


Eye care adherence in pediatric and elderly: Understanding and addressing the challenges

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ABSTRACT

Adherence in pediatric and elderly eye care is a system outcome shaped by patient, caregiver, treatment, service design, and affordability. This narrative review synthesizes recent evidence on magnitude, determinants, and consequences of nonadherence across a representative selection of major pediatric and older adult conditions, and proposes a practice- and policy-ready agenda. Using the ABC taxonomy (initiation, implementation, and persistence) as an organizing frame, we appraise measurement methods, map phase-specific barriers, and collect effective or promising strategies at patient, clinic, and system levels. Evidence indicates that avoidable vision loss often reflects failures in initiation (e.g., delayed start or first follow-up), day-to-day implementation (technique, tolerability, routine friction), or long-term persistence (retention, affordability), with objective measures typically revealing lower adherence than self-report. Multicomponent, age-tailored bundles (relational care, regimen simplification, proactive recall, caregiver support, school- or community-linked access) are more effective and scalable than education alone when co-designed and adequately supported; digital tools show potential but require validation, usability, and equity safeguards. We also identify priorities for research (harmonized, phase-specific outcomes, validation of age- and condition-specific measures, pragmatic and hybrid effectiveness-implementation designs with economic evaluation) and for policy/system reform (quality dashboards with equity-disaggregated indicators, supportive reimbursement for coordination/counseling, and outcome-linked procurement of digital solutions). We define “effective adherence” pragmatically as adherence sufficient to achieve intended clinical outcomes for a given therapy, and outline a three-pillar roadmap (Clinical, Research, Policy/System) to embed measurement, support, and accountability into routine care. Together, these steps can translate conceptual clarity into equitable and sustainable improvements in vision and eye care outcomes.

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1. Introduction

Healthcare adherence, defined as the extent to which a patient's behavior aligns with prescribed recommendations from a healthcare provider (Vrijens et al., 2012), is widely recognized as a primary determinant of patient outcomes and health system performance. Since the early 2000s, the World Health Organization (WHO) has emphasized that improving adherence may yield greater population health benefits than the development of new medical treatments themselves (Kim et al., 2018; World Health Organization, 2003).

Despite decades of research and innovation, poor adherence to long-term therapies remains a pervasive and unresolved challenge, impacting virtually all medical disciplines and patient populations. In high-income countries, it is estimated that only about 50% of patients with chronic diseases adhere to their medication regimens as prescribed and this seems to have remained essentially unchanged for years (Kim et al., 2018). The clinical consequences are profound, accounting for a significant proportion of treatment failures, hospital admissions, and preventable mortality. Economically, nonadherence is associated with an estimated \$100 to \$300 billion in potentially avoidable healthcare costs annually in the United States alone, highlighting its major impact on healthcare systems (Kim et al., 2018; World Health Organization, 2003).

Adherence is not a matter of individual fault, but a dynamic, multifactorial process shaped by patient, therapy, social, cultural, and system-level factors (Lawrence et al., 2017; World Health Organization, 2003). Effective strategies are multicomponent, combining education, behavioral support, regimen simplification, and digital tools (Bayatra et al., 2024; Kim et al., 2018), and require ongoing monitoring across prescribed regimen: initiation, implementation, and persistence phases (Vrijens et al., 2012).

Ophthalmic care presents a particularly compelling context in which to examine adherence. The field is marked by a high burden of chronic (in some cases asymptomatic) diseases, treatment benefits are frequently preventive rather than immediately perceptible (a typical vulnerable setting for both intentional and unintentional nonadherence) (Hughes, 2004; Osterberg and Blaschke, 2005), and common therapies (for example, eye drops, contact lenses, intravitreal schedules, or post-operative positioning) demand fine motor skills, sustained routines, and/or long-term commitment (Friedman et al., 2008; Polat et al., 2017; Yang et al., 2025); lapses can often lead to irreversible vision loss, healthcare system burden, and clinician/caregiver frustration.

Beyond individual and treatment-related factors, eye care is high-volume with growing visit complexity (DeBroff and Andoh, 2024) and uneven access; systemic bottlenecks and long waits foster disengagement, making adherence a proxy for healthcare system accessibility, coordination, and equity (Lin et al., 2020; McDonald and Iordanous, 2022; McMullen and Netland, 2013).

Within this complex framework, pediatric and elderly populations face unique and underappreciated challenges. In pediatric populations, adherence is strongly shaped by developmental stage and depends largely on caregiver involvement, particularly in early childhood (Al-Hassany et al., 2019). In the elderly, multimorbidity, polypharmacy, and declines in cognition, vision, and manual dexterity intersect with fragmented care, frequent involvement of multiple caregivers across different settings, and limited health literacy, undermining day-to-day implementation and persistence (Hughes, 2004). Importantly, pediatric and elderly adherence often extends beyond pharmacologic treatment, encompassing consistent attendance at follow-up visits and scheduled treatments or regular use of supportive/therapeutic devices or procedures.

This narrative review critically synthesizes evidence on adherence in pediatric and older adult eye care, covering its magnitude, determinants, and evidence-based strategies for medication-taking and visit adherence, to set research priorities and support the design of equitable, sustainable, patient-centered models of ophthalmic care.

2. Conceptual framework and common language

Understanding and improving adherence requires conceptual clarity as well as robust measurement and intervention. Over time, terms such as compliance, adherence, and concordance, together with constructs like health literacy, empowerment, and patient-centeredness, have been used (sometimes interchangeably) to describe the evolving relationship among patients, prescribed care, and clinicians.

Compliance traditionally denotes following instructions and has been criticized for implying passivity and a paternalistic model (Aronson, 2007), while adherence would reflect a more active, autonomous stance (Fawcett, 2020). The WHO definition, "the extent to which a person's behavior corresponds with agreed recommendations from a healthcare provider" (Erickson and Polfuss, 2021; World Health Organization, 2003), highlighted collaboration and shared decision, yet the phrase "agreed recommendations" pertains to the prescribing process rather than the operational outcome and can complicate measurement (Vrijens et al., 2012). In this review we therefore treat adherence as the outcome, reserving concordance, shared decision-making, and related constructs as modifiable determinants that interventions can target and that reporting should specify.

Concordance and shared decision-making concern the quality of the prescribing relationship; these are not behavioral outcomes but can facilitate adherence (Bell et al., 2007; Fawcett, 2020). In eye care, technique-dependent regimens (for example, eye drop instillation or patching) amplify this distinction: patients may agree with the plan yet still fail implementation because of motor or visual constraints. These distinctions matter for intervention design: shared decision-making (SDM), considered the "pinnacle" of patient-centered care (Barry and Edgman-Levitan, 2012), integrates evidence with preferences and values, but it does not invariably co-occur with genuinely patient-centered communication (Siebinga et al., 2022). Effective participation depends on health literacy (the ability to obtain, understand, and use health information), which showed a small yet significant correlation with adherence ($r \approx 0.14$) and stronger effects in disadvantaged groups, making adherence an equity-sensitive metric (Miller, 2016). Patient empowerment (including locus of control) generally supports adherence, but without adequate literacy it may foster "intelligent nonadherence," such as prematurely stopping topical steroids when symptoms decline to avoid perceived side effects (Náfrádi et al., 2017).

In sum, the conceptual evolution from paradigms rooted in paternalistic models of care, to frameworks in which adherence is grounded in agreement, shared decision-making, and patient empowerment marks a meaningful shift in how therapeutic relationships are conceived and facilitated (Fig. 1).

Scientific progress has been advanced by standardized frameworks such as the ABC taxonomy (formalizing the distinct phases of adherence: initiation, implementation, and persistence) and the European Society for Patient Adherence, Compliance, and Persistence (ESPACOMP) Medication Adherence Reporting Guideline (EMERGE), which provide a common foundation for research and reporting (De Geest et al., 2018; Vrijens et al., 2012). The remaining challenge lies in translating this conceptual clarity into routine clinical practice and health system organization, while ensuring that language also resonates with patients' lived experience.

2.1. Determinants of adherence: A multilevel framework

Understanding why patients succeed or fail in following prescribed care requires attention to factors operating at multiple, interacting levels. Socioecological models and ophthalmic evidence point to four broad layers of influence: intrapersonal, interpersonal, clinical, and system-level, that jointly condition whether a patient initiates, implements, and persists with prescribed care (Fig. 2). This framework applies across the life course, though the relative weight of each layer shifts with

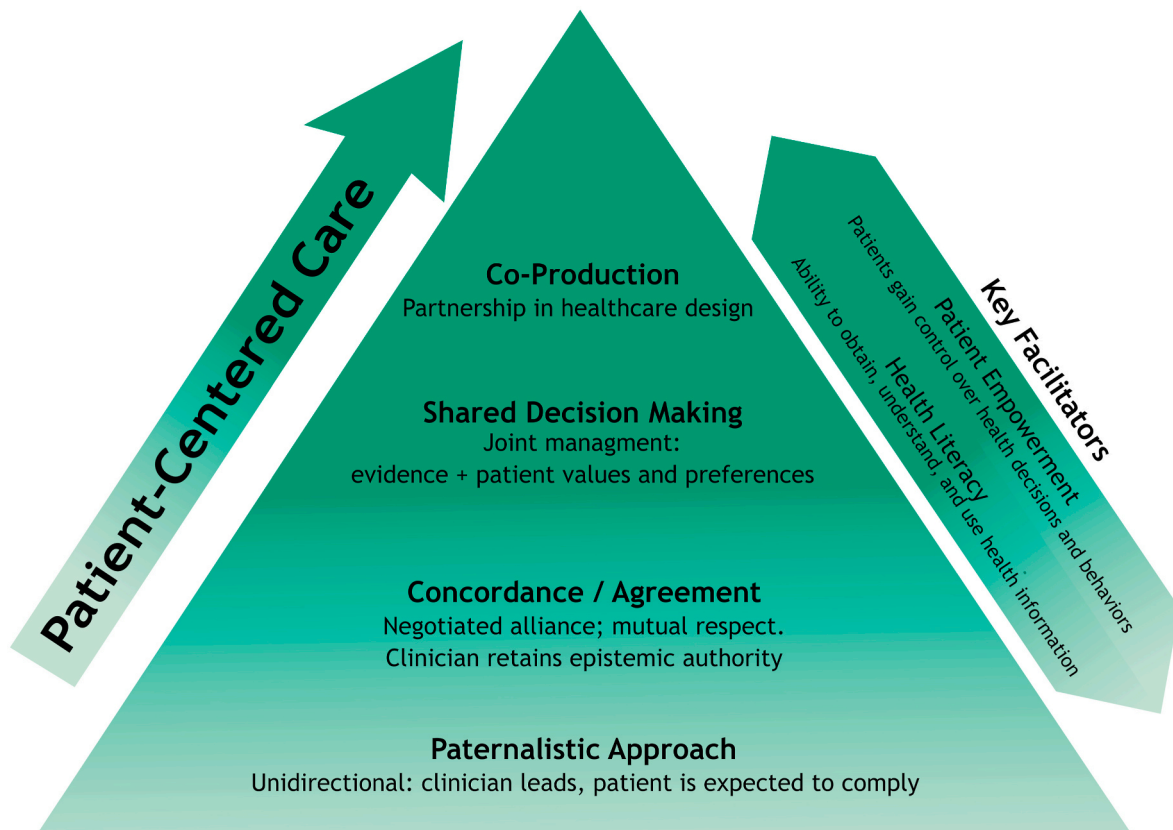


Fig. 1. Conceptual framework for evolving towards increasingly strong patient-centered care paradigm. A conceptual diagram illustrating the evolution of the prescribing and engagement model in the clinician–patient relationship. The process evolves from a paternalistic model (clinician-led decision-making) to concordance/agreement (alignment between clinician recommendations and patient acceptance), to shared decision-making (bidirectional exchange and joint choice), and ultimately to co-production (co-created care planning and management). The intensity of color across stages reflects the progressive implementation of patient-centered care as a guiding paradigm. Health literacy and patient empowerment act as transversal facilitators, increasing in importance and impact throughout the transition. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

developmental stage, functional capacity, and care context.

At the individual level, cognitive function influences the ability to comprehend instructions, remember dosing schedules, and integrate regimens into daily routines; impairment at any age, whether developmental in children or acquired in older adults, predicts poorer implementation and persistence (Freedman et al., 2012; O’Conor et al., 2024). Health beliefs and illness perception modulate motivation: patients who doubt treatment necessity or efficacy, or who perceive low susceptibility to disease progression, are more likely to discontinue care (Loon et al., 2015; Negese Kebede et al., 2024; Náfrádi et al., 2017). Conversely, self-efficacy-confidence in one’s ability to execute the prescribed regimen has been consistently associated with better adherence outcomes (Sleath et al., 2012, 2015). Psychological states also matter: anxiety, depression, and fear of adverse effects can erode illness acceptance and the perceived value of sustained treatment (Albadrani et al., 2024; Horvat et al., 2024; Jeżuchowska et al., 2024). The distinction between intentional nonadherence (deliberate deviation based on beliefs, preferences, or risk-benefit appraisal) and unintentional nonadherence (inadvertent deviation due to forgetfulness, misunderstanding, or practical barriers) carries implications for intervention design: the former may respond to motivational and educational approaches, the latter to simplification and reminder systems (Stirratt et al., 2015).

Beyond individual attributes, relational networks profoundly shape adherence. In pediatric care, the caregiver assumes a central role: parental engagement, health literacy, and family routines are pivotal for day-to-day implementation, particularly in early childhood when the child lacks capacity for self-management (Al-Hassany et al., 2019;

Santer et al., 2014). Low caregiver health literacy is associated with reduced access, lower participation in shared decision-making, and greater reliance on emergency care, thereby undermining long-term ophthalmic regimens (Hekmatjah et al., 2024; May et al., 2018; Yin et al., 2012). Family dynamics add complexity: in divorced families, discordant views and routines across households can fragment care and erode adherence over time (Bergström et al., 2021; O’Hara and Cohen, 2024). In older adults, social isolation, defined as objective reduction in social contact, affects up to one in four individuals and is independently associated with suboptimal adherence and poor health outcomes (Gerlach et al., 2024; Lu et al., 2020). The patient-provider relationship represents another critical lever: patients who receive active reinforcement from their provider or specific encouragement regarding correct dosing demonstrate significantly better adherence outcomes (Sleath et al., 2015). Shared decision-making, when executed with attention to caregiver burden and patient agency, can foster trust, motivation, and ownership of the treatment plan (Barry and Edgman-Levitan, 2012).

Disease characteristics and treatment attributes also condition adherence. Regimen complexity (number of medications, dosing frequency, and technique demands) consistently predicts adherence across settings and populations: simpler regimens with fewer drops and reduced dosing frequency are associated with better implementation and persistence (Barnebey and Robin, 2017; Huo and Pu, 2024; Kim et al., 2017b; Ko et al., 2019; Tsumura et al., 2019). Ophthalmic care adds skill-dependent tasks, such as eye drop instillation, patching, and contact lens handling, requiring manual dexterity and, in pediatric settings, sustained caregiver effort to manage child resistance (Harvey et al., 2024; Pawar et al., 2023). Tolerability is a potent modifier: ocular

discomfort, particularly from preservatives such as benzalkonium chloride, can substantially compromise patients' willingness to maintain therapy (Kolko et al., 2023; Thygesen, 2018), whereas preservative-free and fixed-combination formulations improve persistence (Barnebey and Robin, 2017; Kim et al., 2021). Paradoxically, asymptomatic disease, common in glaucoma and early diabetic retinopathy, may reduce perceived urgency and undermine persistence (Loon et al., 2015; Movahedinejad and Adib-Hajbaghery, 2016). Duration of therapy also matters: longer treatment duration is consistently linked to declining adherence, reflecting the erosion of motivation over time (Frech et al., 2018; Huo and Pu, 2024; Ko et al., 2019).

Structural and policy factors (access, affordability, service organization) form the outermost layer of influence. Affordability emerges as an important barrier in many contexts: low income, self-paying status, and absence of health insurance have been associated with poorer adherence outcomes in multiple studies (Anbesse et al., 2019; Mehari et al., 2016; Newman-Casey et al., 2015a; Saeedi et al., 2015; Yang et al., 2017). However, the magnitude of cost-related barriers varies substantially across settings: in systems with comprehensive coverage or subsidized care, other determinants assume greater relative prominence, and even in low-resource contexts, non-financial barriers such as limited disease knowledge frequently predominate in patient-reported surveys (Foreman et al., 2017; Malhotra et al., 2019; Ramesh et al., 2021). Geographic access—travel distance and transportation difficulties—emerges as a significant barrier and particularly for follow-up-intensive regimens such as intravitreal injections (Killeen et al., 2020; Movahedinejad and Adib-Hajbaghery, 2016; Subathra et al., 2021). Service design shapes adherence opportunity: fragmented care transitions, inadequate discharge planning, unclear written instructions, and poor integration of caregivers contribute materially to non-adherence and medication errors (Gellad et al., 2011; Rogers et al., 2014). Conversely, structured monitoring, proactive recall systems, and community-linked delivery (such as school-based programs) can mitigate individual-level barriers: school-based vision programs and nurse-led counseling have achieved markedly higher adherence than usual care across diverse settings (Burnett et al., 2018; Dhiman et al., 2022).

These layers do not operate in isolation but interact in ways that complicate both explanation and intervention. Even when care is provided free of charge, for instance, low health literacy can still undermine initiation and implementation, a reminder that removing one barrier often exposes another. Similarly, high-burden regimens may prove sustainable for patients with robust caregiver support yet unmanageable for those without, illustrating how interpersonal resources moderate the impact of clinical demands. The broader system context shapes which individual-level factors matter most: in well-coordinated systems with proactive recall, self-efficacy may be less critical than in fragmented systems where patients must navigate care largely on their own. Perhaps most striking is the feedback loop created by visual impairment itself: an outcome adherence seeks to prevent can become a barrier to eye drop instillation, reading instructions, and attending appointments, compounding the risk of further decline. These interactions argue against single-factor explanations and underscore the need for multicomponent interventions that address barriers across levels simultaneously.

Fig. 2 maps these layers against the ABC phases (initiation, implementation, persistence), highlighting where specific determinants assume particular importance for different populations. Sections 4 and 5 apply this framework to pediatric and elderly populations, examining how age-specific factors shape adherence across ophthalmic conditions.

2.2. Prioritizing determinants across contexts

The factors outlined above operate across settings, but their relative importance shifts with health-system context, care occasion, and life-course stage. Recognizing these patterns enables clinicians and policy makers to anticipate which barriers are most likely to be rate-limiting in

each setting and to calibrate interventions accordingly.

The broader health-system context affects both overall adherence rates and which barriers predominate. In low- and middle-income countries (LMICs), adherence rates are generally lower, and structural barriers, such as out-of-pocket costs, geographic distance, and workforce shortages, assume greater relative prominence. A cross-sectional synthesis of pediatric spectacle wear in LMICs reported mean compliance of approximately 40%, with free provision programs consistently improving uptake compared with prescription-only approaches (Dhirar et al., 2020; Huang et al., 2019; Khatri et al., 2024). The contrast is stark for life-threatening conditions: in high-income countries, comprehensive care has made retinoblastoma curable in more than 95% of cases, whereas in sub-Saharan Africa, treatment abandonment reached 27% and enucleation refusal 45% in a recent cohort (Abramson, 2014; Lukamba et al., 2023). For diabetic retinopathy screening, a global meta-analysis documented pooled uptake of 66.9% in high-income settings versus 39.3% in LMICs, with Europe reaching 81.3% and Africa only 36.1% (Rahmati et al., 2024).

Importantly, however, the determinants of adherence appear largely universal across settings; what changes is their relative weight rather than their presence. Regimen complexity, perceived benefit, health literacy, and caregiver involvement emerge as significant predictors in both high- and low-resource contexts (Freedman et al., 2012; Rao et al., 2020; Sleath et al., 2015). In high-income countries where access barriers are partially mitigated by insurance coverage and organized care pathways, implementation challenges (e.g. technique demands, tolerability, and integration into daily routines) assume greater relative prominence. In glaucoma, even within well-resourced European systems, pharmacy claims revealed adherence rates of 66.5% in Germany and 51.6% in the United Kingdom, below annual adherence benchmarks (Frech et al., 2018; Tse et al., 2016). Critically, socioeconomic gradients persist within high-income countries: underserved populations, whether defined by insurance instability, language discordance, or geographic isolation, often exhibit LMIC-like barrier profiles, underscoring the need for equity-disaggregated analysis even in high-resource contexts (Hark et al., 2017; Heckenlaible et al., 2024; Loudon et al., 2006).

Care occasion determines the predominant mode of adherence failure. Screening and initiation challenges dominate in conditions requiring case-finding: reaching undiagnosed populations and ensuring referral completion after positive screening represent the critical vulnerabilities. In diabetic retinopathy, even England's well-organized NHS program, which screened 82.7% of invitees, faced clinically relevant delays from diagnosis to first examination, with waitings exceeding 36 months tripling the odds of referable disease (Scanlon, 2021; Scanlon et al., 2016). The pattern of 'successful screening followed by failed referral' recurs across settings: in a large U.S. tele-retina network, only 30.9% of positive referrals were seen in eye care within six months (Bonilla-Escobar et al., 2024).

For chronic longitudinal care, the dominant failure mode shifts to persistence. The proportion of patients remaining on therapy over time shows remarkably consistent erosion across conditions and health systems. In glaucoma, a meta-analysis of prostaglandin analogues documented persistence declining from approximately 75% at three months to 31% at three years (Baudouin et al., 2025). For intravitreal anti-VEGF therapy, up to 50% of patients discontinue treatment within 24 months, with cumulative loss to follow-up reaching 57% at five years in French cohorts and 51% at two years among the oldest-old in Denmark (Boulanger-Scemama et al., 2015; Okada et al., 2021; Subhi and Sørensen, 2017). Trajectory analyses reveal a characteristic bimodal distribution: roughly 15% of patients are never adherent, 15% are always adherent, and the remainder fluctuate over time, suggesting that interventions must target distinct behavioral phenotypes rather than assuming a homogeneous population (Newman-Casey et al., 2015a).

Acute and short-term regimens present a contrasting profile. Adherence is generally higher when treatment is time-limited and benefit is immediately perceptible, though technique and early

discontinuation remain concerns. Postoperative positioning after vitreoretinal surgery exemplifies this pattern: inpatient observational studies report moderate-to-high mean adherence (88-91%) but wide inter-individual variability, with perfect compliance achieved by fewer than half of patients in most series (Shimada et al., 2017; Suzuki et al., 2018). Tolerability emerges as the primary determinant; less demanding postural instructions (non-supine vs. face-down positioning) yield substantially higher compliance (99.3% vs. 93.7%), confirming that regimen burden is modifiable (Morimoto et al., 2018).

