Clinical Ophthalmology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

PERSPECTIVES

Interventional Keratoconus Management: The Critical Imperative for Early Detection and Treatment

Kathryn M Hatch[1,2], Eric Donnenfeld[3,4], Andrew S Morgenstern[5], Mitch J Ibach[6]

[1]Mass Eye and Ear, Boston, MA, USA; [2]Mass General Brigham, Boston, MA, USA; [3]Ophthalmic Consultants of Long Island, New York, NY, USA; [4]Department of Ophthalmology, New York University, New York, NY, USA; [5]Department of Ophthalmology, Walter Reed National Military Medical Center, Bethesda, MD, USA; [6]Vance Thompson Vision, Sioux Falls, SD, USA

Correspondence: Kathryn M Hatch, Mass Eye and Ear, 110 Hartwell Ave, Lexington, Boston, MA, 02421, USA, Tel +1 (781) 890-1023, Fax +1 (781) 890-2507, Email kathryn_hatch@meei.harvard.edu

Abstract: Keratoconus is an under-diagnosed progressive ectatic degeneration of the cornea associated with significant negative impact on both visual function and quality of life. Historical treatments—including optical refractive correction and penetrating keratoplasty—have significant limitations, the most important of which is that they fail to alter the progressive nature of the disease in some or all of patients. Corneal cross-linking in conjunction with cessation of eye rubbing and mechanical stressors represents a paradigm change in keratoconus therapy that stabilizes the degenerative process and offers both improvement in structural and functional outcomes and long-term stability in both visual function and quality of life. The development of corneal cross-linking and the opportunity to halt keratoconus progression makes imperative the early identification and treatment of subclinical cases when cross-linking offers the greatest long-term benefit. The availability of a less invasive epithelium-on cross-linking option further underscores this imperative. In this perspective, we describe the challenges of detecting early keratoconus and advocate for collaborative partnership with the entire eye care community to implement new and emerging technologies to find patients who would benefit from cross-linking and facilitate early referral to corneal surgeons for definitive treatment.

Keywords: keratoconus, cross-linking, epithelium, transepithelial, intervention, oxygen, diagnosis

Introduction

Keratoconus is an under-diagnosed bilateral and progressive ectatic condition of the cornea most commonly presenting in teenage years and early adulthood and progressing over time.[1] The condition is characterized by progressive thinning and steepening into a conic formation commonly resulting in irregular astigmatism and reductions in best-corrected visual acuity.[2] The exact cause is not fully understood, but factors like genetics, eye rubbing, allergy/atopy, sleeping with a hand or pillow pressed against the eye, and certain connective tissue conditions may play a role. If left untreated, progression can lead to vision loss and reduction in quality of life.[3]

Early keratoconus is frequently asymptomatic and difficult to diagnose on clinical exam, although more advanced imaging techniques may detect early cases before permanent structural changes occur in the cornea leading to vision loss, thereby facilitating earlier intervention to prevent progression of the disorder. The prevalence of keratoconus in the United States using standard diagnostic technology has historically been reported in the range of 17.5–120 per 100,000 persons (0.0175–0.12%),[4–8] while a recent analysis of data from the Centers for Disease Control and Prevention Vision and Eye Health Surveillance System reported the prevalence at 0.03% in 2016 and 0.04% in 2019.[9] With more advanced imaging (eg, Scheimpflug tomography) to capture potential subclinical cases, the prevalence rises to 0.3%.[10]

Traditional keratoconus management involved correction of progressive refractive error with optical modalities in early stages (glasses or soft contact lenses for early myopic changes, followed by gas-permeable, hybrid, or scleral contact lenses as irregular astigmatism develops), with corneal transplantation reserved for advanced or severe cases. The

https://doi.org/10.2147/OPTH.S591113
Received: 23 December 2025
Accepted: 4 May 2026
Published: 18 May 2026

advent of corneal cross-linking has enabled intervention early in the disease course to stabilize corneal shape and structure to prevent cone formation and associated vision loss. This treatment, in addition to cessation of eye rubbing, sleeping with a hand or pillow pressed against the eye, or other chronic mechanical insults to the cornea, is best administered before significant ectasia and vision loss have occurred in order to stabilize the condition. Consequently, there is a significant unmet need to improve early detection of keratoconus to facilitate intervention when it is most effective, before irreversible vision loss. Early detection is especially important given the availability of treatment options for stabilization such as corneal collagen cross-linking. In this paper, we advocate for early interventional keratoconus management, discuss limitations to this approach including low detection rates at the most treatment-amendable stages, and propose strategies to overcome these limitations.

The Cost of Delayed Diagnosis

The natural history of keratoconus includes early asymptomatic stages when treatment to prevent vision loss may be most impactful, as well as later symptomatic stages when visual rehabilitation becomes more difficult (even if the disease itself is stabilized). The disease typically is detected in teenage years and young adulthood, but progression can continue into later age groups.[11] It can begin with early topographic, tomographic, or epithelial-mapping changes before it is detectable on slit lamp examination and even while there is little to no loss of best corrected visual acuity.[12]

Keratoconus represents a spectrum of progressive corneal changes. Forme fruste keratoconus typically describes an extremely early form of keratoconus which includes a normal-appearing cornea on slit-lamp and often normal anterior topography, but may show subtle posterior elevation changes and thinning. Subclinical keratoconus is characterized by tomographic and topographic signs with a normal slit-lamp appearance. Subtle signs of subclinical keratoconus include asymmetric displacement of anterior and posterior corneal apices (skew deviation), corneal thinning, and reduction of corneal volume. Thinning is typically observed in the area of greatest steepening. However, these signs are often unappreciated on routine clinical examination, when early symptoms can easily be attributed to simple refractive error. More advanced imaging techniques, such as corneal tomography, can identify these early, subclinical cases and expedite treatment before structural and functional degradation occur. More subtle signs, including increased epithelial/stromal thickness ratio in the central cornea as well as asymmetric superior-nasal epithelial thinning, may suggest but not establish the diagnosis of keratoconus; such cases are considered keratoconus suspects and warrant close longitudinal observation to detect definitive findings consistent with keratoconus. Patients also should have ongoing counseling regarding the risks of ongoing eye rubbing and the need for cessation of mechanical forces on the cornea. As the disease progresses, ectatic changes leading to cone formation become evident on slit-lamp examination, accompanied by decreased visual acuity that can often be fully corrected early with a variety of refractive devices but not later in the progression.

Corneal cross-linking can yield the most favorable refractive outcomes when performed before significant ectasia has occurred. This is typically in the asymptomatic or early symptomatic phase, when many cases are misdiagnosed as simple myopic/astigmatic refractive error. By the time the disease manifests both symptomatically and clinically, cross-linking stabilizes the structural changes but may not be able to significantly improve refractive outcomes.

