Ophthalmol Ther (2025) 14:2801–2818
https://doi.org/10.1007/s40123-025-01234-8

ORIGINAL RESEARCH

Chronic Ocular Surface Pain: An Optometrist and Ophthalmologist Survey

Anat Galor · Kaleb Abbott · Bonnie Henderson · Steve Pflugfelder · Darrell White · Preeya Gupta · Laura Periman · James A. Stefater · Tomasz P. Stryjewski · Cristos Ifantides · Paul Karpecki

Received: May 27, 2025 / Accepted: August 12, 2025 / Published online: September 5, 2025

ABSTRACT

Introduction: Chronic ocular surface pain (COSP) is defined as ocular pain that is perceived to originate from the ocular surface and persists for more than 3 months. Clear epidemiological data on COSP prevalence are lacking.

Methods: In 2025, a total of 100 eye care providers were surveyed, including 50 optometrists and 50 ophthalmologists. The survey aimed to assess the percentage of their weekly patient volume diagnosed with COSP, the diagnostic methods used, contributing etiologies, and current management strategies. Additionally, practitioners identified key indicators of successful treatment and attributes they believed would have the greatest impact on patient outcomes. Lastly, they rated their satisfaction with current therapeutic options.

Results: An estimated 33% of optometrists' patients and 29% of ophthalmologists' patients had COSP. Of those diagnosed with dry eye disease (DED), 63% also had COSP. Providers managed COSP with over-the-counter (OTC) artificial tears (97% of respondents), OTC gels and ointments (90%), hot compresses (86%), and prescription therapies indicated for DED (30–88%), while a minority routinely used amniotic

Anat Galor, Kaleb Abbott are co-first authors.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40123-025-01234-8.

A. Galor
Bascom Palmer Eye Institute, Miami, FL, USA

K. Abbott · C. Ifantides (✉)
Department of Ophthalmology, University of Colorado Health Sue Anschutz-Rodgers Eye Center, Aurora, CO, USA
e-mail: CristosMD@gmail.com

B. Henderson
Tufts University School of Medicine, Boston, MA, USA

S. Pflugfelder
Department of Ophthalmology, Baylor College of Medicine, Houston, TX, USA

D. White
Skyvision Centers, Westlake, OH, USA

P. Gupta
Triangle Eye Consultants, Durham, NC, USA

L. Periman
Periman Eye Institute, Seattle, WA, USA

J. A. Stefater
Ophthalmic Consultants of Boston, Boston, MA, USA

T. P. Stryjewski
Tallman Eye Associates, Andover, MA, USA

C. Ifantides
Tyson Eye, Cape Coral, FL, USA

P. Karpecki
Kentucky Eye Institute, Lexington, KY, USA

membranes (37%), serum tears (26%), intense pulsed light (18%), and LipiFlow (16%). The proportions of providers who were satisfied or very satisfied with these therapies were as follows: 64% for amniotic membranes and serum tears, 63% for device-based therapies, 40% for prescription medications, and 21% for OTC drops, ointments, and hot compresses.

Conclusions: This survey provides initial insight into the prevalence of COSP among patients in US eye care clinics, along with perspectives on managing this condition from both optometrists and ophthalmologists. The most common therapeutic strategies for COSP (OTC artificial tears, gels, and ointments) were associated with the lowest levels of provider satisfaction. COSP and dry eye disease are distinct but closely linked conditions. These results demonstrate an unmet need for new treatment options to address COSP.

PLAIN LANGUAGE SUMMARY

Chronic ocular surface pain (COSP) refers to eye pain that starts at the surface of the eye and lasts for more than 3 months. Currently, there is a lack of clear data on how common this condition is. To better understand COSP, we surveyed 50 optometrists and 50 ophthalmologists in the United States in 2025. The responders estimated that about one-third of their patients had COSP. Among patients with dry eye disease, nearly two-thirds also experienced COSP. The survey explored how providers diagnose and treat COSP, and what factors they believe lead to better outcomes. Most commonly, COSP was managed using over-the-counter (OTC) artificial tears, gels and ointments, and hot compresses along with prescription treatments for dry eye. More advanced therapies like amniotic membranes, serum tears, and devices such as intense pulsed light and LipiFlow were also listed as options. Despite the widespread use of OTC treatments and prescription dry eye treatments for COSP, providers reported the lowest satisfaction with these options. Overall, this survey sheds light on how common COSP is, the need for it to be a disease distinguished from DED despite having similar symptoms, and the importance of properly diagnosing COSP. The findings reveal a gap between frequently used options for managing COSP and provider satisfaction, pointing to a strong need for better therapies to manage chronic ocular surface pain.

Keywords: Chronic ocular surface pain; Cornea; Dry eye disease; Ocular pain; Ocular surface disease; Sensitization; Neuropathic ocular pain; Neuropathic corneal pain

Key Summary Points

Why carry out this study?

Chronic ocular surface Pain (COSP) was first defined in 2022 as pain perceived as originating from the ocular surface that persists for more than 3 months. However, the prevalence of this disease state remains unknown.

COSP and dry eye disease (DED) are distinct conditions but closely linked. Common prescription and over-the-counter treatments for DED have been unsuccessfully used for COSP, demonstrating an unmet need for treatments with fast onset and durable relief.

This real-world survey study of 100 eye care providers set out to understand how often optometrists and ophthalmologists encounter patients with COSP.

What was learned from the study?

One-third of their patients had COSP. Among patients with dry eye disease, nearly two-thirds also experienced COSP.

Despite the widespread use of OTC treatments and prescription dry eye treatments for COSP, providers reported the lowest satisfaction with these options.

These data reveal that COSP is common, yet a gap exists between frequently used options for managing COSP and provider satisfaction, pointing to a strong need for better therapies to manage chronic ocular surface pain.

INTRODUCTION

Ocular surface pain is a common reason for patient visits to ophthalmologists (MDs) and optometrists (ODs) [1]. A large-scale study using data from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey, spanning from 2008 to 2019, found that eye pain was the most frequent reason patients sought care from ophthalmologists and emergency departments (ED) [2]. Namely, eye pain was the primary reason for 42.0% of outpatient visits and 66.9% of ED visits for eye problems. While the primary diagnoses were non-vision-threatening (78.5% and 69.9% for outpatient and ED visits, respectively), the vast majority of patients in both settings required a follow-up visit (89.4%), highlighting the burden that eye pain puts on the health care system. In the United States, more than 5 million visits to MDs and ODs occur annually due to ocular pain, with the majority taking place in outpatient settings.

For appropriate management of ocular surface pain, it is important to distinguish between acute and chronic pain, although they exist as part of a continuum [3]. Acute pain is a physiological response to tissue damage, usually as a result of trauma, surgery, or infection, that resolves with treatment or time [4, 5]. This type of pain is nociceptive in origin, as it arises from damage (or threatened damage) to tissues and cells of the ocular surface in response to stimuli that activate nociceptors [6, 7]. Chronic ocular surface pain (COSP) is defined as ocular pain that is perceived to originate from the ocular surface and persists for more than 3 months, interfering with daily activities of life such as reading, driving, and sleeping, often leading to poor quality of life (QoL) [3, 7, 8]. The ocular dysesthesia in COSP may arise from various etiologies, including nociceptive pain (such as ocular surface disease, aqueous deficiency, evaporative dry eye, or ocular surface inflammation), neuropathic pain (due to a lesion or disease along the trigeminal somatosensory pathway), or nociplastic pain (nerve abnormalities that occur without a known lesion or disease) [3, 9, 10].

The pathophysiology of COSP is complex and multifaceted, involving various underlying etiologies [1]. While it may arise from nociceptive input, it can also persist without ongoing or apparent ocular surface damage, involving peripheral and/or central pain signaling pathways [3]. COSP can be caused or exacerbated by ocular disorders, non-ocular conditions (chronic pain syndromes, autoimmune conditions, neurological diseases), and/or external factors (environmental exposures) [3]. Patients with COSP may not explicitly describe their discomfort as "pain" but rather as various forms of ocular dysesthesias, including dryness, tenderness, and burning, with symptoms that may fluctuate daily or may be exacerbated by triggers such as wind and light [1, 4].

Diagnosis of COSP is challenging due to substantial overlap in symptoms between COSP and dry eye disease (DED) [11]. According to the DEWS II updated definition, “DED is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles” [12]. Similar to COSP, DED may present with various ocular dysesthesias such as dryness, soreness, itching, fatigue, foreign body sensation, burning, and/or pain [13]. As such, DED can be one cause of COSP, but other causes include ocular pain comorbid with migraine and pain that occurs after ocular surgeries, among other etiologies [3]. In cases when COSP is accompanied by light sensitivity, functional neuroimaging studies can demonstrate central nervous system abnormalities; in some cases the abnormalities may even improve following topical anesthetic application [14]. Given this complexity, COSP should be evaluated considering potential nociceptive and peripheral and central neuropathic/nociceptive etiologies to develop an appropriate treatment plan for each individual patient [15].