Life-course stage further modulates these patterns. Within pediatric populations, adherence capacity evolves with cognitive and motor development, and the balance between caregiver dependence and emerging autonomy shifts across developmental stages. In early childhood (0-5 years), adherence is predominantly caregiver-determined; parental engagement, health literacy, and family routines are the critical levers (Al-Hassany et al., 2019; Santer et al., 2014). In adolescence (12-17 years), peer influence, identity formation, and risk-taking behavior introduce new challenges, and excluding adolescents from treatment decisions fosters frustration and nonadherence (Coyne et al., 2014; Sobode et al., 2024).

Among independent elders, visual function, manual dexterity, and regimen complexity are key constraints on initiation and implementation, while social isolation can undermine persistence. In dependent or cognitively impaired elders, patient-level factors recede because the patient no longer manages therapy directly and caregiver capacity becomes the dominant determinant across all phases (O'Connor et al., 2024). Although the oldest-old show substantial attrition (51% loss to follow-up by two years in Danish intravitreal cohorts) (Subhi and Sørensen, 2017), functional dependence better captures the adherence phenotype than birth year.

Health-system organization can substantially moderate the impact of individual-level barriers. In well-coordinated systems with proactive recall and structured pathways, individual-level self-efficacy may matter less than in fragmented systems requiring patient self-navigation. A school-based vision program may largely neutralize socioeconomic barriers to spectacle uptake that would otherwise dominate (Burnett et al., 2018); integrated ROP tracking systems achieve near-complete screening coverage regardless of individual caregiver characteristics (Arnold et al., 2017). Conversely, in systems without such structures, compounding disadvantages accumulate: the child without a coordinated school program, from a low-literacy household, with an uninsured parent, faces multiplicative rather than additive barriers.

These contextual dimensions interact in ways that argue against simplistic prioritization schemes. Nevertheless, the evidence suggests broad principles for resource allocation: in LMIC settings and underserved populations within high-income countries, structural interventions addressing cost and access are likely to yield substantial gains; in well-resourced systems where access is largely secured, multicomponent interventions targeting implementation and persistence become paramount; across all settings, equity-sensitive stratification ensures that the most vulnerable subgroups-defined by the intersection of age, socioeconomic status, and care complexity-are not left behind. Sections 4 and 5 examine how these principles play out in pediatric and elderly eye care, while Section 6 translates the emerging patterns into a strategic agenda across three interdependent pillars: clinical practice, research priorities, and policy reform.

3. Treatment adherence measurement methods

3.1. Conceptual challenges and unmet needs in adherence measurement

Despite the wide range of available tools, no single method captures the full behavioral spectrum or distinguishes intentional from unintentional nonadherence (Stirratt et al., 2015). Self-report, caregiver-report, and objective methods each provide complementary but incomplete perspectives, and methodological heterogeneity hinders comparability.

Defining clinically meaningful thresholds is equally problematic: the traditional 80% cut-off (Chang and Liao, 2018; Kao et al., 2021; Kim et al., 2017a) conflates heterogeneous behaviors (e.g., sporadic dosing, consistent under-dosing, or early cessation) and lacks evidence across drugs and diseases. Systematic reviews show effective adherence thresholds varying from 46% to over 90% (Baumgartner et al., 2018). Thresholds, if applied, should therefore be phase-specific and disease-contextual.

Best practice favors a multimethod approach, conceptually anchored and tailored to treatment type, patient age, and care setting. Models such as TEOS (Timelines-Events-Objectives-Sources) help align measures with adherence phases and study objectives (Dima et al., 2021). Especially in pediatric and geriatric care, where proxy reporting and cognitive or functional limitations complicate assessment, methodological rigor requires integrated, context-sensitive strategies.

In the following sections, we review available measurement tools with attention to phase-specific application and to their validity, feasibility, and suitability for pediatric and elderly care (Fig. 3).

3.2. Patient-Reported Adherence

Self-report remains the most widely used method because it is inexpensive, feasible, and uniquely able to capture intentionality, including patients' beliefs, motivation, and perceived burden, dimensions largely inaccessible to objective tools (Gackowski et al., 2024; National Academies of Sciences et al., 2016; Stirratt et al., 2015).
















However, while relatively easy to implement, these methods are heterogeneous and susceptible to both intentional and unintentional bias, with reliability varying according to administration context, patient characteristics, and question framing (Green et al., 2024). Moreover, self-reports tend to overestimate true adherence due to recall inaccuracies, social desirability, and fear of disapproval (Kwan et al., 2020; Osterberg and Blaschke, 2005; World Health Organization, 2003; Tesfaye and Peterson, 2022).

Several instruments have been developed with the aim to standardize self-reporting, including the Morisky Medication Adherence Scale (MMAS) (Morisky et al., 1986), the Medication Adherence Report Scale (MARS) (Chan et al., 2020; Cohen et al., 2009), the Adherence to Refills and Medications Scale (ARMS) (Kripalani et al., 2009), the Self-Efficacy for Appropriate Medication Use Scale (SEAMS) (Risser et al., 2007), and the General Medication Adherence Scale (GMAS) (Naqvi et al., 2018), but they vary in psychometric robustness and licensing constraints (Basu, 2021; Gackowski et al., 2024). A recent Consensus-based Standards for the selection of health Measurement Instruments (COSMIN)-compliant review (Kwan et al., 2020), analyzing 121 unique medication adherence PROMs, found that none met full endorsement across all measurement properties.

Notably, the widely used MMAS has recently been implicated in multiple retractions due to unauthorized use and licensing disputes; moreover, the validation study for the 8-item scale (MMAS-8) was retracted in 2023, casting doubt on its psychometric legitimacy, highlighting an underrecognized risk in adherence research, and underscoring the need for transparent permissions and ethical instrument selection (Retraction Watch, 2023).

In ophthalmology, validated patient-reported measures are scarce. A few glaucoma-specific instruments, such as the Glaucoma Treatment Compliance Assessment Tool (Mansberger et al., 2013) and the Glaucoma Medication Self-Efficacy Scale (Sleath et al., 2010, 2012), have been tested but rarely implemented in clinical practice and seldom extended to other eye conditions. Pediatric use adds complexity due to limited self-report ability and developmental appropriateness, with proxy bias often unavoidable.

Despite limitations, patient-reported methods remain indispensable for capturing psychosocial dimensions, but development of ophthalmology-specific validated instruments should be a research priority.

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TIME		Initiation <i>Has the patient started the prescribed treatment?</i>	Implementation <i>To what extent is the patient taking the treatment as prescribed?</i>	Persistence <i>Is the patient still continuing the treatment?</i>		
Adherence measurement methods	Subjective	Patient-report	Structured Questionnaires / Scales			-Feasible in clinical care; capture reasons and intentionality -Recall and social desirability bias; overestimation
			-			
			-	Single-Item Measures		
		Structured or Semi-Structured Interviews			-Flexible; can explore beliefs, barriers, and dexterity issues -Time-consuming; interviewer bias; limited standardization	
						
		Caregiver-completed questionnaires or interviews (adapted from patient tools)				
	Objective	Indirect	Prescription and refill records (MPR, PDC)			-Scalable; no patient burden -Cannot confirm instillation; "stockpiling" issues -Validity depends on healthcare system coverage and data integration -In children and dependent elderly, the chain is longer
				-		
		Direct	-	Drop Counts / Bottle Weighing		-Simple; used in trials -Easily manipulated; not feasible in routine care
			Electronic monitoring devices (such as MEMS caps adapted for eye drop bottles)			
						
Digital health tools (AI-Based mobile apps, wearables)			-Real-time feedback; integrates with reminders -Interactive tools require digital literacy; device cost; privacy and data security			
-						
Direct observation (In-person or Video)			-Verifies actual instillation; potential for VOT -High burden; privacy concerns; low scalability; adherence to the monitoring process can be poor -Mainly in controlled settings			
		-		-		
Therapeutic drug monitoring			-Topical drugs may yield very low systemic levels; not suitable for routine monitoring and not applicable for many topical therapies			
-	-	-		-		



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Fig. 3. Measuring adherence across phases and methods in pediatric and elderly eye care. Adherence assessment methods are organized into subjective patient- and caregiver-reported, and indirect and direct objective approaches; digital health tools include both interactive and automatic apps and wearables, often mixing indirect and direct elements. For each method, the figure summarizes strengths/limitations and maps ABC phases (A Initiation, B Implementation, C Persistence) and age-group hotspots of suitability (infants–preschoolers, school-aged-adolescents, independent elderly, dependent/cognitively impaired elderly). Icons indicate particularly suitable phase × population pairings. Therapeutic drug monitoring is not mapped to specific populations or phases because systemic drug levels are generally undetectable for topical ophthalmic therapies. MEMS = Medication Event Monitoring System; MPR = medication possession ratio; PDC = proportion of days covered; RCTs = randomized clinical trials; VOT = video-observed therapy.

3.3. Caregiver-reported adherence

Caregiver report is crucial in pediatrics, cognitive impairment, and frail older adults, yet it is methodologically underdeveloped. Most studies rely on unstructured diaries or interviews, with little psychometric validation (Alonge and Kostaki, 2022). Reports are influenced by caregivers' health literacy, emotional burden, and family dynamics, often leading to overestimation or underestimation. However, general medicine studies have found moderate agreement between caregiver- and self-report, both potentially overestimating adherence (Gillette et al., 2024; Stirratt et al., 2015).

In pediatric settings, the caregiver is typically a parent, whose dual role as logistical manager and emotional buffer introduces relational and psychological complexity into adherence reporting (Santer et al., 2014). This dynamic is further complicated during adolescence, where tensions between promoting autonomy and ensuring adherence may emerge; these are crucial when interpreting proxy-reported adherence during transitional developmental stages (Anderson et al., 2025; Coyne et al., 2014).

In geriatrics, caregiver type matters: family members may overreport due to emotional involvement, while professional caregivers provide more neutral but less contextual assessments (El-Saifi et al., 2019; O'Connor et al., 2024).

Importantly, no caregiver-reported adherence tools have been psychometrically validated for ophthalmic use and there is a lack of direct comparisons between caregiver- and self-report in eye care. Developing and validating psychometrically sound, condition-specific caregiver-report tools should be prioritized to support both research accuracy and clinical applicability. Systematically and critically integrating caregiver perspectives into adherence assessment may ultimately enhance the precision, relevance, and patient-centeredness of eye care.

3.4. Objective measurement methods

Objective approaches include indirect techniques, which infer adherence from secondary indicators (e.g., pharmacy refill records, electronic monitoring), and direct techniques, which attempt to capture actual drug administration or physiological exposure (e.g., video observation, therapeutic drug monitoring).

Refill-based measures such as medication possession ratio (MPR) and proportion of days covered (PDC) are widely used in chronic disease management and scalable across health systems, but they are poorly suited to ophthalmic care. Eye-drop prescriptions can be collected without instillation, and pharmacy data do not capture laterality, frequency, or technique, all of which critically influence treatment success (Kumar et al., 2016). Pill counts and eye drop bottle weighing, primarily limited to clinical trials, are prone to systematic overestimation due to pill dumping, parallel supplies, and (for eye drops) variable, non-therapeutic product loss; they therefore provide, at best, a noisy proxy of true implementation (Biressaw et al., 2013; Green et al., 2024; Murdoch et al., 2020; Thornburg et al., 2010).

Electronic monitoring devices (EMDs), such as Medication Event Monitoring Systems (MEMS), generate timestamped opening records and consistently detect lower adherence than self-report or counts, highlighting their sensitivity (Friedman et al., 2008; Monnette et al., 2018). Yet adapting them to eyedrops bottles remains technically challenging, and high-cost limits scalability. Pilot adaptations, including smart caps and sensor-equipped dispensers, suggest promising

ophthalmology-specific solutions (Erras et al., 2023; Kinast et al., 2023; Oltramari et al., 2024).

Direct observation, once considered the gold standard in infectious disease, is impractical for chronic therapy (Garfein and Doshi, 2019). Digital variants such as video-observed therapy (VOT) or AI-assisted mobile apps can provide high-resolution tracking but face problems of low engagement, technical failures, and regulatory hurdles (Browne et al., 2018; Gackowski et al., 2024). In ophthalmology, video recording has been used to assess instillation technique (Hennessy et al., 2011; Lee et al., 2024a), but remote verification in real-world longitudinal settings remains unvalidated. An intriguing emerging potential application of wearable sensors, at least in clinical trials, is represented by patches for amblyopia treatment equipped with microsensors and wireless chip (Hwang et al., 2024; Stewart et al., 2017). Similarly, smart contact lenses extend the wearable paradigm beyond diagnostics, with potential therapeutic functions including controlled-release drug delivery and, conceptually, objective monitoring of device use as an implementation/persistence marker. However, measurement accuracy, wireless operation and powering, wearer comfort/acceptability, and clinical translation remain major barriers (Seo et al., 2023).

Therapeutic drug monitoring (TDM) offers high specificity by measuring drug levels or metabolites in biological fluids (Pandey et al., 2015), but it is invasive, costly, and limited by variability in pharmacokinetics and “white-coat adherence” (Eskås et al., 2016). For topical ophthalmic medications, systemic levels are usually undetectable, and no validated biomarkers of ocular exposure exist, restricting TDM utility in eye care.

Across objective methods, feasibility and patient burden remain major limitations, compounded by the lack of consensus thresholds for clinically meaningful adherence. Overall, the choice of objective measure should be guided by adherence phase, treatment modality, and population characteristics. In pediatric and geriatric eye care, where dexterity, cognition, and caregiver involvement are critical, no single objective tool satisfies accuracy, scalability, and acceptability. Multimodal, theory-driven strategies remain the most rigorous path for capturing real-world adherence behavior.

4. Adherence in pediatric eye care

Pediatric eye care unfolds within a triadic model, involving child, caregiver, and healthcare provider, where roles are fluid and negotiated based on context rather than formal principles (De Civita and Dobkin, 2004; Santer et al., 2014). This triad is embedded in broader social and service environments that shape how illness is perceived and care is accessed, making adherence especially vulnerable in chronic conditions (Chapman et al., 2023; Gray, 2018; Zakayo et al., 2020). The determinants of adherence operate within this triadic structure, but their expression is conditioned by the child's developmental trajectory and the distribution of agency between child and caregiver.

A distinctive feature of pediatric adherence is the assent-to-autonomy continuum. Ethics and good practice call for graded participation: assent in infants and near-adult decisional abilities by mid-adolescence (Carter, 2009; Field and Behrman, 2004), matching engagement with maturity as well as with age (Grootens-Wiegers et al., 2017; Sobode et al., 2024). Effective shared decision-making in this context requires age-appropriate communication, respect for evolving autonomy, and sensitivity to the cultural, emotional, and psychological dimensions of pediatric care. The balance between caregiver

dependence and emerging autonomy shifts across developmental stages, with adolescence introducing peer influence, identity formation, and risk-taking behavior as additional modulators of adherence.

Fig. 2 captures these developmental gradients by distinguishing two pediatric subgroups with distinct adherence profiles. In infants and preschoolers, adherence is predominantly caregiver-determined: family dynamics emerge as a critical factor across all ABC phases (including potential risks of poor coparenting quality and fragmented care in divorced families) (Bergström et al., 2021; O'Hara and Cohen, 2024), caregiver health literacy shapes both initiation and persistence, and system-level supports such as community programs assume particular importance. In school-aged children and adolescents, the patient's own intrapersonal factors gain prominence—personal beliefs, illness perceptions, digital literacy, and self-efficacy become relevant during implementation and persistence, while peer interactions and stigma introduce social dimensions largely absent in younger children. This developmental shift has practical implications: interventions targeting younger children must engage caregivers directly, whereas those for adolescents must also address the patient's emerging autonomy, identity concerns, and social context.

A practical challenge in pediatric eye care is that adherence frequently depends on executing technique-dependent tasks, such as eye drop instillation, patching, spectacle wear, and contact lens handling, that demand sustained parental effort and management of child resistance in day-to-day implementation (Harvey et al., 2024; Pawar et al., 2023). These skill demands interact with caregiver factors: health literacy, family routines, and household stability all influence day-to-day success. At the system level, community-linked delivery models, particularly school-based programs, can mitigate socioeconomic barriers and achieve substantially higher adherence than usual care (Burnett et al., 2018; Dhiman et al., 2022).

Taken together, pediatric adherence reflects a dynamic interplay between child development, caregiver capacity, clinical demands, and system organization. Across the ABC phases, misunderstanding and stigma often hinder initiation, manual dexterity and family dynamics drive implementation, and logistics and sustained motivation determine persistence.

Guided by this framework, the following sections review the past decade of evidence for a selection of pediatric conditions: refractive errors, amblyopia, pediatric retinal diseases, glaucoma, congenital cataract, ocular surface diseases, and uveitis. These were selected for prevalence, clinical impact, and the documented complexity of adherence. For each condition we map adherence rates and patterns, describe the network of determinants, and appraise strategies with reported effectiveness, noting phase-specific issues and equity-sensitive barriers.

To keep the section focused, we include evidence tables only for the three pediatric topics with the largest literature: refractive error, myopia progression management, and amblyopia. For each, the main text presents a table of sentinel evidence (phase-specific metrics, determinants, and quality flags), illustrative rather than exhaustive, prioritizing higher-level evidence and representativeness across measurement methods and contexts; corresponding Supplementary tables expand the evidence from the past decade. Other pediatric conditions are synthesized narratively, with representative citations.

4.1. Refractive errors and myopia management

Refractive error is the most common indication for pediatric eye care, and its management spans a continuum from simple optical correction to active myopia control. Both domains share a fundamental adherence challenge, with efficacy depending on sustained daily behavior.

4.1.1. Adherence rates and patterns

Spectacle wear in children is highly variable across settings and measurement methods. A cross-sectional synthesis in low- and middle-

income countries (LMICs) reported mean compliance of approximately 40% (range 9.8–78.6%) (Dhirar et al., 2020), whereas randomized school-based programs with free provision achieved higher rates (~53%) (Wu et al., 2023). Country-level cohorts illustrate the heterogeneity: in India, non-wear reached 20% at 3–6 months, with only 30% wearing consistently at two years (Gajiwala et al., 2021; Pawar et al., 2023); in the UK, 47% maintained consistent wear over three years after screening (Bruce et al., 2018); in Africa and Nepal, approximately 60% wore spectacles at 3–4 months (Khatri et al., 2024; McCormick et al., 2019); and in US school programs, 87% were wearing at scheduled checks versus 63% by self-report, while toddlers achieved ≥ 8 h/day in 74% of cases (Harvey et al., 2024; Huang et al., 2019).

Contact lenses present a more complex picture. Large mixed-age cohorts report approximately 11 h/day average wear (Rajan et al., 2018), but pediatric rigid gas-permeable lens discontinuation can reach 51%, often within three months (Yang et al., 2025). Orthokeratology reveals the starkest gap between self-report and objective measurement: self-reported "good" adherence approached 97%, whereas objectively verified adherence was only 20%, with further declines after the first year (Bian et al., 2021; Chang and Liao, 2018).

For myopia control interventions, such as low-dose atropine, defocus-incorporated spectacles (DIMS/HALT/DOT), soft contact lenses, orthokeratology, repeated low-level red-light therapy (RLRL), and outdoor time, adherence data are increasingly available but inconsistently reported. A 2025 living Cochrane review across 25 RCTs documented wide ranges: spectacles 72–97%, soft lenses 31–100%, and pharmacologic interventions 79–99% (Lawrenson et al., 2025). Atropine trials report high implementation: LAMP achieved >91% compliance at one year across concentrations (Yam et al., 2019), and CHAMP documented 82.8% three-year completion (Zadnik et al., 2023). For spectacles, daily wear in clinical trials typically reaches 12–15 h, though persistence wanes over time (Bao et al., 2022; Lam et al., 2020; Rappon et al., 2023; Yuval et al., 2024), only 49% of the original DIMS cohort completed six years, albeit as full-time wearers (Lam et al., 2023). Real-world adherence to both pharmacologic and optical myopia control remains poorly characterized beyond generic "completion/drop-out" (Nucci et al., 2023; Yang et al., 2024). Soft contact lens adherence is mixed, with $\approx 25\%$ discontinuation before 1 month (and $\approx 24\%$ thereafter over 2 years) in one RCT versus >90% still wearing at 3 years in another (Sankaridurg et al., 2019; Gaume Giannoni et al., 2022). Orthokeratology shows lower, heterogeneous adherence to lens wear and follow-up (Chang et al., 2021a, 2021b; Jun et al., 2018). RLRL adherence (median $\approx 75\%$) correlates with treatment response: higher implementation is associated with less axial elongation (Jiang et al., 2022; Xiong et al., 2023; Kang et al., 2025). School-based outdoor programs achieve 84–88% implementation during supervised sessions (He et al., 2022; Wu et al., 2018), but objective monitoring reveals that actual outdoor exposure often falls short of prescribed targets.

Within the ABC taxonomy, most estimates capture implementation (daily wear or use). Persistence (continued treatment over months or years) is less often measured and frequently conflated with implementation, while initiation is variably reported and often implicit. This measurement heterogeneity limits cross-study comparison and intervention design.

Sentinel evidence for both spectacle correction and myopia control interventions is summarized in Tables 1 and 2; Supplementary Tables S1a, S1b, S2a, and S2b provide an expanded inventory of adherence studies from 2015 to 2025.

4.1.2. Determinants and strategies

The multilevel framework outlined in Section 2.1 applies across spectacles, contact lenses, and myopia-control modalities, with consistent patterns emerging and caregiver engagement standing out as the dominant interpersonal factor. Parental support, consistent reminders, and positive reinforcement associate with better adherence across modalities (Harvey et al., 2024; Huang et al., 2019), while parental

Table 1
Sentinel evidence on adherence to common refractive errors optical correction and follow-up in pediatric: Rates, patterns, and determinants.

