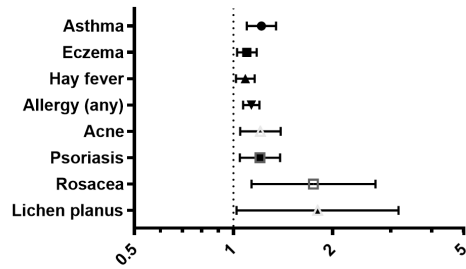
Ophthalmic disorders and traits



Psychiatric and neurological disorders



Atopic and dermatological disorders



Various disorders