Therein lies a critical clinical conundrum: Many eyes with keratoconus are not diagnosed until significant ectasia and vision loss have occurred. There is a vital window of opportunity when treatment is most refractively impactful, but diagnosis is most difficult. If this window of opportunity is missed, not only is visual function permanently impaired, but there are also adverse effects on mental health and quality of life. Multiple studies and several systematic reviews and meta-analyses have demonstrated a detrimental effect of keratoconus on mood, mental health, quality of life, and emotional well-being.[13–15] The detrimental impact of keratoconus on mental health is often disproportionate to the extent of visual impairment and dependence on medical contact lenses, suggesting effects related to stress, anxiety, and fear of going blind; this impact appears to dissipate with time as patients become more familiar and comfortable living with the disease.[13] Additionally, patients with keratoconus have higher depression scores than unaffected individuals.[14] The 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25) is a well-validated instrument for measuring the impact of visual function on quality of life.[16] Most studies utilizing the NEI VFQ-25 have demonstrated a significant reduction in quality of life among patients with keratoconus.[3] Mean scores suggest an impact commensurate

with that of advanced non-exudative age-related macular degeneration (category 3–4),[17] and scores worsen meaningfully over time in many patients.[18]

A second important clinical reason to enhance detection of subclinical keratoconus relates to corneal refractive surgery. In the early days of laser in situ keratomileusis (LASIK), when patients presented with post-refractive corneal ectasia, undetected subclinical keratoconus was recognized as a very strong and likely cause. Post-refractive ectasia is characterized by rapid progression of irregular corneal steepening, increasing myopia, and astigmatism.[19] Myopia is the leading indication for refractive surgery, and patients with undiagnosed keratoconus-related myopia are among those seeking refractive surgery. For instance, in a recent study in Syria, 18% of prospective myopic refractive surgery patients were screened and diagnosed with keratoconus, and another 14% were identified as keratoconus suspects.[20] If misdiagnosed as simple myopia, patients with subclinical keratoconus undergoing corneal refractive surgery are at high risk for postoperative ectasia, further underscoring the importance of improving detection.

In summary, identifying and treating early cases can reduce vision loss and preserve quality of life in patients with keratoconus. Screening for keratoconus will have substantial value from a societal perspective because the benefit is substantial and the missed opportunity for early diagnosis and treatment leads to preventable vision loss in working-age adults; it also is imperative in patients seeking corneal refractive surgery to avoid postoperative ectasia and vision loss.

Current Diagnostic Challenges and Solutions

Keratoconus is most impactfully treated in its earliest and often asymptomatic stages, making early diagnosis critical to preventing vision loss. The diagnosis of keratoconus is challenging given the paucity of clinical findings in the early stages, posing a mismatch between manifest symptoms and subtle or absent clinical signs that compounds the diagnostic dilemma. Suspected cases may be identified by tomographic, topographical, and epithelial mapping analysis of the cornea. Early findings may include posterior corneal elevation, mild focal corneal steepening, widening disparity of the inferior and superior ratio, and the presence of anterior corneal aberrations such as coma.[21,22] Absent a high suspicion and persistent diagnostic testing, many subclinical cases are missed.

Screening may be the best approach for early detection of subclinical cases.[23] However, large-scale mass screening efforts are complicated by the lack of a simple, cost-effective screening test, as corneal topography/tomography is expensive and not easily portable and thus is not well suited for large population screening efforts.[24] Additionally, collaboration with pediatrician societies may be necessary to allow for screening modalities to be considered standard of care for the pediatric population.

Screening using topography can also have other limitations, including poor-quality image acquisition in eyes with concurrent ocular surface disease or epithelial basement membrane disorders, in addition to poor reproducibility, especially in uncooperative children. A smartphone-based system has been developed but may miss subclinical cases due to low sensitivity.[25] Future screening modalities may include artificial intelligence (AI) driven devices. There is most certainly an unmet need for this type of low cost, high specificity and sensitivity device which will allow patients to seek the gold standard tomography study in order to find eyes that need medical assessment. An FDA-approved genetic test evaluating more than 2000 variants in 75 genes associated with keratoconus was developed, but its clinical utility as a screening test has not been demonstrated and it is currently not commercially available.[26]

At present, targeted screening in at-risk populations (eg. in patients with eye rubbing, floppy eyelid syndrome, allergy/atopy, family history, connective tissue disorders, Down Syndrome, frequent prescription changes, or higher-order aberrations) is more viable than mass community screening. As an example of this approach, a tomography-based screening study in 174 Egyptian school children with high myopia (>6 D) using Scheimpflug imaging identified 16 eyes (9.2%) with keratoconus; the degree of myopia and astigmatism was similar in eyes with and without keratoconus, but affected eyes had significantly more spherical and vertical coma aberrations.[27] Effective opportunistic screening requires a high degree of suspicion in at-risk individuals. This includes those with a family history of keratoconus (odds ratio 6.42–25.52), atopy/allergy (odds ratio 1.94–2.95), and eye rubbing (odds ratio 3.09–4.93),[28–30] as well as those with connective tissue disorders, Down Syndrome, frequent prescription changes, or higher order aberrations. In addition, screening remains essential in patients seeking corneal refractive surgery, where the prevalence of undiagnosed

keratoconus has been reported to range from 3–6% in Caucasian populations[31] and 9–18% in Middle Eastern populations.[20,32,33]

In primary eye care settings, the instrumentation available for screening may be limited to the slit-lamp, phoropter, and keratometry. A significant increase in myopia and/or astigmatism alone during a routine eye examination may be a presenting sign of keratoconus and should be considered a screening method. Early slit-lamp findings of keratoconus are often nonexistent, or they are subtle and easily overlooked. Keratometry is inexpensive and provides qualitative information on mire appearance in manifest keratoconus but may be insensitive to early disease, and may miss more peripheral findings as it only evaluates a 3mm region of the cornea, and has largely been superseded by more recent and advanced diagnosing technologies.[34] In specialty eye care settings, additional instruments including corneal topography and tomography, as well as tomography and corneal hysteresis testing, may be available. Placido-based topography provides information on the central anterior corneal surface and can provide evidence of early keratoconus, but it requires clinical experience for best interpretation.[35] Likewise, videokeratography has widely variable sensitivity and specificity for early subclinical keratoconus.[24]