Study design & Reference	Population (n°, age), Condition, Treatment	Outcome & Methods (initiation, implementation, persistence)	Adherence rate (initiation, implementation, persistence)	Determinants of Adherence
Meta-analysis Wu et al. (2023)	n = 14 RCTs Age: <18y Condition: RE Treatment: spectacle	Implementation* Compliance to treatment (reported or direct observation)	Implementation* Compliance: 53.11%	Drivers: low-income, parental attitudes and teacher incentives, higher RE severity, difficulty seeing the blackboard Barriers: age, sex, family income, urban vs. rural residence (inconsistent across studies), teasing and appearance, lack of carer's awareness of glasses necessity
Meta-analysis Dhirar et al. (2020)	n = 23 cross-sectional Age: <18y Condition: RE Treatment: spectacle	Implementation* Compliance to treatment (reported or direct observation)	Implementation* Compliance: 40.14% (95% CI = 32.78-47.50) (9.84% - 78.57%)	Barriers: breakage/lost spectacles, forgetfulness, parental disapproval, headache, teasing by peers, dislike spectacles, unclear vision, fear of injuries, lack of affordability, uncomfortable spectacles, negative attitude of the society
Cluster-randomized CT Thapa et al. (2020)	n = 297 Median age: 13y Condition: RE Treatment: free spectacle, with intervention vs control group	Implementation + Persistence**/* Adherence to treatment (wearing spectacles at 3-, 6- month at unannounced visits)	Implementation + Persistence**/* 3 months: Intervention 51% 6 months: Intervention 57%, control 48%	Driver: higher parents education (p = 0.008) Reported barriers: occasional use only (32% intervention, 35% control), belief that spectacles weaken eyes (40% control, 13% intervention), parental disapproval (19% intervention, 15% control), dislike of frames (21% intervention, 2% control), teasing or aesthetic concerns, broken/lost glasses
Prospective interventional cohort Huang et al. (2019)	n = 206 Mean age: 8.5 ± 0.7y Condition: RE Treatment: free spectacle	Implementation* - Spectacle wear compliance at unannounced school visit and reported as prescribed, at 1y and 2y Persistence* - Follow-up adherence (visit attendance), at 1 y	Implementation * Objective 1y: 87% Self-report: 1y 63%, 2y 71% Persistence* Follow-up: 1y 96%, 2y 33.5%	Not significant: public or private schools Drivers (year 1): satisfaction with glasses (OR = 4.2, p < 0.05); (year 2): parent reminders (OR = 4.2, p < 0.05), teacher reminders (OR = 6.4, p < 0.01) Reported drivers: being happy with glasses 89%, like the appearance 86%, visual reading benefit 72%, vision improvement 69% Reported barriers: need replacements 66%, not perceive benefit 40%, dislike frames 39%, teasing 20%
Prospective longitudinal observational nested within a birth cohort Bruce et al. (2018)	n = 801 Age: 4–5y Condition: RE Treatment: spectacle	Implementation - Adherence to treatment (direct observation at every assessment over 2y) Persistence - LTFU (failed to attend any visit after screening)	Implementation Adherence to treatment: 47% Persistence LTFU 30.4%	Drivers: higher maternal education (≥A-level) 39.1% of adherent vs. 23.3% of non-adherent (p = 0.005) Reported barrier: better baseline VA Not significant: age, gender, ethnicity, birth weight, gestation, or cognitive scores (BPVS), RE type
Retrospective cohort Rajan et al. (2018)	n = 360 Mean age: 31.38 ± 11.75y Condition: RE, aphakia, pseudophakia Treatment: soft CL, RGPCL, scleral	Implementation - Adherence to cleaning regimen (reported) - AWT (reported)	Implementation Adherence to cleaning regimen: 67.3% AWT: 10.92 ± 2.7 h (2–20 h)	Not reported
Cross-sectional Pawar et al. (2023)	n = 3333 (683 examined) Age: 5–17y Condition: RE Treatment: free spectacle	Initiation + Implementation + persistence**/* Spectacle wear compliance at unannounced school visit	Initiation + Implementation + persistence**/* Wear compliance: 79.5% Of them: 74% use at home and sometimes in school, 26% never use spectacles	Barriers: older age 11-15y (OR = 2.34, p = 0.015 in univariate), parents higher education (OR = 1.47, p < 0.05 in univariate), belief that spectacles are not needed (OR = 6.01, p < 0.001), parental disapproval (OR = 5.41, p < 0.001), no family members wearing glasses (OR = 2.17, p < 0.001), lesser RE (p = 0.034) Reported barriers: headache/watering (20.3%), peer pressure or teasing (14.7%), spectacle broken/lost (14.7%, 11.9%), forgot (10.7%), parents dislike spectacles wear (10.7%), spectacle frame is not good (6.8%), eyes are OK (3.4%), dislike spectacles wear (2.8%), vision does not improve (1.7%), wearing only at home (1.1%), fear (1.1%) Not significant: gender, income, school type, urban/rural setting

Sentinel studies evaluating adherence to optical correction in children and adolescents with refractive errors are presented according to the evidence hierarchy, from meta-analyses and randomized controlled trials to cohort, observational, and cross-sectional investigations. Adherence outcomes are mapped to the ABC taxonomy (initiation, implementation, and persistence). Quality flags: entries marked with an asterisk (*) denote phase attribution inferred from indirect or surrogate measures that are not clearly stated; double asterisks (**) indicate composite outcomes spanning multiple or mixed phases. Determinants are categorized as drivers and barriers, with significant quantitative associations (OR, p-values) reported when available, while qualitative determinants are presented as described in the original studies. Acronyms: AOR = adjusted odds ratio; AWT = average wearing time; CI = confidence interval; CL = contact lenses; EMR = electronic medical record; LTFU = loss to follow-up; OR = odds ratio; RCT = randomized controlled trial; RE = refractive error; RGPCL = rigid gas-permeable contact lenses; VA = visual acuity.

Table 2
Sentinel evidence on adherence to myopia control interventions and follow-up in pediatrics: Rates, patterns, and determinants.

Study design & Reference	Population (n°, age), Condition, Treatment	Outcome & Methods (initiation, implementation, persistence)	Adherence rate (initiation, implementation, persistence)	Determinants of Adherence
RCT He et al., in 2022	n = 6295 Age: 6-9y Condition: myopia Treatment: test I (additional 40 min outdoor), test II (additional 80 min outdoor), vs controls	Implementation - AWT (reported) - Compliance to additional outdoor time (wearable wrist-watch light sensor) Persistence - LTFU (visit attendance), at 2y	Implementation AWT: Control: 106 ± 27 min/day, test I: 127 ± 30 min/day, test II: 127 ± 26 min/day Compliance: test I: 84.6%, test II: 88.0% Persistence LTFU: control: 21.1%, test I: 19.4%, test II: 18.0%	Not reported
RCT Zadnik et al. (2023)	n = 573 Age: 3-16y Condition: myopia Treatment: 0.01%, 0.02% atropine vs placebo	Implementation - Compliance (return of unused/used ampules, after 3 months) Persistence - LTFU (visit attendance), at 3y	Implementation Compliance: 87.41% (total), 87.07% (placebo), 86.42% (0.01%), 88.29% (0.02%) Persistence LTFU: 7.3%	Not reported
RCT Bao et al. (2022)	n = 170 Mean age: 10.4 ± 1.2y Condition: myopia Treatment: HAL (58pz), SAL (57pz), or SVL (55pz)	Implementation - AWT (reported) - Full time wearer (reported: ≥12 h/day wear) Persistence - Drop-out (visit attendance), at 2y	Implementation AWT: 1y 13.1 h/day, 2y 14 h/day (p < 0.001) 2y: HAL: 13.4 ± 0.29 h/day, SAL: 13.4 ± 0.24 h/day, SVL: 13.9 ± 0.24 h/day (p = 0.34) Full time wearer 1y: 61%, 2y: 89% (p < 0.001) Persistence Drop-out: 6.5%	Reported barriers: changed therapy, changed to new spectacles, declined cycloplegia, moved
RCT Jiang et al. (2022)	n = 264 Age: 8-13y Condition: myopia Treatment: RLRL, SVL	Implementation - Treatment compliance (device usage logs) Persistence* - Follow-up adherence (visit attendance), at 1y	Implementation Treatment compliance: 75% (14.1%-112.1%) Persistence* Follow-up: Total 85.2%, RLRL 93.3%, SVS 78.6%	Not reported
RCT Weng et al. (2021)	n = 379 Age: 8-13y Condition: myopia Treatment: CL with central/peripheral plus (test 1-2), EDOF (test 3-4), vs SVCL	Implementation - Adherence to contact lens wear schedule (reported ≥6 days/week, >8 h/day) Persistence* - Adherence to all scheduled follow-up (visit attendance)	Implementation Treatment adherence: myopia control 63.7-74.6%, SVCL 79.6% Persistence* Follow-up adherence: myopia control 26.1-45.8%, SVCL 43%	Reported barriers: male (OR = 1.69, p < 0.001), lower baseline RE (OR = 1.42, p < 0.001), lower high contrast VA (OR = 3.26, p = 0.025), esophoria (OR = 1.65, p = 0.005), discontinuation from the study (OR = 3.07, p < 0.001), poor comfort (OR = 0.69, p < 0.001), near vision clarity (OR = 0.70, p = 0.007), lens type test (OR = 2.17 p < 0.001)
RCT Lam et al. (2020)	n = 183 Age: 8-13y Condition: myopia Treatment: DIMS (93pz), SVL (90pz)	Implementation - AWT (telephone questionnaire) Persistence* - Follow-up compliance (visit attendance), at 2y	Implementation AWT: DIMS: 15.5 ± 2.6 h/day, SVL: 15.3 ± 2.1 h/day Persistence* Follow-up compliance: Total 87.4%, DIMS 85%, SV 90%	Reported barriers: long time to wait for delivery of lenses, refuse cycloplegia, try other myopic control methods, not willing or unable to attend follow-up
RCT Yam et al. (2019)	n = 438 Age: 4-12y Condition: myopia Treatment: 0.05%, 0.025%, 0.01% atropine vs placebo	Implementation - Compliance (reported >75% of expected use) Persistence - LTFU (visit attendance), at 1y	Implementation Compliance: 93.6% (0.05%), 95.4% (0.025%), 90.9% (0.01%), 90.1% (placebo) Persistence LTFU: 7.1% (total), 6.4% (0.05%), 15.7% (0.025%), 11.8% (0.01%), 16.2% (placebo)	Not reported
Retrospective + cross-sectional Jun et al., 2018	n = 405 Mean age: 13.1 ± 3.9y Condition: myopia Treatment: Orthokeratology for for a minimum of 1 year	Implementation - Full compliance (wear and care, visits) - Wear & care behaviours compliance Persistence*	Implementation Full compliance rate: 14.1% Wear and care behavior: 18.5% Persistence* Mean follow-up: 63.3% Follow-up: 1day (100%), 1 week (100%), 1 month (100%), 3 months (98.8%), and then every 3 months thereafter (within 2 y): 95.6%,	Drivers: parent responsible for lens vs self care (29.3%, 16.3%, p = 0.046), female juveniles more independent than males in lens handling (p = 0.014) and care (p = 0.004) Reported barriers: no time (39.2%), no discomfort (21.5%), inconvenience (15%), unnecessary (10.3%), forgotten (8.4%),

(continued on next page)

Table 2 (continued)

Study design & Reference	Population (n°, age), Condition, Treatment	Outcome & Methods (initiation, implementation, persistence)	Adherence rate (initiation, implementation, persistence)	Determinants of Adherence
		- Follow-up compliance (EMR: mean, at 1day, 1week, 1-, 3-, every 3-months)	90.9%, 90.4%, 87.9%, 87.9%, 86.2%, and 86.6%	other (3.7%), expenditure (1.9%) Not significant: age, sex, wearing experience

Sentinel studies assessing adherence to myopia control interventions, as well as follow-up attendance, in pediatric populations are presented according to the evidence hierarchy, from randomized controlled trials to retrospective and cross-sectional studies. Adherence outcomes are mapped to the ABC taxonomy (initiation, implementation, and persistence). Quality flags: entries marked with an asterisk (*) denote phase attribution inferred from indirect or surrogate measures that are not clearly stated; double asterisks (**) indicate composite outcomes spanning multiple or mixed phases. Determinants are categorized as drivers and barriers, with significant quantitative associations (OR, p-values) reported when available, while qualitative determinants are presented as described in the original studies.

Acronyms: AL = axial length; CI = confidence interval; CL = contact lenses; DIMS = defocus incorporated multiple segments; EDOF = extended depth of focus; EMR = electronic medical record; HAL = highly aspherical lenses; LTFU = loss to follow-up; OR = odds ratio; RCT = randomized controlled trial; RLRL = repeated low-level red light; SAL = slightly aspherical lenses; SVCL = single-vision contact lenses; SVL single-vision lenses; VA = visual acuity.

disapproval, perceived difficulty, and caregiver fatigue predict discontinuation (Yang et al., 2025; Chang et al., 2021b; Pawar et al., 2023; Thapa et al., 2020). Higher parental education generally correlates with improved adherence (Bruce et al., 2018; Thapa et al., 2020), though findings are not uniform. Misconceptions, notably the belief that spectacles worsen vision, hinder initiation in several settings (Khatri et al., 2024; Thapa et al., 2020). Peer stigma affects both spectacle wear and visible contact lens routines, particularly during adolescence (Gajiwala et al., 2021; Pawar et al., 2023).

Clinical and regimen factors prove equally important. Ocular discomfort consistently predicts poor implementation and early discontinuation, whether from spectacle fit, contact lens intolerance, or atropine side effects (Bian et al., 2021; Ho, 2024; Yang et al., 2024, 2025). Longer treatment duration correlates negatively with continued use. For contact lenses, handling difficulties, dissatisfaction with visual performance, and safety concerns drive early dropout (Sankaridurg et al., 2019; Weng et al., 2021). Paradoxically, lower baseline myopia has been linked to poorer adherence, possibly reflecting reduced perceived benefit (Ilechie et al., 2019; Weng et al., 2021). Refusal of cycloplegia or scheduled visits has also been reported and directly compromises retention (Bao et al., 2022; X. Chen et al., 2024; Lam et al., 2020).

Among children who have received spectacles, socioeconomic status and school type show weak and inconsistent associations with subsequent adherence (Pawar et al., 2023; Li et al., 2024), though as outlined in Section 2.2, cost and access barriers remain critical determinants of whether children receive spectacles in the first place. Cost also emerged as a barrier to orthokeratology persistence in a large retrospective analysis (Ma et al., 2022), while travel burden and inconvenient scheduling compromise retention across modalities.

Evidence for adherence-enhancing interventions remains limited but informative. Free spectacle provision consistently outperforms prescription-only approaches across diverse socioeconomic contexts (Huang et al., 2019; Khatri et al., 2024; McCormick et al., 2019). School-based delivery achieves substantially higher adherence than clinic-based models by reducing logistical barriers and normalizing eye-care routines. Related school-based initiatives support these mechanisms but did not directly measure adherence to active myopia-control treatments, underscoring the need to embed adherence endpoints in future policy trials (Karuppiyah et al., 2021; Li et al., 2021; Nischal, 2025). Caregiver-directed strategies (structured routines, positive reinforcement, and attention to comfort) have demonstrated benefit, particularly in younger children (Harvey et al., 2024). Sharing objective data with families, such as axial-length measurements, improved follow-up adherence in one cohort (Chang et al., 2021a). Anticipatory counseling about myopia “rebound” after discontinuing atropine, and that switching or tapering after orthokeratology does not eliminate rebound risk, may be a lever for persistence (Lee et al., 2024b). Whether this risk-framed counseling improves adherence remains to be tested

prospectively. Digital supports show promise: a smartphone app for orthokeratology improved follow-up attendance from 78% to 100% in a pilot study, with more modest effects on daily implementation (Sun et al., 2021). Future trials should predefine adherence as a secondary outcome with standardized, phase-specific metrics and embed adherence supports as randomized components (Chang et al., 2024).

4.2. Amblyopia

Amblyopia is a neurodevelopmental disorder arising from abnormal visual input during the critical period, most commonly associated with strabismus, anisometropia, or high bilateral ametropia (Pediatric Eye Disease Investigator Group, 2002). Treatment modalities, including occlusion, pharmacological penalization, refractive correction, and emerging binocular/digital therapies, each present distinct adherence challenges. A consistent pattern emerges across modalities: self-reported adherence substantially overestimates objectively measured implementation, and adherence tends to decline over time.

4.2.1. Adherence rates and patterns

For patching, self-reported adherence spans 34–92% across settings and age groups, but occlusion-dose monitors (ODM) typically record lower day-to-day implementation (~60–65% at 12 weeks), exposing systematic diary overestimation (Gao et al., 2021; Maconachie et al., 2016). Sensor-equipped intermittent-occlusion glasses show average adherence of approximately 50% over the first weeks, with small declines by three months, in a narrower and younger age group (Wang et al., 2019).

For atropine penalization, adherence evidence remains relatively sparse and largely caregiver-reported, with compliance estimates ranging from 59% to 94% and often exceeding those for patching (Wang, 2015). Objective tracking, however, reveals lower implementation that declines over time: in a MEMS pilot study, compliance averaged 78% (versus 84% by parental log) at 4 weeks and fell to 62% (versus 84%) at 12 weeks, with significantly higher adherence for twice-weekly than for daily dosing ($p = 0.03$) (Wang et al., 2015). One RCT using dynamic accommodation testing reported 12.9% non-compliance (Tejedor and Ogallar, 2008).

For spectacle correction, whether as primary optical treatment or as a run-in phase, objectively monitored wear reaches moderate-to-high levels within middle childhood. In a 16-week optical-only period, children wore spectacles 9.7 ± 2.4 h/day, corresponding to approximately 73% of estimated waking time (Kadhum et al., 2024). A separate cohort reported median 70% adherence over 18 weeks, with a dose–response relationship between wear time and visual acuity improvement (Maconachie et al., 2016).

Emerging digital and dichoptic platforms, including Occlu-pad, CureSight, and Luminopia, embed real-time usage logging and gamified engagement loops. These technologies have demonstrated higher

adherence rates (70–96%) compared with traditional occlusion under trial conditions, in children of middle childhood (Li et al., 2022; Totsuka et al., 2018; Wagnanski-Jaffe et al., 2025; Xiao et al., 2021). Session fragmentation, parental involvement demands, and daily routine disruption remain relevant challenges even with these novel approaches.

Within the ABC taxonomy, most published estimates reflect implementation (daily wear/use). Persistence (maintenance over months) is less often measured and frequently conflated with implementation; initiation (e.g., starting patching after refractive adaptation) is variably

reported and sometimes inferred rather than captured.

Sentinel studies are summarized in Table 3, with an expanded inventory for 2015–2025 in Supplementary Table S3a and S3b.

4.2.2. Determinants and strategies

No single demographic predictor proves universally robust in amblyopia treatment. Most series report no consistent effect of age or sex on day-to-day implementation, though older age, non-white race, and lack of insurance were associated with loss to follow-up in a large real-world cohort (Shoshany et al., 2021).

Table 3
Sentinel evidence on adherence to amblyopia treatments and follow-up in children: Rates, patterns, and determinants.

Study design & reference	Population (n ^a , age), Condition, Treatment	Outcome & Methods (initiation, implementation, persistence)	Adherence rate (initiation, implementation, persistence)	Determinants of Adherence (initiation, implementation, persistence)
RCT Wagnanski-Jaffe et al. (2025)	n = 149 Age: 4-9y Condition: anisometropia, strabismus, both Intervention: CureSight (75), patching (74)	Implementation - Objective compliance tracking via CureSight (actual treatment hours completed/prescribed treatment hours) and reported for patching - Compliance rate in per protocol (PP) (reported >60% at week 16)	Implementation CureSight 94% (63–178%) Patching 84% (60–130%) Compliance >60%: 73,833 PP binocular: 96% (63–178%) PP Patching: 92% (60–130%)	Drivers: CureSight usage vs patching (p = 0.0038) Reported drivers: better comfort, gamification, absence of occlusion, and passive watching model
Prospective longitudinal interventional (pre RCT) Kadhun et al. (2024)	n = 65 Mean age: 6.0 ± 2.2y Condition: anisometropia, strabismus, combined Intervention: spectacle wear with ODM	Implementation Objective spectacle compliance (ODM-measured wear time vs. estimated wake time)	Implementation ODM mean: 73% ± 18% of estimated waking hours (IQR: 16%–100%)	Reported drivers: parental motivation, structured monitoring (ODM)
Prospective longitudinal Totsuka et al. (2018)	n = 138 Mean age: 5.5 ± 1.6y Condition: anisometropia, strabismus Intervention: Occlupad, patching	Implementation - Objective compliance via Occlu-pad device system - Parent-reported compliance for the patching group (% of prescribed time completed)	Implementation Occlu-pad group: 3 months: 70%, 6 months: 68-72% Patching group: 3 months: 34%	Reported drivers: gamification, immersive and engaging VR environment, absence of occlusion (no patching), and structured supervised in-center sessions
Prospective longitudinal Maconachie et al. (2016)	n = 40 Age: 3-12y Condition: anisometropia, strabismus Intervention: glasses full time, glasses + patching	Implementation Objective adherence measurement via GDM and ODM (% of waking hours, in glasses phase and in combined phase)	Implementation Adherence in glasses phase: 70% ± 25.3% Adherence in patching phase: glasses 76.3% ± 21.5%, occlusion 61.9% ± 27.6%	Reported barriers: loss of the monitor, technical issues Not significant: type of amblyopia
Prospective longitudinal pilot study Xiao et al. (2021)	n = 90 Mean age: 6.7 ± 2.0y Condition: unilateral amblyopia due to strabismus, anisometropia, or both Intervention: Luminopia therapy	Implementation - Objective adherence tracking via therapeutic headset (% of total time prescribed watching videos) Implementation + Persistence**/** - LTFU (visit attendance)	Implementation Median adherence 86% (IQR 70–97%) Implementation + Persistence**/** Follow-up: 82% (9 noncompliant, 7 lost to follow-up)	Reported drivers: gamification, personalized content choice, passive non-occlusive design, automated tracking, and parent access to usage data
Retrospective cohort Shoshany et al. (2021)	n = 2037 Age: 2-12y Condition: deprivation, anisometropia, strabismus, mixed, comorbid ocular condition Intervention: spectacles, patching, atropine	Persistence LTFU (EMR)	Persistence LTFU: 23%	Barriers (in multivariate): lack of insurance (OR = 4.26, p < 0.001), previous atropine treatment (OR = 2.48, p = 0.035), previous glasses treatment (OR = 2.23, p < 0.001), follow-up time ≥3 months (OR = 1.82, p = 0.001), age >6y (OR = 1.51, p = 0.007) Not significant: ethnicity, type of amblyopia and treatment
Retrospective Sabri et al. (2017)	n = 41 Median age: 37months Condition: unilateral amblyopia (esotropia, anisometropia, cataract), unresponsive to patching Intervention: patching post-splint use	Persistence* Non-compliance without continued splint use (reported patching <50% of specified time or consistently removing patch)	Persistence* Post-splint non-compliance: 17%	Reported drivers: inability to remove the patch with elbows immobilized, strong parental motivation, short required splint duration Reported barriers: initial distress in children, need for parental acceptance

Sentinel studies evaluating adherence to amblyopia treatments, as well as follow-up adherence, are presented according to the evidence hierarchy, from randomized controlled trials to longitudinal, retrospective, and cross-sectional studies. Adherence outcomes are mapped to the ABC taxonomy (initiation, implementation, and persistence). Quality flags: entries marked with an asterisk (*) denote phase attribution inferred from indirect or surrogate measures that are not clearly stated; double asterisks (**) indicate composite outcomes spanning multiple or mixed phases. Determinants are categorized as drivers and barriers, with significant quantitative associations (OR, p-values) reported when available, while qualitative determinants are presented as described in the original studies.

