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A behaviour change approach to medication adherence in glaucoma

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A Thesis submitted for the degree of
Doctor of Philosophy



Department of Optometry and Visual Sciences
School of Health and Medical Sciences

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Declaration

I, Deborah Bott, confirm that the work presented in this thesis is my own, conducted under the supervision of Dr. Peter Campbell, Associate Professor Ahayla Subramanian, Emeritus Professor David Edgar, and Professor John Lawrenson. Where information from external sources has been used, I confirm that this has been appropriately acknowledged in the thesis, and full references are provided. This thesis has not been submitted, either in whole or in part, for any other degree or qualification, past or present. I grant the University Librarian of City St George's, University of London, permission to allow the thesis to be copied, in whole or in part, for study purposes, subject to normal conditions of acknowledgment.

Abstract

Background

Poor adherence to intraocular pressure (IOP)-lowering medication remains a major challenge in glaucoma care, contributing to avoidable vision loss. Existing adherence interventions are limited and often lack a robust theoretical foundation. With the growing global burden of glaucoma, there is a pressing need for scalable, effective, evidence-based interventions that are responsive to patients' needs. This thesis adopts a behavioural science approach to develop a patient-level intervention, following UK Medical Research Council (MRC) guidance for complex intervention development. A structured process was followed: understanding the behaviour, identifying influencing factors, and determining what needs to change to support improved adherence.

Objectives:

- Identify key behavioural determinants of glaucoma medication adherence from the literature
- Develop a practical definition of acceptable adherence among UK glaucoma eye care professionals (ECPs)
- Identify modifiable behavioural determinants from the perspectives of patients and ECPs
- Develop a conceptual model for a theory-based, patient-centred intervention

Methods

A systematic review identified modifiable behavioural determinants, mapped to the Theoretical Domains Framework (TDF). A Delphi consensus study with UK ECPs was conducted to establish a benchmark for acceptable adherence to guide when intervention support should be triggered. Qualitative interviews with patients and ECPs explored real-world barriers and enablers, analysed using the TDF. Findings were synthesised to generate a behavioural diagnosis using the COM-B model (Capability, Opportunity, Motivation–Behaviour), informing the selection of relevant Intervention Functions (IFs) and Behaviour Change Techniques (BCTs) via the

Behaviour Change Wheel (BCW). Selected components were integrated into a conceptual intervention model and evaluated for acceptability by key stakeholders.

Results

The systematic review and interview findings revealed three overarching patient-level barriers to adherence: (1) lack of understanding regarding glaucoma and/its treatment, (2) issues with eyedrop administration, (3) difficulties obtaining medication. These mapped to psychological capability, physical capability, and physical opportunity within the COM-B model. The Delphi study found that 80% adherence was generally considered acceptable for most glaucoma patients, with flexibility for clinical discretion. This threshold informed when intervention support should be activated. The behavioural diagnosis informed the selection of three IFs and seven BCTs, which were integrated into the Adherence Resources Toolkit (ART), a personalised adherence support toolkit. Stakeholder feedback indicated high acceptability and strong potential for the ART.

Conclusion

This thesis presents the first behaviourally informed, stakeholder-driven model designed to support glaucoma medication adherence. It provides a robust theoretical and empirical foundation for future feasibility testing and implementation in real-world clinical practice.

List of Abbreviations

AA: Alpha-adrenergic agonist	ESPACOMP: European Society for Patient Adherence, COMpliance, and Persistence
ABC: Ascertaining Barriers to Compliance	FDA: Food and Drug Administration
AHP: Allied health professional	GOC: General Optical Council
AGIS: Advanced Glaucoma Intervention Study	GTCAT: Glaucoma Treatment Compliance Assessment Tool
AI: Artificial Intelligence	HCP: Health care professional
ART: Adherence Resources Toolkit	IF: Intervention Function
BB: Beta-adrenergic blocker	IOP: Intraocular pressure
BCT: Behaviour change technique	LiGHT: Laser in Glaucoma and Ocular Hypertension Study
BCW: Behaviour change wheel	LPI: Laser peripheral iridotomy
CA: Cholinergic agonist	LMIC: Low- and middle-income country
CAI: Carbonic anhydrase inhibitor	MD: Mean deviation
CNTGS: Collaborative Normal Tension Glaucoma Study	MI: Motivational interviewing
COAG: Chronic open angle glaucoma	MIGS: Minimally invasive glaucoma surgeries
COM-B: Capability, Opportunity, and Motivation – Behaviour	MMAS: Morisky Medication Adherence Scale
CPD: Continuing Professional Development	MoD: Mode of delivery
EAGLE: Effectiveness in Angle-closure Glaucoma of Lens Extraction	MRC: Medical Research Council
ECP: Eye care professional	NICE: National Institute for Health and Care Excellence
ECLO: Eye care liaison officer	NTG: Normal tension glaucoma
EGS: European Glaucoma Society	OHT: Ocular hypertension
EMA: European Medicines Authority	OHTS: Ocular Hypertension Treatment Study
EMERGE: ESPACOMP Medication Adherence Reporting Guideline	

PDG: Pigmentary glaucoma
PGA: Prostaglandin analogue
PGD: Patient Group Directive
POAG: Primary open angle glaucoma
PPIE: Public and Patient Involvement
and Engagement
PXG: Pseudo exfoliative glaucoma
QoL: Quality of life
RCT: Randomised Controlled Trial
RGCs: Retinal ganglion cells
RNFL: Retinal nerve fibre layer
RNIB: Royal National Institute of Blind
People
SLT: Selective laser trabeculoplasty
TAGS: Treatment of Advanced
Glaucoma Study
TDF: Theoretical Domains Framework
TFA: Theoretical Framework of
Acceptability
UKGTS: United Kingdom Glaucoma
Treatment Study
UKEGS: UK and Eire Glaucoma
Society
USA: United States of America
WHO: World Health Organization

Chapter 1 Glaucoma and medication adherence

1.1 Chapter overview

This chapter introduces glaucoma and its treatment, then provides background information on medication adherence with a specific focus on adherence in glaucoma. Following this, the chapter explores various interventions designed to improve adherence. Finally, it outlines the aims and objectives of this thesis.

1.2 Glaucoma definition and epidemiology

Glaucoma encompasses a group of optic neuropathies, characterized by the progressive loss of retinal ganglion cells (RGCs) leading to a distinctive appearance of the optic disc and associated visual field loss (Weinreb & Khaw, 2004). If left untreated, glaucoma results in progressive, irreversible vision loss (Jayaram et al., 2023).

While glaucoma damage cannot currently be reversed, early detection and appropriate treatment can prevent most glaucoma-related damage. Individuals diagnosed early can generally expect to maintain their vision throughout their lives. Early detection and initiation of treatment are associated with better outcomes and improved quality of life (QoL) (Latif et al., 2023). The most important risk factor for glaucoma-related blindness is the extent of vision loss at the time of diagnosis. Individuals with advanced disease require significantly more time and resources for management, often needing more frequent medical or surgical interventions (Kastner & King, 2020). Therefore, early detection and treatment are crucial to minimising irreversible vision loss.

Currently, glaucoma is the second most common cause of global blindness (Steinmetz et al., 2021). In 2020, there were 3.6 million individuals worldwide who were blind due to glaucoma. In England and Wales, it accounts for 11% of severe vision impairment and is the second most common cause of certifiable sight loss (Quartilho et al., 2016).

The prevalence of glaucoma increases with age, affecting an estimated 1.1% of individuals over 40 and 9.2% of those over 80 (Zhang et al., 2021a). With an aging global population (Harris, 2013) the prevalence of glaucoma is expected to rise. By 2040, it is projected to affect 111.8 million people, up from 76 million in 2020 (Tham et al., 2014). Consequently, glaucoma and its associated vision loss are set to become a major global burden.

Glaucoma can be broadly classified into two types: open angle and angle closure glaucoma. The main distinction between the two is the anatomy of the anterior chamber angle, which is the space between the iris and the cornea in the front part of the eye. Both forms can be primary diseases or secondary to other causes such as steroid use, trauma, inflammation, pseudo-exfoliation, or pigment dispersion syndrome.

1.2.1 Primary open angle glaucoma

The ciliary body continuously produces aqueous humour in the posterior chamber at a rate of approximately 2 to 3 microlitres per minute (Sunderland & Supra., 2023). This fluid then passes through the pupil into the anterior chamber and drains via two pathways: the conventional outflow pathway (through the trabecular meshwork) and the unconventional outflow pathway (via the uveoscleral route) (Figure 1.1).

Intraocular pressure (IOP) is determined by the balance between aqueous humour production and outflow. In White populations, IOP typically ranges between 11 and 21 mmHg and exhibits diurnal variation, with higher levels commonly observed in the morning (Machiele et al., 2024). In East Asian populations, IOP tends to be lower on average (Chua et al., 2014).

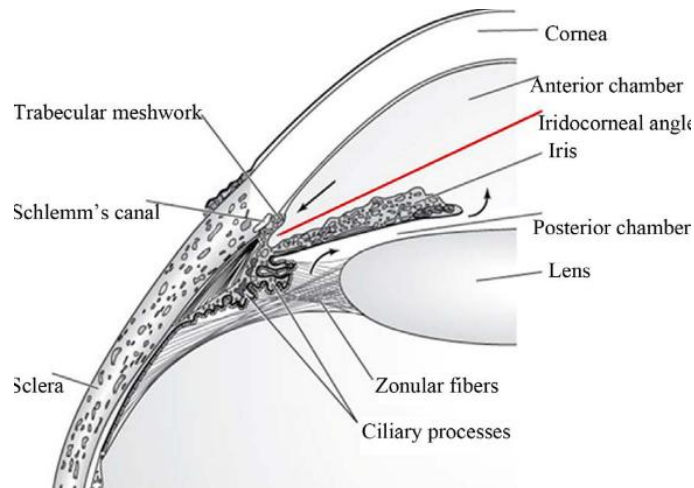


Figure 1.1 Diagram of the anatomical structures of the anterior chamber angle. Black arrows illustrate the flow of aqueous humour.
Image courtesy of Källmark & Sakhi, 2013.

In primary open angle glaucoma (POAG) there is increased resistance to the outflow of aqueous humour through the trabecular meshwork. Over time, this leads to elevated IOP, which results in structural damage to the posterior segment of the eye. Specifically, damage to the optic nerve head, associated with progressive loss of RGCs and thinning of the neuroretinal tissue, produces the characteristic appearance of optic disc cupping. This structural damage leads to a pattern of visual field loss, with peripheral vision being more susceptible to glaucomatous damage (Figure 1.2). Central vision is typically affected in the later stages of the disease when it becomes symptomatic.

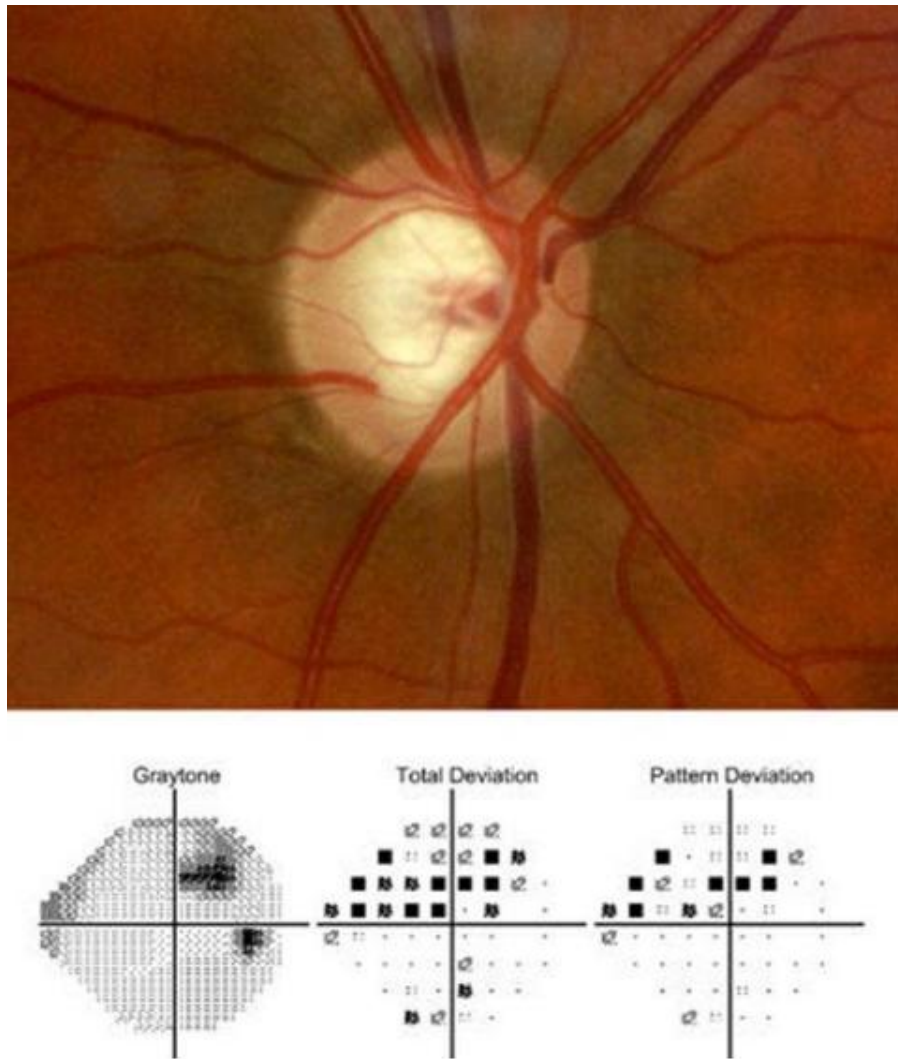


Figure 1.2 Appearance of an optic disc in a glaucomatous eye which illustrates an enlarged cup and thinning of infero-temporal neuroretinal rim (top image) with corresponding visual field defect (bottom image).

Image courtesy of The College of Optometrists <https://www.college-optometrists.org/>

Elevated IOP is the main modifiable risk factor associated with POAG. Longitudinal population-based studies have demonstrated that higher than average baseline IOP increases the risk of developing glaucoma (de Voogd et al., 2006; Le et al., 2003; Leske et al., 2008). However, some individuals are diagnosed with glaucomatous optic neuropathy despite having IOP readings within the statistically normal range (i.e. between 10- 21mmHg). This is classified as normal tension glaucoma (NTG) and is more common in Japanese populations and females (Mallick et al., 2016). NTG has also been linked to factors associated with impaired ocular blood flow.

These include chronic low vascular perfusion, nocturnal systemic hypotension, and systemic hypotension which can be caused by aggressive treatment of high blood pressure. Additionally, conditions such as Raynaud's phenomenon, migraine history, and sleep apnoea have been identified as contributing risk factors (Mallick et al., 2016).

Increasing age is a risk factor for developing glaucoma (Boland & Quigley, 2007). Within the UK, POAG affects approximately three percent of over 60s and eight percent of over 80s, according to the National Institute for Health and Care Excellence (NICE, 2022). African ancestry increases the risk of glaucoma, with prevalence being four to five times higher in those of African descent (Leske et al., 2008; Tielsch et al., 1991). Glaucoma also tends to develop earlier, more severely and can respond less effectively to treatment in these populations (Wilson et al., 1985). A family history of glaucoma is another significant risk factor, the closer the relative the higher the risk, a first-degree relative with POAG increases the risk tenfold (Quigley, 2011).

1.2.2 Ocular hypertension

Ocular hypertension (OHT) is characterised by consistently elevated IOP in one or both eyes, in the absence of glaucomatous optic nerve damage, visual field loss, or other ocular conditions that might explain the raised pressure. While IOP levels above 21 mmHg are generally considered elevated, a diagnosis of OHT requires confirmation of this raised pressure on at least two separate occasions (European Glaucoma Society [EGS], 2021). Importantly, individuals with OHT have open anterior chamber angles and structurally normal optic discs and visual fields.

Longitudinal studies suggest that around 10% of individuals with OHT will develop glaucoma within five years if left untreated (Kass et al., 2002). However, early intervention to lower IOP can reduce this risk by approximately 50%. As a result, the decision to treat OHT is guided on individual risk factors for progression, such as age and baseline level of IOP. According to current UK NICE guidance, treatment should be considered when IOP exceeds 23 mmHg and there is a risk of vision loss within

the person's lifetime (NICE, 2022).