Advances in ophthalmic imaging offer new opportunities for keratoconus screening.[36] These include instruments that provide both structural and biomechanical information. Rotating Scheimpflug imaging is a tomographic technique that provides detailed quantitative information on corneal curvature and elevation of both the anterior and posterior corneal surface.[37] These devices provide an extensive list of calculated parameters with varying but generally highly accurate screening performance in detecting early keratoconus.[38] Posterior corneal elevation abnormalities seen on tomography may also aid in detecting early or subclinical cases.[1,2,37,39] Assessment of both anterior and posterior corneal curvature data with tomography has given rise to a new keratoconus staging system, the Belin/Ambrosio Enhanced Ectasia (BAD) display, which considers the anterior (A) and back (B) corneal radii as well as corneal thickness (C) and distance visual acuity (D).[40] Diagnosis may be further enhanced with epithelial mapping to detect focal epithelial thinning over the area of total corneal thinning, posterior elevation changes, and the cone arising from the epithelial remodeling response.[41–43] Additionally, these instruments model the passage of light through the cornea (wavefront or aberration analysis) to identify structural abnormalities typical of early keratoconus arising from optical aberrations.[44] Optical coherence tomography generates corneal thickness maps that identify focal areas of corneal thinning indicative of early keratoconus.[37] Finally, analysis of air-pulse deformation of the cornea can provide biomechanical information that distinguishes between normal and early keratoconus with a high degree of accuracy.[45]

In isolation, each of these technologies provides information that can identify eyes with early keratoconus. In combination, their diagnostic value is substantially increased. Multi-modal platforms include comprehensive combined metrics to indicate potentially affected eyes. These devices can attune clinicians to the possible presence of the disease, leading to definitive evaluation, diagnosis, and management.

Optimizing collective information gleaned from the wide variety of parameters generated across the various platforms is a logical application for AI. Artificial intelligence has shown promising outcomes in analyzing ophthalmic images for the early detection of diseases including diabetic retinopathy and glaucoma as well as corneal, eyelid, and orbital diseases.[46] With regard to keratoconus, AI may have the potential to enhance diagnosis and improve early detection and treatment planning,[47] when used in conjunction with clinical evaluation and gold-standard diagnostic technologies such as tomography. Both images and the numerical data derived from them can serve as inputs, although the preponderance of research to date utilizes numerical data rather than actual raw images.[48] High accuracy has been achieved with AI models in distinguishing normal eyes from those with manifest keratoconus. However, achieving high diagnostic accuracy using AI to identify subclinical keratoconus has been more challenging and is more successful when data from multiple sources (for example tomographic and biomechanical data) are combined.[49] This underscores a persistent challenge in screening for subclinical keratoconus: the lack of a single diagnostic modality that provides sufficient information to conclusively detect cases across the spectrum of disease severity.

In summary, targeted screening for keratoconus may represent the most feasible and effective strategy for detecting early subclinical cases and facilitating early treatment. Currently, there is a need for simple, portable screening tests, and targeted screening of high-risk populations (eg, those with a family history of keratoconus, atopy/allergy, connective tissue disorders, eye rubbing, Down Syndrome, frequent prescription changes, and higher-order aberrations). There is

also a need for mass screening for the entire pediatric population once a low-cost and highly specific and sensitive screener becomes available for the use in schools, pediatricians' and allergists' offices in addition to eye care provider locations. In addition, screening remains essential in patients seeking corneal refractive surgery, where the prevalence of undiagnosed keratoconus is high and can increase the risk for postoperative ectasia. Optometrists and comprehensive ophthalmologists who suspect early or subclinical keratoconus should refer such patients to a corneal surgeon early so that these patients – if diagnosed with keratoconus - can avail themselves of early interventional therapy to halt disease progression rather than delaying referral and increasing progression risk with non-interventional optical refractive correction.

Comparing Treatment Pathways: Early Intervention vs. Late Management

Treatment options for keratoconus vary by stage of the disease. Historically visual correction was largely compensatory in nature and had no beneficial effect on the natural history of the disease. Early cases were managed with optical correction (spectacles or contact lenses early, rigid scleral contact lenses to address irregular astigmatism later) while advanced cases underwent corneal transplantation. Scleral contact lenses are the most common form of optical correction, and while they provide a smooth and stable interface for vision correction, they can have important limitations, such as handling issues[50] and visual problems (eg, sunburst/starburst patterns within the visual axis).[51] In addition, unfortunately many patients wearing rigid contact lenses have the misconception that the contact lenses are preventing progression of the disease. In reality, none of these compensatory optical correction strategies alters the progressive natural history of the disease, and so they should be considered useful adjuncts if needed, rather than replacing the primary treatment of corneal cross-linking.

In later stages of keratoconus, compensatory strategies typically involve invasive surgical replacement of the affected cornea. These procedures are not curative, have a limited duration of effect given the lifelong course of keratoconus, and unfortunately often represent the trading of one set of problems for a different set of problems. A long-term study of full-thickness corneal transplantation for keratoconus in 219 eyes revealed a cumulative rejection rate of 45%, a 20-year graft failure rate of 12%, and a 10% 20-year probability of keratoconus recurrence.[52] In a larger registry study of 4834 eyes undergoing first transplantation for keratoconus, graft survival rates at 10, 20, and 23 years were 89%, 49%, and 17%.[53] More disheartening, the failure rates for repeat keratoplasty in eyes with keratoconus are even higher than for first grafts.[54] Given that keratoconus presents early in life, the high failure rates at 20 years and later are significant as most patients would be expected to survive at least this long postoperatively, and many would require additional procedures for visual rehabilitation. Partial-thickness transplantation is also an option, although outcomes are generally similar to those with full-thickness procedures.[55] Whether full- or partial thickness, corneal grafting requires consistent lifetime follow-up for surveillance of graft health and survival.

Corneal cross-linking represents a definitive solution-focused approach to keratoconus management. As initially described, the Dresden protocol was an epithelium-off approach using riboflavin 0.1% in 20% dextran administered every 2 minutes for 30 minutes followed by central corneal irradiance with ultraviolet A (UVA) light in the 365–370 nm range for 30 minutes.[56] Long-term studies have since established the safety and efficacy of the treatment in halting progressive ectasia.[57–59] With the advent and FDA approval of corneal cross-linking in 2016 (Photrexa®), the U.S. keratoconus treatment paradigm underwent a significant shift. Cross-linking is a minimally invasive outpatient procedure in which riboflavin, a vitamin B2 derivative, is applied topically to the cornea, followed by ultraviolet light exposure to activate the riboflavin and promote the formation of cross-linking of collagen molecules within the corneal stroma. This network of crosslinked collagen biomechanically strengthens and stabilizes the cornea, preventing further ectasia. Thus, in contrast to corneal transplantation, corneal cross-linking halts progression rather than compensating once progression has occurred.