Acronyms: CI = confidence interval; EMR = electronic medical record; GDM = Glasses Dose Monitor; LTFU = loss to follow-up; ODM = Objective Dose Monitor; OR = odds ratio; PP = per protocol; RCT = randomized controlled trial; VA = visual acuity.

Parental understanding, engagement, and motivation are consistently reported as facilitators of adherence (Dean et al., 2016; Kadhum et al., 2024; Mezaad-Koursh et al., 2018; Sabri et al., 2017; Xiao et al., 2020, 2021). Social stigma and high visibility of the patch act as barriers, particularly among school-aged children (Totsuka et al., 2018; Wang et al., 2019). Complex or lengthy regimens introduce logistical friction that families struggle to sustain (Maconachie et al., 2016), and child resistance, emotional distress, and treatment fatigue frequently drive early discontinuation (Gao et al., 2021; Sabri et al., 2017). Similar considerations apply to pharmacological penalization: reduced-frequency regimens such as weekend atropine dosing may lower daily burden and support implementation, consistent with PEDIG evidence that weekend atropine achieved visual acuity improvement comparable to patching (Scheiman et al., 2008). Tolerability concerns (photophobia, near-blur) and the need for timely follow-up to detect overtreatment remain important constraints (Wang, 2015). At the system level, socioeconomic disadvantages and language discordance further correlate with poorer adherence continuity (Loudon et al., 2006).

Evidence for adherence-enhancing interventions is heterogeneous but informative. Interventions incorporating child-friendly explanations, caregiver guidance, behavioral reinforcement, and visual tools produce a small but significant improvement in patching compliance (meta-analytic effect size $r = 0.249$; $p < 0.001$) (Dean et al., 2016). The Patchbook program showed promising uptake, particularly in low-socioeconomic settings where language barriers and limited health literacy are prevalent (Tjiam et al., 2012, 2016). More recently, a structured nurse-led counseling program achieved adherence exceeding 90% at 12 weeks versus 11% with standard care, with superior visual acuity outcomes (Shivani et al., 2024).

Technology-enabled therapies embed adherence supports directly into treatment delivery: real-time tracking, gamification, and engagement loops strengthen implementation under trial conditions, though effects on long-term persistence require confirmation (Nikolaidou et al., 2024). Objective monitoring via ODMs provides accurate adherence data, exposes systematic diary overestimation, and enables feedback-informed care (Maconachie et al., 2016; Wang et al., 2019).

4.3. Retinal diseases (pediatrics)

Adherence to follow-up and treatment in pediatric retinal diseases is crucial for preventing vision loss, yet it remains challenging across various conditions. Many pediatric retinal diseases require ongoing surveillance or timely interventions during infancy or early childhood, making caregivers and health systems pivotal to maintaining continuity of care. Recent studies over the past decade indicate that while high adherence is attainable in specialized programs, substantial gaps persist in less structured settings. Below, we review adherence rates and patterns, determinants, and strategies for improvement in 3 key pediatric retinal conditions: retinopathy of prematurity (ROP), retinoblastoma, and sickle cell retinopathy.

4.3.1. Adherence rates and patterns

ROP follow-up has been studied more extensively than other pediatric retinal disorders, revealing a stark dichotomy between structured programs and fragmented care. In a multicenter California cohort of 402 neonates, 93.6% were successfully followed until complete retinal vascularization during hospitalization, yet only 53.5% had documented pediatric ophthalmology follow-up within a year after discharge (Mahmud et al., 2023). The clinical consequences are sobering: a Swedish nationwide study found that among very preterm children who developed stage 4–5 ROP, 65% of resulting severe visual disability was potentially avoidable with timely adherence to screening and treatment guidelines (Norman et al., 2019).

Highly structured programs demonstrate that near-perfect adherence is achievable. A US initiative using an electronic platform ("ROP Check")

across 13 units enrolled over 2200 at-risk infants; 98% received initial screening and 97.4% completed all follow-up exams within guideline-recommended intervals, with 99.3% of indicated treatments administered on time (Arnold et al., 2017). Similarly, a Hong Kong regional program achieved 99.7% compliance with all scheduled ROP screenings among 602 premature infants (Luk et al., 2017).

Retinoblastoma exemplifies how adherence dictates survival. In high-income countries, comprehensive care yields cure rates exceeding 95% (Abramson, 2014). In contrast, a cohort from Côte d'Ivoire and D.R. Congo ($n = 175$) reported that 27.4% abandoned treatment prematurely and 18.3% were lost to follow-up after completing therapy; nearly half of families (45.1%) refused enucleation and 22.3% refused chemotherapy at some point (Lukamba et al., 2023). These patterns contribute to the 70–80% retinoblastoma mortality observed in some LMICs.

Sickle cell retinopathy requires periodic surveillance, particularly during adolescence. A quality improvement study at a tertiary pediatric center reported a 49% no-show rate for ophthalmology appointments, despite same-day scheduling with hematology visits (Louie et al., 2025).

Within the ABC taxonomy, ROP adherence challenges span initiation (timely first screening), implementation (maintaining interval fidelity), and persistence (continuity after discharge). Retinoblastoma adherence failures manifest as treatment refusal (initiation) and abandonment (persistence), while sickle cell disease primarily involves implementation gaps in routine surveillance.

4.3.2. Determinants and strategies

System-level factors prove particularly influential in pediatric retinal follow-up: fragmented care systems consistently show higher loss to follow-up, whereas integrated, actively tracked pathways retain patients (Arnold et al., 2017; Louie et al., 2025). In the California multicenter study, infants on public insurance were significantly less likely to attend post-discharge ophthalmology follow-up (OR 0.66); among those at academic centers, only 36.5% received recommended follow-up compared to 59–64% at safety-net hospitals explicitly structured to support vulnerable populations (Mahmud et al., 2023).

Traditional demographic factors show weak or inconsistent associations with follow-up (Mahmud et al., 2023). At the clinical level, extremely low birth weight predicted non-compliance in one Texas cohort, showing that, paradoxically, the smallest infants faced the highest risk, likely reflecting competing medical demands that overwhelm caregivers (Santaineau et al., 2024). The child's immediate health and competing medical needs are real determinants of whether adherence may be implemented at a given time (Crosby et al., 2009). Social services intervention was required in 11% of cases to ensure ROP follow-up (Santaineau et al., 2024). In retinoblastoma, fear, cultural stigma around enucleation, and misperceptions about chemotherapy drive refusal and abandonment (Lukamba et al., 2023).

Effective strategies target specific failure points. Standardized pathways with explicit timing windows dramatically reduce missed care, as demonstrated in Hong Kong's territory-wide implementation and US programs using structured schedules (Luk et al., 2017; Fierison, 2018). Digital tracking tools can eliminate gaps: one unit moved from 11% missed examinations with paper reminders to 0% missed with a cloud-based platform, while reducing documentation time (Arnold et al., 2012). Multi-site analyses drawing on the same platform suggest similar system-level gains (Arnold et al., 2017; Jacob et al., 2018). Telemedicine for ROP has proven cost-effective with high sensitivity and specificity, potentially expanding capacity in resource-limited settings (Brady et al., 2020; Fijalkowski et al., 2014; Morrison et al., 2016).

For multispecialty care, geography matters: relocating ophthalmology to the hematology floor reduced sickle cell no-shows from 49% to 39% within 3.5 months (Louie et al., 2025). In retinoblastoma, addressing decisional conflict through extended counseling, psychosocial support, financial assistance, and peer advocates may enable adherence to life-saving care (Lukamba et al., 2023).

4.4. Childhood glaucoma

Childhood glaucoma, including primary congenital and developmental forms, requires lifelong therapy and close monitoring. Adherence data are limited and highly variable, reflecting differences in populations, methodology, and how adherence is operationally defined.

4.4.1. Adherence rates and patterns

Visit adherence varies widely across settings. In one US retrospective cohort, 43% of pediatric glaucoma patients were lost to tertiary follow-up, with only 54% considered adherent based on visit attendance (Mikolajczyk et al., 2021). Conversely, Heckenlaible et al. (2024) reported 90.4% mean visit completion with no significant variation by patient characteristics. In a South Indian cross-sectional study, only half of children attended their next scheduled visit even after home visits aimed at engaging caregivers (Pillai et al., 2025).

Medication adherence is more difficult to ensure. In a Saudi Arabian cross-sectional study, only 23.6% of parents reported full adherence to prescribed drops, while 34.9% reported missing all doses on at least one of the previous three days (Al-Dawood et al., 2022). Objective monitoring confirms high variability: Moore et al. (2015) reported mean adherence of 93% (range 43–107%) with poor correlation between subjective and objective measures, particularly when the children were responsible for administering their own eyedrops (Moore et al., 2015), while Freedman et al. (2012) found the proportion of doses taken on schedule ranged from 3% to 97% (Freedman et al., 2012).

4.4.2. Determinants and strategies

Demographic correlates (age, sex, travel distance) are inconsistent across series (Freedman et al., 2012; Mikolajczyk et al., 2021), while non-White race predicted missed follow-up in one US cohort (Mikolajczyk et al., 2021). In resource-limited contexts, difficulties obtaining medications and high out-of-pocket costs are associated with poorer adherence (Liu et al., 2022).

Family dynamics prove crucial: doses taken on schedule are higher when parents rather than children administer drops (Freedman et al., 2012). Caregiver health literacy consistently predicts both dose-taking and timing (Freedman et al., 2012; Moore et al., 2015); caregiver burden, forgetfulness, and complexity of the regimen are frequently cited barriers (Al-Dawood et al., 2022). Psychological distress – anxiety, depression, pessimism about benefit – further undermines day-to-day implementation, as reported by two-thirds of caregivers of preschool children with glaucoma (Liu et al., 2022).

Disease stage/control has not shown a consistent relationship with adherence, although prior glaucoma surgery predicted better visit adherence in one study (Pillai et al., 2025). At the system level, long travel distances, low income, and limited access to tertiary care recur among non-adherent patients (Al-Dawood et al., 2022; Mikolajczyk et al., 2021); state-based insurance correlated with lower procedure/monitoring rates in one real-world analysis (Heckenlaible et al., 2024). Sociocultural taboos around chronic eye disease or pediatric surgery may additionally reduce care engagement in specific settings (Rao et al., 2020).

No randomized trials specifically target adherence in childhood glaucoma. Practice recommendations derive from observational correlates: provide literacy-sensitive instruction, assign drop administration to adult caregivers when feasible, and implement pre-booked follow-up with active recall. Childhood glaucoma adherence trials remain a priority research gap.

4.5. Congenital cataract

Visual recovery after congenital cataract depends not only on timely surgery but also on sustained adherence to optical correction, amblyopia therapy, and long-term follow-up. The Infant Aphakia Treatment Study (IATS), which provided contact lenses and spectacles at no cost, offers

the most comprehensive adherence data; real-world studies reveal additional challenges in resource-limited contexts.

4.5.1. Adherence rates and patterns

In the IATS cohort, patching adherence was moderate: an average of 3.7 h/day in the first year and 3.4 h/day thereafter (Drews-Botsch et al., 2016). Contact lens wear was high and durable: the median percentage of waking hours with the lens in place was 95% in year 1 (IQR 84–100), 93% in years 2–3 (IQR 85–99), 93% in year 4 (IQR 75–99), and 89% in year 5 (IQR 71–97); overall, most children wore the lens for >80% of waking hours across follow-up (Cromelin et al., 2018). Spectacle adherence showed greater variability: median 80% at age 4 (IQR 45–91), and children with $\geq 20/40$ VA in the treated eye were more likely to report $\geq 80\%$ wear (66% vs 42%, $P = 0.034$) (Lambert et al., 2019). Among children using both modalities, contact lens adherence exceeded spectacle adherence.

Real-world data reveal context-specific patterns. In South China, among 192 aphakic infants with bilateral congenital cataract, caregiver-reported full-time spectacle wear increased from 30.9% at 3–12 months to 87.0% at 2–3 years, highlighting developmental and routine effects (Cao et al., 2018). In Kinshasa, only 71% of children returned for the first postoperative visit, illustrating retention challenges in resource-limited settings (Schulz et al., 2025).

4.5.2. Determinants and strategies

Adherence after congenital cataract surgery reflects interacting influences at the child/caregiver, relational, clinical, and system levels. Within the ABC taxonomy, most determinants act on implementation (day-to-day patching and optical wear) and persistence (retention over months), while initiation is shaped by access and early postoperative support.

Across IATS analyses, adherence patterns did not vary consistently by sex (Drews-Botsch et al., 2016; Lambert et al., 2019), whereas real-world data from Kinshasa showed lower early follow-up return among girls and younger children, highlighting context-specific vulnerabilities that chiefly affect persistence (Schulz et al., 2025). Caregiver well-being is pivotal: higher parenting stress at 3 months post-surgery predicted subsequent reductions in patching time, identifying an early modifiable barrier (Drews-Botsch et al., 2019). Parental engagement, clear understanding of goals, and consistent clinician reinforcement during visits support adherence (Zhang et al., 2024); conversely, caregiver isolation and inconsistent messaging undermine routines (Cao et al., 2018).

Perceived benefit reinforces implementation. In IATS, contact lenses showed higher adherence than spectacles, signaling stronger implementation with a modality perceived to deliver clearer vision (Lambert et al., 2019). At four years, $\geq 20/40$ visual acuity in the treated eye was associated with $\geq 80\%$ spectacle wear (Cromelin et al., 2018). In Chinese infants, comfortable, well-fitting frames were associated with better compliance (Cao et al., 2018). Real-world studies have reported that children who were blind/severely impaired at baseline had a lower probability of attending the first follow-up, and bilateral cataract carried a 29% lower attendance risk versus unilateral children (Schulz et al., 2025); paradoxically, very good post-op VA also predicted lower attendance, consistent with success-driven drop-off. System-level factors shape all phases: free provision in IATS likely supported initiation and persistence (Cromelin et al., 2018; Lambert et al., 2010, 2019), while in resource-limited settings retention remains a major challenge (Schulz et al., 2025).

The strongest intervention evidence comes from mobile health. In a Chinese RCT ($n = 258$), automated SMS reminders significantly increased follow-up attendance (RR 1.47; number needed to remind ≈ 3) and yielded more timely clinical interventions (Lin et al., 2012). A prospective WeChat-based service combining education, reminders, and appointment management improved cumulative follow-up (93.6% vs 80.5%) and refractive correction compliance (Chang et al., 2018). A

separate RCT of interactive parental education reduced anxiety and improved knowledge and satisfaction, addressing determinants linked to missed visits (Chen et al., 2020). In children with congenital ectopia lentis, WeChat-based follow-up support also increased postoperative attendance versus standard care (Ma et al., 2025).

Actionable strategies include automated reminder systems, app-based education and scheduling, and brief literacy-sensitive caregiver support at initiation and early follow-up. Trials directly linking these interventions to adherence with amblyopia therapy and long-term visit persistence remain an important research gap.

4.6. Corneal and ocular surface disease (pediatrics)

A wide range of corneal and ocular surface diseases often require prolonged topical or systemic therapy and close follow-up. Here, we review adherence rates and patterns, determinants, and strategies for improvement in three high-burden conditions: herpes simplex virus keratitis (HSK), pediatric blepharokeratoconjunctivitis (BKC), and vernal keratoconjunctivitis (VKC). Moreover, we summarize adherence evidence in trachoma, considering that, in endemic settings, preschool-age children form the principal reservoir, and as of April 2025 an estimated 103 million people live in endemic districts at risk (World Health Organization, 2025. <https://www.who.int/news-room/fact-sheets/detail/trachoma>).

4.6.1. Adherence rates and patterns

In HSK, the link between adherence and outcomes is direct. A pediatric cohort reported adherence to acyclovir prophylaxis in 100% of patients with no recurrences versus 36.4% of those with ≥ 1 recurrence (Luccarelli et al., 2021). Consistent with adult HEDS principles (Kalezic et al., 2018), another large retrospective cohort found 35% recurrence in children who stopped prophylaxis versus zero in those completing one year of treatment (Serna-Ojeda et al., 2015).

BKC exemplifies daily-burden adherence, with hygiene measures and multi-drop regimens dominating management (Ortiz-Morales et al., 2023, 2025). Evidence is extremely limited: two Cochrane reviews found no eligible RCT for systemic therapy (O'Gallagher et al., 2016) and only one small trial with very low-certainty evidence and no adherence endpoints for topical therapy (O'Gallagher et al., 2017). A Moorfields longitudinal series reported intentional discontinuation in 64/145 children treated with topical cyclosporine A (CsA) (Dahlmann-Noor et al., 2022).

VKC demands months-to-years of topical immunomodulation. Although RCTs lack pre-specified adherence outcomes, the VEKTIS study reported discontinuation rates of 10.5%, 20.4%, and 15.5% across the two CsA arms and vehicle, respectively, over 4 months (Leonardi et al., 2019). Real-world data reveal marked geographic disparities: in India, a cross-sectional study of 65 children found 86.15% follow-up compliance but 56.92% poor treatment adherence (Wadhvani et al., 2021), whereas a German retrospective series on tacrolimus 0.03% reported poor implementation in only 4/21 patients over 41.3 months (Müller et al., 2019), a contrast that may reflect differences in healthcare access, medication costs, and caregiver support between settings.

In trachoma, adherence to the 6-week tetracycline eye ointment (TEO) regimen during mass drug administration remains critically low in resource-limited endemic settings, predominantly in LMICs. A Cochrane review noted that oral and topical treatments are equivalent if used as prescribed, but single-dose oral azithromycin is more effective operationally due to poor TEO compliance (Evans et al., 2019). An Ethiopian study found only 2% achieved full adherence, with regular use dropping from 49% in week one to 9% by week six (Aragie et al., 2024); similarly, a Nigerian survey reported 87% poor implementation and only 2% completing the full course (Amanyi-Enegela et al., 2025).

4.6.2. Determinants and strategies

Tolerability, regimen burden, caregiver understanding, and access

emerge as recurring determinants, with their relative weight varying by condition and setting.

In HSK, intentional non-adherence often reflects fears of long-term adverse effects, dosing difficulties in young children, and doubts about efficacy, pointing to the need for coordinated messaging between eye care practitioners and pediatricians (Luccarelli et al., 2021). Early, literacy-sensitive counseling, explaining the rationale and safety of prolonged prophylaxis, combined with reliable refill pathways, targets these drivers (Serna-Ojeda et al., 2015; Luccarelli et al., 2021).

In BKC, the daily cumulative burden of lid hygiene and multi-drop regimens is difficult to sustain (Ortiz-Morales et al., 2025; Roust, 2017). The Moorfields series found that CsA discontinuation was most often administrative or perception-related (expired prescriptions, families not seeking re-prescription, or belief that treatment was no longer needed) rather than tolerability-driven (Dahlmann-Noor et al., 2022). These system-level barriers, documented in a high-income setting with universal coverage, may differ substantially in contexts where out-of-pocket costs and medication availability dominate. Pragmatic simplification, explicit training with written guidance for lid-hygiene routines, and proactive discussion of expectations may reduce friction, though the evidence base remains sparse and calls for trials with pre-specified adherence outcomes (O'Gallagher et al., 2016, 2017).

In VKC, tolerability is central: stinging and burning with CsA or tacrolimus can precipitate non-initiation or early discontinuation. Case series also implicate caregivers' knowledge gaps, regimen friction, and psychological burden from the chronic disease course (Müller et al., 2019; Wadhvani et al., 2021). A recent review noted that apparent treatment refractoriness may partly reflect compliance factors (Agarwal et al., 2024). The striking adherence gap between high-income and LMIC settings suggests that access, affordability, and health literacy compound these clinical barriers in resource-limited contexts. Selecting better-tolerated steroid-sparing agents, scheduling structured follow-up, and focusing caregiver education on realistic expectations may support persistence.

In trachoma, regimen burden dominates: 6-week TEO proves operationally inferior to single-dose directly observed therapy with azithromycin (Aragie et al., 2024; Amanyi-Enegela et al., 2025). Effective program-level strategies include clear caregiver-facing instructions, integration with community touch-points, and, critically, active population engagement rather than passive education (Solomon and Burton, 2004; Francis and Turner, 1995).

Across all conditions, direct interventional evidence targeting adherence is limited. Notably, publications emphasizing parental engagement focus on education about disease and treatments rather than shared decision-making and patient-centered approaches (Agarwal et al., 2024; Ortiz-Morales et al., 2023, 2025; Roust, 2017). Most adherence evidence for HSK and BKC derives from high-income settings; how access, medication costs, and health-system factors shape adherence in LMICs remains largely unexplored. Pediatric ocular surface adherence trials with pre-specified endpoints, stratified by economic context, remain a priority research gap.

4.7. Pediatric non-infectious uveitis

Pediatric non-infectious uveitis (NIU) is often asymptomatic yet sight-threatening, requiring chronic immunosuppression and intensive follow-up (Holland et al., 2009; Rosenberg et al., 2004). Adherence spans implementation (day-to-day dosing), persistence (maintaining therapy over months/years), and retention (attending monitoring visits) (Chang et al., 2021c).

4.7.1. Adherence rates and patterns

Links between adherence and inflammatory control are documented in observational cohorts. In a long-term infliximab series, incomplete adherence (missed systemic/topical doses, delayed infusions, or missed visits) was reported in 17/27 patients over a mean follow-up of 42

months, and was associated with approximately 10-fold higher odds of active uveitis while on therapy, despite overall disease control in 89% and steroid-free remission in 58% of patients (Miraldi Utz et al., 2019). In an independent cohort on immunomodulatory therapy, only 59% of children were classified as compliant, and poor adherence correlated with markedly lower steroid-free remission (21% vs 79%) (Ashkenazy et al., 2019).