1.2.3 Primary angle closure glaucoma

In angle closure glaucoma the outflow of aqueous humour is obstructed leading to elevated IOP (Figure 1.3). This may be due to various mechanisms, the most common of which is pupillary block where contact between the iris and lens blocks the flow of aqueous humour from the posterior to the anterior chamber. Less common are non-pupillary block mechanisms, such as plateau iris, which causes closure of the angle.

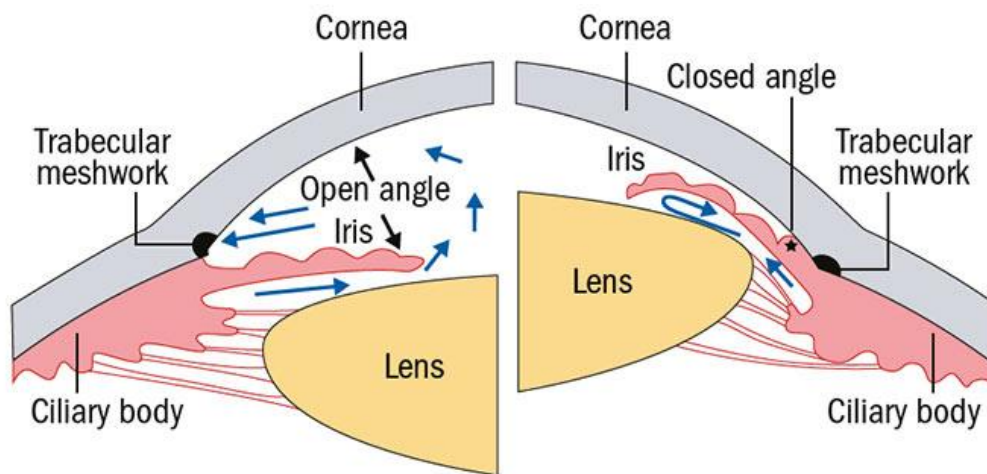


Figure 1.3 Diagram illustrating the difference between an open (left hand side) and closed (right hand side) anterior chamber angle.

Image courtesy of Optician <https://www.opticianonline.net/>

Globally, POAG is more common than primary angle closure glaucoma (PACG), although PACG is more prevalent in Asia (Zhang et al., 2021a, 2021b). Approximately 65 million individuals have open angle glaucoma (OAG) compared to 30 million with angle closure glaucoma. However, the risk of vision loss is greater with angle closure glaucoma (Jayaram et al., 2023); population-based studies have indicated that individuals with PACG are approximately three times more likely to experience severe, bilateral visual impairment than those with POAG (Tham et al., 2014).

For the purposes of further discussion, the term 'glaucoma' will refer to any or all of the conditions outlined above, unless otherwise specified.

1.3 Clinical management

The only proven treatment to slow down or halt disease progression is to reduce IOP. Several multicentre randomised controlled trials (RCTs) have demonstrated the benefits of effective IOP reduction for both early and advanced stages of the disease.

The Ocular Hypertension Treatment Study (OHTS) demonstrated that lowering IOP reduces the risk of patients with OHT developing glaucoma by 50% over five years (Kass et al., 2002). For every 1mmHg reduction in IOP, the risk of developing glaucoma reduces by 10%. The United Kingdom Glaucoma Treatment Study (UKGTS) found that latanoprost eyedrops significantly preserved visual field function compared to placebo over a two-year period (Garway-Heath et al., 2013). A 20% reduction in IOP was associated with a 50% relative risk reduction in visual field deterioration. The Collaborative Normal tension Glaucoma Study (CNTGS) demonstrated lowering IOP by 30% delayed visual field progression in patients with NTG (Collaborative Normal-Tension Glaucoma Study Group, 1998). The Advanced Glaucoma Intervention Study (AGIS) proved IOP consistently lower than 18mmHg slowed visual field progression over a six-year period in patients with OAG compared to those with IOP higher than 18mmHg (Agis Investigators, 2000).

Studies have also demonstrated that treating glaucoma is likely to be economically beneficial. The benefits of preventing vision loss and reducing healthcare costs outweigh the costs of treatment when compared to not treating the condition at all (EGS, 2021).

1.3.1 Treatment goal

The primary goal of glaucoma treatment is to preserve visual function. Defining an acceptable level of IOP to prevent or slow disease progression and minimise the risk

of visual loss (i.e. target IOP) is specific to each disease and patient. Factors such as baseline IOP, severity of visual field loss, amount of optic nerve damage, status of the fellow eye, patient age, general health and predicted life expectancy all play a part in deciding on a target IOP (EGS, 2021).

The EGS guidelines (2021) recommend a 20% reduction in IOP, to below 21mmHg for patients with early glaucoma to prevent deterioration. For patients with moderate disease, a 30% reduction in IOP to less than 18mmHg is advised. In advanced glaucoma even lower levels may be needed, such as less than 14mmHg, to prevent progression (EGS, 2021; Sihota et al., 2018). Target IOP is not a static figure, but a dynamic value that needs to be re-assessed at each follow-up visit to maximise disease stability.

1.3.2 Treatment options

NICE, the EGS, the American Academy of Ophthalmology and the Asia Pacific Glaucoma Society provide guidance on treatment choices for glaucoma. Current treatment options include medical therapy, laser treatments and surgical procedures. All treatment modalities aim to lower IOP by either reducing aqueous humour production, increasing its outflow through the conventional (trabecular) or unconventional (uveoscleral) pathways, or a combination of both mechanisms.

1.3.3 Medical therapy

There are five main classes of topical IOP-lowering drugs: prostaglandin analogues (PGAs), beta-adrenergic blockers (BBs), carbonic anhydrase inhibitors (CAIs), alpha-adrenergic agonists (AAs) and cholinergic agonists (CAs). Guidance suggests initiating treatment with monotherapy (EGS, 2021). If the initial drug does not achieve target IOP or it is not tolerated then it should be substituted by another monotherapy before escalating treatment. If monotherapy does not sufficiently reduce IOP but is well tolerated, adding or combining a second drug class is recommended. The goal of treatment is to achieve the desired therapeutic effect with

the least amount of medication and side effects.

NICE guidelines in England and Wales recommend offering a generic prostaglandin as first-line therapy to patients with OHT, suspect glaucoma, or chronic open-angle glaucoma (COAG), which includes POAG as well as secondary types such as pseudo exfoliative glaucoma (PXG) and pigmentary glaucoma (PDG), who are at risk of visual loss during their lifetime (NICE, 2022). PGAs reduce IOP by increasing aqueous outflow through the uveoscleral pathway (Lee & McCluskey, 2010). They have good efficacy at reducing IOP, require a convenient once a day dosing regime and are well tolerated with limited systemic side effects. A meta-analysis of RCTs found that PGAs achieved the greatest reduction in IOP among topical ocular hypotensive drugs (van der Valk et al., 2005).

Topical BBs, which reduce aqueous humour production, are recommended as second-line therapy. They reduce IOP by approximately 20-35%, have minimal ocular side effects but a higher risk of systemic side effects (Sidjanin et al., 2008).

CAIs and AAs, both of which reduce aqueous humour formation (Cantor, 2006; Eichhorn, 2013) are used as third- and fourth-line therapies respectively.

Topical CAs, which increase aqueous outflow are usually used as a last resort due to the need for multiple daily instillations and high risk of ocular and systemic side effects (Zimmerman & Wheeler, 1982).

NICE recommends prescribing preservative-free eyedrops where there is evidence of preservative toxicity or clinically significant ocular surface disease (NICE, 2022). Preservative-free preparations, which can be available in either single unit or multidose containers, often have greater patient satisfaction and tolerability than unpreserved versions (Muñoz Negrete et al., 2017), although at increased cost (Steven et al., 2018). Fixed combination eyedrops combine ingredients from two different drug classes into one preparation. This has the advantage of simplifying dosing regimens, reduces exposure to preservatives and lowers the risk of developing ocular surface disease (Shirai et al., 2021).

Over the past eight years, a new class of glaucoma drug, Rho kinase inhibitors, has become available. These agents act on the trabecular meshwork, where they relax the cells, reduce stiffness, and decrease fibrosis, thereby enhancing aqueous humour outflow and lowering IOP (Tanna & Johnson, 2018). Rho kinase inhibitors have been approved by the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), and regulatory authorities in Japan for the treatment of OAG and OHT.

RCTs have demonstrated that once daily dosing of a Rho kinase inhibitor is as effective in lowering IOP as the BB eyedrop, Timolol (Khoury et al., 2019; Serle et al., 2018). However, a high incidence of ocular side effects were noted with Rho kinase inhibitors, leading some participants to discontinue the drug (Khoury et al., 2019).

A fixed combination of the Rho kinase inhibitor netarsudil with the PGA latanoprost is also available. Netarsudil lowers IOP by increasing aqueous humour drainage through the trabecular meshwork, reducing its production, and decreasing episcleral venous pressure. This mode of action complements latanoprost, which reduces IOP by increasing the outflow through the uveoscleral pathway. The netarsudil/latanoprost fixed combination has been approved by the FDA, EMA and the UK's Medicines and Healthcare products Regulatory Agency for the treatment of OAG and OHT.

Clinical trials have shown that the fixed combination drug netarsudil/latanoprost is more effective at lowering IOP than either drug alone (Asrani et al., 2019; Walters et al., 2019). However, ocular side effects, such as conjunctival hyperaemia were noted, which lead to some participants discontinuing the drug. Cost analysis of the fixed combination netarsudil/latanoprost found it to be as cost-effective or less costly than other fixed combination drugs (NICE, 2024).

In 2024, NICE updated its guidance for the treatment of OAG and OHT to reflect these advances in drug therapy. NICE now recommends the fixed combination netarsudil/latanoprost for patients with OAG or OHT after a PGA alone has not sufficiently lowered IOP, and a fixed combination drug has been used but has not

achieved target IOP, or if a patient is unsuitable for other fixed combination drugs (NICE, 2024).

1.3.3.1 Ocular and systemic side effects of glaucoma eyedrops

Topical therapy is a mainstay in the management of glaucoma; however, it is not without adverse effects. Both ocular and systemic side effects of ocular hypotensive medication are well-documented and can influence patient adherence, comfort, and the overall success of long-term treatment. A database study conducted in a Glasgow teaching hospital covering the period 1981-99, found that 22% of changes to eyedrop regimens were due to adverse effects (Rahman et al., 2009). These side effects can negatively impact patients' quality of life and may lead to reduced adherence with prescribed therapy (Quaranta et al., 2016).

PGAs are generally well tolerated systemically but are associated with several ocular side effects. These include irreversible darkening of the iris, elongation and darkening of eyelashes, conjunctival hyperaemia, periorbital fat atrophy, and increased pigmentation of the periocular skin (Garg & Gazzard, 2018). Eyelash changes and conjunctival hyperaemia are relatively common, with hyperaemia reported in up to 50% of patients (Feldman, 2003) and eyelash changes in 45-57% of users (Alm et al., 2008). Iris pigmentation changes and periorbital fat atrophy are less common but may be irreversible.

BBs, while often well tolerated locally, carry a higher risk of systemic adverse effects. These include cardiovascular complications such as bradycardia, arrhythmias, and heart failure, as well as respiratory issues like bronchospasm, particularly in patients with asthma or chronic obstructive pulmonary disease (Li et al., 2025). BBs should therefore be prescribed with caution, especially in patients with pre-existing respiratory or cardiac conditions. Neurological side effects such as fatigue, depression, decreased libido, anxiety, and nightmares have also been reported, though these are relatively uncommon.

Topical CAs may cause ocular discomfort, including stinging, burning, and blurred vision. A common systemic side effect is a bitter or metallic taste, reported by nearly

25% of patients (Li et al., 2025). Other systemic effects may include fatigue, nausea, headaches, and paraesthesia.

AAs are associated with allergic conjunctivitis and have a high potential for systemic absorption due to their ability to cross the blood-brain barrier. This can result in side effects such as fatigue, dry mouth, headache, hypotension, and bradycardia (Li et al., 2025).

CAs, though less commonly used today, can cause ocular side effects including miosis-induced blurred vision, ciliary muscle spasm leading to induced myopia, and brow ache. Due to these effects, their use is typically reserved for short-term or specific clinical scenarios (Garg & Gazzard, 2018).

1.3.4 Laser treatment

Several types of laser treatment are available to use in OAG, the most common being selective laser trabeculoplasty (SLT). SLT uses short pulses of low energy light targeted at the trabecular meshwork to induce biological and mechanical reactions, resulting in increased aqueous outflow and reduced IOP (Jha et al., 2012).

The Laser in Glaucoma and Ocular Hypertension Study (LiGHT), a multicentre RCT, compared SLT treatment with eyedrops as initial treatment in newly diagnosed OHT and OAG patients. Over six years, this pivotal trial demonstrated SLT is a safe, repeatable, clinically-effective and cost-effective treatment for OAG and OHT (Gazzard et al., 2019, 2023).

Since January 2022, NICE has recommended offering SLT to newly diagnosed COAG or OHT patients as first-line treatment (NICE, 2022). Similar recommendations have been advocated by the United States of America (USA) and Europe (EGS, 2021; Gedde et al., 2021). As an initial treatment, SLT can delay the need for eyedrops in approximately 70% of patients for up to six years (Gazzard et al., 2023). In patients already on treatment but with uncontrolled IOP, SLT can

potentially reduce the need for further medications or delay more invasive procedures (e.g., surgery).

However, SLT may not always be successful. IOP reduction may not be sufficient or sustained (Khawaja et al., 2020) and while uncommon, severe complications can arise (Garg & Gazzard, 2018; Song, 2016). An observational study, conducted in the UK, reported treatment success in only 27% of participants at two years post SLT, though higher baseline IOP was associated with better success rates (Khawaja et al., 2020).

Laser peripheral iridotomy (LPI) is a treatment option for angle closure. It involves creating a small opening in the peripheral iris to facilitate the flow of aqueous humour from the posterior to the anterior chamber. This relieves pressure behind the iris, preventing it from bowing forward and narrowing or closing the drainage angle. However, evidence from the multicentre EAGLE trial (Effectiveness in Angle-closure Glaucoma of Lens Extraction), which compared clear lens extraction with LPI in patients with primary angle closure and PACG demonstrated that lens extraction is more effective in lowering IOP and is also more cost-effective than LPI (Azuara-Blanco et al., 2016). As a result, current guidelines recommend reserving LPI primarily for acute presentations or individuals at high risk of developing angle closure glaucoma (The Royal College of Ophthalmologists, 2022).

A more destructive form of laser treatment, cyclodiode laser, can be used to treat glaucoma refractory to medical therapy and surgical procedures. Cyclodiode laser ablates the ciliary processes which in turn reduces aqueous humour production and lowers IOP. Whilst this procedure may be beneficial for end stage glaucoma it carries a significant risk of complications such as uveitis, hypotony and phthisis (Scott et al., 2023).

1.3.5 Surgical procedures

NICE recommends filtration surgery as the initial treatment for patients diagnosed with advanced COAG (NICE, 2022). Surgery is often considered a more cost-effective first line option in low- and middle-income countries (LMICs) (Delgado et al.,

2019; Thomas et al., 2003). However, careful consideration needs to be given to possible post-operative complications and accessibility to follow-up care which can result in more indirect costs (Delgado et al., 2019). Filtration surgery is the most effective method for lowering IOP in advanced glaucoma. NICE defines advanced glaucoma damage using a visual field grading system, the Hodapp-Parrish-Anderson (HPA) system (Hodapp et al., 1993) where the visual field loss has to meet four specified criteria (NICE, 2022).

Trabeculectomy is considered the 'gold standard' technique for glaucoma surgery. The Treatment of Advanced Glaucoma Study (TAGS), a multicentre RCT, demonstrated that primary trabeculectomy provided better IOP control over five years compared to medical treatment in patients with advanced glaucoma (King et al., 2024). A trabeculectomy creates an alternative drainage pathway for aqueous humour to flow out of the eye, avoiding the blocked trabecular meshwork. During the procedure, a partial thickness flap is created in the sclera, and a small opening is made in the underlying sclera. The overlying conjunctiva is then loosely sutured back over this area to cover the new drainage site. As aqueous humour drains through the new opening the overlying tissue rises to form a fluid filled blister, known as a 'bleb'. The bleb controls the continuous outflow of aqueous humour, hence reducing IOP and minimising IOP fluctuations (Figure 1.4).