At present, diagnosing when COSP has a neuropathic component is primarily clinical and involves a process of exclusion, with treatment often involving a trial-and-error approach. Diagnosis is largely based on clinical history, identification of risk factors, and the presence

of perceived pain that is out of proportion to observed ocular surface abnormalities, a phenomenon termed "pain without stain" [16]. Despite this term, it is important to note that the presence of corneal staining does not preclude a neuropathic component to pain, as a mixed pain phenotype is common [17]. Once a neuropathic component is suspected, topical ocular anesthetics, such as proparacaine or tetracaine, can be utilized in clinical settings to localize the source of pain. Significant improvement in pain after a topical anesthetic suggests a nociceptive or peripheral neuropathic pain source, while persistent pain signals that central or non-ocular mechanisms may drive pain [18]. By temporarily numbing the eye, topical ocular anesthetics can help determine the origin of the pain based on the patient's response [1]. In many cases, the severity of ocular pain symptoms significantly disrupts daily activities. Beyond physical discomfort, COSP imposes a substantial burden on QoL, often leading to impairments in both physical and mental health [3]. Some patients develop depression, and in severe cases, even exhibit suicidal tendencies [1, 8, 19].

While there is often vigorous and appropriate attention paid to addressing the identifiable causes of dry eye disease, most practitioners do not currently think about concurrently treating COSP, which is usually the patient's main symptom [11]. This is likely because there are no approved devices or medications specifically for COSP, nor does a standardized treatment protocol exist [4, 20]. While some published reports have discussed contributing etiologies, diagnostic techniques, and potential management strategies, data on the prevalence of COSP remain limited. This is further complicated by the fact that COSP overlaps with other conditions such as DED, migraine, and glaucoma. Unlike some other chronic pain conditions, there is no universally accepted diagnostic framework or biomarker for COSP, leading to underdiagnosis and variability in reported prevalence rates. There also remains an unmet need for novel therapeutic approaches targeting the underlying mechanisms of eye pain [21].

Several existing prevalence studies have been based on participants from the general public rather than MDs and ODs [22–26]. Herein, we describe a survey on COSP that includes both practicing ophthalmologists and optometrists. This study is the first to estimate the prevalence and impact of COSP in US eye care clinics as well as provide insight into provider experiences with current management approaches for COSP as a bridge to identifying new diagnostic and therapeutic approaches in this population.

METHODS

In 2025, a total of 100 providers completed an online survey conducted by a third-party life-sciences research firm (Fletcher Spaght, Inc.) (Supplemental Table 1). This research was determined to be secondary research and therefore deemed exempt by the institutional review board (Alpha IRB, reference number EC-01). Survey questions included a list of pre-specified options, with some including a write-in text entry to describe "other." Ophthalmology specialties included comprehensive/general, cataract and refractive, cornea and external disease, and glaucoma. Optometry specialties included ocular surface disease and comprehensive/general.

The questions in the online survey were based on having spoken in-depth on the same topics with 30 clinicians (15 ophthalmologists and 15 optometrists) to ensure that unexpected responses were incorporated in the answer choices. Also, many questions allowed open responses ("other, please specify"), to capture further inputs. Where appropriate, answer choices were randomized, which also decreases bias. In addition, technologies were in place to verify respondents and to ensure that no duplication of respondents occurred.

This survey was intentionally limited to US-based ophthalmologists and optometrists to focus on clinical patterns within the American healthcare system. Respondents resided in 33 different states within the USA. Additional inclusion criteria were as follows: ophthalmology and optometry specialists; began practicing between 1985 and 2021; between 30 and 300 patients per week. Of the 196 respondents who started the survey, 89 were excluded (based on

years in practice outside the limits, wrong subspecialty, too few or too many patients/week), and seven were excluded due to being in excess of the desired target number of respondents (100). Fifty optometrists and 50 ophthalmologists participated. The online survey aimed to determine the percentage of their weekly patient volume diagnosed with COSP, diagnostic methods used, contributing etiologies, and current management strategies. Additionally, respondents identified key indicators of successful treatment and attributes they believed would have the greatest impact on patient outcomes. Lastly, they rated their satisfaction with available management options on a scale from 0 (very unsatisfied) to 7 (very satisfied).

RESULTS

Ophthalmology specialties represented in the survey included comprehensive/general, cataract and refractive, cornea and external disease, and glaucoma. Optometry specialties included ocular surface disease and comprehensive/general.

The total weekly patient volume among the 100 surveyed providers was on average 153 for ophthalmologists and 94 for optometrists. Five of these providers were in ophthalmologist-only practices, 26 were in optometrist-only practices, and 69 were in mixed practices with both ophthalmologists and optometrists. Eleven percent of the providers practiced in hospital settings, 79% in private practice, and 10% in corporate or private equity-owned facilities. All surveyed providers had at least 4 years of clinical practice; 44% were early-career (<8 years of practice), 33% were mid-career (9 to 19 years of practice), and 23% had more than 20 years of practice following training.

An estimated 29% (44/153 patients/week) of ophthalmologists' patients and 33% (31/94 patients per week) of optometrists' patients had COSP based on presenting with a chief complaint that would be diagnosed as chronic ocular surface pain (Fig. 1).

The most commonly used tools to diagnose underlying causes of chronic ocular surface pain (COSP) were corneal fluorescein staining (96%), tear film breakup time (92%), lid margin evaluation (91%), and slit lamp examination (90%). The severity of diagnosed COSP was reported as severe in 53% of patients, moderate in 33% of patients, and mild in 14% of patients (Fig. 2).

Of the patients diagnosed with COSP, survey respondents stated that 85% were also diagnosed with DED, confirming the overlap of the two conditions (Fig. 3). Likewise, of the patients diagnosed with DED, and an estimated 63% were also diagnosed with COSP.

According to survey respondents, meibomian gland disease (MGD) and local ocular etiologies (e.g., poor tear film) were coincident with COSP (48% of respondents), followed by autoimmune and inflammatory related conditions (21%) medication induced (15%), diabetic neuropathy (8%), and fibromyalgia (7%) (Fig. 4).

The most common treatments utilized for managing COSP included over-the-counter (OTC) artificial tears (97%), OTC gels and ointments (90%), and hot compresses (86%) in combination with prescription medications including Restasis 88% [Allergan/AbbVie, Irvine, CA]; steroids other (76%), Xiidra 69% [Bausch & Lomb Americas Inc., Bridgewater, NJ], punctal plugs 68%, cyclosporine other 56%, doxycycline 52%, Cequa 47% [Sun Pharma, Princeton, NJ], Miebo 43% [Bausch & Lomb Americas Inc., Bridgewater, NJ], Maxitrol 41% [Harrow Eye, LLC, Nashville, TN], Tyrvaya 31% [Oyster Point Pharma, Inc., Princeton, NJ], and Eysuvis 30% [Alcon Laboratories, Inc. Fort Worth, TX] (Fig. 5). Amniotic membranes and serum tears were also stated as options among 37% and 26% of respondents, respectively. Less than one-fifth of surveyed MDs and ODs offer device-based therapies for their patients with COSP: Intense Pulsed Light (IPL) (Lumenis) (18%), LipiFlow (Johnson and Johnson Vision, Irvine, CA) (16%), iLux (Alcon) 9%, TearCare (Sight Sciences, Menlo Park, CA) (7%) with devices more commonly used among the ophthalmologists (44% of MD and 16% of OD survey respondents offer at least one device therapy for COSP).

Respondents surveyed were asked how satisfied they were with current forms of management for their COSP patients (on a 7-point scale from very unsatisfied to very satisfied) (Fig. 6). Of those using amniotic membranes