Prior to October 2025, the only FDA-approved procedure was performed by removing the central 7–9mm of corneal epithelium to enhance riboflavin absorption (epithelium-off corneal cross-linking). However, on October 20, 2025, the FDA approved epithelium-on cross-linking (Epioxa®): a new incision-free drug therapy, catalyzed by oxygen and light, which leaves the epithelium intact and has been shown to arrest progression of keratoconus with a single administration. This novel procedure may substantially increase the benefit-risk ratio by reducing complications, decreasing the

rehabilitation process to a day rather than a week, reducing the treatment time, and reducing the discomfort associated with epithelial removal. In addition, the FDA indication for epithelium-on cross-linking does not require that disease progression be demonstrated before initiating therapy, further facilitating earlier intervention. Finally, epithelium-on cross-linking is approved for corneas with epithelium-on pachymetry of ≥325 microns (vs epithelium-off cross-linking was approved for corneas ≥400 microns thick after epithelium removal), further broadening the range of patients who may undergo the treatment. Altogether these advantages may accelerate the acceptance of corneal cross-linking. Multiple randomized trials and several meta-analyses of these trials have concluded that both approaches provide similar outcomes in terms of maximal keratometry, best-corrected and uncorrected visual acuity, spherical equivalent, and corneal curvature parameters; however, the epithelium-off approach has higher rates of corneal haze, delayed epithelial healing, inflammatory and infectious keratitis, and postoperative discomfort compared to epithelium-on.[60,61] In addition, several systematic reviews have shed light on the efficacy of both epithelium-on and epithelium-off crosslinking for keratoconus. A Cochrane systematic review evaluated 13 international randomized trials with 567 patients comparing epithelium-on and -off techniques and found no between-group differences in maximal keratometry (in 5 studies) or visual acuity (in 2 studies) and concluded insufficient evidence supporting either treatment over the other.[62,63] Borchert et al conducted a systematic review and meta-analysis of 27 randomized trials comparing epithelium-on and -off crosslinking in 1399 patients and found no differences in maximal keratometry or corrected distance VA between groups at 12 months; however, uncorrected distance VA was better in the epithelium-off group albeit with greater progressive corneal thinning than in the epithelium-on group.[64] Jaruseviciene and coworkers conducted a review of 39 publications and concluded that compared to the Dresden epithelium-off technique, while epithelium-on or iontophoretic protocols improved patient comfort and recovery time, these modifications appeared to provide less stromal stiffening and potentially lower efficacy in preventing keratoconus progression.[65] Alajmi et al conducted a systematic review and meta-analysis of 14 studies comparing epithelium-on and -off techniques in 629 patients and concluded that both approaches effectively stabilized the disease, however the epithelium-off technique yielded greater corneal flattening while the epithelium-on technique offered better visual acuity and a more favorable patient experience[66] Due to heterogeneity of study designs, treatment protocols, outcome parameters, and presence or absence of oxygen supplementation or UVA pulsing across studies, comparative conclusions should be interpreted with caution.

Long-term outcomes of cross-linking in early keratoconus confirm its effectiveness. A 10-year follow-up of participants in the pivotal trial supporting FDA approval revealed that 81.8% of keratoconus eyes remained stable following the procedure.[67] A review of several other studies have confirmed the long-term efficacy of cross-linking in stabilizing progressive keratoconus through up to 13 years of follow-up.[68] Likewise in eyes with early keratoconus, a 9-year study revealed that visual acuity, refractive, and curvature parameters were all stable or improved with no significant postoperative complications.[69]

Given the high long-term failure rates of keratoplasty, it is not surprising that keratoconus treatment has dramatically shifted toward earlier less-invasive intervention, particularly once corneal cross-linking was available.[70] In a Dutch study conducted after the introduction of cross-linking, keratoplasty rates for keratoconus dropped by 25%.[71] In a similar study conducted in Norway, a greater than 50% reduction in keratoplasty was seen.[72] A similar decline in keratoplasty rates for keratoconus has been observed in the United States,[73] Japan,[74] and New Zealand.[75]

A transition from keratoplasty to corneal cross-linking is expected to have beneficial effects not only on visual acuity and corneal parameters, but also—and arguably more importantly—on quality of life and safety for patients with keratoconus. It is well established that quality of life is impaired in patients with keratoconus[76] and deteriorates further as keratoconus progresses.[77] The impact of keratoconus on life and lifestyle can be profound. In a New Zealand study, 15% reported that keratoconus impacted their employment, including 9% who missed work due to the disease, and 5% who altered their educational plans because of the diagnosis.[78]

In a prospective French study, vision-related quality of life scores (including both overall score and subscale scores such as ocular pain, social function, mental health, role difficulties, and dependency) decreased proportionally as the severity of keratoconus increased.[79] In contrast, with stabilization of visual acuity and corneal morphology, quality of life scores measured with both general vision and keratoconus-specific instruments stabilize after cross-linking.[80] Thus, early intervention can stabilize the disease and preserve quality of life, and it is best implemented before significant structural

and/or functional impairment has already compromised quality of life. In contrast, quality of life following penetrating keratoplasty for keratoconus demonstrates significant impairment in domains such as role difficulties, dependency, driving, and peripheral vision,[81] further supporting the importance of early intervention to avoid keratoplasty and reduction in quality of life.

Other procedures that have been employed for keratoconus include corneal tissue addition keratoplasty and synthetic or allogenic corneal intrastromal ring segments. Collectively these procedures consist of implantation of corneal or synthetic materials into the cornea in an effort to flatten the cone and improve visual function. In clinical studies, variable effects on visual acuity and topography have been reported.[82,83]

In summary, early optical correction in keratoconus addresses visual symptoms but does not alter the course of the disease. In contrast, early corneal cross-linking stabilizes corneal ectasia and preserves visual function and quality of life. These outcomes are stable over time through up to 13 years of follow-up. This is in marked contrast to the postoperative course of penetrating keratoplasty, which has a high long-term failure rate requiring regrafting with even higher subsequent failure rates. Consequently, keratoplasty rates are falling as early cross-linking becomes the standard of care for keratoconus. This paradigm shift preserves visual function and maintains quality of life. Now FDA-approved, epithelium-on oxygen-enriched cross-linking will further improve upon epithelium-off techniques by providing similar outcomes with less postoperative discomfort and lower risk of corneal haze, thereby facilitating earlier intervention.

Interventional Keratoconus: An Evidence-Based New Paradigm

The development and further refinement of corneal cross-linking offer an impactful opportunity to transform our approach to the management of keratoconus at all stages of the disease. As procedural therapy becomes the preferred first-line treatment, the paradigm shifts to a more interventional approach to halt disease progression and prevent vision loss. Interventional keratoconus is a proactive approach, with interventions applied earlier in the disease—ideally in the pre-symptomatic stages—to prevent structural and functional decline rather than reactive attempts to stabilize or slow progression once vision is adversely affected. Such an approach incorporates new and emerging technology to improve diagnosis, and more active patient monitoring to detect subtle evidence of progression before visual function declines. The goal of interventional keratoconus is to proactively identify, treat, and monitor patients with keratoconus throughout their lives and disease course to prevent visual dysfunction and preserve quality of life.