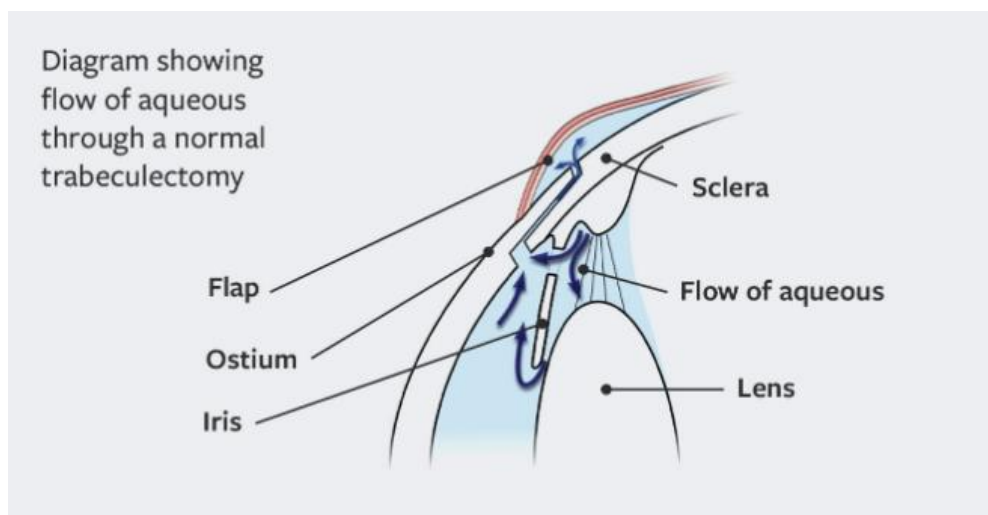


Figure 1.4 Diagram to illustrate the flow of aqueous humour following a Trabeculectomy.

Image courtesy of Glaucoma UK <https://glaucoma.uk/>

To minimise the risk of post-operative bleb failure caused by scar tissue formation during the healing process, anti-metabolites, such as mitomycin, can be applied into the eye during surgery. Anti-metabolites prevent the growth of cells which are responsible for producing the scar tissue. The use of anti-metabolites in trabeculectomy is in line with NICE guidance (NICE, 2022).

However, trabeculectomy is not without its risks. Potential complications include bleb failure, surgical complications, post-operative infection, bleeding or inflammation, all of which can cause loss of vision (Rulli et al., 2013). As a result, trabeculectomy requires intensive post-operative management to closely monitor and address these issues.

In cases of advanced glaucoma, or when IOP cannot be adequately controlled with medications, laser, or conventional filtration surgery, glaucoma tube surgery may be indicated. This procedure involves implanting a small drainage device to create an alternative outflow pathway for aqueous humour, bypassing the obstructed trabecular meshwork. The device consists of a tube that is inserted into the anterior chamber of the eye and connected to a plate positioned on the sclera beneath the conjunctiva. Aqueous humour flows through the tube to the plate, where it is absorbed by surrounding tissues and drained into the episcleral blood vessels. Evidence from long-term studies has shown that tube surgery is effective in lowering IOP and is associated with lower failure rates over a five-year period compared to trabeculectomy (Gedde et al., 2012).

Newer minimally invasive glaucoma surgeries (MIGS) have been developed in recent years to mitigate the risks associated with traditional filtration surgery. MIGS encompasses a range of procedures that use microscopic implants or devices inserted through tiny incisions, usually made through the cornea, thereby minimising trauma to the surrounding sclera and conjunctiva. These procedures reduce IOP by bypassing the trabecular meshwork, increasing outflow through Schlemm's canal, increasing uveoscleral outflow, diverting aqueous to the subconjunctival space or ablating the ciliary body to reduce aqueous production (Gillmann & Mansouri, 2020).

Whilst MIGS procedures have an improved safety profile, shorter surgery and recovery they achieve less IOP reduction compared to trabeculectomy (Mathew & Buys, 2020). MIGS procedures can be performed with cataract surgery and may reduce or eliminate the need for glaucoma eyedrops post-operatively (Bicket et al., 2021). Ideal candidates for MIGS are those with mild to moderate glaucoma damage or those intolerant to medications.

For PACG, clear lens extraction surgery can effectively open the drainage angle and reduce iridotrabecular contact, thereby reducing IOP. Findings from the EAGLE study demonstrated that clear lens extraction is an effective, safe, and cost-effective initial treatment for PACG (Azuara-Blanco et al., 2016). These results have been reflected in updated clinical guidelines (The Royal College of Ophthalmologists, 2022).

1.4 Medication adherence in glaucoma

Despite the availability of laser and surgical options, the majority of glaucoma patients rely on long-term medication to manage their condition (Haga et al., 2022; Perera et al., 2020). To achieve therapeutic benefits ongoing medication adherence is required. For example, if medication is not routinely administered, it will not be effective, potentially leading to sight loss. The following section will explore the importance of medication adherence in glaucoma, the factors influencing adherence, and strategies to improve it.

1.4.1 Terminology

The taking of medication is a complex issue, made even more complicated by the different terminology used in the literature. Definitions such as adherence, compliance, persistence and concordance all describe different aspects of medication-taking following a consultation with a health care professional (HCP).

1.4.1.1 Adherence

Adherence refers to a change in a patient's health behaviour, in response to an agreed care plan with their HCP in order to achieve a desired outcome (Martos-Méndez, 2015). Health behaviour relates to any form of "overt behavioral patterns, actions and habits" that influence a patient's health status (Williams et al., 2018). According to the World Health Organisation (WHO), adherence involves changes in health-related behaviour such as "taking medication, following a diet, and/or executing lifestyle changes" (Sabaté, 2003). Adherence assumes that a patient has the necessary knowledge, motivation, skills and resources to follow a management plan (Vrijens et al., 2012). In this thesis, adherence refers to the behaviour of taking prescribed medication.

Adherence can be classified into primary or secondary, the opposite being primary or secondary nonadherence. Primary nonadherence occurs when patients fail to collect their first prescription for a new medication from the pharmacy (Raebel et al., 2013). Secondary nonadherence occurs when patients collect their medication but do not take it as prescribed. A systematic review with meta-analysis found that 17% of patients with chronic diseases were primary nonadherent to newly prescribed medications (Cheen et al., 2019). Approximately half of all patients on chronic medications are thought to be secondary nonadherent, which is why most research focusses on this category (Lee et al., 2016).

Nonadherence can also be intentional, unintentional or a combination of both (Figure 1.5). Intentional nonadherence occurs when a patient deliberately chooses to not take their medication, often influenced by their beliefs and concerns about their condition and treatment. Unintentional nonadherence happens when a patient is unable to follow their medication regime due to factors such as forgetfulness, physical difficulties in taking medication, difficulty understanding instructions or complex treatment regimens (Hugtenburg et al., 2013).

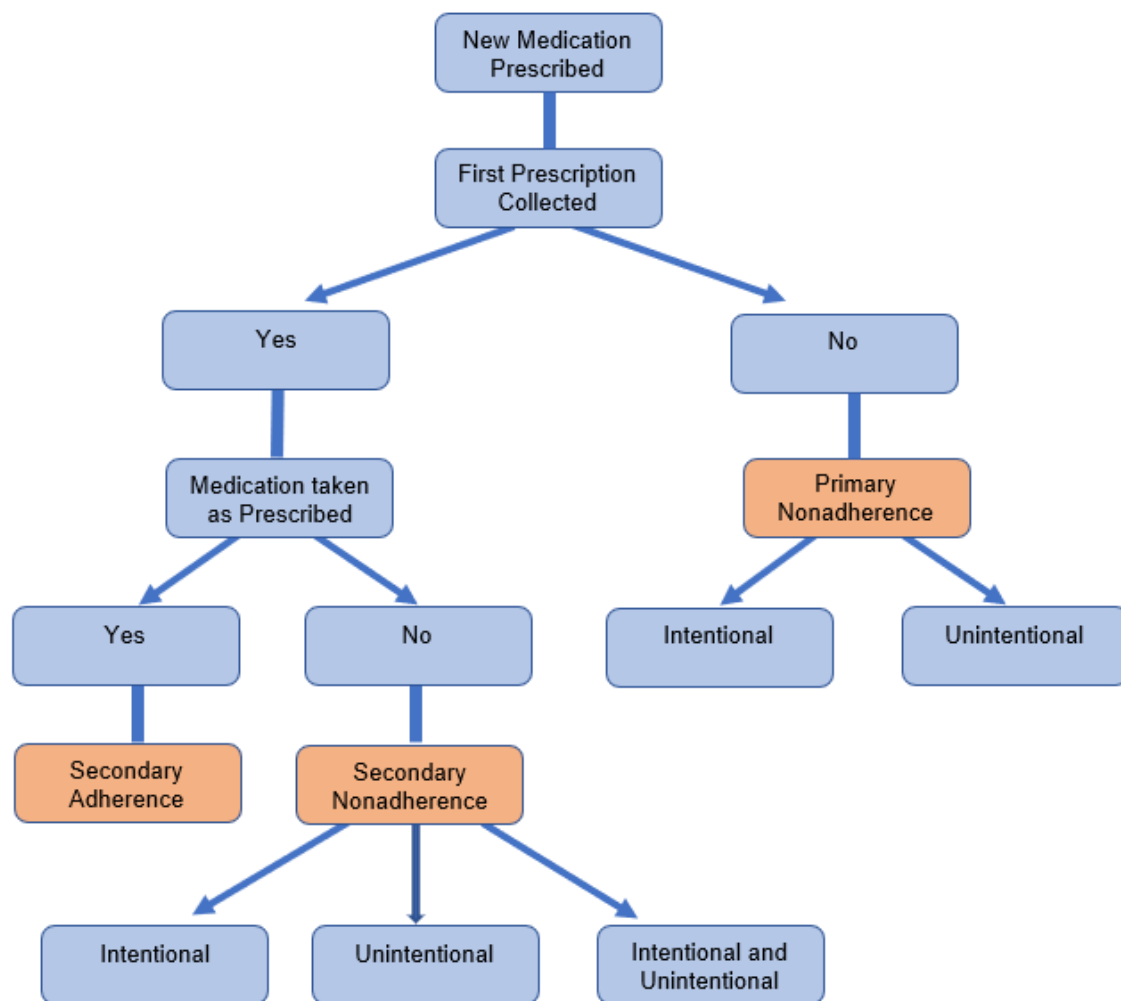


Figure 1.5 Diagram representing the complex nature of medication adherence. Image adapted from Raebel et al., 2013.

Adhering to ocular hypotensive medication involves four key steps that require changes in patient health-related behaviour: (a) obtaining repeat prescriptions; (b) correctly instilling eyedrops; (c) instilling eyedrops every day and (d) doing so at the appropriate times (Muir & Lee, 2011). Nonadherence can occur at any of these four steps.

1.4.1.2 Compliance

Traditionally, compliance has been used to describe the extent to which a patient follows practitioner recommendations (Muir & Lee, 2011). However, with a better understanding of patient–practitioner dynamics, the term 'adherence' has largely

replaced compliance (Vrijens et al., 2012). Compliance suggests a passive act by the patient to follow orders, whereas adherence implies a behavioural change to achieve actual medication use.

1.4.1.3 Persistence

Persistence refers to the continuation of therapy for the prescribed timescale (Robin & Muir, 2019). It is characterised by the duration from initiation to discontinuation of treatment.

1.4.1.4 Concordance

Concordance involves a collaborative interaction between the patient and the HCP. In this approach, the HCP seeks to understand the patient's beliefs and concerns to provide the most suitable treatment options. Together a management plan can be jointly agreed upon. While concordance does not necessarily imply medication-taking, it may promote behaviours that support adherence to the agreed upon treatment plan (Bell et al., 2007).

1.5 Addressing adherence terminology

The varied terminology used for medication-taking complicates the comparison between research studies and the application of their findings in clinical practice. To standardise adherence terminology, the European Commission funded an international research project, led by the Ascertaining Barriers to Compliance (ABC) team. This project aimed to develop a standardised definition for medication adherence (Vrijens et al., 2012).

1.5.1 ABC Terminology

As part of the ABC project, Vrijens et al (2012) conducted a systematic literature review of the different terms used to describe medication-taking. They proposed a

new ABC taxonomy based on behavioural and pharmacological science, defining adherence as “the process by which patients take their medication as prescribed,” consisting of three steps:

- Initiation: When a patient first starts taking their prescribed medication
- Implementation: A longitudinal comparison of how closely a patient’s actual medication dosing matches the prescribed amount from initiation to the last dose
- Persistence: The time interval from initiation to discontinuation of treatment

To achieve optimal treatment benefits, all three steps must occur. Nonadherence can be identified as not starting medication, poor implementation of the treatment regimen, or early discontinuation. The ABC taxonomy allows for the quantification of each step, facilitating the identification of where nonadherence occurs. Although the taxonomy has not been widely adopted, it has been validated and translated into several languages (Bernardo et al., 2024; Haag et al., 2020; Mucherino et al., 2023).

1.5.2 Standardizing adherence reporting

To improve the reliability of adherence study results, the European Society for Patient Adherence, COMpliance, and Persistence (ESPACOMP) developed the ESPACOMP Medication Adherence Reporting Guideline (EMERGE). This guideline follows the ABC taxonomy’s three steps to enhance the consistency of reporting, making it easier to evaluate and synthesise study findings and understand their clinical relevance (De Geest et al., 2018). Improving the consistency of reporting will, it is hoped, make evaluation and synthesis of study findings easier and provide a better understanding of their relevance and applicability to clinical practice. Global adoption of the EMERGE guidelines could promote international consensus on medication adherence terminology, measurement, and reporting (Eliasson et al., 2020; Piña et al., 2021).

1.6 Extent of glaucoma medication nonadherence

Nonadherence to medication is a global issue. According to the WHO, nonadherence in chronic diseases in developed countries is approximately 50% (Sabaté, 2003). In LMICs, this figure is even higher due to limited medical resources, poor access to healthcare, financial constraints and social and cultural beliefs (Macquart de Terline et al., 2019; Sabaté, 2003).

1.6.1 *Glaucoma nonadherence rates*

Nonadherence rates in glaucoma vary widely, depending on how adherence is measured and defined. Consequently, the true extent of nonadherence is likely to be underestimated. A systematic review, with meta-analysis of 34 glaucoma studies, found that the percentage of patients who use their medication correctly ranged from 5-80% (Olthoff et al., 2009). Several studies indicate there is room for improvement, with estimates suggesting that fewer than 50% of glaucoma patients are adherent (Newman-Casey et al., 2015a; Nordstrom et al., 2005a; Olthoff et al., 2009). Self-reported nonadherence rates also vary, with studies reporting rates from 30% in Germany (Wolfram et al., 2019) to 67.5% in Ethiopia (Tamrat et al., 2015). An observational study in a major NHS hospital in the UK found poor adherence rates around 26% when measured with an electronic eyedrop monitoring device (Ajit et al., 2010). Persistence rates are also low, with only 10% of patients repeatedly collecting ongoing prescriptions in the first year of diagnosis (Erras et al., 2021). A USA retrospective cohort study found that approximately half of patients discontinued their treatment within the first six months (Nordstrom et al., 2005).

1.6.2 *Unintentional vs Intentional adherence*

Unintentional nonadherence is more common than intentional nonadherence in glaucoma. A cross-sectional interview study in Australia with 130 glaucoma patients found that while both types of nonadherent behaviour may be present, unintentional nonadherence was more common (Rees et al., 2010). Stronger beliefs in the need for taking eyedrops were associated with lower rates of unintentional nonadherence,

possibly because participants had employed strategies to adhere to their treatment regimen. Intentional nonadherence was more strongly associated with greater concerns over medication use.

1.7 Impact of glaucoma medication nonadherence

Sub-optimal adherence compromises treatment outcomes, accelerates disease progression and increases societal and economic costs.

1.7.1 Clinical impact

Enhanced glaucoma screening, improved detection rates, and the application of evidence-based medicine have led to increased prescribing of long-term glaucoma medication. As people live longer and more cases of glaucoma are identified, a growing number of patients are being diagnosed and started on treatment. Consequently, the burden and impact of poor medication adherence becomes increasingly significant (Sabaté, 2003). Sub-optimal adherence reduces the effectiveness of treatment, leading to disease progression and subsequent visual loss. The Collaborative Initial Glaucoma Treatment Study (CIGTS) demonstrated a significant association between medication nonadherence and loss of visual function (Newman-Casey et al., 2020). Participants who missed doses experienced greater visual field loss compared to those who adhered to their regimen.