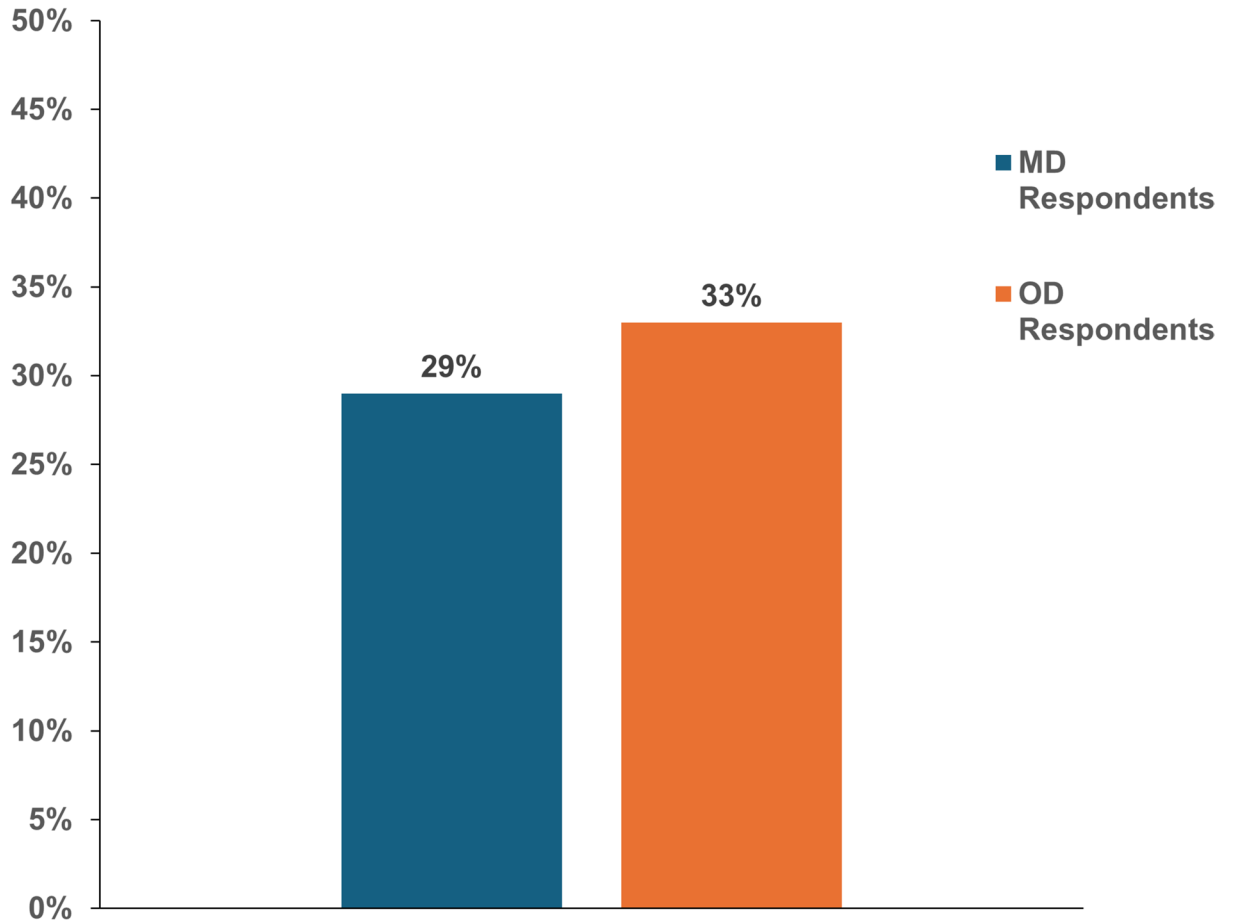

Fig. 1 Prevalence of patients who present with chronic ocular surface pain symptoms. A total of 100 eye care providers were surveyed, including 50 optometrists and 50 ophthalmologists. Respondents were queried about the proportions of their patients who have COSP. *MD* Medical doctor, *OD* Doctor of optometry

and serum tears, 64% were satisfied or very satisfied. Of those using device-based therapies, 63% stated they were satisfied or very satisfied, and for prescription medicines and OTC therapies (artificial tears, gels, ointments, and hot compresses), 40% and 21% of physicians responded as satisfied or very satisfied, respectively.

Improvements in patient-reported symptoms were noted as the key indicator of successful treatment (66%), followed by a marked improvement in physical signs such as inflammation and redness (43%). When physicians were asked what COSP treatment attributes would make a positive impact on their patients, the two most common responses were fast onset of pain relief (85%) and durability of treatment (77%).

Overall, the providers stated that 41% of their patients had commercial insurance, 36% were on Medicare, 13% had Medicaid, 8% were cash pay, and 3% had an unknown insurance status. MD respondents see a greater percentage of Medicare patients, while OD respondents see more commercial and Medicaid patients (Fig. 7).

DISCUSSION

This survey provides an initial look at the prevalence of COSP patients in US eye care clinics, along with perspectives on managing this disease from both optometrists and ophthalmologists. In our study, approximately one-third of

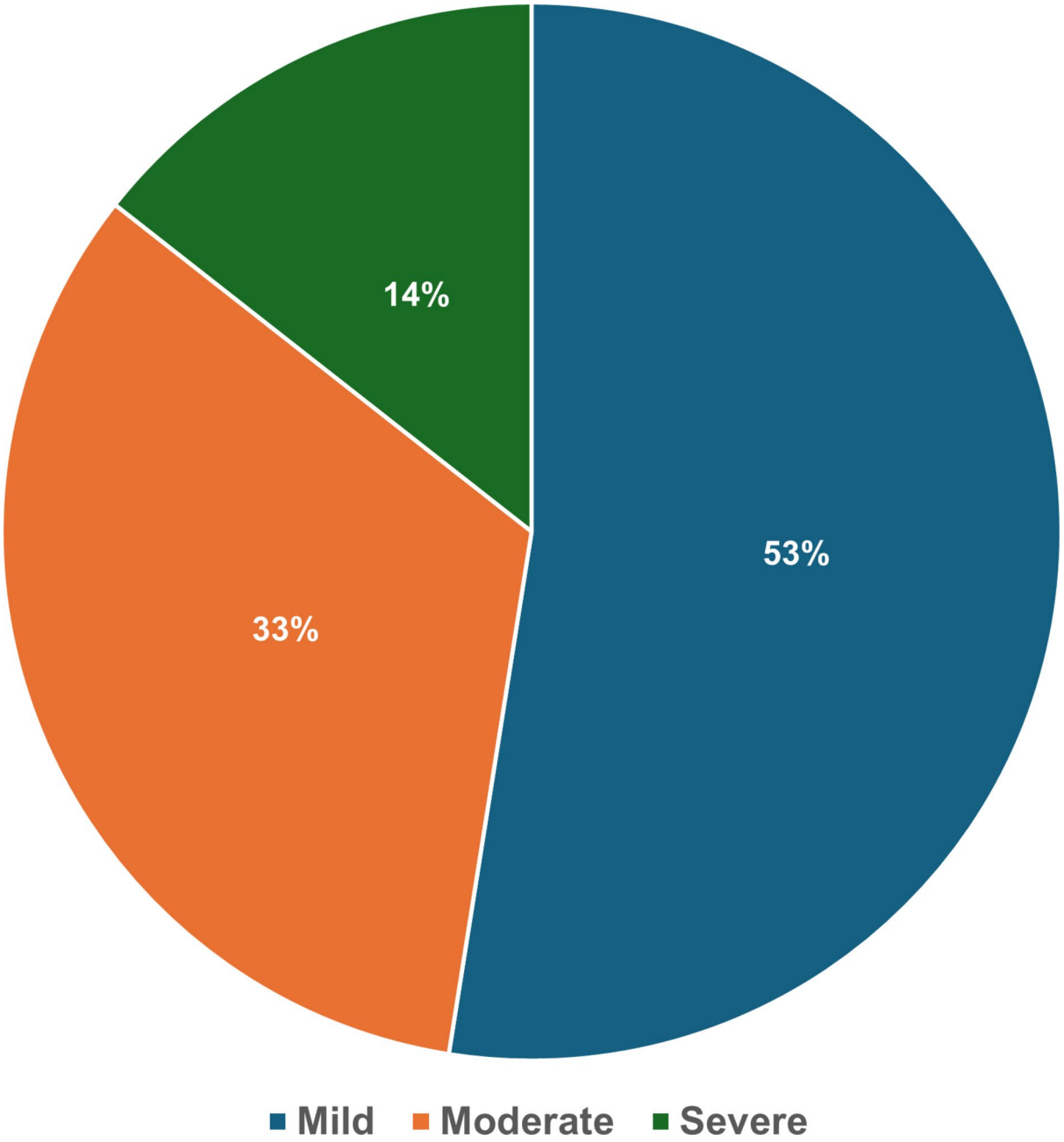

Fig. 2 Severity of chronic ocular surface pain (COSP) as reported by surveyed providers in their patients. A total of 100 eye care providers were surveyed, including 50 optometrists and 50 ophthalmologists. The severity of COSP was categorized as mild, moderate, or severe based on provider assessments

patients visiting an OD or MD had COSP. Of those patients with COSP, the vast majority (85%) of the patients seen were diagnosed with DED. Therefore, the most common underlying comorbidities for patients with COSP were conditions that contribute to DED, meibomian gland disease and autoimmune/inflammation. In addition, medications were contributors to approximately one in five patients with COSP. Of the providers surveyed, the most commonly