A Call to Action: Implementing Interventional Keratoconus Management

The paradigm shift to early corneal cross-linking to preserve visual function and quality of life for patients with keratoconus mandates a broader shift in our approach to the disease. In addition to individualized clinical care at the patient level, we must develop a broader strategy for addressing the impact of keratoconus on society as a public health issue. Such a shift starts with a redesign of clinical pathways to incorporate early diagnosis and cross-linking to prevent avoidable vision loss. This in turn requires the development of cost-effective targeted screening strategies, in the future perhaps incorporating artificial intelligence to parse the multi-modal data arising from various diagnostic modalities. Educational initiatives will be necessary for all eyecare providers—both ophthalmologists and optometrists—to identify and screen at-risk individuals and recommend early treatment rather than following these patients, waiting for them to progress. Likewise, patient awareness campaigns and education regarding the impact of eye rubbing as well as identifying patients at risk and empower them to self-advocacy for screening. This may include public service announcements distributed via both traditional and social media, as well as an awareness month as has been implemented for other eye conditions. For instance, January is Glaucoma Awareness Month, when multiple stakeholders from industry partners to private foundations to the American Glaucoma Society and the American Academy of Ophthalmology actively promote glaucoma awareness and screening. A similar approach to keratoconus could significantly increase awareness and screening among at-risk individuals. Such efforts are ongoing. For instance, the National Keratoconus Foundation has proclaimed November 10 as World Keratoconus Day as a means of raising awareness about keratoconus as well as to support and advocate for those living with keratoconus. Additionally if mass screening is the future state for diagnosing keratoconus, working with our pediatrician and allergist colleagues as well as working with local schools may ultimately increase early detection rates once mass screening tools are more widely available.

In combination with these patient-centered activities, there must be parallel advocacy for changes in health policy to provide coverage for screening and treatment costs associated with diagnosis and treatment of keratoconus. Waiting to treat patients with a high likelihood of progression, or those with already advanced progression, is poor preventive medicine. Specifically, corneal cross-linking coverage should be widely available early in the course of the disease, before symptoms appear, and with or without documented disease progression. The case for broader insurance coverage could be bolstered by more robust economic models describing both the direct and indirect costs of the disease and its consequences at both the patient and the society level, as well as the expected savings from early, effective case detection and intervention. The introduction of a diagnostic code for keratoconus suspects in the International Classification of Disease-10 system and a keratoconus screening code in the Current Procedural Terminology system would further enhance efforts to identify and treat early cases. The evidence to support these system-wide changes in our approach to keratoconus would be strengthened by additional research to refine screening performance, quantify long-term clinical outcomes, and model costs and savings associated with comprehensive screening and management.

Summary and Conclusion

Keratoconus is an under-diagnosed but important cause of irreversible vision loss in young and working-age adults with a profound effect on quality of vision and quality of life. Corneal cross-linking effectively stabilizes the disease and prevents vision loss, and it is most beneficial when applied early in the course of the disease before irreversible corneal structural changes occur. Early diagnosis is often challenging due to lack of symptoms and signs when treatment is most effective, and/or to the lack of a corneal tomographer or topographer. Innovation in ocular imaging and application of artificial intelligence enhance early detection and identify patients most likely to benefit from treatment. Once keratoconus is diagnosed, the availability of a new epithelium-on oxygen-enriched topical drug therapy may be able to arrest its progression sooner with a single administration. A proactive public health approach is imperative to identify and treat patients with early keratoconus to prevent avoidable vision loss and preserve quality of life. A paradigm shift for the condition including diagnosis and treatment with less invasive epithelium-on options is critical for the future of patients and doctors treating this condition. This shift will also include provider education to improve screening and detection rates, patient awareness to encourage self-advocacy, expansion of insurance coverage for both screening and treatment, and ongoing robust research to quantify the societal costs and savings of comprehensive interventional keratoconus management.

Acknowledgments

The authors received no compensation for their work on this manuscript. The authors would like to thank Dr. Dana M. Hornbeak, MD, MPH (Glaukos Corporation) and Dr. Tony Realini, MD, MPH (Hypotony Holdings LLC; funded by Glaukos Corporation) for medical writing and editing support.

Disclosure

Dr Kathryn M. Hatch reports non-financial support from Glaukos, during the conduct of the study; is a consultant and stockholder of Glaukos and EpiON, outside the submitted work; and has a patent “AI screener to keratoconus” pending to Tilleron. Dr. Eric Donnenfeld is a consultant to Alcon, Bausch + Lomb, Glaukos, and Johnson & Johnson, outside the submitted work. Dr. Andrew S. Morgenstern is an advisory board member for LENZ, Virtual Field/Carrot, and EpiON, and is a consultant for Glaukos, outside the submitted work. Dr Mitch J. Ibach is a consultant and speaker for Glaukos, outside the submitted work. The authors report no other conflicts of interest in this work.

References

1. Gomes JA, Rapuano CJ, Belin MW, Ambrosio R Jr.; Group of Panelists for the Global Delphi Panel of K, Ectatic D. Global consensus on keratoconus diagnosis. *Cornea*. 2015;34(12):e38–e39. doi:10.1097/ICO.0000000000000623
2. Santodomingo-Rubido J, Carracedo G, Suzaki A, Villa-Collar C, Vincent SJ, Wolffsohn JS. Keratoconus: an updated review. *Cont Lens Anterior Eye*. 2022;45(3):101559. doi:10.1016/j.clae.2021.101559
3. Kandel H, Pesudovs K, Watson SL. Measurement of quality of life in keratoconus. *Cornea*. 2020;39(3):386–393. doi:10.1097/ICO.0000000000002170