1.7.2 Impact on quality of life

Visual impairment from glaucoma progression negatively impacts both patients' and carers' QoL. A study of 244 glaucoma patients found a significant correlation between visual field loss and vision related QoL (Orta et al., 2015). Poor adherence also impacts QoL with nonadherent participants experiencing reduced vision-related QoL compared to adherent participants (Thompson et al., 2018). Advanced visual field loss significantly affects mobility, independence, and emotional wellbeing (Gazzard et al., 2021). Carers of glaucoma patients also face considerable strain.

According to the US National Glaucoma Patient and Caregiver Survey, 52% of carers reported a constant impact on their lives, and 53% found caregiving to be a moderate to extreme burden (Glaucoma Research Foundation, 2019). Similarly, a UK study found that carer strain increased as visual impairment in patients worsened (McDonald et al., 2020).

1.7.3 Economic impact

Glaucoma progression increases healthcare costs due to more frequent hospital visits, medication changes, increased pharmacy costs, greater use of diagnostic testing, more hospitalisations, and potential surgical interventions. A systematic review found that poor adherence across chronic conditions is associated with higher healthcare costs (Cutler et al., 2018). In Europe, nonadherence is estimated to cost 1.25 billion euros annually, and in the USA, between 100 to 290 billion US dollars each year. A European study demonstrated that resource utility and direct costs of glaucoma management increased with disease severity (Traverso et al., 2005). Similarly, a Canadian study found that glaucoma care costs increased with disease progression (Iskedjian et al., 2003). Indirect costs, such as time taken off work by patients and carers for extra hospital visits, also contribute to the economic burden (Iuga & McGuire, 2014).

Intensifying an eyedrop regimen (i.e., adding medications) due to poor adherence further increases the economic pressure on healthcare systems. A study in the USA, analysing administration claims data from glaucoma patients whose treatment was escalated from one to four eyedrops, found that for every additional eyedrop added, ophthalmic outpatient costs also rose (Patel et al., 2021).

The financial impact of issuing glaucoma medications is also a concern. In 2018, the cost to the National Health Service (NHS) from glaucoma prescribing was £114.2 million (Hogg & Connor, 2020). This amount is likely to rise due to an ageing population and increased detection of the disease. The Royal College of Ophthalmologists predicts a 44% increase in glaucoma cases in the UK between 2015 and 2035 (The Royal College of ophthalmologists, 2017). This projected rise in

case numbers, driven by an aging population, advances in diagnostic technology, and improved clinical detection, will likely lead to earlier diagnosis and treatment, thereby increasing demand for glaucoma medication.

1.7.4 Generic medications

To reduce medication costs, generic preparations can be prescribed. Generic medications must contain the same active ingredient in the same dosage form as the branded version. A generic preparation can be used once the branded medication's patent has expired, usually ten years after it was first approved (Tatham, 2020). Despite an increase in the number of medications issued in England from 2008 to 2018, the cost of glaucoma prescribing proportionally decreased due to the use of non-branded preparations. NICE recommends that first-line drug therapy be a generic PGA (NICE, 2022). In 2018, 55.2% of glaucoma prescriptions in England were generic, compared to 11.9% in 2009 (Tatham, 2020). Generic PGAs are as effective as branded PGAs at lowering IOP (Diagourtas et al., 2018; Digiuni et al., 2013).

However, different bottle designs of generic PGAs can promote nonadherence. Some preparations are difficult to open, some are difficult to squeeze, others only require a light touch to expel a drop, and some do not work with eyedrop dispensing aids. These design inconsistencies can ironically negate the benefits of reduced medication costs by increasing overall healthcare costs (Tatham, 2020).

1.8 Risk factors for glaucoma medication nonadherence

Understanding the risk factors for nonadherence can help identify “at risk” patients, allowing for targeted strategies to improve adherence among the highest risk groups. The CIGTS evaluated baseline predictors for nonadherence (Newman-Casey et al., 2020). Consistent with previous research, they found younger age (McClelland et al., 2019; Newman-Casey et al., 2015; Olthoff et al., 2009), Afro-Caribbean ethnicity (Dreer et al., 2013; Friedman et al., 2009a; Rees et al., 2014), depression and lower levels of education (Boland et al., 2014; Castel et al., 2014) were predictors of

nonadherence. In Boland et al.'s (2014) study, education was defined by the highest level attained – postgraduate, college, high school or primary school. Castel et al. (2014) specified education level in terms of years of education (good adherers had 12 ± 4 years of education compared to poor adherers with 11 ± 4 years, $p = 0.002$). Additionally, living alone and being male (Olthoff et al., 2005) are also known risk factors for poor adherence.

1.9 Determinants of glaucoma medication nonadherence

Understanding the determinants that contribute to glaucoma medication nonadherence is crucial for improving patient outcomes. Medication adherence is a complex behaviour influenced by various factors, which differ for each individual.

1.9.1 World Health Organization's five medication themes

The WHO has classified these factors into five themes (figure 1.6): health system/healthcare team, socioeconomic aspects, disease-related, therapy-related and patient-related causes (Sabaté, 2003).

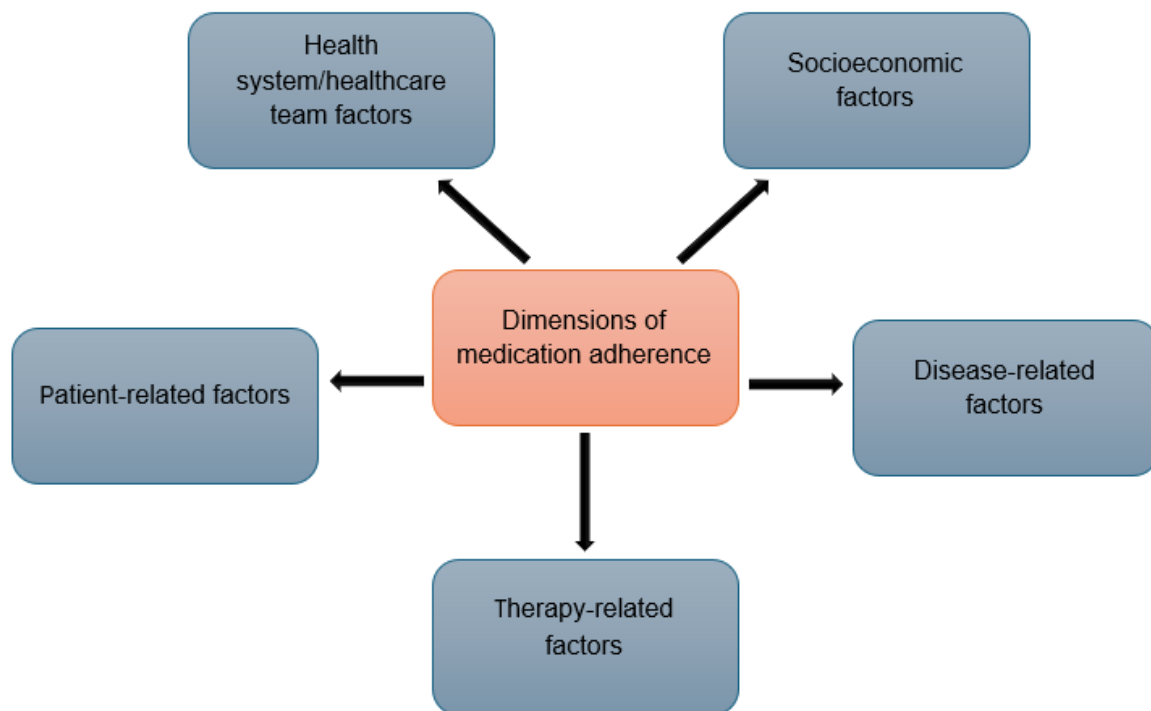


Figure 1.6 World Health Organization's five themes that influence medication adherence behaviour. Image adapted from Sabaté, 2003.

1.9.2 Barriers to glaucoma medication nonadherence

A range of factors within these categories can affect adherence. One USA-based qualitative study identified as many as 71 barriers covering four of the WHO categories (Tsai et al., 2003). Another multicentre USA-based study identified 11 main barriers to glaucoma medication adherence, categorised into four of the WHO's five themes (Newman-Casey et al., 2015). Of the 185 glaucoma patients surveyed, the authors found that the most significant barriers for nonadherent participants were:

- Forgetfulness (62%)
- Lack of self-efficacy (59%)
- Scepticism about glaucoma causing blindness (52%)
- Scepticism about medications preventing visual loss (50%)
- Insufficient knowledge about glaucoma (50%)

For adherent participants, the most significant barriers were:

- Scepticism about glaucoma causing blindness (51%)
- Scepticism about medications preventing visual loss (50%)
- Insufficient knowledge about glaucoma (40%)

Nonadherent participants were more likely to report multiple barriers to adherence than adherent participants (80% compared to 55%).

1.9.3 Healthcare system/team factors

Healthcare system/team factors relate to patient-practitioner relationships, quality of communication, access to healthcare, and out-of-pocket costs. Poorly developed healthcare systems, fragmented care, and inadequate patient-practitioner relationships can negatively impact adherence (Sabaté, 2003). A study of 300 newly diagnosed OAG patients found doctor-patient relationships to be crucial for medication adherence (Friedman et al., 2008). Effective communication, including educating patients about glaucoma and discussing their views on the disease and treatment, enhances patient confidence in overcoming adherence barriers (Carpenter et al., 2016).

1.9.4 Social/environmental factors

Socioeconomic factors such as poverty, low literacy and education levels, poor social support, erratic living conditions, age and high treatment costs can affect adherence. Friedman et al. (2008) found that newly diagnosed nonadherent glaucoma patients had lower incomes and education levels compared to adherent patients. Changes in environment also affect adherence levels. A UK-based multicentre qualitative study found that disruptions in routine, such as travelling, increased the likelihood of missing doses (Lacey et al., 2009).

1.9.5 Disease-related factors

Disease-related factors include the presence and severity of symptoms and the rate of disease progression. Disease severity positively affects adherence (Kardas et al., 2013). A cross-sectional USA study found patients with more severe glaucoma were more adherent to treatment than those with mild or moderate disease (Ung et al., 2013).

1.9.6 Therapy-related factors

Treatment characteristics such as regimen complexity, polypharmacy, length of treatment, frequent changes in therapy and medication side effects influence adherence (Yap et al., 2016). High numbers of medications and frequent dosing can worsen adherence (Kardas et al., 2013).

A review of 29 quantitative studies found for glaucoma patients a dose frequency of more than twice daily was associated with worse adherence than a dose frequency of twice daily or less (Olthoff et al., 2005). In contrast, an Israeli mixed-methods study found a higher number of daily instillations promoted adherence (Castel et al., 2014). Simplifying eyedrop regimes using fixed combinations has also been associated with better adherence (Barnebey & Robin, 2017).

1.9.7 Patient-related factors

Both psychological and physical patient-related factors can influence adherence. Psychological patient factors include knowledge about the condition and treatment, attitudes towards medicines, perceived benefits, motivation and self-confidence. Lack of knowledge about glaucoma is a key barrier to adherence (Friedman et al., 2008; Newman-Casey et al., 2016a; Tsai et al., 2003). Self-efficacy, or confidence in one's ability to adhere to the medication regimen, is associated with better adherence (Carpenter et al., 2016). Higher self-efficacy is associated with better levels of glaucoma medication adherence. Low motivation and fear of blindness also impact adherence (McDonald et al., 2019; Spencer et al., 2019).

Physical factors include hearing and sight loss, reduced dexterity, poor mobility and cognitive impairment. Difficulties with drop instillation are common barriers (Olthoff et al., 2009). A USA-based qualitative study investigating instillation technique of experienced glaucoma patients found that while 93% reported having no problems instilling eyedrops, only 31% were administering them correctly (Stone et al., 2009). Forgetfulness is consistently reported as a key reason for missing doses (McClelland et al., 2019; Olthoff et al., 2005, 2009; Robin & Muir, 2019; Tsai et al., 2003). A multicentre prospective Australian study found almost a quarter of participants had difficulty remembering to instil drops in the middle of the day (Spencer et al., 2019).

1.9.8 Multifactorial nature of nonadherence

A systematic review found that medication nonadherence is influenced by multiple factors from different categories, and not all determinants are amenable to change (Kardas et al., 2013). While identifying possible determinants is important, recent research suggests that the WHO classification may be too broad to provide valuable guidance for improving adherence behaviours (Allemann et al., 2016).

1.10 Medication adherence measurements in glaucoma

To address issues with medication adherence, it is essential to quantify when and how much of a dose has been taken. But what constitutes an “acceptable” level of adherence? Defining an acceptable level to maintain therapeutic efficacy and clinical relevance is challenging, as no standardised threshold exists for glaucoma.

Establishing a universal cut-off point at which nonadherence becomes clinically significant is difficult due to factors such as drug type, patient characteristics and disease specifics (Paterson et al., 2000; Stauffer et al., 2017; Wu et al., 2009). Most glaucoma research studies use a cut-off point of 80% to signify adequate adherence, meaning a patient receives at least 80% of the prescribed medication over a specified time interval (Andrade et al., 2006). This threshold, supported by regression analysis, originated from a study on blood pressure, where adequate blood pressure control was achieved by taking at least 80% of antihypertensive oral

medication (Haynes et al., 1980).

1.10.1 Thresholds for adherence

In glaucoma, an 80% adherence threshold has been supported by a cross-sectional study (Sleath et al., 2011) which found that adherence below 80% increased the likelihood of severe visual field loss by seven times compared to adherence above 80%.

The CIGTS demonstrated that increased rates of visual field progression were associated with more frequent missed doses (Newman-Casey et al., 2020). This longitudinal study assessed the relationship between medication adherence and visual field progression over a ten-year period. Patients who did not miss doses had a mean deviation (MD) loss consistent with normal age-related loss (0.62 dB), while those missing doses at two-thirds of follow-up visits lost on average, 2.23 dB of MD.

1.10.2 Variability in adherence definitions

Different glaucoma studies use varying adherence cut-off points, often without empirical evidence to support these thresholds, complicating the interpretation and applicability of findings. For example, some studies define nonadherence as missing a dose once or more (Olthoff et al., 2009; Tsai et al., 2003), while others use the 80% adherence threshold (Cate et al., 2014; Thompson et al., 2018). Additionally, some studies use arbitrary values, such as missing five percent or more of prescribed doses (Wolfram et al., 2019) or less than 75% adherence to represent poor adherence (Oltramari et al., 2024). A feasibility study conducted at a large hospital in Northwest England suggested aiming for 100% adherence to avoid the adverse outcomes associated with missed doses (Richardson et al., 2013).

1.10.3 Adherence and persistence patterns

Adherence is a complex behaviour that can vary over time. An 80% threshold measures initial adherence but does not consider continued persistence. Patients can be nonadherent but persistent with treatment. For example, if a patient consistently instils eyedrops once a day instead of the prescribed twice daily dose, they would be considered persistent but only 50% adherent. A single threshold value would fail to capture this pattern of adherence. Persistence is typically measured as a continuous variable, often defined by the number of days on which the patient continued treatment without discontinuation (Robin & Muir, 2019).

Group-based trajectory models (GBTM) have been proposed as a more suitable method for describing adherence behaviours in chronic conditions requiring long-term therapy. GBTM provides longitudinal measures of adherence patterns by identifying patients with similar behaviours and categorising them into groups. Newman-Casey et al. (2015a) used GBTM to identify five adherence patterns over a four-year period in newly diagnosed POAG patients:

- Never adherent
- Persistently poor adherers
- Declining adherence
- Moderate adherence
- Persistently good adherers

Adherence patterns formed in the first year were good predictors of long-term behaviour. Sub-optimal adherence in the first year often remained poor or worsened, while persistently adherent patients in year one continued to adhere well in year four. Therefore, investing resources in identifying and helping patients with sub-optimal adherence patterns during the first year could have a significant impact on long-term adherence.

1.11 Measuring glaucoma medication adherence

To effectively address and manage nonadherent behaviour requires successful detection. However, there is no gold standard method for measuring medication adherence in glaucoma (Waterman et al., 2013). Several methods exist, but each has its own advantages and disadvantages, leading to fundamental problems either within the clinical environment or when interpreting, comparing and applying research findings. Adherence can be measured objectively or subjectively and can also be categorised into direct and indirect methods.

The Norwich Adherence Glaucoma Study, an RCT conducted in a teaching hospital in the UK, highlighted the difficulties and variations in measuring adherence (Cate et al., 2015). Over an eight-month period, Cate et al. (2015) analysed several methods for measuring glaucoma medication adherence, along with different ways of calculating adherence and collecting data and concluded that no definitive measurement method could be recommended.