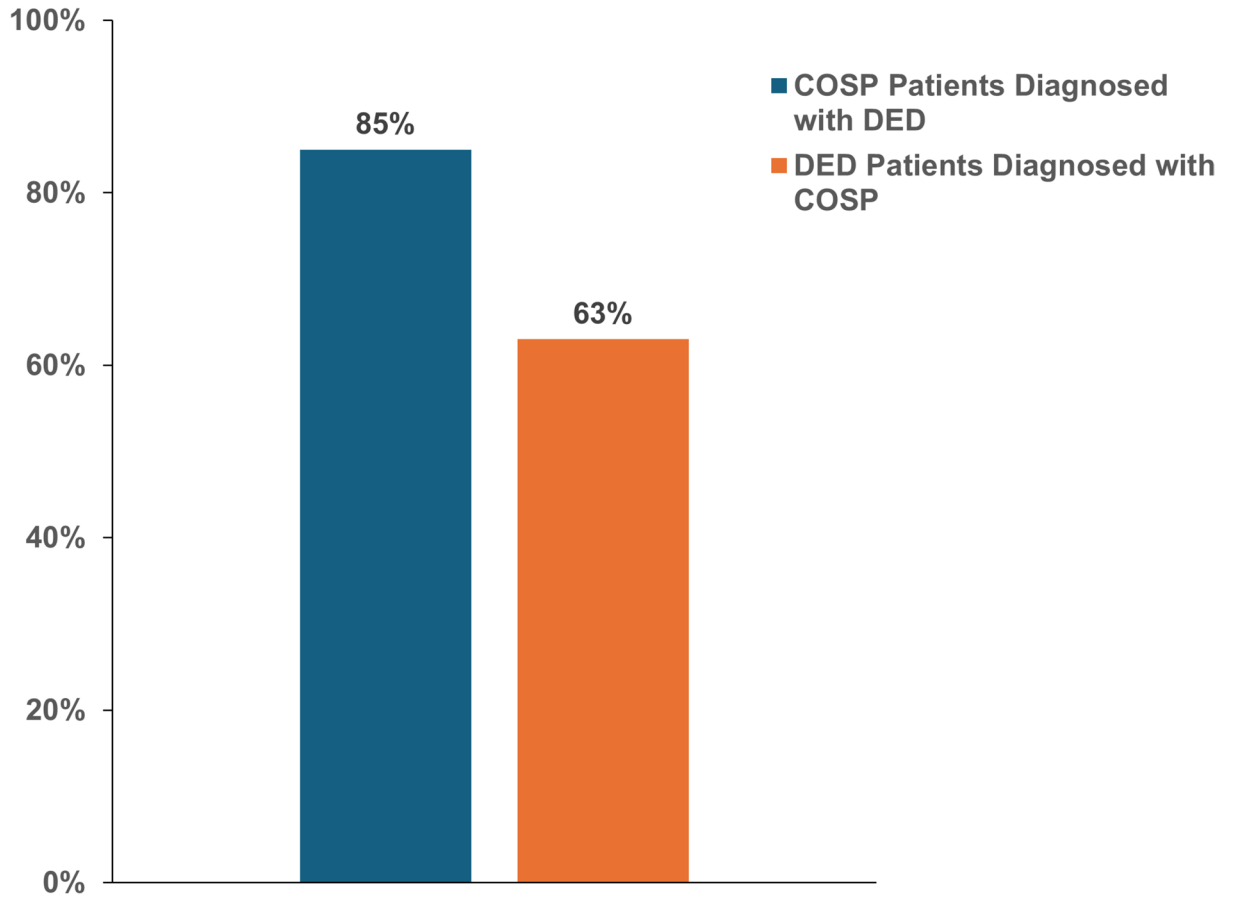

Fig. 3 Overlap in prevalence of patients who present with chronic ocular surface pain (COSP) and dry eye disease (DED). A total of 100 eye care providers were surveyed, including 50 optometrists and 50 ophthalmologists. Clinicians were asked about their patients with chronic ocular surface pain (COSP), roughly what percentage have DED

used methods to diagnose underlying causes of COSP align with those reported in the 2024 Market Scope Ocular Surface Disease Survey Report [27].

The variability in symptom reporting makes it challenging to accurately capture COSP prevalence. However, DED is a common driver of COSP and was the most common comorbidity in our survey [1, 28]. The prevalence of diagnosed DED depends on the definition used. In the United States, a systematic review and meta-analysis of 13 studies estimated DED prevalence of 8.1% of the US population [29]. Our investigation found that 85% of patients diagnosed with COSP were also diagnosed with DED, confirming the substantial overlap between these conditions and highlighting that DED (e.g., tear abnormalities) is a common cause of COSP. Many individuals with DED may have COSP findings beyond tear abnormalities. For instance, a 2021 survey of 415 individuals living with dry eye revealed that only 13% felt their dry eye symptoms were adequately managed [30]. Additionally, 60% of dry eye patients self-discontinue their prescription medications, with a mean time to discontinuing traditional dry eye therapies such as cyclosporine and lifitegrast being just 3 months and 1 month, respectively [31].

COSP is often overlooked due to the fact that many DED studies are based on assessments of symptoms. These symptoms are not described as "pain" but use terms such as grittiness, burning, and aching [3]. The presence of neuropathic/

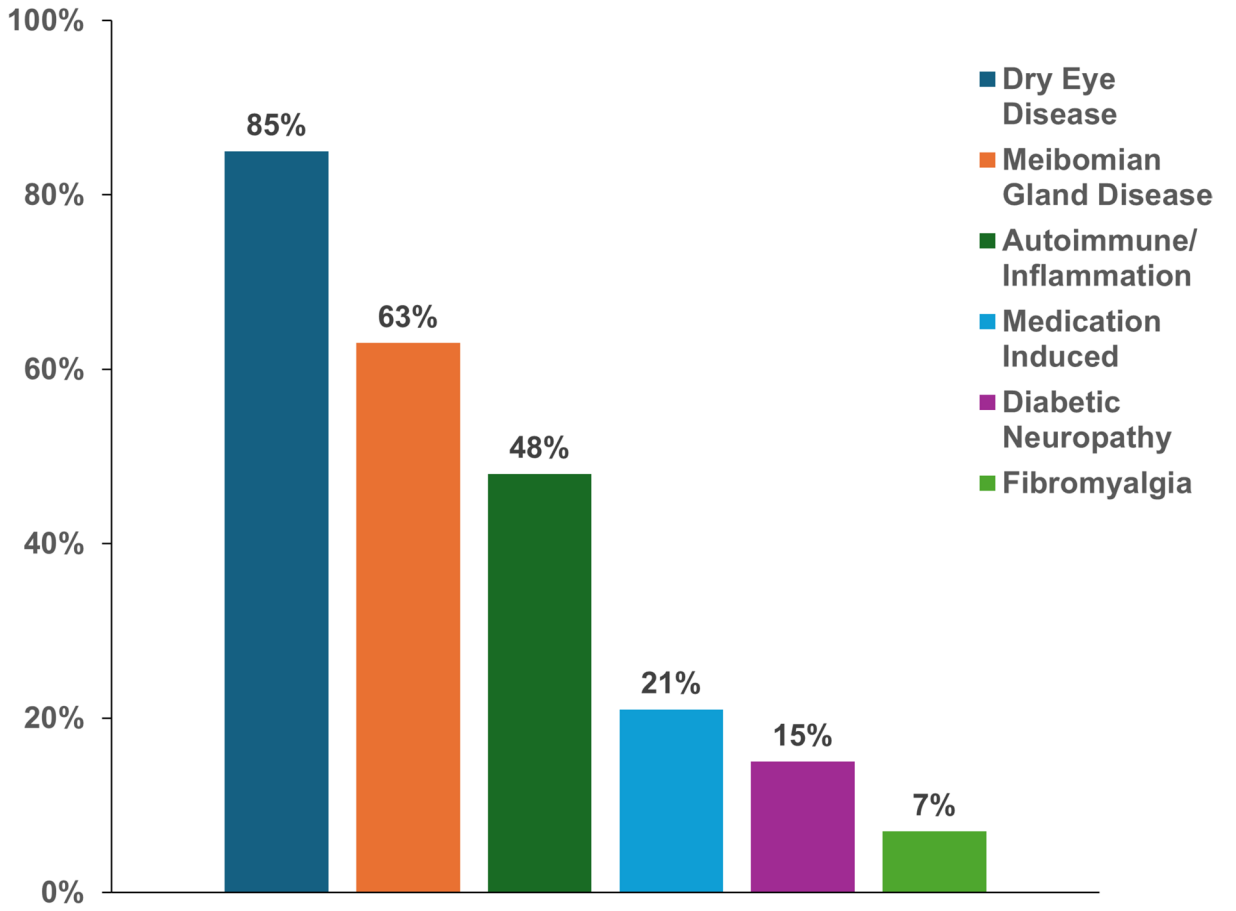

Fig. 4 Underlying comorbidities of chronic ocular surface pain. A total of 100 eye care providers were surveyed, including 50 optometrists and 50 ophthalmologists. Choices were dry eye disease; meibomian gland disease, poor tear film, etc.; autoimmune and inflammatory; diabetic neuropathy; fibromyalgia and associated conditions; and glaucoma drops/other medications; other

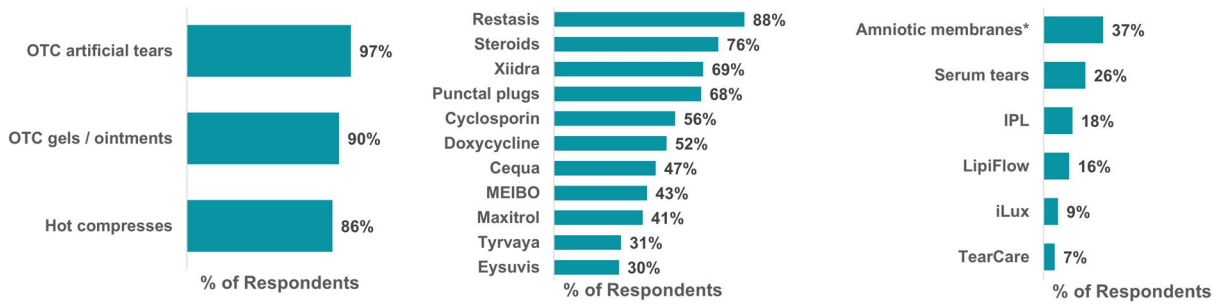

Fig. 5 Options used for chronic ocular surface pain management (percentages of OD and MD respondents). A total of 100 eye care providers were surveyed, including 50 optometrists and 50 ophthalmologists. **A** OTC therapies offered including hot compresses. **B** Prescription medications offered. **C** Device-based therapies offered. *OTC* over the counter

