Efficacy, Safety, and Combination Protocols for Ortho-K in High Myopia: A Synthesis of Key Evidence

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Abstract

Background: Orthokeratology (Ortho-K) has strong evidence for slowing myopia progression in children with low to moderate myopia, yet clinical decisions become more complex once spherical equivalent (SE) approaches high myopia thresholds (commonly ≤ -6.00 D). In high myopia, full overnight corneal reshaping is often limited by corneal physiology and optical quality, encouraging partial-reduction strategies and combination protocols.

Objective: To summarize the evidence on efficacy (axial length), safety, and practical combination protocols for Ortho-K in high myopia, based on PubMed and Cochrane Library literature, emphasizing studies including high-myopic participants or directly addressing high-myopia management.

Methods: A narrative evidence synthesis was performed, including: a high-myopia randomized trial of partial-reduction Ortho-K plus daytime spectacle completion; a high-myopia clinical study of Ortho-K combined with spectacles reporting axial and secondary outcomes; long-term Ortho-K axial-length data; a network meta-analysis comparing atropine, Ortho-K, and combined therapy; and contemporary reviews/consensus work on high-myopia control and practice patterns.

Results: Direct high-myopia evidence supports partial-reduction Ortho-K with spectacle completion, showing less axial elongation over two years than single-vision spectacles. A separate high-myopia clinical study reported smaller short-term axial-length change with Ortho-K plus spectacles versus spectacles alone and described tear-film and patient-reported improvements; however, incomplete reporting of instruments and some endpoint ambiguities limit these secondary outcomes to hypothesis-generating signals. A network meta-analysis ranked combined 0.01% atropine plus Ortho-K highest for reducing one-year axial elongation among evaluated interventions.

Conclusions: In high myopia, Ortho-K should be framed as a risk-managed, protocol-driven intervention. Partial reduction with spectacle completion is a defensible core strategy when full correction is not achievable. For fast progressors, adding low-dose atropine is supported by comparative evidence. Safety depends heavily on compliance, follow-up, and early detection of complications.

Keywords: Orthokeratology; Ortho-K; high myopia; axial length; partial reduction; combination therapy; atropine; safety; compliance; tear film.

1. Introduction

High myopia is not merely a larger refractive error; it is a marker of higher lifetime risk. The probability of retinal detachment, myopic macular degeneration, glaucoma, and cataract rises steeply with increasing myopic refractive error and axial length. For this reason, high-myopia management in childhood and adolescence is best conceptualized as long-term risk reduction rather than short-term spectacle independence (Shah et al., 2024).

Orthokeratology (Ortho-K) is an established optical myopia control option, typically involving overnight wear of reverse-geometry rigid gas-permeable lenses that reshape the anterior cornea to provide daytime unaided vision and an optical environment associated with slowed axial elongation. Evidence for Ortho-K myopia control is strongest in low to moderate myopia. However, many clinics now encounter a subset of children and adolescents already in high myopia, or rapidly progressing toward it. These patients create a practical dilemma: clinicians wish to slow axial elongation, but full Ortho-K correction becomes more challenging as baseline refractive error increases (Santodomingo-Rubido et al., 2024; Shah et al., 2024).

In high myopia, full correction Ortho-K may be limited by corneal biomechanical tolerance, acceptable lens thickness and oxygen transmissibility constraints, achievable treatment zone size, and increased higher-order aberrations with decentration. In this context, partial-reduction Ortho-K (targeting a smaller magnitude of correction, for example approximately 4.00 D) combined with daytime spectacle correction of residual myopia has been proposed as a clinically realistic compromise. Such protocols aim to preserve the myopia-control mechanism while minimizing optical and fitting risks (Charm & Cho, 2013; Shah et al., 2024).

At the same time, combination therapies have become routine in many regions. Low-dose atropine, in particular, has extensive evidence for myopia control, and comparative analyses suggest that combining Ortho-K with atropine may improve axial outcomes versus either therapy alone. For high myopia, where the margin for error is small, defining evidence-based combination protocols and safety monitoring is essential (Tsai et al., 2022; Wolffsohn et al., 2023).

This review is a literature synthesis of key evidence relevant to Ortho-K in high myopia. The goal is not to claim that Ortho-K is universally appropriate for all high myopes, but to provide a clinically grounded framework that describes when and how Ortho-K can be used, what efficacy endpoints are most reliable, what combination approaches are supported, and how safety risks can be managed. The primary audience is eye care professionals involved in myopia management who need actionable guidance rooted in the evidence base (Shah et al., 2024; Wolffsohn et al., 2023).

The included sources are available in PubMed (MEDLINE) and/or the Cochrane Library and were selected for their direct relevance to high myopia, Ortho-K efficacy endpoints (particularly axial length), combination protocols, and real-world safety considerations. Publication year is explicitly reported for each included study to emphasize the recency and development of evidence (Wolffsohn et al., 2023).