Adherence challenges also extend to screening/monitoring pathways in juvenile idiopathic arthritis (JIA). In the ICON-JIA prospective cohort, only 63.9% of children adhered to recommended ophthalmic screening intervals over approximately 3 years; nonadherence was more frequent in higher-risk phenotypes and associated with worse visual acuity at uveitis diagnosis (Walscheid et al., 2020). These data should be interpreted against the benchmark of the 2019 American College of Rheumatology/Arthritis Foundation guideline on screening for JIA-associated uveitis (Angeles-Han et al., 2019).

For topical steroids, objective measures highlight a substantial implementation gap. In a prospective clinic study using bottle-weighing of prednisolone 1%, 75% of children used less than prescribed and 25% used less than half the expected volume; discrepancies between parent and child reports were common, with frequent dosing errors admitted by 33.3% of children versus only 9.7% of parents, and 40.6% of parents unable to recall the correct frequency (Green et al., 2024).

4.7.2. Determinants and strategies

At the individual level, younger age, shorter disease duration, oligoarticular subtype, and ANA positivity have been associated with higher nonadherence to JIA screening schedules (Walscheid et al., 2020). In NIU more broadly, a high proportion of nonadherent children have associated systemic disease, suggesting that the complexity of managing comorbid conditions may further hinder adherence (Ashkenazy et al., 2019; Miraldi Utz et al., 2019). At the interpersonal level, caregiver negligence and family strife have been independently associated with nonadherence, underscoring that relational stability and informational competence are critical to sustained engagement with care (Ashkenazy et al., 2019).

Clinical complexity interplays with logistic issues: polypharmacy, travel burden for infusions/visits, and family stressors recur as barriers in observational cohorts (Ashkenazy et al., 2019; Walscheid et al., 2020); bottle-weighing data suggested misunderstanding of topical regimens (frequency/technique) and mismatches between child and parent reports (Green et al., 2024). Recent multicenter U.S. surveys (mixed adult–pediatric) from high-income settings with variable insurance coverage investigated self-reported barriers: over 6 months, 21% reported a missed/cancelled visit, copay costs limited visit frequency for 7%, 8% could not take time off work, 5% cited transportation barriers, and 11.5% lived more than 100 miles from the clinic (Sun et al., 2025a). For immunosuppressive therapy, 52% needed reminders, 20% had difficulty taking medications regularly, 12% struggled with multiple daily dosing, and 15% missed doses due to refill gaps (Sun et al., 2025b). Because these samples are adult-weighted, pediatric-specific barriers, such as dependence on caregivers and school schedules, are likely under-represented. These barriers, documented in high-income settings, are likely amplified in LMICs where biologic therapies remain largely inaccessible and out-of-pocket costs dominate.

No randomized or prospective adherence-targeted trials exist in pediatric uveitis. Accordingly, practice suggestions align with observed determinants: literacy-sensitive instruction (clear written/visual schedules, teach-back), assigning drop administration to an adult when feasible, and simplification of topical regimens may address common day-to-day errors. Coordinated rheumatology–ophthalmology calendars with pre-booked visits and active recall can target the work/transport frictions flagged in observational studies. For immunosuppressive therapy, embedding reminder systems and providing injection training/assistance align with frequently reported implementation hurdles; proactively managing refill continuity and lowering the burden of

laboratory monitoring represent practical, testable levers. For biologics, the infusion-center delivery experience provided verifiable administration and predictable scheduling, mitigating nonadherence compared with fully self-administered regimens (Miraldi Utz et al., 2019). When clinical control wanes, therapeutic drug monitoring can help separate missed doses/under-dosing from pharmacokinetic or immunogenic causes, guiding interval/dose optimization and consideration of cDMARD co-therapy (Dehoorne et al., 2023).

Notably, all adherence evidence in pediatric NIU derives exclusively from high-income countries (USA, UK, Germany, Israel); how limited specialist access, medication costs, and health-system fragmentation shape adherence in LMICs remains largely unexplored. Pediatric uveitis trials should pre-specify phase-specific adherence endpoints and pair caregiver- and child-reported measures with objective metrics, with stratification by economic context as a priority.

5. Adherence in elderly eye care

Aging is a dynamic, multifactorial process marked by declining physiologic reserve and cognitive flexibility, driven by interconnected mechanisms that increase multimorbidity and reduce capacity to manage complex regimens (López-Otín et al., 2023). The 65-year cutoff is policy-driven and biologically arbitrary (Beard et al., 2016), yet at this stage multimorbidity, polypharmacy, and functional decline are common, undermining adherence and increasing reliance on health systems (Gellad et al., 2011).

A critical distinction for this population is functional status rather than chronological age. Fig. 2 separates independent elderly (those who retain capacity for self-management) from dependent or cognitively impaired elderly, for whom adherence becomes largely caregiver-mediated. These two groups present strikingly different adherence profiles. For independent elderly, visual acuity and manual dexterity are pivotal during initiation and implementation: the ability to instill eye drops correctly, handle bottle applicators, and read medication instructions determines day-to-day success. Regimen complexity, tolerability, and polypharmacy also assume prominence, as does social isolation during implementation and persistence. For dependent or cognitively impaired elderly, by contrast, individual-level (clinical factors–regimen complexity, bottle usability, technique demands) recede in importance because the patient no longer manages therapy directly; instead, formal caregiver involvement becomes the critical determinant across all ABC phases, and the aging trajectory itself shapes the progressive transfer of adherence responsibility. While advanced age correlates with functional decline (loss to follow-up reached 51% by two years among those aged 90 and older in Danish intravitreal injection cohorts) (Subhi and Sørensen, 2017), it is functional status that determines which barriers are rate-limiting.

A related distinction is living situation: most adherence evidence pertains to community-dwelling older adults, yet those in residential or nursing-home care face a different barrier profile. In institutional settings, medication administration is typically systematized, and adherence responsibility shifts entirely to professional caregivers, potentially improving implementation but introducing new vulnerabilities around care transitions, staff turnover, and coordination with external eye-care providers. The functional status framework in Fig. 2 partially captures this gradient, since institutionalized individuals are predominantly in the dependent category, but the organizational context of care delivery adds a distinct layer of determinants that warrants explicit consideration in service design.

Moreover, frailty, a multidimensional expression of cumulative decline, predicts poor outcomes better than chronological age alone and is associated with hospitalization, institutionalization, and non-adherence (Clegg et al., 2013). In ophthalmic care, frailty can limit follow-up attendance, eye drop instillation, and management of complex regimens, particularly without caregiver support (Killeen et al., 2020; Sobolewska et al., 2021). Importantly, in advanced frailty or limited life

expectancy, adherence goals should be recalibrated to reflect patient values, prioritizing quality of life and ethical deprescribing where appropriate (Gellad et al., 2011). More broadly, adherence in later life reflects interacting relational, cognitive, psychological, pharmacologic, and system factors, well-illustrated by the geriatric 'flower model' (Yap et al., 2016).

In eye care, these challenges are compounded by visual impairment and reduced manual dexterity, which affect both self-administration of topical medications and the ability to navigate care systems (Gellad et al., 2011). For patients who remain independent, individual-level factors, such as self-efficacy, psychological burden, and health literacy, assume particular salience. For those who are dependent or cognitively impaired, the interpersonal dynamics of caregiver involvement become paramount, where responsibility often shifts reactively after adverse events without structured guidance (O'Connor et al., 2024).

Taken together, these considerations argue for a multi-tiered approach: simplify regimens, use clear and accessible communication, involve caregivers early, and coordinate services across transitions. Adherence should be treated as a shared responsibility embedded within relational, cognitive, and institutional frameworks.

The following sections apply this lens to glaucoma, macular diseases treated with intravitreal injections, diabetic retinopathy screening and follow-up, ocular surface diseases, and refractive-error optical correction, mapping determinants across individual, relational, clinical, and system levels. Together, these conditions span pharmacologic, procedural, and behavioral regimens with heterogeneous follow-up intensity and patient-caregiver dynamics; they also incorporate canonical equity and accessibility indicators (most notably refractive-correction uptake and the programmatic reach of retinopathy screening and injection pathways), yielding a broad yet representative overview of adherence challenges in geriatric eye care, while deliberately excluding conditions for which adherence-specific evidence remains sparse.

The sections on the three conditions with the largest adherence-related literature (glaucoma, macular diseases, and diabetic retinopathy) include illustrative sentinel evidence tables (phase-specific adherence metrics, key determinants, and quality flags) and corresponding Supplementary tables expanding the evidence from the past decade. Other elderly conditions are synthesized narratively, with representative citations.

5.1. Glaucoma

Glaucoma in older adults typically requires lifelong topical therapy, regular monitoring, and often surgical intervention. As one of the leading causes of irreversible blindness globally, adherence to IOP-lowering regimens and follow-up schedules directly shapes long-term visual outcomes.

5.1.1. Adherence rates and patterns

Adherence in glaucoma spans three interlocking behaviors: correct day-to-day use of topical IOP-lowering drops, reliable attendance at monitoring visits, and completion of postoperative therapy. Across these domains, real-world performance is suboptimal and time-sensitive. A meta-analysis of 43 observational studies on prostaglandin analogues found persistence declining from approximately 75% at 3 months to 31% at 3 years (Baudouin et al., 2025), illustrating the steep attrition typical of chronic glaucoma therapy.

Self-report systematically overestimates dosing compared with pharmacy records and electronic monitoring (Buehne et al., 2022; Cate et al., 2015; Gatwood et al., 2017; Okeke et al., 2009). MEMS data reveal this discrepancy across economic settings: in the U.S., 31% and 74% of patients overestimated their percent- and timing-adherence, respectively (Sayner et al., 2015); in Ghana, only 33.8% self-reported non-adherence whereas MEMS identified 77% as nonadherent, with mean adherence of just 48.5% (Kyei et al., 2023). This contrast between a high-income and a lower-middle-income setting underscores that

objective monitoring captures barriers invisible to self-report, particularly in resource-constrained environments. European pharmacy claims corroborate variable adherence: 66.5% in Germany (Frech et al., 2018), with 51.6% of UK patients failing annual benchmarks (Tse et al., 2016). Trajectory analyses in U.S. cohorts reveal bimodal behavior: 15% never adherent, 15% always adherent, remainder fluctuating (Newman-Casey et al., 2015a). Medication Possession Ratio-based studies confirmed this distribution, with 29% low, 32% moderate, and 32% high adherence (Jones et al., 2016).

Visit adherence is equally fragile. Even in organized systems, silent dropout occurs: in South Korea, 3.6% of patients missed more than 12 months of follow-up (Kim et al., 2017b); a UK national safety investigation recorded over 100 reports of sight loss linked to delayed follow-up between 2010 and 2019 (HSSIB, 2020). Disparities across health-system contexts are pronounced: in underserved urban Philadelphia, only 61.2% of newly diagnosed patients attended first scheduled follow-up (Hark et al., 2017); in a multicenter Chinese series from resource-limited settings, postoperative attendance fell from 75.9% at two weeks to 26.9% at one month (Yang et al., 2017), highlighting the compounded access and retention challenges in lower-resource environments.

Major glaucoma trials rarely measure adherence prospectively, relying on in-clinic IOP as a proxy. The LiGHT trial, where SLT outperformed topical medication despite comparable IOP, exemplifies this gap: poor drop adherence causing between-visit IOP fluctuations was proposed but never assessed (Gazzard et al., 2019). The CIGTS trial, which included self-reported adherence, demonstrated an adherence-outcome gradient: patients reporting never missing doses showed 0.62 dB mean deviation loss over 8 years versus 2.23 dB in those missing doses at two-thirds of visits (Newman-Casey et al., 2020a).

Sentinel studies are summarized in Table 4, with an expanded 2015–2025 inventory in Supplementary Table S4a and S4b.

5.1.2. Determinants and strategies

Adherence in glaucoma reflects the interplay of intrapersonal, relational, clinical, and health-system determinants that shape both implementation and persistence: in a prospective Brazilian MEMS cohort, 28.2% were low adherers; low adherence correlated with visual-field progression and subsequent loss-to-follow-up, aligning with lower education/income, lack of insurance, longer disease duration, and higher peak IOP (Oltamari et al., 2024). These signals are concordant with claims-based studies in high-income settings, reinforcing that patient-level constraints and health-system frictions interact to shape day-to-day adherence regardless of economic context.

Individually, younger age within older cohorts and male sex recur as risk markers, though inconsistently across multivariable models (Adeghate et al., 2019; Barnebey and Robin, 2017; Cheng et al., 2023; Frech et al., 2018; Guven et al., 2021; Hark et al., 2017; Kim et al., 2017b; Kolko et al., 2024; Kyei et al., 2023; Lešin Gačina et al., 2023; Loon et al., 2015; Mehari et al., 2016; Racette et al., 2022; Shirai et al., 2021; Yang et al., 2017). Racial disparities emerge in U.S. studies (lower adherence among Black vs White patients) (Delavar et al., 2022; Newman-Casey et al., 2015a, 2020a; Poleon et al., 2025; Racette et al., 2022; Saeedi et al., 2015; Sleath et al., 2015), though not universally (Barnebey and Robin, 2017; Loon et al., 2015; Negese Kebede et al., 2024; Salman et al., 2020). Multimorbidity shows variable associations; in Taiwan, ≥ 4 comorbidities predicted 11.8% adherence reduction at five years (Hou and Pu, 2024). Forgetfulness (Kumar et al., 2016; Movahedinejad and Adib-Hajbaghery, 2016; Negese Kebede et al., 2024; Newman-Casey et al., 2015b; Spencer et al., 2019; Tsumura et al., 2019), particularly in those with low self-rated memory, limited self-efficacy and difficulties with drop instillation (Cheng et al., 2023; Movahedinejad and Adib-Hajbaghery, 2016; Negese Kebede et al., 2024; Newman-Casey et al., 2015b; Sanchez et al., 2020; Slota et al., 2015; Spencer et al., 2019) are ubiquitous barriers. Psychological burden, including depression, anxiety, and post-traumatic stress symptoms

Table 4
Sentinel evidence on adherence to glaucoma treatments and Follow-up: Rates, patterns, and determinants.

Study design & Reference	Population (n ^o , age), Condition, Treatment	Outcome & Methods (initiation, implementation, persistence)	Adherence rate (initiation, implementation, persistence)	Determinants of Adherence
Meta-analysis Baudouin et al. (2025)	n = 961000 patients n = 47 studies Mean age: 67.5y Condition: glaucoma Treatment: Prostaglandin analogues	Implementation Medication adherence (MPR/PDC >80%, mean) Persistence Persistence (not switch or discontinue treatment, with a refill gap ≤90 days)	Implementation MPR/PDC >80%: 1y: 44% (95% CI: 31%-58%) MPR/PDC mean: 1y 54% (38–75%), 2y 60% (39–94%) Persistence Persistence: 6-months 75% (95% CI: 66%-85%), 1y 56% (95% CI: 45%-66%), 2y 53% (95% CI: 45%-62%), 3y 31% (95% CI: 12%-55%)	Not reported
Retrospective cohort Hou and Pu (2024)	n = 50408 Age: >40y (age at diagnosis 58.99 ± 15.12y) Condition: glaucoma Treatment: IOP-lowering drops	Adherence/nonadherence phase not reported* Medication non-adherence (discontinuation after initial prescription, via MPR, pharmacy refill data per year over 5 year) in GBTM	Adherence/nonadherence phase not reported* Persistently declining adherence 8.2% Moderately persistently low adherence 19.4% Persistently low adherence 47.0% Persistently high adherence 25.5%	Barriers: corneal opacity (p = 0.007), macular degeneration (p < 0.001), uveitis (p < 0.001), age at diagnosis (p = 0.003), n ^o of medications at onset (p < 0.001), male sex (p < 0.001), low income (p < 0.001), ≥4 comorbidities reductions of 6.4% (p = 0.033) and 11.8% (p < 0.001) in 4 ^o and 5 ^o y after glaucoma onset (p < 0.001)
Retrospective cohort Jones et al. (2016)	n = 17943 newly diagnosed Mean age: 66y Condition: glaucoma Treatment: IOP-lowering drops	Implementation Medication adherence (pharmacy claims: MPR low <20%, mid 20–79%, high ≥80%), over 5y	Implementation Adherence: low 29%, mid 32%, high 32%	Reported drivers: older age, female sex, White race Reported barriers: more severe systemic diseases
Cross-sectional Tsumura et al. (2019)	n = 3853 Mean age: 68.5 ± 12.2y Condition: POAG, ocular hypertension, NTG or pseudoexfoliation glaucoma Treatment: IOP-lowering drops in fixed-combination	Implementation* Medication adherence (self-reported never forget an instillation in the past week, physician assessment)	Implementation* Self-report: 72.4%, Physician-report: 78.5%	Drivers (patient): female (OR = 1.25, p = 0.02), clinic setting (vs. hospital) (OR = 0.71, p = 0.013), better MD value (OR = 1.02 per dB, p = 0.0045), shorter treatment duration (OR = 1.31, p = 0.0345), lower burden of eyedrops (OR = 1.51, p < 0.0001, acceptable n ^o of eyedrops (OR = 1.67, p < 0.0001), acceptable frequency of instillation (OR = 1.43, p < 0.000), glaucoma knowledge score (inverse) (OR = 0.41, p = 0.0079) Drivers (ophthalmologist): n ^o of eyedrops (OR = 1.38, p < 0.0001), acceptable n ^o of drops (OR = 1.51, p < 0.0001), acceptable instillation frequency (OR = 1.24, p = 0.0005) Barriers (both): age and forgetting instillation (p < 0.0001, p = 0.03)
RCT Cate et al. (2015)	n = 208 Mean age: 70.4y Condition: glaucoma Treatment: IOP-lowering drops (travoprost)	Implementation Medication adherence (TDA ≥80%, MMAS score = 0, FDM missed ≤1 dose a month, MPRA >1 "refill on expiration of bottle", MPRb >1 "expected refill bottle every 28 days"), at 8-months	Implementation Adherence: TDA: 54%, MMAS 60%, FMD 57%, MPRA 1.89 ± 0.66, MPRb 0.94 ± 0.34	Not reported
Prospective cohort Yang et al. (2017)	n = 212 Mean age: 60.2 ± 15.6y Condition: glaucoma Treatment: trabeculectomy	Implementation* Follow-up adherence (attendance at 1-week, 2-week, and 1 month) Persistence LTFU (no follow-up over 1 month by visit attendance)	Implementation* Follow-up: 1 week 60.8%, 2 week 75.9%, 1 month 26.9% Persistence LTFU: 5.2%	Barriers: no formal education (OR = 0.37 p = 0.002), belief follow-up not important (OR = 0.62 p = 0.02), lack of escort (OR = 0.14 p < 0.001), income < USD800 (OR = 0.28 p = 0.008), no post-op suture removal (OR = 0.11 p < 0.001) Not significant: age, sex, employment, transportation modality, distance, time and cost of travel, pre-operative patient clinical factors, physician factors
Prospective longitudinal pilot Jones et al. (2021)	n = 20 Median age: 71y Condition: POAG, angle closure or secondary glaucoma Treatment: Home VF	Persistence* Home VF test adherence (% of tests done at 6 months)	Persistence* Adherence: 98.3%	Reported barriers: chronic symptoms of vertigo

Sentinel studies evaluating adherence to glaucoma treatment and follow-up are presented according to evidence hierarchy and population size. Adherence outcomes are mapped to the ABC taxonomy (initiation, implementation, and persistence). Quality flags: entries marked with an asterisk (*) denote phase attribution inferred from indirect or surrogate measures that are not clearly stated; double asterisks (**) indicate composite outcomes spanning multiple or mixed phases. Determinants are categorized as drivers and barriers, with significant quantitative associations (OR, p-values) reported when available, while qualitative determinants are presented as described in the original studies.

Acronyms: AOR = adjusted odds ratio; CI = confidence interval; EMR = electronic medical record; FDM = frequency of missed dose; GBTM = group-based trajectory model; HR = hazard ratio; IOP = intraocular pressure; LTFU = loss to follow-up; MEMS = medication event monitoring system; MMAS = Morisky Medication

Adherence Scale; MPR = medication possession ratio; NTG = normal-tension glaucoma; OAG = open-angle glaucoma; OR = odds ratio; PDC = proportion of days covered; POAG = primary open-angle glaucoma; PP = per protocol; RCT = randomized controlled trial; TDA = Travalert Dosing Aid; VA = visual acuity; VF = visual field.

(Gamiochipi-Arjona et al., 2021; Newman-Casey et al., 2020a; Salman et al., 2020; Sanchez et al., 2020; Spencer et al., 2019; Stringham et al., 2018), consistently predicts poor adherence, sometimes outweighing demographics. Lower education (Ko et al., 2019; Kyei et al., 2023; Lešin Gačina et al., 2023; Mehari et al., 2016; Newman-Casey et al., 2020a; Oltramari et al., 2024; Saeedi et al., 2015; Salman et al., 2020; Yang et al., 2017), inadequate disease knowledge and limited health literacy (Oltramari et al., 2024; Sanchez et al., 2020; Slota et al., 2015; Thompson et al., 2015; Tsumura et al., 2019), and poor digital literacy and absence of guidance in navigating e-health resources (Newman-Casey et al., 2018; Saeedi et al., 2015), further hinder adherence.

At the interpersonal level, caregiver support strongly influences adherence: regular assistance with transport or drop instillation correlates with higher adherence (Anbesse et al., 2019; Assem et al., 2020; Lešin Gačina et al., 2023; Saeedi et al., 2015). However, living situation matters critically. High care dependency (care level 3+) was associated with 18.2% adherence reduction (Frech et al., 2018), and lack of escort to appointments increased missed visits (Killeen et al., 2020; Movahedinejad and Adib-Hajbaghery, 2016; Yang et al., 2017). These findings suggest that community-dwelling older adults with adequate caregiver networks fare better than those in high-dependency or institutional settings, where competing demands and staff-mediated administration introduce additional barriers. Provider communication and trust also matter: patients receiving active reinforcement regarding correct dosing demonstrate better outcomes (Sleath et al., 2015).