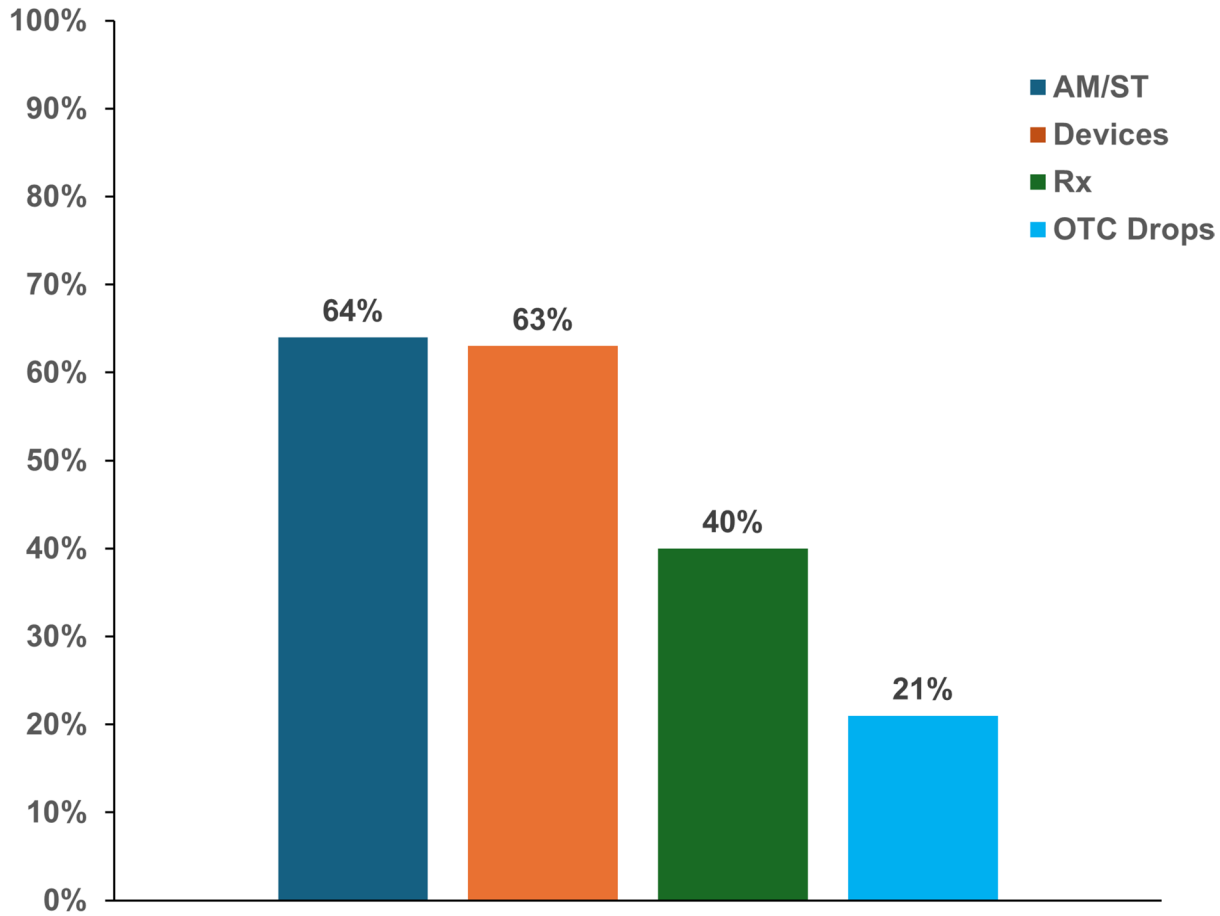

Fig. 6 Eye care provider satisfaction with treatments used for chronic ocular surface pain management. A total of 100 providers were surveyed, including 50 optometrists and 50 ophthalmologists. Proportions of the overall (OD and MD) providers who were satisfied or very satisfied (on a 7-point scale from very unsatisfied to very satisfied). They were asked to rate each of the treatment categories. *AM/ST* amniotic membranes/serum tears, *Rx* prescription medications, *OTC* over the counter

nociplastic contributors in these patients is rarely measured, but studies have found that such somatosensory abnormalities are common in individuals with DED. In a population-based cross-sectional study of 689 volunteers who completed the Ocular Surface Disease Index (OSDI) questionnaire, investigators concluded that high pain sensitivity and low pain tolerance were associated with symptoms of DED [24].

Systemic health conditions can also complicate COSP diagnosis or treatment decisions [32]. Systemic pain syndromes commonly coexist in patients with chronic ocular pain [32]. Similar to other chronic pain syndromes, forms of chronic ocular pain such as DED and neuropathic ocular pain are often associated with psychiatric conditions such as anxiety and depression [33–35]. Chronic ocular pain has also been linked to conditions such as migraines and post-COVID-related pain [36, 37]. COSP can exist as a comorbid condition with systemic pain conditions, with fibromyalgia noted as a comorbidity in 7% of the current survey population [38]. Vehof *et al* reported the results from a cross-sectional study of 425 patients in a tertiary care DED patient cohort with chronic pain syndrome. A total of 74 out of 425 DED patients (17%) had at least one chronic pain syndrome. The total symptom score was significantly higher in DED patients with a chronic pain syndrome than

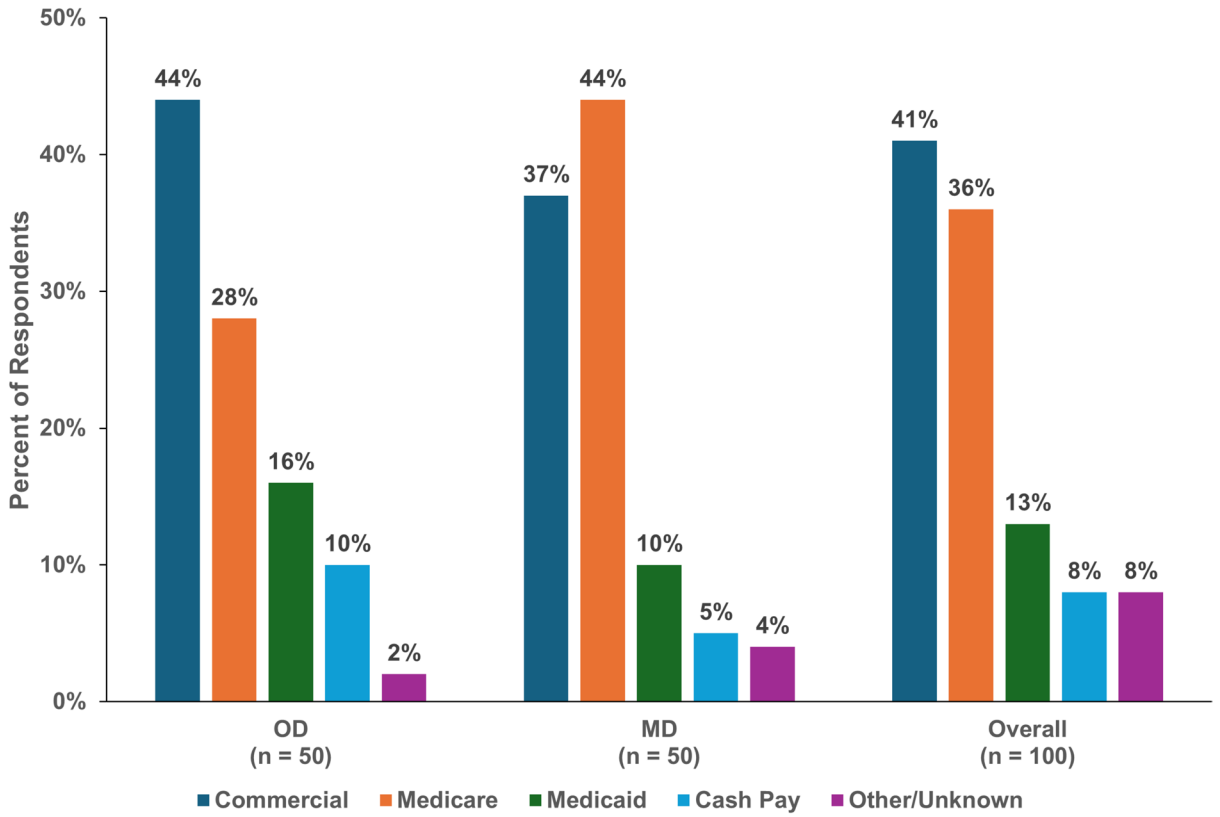

Fig. 7 Respondent-reported patient insurance coverage. A total of 100 eye care providers were surveyed, including 50 optometrists and 50 ophthalmologists. Choices were commercial, Medicare, Medicaid, uninsured, other, and unknown

in those without (45.8 vs. 33.8, $P<0.0005$). These patients reported increased severity of DED symptoms across all domains of the OSDI, despite having similar or less severe objective ocular signs compared to those without chronic pain syndromes, pointing toward neuropathic/nociplastic mechanisms as contributors to pain in this population.

Ocular surgery as a contributing factor to COSP has also been described, but was seen infrequently as a cause of COSP in our survey, as it was not an option provided within the survey questions. Vazquez and colleagues [39] conducted a cross-sectional, observational study in 104 refractive surgery patients to evaluate dry eye-, pain-, and psychological-related symptoms using specific questionnaires. They found that 78.8% of patients seeking consultation for persistent dry eye symptoms after refractive surgery were diagnosed with COSP, with 63.5% identified as having a neuropathic subtype.

Survey respondents reported that comorbidities with COSP were most often conditions that contribute to dry eye, such as meibomian gland dysfunction (MGD), autoimmune and inflammatory-related conditions, and medications. Diabetic neuropathy and fibromyalgia were also reported by the respondents. A study of 464 posts on social media examined the comorbidities associated with COSP [8]. There were 282 mentions of the underlying ocular medical conditions occurring with COSP, of which 46.1% were dry eye disease and ocular surgery, while 53.9% ($n=152$) pertained to non-ocular conditions such as migraine and COVID-19. A retrospective study of nearly 1 million US veterans with a DED diagnosis found that chronic ocular pain in these patients was most strongly associated with headache (odds ratio [OR] 2.98), tension headache (OR 2.64), and migraine (OR 2.58) [40]. These comorbidities suggest a central sensitization component that can complicate COSP

diagnosis and treatment [32]. Delayed diagnosis and suboptimal treatment can contribute to low patient and provider satisfaction, which was observed in this study. Irrespective of the etiology, COSP has a profound impact on patient lifestyle and QoL [3]. Unlike traditional DED, for which many of these patients are initially diagnosed and treated, OTC therapies and prescription treatments often fail to provide relief for COSP, leaving patients with chronic pain and limited options for effective management [41]. COSP can negatively impact a wide array of QoL aspects. A person with COSP can experience difficulties in driving and reading, which can affect routine activities and work performance. Blurry vision and difficulties with continuous screen use from chronic pain can interfere with sleep patterns. Individuals with COSP, particularly the severe form, can experience frustration, impaired personal relationships, and depression, highlighting the burden of the disease [3].