1.11.1 Objective measures

Electronic Monitoring Systems

Electronic monitoring, such as with the Medication Event Monitoring System (MEMS), is the most accurate way of indirectly measuring patient adherence (Zaharia et al., 2022) and is considered the gold standard for clinical trials (Nieuwlaat et al., 2014). A computer chip embedded in the cap of a medication bottle allows the MEMS to record the exact date and time the bottle was opened, implying the medication has been administered. One commonly used ophthalmic MEMS is the Travatan Dosing Aid (TDA), produced by Alcon, which electronically stores data on the time, date, and number of drops administered. These data allow for the identification of individual dosing history, as opposed to a single adherence value, thus providing better insight into adherence behaviour. Four distinct patterns of adherence have been reported with TDA use (Ajit et al., 2010):

- Good adherence
- Discontinued usage
- Frequent drug holidays
- Frequent missed doses with low adherence rates

The TDA has been proven to successfully measure adherence (Friedman et al., 2007) however, its accuracy appears to wane after an initial two-month period due to lost data from failings with the device (Cate et al., 2015). It is only compatible with Travoprost and Travoprost/timolol combination eyedrops due to the size of the device opening.

Electronic monitoring systems have several limitations. Recording an event merely indicates the bottle has been opened and does not guarantee the patient actually instilled their eyedrop, which can cause adherence to be overestimated. Electronic monitoring devices are often expensive, cumbersome, and difficult to operate, making their use in everyday clinical settings involving large numbers of patients less feasible (Zaharia et al., 2022).

Monitoring devices can act as either a visual reminder for patients to take their medications or provide a physical barrier to administration (Waterman et al., 2013). Either way, adherence can be altered by their presence, and actual adherence behaviour may not be accurately measured, a phenomenon known as the “Hawthorne effect” (Okeke et al., 2009a). When patients are made aware their adherence is being monitored, either from the visual stimulus of the device or by a clinician informing them, they may modify their behaviour to enhance their levels of adherence simply because they know they are being observed. This can jeopardise the validity of any research findings by introducing an element of reactivity bias. However, a study electronically monitoring glaucoma medication adherence found that participants aware they were being monitored displayed no significant difference in adherence compared to those who were unaware of being monitored (Hermann et al., 2011). A multicentre study also found that patient reactivity bias to the presence of an electronic monitoring device was short-lived, and usual adherence behaviour resumed after approximately two months (Cook et al., 2015).

Electronic Databases

Electronic databases accessing pharmacy and insurance claims data provide an estimate of adherence or persistence based on the number of new prescriptions issued, which is assumed to correspond to medication-taking behaviour (Lam & Fresco, 2015). These databases are widely used in research trials because they allow for the analysis of large populations on multiple medications over extended periods. They rely on access to accurate and up-to-date data. Adherence measures from electronic databases are particularly popular in the USA, where electronic data from health insurance companies is readily available, unlike in the UK. The Norwich Adherence Glaucoma Study encountered difficulties, reporting that health centres failed to provide almost a quarter of the prescribing data needed for adherence calculations (Cate et al., 2015).

Electronic database data provides an objective method of measuring adherence and, unlike self-reported measures, is less likely to be affected by patients' desire to appear adherent (Cate et al., 2015). While demographic information can be assessed in relation to nonadherence, electronic database measures do not provide detailed information about barriers to nonadherence behaviour and do not account for patients who collect but do not use their medications.

Electronic databases use the Medication Possession Ratio (MPR) to gauge adherence. MPR is defined as the proportion of days' supply of medication a patient has divided by the days between prescription refills (Lam & Fresco, 2015). An MPR of less than one indicates less than perfect adherence. The Glaucoma Adherence and Persistence Study (GAPS) retrospectively analysed electronic database claims for over 13,000 glaucoma patients and calculated a mean MPR of 0.64 over a 22-month period (Friedman et al., 2008). One advantage of MPR is its ability to distinguish between the addition of a new medication and the replacement (or switching) of an existing one in treatment regimens (Erras et al., 2021).

Direct Methods

Directly measuring the concentration of a therapeutic drug in a person's blood as proof they have instilled their medication is an adequate objective method for assessing adherence. However, it has some drawbacks that need to be considered. Due to differences in drug metabolism and individual variability in drug absorption and elimination rates, drug plasma levels can differ from person to person, despite the same dose of medication having been taken. This method provides no insight into the cause of nonadherence or any information about nonadherence patterns. It is also costly, involves invasive procedures, and requires input from several professionals, making it impractical to carry out routinely in glaucoma clinics (Kreys, 2016; Zaharia et al., 2022).

Directly observing a patient instilling their eyedrops is a simple way of assessing administration technique at a single follow-up appointment. However, it does not necessarily represent adherence behaviour outside of the clinic environment and consequently is not used frequently as an adherence measurement (Stone et al., 2009).

1.11.2 Subjective measures

Clinician Estimates

While it is easy, quick, and simple for clinicians to assess adherence during a follow-up visit, this method is considered unreliable. Research has shown that doctors are not good at predicting which patients are adherent (Djafari et al., 2009). Djafari et al. (2009) found that 71.1% of patients considered by their doctor to be nonadherent to glaucoma medication were actually adherent. Similarly, Okeke et al. (2009a) found poor correlation between clinician estimates of adherence and electronically measured adherence with the TDA.

Patient Self-Report Measures

Patient self-report adherence measures use surveys, questionnaires, or interviews administered by the patient, clinician, or an assistant. While these measures are frequently used in clinical and research settings because they are cheap, simple,

and quick to perform, they are prone to overestimation. A UK-based prospective observational study found that glaucoma patients overreported their adherence (how many drops they missed in the past month) when compared to TDA adherence measures (Ajit et al., 2010). In some cases, patients reported not missing any drops when TDA adherence levels were below 40%. The Norwich Adherence Glaucoma Study also found inaccuracies between patient-perceived adherence and TDA adherence measures (Cate et al., 2015). Patient self-reported nonadherence became less reliable over the eight-month study period compared to TDA measures, which remained consistent.

A USA-based multi-site observational study (Sayner et al., 2015) compared the accuracy of self-reported adherence to glaucoma medications, measured on a visual analog scale (VAS), to electronically measured adherence with a MEMS. They found that patients overestimated the percentage doses taken by 31% and timing adherence by 74%. A prospective cohort USA-based study, comparing the accuracy of self-reported adherence measures with electronically monitored nonadherence, found that a single question (“Over the past month, what percentage of your drops do you think you took correctly?”) correlated best with electronically measured adherence (Cho et al., 2022). The authors recommend using this single question as an effective way of identifying nonadherent patients in practice when time, resources, or money are limited.

Another limitation of self-report measures is that they rely on patient recall and “social desirability bias,” where patients feel the need to please their clinician by reporting better adherence than actually occurred (Sayner et al., 2015). Errors with self-report adherence are further complicated by the fact that research has shown patients are reluctant to tell their doctor when they are having problems with eyedrops (Winfield et al., 1990). To promote an environment where patients can be honest about their adherence behaviour without the fear of feeling judged, clinicians need to have good communication skills and employ non-judgemental interview techniques to encourage a healthy patient-practitioner relationship (Hahn et al., 2010). To overcome these issues, McClelland et al. (2019) suggest that patients self-complete a questionnaire prior to their clinic visit to eliminate the bias of it being

administered by a clinician involved in their care. Self-report measures do, however, have the benefit of providing an understanding of adherence behaviours, barriers, and patient beliefs and attitudes, information which can be used to develop effective strategies to overcome poor adherence.

1.11.3 Issues with measuring nonadherence

Issues with measuring nonadherence have implications from both a research and clinical perspective. As no current standardised consensus exists for choosing a measurement tool, it makes interpretation and application of clinical trial results difficult. Understanding relevant research findings becomes further complicated when adherence is inaccurately estimated due to the “Hawthorne effect,” varying lengths of study follow-up, and sample sizes and demographics that are not representative of the population as a whole.

From a clinical perspective, detecting and accurately assessing nonadherence is key to effective management of medication-taking. In practice, however, HCPs can encounter problems when patients withhold information because they want to appear adherent and “please” their clinician. One solution to this problem is to have open, honest, and non-judgemental conversations that encourage patient participation. To support this, within England, NICE (2009) has produced a guideline for medication-taking which promotes informed patient decisions. NICE recommends that patients become more involved in their care by encouraging:

- Good open communication between patient and healthcare professional
- Practitioners to gain an understanding of patients’ beliefs and knowledge around medicines
- Practitioners to provide relevant information for patients about their condition and treatment

Each step should be tailored to the individual needs of a patient. Based on this approach, patients can make an informed choice, in conjunction with their HCP, as

to whether they take a prescribed medication and be supported to adhere to treatment.

1.12 Impact of COVID-19 on glaucoma medication adherence

The COVID-19 pandemic, caused by the acute respiratory syndrome coronavirus 2 (SARS-CoV-2), placed immense strain on healthcare systems globally in 2020. A WHO survey highlighted the significant impact and disruption to healthcare services worldwide (World Health Organization, 2020). To mitigate the spread of the virus, governments implemented travel restrictions, quarantine orders and lockdown measures, creating substantial barriers for patients seeking healthcare services. A systematic review found that global healthcare utilisation decreased by approximately one-third from February to August 2020, with the most significant reductions occurring in March and April (Moynihan et al., 2021).

These disruptions posed extreme challenges for glaucoma patients, who faced difficulties accessing hospital visits, obtaining medications and experienced delays in their appointments. In the UK, the discontinuation of routine care led to prioritising patients at the greatest risk of glaucoma-related sight loss (Jayaram et al., 2022; The Royal College of Ophthalmologists, 2020). The pandemic also induced significant anxiety and stress across the population, particularly affecting those with chronic health conditions (Galea et al., 2020). This added stress negatively impacted health behaviours, such as medication adherence (Subathra et al., 2021).

Several studies conducted in various countries, including the USA, India, Croatia, Turkey and Egypt have shown that glaucoma medication adherence decreased during the pandemic. This decline was attributed to factors such as reduced access to healthcare appointments, difficulty obtaining medications, financial concerns and psychosocial effects (Awwad & Masoud, 2021; Firat et al., 2023; Lešin Gaćina et al., 2022; Racette et al., 2022; Subathra et al., 2021). This trend is concerning, as reduced adherence is known to negatively impact health outcomes and increase healthcare costs.

The provision of glaucoma care post-pandemic has been challenging, with an increased backlog of patients awaiting appointments. The delivery of care is expected to undergo major changes in the future and continues to face challenges (Jayaram et al., 2020). In 2023, the Royal College of Ophthalmologists reported approximately 650,000 individuals were awaiting consultant-led ophthalmology appointments in England, representing about 10% of the total NHS backlog (The Royal College of Ophthalmologists, 2023). This delay in care can further affect adherence. The impact of COVID-19 on glaucoma medication adherence remains a concern, with effects persisting long after the pandemic ended.

1.13 Glaucoma medication adherence as a research priority

Nonadherence to glaucoma medication is a significant global healthcare issue. Ensuring patients are adherent, whether they are commencing or already on treatment, is crucial for improving clinical, social, and economic outcomes for both individuals and society. The UK Clinical Eye Research Strategy, which seeks to prioritise key areas of eye health research, has recognised this problem, highlighting glaucoma medication nonadherence as a significant concern and ranking it among the top 10 research priorities for glaucoma care in the UK (Bourne et al., 2024).

In collaboration with patients, carers, eye care providers, professional organisations, and charity organisations, the Clinical Eye Research Strategy conducted exercises to establish a consensus on research priorities. One of the top priorities identified for glaucoma was to investigate the link between treatment adherence and glaucoma progression, and to explore ways to improve adherence. This priority is also endorsed by Glaucoma UK, a patient advocacy charity dedicated to ending preventable glaucoma-related sight loss (Glaucoma UK, 2024). Glaucoma UK actively funds research aimed at improving treatment adherence.

1.14 Improving glaucoma medication adherence

As previously discussed in Section 1.7 (page 43), poor adherence to glaucoma medication compromises treatment effectiveness, accelerates disease progression and increases both societal and economic costs. Strategies aimed at improving

adherence can potentially alleviate these consequences. These strategies can broadly be categorised into reminder systems, simplifying medication regimens, behaviour change programs, educational programmes and alternative engagement strategies (Buehne et al., 2022). Often, a multifaceted approach is necessary to address the complex multifactorial nature of glaucoma medication adherence.

1.14.1 Interventions to aid glaucoma medication adherence

Reminder strategies

Achieving persistent medication adherence involves developing a routine that is conducive to a patient's lifestyle rather than changing a patient's lifestyle to incorporate adherence (Arlinghaus 2019). Practical reminder strategies tailored to a patient's lifestyle encourage the development of a routine, making the behaviour automatic and habitual (Gardner et al., 2012). For example, everyday memory strategies may include setting a specific time of day for eyedrop instillation, such as after the six o'clock news, linking eyedrop instillation with other activities like brushing teeth, or placing eyedrops in a prominent location such as on a bedside cabinet (Boron et al., 2013; Granström, 1982). Granström (1982) reported that patients linking taking their pilocarpine eyedrops to a daily event might have better adherence, as measured electronically.

Planning strategies, such as visual written charts, can help serve as a reminder for eyedrop administration and overcome difficulties with treatment schedules. A cross-sectional prospective pilot study in the UK found an improvement in self-reported eyedrop administration when glaucoma patients used a scheduled eyedrop chart. The chart helped patients to remember their dosing schedule and included an educational leaflet outlining correct instillation techniques (McVeigh & Vakros, 2015).

Studies have shown that reminder strategies, such as timed text messages, phone calls or emails targeting forgetfulness are beneficial in improving adherence. For instance, a prospective RCT in Singapore found improved self-reported adherence among glaucoma patients who received telereminders along with a reference chart for viewing their treatment schedule, compared to those who did not receive these interventions (Lai et al., 2020). However, a limitation of this study was the short

follow-up period (six weeks), which may not be appropriate when assessing the effectiveness of an intervention in a chronic condition such as glaucoma. Similarly, a USA-based cohort study demonstrated that automated telecommunication reminders, either by daily telephone or text message, improved adherence rates from 53% to 64% in nonadherent patients using once-daily prostaglandin medication (Boland et al., 2014). Adherence was measured objectively using an electronic monitoring system. One point of note was the high dropout rate in the study; almost half of the patients recruited did not successfully complete the trial, hence these findings should be interpreted with caution.

Digital interventions have modernised more traditional reminder systems with the use of smartphone applications (referred to as apps). These apps can provide reminders, track medication usage and offer educational resources. They have shown promise in improving medication adherence in chronic conditions. A systematic review with meta-analysis showed that smartphone apps significantly improved medication adherence in hypertension (Xu & Long, 2020). Similarly, a systematic review evaluating the use of apps in diabetes management demonstrated their efficacy in improving treatment adherence (Islam et al., 2022). Although limited clinical studies exist for glaucoma, initial findings suggest positive improvements with the use of medication reminder apps. A multisite interventional study in Israel found that after using a smartphone medication reminder app, glaucoma patients reported significant improvements in adherence and QoL (Leshno et al., 2021). The app sent audio and visual reminders to patients when an eyedrop dose was due, and patients had to confirm dose intake to deactivate the reminders. A feedback system also allowed patients to review their adherence behaviour over time. However, the study duration was only one month, so caution is needed when extrapolating these findings to long-term adherence. A Nigerian-based RCT found that using a medication reminder app significantly improved self-reported adherence among glaucoma patients. The app provided automated reminders for medication schedules, helping patients remember to take their eyedrops consistently (Osahon et al., 2020).

Reminder strategies can also be recommended for patients who struggle to remember to order repeat prescriptions. These strategies might include setting an alert in a mobile phone diary or physically writing reminders on a calendar. Additionally, promoting the use of mail-order services for delivering eyedrops can facilitate long-term adherence. A retrospective longitudinal cohort analysis found that using mail-order services for prescription delivery was associated with better adherence to glaucoma medications (Newman-Casey et al., 2015a).

Simplifying treatment regimen

Deciding on a treatment regimen is an important factor that can influence adherence and long-term persistence. Simplifying medication regimens can improve a patient's medication-related self-efficacy and adherence.