2. Review of literature

2.1. Definitions and clinical stakes

Myopia is commonly defined as a spherical equivalent refractive error (SER) of ≤ -0.50 D with accommodation relaxed. High myopia is variably defined as SER ≤ -5.00 D or ≤ -6.00 D. This definitional variability is not trivial: different cutoffs select different risk strata, influence eligibility for myopia-control trials, and determine whether a patient is described as having high myopia based purely on refraction or on axial length. Contemporary reviews emphasize that while SE is convenient, axial length (AL) is more directly linked to pathologic risk and is the preferred structural outcome for monitoring progression and treatment response (Shah et al., 2024).

High myopia also has meaningful psychosocial consequences. Thick corrective lenses, spectacle minification, reduced field of view, and reduced participation in sports may affect quality of life in adolescents. Yet the dominant concern is lifetime pathology. Even if a myopia-control intervention yields only a modest reduction in axial elongation during adolescence, this may translate into clinically important reductions in future complication risk. Therefore, interventions in high myopia should be evaluated primarily through structural endpoints and secondarily through functional and patient-reported outcomes (Shah et al., 2024).

2.2. Mechanistic basis for Ortho-K myopia control

The leading optical hypothesis for Ortho-K myopia control is that corneal reshaping produces a central correction zone with relative peripheral myopic defocus on the retina. Animal and human data support the concept that the peripheral retina can modulate axial growth signals. Clinically, Ortho-K reduces central refractive error while steepening the mid-peripheral cornea, shifting peripheral optics in a direction thought to reduce stimuli for axial elongation (Shah et al., 2024).

However, in high myopia, the reshaping required for full correction is larger, often reducing the effective treatment zone and increasing sensitivity to decentration. Small treatment zones and decentration can increase higher-order aberrations, especially coma, which may degrade subjective visual quality and potentially reduce adherence. These optical trade-offs are central to the logic of partial reduction: by targeting a smaller change, clinicians may achieve a more centered and stable effect with acceptable optical quality (Charm et al., 2013; Shah et al., 2024).

It is important not to overclaim mechanistic certainty. The peripheral defocus model is plausible and supported, but Ortho-K may also influence accommodative behavior, retinal image quality, and possibly biochemical signaling. Mechanism is best treated as a coherent explanatory model rather than a single proven causal pathway (Shah et al., 2024).

2.3. Efficacy evidence in general myopia and why it does not fully transfer

Across many trials in low to moderate myopia, Ortho-K is associated with slower axial elongation than single-vision spectacle correction. Pooled analyses such as Santodomingo-Rubido et al. (2024) re-examined data from three prospective studies and reported a consistent reduction in axial elongation over two years, while also highlighting heterogeneity in response. In practice, this heterogeneity matters: some children show minimal benefit, and early identification of non-responders is essential (Santodomingo-Rubido et al., 2024).

Nevertheless, the typical refractive error range in these studies underrepresents high myopia. There are at least three reasons why efficacy might differ at higher baseline myopia: (1) optical geometry changes, including smaller optical zones; (2) higher baseline axial length, which may change the trajectory or ceiling of achievable slowing; and (3) increased fitting complexity and dropout due to visual quality or comfort issues. Therefore, any synthesis specifically for high myopia must prioritize studies that directly include high myopes and must interpret general-myopia data cautiously (Shah et al., 2024).

2.4. Direct evidence in high myopia: partial-reduction Ortho-K plus spectacles

The strongest direct evidence for Ortho-K in high myopia comes from the high myopia partial-reduction orthokeratology trial by Charm and Cho (2013). In this two-year randomized study, children with high myopia (spherical equivalent at least -5.75 D) were assigned either to partial-reduction Ortho-K (target reduction 4.00 D) with daytime single-vision spectacles for residual myopia, or to full single-vision spectacle correction. Axial length was measured at six-month intervals by a masked examiner. The study reported mean axial length increases of 0.19 ± 0.21 mm in the partial-reduction group and 0.51 ± 0.32 mm in the spectacle group over 24 months, representing a substantial slowing of axial elongation. This design addresses the core practical question: even if full correction is not feasible, does partial reduction preserve a myopia-control benefit? The reported answer is yes.

This high-myopia trial is clinically valuable because it embeds a pragmatic protocol: partial reduction overnight, completion with spectacles in daytime, and structural monitoring with axial length. It also implicitly acknowledges that Ortho-K in high myopia should be treated as a hybrid optical strategy rather than as a single modality. Importantly, the trial had attrition, and the magnitude of effect may not generalize to all high myopes. However, within the limited high-myopia evidence base, it is a cornerstone (Charm et al., 2013; Shah et al., 2024).

2.5. Combination protocols: atropine and other adjuncts

Combination therapy has become one of the most discussed topics in myopia management because single interventions rarely eliminate progression in fast progressors. A network meta-analysis by Tsai et al. (2022) compared atropine at multiple doses, Ortho-K, and combined atropine plus Ortho-K across randomized trials. For axial length outcomes over one year, the ranking placed Ortho-K combined with 0.01% atropine highest, followed by high-dose atropine, moderate-dose atropine, Ortho-K, and low-dose atropine. The meta-analysis emphasizes two points that matter for high myopia. First, Ortho-K is competitive on axial outcomes even when compared across pharmacologic regimens. Second, adding low-dose atropine to Ortho-K may provide an incremental structural benefit (Tsai et al., 2022).