At the clinical level, glaucoma severity shows inconsistent associations with adherence (Kim et al., 2017a; Salman et al., 2020), but longer disease duration consistently predicts poorer adherence (Frech et al., 2018; Hou and Pu, 2024; Ko et al., 2019; Oltramari et al., 2024; Tsumura et al., 2019). Simpler regimens (fewer drops, reduced dosing frequency) improve adherence (Huo and Pu, 2024; Kim et al., 2017a; Ko et al., 2019; Movahedinejad and Adib-Hajbaghery, 2016; Sleath et al., 2015; Tsumura et al., 2019), while asymptomatic disease reduces perceived urgency (Loon et al., 2015; Movahedinejad and Adib-Hajbaghery, 2016). Low belief in treatment necessity or effectiveness represents an important attitudinal barrier (Lešin Gačina et al., 2023; Loon et al., 2015; Negese Kebede et al., 2024; Oltramari et al., 2024; Yang et al., 2017). Therapy-related side effects, particularly ocular discomfort from preservatives such as benzalkonium chloride, substantially compromise persistence (Kolko et al., 2023; Thygesen, 2018), increasing dropout rates (Kim et al., 2021; Stringham et al., 2018). Preservative-free and fixed-combination formulations improve tolerability and adherence (Amiri et al., 2024; Barnebey and Robin, 2017; Kim et al., 2021; Shirai et al., 2021).

At the systemic level, travel distance and transportation difficulties consistently emerge as barriers globally (Killeen et al., 2020; Movahedinejad and Adib-Hajbaghery, 2016; Subathra et al., 2021). Low income, self-paying status, and absence of insurance are associated with poorer adherence, though context matters (Anbesse et al., 2019; Hou and Pu, 2024; Mehari et al., 2016; Movahedinejad and Adib-Hajbaghery, 2016; Newman-Casey et al., 2015a; Oltramari et al., 2024; Saeedi et al., 2015; Salman et al., 2020; Yang et al., 2017). In South India, where most patients lacked insurance coverage, cost was not the predominant barrier, suggesting that when structural access is broadly limited, other factors (difficulty obtaining drops, distance, lack of escort) may dominate (Ramesh et al., 2021). These geographic disparities underscore that adherence determinants, and therefore interventions, must be stratified by health-system context.

Regarding strategies, a 2022 systematic review identified five intervention classes: reminder systems, medication simplification, behavioral change programs, education, and alternative engagement

strategies; multimodal approaches were most effective (66% vs 58% for singular interventions) (Buehne et al., 2022). Emerging therapeutic strategies, such as intracameral sustained-release systems, MIGS, injectable implants, aim to bypass daily drop barriers but require system-level integration to achieve durable improvements (Droste and Newman-Casey, 2023). Educational and counseling approaches incorporating motivational interviewing show short-term improvements, though benefits often wane after intervention cessation. Passive educational mailings proved ineffective: a U.S. trial in 1800 high-risk older adults showed only 36.9% achieving PDC $\geq 80\%$ versus 35.7% in controls (Fiscella et al., 2018), underscoring the need for sustained, personalized engagement. Digital platforms and telemedicine, including technician-led remote glaucoma clinics (Cheng et al., 2023), offer scalable solutions, though effectiveness varies with digital literacy. This extends to remote disease monitoring: in a 6-month pilot of tablet-based home visual field testing, adherence was high (98.3% of scheduled tests completed) with good concordance versus in-clinic perimetry (Jones et al., 2021). Family-inclusive interventions, pharmacist-led support, and culturally tailored modules show promise in underserved and elderly populations (Aleem et al., 2024; Assem et al., 2020; Killeen et al., 2020; Ramesh et al., 2021).

Finally, for older adults with severe frailty or limited life expectancy, treatment decisions should reflect individualized care goals, with deprescribing and shared decision-making replacing rigid adherence mandates (AGS Beers Criteria, 2023). Beyond individual interventions, durable improvements require systemic changes: removing access barriers, integrating adherence monitoring into EHRs, and policy-level commitment to reduce avoidable discontinuation, as emphasized by the UK national safety investigation recommending automated tracking and risk-based recall protocols (HSSIB, 2020).

5.2. Neovascular age-related macular degeneration, diabetic macular edema, and retinal vein occlusion

Neovascular AMD, DME, and RVO are chronic retinal diseases requiring frequent intravitreal anti-VEGF injections or corticosteroid implants to preserve vision. While clinical trials with fixed or monthly dosing achieve substantial vision gains, real-world outcomes frequently show only stabilization or loss of early gains, largely attributable to suboptimal adherence and persistence in populations predominantly comprising older adults with cognitive/sensory decline, multimorbidity, and caregiver reliance.

5.2.1. Adherence rates and patterns

A systematic review of 52 studies (over 409,000 patients) reported non-adherence rates ranging from 15% to 95%, reflecting widely varying definitions; patient-led non-adherence (missing or delaying injections without provider guidance) was estimated at 17.5–35.0% (Shahzad et al., 2023). In a complementary mixed-methods review, up to 50% of nAMD patients discontinued treatment within 24 months (Okada et al., 2021).

Large database studies confirm high attrition. In 9007 nAMD patients, 22.2% were lost to follow-up (LTFU) for ≥ 12 months within 4 years (Obeid et al., 2018). The IRIS Registry analysis of 156,327 treatment-naïve nAMD patients found 12-month LTFU of 11.6% and non-persistence of 14.3% at 6 months after last injection (Khurana et al., 2023). By contrast, trial settings achieve near-perfect adherence: in the CATT trial, 92.6% maintained 100% visit constancy over 2 years (Ramakrishnan et al., 2020), underscoring the efficacy-effectiveness gap.

Clinicians underestimate the problem: in a multinational survey, 42% of retina specialists reported not formally tracking adherence, most

estimating non-adherence at only 0–20%, whereas patient self-reports indicated 14% (nAMD) and 30% (DME) missed at least one injection visit in the prior year (Giocanti-Aurégan et al., 2022).

Geographic variation reflects health-system differences. In high-income European settings, cumulative LTFU reached 57% at 5 years in a French nAMD cohort (15.6% in first year) (Boulanger-Scemama et al., 2015), 51% first-year discontinuation in Sweden nAMD cohorts (Westborg and Rosso, 2018), 49% 4-year LTFU in Austrian DME (Angermann et al., 2022), and 44–46% one-year non-adherence/discontinuation in German DME cohorts (Ehlken et al., 2018; Weiss et al., 2018). In the U.S., 33.7% of AMD patients missed follow-up appointments defined as not occurring within 1 month of the desired date (Thompson et al., 2015), while a Canadian survey found non-adherence in 16.5% of DME and 6–7% of nAMD patients, defined as failure to attend or cancellation of ≥ 2 scheduled visits (Holekamp et al., 2024a). In Japan, under universal coverage, LTFU in nAMD rose from 6.8% at 3 months to 21.2% by 2 years (Sugisawa et al., 2025).

In resource-limited settings, adherence is markedly lower: 51.5% overall LTFU in India (Kelkar et al., 2020), 39.8% non-adherence in Turkey under PRN ranibizumab (Polat et al., 2017), and nearly 60% non-adherence in Palestine within 3 months (Abualhasan et al., 2025). This HIC-LMIC gradient underscores how affordability and healthcare infrastructure shape treatment persistence.

Adherence differs by disease: DME patients were significantly more likely to cancel or miss appointments than nAMD patients—by a factor of ~ 1.6 in the U.S. and ~ 1.9 in Europe—possibly reflecting inclusion of middle-aged patients with competing demands (Jansen et al., 2018).

Sentinel studies are summarized in Table 5, with expanded evidence in Supplementary Table S5a and S5b.

5.2.2. Determinants and strategies

In this high-burden treatment context, adherence is shaped by interacting intrapersonal, interpersonal, clinical, and health-system determinants, with advanced age emerging as one of the most consistently identified risk factors: patients ≥ 80 –85 years show higher LTFU across multiple cohorts (Angermann et al., 2022; Boulanger-Scemama et al., 2015; Ehlken et al., 2018; Khurana et al., 2023; Obeid et al., 2018; Polat et al., 2017; Talks et al., 2022), reaching 51% by two years in those ≥ 90 in Denmark (Subhi and Sørensen, 2017), reflecting compounded frailty, comorbidities, and competing health priorities. However, younger patients may also face barriers from busy schedules. Male sex independently predicts LTFU in IRIS data, as does non-White race even after insurance status adjustment (Khurana et al., 2023). Socioeconomic deprivation correlates with worse outcomes in UK DME cohorts (Talks et al., 2022).

Cognitive impairment directly jeopardizes adherence: patients with dementia and nAMD had fewer eye-care visits and received fewer injections than matched peers in U.S. claims data (Hamedani et al., 2024). Patients with multiple medical comorbidities may struggle to adhere due to polypharmacy, frequent doctor visits for other conditions, and functional impairments (Giocanti-Aurégan et al., 2022; Müller et al., 2017; Polat et al., 2017; Weiss et al., 2018); however, real-world evidence is inconsistent. In a systematic review, only 15.5% of patients reported comorbidities as barriers versus 68% of retina specialists (Shahzad et al., 2023; Giocanti-Aurégan et al., 2022), suggesting that comorbidity burden per se may not be the ideal predictor and that specific patterns posing the highest risk require further research. Mental health similarly shapes engagement: depression was identified as a barrier by $\sim 29\%$ of non-adherent patients in a German study (Müller et al., 2021), while fear and anxiety about injections were reported by 54% of patients and 42% of caregivers (Giocanti-Aurégan et al., 2022). Treatment fatigue accumulates; qualitative interviews reveal some elderly patients questioning continued therapy, expressing futility if vision is not improving (Shahzad et al., 2023; Subhi and Sørensen, 2017).

Health literacy strongly influences adherence. A Danish study using

the European Health Literacy Survey questionnaire found 65% of nAMD, 73% DME, and 63% RVO patients had inadequate or problematic health literacy, and these patients reported worse self-rated health and lower education levels (Jandorf et al., 2019). Many may experience difficulty navigating complex treatment plans or recognizing early recurrence. Disease-specific knowledge is often poor, only one-third felt fully educated on anti-VEGF therapy purpose and expectations. Misconceptions can lead to premature discontinuation: some patients erroneously believe injections will dramatically improve vision, so when only stabilization occurs, they lose trust. "No perceived improvement" was cited by 28–35% as a discontinuation reason (Boulanger-Scemama et al., 2015; Kelkar et al., 2020), potentially triggering a vicious cycle given that non-adherence itself may worsen visual acuity outcomes (Ehlken et al., 2020). Subgroup analyses suggested that countries with more frequent follow-ups and education achieved better outcomes, implying that informed patients adhere better (Ehlken et al., 2018).

At the interpersonal level, caregiver involvement is critical for older adults with frailty, mobility issues, or advanced vision loss. Barriers arise when caregiver availability is limited by work or family obligations, amplified by the need for caregivers to accompany patients to appointments, often requiring time off or rearrangement of daily responsibilities (Abualhasan et al., 2025; Boulanger-Scemama et al., 2015; Sobolewska et al., 2021; Weiss et al., 2018). A multinational qualitative study documented caregiver burden: schedule disruptions (45.6%), work absenteeism (70.5%), and emotional strain; about half reported dealing with feelings of concern and worry for the patient, managing their own emotions while helping alleviate patients' anxiety about illness and treatment (Viola et al., 2024). Caregiver involvement is not only a logistical necessity but also shapes adherence through expectation management and quality-of-life considerations. Provider relationships matter profoundly. Care outside specialist settings, changes in treating physicians, and inadequate communication about disease status or treatment plans have been associated with reduced adherence (Weiss et al., 2018). Patients most frequently cited the doctor-patient relationship (70%) as their top adherence driver, whereas retina specialists emphasized patient education (45%) (Giocanti-Aurégan et al., 2022). This subtle misalignment suggests that patients equate adherence with trust, continuity, and feeling heard, whereas clinicians may foreground education in ways that can become one-way messaging if not coupled with shared decision-making.

At the clinical level, diagnosis and perceived disease severity were not significantly associated with adherence in some cohorts (Polat et al., 2017; Thompson et al., 2015), although lower adherence in DME versus nAMD may reflect inclusion of middle-aged, less committed adults (Jansen et al., 2018). Patients with worse baseline visual acuity or advanced retinal damage show higher dropout rates (Angermann et al., 2019; Boulanger-Scemama et al., 2015; Ehlken et al., 2018; Khurana et al., 2023; Polat et al., 2017; Talks et al., 2022), while unilateral disease may reduce motivation to endure frequent injections (Khurana et al., 2023; Obeid et al., 2018). Both objective and perceived visual outcomes emerge as key drivers: lack of perceived benefit or perceived stability may reduce motivation, leading patients to extend intervals or stop therapy (Shahzad et al., 2023). Treatment-related barriers include injection pain and discomfort (Giocanti-Aurégan et al., 2022; Holekamp et al., 2024a) and cumulative injection burden (Kelkar et al., 2020; Ramakrishnan et al., 2020; Weiss et al., 2018).

At the systemic level, financial barriers remain prominent: anti-VEGF therapy is expensive, and despite reimbursement mechanisms, patients often face co-pays and indirect expenses such as travel and income loss. Higher non-adherence is consistently reported in cohorts with inadequate insurance or high out-of-pocket costs (Abualhasan et al., 2025; Jackson and Stokes, 2020; Khurana et al., 2023; Obeid et al., 2018; Polat et al., 2017). In Australia, lower out-of-pocket costs correlated with better initiation, implementation, and persistence across 11,592 patients (Jackson and Stokes, 2020). IRIS data showed Medicaid patients had higher LTFU odds than those on Medicare or private insurance (Khurana

Table 5
Sentinel evidence on adherence to intravitreal therapy and follow-up in macular diseases: Rates, patterns, and determinants.

Study design & reference	Population (n ^o , age), Condition	Outcome & Methods (initiation, implementation, persistence)	Adherence rate (initiation, implementation, persistence)	Determinants of Adherence
Meta-analysis Shahzad et al. (2023)	n = 52 studies (409215 patients) Age: adult ≥18y Condition: nAMD, DME, RVO (Treatment-naïve, -experienced)	Persistence**/* - Non-adherence (irregular attendance or gaps in treatment) - Non-persistence (discontinuation of the treatment against the prescriber's recommendation) - Non-adherence during COVID-19	Persistence**/* Non-adherence: 17.5-35.0% Non-persistence: 2.9-43%, mean 30.0% (p = 0.000) COVID-19 Non-adherence (3 studies) 51.6-68.8%	Barriers: treatment results dissatisfaction (29.9%), financial burden (19%), older age/comorbidities (15.5%), difficulty booking appointments (8.5%), travel distance/social isolation (7.9%), lack of time/job/family commitments (5.8%), perceived improvement (4.4%), fear of injection (4.0%), loss of motivation/burden of frequent visits (4.0%), apathy towards eyesight (2.5%), facilities dissatisfaction 2.3%, discomfort/pain (0.3%), personality clash with physicians/unspecified personal reasons (1.9%), fear of COVID-19 exposure, difficulties travelling during lockdown. Drivers: female sex (OR = 0.87, p < 0.001), bilateral disease (OR = 0.37, p < 0.001), Medicare FFS vs private insurance (OR = 0.68, p < 0.001). Barriers: older age 76-80y (OR = 1.43, P < 0.001), older age 81-84y (OR = 2.48, p < 0.001), older age ≥85y (OR = 1.29, p < 0.001), unilateral disease (OR = 2.68 for LTFU, OR = 2.70 for non-persistence, both p < 0.001), black race (OR = 1.34 LTFU, p = 0.003; OR = 1.39 non-persistence, p < 0.001), Hispanic ethnicity (OR = 1.13, p = 0.006 for non-persistence), diabetes (OR = 1.12, p = 0.005), poorer baseline VA 20/50-20/200 (OR = 1.41, p < 0.001), Medicaid insurance (OR = 1.27, p = 0.027 for non-persistence), patients treated in Midwest-Northeast-West vs south of USA (all p < 0.001)
Retrospective cohort Khurana et al. (2023)	n = 156327 Age: <70- >85 Condition: nAMD (Treatment-naïve)	Persistence - Non-persistence (IRIS registry no follow-up within 6 months after last injection) - LTFU (IRIS registry no follow-up within 12 months after last injection)	Persistence Non-persistence: 14.3% LTFU: 11.6%	
Retrospective cohort Obeid et al. (2018)	n = 9007 Mean age: 81.2 ± 8.8y Condition: nAMD (Treatment-experienced)	Persistence LTFU (EMR no follow-up within 12 months after injection)	Persistence LTFU: 22.2%	Barriers: older age (81-85 y OR = 1.58; 86-90 y OR = 2.29; >90 y OR = 3.31), non-white race (Asian OR = 2.63, Black OR = 1.47), lower income (≤\$50k OR = 1.52), greater distance (>30 miles OR = 1.55), unilateral disease (OR = 1.44), worse VA at final injection (VA <20/200 OR = 1.45, p = 0.001). Barriers: older age, transportation difficulties, treatment fatigue, frequent injections burden
Secondary analysis of RCT Ramakrishnan et al. (2020)	n = 1178 Mean age: 79.1 ± 7.3y Condition: nAMD (Treatment-naïve)	Implementation Visit constancy (3-month periods with at least 1 visit attended) - Adherence of on-time visits	Implementation Visit constancy: 92.6% On-time (28-35day) 90%, late (36-60day) 9.2%, very late (>60day) 0.8%	
1 Arm CT Holekamp et al. (2024b)	n = 15 Mean age: 75.1 ± 5.7y Condition: nAMD (Treatment-experienced)	Implementation - Adherence to home-OCT scan via device logs (~6 scans/eye/week) - Mean n ^o of OCT scan/eye/week (at 1-, 3-, 6- months)	Implementation Adherence to scan: 100% OCT adherence 1 months: 6.16/7day, 3 months: 6.37/7day, 6 months: 6.2/7day	Not reported
Retrospective cohort Ehlken et al. (2018)	n = 708 Condition: nAMD (466) age: ~78y DME (134) age: ~66y BRVO (108) age: ~69y (Treatment-experienced)	Implementation - Continuous adherence (EMR treatments or follow-up at least every 56 days) Persistence - Non-adherence visit/treatment (EMR gap >56 days)	Implementation Continuous adherence: nAMD 53.4%, DME 44%, BRVO 43.5% Persistence Non-adherence: nAMD: 32.2%, DME: 44%, BRVO: 25%	Barriers (nAMD): older age (OR = 1.04 per year increase, p = 0.013), poor baseline VA (OR = 2.37 for VA >0.3 logMAR vs < 0.1, p = 0.048) Not significant: sex, mobility impaired, upload successful, study eye better than fellow eye, both eyes treated No significant predictors in DME or BRVO
Retrospective cohort Subhi and Sørensen (2017)	n = 116 Median age: 92y Condition: nAMD (Treatment-naïve)	Persistence LTFU (EMR no follow-up within 24 months)	Persistence LTFU: 51%	Reported barriers: death (13.8%), treatment burden (13.8%), inactive CNV -dry macula -and referral of patient to the primary sector (6.9%), development of fibrotic/untreatable lesion (14.7%)
Cross-sectional qualitative Giocanti-Aurégan et al. (2022)	n = 94 patients (49 nAMD, 46 DME; 1 with both) n = 79 caregivers (47 nAMD, 33 DME) n = 62 retina specialists Age: <60-80y (Treatment-experienced)	Implementation* Non-adherence to visit (missed 1 injection visits)	Implementation* Non-adherence: nAMD: 14%, DME: 30%	Drivers (patients): doctor-patient relationship (70%), perceived treatment effectiveness (35%), fear of vision loss (34%) (caregivers): ease of booking (32%), caregiver support/motivation (30%); (specialist): patient education (45%), perceived treatment effectiveness (31%), and fear of vision loss (34%) Barriers (patients): tolerability (67% patients, 66% caregivers), injections anxiety (54% patients, 42% caregivers), logistical challenges (20% patients, 19% caregivers, 71% specialists), frequency of visits (26% patients, 18% caregivers, 19% specialists), appointment scheduling difficulties, perceived ineffectiveness, comorbidities, being ill on injection day, lack of education (21% patients), poor doctor-patient relationship (18% patients)

Sentinel studies evaluating adherence to intravitreal anti-VEGF therapy, follow-up, and monitoring strategies in patients with nAMD, DME, and RVO are presented according to the evidence hierarchy, from meta-analyses and large registry cohorts to randomized controlled trials, observational studies, and qualitative investigations. Adherence outcomes are mapped to the ABC taxonomy (initiation, implementation, and persistence). Quality flags: entries marked with an asterisk (*) denote phase attribution inferred from indirect or surrogate measures that are not clearly stated; double asterisks (**) indicate composite outcomes spanning multiple or mixed phases. Determinants are categorized as drivers and barriers, with significant quantitative associations (OR, p-values) reported when available, while qualitative determinants are presented as described in the original studies.

Acronyms: CI = confidence interval; CNV = choroidal neovascularization; DME = diabetic macular edema; EMR = electronic medical record; HR = hazard ratio; IRIS = Intelligent Research in Sight; LTFU = loss to follow-up; nAMD = neovascular age-related macular degeneration; OCT = optical coherence tomography; OR = odds ratio; PRN = pro re nata; RCT = randomized controlled trial; RVO = retinal vein occlusion; T&E = treat-and-extend; VA = visual acuity.

et al., 2023). Beyond cost, clinic accessibility issues (long waiting times, difficulty scheduling appointments, limited hours) deter patients and contribute to unintended delays or complete LTFU (Giocanti-Aurégan et al., 2022; Holekamp et al., 2024a; Thompson et al., 2015). Busy retina clinics and high-volume public hospitals may have particularly long waits and crowded environments that overwhelm elderly patients.

Regarding strategies, interventions target modifiable barriers at multiple levels. At the individual level, patient-centered communication, clearly defined treatment goals, and tailored education are critical for sustaining engagement. Patients should understand that therapy aims for long-term vision maintenance, not short-term cure, and that discontinuation can lead to irreversible loss often worse than baseline (Okada et al., 2021). Multinational surveys showed retina specialists felt improved patient education on disease course and treatment purpose might be a top adherence driver (Giocanti-Aurégan et al., 2022). European DME guidelines recommend frank discussions about expectations and the importance of continuous follow-up from the outset (Gale et al., 2017). Although not formally tested in interventional studies, repetition of key messages, written materials, and dedicated educators may improve adherence, particularly for those with low health literacy (Boulangier-Scemama et al., 2015). Education should be bidirectional, incorporating shared decision-making: respecting patients' preferences and values in follow-up scheduling, drug choice, regimen selection, and even the option to discontinue when appropriate (Barry and Edgman-Levitan, 2012). Caregiver education and involvement in the therapeutic alliance play a relevant role for dependent patients, particularly those with significant visual or cognitive impairment.