Studies have shown that complex eyedrop regimens requiring multiple daily instillations, especially those around the middle of the day, lead to poorer adherence (Dreer et al., 2013; Spencer et al., 2019). For example, a prospective observational cohort study found that glaucoma patients using twice-daily Brimonidine eyedrops had significantly better adherence compared to those using Brimonidine three times daily (Hermann et al., 2011). Adherence was measured objectively with an electronic monitoring device. Fewer glaucoma medications also improve adherence. A Japanese study found that a greater number of eyedrops negatively impacted adherence levels (Tsumura et al., 2019). Similarly, another Japanese study found that fixed combination eyedrops improved adherence compared to unfixed combination eyedrops (Shirai et al., 2021).

Medication side effects, such as irritation, dry eye symptoms or allergic responses, can be barriers to adherence. A USA-based qualitative study found that dry eye symptoms were associated with reduced self-reported adherence among glaucoma veterans (Stringham et al., 2018). Interestingly, another study found that patients experiencing burning or stinging with their eyedrops had higher objectively measured adherence levels (Friedman et al., 2008). This was thought to be because these patients were more aware of their medication's effects and, therefore, more likely to

remember to take it regularly. The discomfort could serve as a reminder of the medication's presence and importance, reinforcing adherence.

Switching to preservative-free preparations and reducing exposure to preservatives can reduce the risk of developing ocular surface disease and improve adherence. A multicentre epidemiological study in four European countries found that symptomatic ocular side effects and signs were significantly more likely in glaucoma patients using preserved BB eyedrops compared to those using preservative-free BB eyedrops (Jaenen et al., 2007).

Practitioners should consider reducing the burden of instilling eyedrops by simplifying dosing regimens, prescribing fixed combination regimens where possible, and using preservative-free preparations. A successful choice of therapy is likely to promote better long-term adherence with fewer medication changes and fewer new prescription collections for patients (Nordstrom et al., 2005).

Devices can also help simplify medication-taking for patients. For those with limited manual dexterity, poor hand-eye coordination or reduced grip strength eyedrop dispensing aids can help administer medication more easily and accurately. A French-based multicentre RCT evaluated the Xal-Ease® (Pfizer, USA) device, which is a dispensing aid used with the eyedrops Xalatan® (latanoprost; Pfizer, USA) or Xalacom® (latanoprost/timolol; Pfizer, USA). After one month of use, patients reported a reduced need for assistance with administering their medication and a decrease in reports of the issue of the bottle tip touching the eye (Nordmann et al., 2009).

Behaviour change programmes

Behaviour change programmes, which specifically target patient behaviour to improve medication adherence, are discussed in detail in Section 1.15 on page 68.

Education programmes

Poor understanding of glaucoma and its treatment rationale is consistently reported as a contributing factor to nonadherence (Bott et al., 2023; Gatwood et al., 2022;

Tshivhase et al., 2021). A prospective cross-sectional study conducted in Saudi Arabia found that 76.2% of self-reported nonadherent participants lacked background information on glaucoma and its treatment (Khaled et al., 2021).

Educational programmes, such as in-person education, videos, illustrative picture or information leaflets provided by HCPs or research assistants can help patients better understand their condition, appreciate the importance of adherence and adopt practical strategies for managing their medication regimen.

While studies have demonstrated positive effects of educational interventions, improvements in adherence are often attributed to education combined with other strategies. For example, an intervention study in Pakistan found improved self-reported adherence among elderly glaucoma patients following pharmacy-led sessions that included eyedrop instillation techniques, visual aids, and tailored counselling (Aleem et al., 2021). Similarly, a prospective interventional study in Jordan found improvements in self-reported adherence after patients received an educational booklet and face-to-face discussions (Barakat et al., 2024).

In contrast, a Dutch multisite RCT that included patient education in two of the four intervention arms found that education alone did not improve adherence (Beckers et al., 2013). A UK-based RCT similarly reported that improvements in adherence within a nurse-led glaucoma monitoring clinic were attributable to the combination of education and counselling, rather than education alone (Sheppard et al., 2003). A review of RCTs using network meta-analysis (NMA) comparing the effectiveness of interventions to improve adherence to ocular hypotensive therapy found that multifaceted interventions including personalised care and digital educational resources were more effective (Ha et al., 2022). NMA allows for the evaluation of multiple interventions within a single review, provides effectiveness estimates, and ranks each intervention (Nikolakopoulou et al., 2014).

Educational programmes can be delivered one-to-one or in group settings. Group education has also shown to be beneficial. A Canadian-based RCT demonstrated significant improvements in objectively measured adherence over 12 months among

patients who received two 60–90-minute group education sessions on glaucoma (Djafari et al., 2015).

Providing glaucoma education need not be limited to the patient alone, where appropriate formal or informal caregivers can also be involved. One RCT found that self-reported poorly adherent glaucoma patients improved their adherence when both they and their caregivers received educational support (Muir et al., 2022).

The patient-practitioner relationship also plays an important role in education and medication adherence. While it is difficult to prove that practitioner communication alone improves adherence, studies have concluded that effective communication can contribute to better outcomes. For instance, a USA-based longitudinal study over eight months suggested that strong patient-practitioner communication could improve adherence (Carpenter et al., 2016). Similarly, a Taiwan-based retrospective population-based study showed that good patient-practitioner relationships enhanced adherence by improving patient understanding (Hwang et al., 2014). In contrast, Friedman et al. (2008) found that passive, practitioner-led relationships can be lead to poorer adherence. Educational interventions should therefore not only consider the content being delivered but also the manner in which it is conveyed, taking into account the dynamics between the patient and the practitioner.

Alternative Engagement Strategies

Alternative engagement strategies involve ways of engaging patients with their healthcare team or other individuals to improve adherence. For example, in a USA-based RCT, patients received a birthday card as part of the intervention to improve adherence. The birthday card was one of the tailored print materials designed to engage patients and remind them of the importance of adhering to their glaucoma treatment regimen. In The Norwich Adherence Glaucoma Study, a telephone advice line was provided by a glaucoma assistant, available Monday to Friday from 9 am to 5 pm. This service was designed to offer additional support and information to patients and their caregivers to help improve adherence (Cate et al., 2014). However, neither of these RCTs demonstrated any significant improvements when the intervention and control groups were compared.

1.14.2 Effectiveness of interventions to improve glaucoma medication adherence

Whilst there has been a wealth of research on strategies to improve glaucoma medication adherence, the overall effectiveness of these strategies has been limited, and it remains unclear which intervention is most effective. A Cochrane systematic review investigated the effectiveness of interventions aimed at improving glaucoma medication adherence (Waterman et al., 2013). Overall, the review found that while some interventions appeared beneficial, there was no single strategy that could be universally recommended. Specifically, the authors reported that there was some evidence that complex interventions, which combine patient education with personalised behavioural change strategies, may be effective in improving adherence. However, the overall quality of the included studies was generally low. Due to clinical and methodological heterogeneity, no meta-analysis was performed, and there was insufficient evidence to recommend any particular intervention. The authors also concluded that simplifying eyedrop regimens and using reminder devices showed potential benefits; however, the evidence was not conclusive. The review emphasised the need for more high-quality research to identify the most effective strategies for improving glaucoma medication adherence. Several reviews have indicated that multifaceted interventions generally lead to improved adherence to glaucoma medication (Buehne et al., 2022; Tapply & Broadway, 2021; Waterman et al., 2013).

Such multifaceted interventions would be considered complex in nature. An intervention is deemed complex if it contains numerous interrelating elements that can be flexible depending on need, targets several behaviours, or requires skill and expertise to implement and carry out (Skivington et al., 2021). In general, complex interventions aimed at improving medication adherence have met with several challenges. Two systematic reviews (Nieuwlaat et al., 2014; Patton et al., 2017) highlighted several factors contributing to this. One issue identified was the inadequate description of the individual components within these interventions, making it difficult to replicate and implement them in a clinical setting. Another factor was the difficulty in determining the impact of each component on adherence. It was unclear whether a single component could improve adherence or if a combination of

strategies was necessary. Furthermore, Nieuwlaet et al. (2014) and Patton et al. (2017) highlighted that many interventions lack a robust theoretical foundation. They noted insufficient justification for the selection of specific components and their expected influence on adherence behaviour. This lack of theoretical underpinning can undermine the effectiveness of the interventions and their applicability in different contexts. By addressing these challenges, future research can develop more effective and replicable interventions to improve glaucoma medication adherence.

1.15 A behavioural approach to intervention development

The increasing global burden of glaucoma, combined with the limitations of existing adherence interventions, highlights a pressing need for more effective, scalable, and evidence-based solutions for individuals with poor adherence. As medication adherence is fundamentally a health-related behaviour, improving it requires sustained behaviour change. This involves more than simply providing information or reminders, it requires a systematic understanding of why people behave as they do and what needs to change to support better adherence. Identifying the specific behaviours requiring change, along with the underlying influences, allows for the selection of appropriate strategies to support that change (Abraham et al., 2009). Behavioural science provides a robust foundation for designing such interventions, with evidence that theory-driven approaches are generally more effective than those lacking a theoretical underpinning (Rahman et al., 2022).

This approach aligns with best practice guidance. The UK Medical Research Council (MRC) framework for developing complex interventions emphasises the importance of theoretically grounded and transparent intervention development processes (Skivington et al., 2021). One comprehensive framework that meets these requirements is the Behaviour Change Wheel (BCW). Developed by Michie et al. (2011) through a synthesis of 19 existing behaviour change frameworks, the BCW provides a structured, systematic, and theory-informed method for moving logically from understanding a behavioural problem to designing and implementing practical interventions.

Behaviour Change Programmes

Building on the behavioural science foundation outlined above, a variety of behaviour change programmes have been developed and tested to improve glaucoma medication adherence. These programmes typically use tailored, patient-centred approaches designed to modify individual behaviours through counselling, education, and motivational techniques.

For example, a New Zealand-based study found that patient adherence improved with counselling from a trained glaucoma assistant, and the approach was feasible and practical to implement in everyday practice (Cook et al., 2010). A Swedish RCT demonstrated that patients who received a 30-minute education and tailored programme showed a statistically significant improvement in adherence to three-times-daily pilocarpine eyedrops, as measured with a medication monitor (Norell, 1979). Similarly, a UK-based RCT found that treatment-naïve glaucoma patients who received a tailored care package delivered by a trained glaucoma nurse, which included an assessment of patient needs, a training session on instillation techniques, and an educational session, showed better prescription collection rates and improved self-reported adherence (Gray et al., 2012).

Behavioural interventions can be applied at the individual, community, or national level (Anderson et al., 2004). Interventions at the individual level focus on personal behaviour change. Community-level interventions target groups of people within a specific community with the goal of influencing the behaviour of a larger group rather than just individuals. National-level interventions are implemented on a broader scale, often through policies, regulations, or nationwide campaigns aimed at promoting healthy behaviours across the entire population.

Motivational interviewing (MI) is a communication technique designed to enhance a person's motivation to change behaviour (Palacio et al., 2016). It can help patients with glaucoma overcome barriers to medication adherence and increase their motivation to follow their treatment plan without imposing solutions on them. A study evaluating the acceptability of a culturally informed health program to improve glaucoma medication adherence among African American patients used MI

combined with problem solving training and education. The study found an overall improvement in adherence and the program was acceptable to patients (Dreer et al., 2016). MI was provided by health educators who were trained to deliver the culturally informed, individually tailored health promotion program, of which MI was a key component.

1.15.1 The Behaviour Change Wheel

The BCW can be visualised as a series of concentric layers (see Figure 1.7), each representing a key stage of intervention development. Together, these layers enable a thorough behavioural diagnosis and informed strategy selection. This ensures interventions are both theoretically robust and practically applicable.

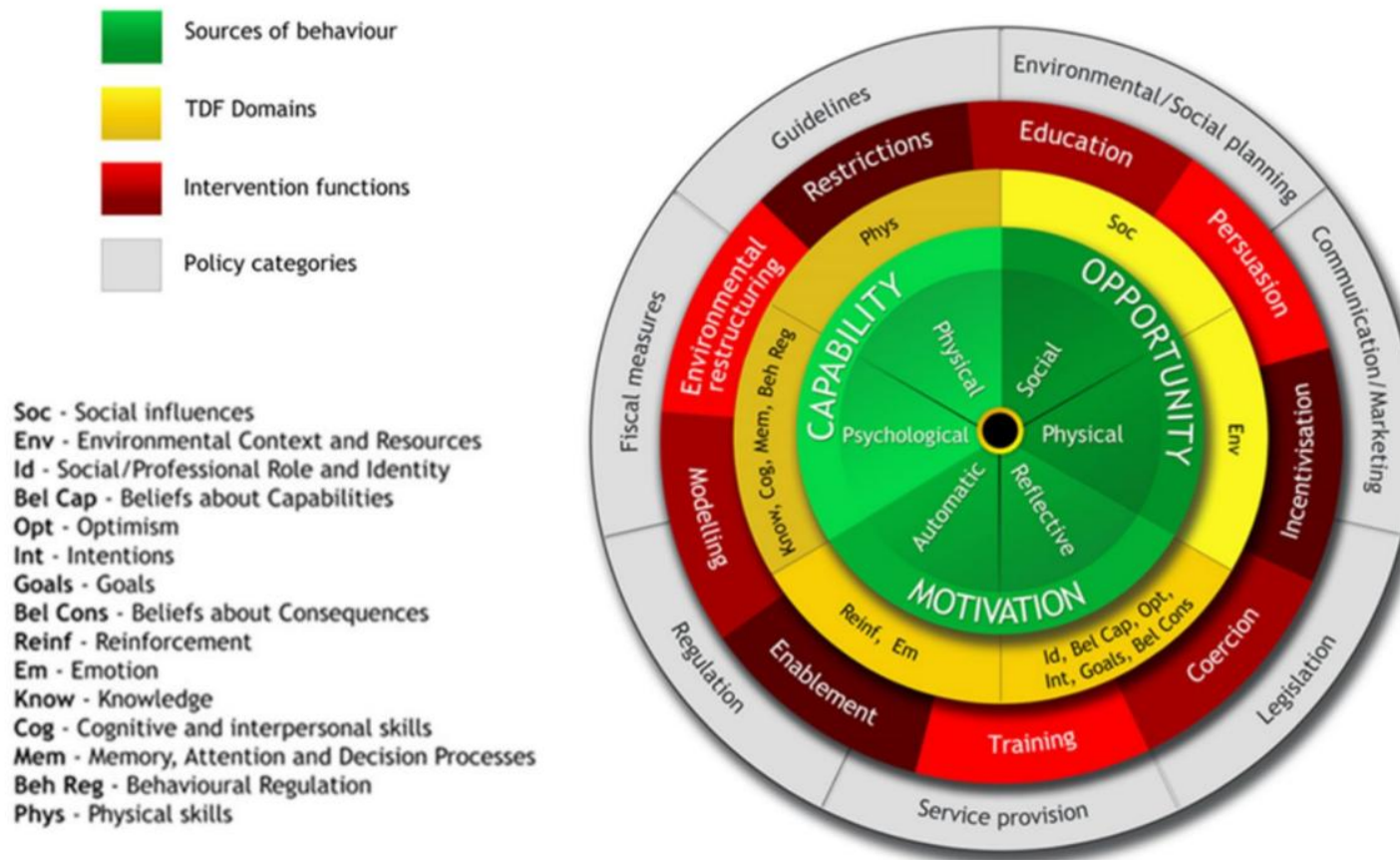


Figure 1.7 The key components of the Behaviour Change Wheel, including the COM-B model at the centre, surrounded by the TDF domains, Intervention Functions, and policy categories.
Image courtesy of Michie et al., 2014

1.15.2 Applying the Behaviour Change Wheel in practice

The BCW guides intervention development through three main stages, each of which builds on the last to design an evidence-informed intervention.

Stage 1: Understanding the Behaviour (Behavioural Diagnosis)

The first step involves defining the target behaviour and conducting a behavioural diagnosis to determine what needs to change. This is facilitated by the COM-B (Capability, Opportunity, Motivation - Behaviour) model (Michie et al., 2011), which forms the innermost core of the BCW (see Figure 1.7). COM-B proposes that behaviour (B) results from the interaction of three components: Capability (C) both psychological and physical, Opportunity (O) both social and environmental, and Motivation (M) both reflective and automatic (Figure 1.8). If one or more of these components is lacking, the target behaviour is unlikely to occur. The COM-B model thus provides a systematic framework for identifying which components must be addressed to facilitate behaviour change.