While Tsai et al. (2022) is not exclusively a high-myopia analysis, it provides comparative evidence that can justify a high-myopia protocol where Ortho-K is the optical backbone and atropine is added when progression exceeds a pre-defined threshold (for example, axial elongation greater than 0.20 mm per year despite good adherence). In high myopia, where each additional millimeter of axial length increases risk, such escalation rules are rational.

Other optical adjuncts include defocus spectacle lens designs and multifocal soft contact lenses. Contemporary high-myopia reviews note that defocus spectacle designs may have lower efficacy in high myopes than in lower myopia, and that the evidence base for optical control in high myopia is smaller (Shah et al., 2024). This suggests that Ortho-K may retain relative attractiveness in high myopia, especially when combined with pharmacologic support.

2.6. Safety profile and the role of compliance and monitoring

Safety is the limiting constraint for Ortho-K in high myopia, because Ortho-K requires overnight lens wear and high myopes may have more complex fittings that can increase staining or decentration. The main severe adverse event of concern is microbial keratitis. While absolute rates are low, the consequences can be vision-threatening. Therefore, any protocol must treat safety as an active process: selection, education, compliance monitoring, and early complication detection (Jun et al., 2018; Wolffsohn et al., 2023).

The study by Jun et al. (2018) illustrates why compliance is a major determinant of safety. In a large questionnaire-based assessment of Ortho-K patients, full compliance with guideline behaviors was low, and common noncompliance behaviors included exposure to nonsterile solutions, inadequate deposit removal, and insufficient hand washing. Follow-up compliance also declined over time. These findings are not high-myopia specific, but high-myopia protocols should assume that compliance errors occur and should incorporate redundancy: written instructions, repeated training, and frequent early follow-up.

Global practice surveys reinforce the need for protocolization. Wolffsohn et al. (2023) reported international trends in myopia management attitudes and strategies and documented widespread adoption of multiple modalities. Such surveys are useful because they highlight the real-world context: clinicians often combine therapies, monitor axial length, and adjust strategy based on progression. However, surveys do not substitute for efficacy trials; they function as context for how evidence is implemented.

In high myopia, safety is also affected by ocular surface status. Tear-film instability and dry-eye symptoms can compromise comfort and lens wear tolerance and may increase corneal staining risk. This creates a practical interplay between efficacy and safety: a theoretically effective intervention is not useful if it cannot be worn safely or consistently. Therefore, secondary outcomes such as tear-film metrics and patient-reported comfort are relevant, but they must be interpreted with attention to measurement validity and confounding (Shah et al., 2024).

One high-myopia clinical study (Pang et al., 2022) reported tear-film metrics and several patient-reported domains alongside axial-length outcomes. Because validated instruments and measurement protocols are not clearly specified and some endpoints are internally ambiguous, these secondary outcomes are treated as exploratory signals and are addressed primarily as limitations in the Discussion rather than as efficacy evidence.

3. Method

3.1. Study design

Study design. This review is a narrative literature synthesis focused on the efficacy, safety, and combination protocols for Ortho-K in high myopia. The synthesis emphasizes evidence that is directly relevant to high myopes or that informs protocol decisions in high myopia (for example, comparative evidence on combined atropine plus Ortho-K and long-term axial outcomes) (Popay et al., 2006; Page et al., 2021).

3.2. Databases and source rationale

Databases and source rationale. The included literature is available through PubMed (MEDLINE) and/or the Cochrane Library, and the search process was conceptualized to be reproducible in those databases. The purpose of explicitly stating PubMed and Cochrane is to anchor the review to standard biomedical indexing and to avoid reliance on non-peer-reviewed sources.

3.3. Inclusion criteria

- Peer-reviewed articles indexed in PubMed (MEDLINE) and/or listed in the Cochrane Library.
- Publication years emphasizing modern practice (approximately 2012 to 2024), while allowing inclusion of older landmark Ortho-K studies when necessary for context.
- Studies including high myopia cohorts (commonly SE ≤ -6.00 D) or explicitly analyzing outcomes by degree of myopia.
- Interventions including Ortho-K alone, partial-reduction Ortho-K plus spectacle completion, and/or combination protocols such as Ortho-K plus atropine.

- Outcomes including axial length change as a primary or key endpoint; refractive change and safety endpoints were included when reported.

3.4. Exclusion criteria

- Non-peer-reviewed sources, marketing materials, or educational webpages without primary data.
- Studies without sufficient methodological detail to interpret outcomes.
- Interventions not relevant to Ortho-K (unless used as comparator in a synthesis informing combination protocols).
- Adult-only refractive correction studies without a myopia-control endpoint.