Patient access to a provider with a keen interest or knowledge of COSP can delay COSP diagnosis or complicate treatment choices [42]. Disparities in access to specialized cornea eye care across geographic and socioeconomic lines have been demonstrated. Many patients in rural or underserved areas are unable to obtain advanced diagnostics that are critical for differentiating nociceptive and neuropathic pain components. A survey published by Patel and colleagues in 2025 [42] found that the number of cornea specialists in the US was as low as 1.7 per million people in rural states. This low access to care may contribute to the low patient and provide satisfaction that was observed in the current study.

Beyond reasons such as no existing Food and Drug Administration (FDA)-approved treatment for COSP, other factors such as a lack of provider education can confound COSP diagnosis or treatment choices [43]. These may contribute to the low treatment satisfaction observed in the current study for both patients and their providers. Inadequate initial provider education regarding the neurosensory mechanisms underlying COSP frequently leads to misdiagnosis as simple dry eye disease, driving reliance on tear-based therapies while central sensitization and neuropathic contributions remain unrecognized [32, 44]. Many clinicians do not have standardized evaluation protocols for ocular pain. They may overlook key diagnostic indicators such as pain persistence despite topical anesthesia, which confounds differentiation between peripheral and centralized pain sources. A survey of 441 ophthalmologists found that only 38% could correctly identify neuropathic causes of ocular surface pain and only 68% could choose assessment methods to distinguish central from peripheral origins [43]. Online education targeted at ocular surface pain increased these rates to 71% and 88%, respectively. This enhanced training can shorten time to diagnosis, and disseminate the latest clinical data for emerging treatments and evidence-based patient selection guidance for clinical practice.

For the clinician, there is a need for better diagnostic tools to assess the underlying mechanisms of ocular pain [3]. In our study, the most common methods used to diagnose the underlying causes of COSP—corneal fluorescein staining, tear film breakup time, lid margin evaluation, and general slit lamp examination—did not accurately reflect the pain that patients were experiencing. This is unsurprising, as the discrepancy between ocular surface signs and patient-reported symptoms is well established [45–51]. Even tear film parameters, such as matrix metalloproteinase-9 (MMP-9), often do not correlate with patient symptoms [51, 52]. To highlight the importance of COSP as a separate clinical entity, new patient-reported outcome (PRO) tools have been developed to differentiate between COSP and other ocular surface diseases such as DED [53, 54]. Many experts recommend, for example, the use of a screening questionnaire, such as the Ocular Pain Assessment Survey (OPAS) or the Chronic Ocular Pain Questionnaire (COP-Q), to identify COSP symptoms.

The COP-Q has been developed as a PRO instrument designed to assess symptoms of COSP and their effects [53, 54]. Eye symptoms of pain, itch, dryness, fatigue, irritation, burning sensation, foreign body sensation, and grittiness were the most frequently reported affecting vision-dependent activities of daily life (e.g., reading and driving) and health-related quality of life, which includes emotional well-being, work, and social functioning [54]. The authors

concluded that the revised COP-Q showed excellent internal consistency, with fair to excellent test–retest reliability [53]. The creation and validation of novel PROs highlights the importance of recognizing COSP as a distinct disease state that differs from other ocular surface diseases such as DED [11].

The development of specific diagnostic tests to detect abnormalities in the nervous system and pain perception enables a more individualized and effective approach to ocular pain management [3, 55]. To better understand the origin of COSP, proparacaine testing may be used to differentiate between pain originating from the ocular surface (e.g., nociceptive or peripheral neuropathic pain) and pain arising from centralized or non-ocular mechanisms [7, 18]. If ocular dysesthesia originates from the level of the ocular surface and corneal nerves, treatments applied to the eye may be effective in alleviating symptoms. In contrast, if the pain originates upstream of the corneal nerves, treatments targeting the ocular surface are unlikely to provide significant relief. However, it is important to note that mixed pain mechanisms can exist, where patients may have both peripheral (neuropathic corneal pain or nociceptive pain) and central neuropathic pain components [7]. In these cases, even when central neuropathic pain is present, ocular surface treatments may still offer relief for COSP.

Perhaps due to its multifactorial nature and due to the lack of approved therapies and recognized treatment protocols, treatment options remain inadequate for COSP. Pharmacological agents under investigation for ocular surface pain include SAF312 (Libvatrep), a transient receptor potential vanilloid 1 (TRPV1) antagonist, for post-photorefractive keratectomy pain (NCT04630158, NCT06479382) [56–58] and OK-101, a lipid-conjugated chemerin peptide agonist that is being evaluated for peripheral neuropathic pain (i.e., neuropathic corneal pain; NCT06637527) [59, 60]. Anti-inflammatory agents such as reproxalap, a reactive aldehyde species inhibitor (NCT05424549, NCT05062330, NCT04735393, NCT03404115, NCT06493604, NCT04674358, NCT06389214, NCT03879863, NCT05062330, NCT06424444) [61, 62], tanfanercept, a tumor necrosis factor alpha (TNF-α) inhibitor (NCT05109702) [63], and A197, an immunomodulatory agent (NCT05238597), are being evaluated for DED, a contributor to COSP [64]. Varenicline, a selective nicotinic acetylcholine receptor agonist, perfluorohexyloctane (NOV03), a semifluorinated alkane, and a melastatin 8 receptor agonist have been approved for DED [64–69]. A search of global clinical trials on COSP also revealed an ocular cooling device (ETX-4143 2.0) intended to treat patients with eye pain (NCT06479382) [70]. The limited effectiveness of current treatments for COSP, coupled with the general lack of compliance with existing topical medications, demonstrates an unmet need for new therapeutic modalities for patients suffering from COSP, and thus there is a hope that one or more of the above products will change the landscape of COSP therapeutics.

ODs, MDs, and patients may prefer device-based in-office procedures; however, such treatments are not always covered by insurance (e.g., intense pulsed light and thermal pulsation). In-office medical device procedures, however, can help alleviate the daily burden of chronic topical treatments for patients. Compliance is a well-documented issue with at-home prescription and nonprescription treatments. For example, a survey of 2645 individuals with dry eye found that only 10% instilled their eye drops at the frequency specified by the package insert [71]. Providers seek fast-acting pain relief for their patients; however, many prescriptions take weeks to months before demonstrating efficacy [72, 73]. Although less common with prescriptions specific to dry eye, OTC drops and topical corticosteroids—often used for COSP—may contain preservatives to maintain sterility. These challenges underscore the need for alternative therapeutic modalities for chronic conditions such as COSP.

This study was limited by its small sample size and survey methodology. It may also be subject to selection bias, as voluntary participation could favor providers with greater interest or awareness of COSP. While this may lead to higher reported prevalence, it also raises the possibility that the unmet need may be even greater in the broader clinician population, where underdiagnosis is more likely. Hypothesis testing was not performed. COSP as a result of

surgery was not specifically addressed in the survey. Although the definition of COSP aligns with the broader definition of chronic pain from the Centers for Disease Control and Prevention and International Association for the Study of Pain (IASP) [74], COSP diagnoses in this study were based solely on clinician perception based on the definition of COSP, without the use of standardized diagnostic tools or validated pain scales. This may introduce variability in case identification and underscores the need for structured diagnostic frameworks in future research. The survey did not capture data on the use of topical anesthetic testing (e.g., proparacaine challenge), which is an important clinical tool to help distinguish between peripheral and central mechanisms of ocular surface pain. Future studies should assess how often this approach is used in routine practice. The survey focused on traditional and widely used ocular treatments and did not capture the use of less commonly utilized off-label systemic therapies for COSP (e.g., gabapentinoids, serotonin–norepinephrine reuptake inhibitors [SNRIs]). Future studies should expand to include international respondents to explore global variations in COSP diagnosis and management, including the role of systemic and multidisciplinary approaches in managing neuropathic ocular pain. Additionally, future longitudinal studies are warranted to assess trends and evolving management strategies over time. Finally, studies that include patient surveys, patient-reported symptoms, and patient-reported outcomes after COSP treatment would provide additional insight into the burden and impact of disease, along with treatment preference.

CONCLUSION

This study is the first to estimate the prevalence and impact of COSP in US eye care clinics, including provider experiences with current management approaches for COSP, as an attempt to highlight the need for new diagnostic and therapeutic approaches in this population.

Approximately one-third of the respondents' patients had COSP, and levels of satisfaction are poor among both patients and providers. This survey provides initial insight into the prevalence of COSP among patients in US eye care clinics, along with perspectives on managing this condition. These results confirm that COSP is a significant problem for patients, which can be very severe and life-altering, and that practitioners are generally unsatisfied with their treatment options. New and effective treatments are urgently needed.

Medical Writing/ Editorial Assistance. Editorial assistance in the preparation of this article was provided by Julie Crider, PhD, of Collaborative Medical Writing, LLC, and Arthur Chan, PhD, MBA. Support for this assistance was funded by EyeCool Therapeutics.