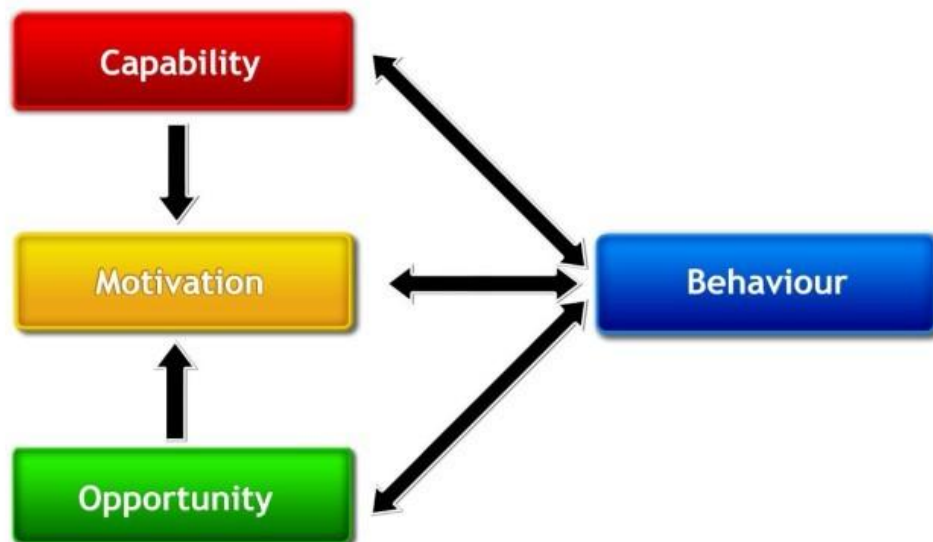


Figure 1.8 Capability, Opportunity, Motivation - Behaviour (COM-B) model. Image courtesy of Michie et al., 2011

To enhance this behavioural diagnosis, the Theoretical Domains Framework (TDF) can be used alongside the BCW (Cane et al., 2012). The TDF, a validated framework, consolidates constructs from multiple behavioural theories into 14 domains (See Table 1.1), providing a more detailed understanding of the psychological, social, and contextual factors influencing behaviour. A strength of the TDF is its ability to capture perspectives from all relevant actors (including patients and HCPs), and it has been successfully applied across a wide range of healthcare behaviours (Atkins et al., 2017).

Table 1.1 The Theoretical Domains Framework. Adapted from Cane et al., 2012.

Domain - Definition	Constructs
Knowledge - An awareness of the existence of something	Knowledge (including knowledge of condition /scientific rationale) Procedural knowledge Knowledge of task environment
Skills - An ability or proficiency acquired through practice	Skills Skills development Competence Ability Interpersonal skills Practice Skill assessment
Social/Professional Role and Identity - A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting	Professional identity Professional role Social identity Identity Professional boundaries Professional confidence Group identity Leadership Organisational commitment
Beliefs about Capabilities - Acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use	Self-confidence Perceived competence Self-efficacy Perceived behavioural control Beliefs Self-esteem Empowerment Professional confidence
Optimism - The confidence that things will happen for the best or that desired goals will be attained	Optimism Pessimism Unrealistic optimism Identity
Beliefs about Consequences - Acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation	Beliefs Outcome expectancies Characteristics of outcome expectancies Anticipated regret Consequents
Reinforcement - Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus	Rewards Incentives Punishment Consequents Reinforcement Contingencies Sanctions

Intentions - A conscious decision to perform a behaviour or a resolve to act in a certain way	Stability of intentions Stages of change model Transtheoretical model and stages of change
Goals - Mental representations of outcomes or end states that an individual wants to achieve	Goals (distal / proximal) Goal priority Goal / target setting Goals (autonomous / controlled) Action planning Implementation intention
Memory, Attention and Decision Processes - The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives	Memory Attention Attention control Decision making Cognitive overload / tiredness
Environmental Context and Resources - Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behaviour	Environmental stressors Resources / material resources Organisational culture /climate Salient events / critical incidents Person x environment interaction Barriers and facilitators
Social influences - Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviours	Social pressure Social norms Group conformity Social comparisons Group norms Social support Power Intergroup conflict Alienation Group identity Modelling
Emotion - A complex reaction pattern, involving experiential, behavioural, and physiological elements, by which the individual attempts to deal with a personally significant matter or event	Fear Anxiety Affect Stress Depression Positive / negative affect Burn-out
Behavioural Regulation - Anything aimed at managing or changing objectively observed or measured actions	Self-monitoring Breaking habit Action planning
All definitions are based on definitions from the American Psychological Association's Dictionary of Psychology (VandenBos, 2007)	

Stage 2: Identifying Intervention Options

Following the behavioural diagnosis, the BCW framework guides the identification of appropriate Intervention Functions (IFs) and supporting policy categories (the two outer rings of the BCW, Figure 1.7). IFs represent broad mechanisms through which behaviour can be influenced, such as *Education*, *Training*, *Enablement*, or *Environmental Restructuring*. These functions are then mapped to policy categories, such as service delivery changes or clinical guidelines, which can support wider implementation and sustainability. This stage ensures that the intervention is not only

theoretically informed but also feasible and applicable within real-world healthcare settings.

Stage 3: Identifying Content and Implementation Options

The final stage focuses on identifying the specific content of the intervention. This is achieved by selecting specific evidence-based Behaviour Change Techniques (BCTs), which are the active components of interventions known to drive behaviour change. BCTs are drawn from a standardised taxonomy (Michie et al., 2013) and include strategies such as *goal setting*, *action planning*, *prompts/cues*, and *feedback*. Importantly, each BCT is chosen based on its established link to the specific behavioural determinants identified during earlier stages, thus providing a clear rationale for 'why' and 'how' the intervention is expected to work (Michie & Abraham, 2004).

BCTs are then translated into practical delivery strategies tailored to the needs and preferences of the target population. Examples may include face-to-face sessions, digital interventions, group-based workshops, or integration into clinical workflows. This ensures that the intervention is not only theoretically sound but also acceptable, feasible, and contextually appropriate.

Taken together, the BCW, COM-B model, TDF, and BCT taxonomy offer a rigorous, transparent, and practical framework for designing behavioural interventions. By grounding intervention design in theory and evidence, this approach increases the likelihood that strategies will be appropriately targeted, effective, replicable and scalable.

1.15.3 Behavioural interventions used in other healthcare contexts

Behaviour change methodologies using the BCW have been successfully applied across a range of health contexts beyond eyecare. For example, interventions targeting smoking cessation, physical activity, and dietary change have used theory-informed strategies to improve long-term outcomes (Michie et al., 2011, Gould et al., 2017). In diabetes care, Murphy et al. (2023) used the BCW to develop an

intervention for pregnant women with gestational diabetes, aiming to reduce the risk of progression to type 2 diabetes postpartum and to improve pregnancy outcomes. Similarly, behaviour change frameworks have informed interventions to enhance nutritional and psychosocial outcomes for mothers and infants in Sub-Saharan Africa, demonstrating their versatility across different diseases and healthcare settings (Watson et al., 2023). These examples highlight the value of theory-informed approaches in designing interventions that are both targeted and scalable and support their application in glaucoma care.

This thesis applies the above behavioural methodology to develop an intervention aimed at improving glaucoma medication adherence, with each phase of the research aligned to a stage of the BCW. By identifying and addressing the underlying drivers of nonadherence, the intervention is more likely to be effective, feasible, and acceptable in real-world settings. This structured, theory-informed approach reflects best practice in complex intervention development and is consistent with MRC guidance (Skivington et al., 2021).

1.16 Conclusion

Glaucoma medication adherence is a complex and multifaceted issue that poses significant challenges in terms of how it is defined, measured and monitored. Adherence may be categorised as primary or secondary, intentional or unintentional, and is shaped by a variety of interrelated factors. For a chronic condition like glaucoma, which requires long-term treatment, it is important to measure adherence longitudinally using reliable tools and where possible, a combination of methods.

Despite various interventions aimed at improving adherence, success has been inconsistent. Interventions that have shown most promise tend to be multi-component, combining educational content with personalised behavioural strategies. The variability in outcomes is particularly concerning given the progressive nature of glaucoma and the important role of adherence in preventing vision loss. Maximising adherence is therefore essential for achieving optimal therapeutic outcomes and preserving sight.

The use of theory to underpin intervention development is key. Theoretical frameworks provide a structured approach to understanding the behavioural drivers of adherence and inform the design of more targeted, systematic, and potentially effective interventions. A theory-informed approach also facilitates greater consistency, transparency, and replicability across settings, which are key considerations in intervention design and implementation.

1.17 PhD rationale and aims

The overall aim of the research in this thesis is to develop a conceptual model for an intervention to support adherence to ocular hypotensive medication, using a behaviour change approach. This is grounded in the understanding that adherence is a persistent and major challenge in glaucoma care, yet essential for preventing vision loss. Consistent with MRC guidance, this research is a theoretically and empirically informed approach to intervention development (Skivington et al., 2021).

From the outset of the project, it was decided the intervention would operate at a patient-level, to maximise engagement and empower individuals to manage their own treatment. Patient engagement is associated with improved adherence to treatment plans, which is essential for managing a chronic condition such as glaucoma (Bosworth et al., 2017). To enhance relevance and acceptability, a person-centred approach will be adopted, involving collaboration with individuals who are likely to use or deliver the intervention (Yardley et al., 2015).

Recognising the increasing integration of technology into healthcare and the widespread use of smartphones, the intervention also aims to incorporate a digital component. Digital tools have shown promise in improving medication adherence in other conditions (Mikulski et al., 2022) and are anticipated to enhance the scalability, accessibility, and real-world feasibility of the proposed intervention.

The key objectives of this research project are to:

- Identify the key behavioural determinants of glaucoma medication adherence from the existing literature (Chapter 2).

- Develop a practical, consensus-based definition of acceptable glaucoma medication adherence among UK eye care professionals (ECPs) (Chapter 3).
- Identify modifiable behavioural determinants of adherence from the perspectives of patients and ECPs in the UK (Chapter 4).
- Develop the theoretical basis of a patient-focussed intervention to support glaucoma medication adherence, select appropriate components, and evaluate its feasibility (Chapter 5 and 6).

The final chapter (Chapter 7) summarises the main findings and considers their implications for glaucoma care and future intervention research.

Chapter 2 Barriers and enablers to medication adherence in glaucoma: A systematic review of modifiable factors using the Theoretical Domains Framework

2.1 Chapter overview

This chapter presents a systematic review of modifiable factors influencing medication adherence in glaucoma, structured using the TDF (Theoretical Domains Framework). The review identifies key factors that influence adherence behaviours in glaucoma, forming the theoretical basis for the intervention development in later chapters.

2.2 Introduction

As outlined in Section 1.9 (page 46), despite the availability of effective glaucoma therapies, many patients struggle to adhere to their prescribed medication regimens due to a range of behavioural, psychological, and practical barriers. These challenges can reduce treatment effectiveness and increase the risk of disease progression (Newman-Casey et al., 2020). Given the importance of medication adherence in managing glaucoma and preventing vision loss, it is essential to identify and understand the modifiable factors that influence patient adherence to treatment. This understanding is key for the development of targeted, theory-informed interventions that can effectively support sustained medication adherence. It is equally important for clinicians to be aware of these influences so they can provide individualised support and promote continued adherence.

The overarching aim of this thesis is to develop an intervention to support glaucoma medication adherence using a behaviour change approach, as outlined in Section 1.17 (page 77). This chapter presents a systematic review of the evidence in order to lay the foundation for the intervention development. The review specifically investigates modifiable barriers and enablers to glaucoma medication adherence through the lens of the TDF. As highlighted in Section 1.14.2 (page 67), interventions designed to improve adherence have demonstrated limited effectiveness and often lack a robust theoretical foundation (Gray et al., 2009; Waterman et al., 2013).

Research suggests that interventions are more likely to be effective if they address the causal determinants of adherence behaviour (Rahman et al., 2022). These determinants may act as enablers (factors that support medication use), barriers (factors that hinder it), or be mixed (having the potential to either support or hinder adherence).

The TDF is a well-established framework that synthesises key behavioural determinants across multiple domains, providing a comprehensive lens through which to examine the psychological and contextual factors influencing behaviour (Cane et al., 2012). A key advantage of the TDF is its linkage to evidence-based BCTs, which represent the ‘active’ components of interventions (Michie et al., 2008). By categorising existing evidence according to the TDF, this review highlights the factors most likely to influence adherence behaviours and identifies areas with potential for effective intervention. This structured approach ensures that strategies to improve adherence are designed to address the root causes of nonadherence (i.e. identifying and overcoming the barriers to eyedrop use) and aligns with the MRC Framework for developing complex interventions.

While the TDF has been applied to systematic reviews within the field of eye care (Graham-Rowe et al., 2018; Spillane et al., 2021; Toomey et al., 2021) and in medication adherence studies for conditions such as bipolar disorder (Prajapati et al., 2021), it has not, to date, been applied specifically to glaucoma medication adherence.

2.2.1 Aims and objectives

The aim of this review was to identify modifiable behavioural determinants influencing adherence to glaucoma medication. The specific objectives were to:

1. Systematically review the literature to identify modifiable barriers and enablers of adherence to prescribed glaucoma medications
2. Extract and categorise these determinants according to the TDF

3. Determine which domains are most influential in shaping adherence behaviour, using pre-determined criteria.

2.3 Method

The study protocol was pre-registered with PROSPERO (CRD42022330637) and can be accessed at <https://www.crd.york.ac.uk/PROSPERO/view/330637>

2.3.1 Eligibility criteria

Primary studies, of any empirical design, describing modifiable determinants of glaucoma medication adherence in adults were included. Non-primary studies, systematic or non-systematic reviews, conference abstracts, commentaries, editorials, studies relating to non-prescribed medications, studies reporting on unmodifiable factors (e.g. age, race) or factors not modifiable within an ophthalmology setting (e.g. treatment for depression) were excluded.

2.3.2 Search strategy

Five bibliographic databases were searched - CINAHL Complete, MEDLINE Complete, PsycINFO (via EBSCOhost), EMBASE and the Cochrane Library (via OVID). The search terms were classified into three concepts “barrier or enabler”, “adherence” and “glaucoma medication” and adapted for each database accordingly. An example search strategy for MEDLINE is provided in Appendix A1. The search was restricted to studies reported in English and conducted from inception to August 2022.

Grey literature was identified using the following resources: Google, limited to the first five pages of results; searching the National Grey literature collection (<https://allcatsrgrey.org.uk/wp/>) and the patient experience library (<https://www.patientlibrary.net/cgi-bin/library.cgi?page=Welcome;prevref=>).

2.3.3 Screening

Retrieved studies were uploaded to Zotero (<https://www.zotero.org/>), an online reference management tool where duplicates were removed. Following elimination of duplicates one author (DB) screened the abstracts of all identified records against pre-determined inclusion/exclusion criteria. One hundred records (approximately 25%) were rescreened by a second author (PC) to check for screening reliability. Cohen's kappa was calculated as 0.89 i.e. high agreement (Landis & Koch, 1977). The remaining eligible records had their full texts retrieved and screened by one reviewer (DB). Full text screen reliability was calculated for 39 studies (28%) between DB and a second author (DE) with a similarly high agreement (Cohen's kappa= 0.78). Throughout the screening process any uncertainty regarding eligibility was resolved by consensus or if needed discussed with a third reviewer (PC or DE).

2.3.4 Data extraction and analysis

Data analysis followed a standard four-step method using a content and framework analysis approach (see Figure 2.1), as described in previous systematic reviews using the TDF (Graham-Rowe et al., 2018; Toomey et al., 2021).