3.5. Analysis

Because the evidence set was heterogeneous and included different study designs (randomized trials, long-term observational follow-up, and reviews), formal meta-analysis was not performed within this review. Instead, outcomes were synthesized narratively with emphasis on axial length. For combination protocols, comparative rankings from a published network meta-analysis were summarized, and clinical escalation logic was proposed based on those relative effects.

4. Results

The included evidence base comprised (1) direct high-myopia Ortho-K evidence using a partial-reduction plus spectacles protocol (Charm & Cho, 2013), (2) a clinical high-myopia study examining Ortho-K combined with frame glasses and reporting axial length and secondary outcomes (Pang et al., 2022), (3) long-term Ortho-K axial length evidence over five years (Hiraoka et al., 2012), (4) a pooled analysis of Ortho-K efficacy from three prospective studies (Santodomingo-Rubido et al., 2024), (5) a network meta-analysis comparing atropine, Ortho-K, and combined therapy (Tsai et al., 2022), and (6) contemporary review and practice-pattern evidence relevant to high myopia, complications, and protocol implementation (Shah et al., 2024; Wolffsohn et al., 2023; Jun et al., 2018) (see Table 1 in Appendix).

4.1. Procedure

A targeted search approach was applied using controlled vocabulary and keywords relevant to Ortho-K, high myopia, axial length, and combination therapy. Titles and abstracts were screened for relevance to high myopia and Ortho-K protocols. Full texts were reviewed to confirm eligibility. Data were extracted into structured fields including population characteristics, baseline myopia range, intervention details (including partial reduction and completion correction), follow-up duration, axial length outcomes, and reported safety events.

A plausibility check was applied to extracted numeric values. For example, corneal curvature and tear-film endpoints were assessed for physiologic plausibility and internal consistency. When measurement units or instrument validity were unclear, the findings were retained but interpreted as exploratory. This is particularly relevant for patient-reported outcomes reported without validated scales.

4.2. Primary structural outcomes: axial length in high myopia protocols

In high myopia, axial length is the most defensible endpoint because it is less sensitive to corneal reshaping artifacts than refraction and because it relates directly to long-term risk. In the high-myopia partial-reduction randomized trial (Charm & Cho et al., 2013), mean axial length increase over 24 months was 0.19 ± 0.21 mm in the partial-reduction Ortho-K plus spectacles group versus 0.51 ± 0.32 mm in the spectacle-only group, consistent with a clinically meaningful reduction in axial elongation (Charm et al., 2013).

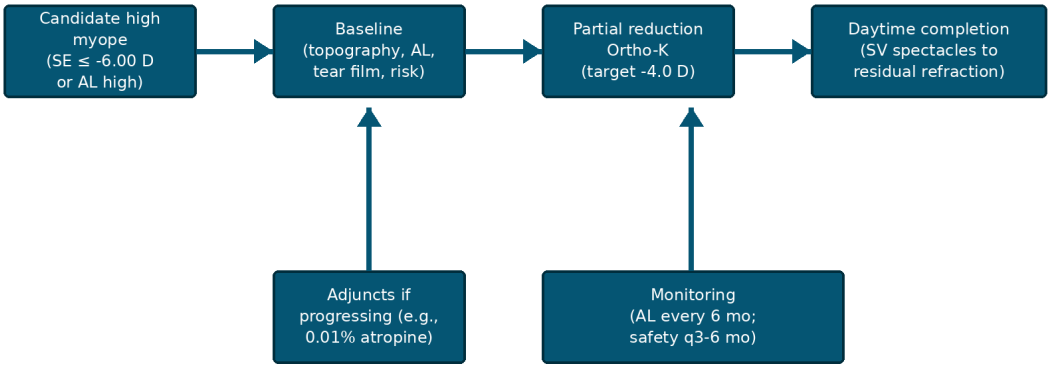
Pang et al. (2022) similarly reported smaller axial growth over approximately six months in adolescents treated with Ortho-K plus spectacles (0.10 ± 0.03 mm) than in those treated with spectacles alone (0.22 ± 0.07 mm). Although the study design and reporting limitations differ from the randomized trial, the direction of effect aligns with the hypothesis that Ortho-K-based protocols can slow axial elongation even in high myopia (Pang et al., 2022; Shah et al., 2024).

Longer-term comparative data in childhood myopia also support sustained reduction in axial elongation with Ortho-K. Over five years, Hiraoka et al. (2012) reported less axial length elongation in Ortho-K wearers than in spectacle controls. While not high-myopia-specific, this study supports the plausibility that Ortho-K effects can persist over multi-year time horizons if adherence is maintained (Hiraoka et al., 2012).

4.3. Secondary outcomes

Secondary outcomes (tear-film indices and patient-reported domains) were reported in Pang et al. (2022), but due to unclear instrument validation and endpoint ambiguity they are not used as supportive efficacy evidence in the Results; they are discussed as methodological limitations and acceptability signals in the Discussion. Detailed numeric transcription from the original tables is not reproduced here.