Author Contributions. Anat Galor, Kaleb Abbott, Bonnie Henderson, Stephen Pflugfelder, Darrell White, Preeya Gupta, Laura Periman, James A. Stefater, Tomasz Stryjewski, Cristos Ifantides, and Paul Karpecki contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Anat Galor, Cristos Ifantides, Tomasz Stryjewski, Tony Stefater, and Bonnie Henderson. The first draft of the manuscript was written by Kaleb Abbott, Anat Galor, and Cristos Ifantides, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Funding. Sponsorship for this study was provided by EyeCool Therapeutics to Fletcher Spaght to independently conduct the survey and perform analysis on the data. EyeCool Therapeutics also provided funding for professional writing support and a Rapid Service Fee for publication in Ophthalmology and Therapy.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Anat Galor—Alcon Bausch + Lomb, Eyecool, OKYO. Supported by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Clinical Sciences R&D (CSRD) I01 CX002015 (Dr. Galor) and 1I01CX002633 (Dr. Galor), Biomedical Laboratory R&D (BLRD) Service I01 BX004893 (Dr. Galor), Rehabilitation R&D (RRD) I21 RX003883 (Dr. Galor). Supported by the Department of Defense Gulf War Illness Research Program (GWIRP) W81XWH-20–1-0579 (Dr. Galor) and Vision Research Program (VRP) W81XWH-20–1-0820 (Dr. Galor) and HT9425-23–1-0608 (Dr. Galor). Supported by National Eye Institute U01 EY034686 (Dr. Galor), U24EY035102 (Dr. Galor), R33EY032468 (Dr. Galor). Supported by NIH Center Core Grant P30EY014801 (institutional) and Research to Prevent Blindness Unrestricted Grant GR004596-1 (institutional). Sjögren's Foundation 2023-PltGr-109. Darrell White—Aldeyra, Allergan/AbbVie, Bausch + Lomb, Bruder, Orasis, Nordic Pharma, Spyglass, Sun, Tarsus, Viatris/Oyster Point. Preeya Gupta—Azura, Alcon, Aldeyra, AbbVie, Bausch + Lomb, Dompe, HanAll Biopharma, Johnson & Johnson Vision, Kala, Mazado Inc, Nordic Pharma, Ocular Science, Oculis, Orasis, Sight Sciences, Science Based Health, Spyglass, Surface Ophthalmics, Tarsus, Tear Clear, Thea, Tissue Tech, Inc, Trukera, Viatris, Visionology, Vital Tears, Zeiss. James A. Stefater—EyeCool Therapeutics. Tomasz Stryjewski—EyeCool Therapeutics. Stephen Pflugfelder—Alcon, Dompe, Kala, Kowa, Unfold. Bonnie Henderson—Eyecool Therapeutics. Kaleb Abbott—Consultant: AbbVie, Alcon, Bausch + Lomb, Barti, Dompe, Harrow, Optase, Tarsus. Laura Periman – Alcon, Alderyra, Allergan/AbbVie, Amgen, Azura, Bausch + Lomb, Bruder, Dompe, Eyedetec, Kala, Lumenis, Mallinckrodt, Myze, Nordic Pharma, Novartis, Nusight Medical, Olympic Ophthalmics, Quench Method, Science Based Health, Scope, Sun, Tarrsus, Thea, Versea, Viatris, Visant. Cristos Ifantides—AbbVie, Alcon, Bausch + Lomb, EyeCool Therapeutics, JnJ, Tarsus Pharmaceuticals, Trefoil. Paul Karpecki—AbbVie, Able Therapeutics, AdOM, Alcon, Aldeyra, Aramis, Atlas, Azura, B + L, BioTissue, Blephex, Bruder, Cambium, Dompe, EyeCool Therapeutics, Harrow Health, Kala Biopharma, Lubris, Mazado, Neurolens, Nordic Pharma, Oasis Medical, Oculus, Oculis, OcuSoft, RegenerEyes, Rendia, Science Based Health, Scope, Sight Sciences, Signal 12, SilkTears, Surface, Tarsus, Thea, Tracey Tech, Viatris, Vial, Vital Tears.

Ethical approval. The subsequent analysis of these market data was deemed secondary research and obtained institutional review board exemption from Alpha IRB (reference number EC-01).

REFERENCES

1. Mehra D, Cohen NK, Galor A. Ocular surface pain: a narrative review. Ophthalmol Ther. 2020;9:1–21.
2. Shapiro JN, Abuzaitoun RO, Pan Y, et al. Health care use for eye pain. JAMA Ophthalmol. 2024;142:655–60.
3. Galor A, Hamrah P, Haque S, et al. Understanding chronic ocular surface pain: An unmet need for targeted drug therapy. Ocul Surf. 2022;26:148–56.
4. Jacobs DS. Diagnosis and treatment of ocular pain: the ophthalmologist's perspective. Curr Ophthalmol Rep. 2017;5:271–5.

5. Ebrahimiadib N, Yousefshahi F, Abdi P, et al. Ocular neuropathic pain: an overview focusing on ocular surface pains. Clin Ophthalmol. 2020;14:2843–54.

6. Belmonte C, Acosta MC, Merayo-Lloves J, Gallar J. What causes eye pain? Curr Ophthalmol Rep. 2015;3:111–21.

7. Dieckmann G, Borsook D, Moulton E. Neuropathic corneal pain and dry eye: a continuum of nociception. Br J Ophthalmol. 2022;106:1039–43.

8. Sloesen B, O'Brien P, Verma H, et al. Patient experiences and insights on chronic ocular pain: social media listening study. JMIR Form Res. 2024;8: e47245.

9. Guerrero-Moreno A, Baudouin C, Melik Parsadaniantz S, Reaux-Le GA. Morphological and functional changes of corneal nerves and their contribution to peripheral and central sensory abnormalities. Front Cell Neurosci. 2020;14: 610342.

10. De Lott LB, Kaplan C, Harte S, et al. Nociplastic pain among individuals with chronic ocular surface pain: one cause for "pain without stain"? Surv Ophthalmol. 2025. https://doi.org/10.1016/j.survophthal.2025.01.004.

11. Galor A, De Lott LB. A Call to Abandon the Term Dry Eye When We Really Mean Pain. Ophthalmology. 2025;S0161–6420(25):00385–9. https://doi.org/10.1016/j.ophtha.2025.06.015.

12. Nelson JD, Craig JP, Akpek EK, et al. TFOS DEWS II introduction. Ocul Surf. 2017;15:269–75.

13. Tsubota K, Pflugfelder SC, Liu Z, et al. Defining dry eye from a clinical perspective. Int J Mol Sci. 2020. https://doi.org/10.3390/ijms21239271.

14. Choudhury A, Reyes N, Galor A, et al. Clinical neuroimaging of photophobia in individuals with chronic ocular surface pain. Am J Ophthalmol. 2023;246:20–30.

15. Sanchez V, Baksh BS, Cabrera K, et al. Dry eye symptoms and signs in US veterans with gulf war illness. Am J Ophthalmol. 2022;237:32–40.

16. McNally TW, Figueiredo FC. Corneal neuropathic pain: a patient and physician perspective. Ophthalmol Ther. 2024;13:1041–50.

17. Rosenthal P, Baran I, Jacobs DS. Corneal pain without stain: is it real? Ocul Surf. 2009;7:28–40.

18. Crane AM, Feuer W, Felix ER, et al. Evidence of central sensitisation in those with dry eye symptoms and neuropathic-like ocular pain complaints: incomplete response to topical anaesthesia and generalised heightened sensitivity to evoked pain. Br J Ophthalmol. 2017;101:1238–43.

19. Um SB, Yeom H, Kim NH, et al. Association between dry eye symptoms and suicidal ideation in a Korean adult population. PLoS ONE. 2018;13: e0199131.

20. Goyal S, Hamrah P. Understanding neuropathic corneal pain–gaps and current therapeutic approaches. Semin Ophthalmol. 2016;31:59–70.

21. Roberts CJ, MacLeod JD, Elkington AR. Ocular pain: a casualty study. The spectrum and prevalence of pain in acute eye disease. Eye (Lond). 1997;11(Pt 3):342–4.

22. Chia EM, Mitchell P, Ojaimi E, et al. Assessment of vision-related quality of life in an older population subsample: the Blue Mountains Eye Study. Ophthalmic Epidemiol. 2006;13:371–7.

23. Chia EM, Mitchell P, Rochtchina E, et al. Unilateral visual impairment and health related quality of life: the Blue Mountains Eye Study. Br J Ophthalmol. 2003;87:392–5.

24. Vehof J, Kozareva D, Hysi PG, et al. Relationship between dry eye symptoms and pain sensitivity. JAMA Ophthalmol. 2013;131:1304–8.

25. Schaumberg DA, Dana R, Buring JE, Sullivan DA. Prevalence of dry eye disease among US men: estimates from the Physicians' Health Studies. Arch Ophthalmol. 2009;127:763–8.

26. Schaumberg DA, Sullivan DA, Buring JE, Dana MR. Prevalence of dry eye syndrome among US women. Am J Ophthalmol. 2003;136:318–26.

27. Market Scope. 2024 Ocular Surface Disease Survey Report. October, 2024. Available at: https://www.market-scope.com/pages/reports/467/2024-ocular-surface-disease-survey-report-october-2024. Accessed 11 Mar 2025.

28. Sanchez V, Cohen NK, Felix E, Galor A. Factors affecting the prevalence, severity, and characteristics of ocular surface pain. Expert Rev Ophthalmol. 2023;18:19–32.

29. McCann P, Abraham AG, Mukhopadhyay A, et al. Prevalence and incidence of dry eye and meibomian gland dysfunction in the United States: a systematic review and meta-analysis. JAMA Ophthalmol. 2022;140:1181–92.