4. Hofstetter HW. A keratoscopic survey of 13,395 eyes. *Am J Optom Arch Am Acad Optom*. 1959;36(1):3–11. doi:10.1097/00006324-195901000-00002
5. Kennedy RH, Bourne WM, Dyer JA. A 48-year clinical and epidemiologic study of keratoconus. *Am J Ophthalmol*. 1986;101(3):267–273. doi:10.1016/0002-9394(86)90817-2
6. Reeves SW, Ellwein LB, Kim T, Constantine R, Lee PP. Keratoconus in the Medicare population. *Cornea*. 2009;28(1):40–42. doi:10.1097/ICO.0b013e3181839b06
7. Lopes-Junior LC, Ferraz VEF, Lima RAG, et al. Health policies for rare disease patients: a scoping review. *Int J Environ Res Public Health*. 2022;19(22). doi:10.3390/ijerph192215174
8. Gov.UK. The UK rare disease framework. Available from: https://www.gov.uk/government/publications/uk-rare-diseases-framework/the-uk-rare-diseases-framework#introduction. Accessed May 23, 2025.
9. Singh RB, Parmar UPS, Jhanji V. Prevalence and economic burden of keratoconus in the United States. *Am J Ophthalmol*. 2024;259:71–78. doi:10.1016/j.ajo.2023.11.009
10. Harthan JS, Gelles JD, Block SS, et al. Prevalence of keratoconus based on scheimpflug corneal tomography metrics in a pediatric population from a Chicago-based school age vision clinic. *Eye Contact Lens*. 2024;50(3):121–125. doi:10.1097/ICL.0000000000001072
11. Flockerzi E, Xanthopoulou K, Goebels SC, et al. Keratoconus staging by decades: a baseline ABCD classification of 1000 patients in the Homburg Keratoconus Center. *Br J Ophthalmol*. 2021;105(8):1069–1075. doi:10.1136/bjophthalmol-2020-316789
12. Henriquez MA, Hadid M, Izquierdo L Jr. A systematic review of subclinical keratoconus and forme fruste keratoconus. *J Refract Surg*. 2020;36(4):270–279. doi:10.3928/1081597X-20200212-03
13. Durakovic E, Kandel H, Watson SL. Mental health impact of keratoconus: a systematic review. *Cornea*. 2023;42(9):1187–1197. doi:10.1097/ICO.0000000000003263
14. Moshfeghinia R, Arman A, Sobhi N, Mahmoudinezhad G, Molavi Vardanjani H. Depression among keratoconus patients: a systematic review and meta-analysis. *Front Public Health*. 2024;12:1477411. doi:10.3389/fpubh.2024.1477411
15. Al Zabadi H, Shehadeh M, Amro L, Ghattass N, Taha I. Vision-related quality of life among patients with keratoconus: a cross sectional study. *Front Med*. 2023;10:1208911. doi:10.3389/fmed.2023.1208911
16. Mangione CM, Lee PP, Gutierrez PR, Spritzer K, Berry S, Hays RD. Development of the 25-item National Eye Institute Visual Function Questionnaire. *Arch Ophthalmol*. 2001;119(7):1050–1058.
17. Kymes SM, Walline JJ, Zadnik K, Gordon MO. Quality of life in keratoconus. *Am J Ophthalmol*. 2004;138(4):527–535.
18. Kymes SM, Walline JJ, Zadnik K, Sterling J, Gordon MO. Changes in the quality-of-life of people with keratoconus. *Am J Ophthalmol*. 2008;145(4):611–617e1.
19. Wolle MA, Randleman JB, Woodward MA. Complications of refractive surgery: ectasia after refractive surgery. *Int Ophthalmol Clin*. 2016;56(2):127–139. doi:10.1097/IIO.0000000000000102
20. Salman A, Darwish T, Badla AA, et al. Prevalence of keratoconus and keratoconus suspect among patients seeking refractive surgery in Syria. *Middle East Afr J Ophthalmol*. 2022;29(4):181–185. doi:10.4103/meajo.meajo_50_23
21. Toprak I, Vega A, Alio Del Barrio JL, Espla E, Cavas F, Alio JL. Diagnostic value of corneal epithelial and stromal thickness distribution profiles in forme fruste keratoconus and subclinical keratoconus. *Cornea*. 2021;40(1):61–72. doi:10.1097/ICO.0000000000002435
22. Martinez-Abad A, Pinero DP. New perspectives on the detection and progression of keratoconus. *J Cataract Refract Surg*. 2017;43(9):1213–1227. doi:10.1016/j.jcrs.2017.07.021
23. Song P, Ren S, Liu Y, Li P, Zeng Q. Detection of subclinical keratoconus using a novel combined tomographic and biomechanical model based on an automated decision tree. *Sci Rep*. 2022;12(1):5316. doi:10.1038/s41598-022-09160-6
24. Gideon Abou Said A, Gispets J, Shneor E. Strategies for early keratoconus diagnosis: a narrative review of evaluating affordable and effective detection techniques. *J Clin Med*. 2025;14(2). doi:10.3390/jcm14020460
25. Askarian B, Chong JW, Tabei F, Askarian A. An affordable and easy-to-use diagnostic method for keratoconus detection using a smartphone. In: Mori K, Petrick N, editors. *Medical Imaging 2018: Computer-Aided Diagnosis*. Society of Photo-Optical Instrumentation Engineers; 2018.
26. American Academy of Ophthalmology. Corneal ectasia preferred practice pattern; 2023.
27. Omar IAN. Keratoconus screening among myopic children. *Clin Ophthalmol*. 2019;13:1909–1912. doi:10.2147/OPTH.S225326
28. Ozalp O, Atalay E, Yildirim N. Prevalence and risk factors for keratoconus in a university-based population in Turkey. *J Cataract Refract Surg*. 2021;47(12):1524–1529. doi:10.1097/j.jcrs.0000000000000669
29. Almusawi LA, Hamied FM. Risk factors for development of keratoconus: a matched pair case-control study. *Clin Ophthalmol*. 2021;15:3473–3479. doi:10.2147/OPTH.S248724
30. Hashemi H, Heydarian S, Hooshmand E, et al. The prevalence and risk factors for keratoconus: a systematic review and meta-analysis. *Cornea*. 2020;39(2):263–270. doi:10.1097/ICO.0000000000002150
31. Al-Amri AM. Prevalence of keratoconus in a refractive surgery population. *J Ophthalmol*. 2018;2018:5983530. doi:10.1155/2018/5983530
32. Althomali TA, Al-Qurashi IM, Al-Thagafi SM, Mohammed A, Almalki M. Prevalence of keratoconus among patients seeking laser vision correction in Taif area of Saudi Arabia. *Saudi J Ophthalmol*. 2018;32(2):114–118. doi:10.1016/j.sjopt.2017.11.003
33. Gilevska F, Kostovska B, Osmani I, et al. Prevalence of keratoconus in refractive surgery practice population in North Macedonia. *Int Ophthalmol*. 2022;42(10):3191–3198. doi:10.1007/s10792-022-02319-0
34. Bevara A, Vaddavalli PK. The evolution of diagnostics for keratoconus: from ophthalmometry to biomechanics. *Semin Ophthalmol*. 2023;38(3):265–274. doi:10.1080/08820538.2022.2152716
35. Toprak I, Cavas F, Velazquez JS, Alio Del Barrio JL, Alio JL. Subclinical keratoconus detection with three-dimensional (3-D) morphogeometric and volumetric analysis. *Acta Ophthalmol*. 2020;98(8):e933–e942. doi:10.1111/aos.14433
36. Kuo AN, Cortina MS, Greiner MA, et al. Advanced corneal imaging in keratoconus: a report by the American academy of ophthalmology. *Ophthalmology*. 2024;131(1):107–121. doi:10.1016/j.ophtha.2023.07.030
37. Wang X, Maeno S, Wang Y, et al. Early diagnosis of keratoconus using corneal biomechanics and OCT derived technologies. *Eye Vis*. 2025;12(1):18. doi:10.1186/s40662-025-00435-3