Clinically, treatment choices should reduce injection and visit burden: treat-and-extend regimens (Debourdeau et al., 2024; Li et al., 2020), longer-duration anti-VEGF agents (Korobelnik et al., 2026; Nichani et al., 2024), sustained drug-delivery devices such as Port Delivery System (Regillo et al., 2023), and alternative classes like dexamethasone implants for selected cases (Querques et al., 2025) should be weighed in a patient-centered framework.

System-level strategies include service redesign and technology. In a U.S. study, the most frequent patient-reported suggestion was pre-appointment reminders (81.7%), followed by parking vouchers (47.9%), transportation services (44.6%), and peer support networks (41.3%) (Thompson et al., 2015). However, an Indian RCT found SMS reminders did not improve DME attendance (Kumar et al., 2021), suggesting forgetfulness may not be the primary barrier in resource-limited settings where cost and access dominate. Clinic flow redesign (one-stop testing and injection, fast-track lanes, streamlined injection clinics) can minimize waits without compromising safety (Amoaku et al., 2020).

Emerging hybrid care models leverage home-based OCT, tele-ophthalmology, and AI triage. In a 6-month study, home-OCT monitoring doubled treatment intervals (from 8.0 to 15.3 weeks) with stable acuity and high adherence; missed scans triggered phone recalls (Holekamp et al., 2024b). However, visual, cognitive, and technological barriers limit generalizability, and long-term outcome data remain limited (Willis et al., 2024). Many strategies derive from observational studies; prospective trials with standardized adherence measurement are needed.

5.3. Diabetic retinopathy screening and follow-up

Diabetic retinopathy (DR) affects approximately 22.3% of adults with diabetes (around 103 million people in 2020) and remains a leading cause of preventable blindness worldwide (Teo et al., 2021). Regular screening, applied to patients with diabetes at risk for retinopathy without established retinal disease, and timely follow-up after diagnosis are central to vision preservation. In older adults, who accumulate both longer diabetes duration and higher prevalence of vision-threatening DR and macular edema, adherence is particularly critical, as visual decline in this age group strongly impacts independence, risk of falls, and overall frailty (Teo et al., 2021; Wong et al., 2016). Unlike the chronic treatment paradigm of nAMD/DME requiring frequent injections, DR screening represents a prevention context where the goal is early detection rather than ongoing therapy, yet adherence challenges parallel those seen across geriatric eye care. Most primary studies report on general adult populations; throughout this section, we report population-level data and extract age-stratified signals for older adults whenever available.

5.3.1. Adherence rates and patterns

A meta-analysis of 77 studies (>11 million people) estimated global pooled screening uptake at 63.2%, substantially higher in high-income countries (66.9%) than in LMICs (39.3%), with Europe leading (81.3%) and Africa lowest (36.1%) (Rahmati et al., 2024). This analysis captured ≥ 1 exam within 1–3 years, conflating initiation and implementation; persistence across multiple cycles was not assessed.

Longitudinal data confirm an implementation/persistence gap. In a U.S. claims cohort (n = 204,073; mean age 61), 71.1% were adherent to American Diabetes Association interval rules over ~ 5 years; when annual exams were required, adherence eroded from 71.5% in year 1 to 21.5% by year 5 (An et al., 2018). Organized programs can raise uptake: England's NHS invitation-based program screened 82.7% of 2.7 million invitees in 2017–2018 (Scanlon, 2021), yet delays from diagnosis to first screen remained clinically relevant, with ≥ 36 -month delays (11.6% of those ≥ 60 years) tripling the odds of referable DR (Scanlon et al., 2016).

In other settings, patterns are consistent with erosion of persistence: an Australian cohort showed that among those with diabetes ≥ 10 years, just 21–28% met annual schedules (Gibson et al., 2020). In LMICs, adherence is markedly lower: in Nepal, 79.4% had ever had a dilated exam but only 62.4% followed recommended intervals (Suwal et al., 2024), while in Iran, 50.8% were non-adherent despite tertiary access (Anvari et al., 2024).

Follow-through after a positive test is a recurrent weak link. In a large U.S. tele-retina network, only 30.9% of referrals were seen in eye care within 6 months (42.2% for vision-threatening DR); older age improved but did not close this gap (Bonilla-Escobar et al., 2024). At advanced stages, IRIS Registry data (73,595 eyes) showed 10–12% LTFU among patients with proliferative DR treated with anti-VEGF and/or PRP (Khurana et al., 2024). Older adults thus show better initiation but insufficient maintenance of guideline-concordant intervals and incomplete follow-through after abnormal findings.

Sentinel studies are summarized in Table 6, with expanded evidence in Supplementary Table S6a and S6b.

Table 6
Sentinel evidence on adherence to diabetic retinopathy screening and Follow-up: Rates, patterns, and determinants.

Study design & reference	Population (n ^o , age), Condition, Intervention	Outcome (initiation, implementation, persistence)	Adherence rate (initiation, implementation, persistence)	Determinants of Adherence (initiation, implementation, persistence)
Meta-analysis Lawrenson et al. (2018)	n = 352879 (from 66 RCTs) Median age: 60.7y Condition: DM 56 RCTs: intervention vs usual care 10 RCTs: more intensive vs less intensive intervention	Adherence/nonadherence phase not reported* - Baseline DRS adherence (visit attendance, EMR) - DRS adherence, after intervention (in previous 12 or 24 months)	Adherence/nonadherence phase not reported* Baseline screening adherence: median 35.4% (0-87.8%) Intervention vs. usual care: +12% attendance (RD 0.12, 95% CI 0.10-0.14). More vs less intensive intervention: +5% attendance (RD 0.05, 95% CI 0.02-0.09).	Drivers: goal setting (outcome) (RD 0.26, 95% CI 0.16-0.36), feedback on outcomes of behavior (RD 0.22, 95% CI 0.15-0.29), restructuring the social environment (RD 0.19, 95% CI 0.12-0.26), credible source (RD 0.16, 95% CI 0.08-0.24)
Retrospective cohort Khurana et al. (2024)	n = 56590 patients (73595 eyes) Age: stratified (<55, 56-85+) Condition: DM with DR Intervention: none	Persistence LTFU (no visit within 12 months after last treatment by EMR IRIS Registry)	Persistence LTFU: all 11.7%, anti-VEGF 12.2%, PRP 12.6%, both 10.8%	Barriers: age 66-70 vs 55y (OR = 0.79, p < 0.001), age 71-75 vs 55y (OR = 0.84, p = 0.023), back race (OR = 1.26, p < 0.001), Hispanic ethnicity (OR = 1.28, p < 0.001), native American/Alaska Native/Native Hawaiian/Other Pacific Islander (OR = 2.69, p < 0.001), unilateral disease (OR 2.05, p < 0.001), baseline VA 20/50-20/200 (OR = 1.25, p < 0.001), baseline VA worse than 20/200 (OR = 1.22, p = 0.012), T2DM vs T1DM (OR = 1.20, p = 0.022), Midwest region (OR = 0.72, p < 0.001), West region (OR = 0.83, p = 0.003); Medicare FFS vs private insurance (OR = 0.71, p < 0.001), Medicare Managed vs private (OR = 0.66, p < 0.001), combination therapy vs PRP (OR 0.85, p = 0.005) Drivers: age 12-17 and 35-59 vs ≥ 60 (p < 0.0001), male sex Barriers: age 18-34 vs ≥ 60 (p < 0.0001)
Retrospective analysis of screening programme Scanlon et al. (2016)	n = 689025 Age: 12- ≥60y Condition: DM Intervention: none	Initiation + Implementation**/** - Adherence to DRS (EMR to 12-, 36-months) Persistence - LTFU (over 3 y)	Initiation + Implementation**/** Adherence: 12 months: 63%-85%, 36 months: 81%-91% Persistence LTFU over 3y: 11.6% (≥60y)	Drivers: older age (OR = 1.75), statin use (OR = 1.21), diabetes education (OR = 1.22), prior eye exam (OR = 1.38), adherence to oral diabetes meds (OR = 1.09). Barriers: Black race (OR = 0.95), male (OR = 0.95), insulin use (OR = 0.62), HbA1c > 9% (OR = 0.84), smoking (OR = 0.90), DR (OR = 0.24), higher specialist copayment (OR = 0.91) Not significant: distance to clinic
Retrospective cohort An et al. (2018)	n = 204073 Mean age: 60.8 ± 13.1y Condition: DM Intervention: none	Persistence* - Adherence to ADA retinal visit guidelines by EMR IRIS Registry	Persistence* Adherence: 71.1%	Drivers: older age (OR = 1.75), statin use (OR = 1.21), diabetes education (OR = 1.22), prior eye exam (OR = 1.38), adherence to oral diabetes meds (OR = 1.09). Barriers: Black race (OR = 0.95), male (OR = 0.95), insulin use (OR = 0.62), HbA1c > 9% (OR = 0.84), smoking (OR = 0.90), DR (OR = 0.24), higher specialist copayment (OR = 0.91) Not significant: distance to clinic
RCT Chen et al. (2018a)	n = 233 Condition: DM Intervention: educational SMS (119) mean age: 59.7 ± 11.3y, vs controls (114) mean age: 58.7 ± 9.5y	Implementation* Adherence to scheduled DRS (visit attendance within ±1 week, after receiving SMS containing DR information)	Implementation* Adherence: p < 0.001 SMS 42.9%, Controls 14.0%	Drivers: SMS intervention (RR = 3.04, p < 0.001), higher baseline DR knowledge (RR = 1.47, p < 0.001) Not significant: age, sex, education, income, travel time, visual acuity, diabetes duration, payment method, prior dilated exam, satisfaction score
RCT + cost effective analysis Winters et al. (2017)	n = 206 Age: ≥65y Condition: DM Intervention: BA 103, ST 103	Persistence* Adherence to dilated fundus exam (attendance within 6 months)	Persistence* Visit adherence: BA 87.91%, ST 34.48%	Reported Drivers: goal-directed behavior, action planning, reduced procrastination, improved diabetes-eye health awareness, structured routines promoted through BA Reported barriers: lack of directive guidance or education, limited engagement beyond active listening
RCT Mansberger et al. (2015)	n = 567 Mean age: 51.1 ± 11.8y Condition: DM Intervention: Telemedicine (296), Traditional surveillance (271)	Implementation + Persistence**/** * Adherence to annual DRS (attendance at ≤6, 6-18, months visits)	Implementation + Persistence**/** Visit adherence: ≤6 months: (p < 0.001) Telemedicine 94.6% Traditional 43.9% 6-18 months: (p < 0.001) Telemedicine 53.0% Traditional 33.2%	Drivers: telemedicine strongly improved short-term adherence (p < 0.001) Barriers: logistical barriers, need for improved technology, lack of comprehensive systems for follow-up care

Sentinel studies evaluating adherence to DR screening and follow-up recommendation are presented according to the evidence hierarchy, from meta-analyses and large registry cohorts to randomized controlled trials and observational studies. Adherence outcomes are mapped to the ABC taxonomy (initiation, implementation, and persistence). Quality flags: entries marked with an asterisk (*) denote phase attribution inferred from indirect or surrogate measures that are not clearly stated; double asterisks (**) indicate composite outcomes spanning multiple or mixed phases. Determinants are categorized as drivers and barriers, with significant quantitative associations (OR, RD, RR, p-values) reported when available, while qualitative determinants are presented as described in the original studies.

Acronyms: ADA = American Diabetes Association; BA = behavior activation; CI = confidence interval; DM = diabetes mellitus; DR = diabetic retinopathy; DRS = diabetic retinopathy screening; EMR = electronic medical record; HR = hazard ratio; IRIS = Intelligent Research in Sight; LTFU = loss to follow-up; OR = odds ratio; PRP = panretinal photocoagulation; RCT = randomized controlled trial; RD = risk difference; RR = relative risk; ST = supportive therapy; VA = visual acuity.

5.3.2. Determinants and strategies

Age effects show distinctive patterns in DR screening adherence: in broad adult cohorts, older age correlates with higher uptake; however, within the elderly, this "age advantage" may reverse at very advanced ages. Ireland's Diabetic RetinaScreen (653,969 appointments; median age 65) showed a U-shaped pattern: odds of missing an appointment increased by 23% for each 10-year deviation from age 70 (OR 1.23 per decade, 95% CI 1.22–1.24), indicating excess non-attendance in the oldest-old (Kelly et al., 2021). Similarly, Australia's National Eye Health Survey found increasing age independently predicted poorer adherence (adjusted OR 0.70 per decade) despite generally high coverage (Foreman et al., 2017).

Sex showed no consistent association with adherence across studies. Racial/ethnic disparities appear in U.S. data (Shi et al., 2014; An et al., 2018), though in homogeneous low-income settings race was not significant after adjustment (Kuo et al., 2020). Lower educational attainment was consistently associated with reduced uptake (Boucher et al., 2020; Moinul et al., 2020; Anvari et al., 2024). Health literacy, diabetes-specific knowledge, and awareness of screening purpose emerged as some of the most consistent and modifiable predictors: limited literacy is a key barrier to initiation, leaving patients who never enter screening pathways invisible to LTFU statistics (Chen et al., 2018a; Lian et al., 2018; Liu et al., 2018; Moinul et al., 2020; Anvari et al., 2024; Winters et al., 2017). Other patient-level factors include psychological barriers (anxiety, depression, low self-efficacy) and reduced perceived benefit of screening (Gibson et al., 2020; Liu et al., 2018). In a screening context where patients are typically asymptomatic, perceived benefit is inherently lower than in symptomatic treatment settings, amplifying the importance of health literacy and proactive physician recommendation.

On the other hand, depression may be particularly influential in the follow-up phase for patients already diagnosed with DR, though direct DR-specific adherence links in older adults remain understudied (Kalva et al., 2024).

Comorbidity and care engagement pull adherence in opposite directions. In low-income U.S. primary care, DR screening attendance tracked with broader chronic-care engagement (attendance at diabetes education or foot-care visits was the strongest predictor, OR 2.41) (Kuo et al., 2020). Conversely, multimorbidity and competing appointments displace eye-care visits, amplified in frail elders (Liu et al., 2018). Cognitive and sensory decline further erode adherence: in homebound nursing-home residents, only 12 of 29 screen-positive patients attended referral assessment despite on-site photographic screening (Anderson et al., 2003). German claims data confirmed that higher disability level (a proxy for functional/cognitive impairment) was strongly associated with lower screening likelihood (HR 0.30, 95% CI 0.25–0.36) (Kreft et al., 2018).

At the interpersonal level, physician advice is powerful: in a Nepal study, recommendation to obtain an eye exam was associated with ~25-fold higher odds of adherence (OR 25.1, 95% CI 6.8–92.1) (Suwal et al., 2024). Family experiences with DR complications heighten perceived vulnerability and foster motivation to attend screening (Liu et al., 2018; Boucher et al., 2020). Conversely, experiences of judgment or criticism from family or providers have been reported as barriers (Liu et al., 2018).

Clinically, longer diabetes duration correlates with erosion of persistence: only 21–28% met annual-exam guidance with ≥10 years' duration in an Australian cohort, arguing for recall intensity calibrated to disease duration (Gibson et al., 2020). Paradoxically, patients with vision-threatening DR were less likely to attend recommended visits despite being at highest risk of irreversible vision loss (Chen et al., 2018b; Hinkle et al., 2020; Keenum et al., 2016; Zhu et al., 2020), potentially reflecting lower perceived benefit, fear of diagnosis, or disease severity.

At the systemic level, rural residence, transportation difficulties, prolonged wait times, and absence of reminders are recurrent barriers (Gibson et al., 2020; Liu et al., 2018; Hinkle et al., 2020). These

inefficiencies disproportionately burden publicly funded or resource-constrained systems. Insurance coverage significantly influences patterns: patients with Medicaid, low income, or fragmented care show lower attendance, while universal or incentive-based systems improve adherence (Chen et al., 2018b; Gibson et al., 2020; Hinkle et al., 2020).

Regarding strategies, a 2018 Cochrane review of 66 RCTs (≥329,000 participants) showed quality-improvement strategies produce ~12% absolute increase in DR screening attendance versus usual care, with larger gains where baseline uptake is low (Lawrenson et al., 2018). Health education and reminders have consistently positive effects: in rural China, automated SMS messages tripled on-time attendance (42.9% vs 14.0%; RR 3.04) at negligible cost (US\$5.40) (Chen et al., 2018a). In older adults specifically, Behavioral Activation in African American seniors (≥65 years) increased dilated fundus examination to 87.9% vs 34.1% (RR 2.58), illustrating value of structured goal-setting in geriatric care (Winters et al., 2017). Canadian tele-education plus on-site tele-retina improved compliance from 35.6% to 50.5% (Moinul et al., 2020).

Embedding screening in primary care reduces travel, coordination, and mobility barriers. A 5-year U.S. trial showed primary-care tele-ophthalmology more than doubled early screening completion (94.6% vs 43.9% within 6 months) compared with referral to in-person clinics (Mansberger et al., 2015). In Montréal, 91.9% flagged after tele-screening attended recommended eye care (Boucher et al., 2020). For the most access-constrained older adults, on-site tele-retinal screening in long-term-care settings reaches residents who rarely attend off-site appointments (Lim et al., 2024).

Autonomous AI tools for diabetic eye screening show promise in addressing logistical barriers. AI-integrated platforms can automate image grading and triage, alleviate specialist workload, and improve diagnostic throughput (Huang et al., 2024; Nakayama et al., 2023). In a study of over 17,000 adults, introduction of the FDA-cleared LumineCore AI system increased adherence from 46.1% to 54.5% at AI-switched sites (vs unchanged 40.3% at non-AI sites), corresponding to an overall increase of 7.6 percentage points ($p < 0.001$), with greatest gains in underserved populations (+12.2% in Black patients, +13.7% in Medicaid-insured) (Huang et al., 2024). Although observational and single-system in scope, these findings strengthen the case that technology-enabled point-of-care testing can enhance equity when implemented with appropriate governance. However, AI implementation requires robust infrastructure and raises concerns about bias, representativeness of training datasets, and limited post-deployment monitoring.

Cost reduction enhances equity. In Hong Kong primary care, waiving copayment increased uptake and uncovered more retinopathy in the free arm (Lian et al., 2013); a subsequent RCT found half-subsidy (HK\$150) achieved uptake comparable to free without deterring higher-risk patients (Lian et al., 2021). Programs pairing cost reduction with active recall, flexible scheduling, and multilingual outreach perform best within organized systems (Lawrenson et al., 2018).

Important caveats remain: much of the trial evidence predated contemporary delivery models, geriatric subgroups were seldom reported, maintenance beyond one screening cycle was rarely assessed, and component-level cost-effectiveness evidence is sparse. A critical gap lies in the absence of caregiver-inclusive approaches: although caregivers often play a decisive role in ensuring follow-up for elderly, visually impaired, or dependent patients, few interventions formally incorporate them into care pathways. Systems aiming to raise DR screening among older adults should prioritize a pragmatic multicomponent package: reduce financial friction, embed point-of-care screening with same-day results in primary and long-term care, and pair patient education with reminder cascades and care navigation.

5.4. Corneal and ocular surface diseases

Management of corneal and ocular surface disease in older adults relies heavily on topical therapy, where adherence is challenged by both duration and intensity. Long-term regimens for dry eye disease (DED) and post-keratoplasty care strain persistence over months, whereas infectious keratitis entails shorter but demanding multi-agent schedules testing day-to-day implementation. Unlike the visit-based adherence challenges of anti-VEGF therapy (Section 5.2) or the once-daily simplicity often achievable in glaucoma (Section 5.1), ocular surface conditions frequently require multiple daily instillations with variable dosing intervals, a regimen complexity that amplifies barriers for older adults with cognitive or dexterity limitations. Given the lack of elderly-specific studies, we draw on adult cohorts that include substantial proportions of older adults.

5.4.1. Adherence rate and patterns

Real-world implementation and persistence are consistently modest across corneal and ocular surface conditions. In a U.S. cohort of 196 adults with corneal diseases (infectious keratitis, post-keratoplasty, other conditions), nonadherence was self-reported by 72% using the 12-question ARMS scale versus 33% using the 3-question VMAS, highlighting how simplified scales with shorter recall periods may further inflate the well-known overestimation of self-reported adherence (Khan et al., 2021). A UK audit of patients with inflammatory eye disease (mean age 50) found 64% reported poor implementation and 27% daily lapses (Javidi et al., 2021).

DED poses unique challenges. A Japan Dry Eye Society survey of 2645 patients (approximately one-third >60 years) found only 10.2% administered drops at prescribed frequency, just 18.3% were aware of recommended dosing intervals, and 61.3% used lubricants "as needed", a symptom-driven PRN pattern that undercuts therapeutic regimens (Uchino et al., 2022). Pharmacy-claims analysis of 9772 adults (mean age 59) confirmed poor persistence with anti-inflammatory therapies: 12-month adherence (PDC \geq 80%) was 5.9% for cyclosporine 0.05% and 9.7% for lifitegrast, with 65–71% discontinuation and median time to discontinuation of 1–3 months (White et al., 2019). Among Sjögren syndrome patients with DED, 82.9% admitted intentionally rationing drops, and nearly one-quarter concealed nonadherence from physicians (Michaelov et al., 2022).

Post-keratoplasty adherence shows contrasting patterns between implementation and visit attendance. A prospective 12-month study using electronic monitoring (27 patients, mean age 58) found mean steroid adherence of $95.2 \pm 4\%$ (range 80.4–100%), with self-reports exceeding electronic capture, likely reflecting motivated candidates, frequent early follow-up, and Hawthorne effect (Poinard et al., 2022). Conversely, a regional PK cohort (n = 695) reported 10.5% missed appointments overall, with only 68.5% achieving "good" attendance (>90% kept) and 4.9% classified as "poor" (Crawford et al., 2015).

5.4.2. Determinants and strategies

The multilevel framework outlined in Section 2.1 applies to ocular surface conditions, though with a distinctive age paradox: younger age is repeatedly associated with lower adherence (Javidi et al., 2021; Khan et al., 2021; Michaelov et al., 2022; Uchino et al., 2022). Older adults more often organize daily activities around medication schedules, whereas younger patients fit drops into busy routines with lower prioritization.

At the individual level, forgetfulness is a leading barrier across studies, frequently coupled with concerns about medication necessity or clinical judgment (Anitha et al., 2022; Javidi et al., 2021; Khan et al., 2021; Michaelov et al., 2022; Uchino et al., 2022). Mental health is an under-recognized determinant: depression and anxiety are prevalent in DED patients, likely mediated by chronic discomfort and undiagnosed neuropathic pain, eroding both implementation and persistence (Wan et al., 2016; Levitt et al., 2017). Critically, discrepancies

between patient perception and clinician grading of DED severity diminish perceived benefit and foster intentional rationing or "as-needed" use (Villani et al., 2025).