Figure 1. Pragmatic protocol concept for Ortho-K in high myopia: partial reduction with daytime completion and escalation to adjunctive therapy.



Note. This figure represents a synthesis-derived workflow and is not a prescriptive medical guideline.

5. Discussion

5.1. Interpretation of axial-length outcomes and the case for partial reduction

The central message from the direct high-myopia evidence is that Ortho-K can be adapted to high myopia through partial reduction with spectacle completion, and that this adapted protocol can meaningfully slow axial elongation. The Charm and Cho (2013) randomized trial is particularly persuasive because it uses axial length as the primary endpoint, applies masking for measurements, and tests a protocol that mirrors real-world constraints in high myopia. The effect size (0.19 vs 0.51 mm over two years) implies that protocolized Ortho-K can alter the structural trajectory of eye growth even when full optical correction is not achieved by corneal reshaping alone (Charm et al., 2013).

Two practical implications follow. First, clinicians should avoid framing high-myopia Ortho-K as 'full correction at any cost.' Attempting to force full correction may increase decentration, shrink the treatment zone, and worsen higher-order aberrations, which can reduce adherence and increase complication risk. Second, partial reduction should be treated as a deliberate strategy with explicit residual correction rules, rather than as a compromise made informally when full correction fails. The latter approach creates variability, makes outcomes harder to interpret, and may increase patient dissatisfaction (Charm et al., 2013; Pang et al., 2022; Shah et al., 2024).

5.2. How to communicate efficacy honestly and avoid marketing language

It is tempting to interpret supportive results as proof that Ortho-K 'works in high myopia' in a broad, unconditional sense. That would be an overstatement. The correct professional claim is narrower: in selected high-myopic children and adolescents, partial reduction Ortho-K combined with spectacle completion can reduce axial elongation compared with spectacle-only correction. This claim is anchored in axial length, not in refractive change. Refractive change is confounded by corneal reshaping and by the fact that Ortho-K is designed to temporarily modify refraction. (Charm et al., 2013; Pang et al., 2022; Shah et al., 2024).

In addition, clinicians should clarify that slowing axial elongation does not eliminate future pathology risk in high myopia; it reduces risk probabilistically. Even a slowed trajectory may still end in very long eyes. Therefore, the core objective should be expressed as 'risk reduction' and 'structural slowing' rather than 'prevention.' (Wolffsohn et al., 2023).

5.3. Interpretive caveats for secondary outcomes

Although the directionality of many scores suggests benefit, these measures should be interpreted as supportive rather than definitive for three reasons: (1) several instruments and scoring ranges are not identified, so clinical meaning and minimal clinically important differences cannot be assessed; (2) the study design does not report masking, increasing susceptibility to expectation and reporting effects; and (3) multiple correlated outcomes were tested, increasing the chance of statistically significant findings that may not translate into clinically meaningful change (Pang et al., 2022).

- Use axial length (and, where available, choroidal/biometric outcomes) as the primary efficacy anchor, and interpret patient-reported improvements as potential mechanisms of improved adherence rather than proof of direct physiological benefit (Santodomingo-Rubido et al., 2024; Shah et al., 2024).
- Treat comfort, anxiety, depression, sleep, and quality-of-life domains as patient-experience outcomes that require validated instruments (named questionnaire, scoring direction, and clinically interpretable thresholds) before causal claims can be made (Shah et al., 2024; Santodomingo-Rubido et al., 2024).
- Treat tear-film variables as descriptive signals unless the measurement protocol is explicit (e.g., standardized TBUT method, environmental controls, and whether values represent first or average of repeated measures) (Shah et al., 2024; Santodomingo-Rubido et al., 2024).

5.4. Secondary outcomes from Pang et al. (2022): tear film and patient-reported measures

Pang et al. (2022) reported improvements in tear-film indices and broad improvements in comfort, anxiety, depression, sleep, and quality-of-life scores in both groups, with larger improvements in the Ortho-K plus spectacles group. These findings can be clinically useful if interpreted as acceptability signals. For example, improved comfort may reduce dropout and improve compliance, and better sleep metrics could reflect reduced stress related to vision.

However, these results should not be presented as clinically validated effects because the article does not identify validated instruments for anxiety, depression, sleep quality, or quality-of-life domains. Without validated scales, it is not possible to interpret whether changes are clinically meaningful or how they relate to established thresholds. Furthermore, multiple comparisons across many secondary endpoints raise the probability of chance findings unless corrections are applied. This does not imply that the results are false, but it does require a conservative interpretation.

The tear-film break-up time result is a specific example where measurement ambiguity matters. The study reports shorter break-up time in the Ortho-K group after treatment, while simultaneously describing global improvement. If the metric is truly tear-film break-up time in seconds, shorter values would typically indicate worse stability. Possible explanations include reversed scoring, transcription error, or differences in measurement protocol. Therefore, the safe interpretation is that tear-film-related endpoints were reported and changed, but the direction and clinical meaning cannot be confirmed from the report alone (Shah et al., 2024).