38. Owusu S, Zaabaar E, Kwarteng MA, Ankamah S, Abowine JBV, Kyei S. Scheimpflug-derived keratometric, pachymetric and pachymetric progression indices in the diagnosis of keratoconus: a systematic review and meta-analysis. *Clin Ophthalmol*. 2023;17:3941–3964. doi:10.2147/OPTH.S436492
39. Gomes JA, Tan D, Rapuano CJ, et al. Global consensus on keratoconus and ectatic diseases. *Cornea*. 2015;34(4):359–369. doi:10.1097/ICO.0000000000000408
40. Belin MW, Kundu G, Shetty N, Gupta K, Mullick R, Thakur P. ABCD: a new classification for keratoconus. *Indian J Ophthalmol*. 2020;68(12):2831–2834. doi:10.4103/ijo.IJO_2078_20
41. Dutra BAL, Hammoud B, Susanna BN, et al. Epithelial mapping efficacy for subclinical keratoconus identification. *Am J Ophthalmol*. 2025;274:209–220. doi:10.1016/j.ajo.2025.02.042
42. Koh S, Inoue R, Ambrosio R Jr, et al. Corneal layer thickness mapping with optical coherence tomography in different stages reveals pathologic processes of keratoconus. *Cornea*. 2024. doi:10.1097/ICO.0000000000003693
43. Kenia VP, Kenia RV, Maru S, Pirdankar OH. Role of corneal epithelial mapping, Corvis biomechanical index, and artificial intelligence-based tomographic biomechanical index in diagnosing spectrum of keratoconus. *Oman J Ophthalmol*. 2023;16(2):276–280. doi:10.4103/ojo.ojo_336_22
44. Ning R, Yang Y, Xu H, et al. Precision of corneal aberrometric measurements with a new hybrid device and comparison with a scheimpflug/placido topography in different grades of keratoconus. *J Refract Surg*. 2025;41(5):e460–e471. doi:10.3928/1081597X-20250401-03
45. Herber R, Ramm L, Spoerl E, Raiskup F, Pillunat LE, Terai N. Assessment of corneal biomechanical parameters in healthy and keratoconic eyes using dynamic bidirectional applanation device and dynamic Scheimpflug analyzer. *J Cataract Refract Surg*. 2019;45(6):778–788. doi:10.1016/j.jcrs.2018.12.015
46. Labib KM, Ghumman H, Jain S, Jarstad JS. Applications of artificial intelligence in ophthalmology: glaucoma, cornea, and oculoplastics. *Cureus*. 2024;16(11):e73522. doi:10.7759/cureus.73522
47. Accardo PA, Pensiero S. Neural network-based system for early keratoconus detection from corneal topography. *J Biomed Inform*. 2002;35(3):151–159. doi:10.1016/s1532-0464(02)00513-0
48. Muhsin ZJ, Qahwaji R, Ghafir I, et al. Advances in machine learning for keratoconus diagnosis. *Int Ophthalmol*. 2025;45(1):128. doi:10.1007/s10792-025-03496-4
49. Ferreira-Mendes J, Lopes BT, Faria-Correia F, Salomao MQ, Rodrigues-Barros S, Ambrosio R Jr. Enhanced ectasia detection using corneal tomography and biomechanics. *Am J Ophthalmol*. 2019;197:7–16. doi:10.1016/j.ajo.2018.08.054
50. Segal O, Barkana Y, Hourovitz D, et al. Scleral contact lenses may help where other modalities fail. *Cornea*. 2003;22(4):308–310. doi:10.1097/00003226-200305000-00006
51. Shorter E, Schornack M, Harthan J, et al. Keratoconus patient satisfaction and care burden with corneal gas-permeable and scleral lenses. *Optom Vis Sci*. 2020;97(9):790–796. doi:10.1097/OPX.0000000000001565
52. Niziol LM, Musch DC, Gillespie BW, Marcotte LM, Sugar A. Long-term outcomes in patients who received a corneal graft for keratoconus between 1980 and 1986. *Am J Ophthalmol*. 2013;155(2):213–219e3. doi:10.1016/j.ajo.2012.08.001
53. Kelly TL, Williams KA, Coster DJ; Australian Corneal Graft R. Corneal transplantation for keratoconus: a registry study. *Arch Ophthalmol*. 2011;129(6):691–697. doi:10.1001/archophthalmol.2011.7
54. Kelly TL, Coster DJ, Williams KA. Repeat penetrating corneal transplantation in patients with keratoconus. *Ophthalmology*. 2011;118(8):1538–1542. doi:10.1016/j.ophtha.2011.01.002
55. Janiszewska-Bil D, Czarnota-Nowakowska B, Krysik K, et al. Comparison of long-term outcomes of the lamellar and penetrating keratoplasty approaches in patients with keratoconus. *J Clin Med*. 2021;10(11). doi:10.3390/jcm10112421
56. Spoerl E, Huhle M, Seiler T. Induction of cross-links in corneal tissue. *Exp Eye Res*. 1998;66(1):97–103. doi:10.1006/exer.1997.0410
57. Raiskup F, Spoerl E. Corneal crosslinking with riboflavin and ultraviolet A. Part II. Clinical indications and results. *Ocular Surf*. 2013;11(2):93–108. doi:10.1016/j.jtos.2013.01.003
58. Wittig-Silva C, Chan E, Islam FM, Wu T, Whiting M, Snibson GR. A randomized, controlled trial of corneal collagen cross-linking in progressive keratoconus: three-year results. *Ophthalmology*. 2014;121(4):812–821. doi:10.1016/j.ophtha.2013.10.028
59. Tasci YY, Taslipinar G, Eyidogan D, Sarac O, Cagil N. Five-year long-term results of standard collagen cross-linking therapy in patients with keratoconus. *Turk J Ophthalmol*. 2020;50(4):200–205. doi:10.4274/tjo.galenos.2020.53810
60. Nughays RO, Bazayd AS, Alshamekh LA, et al. Efficacy and safety of epi-on vs epi-off corneal cross-linking in corneal ectasia: a systematic review and meta-analysis of randomized controlled trials. *Clin Ophthalmol*. 2025;19:1531–1541. doi:10.2147/OPTH.S508618
61. D'Oria F, Palazon A, Alio JL. Corneal collagen cross-linking epithelium-on vs. epithelium-off: a systematic review and meta-analysis. *Eye Vis*. 2021;8(1):34. doi:10.1186/s40662-021-00256-0
62. Ng SM, Ren M, Lindsley KB, Hawkins BS, Kuo IC. Transepithelial versus epithelium-off corneal crosslinking for progressive keratoconus. *Cochrane Database Syst Rev*. 2021;3(3):CD013512. doi:10.1002/14651858.CD013512.pub2
63. Ng SM, Hawkins BS, Kuo IC. Transepithelial versus epithelium-off corneal crosslinking for progressive keratoconus: findings from a cochrane systematic review. *Am J Ophthalmol*. 2021;229:274–287. doi:10.1016/j.ajo.2021.05.009
64. Borchert GA, Kandel H, Watson SL. Epithelium-on versus epithelium-off corneal collagen crosslinking for keratoconus: a systematic review and meta-analysis. *Graefes Arch Clin Exp Ophthalmol*. 2024;262(6):1683–1692. doi:10.1007/s00417-023-06287-8
65. Jaruseviciene R, Tamuleviciute R, Galgauskas S. Corneal cross-linking in keratoconus: comparative analysis of standard, accelerated and transepithelial protocols. *J Clin Med*. 2026;15(2). doi:10.3390/jcm15020490
66. Alajmi TS, Alasmari FF, Alasmari TF, et al. Comparison of epithelium-off versus iontophoresis-assisted transepithelial corneal collagen cross-linking in keratoconus: a systematic review and meta-analysis. *Int Ophthalmol*. 2026;46(1):107. doi:10.1007/s10792-026-03977-0
67. Greenstein SA, Yu AS, Gelles JD, Huang S, Hersh PS. Long-term outcomes after corneal cross-linking for progressive keratoconus and corneal ectasia: a 10-year follow-up of the pivotal study. *Eye Contact Lens*. 2023;49(10):411–416. doi:10.1097/ICL.0000000000001018
68. Cehelyk EK, Syed ZA. Long-term outcomes of corneal crosslinking. *Curr Opinion Ophthalmol*. 2024;35(4):315–321. doi:10.1097/ICU.0000000000001054
69. Derakhshan A, Heravian J, Abdolahian M, Bamdad S. Long-term outcomes of collagen crosslinking for early keratoconus. *J Ophthalmic Vis Res*. 2021;16(2):151–157. doi:10.18502/jovr.v16i2.9077