Clinically, adherence declines with complex schedules (multiple bottles, dosing intervals, taper plans) and treatment-related discomfort (Javidi et al., 2021; Khan et al., 2021; Michaelov et al., 2022; Uchino et al., 2022; Puente-Iglesias et al., 2024). System-level gaps compound these barriers: a UK audit found 33% of patients failed to correctly name their topical medications, 16% did not know the indication, 58% had never been instructed on correct instillation, and 26% used incorrect intervals (Javidi et al., 2021). Financial burden leads to rationing strategies including reusing single-use vials and using drops past expiry (Michaelov et al., 2022). For post-PK patients, ethnicity, care setting, travel logistics, and social deprivation shape visit retention (Crawford et al., 2015).

Regarding strategies, evidence for ocular surface regimens is limited but points to pragmatic levers. After keratoplasty, audiovisual counseling improved knowledge and self-reported compliance, with video outperforming verbal instruction (Anitha et al., 2022). Digital nudges show promise: SMS reminders combined with technique demonstration achieved high competence in an eyelid hygiene trial (Qiu et al., 2018), and blink-reminder prompts improved DED symptoms in another RCT (Ashwini et al., 2021). For chronic DED, patient-centered approaches, acknowledging disease experience, shared decision-making, sustained therapeutic alliance, address the perception-severity mismatch that drives intentional nonadherence (Lienert et al., 2016; Nichols et al., 2016; Villani et al., 2025).

Clinically, regimen simplification (e.g., switching from six-times-daily to long-acting three-times-daily formulations) improves implementation and persistence (Ishikawa et al., 2023). For corneal grafts, adherence-independent drug delivery is emerging: a subconjunctival dexamethasone implant reduced early reliance on patient-instilled steroids (Trone et al., 2023), while electronic monitoring exposed patterns not captured by self-report, suggesting a role for targeted feedback (Poinard et al., 2022).

A low-burden, patient-centered package can target both implementation and persistence while respecting the constraints of older adults, but dedicated trials in elderly ocular surface populations remain needed.

5.5. Refractive errors optical correction

Uncorrected refractive error remains highly prevalent in older adults and is closely tied to equity and access. In 2020, globally, an estimated 419 million people aged \geq 50 years had near-vision impairment from uncorrected presbyopia (age-standardized prevalence \sim 22%), with marked regional and sex disparities (Little et al., 2024). Unlike medication- or procedure-based adherence discussed in prior sections, refractive correction requires sustained spectacle wear (implementation) and timely replacement (persistence), behaviors shaped more by access and affordability than treatment complexity. The multilevel framework outlined in Section 2.1 applies, though system-level barriers predominate.

5.5.1. Adherence rates and patterns

Effective refractive error coverage (eREC) captures population-level adherence. Recent syntheses estimated global adult eREC at \sim 66% in 2023, ranging from \sim 84% in high-income regions to \sim 28% in sub-Saharan Africa, with age-related decline across \geq 50-year cohorts and lower coverage in women (Bourne et al., 2025). Patterns diverge sharply by setting: in residential aged-care facilities, on-site refraction/dispensing yields high uptake and wear, whereas community surveys (e.g., rural India) report substantially lower spectacle use, underscoring logistical and cost barriers outside institutions (Marmamula et al., 2017, 2023). Most data capture day-to-day wear rather than replacement or refractive updates, yet persistence is critical to sustained function, fall

prevention, and quality of life.

5.5.2. Determinants and strategies

At the individual level, low perceived need (a proxy for health literacy), comfort/fit problems, and aesthetics blunt initiation and implementation, while breakage, loss, and financial barriers erode persistence (Malhotra et al., 2019; Marmamula et al., 2023). These frictions intensify when practical support is limited, such as among individuals living alone (Malhotra et al., 2019). Clinically, multifocal lenses can dampen outdoor mobility and depth perception, reinforcing the need for task-specific prescribing in active seniors (Haran et al., 2010).

System forces are pivotal: financial protection is variably structured, and stand-alone screening without integrated follow-through shows no evidence of reducing vision impairment; integration and affordability are prerequisites for shifting access to refractive care (Goodman et al., 2023). Service proximity is itself a determinant: when refraction/dispensing is brought to residential care, uptake and wear substantially exceed community levels (Man et al., 2020).

Regarding strategies, the strongest evidence supports reducing distance to care, minimizing cost, and aligning prescribing with task demands. In residential care, a randomized trial of on-site comprehensive ocular care improved near vision versus usual referral (Man et al., 2020). In the community, syntheses favor integrated services with follow-up

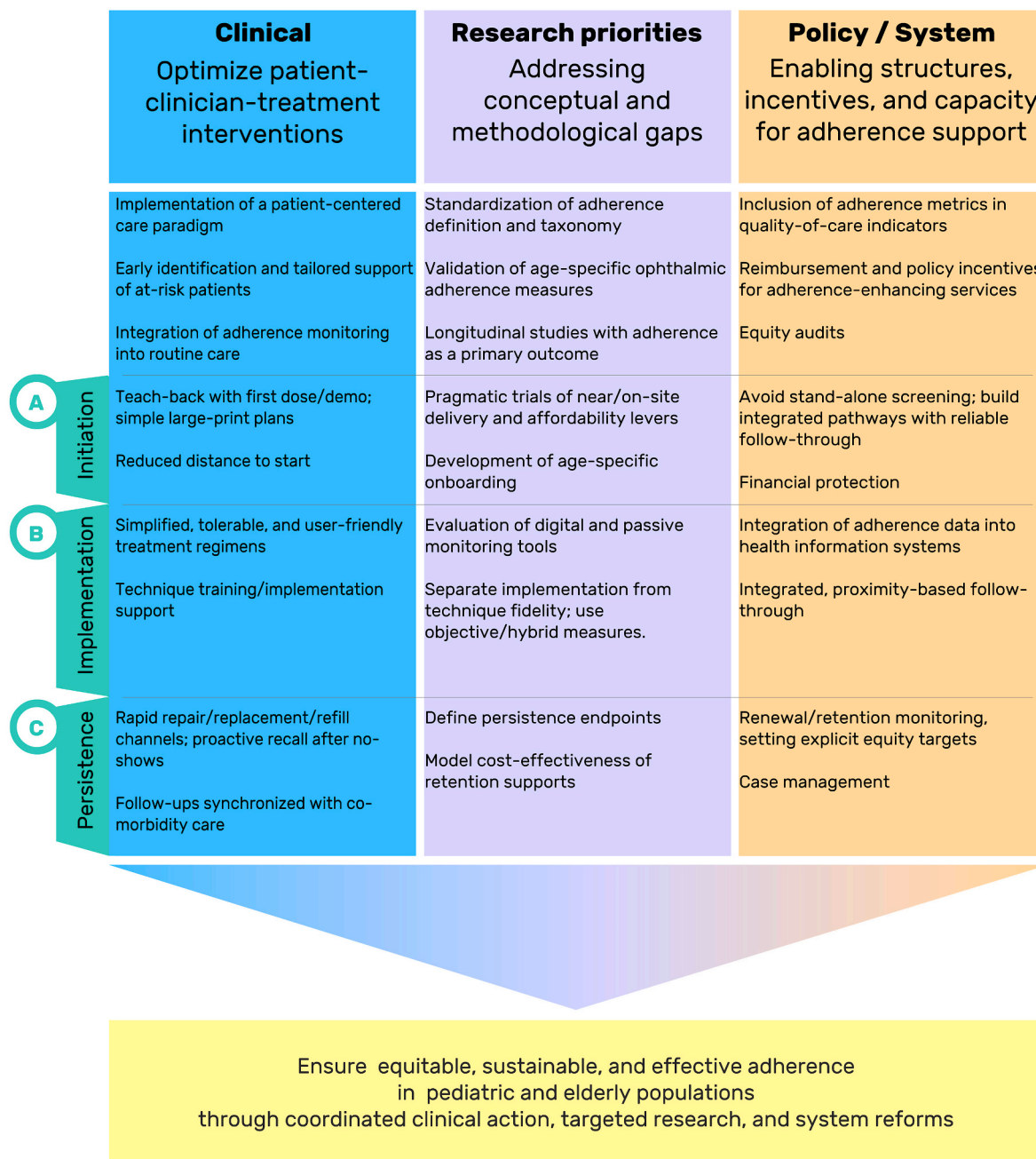


Fig. 4. Strategic roadmap for improving treatment adherence in pediatric and elderly eye care. The figure maps three interdependent pillars — Clinical, Research, and Policy/System — across the ABC phases (A Initiation, B Implementation, C Persistence). The top row lists cross-cutting actions applicable to all phases; rows A–C are phase-specific and anchored to care-pathway timing. The color gradient within the bottom arrow depicts cross-pillar interactions. “Effective adherence” here denotes adherence levels sufficient to achieve intended clinical outcomes of prescribed ophthalmic therapies. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

and financial protection over detection alone (Goodman et al., 2023). Same-day low-cost solutions and safety-oriented single-vision prescribing help initiation and persistence, respectively (Haran et al., 2010; Keay et al., 2010). Community programs bundling education, outreach, teleophthalmology, and affordability mechanisms show better uptake in ≥ 75 -year-olds than single-component efforts (Jensen et al., 2025).

At the policy level, eREC reveals geographic, age, and sex inequities, with current trajectories insufficient for the 2030 target. Economic returns strengthen the case: in rural Bangladesh, providing reading glasses increased income in near-vision-intensive occupations (Sehrin et al., 2024). Programs should embed affordability, bring refraction closer with assured follow-through, and monitor eREC with age- and sex-disaggregation to track whether equity-minded delivery translates into real-world wearing and renewal (Bourne et al., 2025).

6. Conclusion: framing the challenge, setting the agenda

Adherence in pediatric and older adult eye care is not an individual shortcoming but the emergent property of an ecosystem, where cognition, motivation, caregiver dynamics, treatment burden, service design, and affordability converge (Fig. 2). Treating nonadherence as a behavioral lapse has yielded limited progress; treating it as a system outcome provides the basis for durable gains in vision and equity. Our synthesis shows that, across several conditions, avoidable vision loss often tracks breakdowns in initiation, implementation, or persistence rather than lack of therapeutic efficacy.

Fig. 4 organizes the way forward around three interdependent pillars: Clinical, Research, and Policy/System; “effective adherence” may be defined pragmatically as the level of adherence sufficient to achieve intended clinical outcomes for a given therapy.

The agenda below translates that scaffold into near-term, practice- and policy-actionable commitments. Taken together, this agenda reframes adherence as a shared, measurable responsibility of clinicians, services, and payers as much as of families, while keeping patient and caregiver realities at the center. By coupling standardized measurements with age-appropriate clinical bundles and equity-aware system design, ophthalmic care can convert conceptual clarity into routine practice and close this longstanding implementation gap.

6.1. Driving change in clinical practice

Improving adherence in pediatric and older adult eye care demands more than stricter regimens; it calls for a shift to patient-centered, relationship-driven, and developmentally attuned care across the life course. In practice, this means embedding relational competence and flexible delivery into routine workflows rather than treating them as adjuncts to “standard” care (Barry and Edgman-Levitan, 2012; World Health Organization, 2003).

First, risk-aware personalization can be used at intake and at each transition point to profile cognitive, emotional, functional, and logistical factors that shape capacity to adhere (developmental stage and caregiver dynamics in children; executive function, vision, dexterity, and multimorbidity in older adults), so that barriers are anticipated and addressed proactively (Anderson et al., 2025; Hughes, 2004). Second, treating the therapeutic alliance as workflow, through context-calibrated shared decision-making that acknowledges caregiver burden while sustaining patient agency, can foster trust, motivation, and ownership of the plan (Barry and Edgman-Levitan, 2012). Third, treatment and pathway design may prioritize regimen simplification, discomfort reduction, and integration into daily routines (e.g., school-based supports, gamification), paired with low-friction follow-up options and selective home monitoring where feasible (e.g., early home-OCT pilots) to decrease visit burden without compromising safety.

Moreover, measurement should be procedural and transparent. The use of ABC phases with EMERGE-aligned reporting can ensure that “on-time” windows, missed visits, and LTFU are defined consistently, with

condition-specific timing anchored to the care pathway rather than ad hoc (De Geest et al., 2018; Vrijens et al., 2012). Tracking outcomes and processes together (e.g., visual function alongside implementation/persistence), with stratification by equity-sensitive variables such as distance, insurance status, and out-of-pocket costs, can turn adherence into a learning signal for clinic redesign and population health.

Finally, to avoid arbitrariness when designing indicators, a pragmatic approach is to co-develop a small set of phase-specific key performance indicators (KPIs) with clinicians and caregivers, each with a clear ABC mapping and pathway-anchored timing window, an explicit data source (EMR, device log, pharmacy/administrative records), and predefined equity stratifiers (age, sex, deprivation/distance). Targets may be best expressed as relative improvement from local baseline and against pathway benchmarks rather than universal cut-offs, while regular review can support rapid-cycle improvement; financing, accountability, and cross-site comparability are addressed in Section 6.3 (Policy/System).

6.2. Evidence gaps and research agenda

Despite growing recognition, evidence on adherence in eye care, particularly for pediatric and elderly populations, remains fragmented. Studies often use heterogeneous definitions and outcomes, seldom distinguish phases or forms of nonadherence (e.g., initiation vs implementation vs persistence; intentional vs unintentional), and rarely align measurement with care-pathway timing. This hampers meta-analyses, cross-study comparability, and the design of targeted interventions (World Health Organization, 2003; Vrijens et al., 2012).

A first priority is measurement: future work should develop and validate age-appropriate, disease- and phase-specific adherence metrics that move beyond self-report and simple refill proxies toward objective and behaviorally sensitive tools. Where digital health is considered (e.g., connected devices, electronic monitoring, conversational agents), validation in ophthalmic pathways, alongside usability, accessibility, and caregiver-acceptability, will be essential, with clear documentation of data provenance and equity-relevant stratifiers. Proxy reporting for children and cognitively impaired elders should be standardized and explicitly mapped to ABC phases, enabling cumulative synthesis rather than ad hoc interpretation.

A second priority concerns study designs: longitudinal cohorts that track adherence trajectories against clinical and patient-reported outcomes may clarify causal pathways between adherence, disease progression, and vision-related quality of life. Such cohorts would benefit from diverse settings and systematic capture of social and logistical determinants to clarify context-specific barriers and facilitators. Mediation and moderation analyses can help specify when and for whom adherence drives outcomes, informing more precise intervention targets.

Intervention testing should be patient-centered and theory-informed, with designs that explicitly target the phase and mechanism of nonadherence identified in formative work. Education-only approaches may be insufficient; shared decision-making and burden-aware caregiver integration are likely to be more productive, especially at developmental extremes (Barry and Edgman-Levitan, 2012; Piña et al., 2021). Trials should report objective, phase-resolved adherence alongside fidelity, dose delivered, and feasibility, and include caregiver burden and usability where relevant. Notably, cost-effectiveness and potential unintended consequences (e.g., increased visit load, digital exclusion) should also be assessed routinely.

Finally, implementation science can accelerate real-world uptake. Pragmatic and hybrid effectiveness-implementation designs, process evaluations, and health-economic analyses can help characterize acceptability, feasibility, and workflow impact, while identifying the conditions for scale-up (Moore et al., 2015). For digital and AI-enabled approaches, transparent governance, including bias auditing, privacy safeguards, and procurement linked to outcome improvement rather

than feature counts, would support trustworthy adoption.

Taken together, a field-wide core adherence outcome set (EMERGE-aligned, with pediatric and geriatric adaptations), a minimal common data-element and reporting template for trials and registries, and template protocols for cohorts and pragmatic trials would make future studies more comparable and readily translatable (Vrijens et al., 2012).

6.3. Policy and system-level reforms

Sustaining long-term adherence in pediatric and elderly eye care requires more than clinic-level improvements: it depends on systems that lower structural and contextual barriers. Yet adherence is rarely framed as an explicit policy goal, a reimbursable service component, or a quality metric, which limits accessibility, scalability, and sustainability (World Health Organization, 2003). A policy shift toward person-centeredness, co-production, and equity would move services from fragmented, reactive care to integrated, proactive pathways that support patients and caregivers across the entire journey, from detection to treatment, follow-up, and transitions across developmental and aging trajectories. Within this multilayer framework, as outlined in Section 2.2, priorities differ by health-system context: in LMICs and underserved populations, structural interventions addressing cost and access barriers are likely to yield the largest gains and should anchor policy investment; in well-resourced systems where access is largely secured, policy focus shifts to implementation support and retention.

In practical terms, health systems can make adherence a routine objective of service design and accountability. This includes incorporating phase-specific adherence indicators (aligned with the ABC framework) into quality dashboards and contracts, requiring disaggregated reporting by age, sex, deprivation, and distance (making inequities visible and actionable), and linking improvement cycles to feedback from clinics and communities (see Sections 6.1 and 6.2; Vrijens et al., 2012). Because adherence is shaped by logistics and affordability, financing models should recognize counseling, shared decision-making, recall/coordination, and case management as reimbursable activities, support low-friction access (e.g., synchronized prescriptions, on-site dispensing where feasible, transport support for high-risk groups), and avoid stand-alone screening without assured follow-through.

System integration and workforce capacity are equally important. Shared electronic records, cross-specialty coordination, and structured transition protocols can reduce loss to follow-up, while training clinicians to recognize nonadherence and to communicate with children, caregivers, and cognitively impaired older adults strengthens the therapeutic alliance at scale. Protecting time and clarifying roles can help; patient navigators, pharmacists, and community health workers may be embedded in care pathways to sustain adherence support bundles described in Section 6.1.

Digital innovation should ideally be procured and reimbursed on the basis of demonstrated outcomes rather than features. Where digital and AI-enabled tools are adopted, policy can require interoperability, privacy safeguards, bias auditing, and usability testing in ophthalmic pathways, with analog alternatives to prevent digital exclusion. Reimbursement should follow evidence, prioritizing tools that demonstrate improvements in phase-resolved adherence and clinically meaningful outcomes in diverse populations.

Finally, global learning with local adaptation can accelerate progress. International organizations such as the WHO and the International Agency for the Prevention of Blindness (IAPB) are well placed to align measurement, disseminate good practice, and embed adherence within universal eye-health agendas, especially in resource-constrained settings where fragmented care and limited medication access magnify non-adherence (International Agency for the Prevention of Blindness, 2021; World Health Organization, 2003). In parallel, leading professional societies can translate evidence into standards, curricula, and registries, mobilizing multicenter studies and implementation at scale.

Embedding adherence in policy, financing, and quality improvement

makes it a shared system objective, directing support to those at greatest risk and facilitating the equitable, practice-ready translation of improvements into routine care.

6.4. Review scope and limitations

This narrative review synthesized evidence on medication-taking and visit adherence in pediatric and older adult eye care, applying the ABC taxonomy and a multilevel determinant framework to enable systematic comparison across conditions and populations. The opening sections (2–3) established conceptual foundations and measurement considerations; disease-specific chapters (4–5) then examined conditions selected for evidence maturity and clinical representativeness (spanning pharmacologic, device-based, and visit-dependent regimens) before converging on an integrated agenda (Section 6).

As a narrative synthesis, this review did not follow systematic-review protocols: study selection was guided by relevance and recency rather than exhaustive search algorithms, no formal risk-of-bias assessment was applied, and meta-analysis was precluded by heterogeneity in adherence definitions, timeframes, and measurement methods across primary studies. These choices reflect the review's purpose: to map the field, surface cross-cutting themes, and propose a practice-ready framework, rather than to quantify pooled effect sizes. Condition-specific systematic reviews with harmonized outcomes remain an important next step.

Thematically, the medication-and-visit frame excluded relevant topics such as behaviors operating outside scheduled clinical contact (e.g. home self-monitoring, lifestyle modification), systemic outcomes influenced by vision (e.g. fall prevention), acute procedural follow-through (e.g. narrow-angle management), and short-term post-operative positioning (briefly discussed in Section 2.2). Each of these domains warrants dedicated synthesis.

CRedit authorship contribution statement

Edoardo Villani: Writing – review & editing, Writing – original draft, Supervision, Data curation, Conceptualization. **Alessandra Curci:** Writing – review & editing, Writing – original draft, Data curation, Conceptualization. **Francesco Bonsignore:** Writing – review & editing, Visualization, Conceptualization. **Diana V. Do:** Writing – review & editing, Validation. **Murat Dogru:** Writing – review & editing, Validation. **Miriam Kolko:** Writing – review & editing, Validation. **Ken K. Nischal:** Writing – review & editing, Validation, Data curation. **Mario R. Romano:** Writing – review & editing, Validation, Data curation. **Matteo Sacchi:** Writing – review & editing, Validation, Data curation. **Bernard Vrijens:** Writing – review & editing, Methodology, Data curation, Conceptualization. **Paolo Nucci:** Writing – review & editing, Supervision, Conceptualization.

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Declaration of competing interest

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Glossary

- ABC taxonomy (medication adherence framework)** a standardized taxonomy that conceptualizes adherence to prescribed care as a process composed of three quantifiable phases (initiation, implementation, and persistence)
- Adherence** extent to which a patient's behavior matches prescribed recommendations (operational outcome)
- Compliance** extent to which a patient's behavior matches prescribed recommendations; this traditional term has been criticized for implying passivity and a clinician-directed, paternalistic model of care (often framed as "obedience")
- (Patient/caregiver) empowerment** perceived agency and capability to participate in decisions and self-managed care; a facilitator of adherence when paired with adequate health literacy, but potentially associated with reasoned deviation when understanding is incomplete
- Health literacy** the capacity to access, understand, appraise, and use health information and services to make appropriate decisions and enact care plans
- Intelligent nonadherence (also termed "reasoned nonadherence")** intentional deviation from the prescribed recommendations, based on the patient's own risk-benefit appraisal
- Intentional nonadherence** deliberate behavioral deviation from the prescribed recommendations, driven by beliefs, preferences, or perceived side effects
- Sentinel evidence** pre-specified, studies selected for illustrative tables based on methodological rigor, representativeness, or foundational contribution; these are illustrative rather than exhaustive.
- Unintentional nonadherence** inadvertent deviation from the prescribed recommendations, due to forgetfulness, misunderstanding, or practical barriers (cost, access, dexterity)

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.preteyeres.2026.101448>.

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