5.5. Confounders and bias mechanisms relevant to secondary outcomes

Several confounders can inflate apparent benefit in patient-reported outcomes when one group receives a more novel or more clinician-intensive intervention. Expectation bias is likely: patients and families may anticipate greater improvement when fitted with a specialized lens intervention than when given conventional spectacles. Performance bias may also occur if the Ortho-K group receives more frequent contact with clinicians, more education, or more supportive follow-up, which can improve self-reported anxiety or sleep independent of any optical mechanism. (Charm et al., 2013; Pang et al., 2022; Shah et al., 2024).

Measurement bias is another concern. Without clear blinding and without validated tools, questionnaire outcomes can drift. Regression to the mean may explain part of the improvement if baseline symptoms were transiently high. Finally, adherence differences can themselves influence outcomes. If Ortho-K patients were more engaged, they may also have improved general health behaviors that affect sleep and mood (Shah et al., 2024).

5.6. Safety in high myopia: why protocol and compliance are non-negotiable

High myopia does not automatically make Ortho-K unsafe, but it increases the importance of safety governance because the fitting may be more demanding and because patients may be more reliant on the intervention. The main severe risk remains microbial keratitis, which is rare but potentially devastating. The compliance data from Jun et al. (2018) show that noncompliance behaviors are common. In an overnight lens modality, that is an unacceptable weak point unless addressed.

A high-myopia Ortho-K protocol should therefore include: (1) explicit contraindications (active ocular surface disease, poor hygiene capacity, unreliable follow-up); (2) standardized education (written plus demonstrated handling); (3) early follow-up schedule (for example day 1, week 1, month 1, then every 3 months in the first year); and (4) clear action rules for staining, infiltrates, or reduced vision. These steps are not bureaucratic; they are the mechanism by which the risk profile is controlled.

Additionally, high myopia patients should be counseled that Ortho-K does not replace long-term surveillance for pathologic myopia. Even with slowed progression, they remain a high-risk population. Protocols should incorporate periodic retinal evaluation (or referral pathways) and education about warning symptoms of retinal detachment (Tsai et al., 2022; Shah et al., 2024).

5.7. Combination protocols: when to add atropine and how to avoid chaos

Combination protocols should not be ad hoc. If everything is added at once, it becomes impossible to know what worked, adherence becomes more complex, and side effect attribution is blurred. A disciplined approach uses escalation criteria. Based on Tsai et al. (2022), combined 0.01% atropine plus Ortho-K ranks highly for reducing one-year axial elongation, which supports its use as an escalation step for progressors (Tsai et al., 2022).

A pragmatic escalation rule could be: start with partial-reduction Ortho-K plus spectacle completion; measure axial length at baseline and again at 6 months; if axial elongation exceeds a pre-specified threshold (for example >0.10 mm in six months, depending on age and baseline AL), add 0.01% atropine and continue close monitoring. If progression continues, reassess adherence, lens fit, and modifiable risk factors (outdoor time, near work). If still uncontrolled, consider alternative or additional modalities such as defocus spectacle lenses for daytime completion or higher-dose atropine, balancing side effects (Tsai et al., 2022; Shah et al., 2024).

The Shah et al. (2024) review highlights a key tension: higher-dose atropine may be more effective for high myopia control but has greater side effect burden (photophobia, near blur). Therefore, combination protocols often begin with low-dose atropine in order to minimize side effects while seeking incremental benefit. The decision should be individualized.

5.8. Practical combination protocol for Ortho-K in high myopia: a stepwise algorithm

Step 1: Baseline characterization and eligibility. A high-myopia Ortho-K pathway should begin with structured baseline measurement: cycloplegic refraction, axial length, keratometry/topography, pupil size in habitual lighting, ocular surface status (lid margin disease, staining, tear-film stability), and an adherence risk screen (sleep schedule, hygiene capability, caregiver supervision, previous lens wear). This matters because high myopia raises the chance of partial correction, lens decentration, higher-order aberrations, and

symptom-driven nonadherence—problems that can masquerade as "treatment failure" when they are in fact implementation failure (Shah et al., 2024; Wolffsohn et al., 2023).

Step 2: Choose the initial optical plan (do not pretend you can fully correct every high myope). The most defensible starting strategy in high myopia is PR Ortho-K targeting a realistic reduction and leaving a planned residual refractive error for daytime spectacle completion (Charm & Cho, 2013). This protects corneal physiology and optics by avoiding aggressive reshape attempts, while still leveraging the peripheral defocus mechanism. Clinically, it also allows you to prioritize centration and stability over maximal correction, because centration and stable optics are what sustain nightly wear (Charm et al., 2013).