70. Malleron V, Bloch F, Zevering Y, et al. Evolution of corneal transplantation techniques and their indications in a French corneal transplant unit in 2000–2020. *PLoS One*. 2022;17(4):e0263686. doi:10.1371/journal.pone.0263686
71. Godefrooij DA, Gans R, Imhof SM, Wisse RP. Nationwide reduction in the number of corneal transplantations for keratoconus following the implementation of cross-linking. *Acta Ophthalmol*. 2016;94(7):675–678. doi:10.1111/aos.13095
72. Sandvik GF, Thorsrud A, Raen M, Ostern AE, Saethre M, Drolsum L. Does corneal collagen cross-linking reduce the need for keratoplasties in patients with keratoconus? *Cornea*. 2015;34(9):991–995. doi:10.1097/ICO.0000000000000460
73. Sarezky D, Orlin SE, Pan W, VanderBeek BL. Trends in Corneal Transplantation in Keratoconus. *Cornea*. 2017;36(2):131–137. doi:10.1097/ICO.0000000000001083
74. Takahashi A, Yamaguchi T, Tomida D, Nishisako S, Sasaki C, Shimazaki J. Trends in surgical procedures and indications for corneal transplantation over 27 years in a tertiary hospital in Japan. *Jpn J Ophthalmol*. 2021;65(5):608–615. doi:10.1007/s10384-021-00849-1
75. Chilibeck CM, Brookes NH, Gokul A, et al. Changing trends in corneal transplantation in Aotearoa/New Zealand, 1991 to 2020: effects of population growth, cataract surgery, endothelial keratoplasty, and corneal cross-linking for keratoconus. *Cornea*. 2022;41(6):680–687. doi:10.1097/ICO.0000000000002812
76. Aydin Kurna S, Altun A, Gencaga T, Akkaya S, Sengor T. Vision related quality of life in patients with keratoconus. *J Ophthalmol*. 2014;2014:694542. doi:10.1155/2014/694542
77. Steinberg J, Bussmann N, Frings A, Katz T, Druchkiv V, Linke SJ. Quality of life in stable and progressive 'early-stage' keratoconus patients. *Acta Ophthalmol*. 2021;99(2):e196–e201. doi:10.1111/aos.14564
78. Angelo L, Gokul A, Samuels I, McGhee CN, Ziaei M. Patient evaluated economic impact of keratoconus in New Zealand. *Clin Exp Optom*. 2024;1–6. doi:10.1080/08164622.2024.2410026
79. Panthier C, Moran S, Bourges JL. Evaluation of vision-related quality of life in keratoconus patients, and associated impact of keratoconus severity indicators. *Graefes Arch Clin Exp Ophthalmol*. 2020;258(7):1459–1468. doi:10.1007/s00417-020-04680-1
80. Steinberg J, Fischer P, Frings A, Druchkiv V, Katz T, Linke SJ. Quality of life in patients with progressive keratoconus treated with corneal collagen crosslinking. *Int Ophthalmol*. 2025;45(1):103. doi:10.1007/s10792-024-03400-6
81. Yildiz EH, Cohen EJ, Virdi AS, Hammersmith KM, Laibson PR, Rapuano CJ. Quality of life in keratoconus patients after penetrating keratoplasty. *Am J Ophthalmol*. 2010;149(3):416–22e1–2. doi:10.1016/j.ajo.2009.10.005
82. Greenstein SA, Yu AS, Gelles JD, Eshraghi H, Hersh PS. Corneal tissue addition keratoplasty: new intrastromal inlay procedure for keratoconus using femtosecond laser-shaped preserved corneal tissue. *J Cataract Refract Surg*. 2023;49(7):740–746. doi:10.1097/j.jcrs.0000000000001187
83. Tlaiss Y, Warrak J, Warrak E. Intrastromal corneal ring segments for keratoconus: a comprehensive review of different types. *Ther Adv Ophthalmol*. 2025;17:25158414251371521. doi:10.1177/25158414251371521