30. 2021 In America Survey Findings: Living With Chronic Dry Eye. 2021. Available at: https://chronicdryeye.net/infographic/in-america-findings. Accessed 1 Apr 2025.

31. White DE, Zhao Y, Ogundele A, et al. Real-world treatment patterns of cyclosporine ophthalmic emulsion and lifitegrast ophthalmic solution among patients with dry eye. Clin Ophthalmol. 2019;13:2285–92.

32. Weiner G, Galor A, Jacobs DS, Levitt RC. Pain without stain. Clinical Update, December 1, 2018 ed: American Academy of Ophthalmology, 2025; v. 2025.

33. Crane AM, Levitt RC, Felix ER, et al. Patients with more severe symptoms of neuropathic ocular pain report more frequent and severe chronic overlapping pain conditions and psychiatric disease. Br J Ophthalmol. 2017;101:227–31.

34. Fishbain DA, Cutler R, Rosomoff HL, Rosomoff RS. Chronic pain-associated depression: antecedent or consequence of chronic pain? A review Clin J Pain. 1997;13:116–37.

35. Wan KH, Chen LJ, Young AL. Depression and anxiety in dry eye disease: a systematic review and meta-analysis. Eye (Lond). 2016;30:1558–67.

36. Parrey MUR. The link between migraine and eye pain: a review of current evidence. Anaesh, Pain Intensive Care. 2025;29:681–8.

37. Woltsche JN, Horwath-Winter J, Dorn C, et al. Neuropathic corneal pain as debilitating manifestation of LONG-COVID. Ocul Immunol Inflamm. 2023;31:1216–8.

38. Vehof J, Sillevis Smitt-Kamminga N, Kozareva D, et al. Clinical characteristics of dry eye patients with chronic pain syndromes. Am J Ophthalmol. 2016;166:203–4.

39. Vazquez A, Martinez-Plaza E, Fernandez I, et al. Phenotypic characterization of patients developing chronic dry eye and pain after refractive surgery: a cross-sectional study. Ocul Surf. 2022;26:63–74.

40. Lee CJ, Levitt RC, Felix ER, et al. Evidence that dry eye is a comorbid pain condition in a U.S. veteran population. Pain Rep. 2017;2: e629.

41. Galor A, Batawi H, Felix ER, et al. Incomplete response to artificial tears is associated with features of neuropathic ocular pain. Br J Ophthalmol. 2016;100:745–9.

42. Patel RH, Mothy D, Choudhry HS, et al. Cornea eye care coverage based on geographic distribution and population demographics in the United States. AJO International. 2025;2: 100139.

43. Trier S, Aboulsaoud P, Schoonheim P, et al. Ocular surface pain: Online medical education can significantly improve ophthalmologists' knowledge on causative factors, diagnostic methods and emerging therapies and increase confidence for patient assessment. Invest Ophthalmol Vis Sci. 2022;63:1186.

44. Bloomenstein MR Periman, LM.COSP comanagement and making COSP part of every eye exam. Updated June 25, 2025. Available at: https://eyetube.net/spotlight/challenge-the-pain/cosp-comanagement-and-making-cosp-part-of-every-eye-exam. Accessed 9 July 2025.

45. Vehof J, Sillevis Smitt-Kamminga N, Nibourg SA, Hammond CJ. Predictors of discordance between symptoms and signs in dry eye disease. Ophthalmology. 2017;124:280–6.

46. Galor A, Feuer W, Lee DJ, et al. Ocular surface parameters in older male veterans. Invest Ophthalmol Vis Sci. 2013;54:1426–33.

47. Martinez JD, Galor A, Ramos-Betancourt N, et al. Frequency and risk factors associated with dry eye in patients attending a tertiary care ophthalmology center in Mexico City. Clin Ophthalmol. 2016;10:1335–42.

48. Sullivan BD, Crews LA, Messmer EM, et al. Correlations between commonly used objective signs and symptoms for the diagnosis of dry eye disease: clinical implications. Acta Ophthalmol. 2014;92:161–6.

49. Kyei S, Dzasimatu SK, Asiedu K, Ayerakwah PA. Association between dry eye symptoms and signs. J Curr Ophthalmol. 2018;30:321–5.

50. Schmidl D, Witkowska KJ, Kaya S, et al. The association between subjective and objective parameters for the assessment of dry-eye syndrome. Invest Ophthalmol Vis Sci. 2015;56:1467–72.

51. Galor A, Felix ER, Feuer W, et al. Dry eye symptoms align more closely to non-ocular conditions than to tear film parameters. Br J Ophthalmol. 2015;99:1126–9.

52. Lanza NL, McClellan AL, Batawi H, et al. Dry eye profiles in patients with a positive elevated surface matrix metalloproteinase 9 point-of-care test versus negative patients. Ocul Surf. 2016;14:216–23.

53. Findley A, Sloesen BJ, Hodson N, et al. Psychometric validation of the chronic ocular pain questionnaire (COP-Q). J Patient Rep Outcomes. 2025;9:32.

54. Karpecki PM, Findley A, Sloesen BJ, et al. Qualitative research to understand the patient experience and evaluate content validity of the chronic ocular pain questionnaire (COP-Q). Ophthalmol Ther. 2024;13:615–33.

55. Patel S, Mittal R, Felix ER, et al. Differential effects of treatment strategies in individuals with chronic ocular surface pain with a neuropathic component. Front Pharmacol. 2021;12: 788524.

56. Thompson V, Moshirfar M, Clinch T, et al. Topical ocular TRPV1 antagonist SAF312 (libvatrep) for postoperative pain after photorefractive keratectomy. Transl Vis Sci Technol. 2023;12: 7.

57. Study of efficacy and safety of SAF312 eye drops in subjects with post-operative corneal induced chronic pain (CICP). NCT04630158. Available at: https://cdn.clinicaltrials.gov/large-docs/58/NCT04630158/Prot_000.pdf. Accessed 25 Mar 2025.

58. Stasi K, Thompson V, Moshirfar M, et al. Topical ocular TRPV1 antagonist SAF312 was well tolerated and effectively reduced pain after photorefractive keratectomy (PRK). Invest Ophthalmol Vis Sci. 2021;62:967.

59. The study assessing the safety and efficacy of OK-101 treatment in subjects with neuropathic corneal pain. NCT06637527. Accessed March 25, 2025. Available at: https://clinicaltrials.gov/study/NCT06637527?term=OKYO%20and%20pain&rank=1.

60. Patil S, Sawale G, Ghuge S, Sathaye S. Quintessence of currently approved and upcoming treatments for dry eye disease. Graefes Arch Clin Exp Ophthalmol. 2025;263:269–78.

61. Clark D, Sheppard J, Brady TC. A randomized double-masked phase 2a trial to evaluate activity and safety of topical ocular reproxalap, a novel RASP inhibitor, in dry eye disease. J Ocul Pharmacol Ther. 2021;37:193–9.

62. Clark D, Tauber J, Sheppard J, Brady TC. Early onset and broad activity of reproxalap in a randomized, double-masked, vehicle-controlled phase 2b trial in dry eye disease. Am J Ophthalmol. 2021;226:22–31.

63. Dong Y, Wang S, Cong L, et al. TNF-alpha inhibitor tanfanercept (HBM9036) improves signs and symptoms of dry eye in a phase 2 trial in the controlled adverse environment in China. Int Ophthalmol. 2022;42:2459–72.

64. Mangwani-Mordani S, Goodman CF, Galor A. Novel treatments for chronic ocular surface pain. Cornea. 2023;42:261–71.

65. Pflugfelder SC, Cao A, Galor A, et al. Nicotinic acetylcholine receptor stimulation: a new approach for stimulating tear secretion in dry eye disease. Ocul Surf. 2022;25:58–64.

66. Gupta AS, Linaburg TJ, Iacobucci E, et al. Varenicline solution nasal spray for the treatment of dry eye disease in Sjogren's disease: a pilot study. Clin Ophthalmol. 2025;19:1073–84.

67. Tauber J, Wirta DL, Sall K, et al. A randomized clinical study (SEECASE) to assess efficacy, safety, and tolerability of NOV03 for treatment of dry eye disease. Cornea. 2021;40:1132–40.

68. Kaido M, Inoue S, Kawashima M, et al. Role of transient receptor potential melastatin 8 activity in menthol-induced cold sensitivity and its qualitative perception in dry eye. Ocul Surf. 2021;19:307–12.

69. Yoon HJ, Kim J, Yang JM, et al. Topical TRPM8 agonist for relieving neuropathic ocular pain in patients with dry eye: a pilot study. J Clin Med. 2021;10.

70. Study of the ETX-4143 2.0 device in subjects with eye pain. NCT06479382. Accessed March 25, 2025. Available at: https://clinicaltrials.gov/study/NCT06479382.

71. Uchino M, Yokoi N, Shimazaki J, Hori Y, Tsubota K, on behalf of the japan dry eye society. Adherenceto eye drops usage in dry eye patients and reasons for non-compliance: aweb-based survey. J Clin Med. 2022;11(2):367. https://doi.org/10.3390/jcm11020367.

72. XIIDRA®. Lifitegrast ophthalmic solution [package insert]. Bausch & Lomb Americas Inc., Bridgewater, NJ, 2023.

73. Restasis efficacy and safety. What to expect when expecting results. Accessed March 11, 2025. Available at: https://www.restasis.com/about-restasis/efficacy-and-safety.

74. Lucas JW, Sohi I. Chronic pain and high-impact chronic pain in U.S. adults, 2023. NCHS Data Brief. 2024.