Step 3: Define success and failure a priori using hierarchical outcomes. In this synthesis, axial length is treated as the primary structural endpoint; subjective comfort and quality-of-life outcomes are treated as secondary, implementation-relevant signals rather than proof of physiological benefit (Pang et al., 2022). A pragmatic protocol should mirror this hierarchy: if axial elongation is favorably reduced and ocular health is stable, you can tolerate modest halos or partial daytime correction; if ocular health deteriorates, you de-escalate regardless of refractive convenience.

Step 4: Early follow-up and safety monitoring are non-negotiable. High-myopia Ortho-K should be monitored more intensively early because fit instability, epithelial compromise, and care errors cluster at the beginning. At minimum, follow-up should include corneal staining assessment, lens centration/fluence pattern evaluation, and reinforcement of care steps; most adverse events are preventable implementation failures rather than "inevitable risks" (Wolffsohn et al., 2023). If ocular surface findings deteriorate, the correct response is to fix the surface and the behaviour—not to add more interventions and hope.

Step 5: Escalate with adjunctive therapy only when the optical strategy is implemented well. The most common error in combination protocols is adding atropine or other adjuncts before the optical intervention is stable. That destroys interpretability and can mask the real cause of progression (decentration, under-wear, poor sleep, missed visits). When PR Ortho-K plus spectacle completion is stable and adherence is confirmed, adjunctive pharmacologic therapy can be considered, especially when risk is high (young age, rapid axial elongation trajectory, strong family history, high baseline axial length) (Shah et al., 2024; Tsai et al., 2022). Because atropine concentration and regimen vary across the literature, the defensible clinical position is not to prescribe a dose, but to document that "low-dose atropine" is the most common adjunct in combination strategies and to emphasize monitoring of side-effects and adherence (Jun et al., 2018; Shah et al., 2024; Tsai et al., 2022).

Step 6: Manage the tear film proactively because comfort is an adherence lever. Pang et al. (2022) reported improvements in tear-related indices and multiple patient-reported domains in the Ortho-K plus spectacle group, but the measurement protocols and instrument validity were not fully specified. The correct interpretation is: ocular surface comfort may improve with a well-run program (education, frequent contact, better hygiene) and/or may worsen if the surface is neglected. Therefore, a protocol should include proactive lid hygiene, lubricant strategy when appropriate, and clear stop-rules for persistent staining or recurrent inflammatory events (Pang et al., 2022; Wolffsohn et al., 2023).

Step 7: Decide when to stop or switch. A high-myopia protocol needs explicit exit criteria to avoid harm-by-persistence. Examples include recurrent significant staining, recurrent infiltrative events, inability to achieve acceptable centration without unsafe bearing patterns, or sustained intolerance that threatens adherence. Switching does not mean "failure"; it means you are protecting the cornea while still pursuing myopia control using alternative optical designs or pharmacologic approaches described in current reviews (Shah et al., 2024).

High myopia is where "one-size-fits-all" myopia control becomes unsafe and inefficient. The evidence base supports a defensible core: (a) use partial-reduction orthokeratology (PR Ortho-K) when full correction is not feasible, and (b) complete the daytime refractive requirement with spectacles, then (c) escalate using adjunctive therapy when axial elongation remains clinically concerning or when adherence/visual quality limits the optical strategy (Charm & Cho, 2013; Pang et al., 2022; Shah et al., 2024). A stepwise protocol is not merely administrative; it is how you preserve causal interpretability (what helped, what harmed) and how you reduce preventable adverse events.

5.9. Implementation checklist (high myopia Ortho-K pathway)

- Document baseline cycloplegic refraction and axial length; repeat axial length on the same device where possible.
- Prefer PR Ortho-K with explicit daytime completion rather than maximal correction attempts in very high refractive error.
- Define primary (axial length) and secondary (patient-reported) outcomes before treatment begins.
- Confirm adherence and fit stability before escalation to combination therapy.
- Schedule early and frequent safety reviews focused on staining, centration, and care technique.
- Treat ocular surface disease proactively; do not "push through" repeated staining.
- Use adjunctive pharmacologic therapy as an escalation tool, not as a substitute for poor optical implementation.
- Maintain explicit stop/switch criteria to prevent corneal harm.
- Record adverse events and protocol deviations transparently; interpret outcomes in that context.
- Communicate uncertainty honestly: secondary outcomes may reflect experience and adherence, not proven physiological change.

5.10. Limitations of the evidence base and of this synthesis

The high-myopia Ortho-K evidence base remains limited. Only a small number of studies directly test high-myopia cohorts, and sample sizes are often modest. Attrition is common and can bias estimates if dropouts are related to poor response or adverse effects. In

addition, many Ortho-K trials are conducted in specific geographic regions, and generalizability to other populations and practice settings must be considered (Wolffsohn et al., 2023).

This review is a narrative synthesis rather than a formal systematic review. While the search strategy is described and anchored in PubMed and Cochrane, the synthesis does not calculate pooled effect sizes across all available studies. The choice to prioritize a small set of 'key evidence' trades breadth for depth and clinical interpretability. (Santodomingo-Rubido et al., 2024; Shah et al., 2024).

For Pang et al. (2022), the secondary outcomes are limited by unclear measurement validity and some internal inconsistencies, which prevents strong causal inference. Nonetheless, these data are included because they address patient-centered domains relevant to adherence and because they reflect real-world interest in tear-film and comfort outcomes.

5.11. Research gaps and recommendations for future trials

Future high-myopia Ortho-K trials should use standardized, validated outcome measures: axial length as a primary endpoint; validated dry eye instruments (e.g., OSDI or DEQ-5) for symptom reporting; standardized tear-film protocols; and validated mood, sleep, and quality-of-life instruments with pre-specified hypotheses. Trials should explicitly define high myopia using both SER and AL, report treatment-zone size and decentration, and analyze whether these optical parameters mediate response (Shah et al., 2024).

Combination trials should use factorial or stepped designs to isolate incremental benefit. For example, Ortho-K alone versus Ortho-K plus 0.01% atropine with pre-defined escalation criteria would provide actionable guidance. Finally, longer follow-up is essential to determine whether early slowing persists and whether rebound occurs after discontinuation (Tsai et al., 2022; Shah et al., 2024).

6. Conclusion

High myopia requires risk-managed myopia control strategies that prioritize axial length. The strongest direct high-myopia evidence supports partial-reduction Ortho-K paired with daytime spectacle completion, showing substantially less axial elongation than spectacle-only correction. Comparative evidence indicates that adding low-dose atropine to Ortho-K can further improve axial outcomes, providing a rational escalation path for progressors. Safety is tightly linked to adherence and follow-up; compliance data underscore that education and monitoring are essential. Secondary outcomes related to tear film and patient-reported well-being are clinically relevant for acceptability but must be presented conservatively when measurement validity is unclear.

When implemented as a structured protocol rather than as a purely refractive correction tool, Ortho-K can be a defensible component of high-myopia management. The professional obligation is to communicate benefits precisely, monitor structural outcomes, and treat safety as an ongoing process.

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Conflict of interest

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Ethics approval

Not applicable. This article is a narrative literature synthesis and does not report new human-subject data.

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Appendix A. Search strings

Search strings used (PubMed and Cochrane Library; last searched: 2026-01-17).

("orthokeratology" OR "Ortho-K" OR "orthokeratology lens") AND ("high myopia" OR "severe myopia" OR "-6.00" OR "-5.75") AND (axial length OR axial elongation OR myopia progression).

("partial reduction" OR "partial correction" OR "residual refractive" OR "spectacle completion") AND (orthokeratology OR Ortho-K) AND (high myopia OR severe myopia).

(orthokeratology OR Ortho-K) AND atropine AND (combination OR combined) AND (axial length OR myopia progression).

(orthokeratology OR Ortho-K) AND (safety OR adverse events OR microbial keratitis OR compliance OR follow-up).

(high myopia) AND (myopia control) AND (spectacle lenses OR defocus incorporated multiple segments OR multifocal).

Appendix B. Screening overview and characteristics of key included evidence

Table 1. Characteristics of key included evidence (high myopia, Ortho-K efficacy, safety, and combination protocols).

Source (year)	Design	Population	Intervention	Follow-up	Key endpoints
Charm & Cho (2013)	Randomized, single-masked	Children 8-11 y; SE ≤ -5.75 D	Partial-reduction Ortho-K (target 4.00 D) + SV spectacles	24 months	AL change; residual myopia
Pang et al. (2022)	Controlled clinical study	Adolescents with high myopia (≥ -6.00 D)	Ortho-K + frame glasses vs frame glasses	~6 months	AL growth rate; tear-film indices; PROs
Hiraoka et al. (2012)	Prospective comparative	Children with myopia; Ortho-K vs spectacles	Overnight Ortho-K vs SV spectacles	5 years	AL elongation
Santodomingo-Rubido et al. (2024)	Pooled analysis (3 prospective studies)	Children; typical low-moderate baseline myopia	Ortho-K vs SV spectacles	2 years	AL change; response heterogeneity
Tsai et al. (2022)	Network meta-analysis	19 RCTs; 3435 children	Atropine (various) vs Ortho-K vs combined atropine + Ortho-K	1 year	AL change; refractive change; SUCRA ranking
Jun et al. (2018)	Questionnaire + retrospective follow-up	Ortho-K wearers (mostly <18 y)	Compliance behaviors and follow-up adherence	≥1 year wear	Compliance domains; noncompliance behaviors

Note. AL = axial length; PROs = patient-reported outcomes; SV = single-vision. (Shah et al., 2024; Santodomingo-Rubido et al., 2024).

Appendix C. Supplementary note on Pang et al. (2022) secondary outcomes

Detailed secondary-outcome tables from Pang et al. (2022) (tear film indices and multiple patient-reported scores) are not reproduced in this review. They were directly transcribed from the source study and, given the unclear validation of several instruments and ambiguous endpoint interpretation, reproducing them would over-weight a methodologically limited dataset. Readers should consult the original publication for the complete numeric tables.