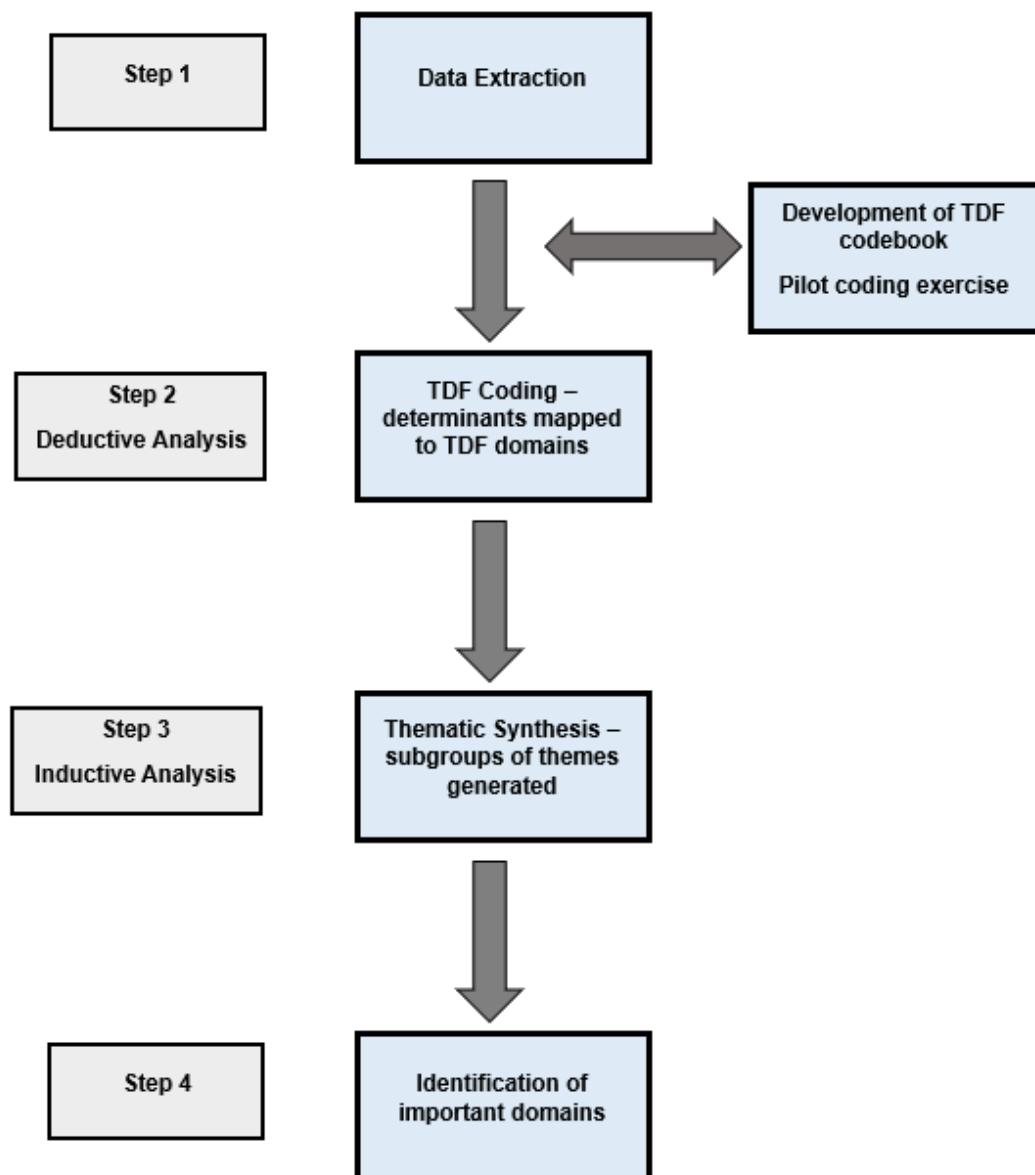


Figure 2.1 Flowchart representing 4-step method of data analysis

Step 1 Data extraction

Data extraction was piloted on five studies and discussed by the whole review team (DB, PC, AS, DE and JGL). Two authors (DB and DE) then extracted data from the remaining studies and uploaded the results to Excel. Extracted data included author, date, study aims and design, country, patient demographics, conditions treated, medications, duration of follow-up, adherence measures, extent of adherence, data collection methods, data analyses and modifiable determinants of adherence.

Extracted determinants comprised participant quotations from qualitative studies, statistical analysis findings from quantitative studies or authors' interpretations from study results. Eighteen studies (22%) had data extraction reassessed by another reviewer (PC) and any minor disagreements found were resolved by discussion.

Step 2 Deductive analysis (TDF coding)

Extracted data were mapped to one of the 14 TDF domains. To aid mapping decisions a codebook including definitions for each domain was developed (see Appendix A2). The codebook went through several iterations to reflect increased knowledge gained from exposure to more studies. Three reviewers (DB, PC, and DE) collaboratively piloted coding for five studies, using the codebook as a guide.

The remaining studies were independently coded by two reviewers (DB and DE). Data were only coded to the single most salient domain. Finally DB and DE reviewed their co-reviewers' coding decisions for each study and any disagreements were discussed until consensus was achieved, with input from a third reviewer (PC) if required.

Step 3 Inductive analysis (thematic synthesis)

One reviewer (DB) sifted and sorted the data coded to each TDF domain, grouping determinants of medication adherence into overarching themes/subthemes representing similar patterns. DE reviewed and verified all generated themes/subthemes. Any disagreements were resolved by discussion or if needed with another reviewer (PC).

Step 4 Identification of important domains

The importance of each domain, as identified in step 2, in influencing glaucoma medication adherence was determined using a previously established set of importance criteria (Graham-Rowe et al., 2018); (1) frequency (the number of studies identified per domain and number of barriers/enablers identified per domain), (2) level of elaboration (number of themes/subthemes generated within each domain) (3) expressed importance (denoted by study authors' comments in discussion,

quotations from study participants signifying importance, or statistically significant findings).

2.3.5 Quality assessment

The Mixed Methods Appraisal Tool (MMAT) version 2018 was used to assess study quality as it is a single tool, with good content validity, that enables concomitant appraisal of different study designs (Hong et al., 2019). Initially, four reviewers (DB, DE, PC and JGL) appraised 10 studies (12%) as a training exercise. Two of these reviewers (DB and DE) then independently quality assessed the remaining studies. Any disagreements in study quality were resolved by discussion until consensus was achieved, with input from a third reviewer (PC) if necessary.

2.4 Results

From the initial total of 565 identified records (comprising 553 from the database search and 12 from other sources such as grey literature) 167 duplicates were removed and after screening the titles and abstracts, 150 were eligible for full-text screening. From these 150 records, 83 were included in the final synthesis. Overall, the main reason for excluding records was that reported determinants were non-modifiable. Figure 2.2 outlines the process of identifying included eligible studies.

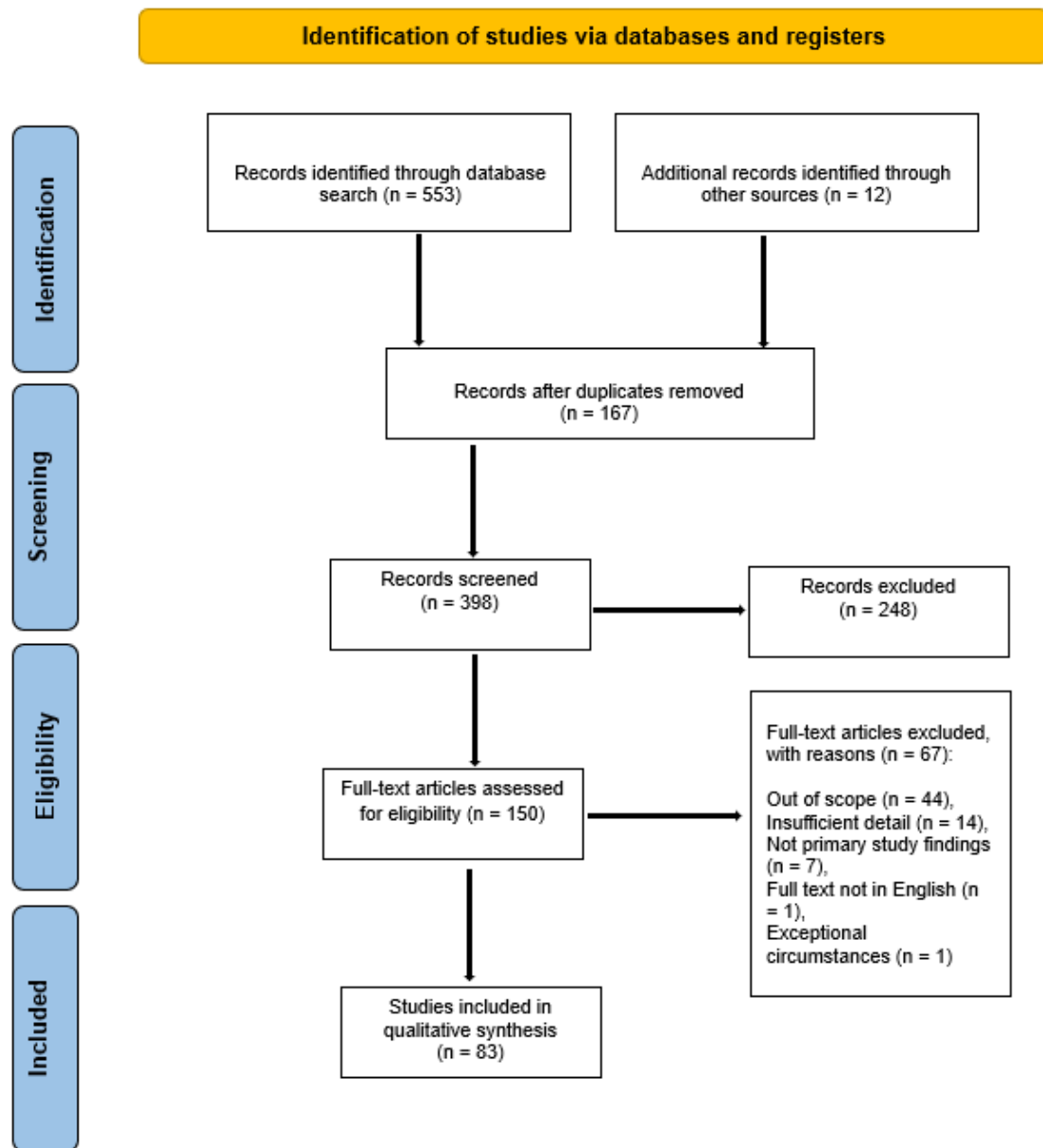


Figure 2.2 Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) flow diagram

2.4.1 Study Characteristics

Nearly half of eligible studies ($n=34$, 41%) were conducted in the USA. Fifteen studies (18%) were conducted in low- and middle-income countries (LMICs), as defined by the Organisation for Economic Co-operation and Development (GOV.UK, 2021) and three studies (4%) were conducted across multiple countries. Most studies ($n=75$, 90%) reported determinants from a patient perspective and seven

(8%) were multi perspective, describing determinants from both patient and practitioner viewpoint. No studies reported determinants from a carer's perspective.

Of 71 studies that reported medication adherence levels 48 (68%) measured adherence subjectively either by questionnaire, survey or interview and 20 (28%) measured adherence objectively using pharmacy databases, electronic monitoring systems or weighing of eyedrop bottle. Three studies (4%) measured adherence both subjectively and objectively. Sample sizes varied between 20 and 12,899. Included studies were published between 1977 and 2022.

An overview of included study characteristics is in Table 2.1, with a more detailed analysis in Appendix A3.

Table 2.1 An overview of included study characteristics

Study Characteristics	Frequency N (%) Total No of studies N=83
Study location [†]:	
North America	37 (45%)
Asia	22 (27%)
Europe	18 (22%)
Africa	7 (8%)
Australia	6 (7%)
Study Design:	
Quantitative	72 (87%) of which 24 (33%) were quantitative non-randomised and 48 (67%) quantitative descriptive
Qualitative	8 (10%)
Mixed Methods	3 (4%)
Reported Adherence Rate [‡]:	
Subjectively	48 (68%)
Objectively	20 (28%)
Subjectively & Objectively	3 (4%)
Determinants reported from:	
Patient perspective	75 (90%)
Practitioner perspective	1 (1%)
Patient & practitioner perspective	7 (8%)
[†] 3 studies conducted in multiple countries	
[‡] 71 studies reported adherence rate	

2.4.2 Quality assessment

A summary of the overall quality of included studies can be found in Table 2.2, (Hong et al., 2018) with a more detailed analysis provided in Appendix A4. In general, mixed methods and qualitative studies were reported as being of very high quality and quantitative studies were of reasonable to high quality. The main sources of bias were due to adherence measurement tools not being validated or piloted prior to administration. Other sources of bias related to the sample not being representative of the target sample and lack of detailed information regarding participant selection processes or response rates, and these lead to several “Can’t tell” decisions on quality.

Table 2.2 Summary of the quality of included studies

Study	Quality				
	*	**	***	****	*****
Qualitative studies					
Dreer et al (2013)					*****
Lacey et al (2009)					*****
Mansberger et al (2013)					*****
Newman-Casey et al (2016b)					*****
Nordmann et al (2007)					*****
Park et al (2013)					*****
Taylor et al (2002)					*****
Tsai et al (20013)					*****
Quantitative non-randomized studies					
Barker et al (2019)				****	
Boland et al (2014)				****	
Carpenter et al (2015)				****	
Castel et al (2014)					*****
Cook et al (2015)			***		
Dasgupta et al (2002)				****	
Djafari et al (2009)			***		
Friedman et al (2008)			***		
Gurwitz et al (1993)				****	
Gurwitz et al (1998)					*****
Hwang et al (2014)					*****
Kashiwagi et al (2014)				****	

Newman-Casey et al (2015a)		*****
Nordstrom et al (2005)		*****
Norell et al (1981)	****	
Owen et al (2009)		*****
Reardon et al (2003)		*****
Sanchez et al (2020)	****	
Shirai et al (2021)	****	
Sleath et al (2015a)	****	
Sleath et al (2015b)	****	
Stein et al (2015)		*****
Welge-Lussen et al (2015)	***	
Zhu et al (2019)	****	
Quantitative descriptive studies		
Anbesse et al (2019)	****	
Balkrishnan et al (2003)	****	
Bloch et al (1977)	****	
Chen et al (2022)	***	
Day et al (2006)		*****
Effendi et al (2018)	**	
Friedman et al (2009b)	***	
Gelb et al (2008)	***	
Gray et al (2010)		*****
Guyen et al (2021)	****	
Hoevenaars et al (2008)	****	
Kawai-Tsuboi et al (2015)	***	

Kayode et al (2019)		****	
Khaled et al (2021)	**		
Khandekar et al (2005)			*****
Kholdebarin et al (2008)		****	
Kim et al (2017)		***	
Konstas et al (2000)		***	
Lai et al (2020) †	**		
Loon et al (2015)		***	
Lunnela et al (2011)		****	
Mansouri et al (2011)		****	
Masoud et al (2013)	**		
McClelland et al (2019)		****	
Mehari et al (2016)			*****
Mowatt et al (2011)		***	
Newman-Casey et al (2015b)			*****
O'Hare et al (2009)		***	
Olthoff et al (2009)			*****
Omolase et al (2013)		***	
Onwubiko et al (2020)		***	
Osman et al (2016)		***	
Patel et al (1995)	*		
Ramesh et al (2021)		***	
Rees et al (2010)		****	
Rees et al (2014)		****	
Schwartz et al (2009)		****	

Sleath et al (2006)	***	
Sleath et al (2009a)		****
Sleath et al (2009b)	***	
Sleath et al (2014)	**	
Stewart et al (2004)	***	
Suet et al (2018)		****
Stringham et al (2018)		****
Tamrat et al (2015)	***	
Tshivhase et al (2021)		*****
Tsumura et al (2019)	***	
Wolfram et al (2019)	**	
Mixed Methods studies		
Gatwood et al (2022)		****
Killeen et al (2020)		*****
Spencer et al (2019)		*****
[†] main study was a randomized control trial but for this review the relevant part was a pre-RCT questionnaire and classified as 'quantitative descriptive' ***** denotes 100% quality criteria met; **** denotes 80% quality criteria met; *** denotes 60% quality criteria met; ** denotes 40% quality criteria met; * denotes 20% quality criteria met		

2.4.3 Outcomes

Deductive Analysis

In total 579 units of data (234 modifiable enablers and 345 modifiable barriers) were extracted and coded to relevant TDF domains. For example, extracted data *“non adherent patients were less aware of the permanent nature of glaucoma compared to adherent patients”* was assigned to the *“Knowledge”* domain as a barrier. An example quotation from a qualitative study *“I think it’s when you go and do other things that take you away from the general routine, then you might forget it”* was mapped to *“Environmental Context and Resources”* domain as a barrier. Both enablers and barriers were extracted from the majority of studies (n=60, 72%), whereas enablers only were extracted from eight (10%) studies and barriers only from 15 (18%) studies. Overall, determinants spanned all 14 domains except *Optimism*, where no reported barriers were assigned.

Inductive Analysis

In total 32 themes and 24 sub-themes were generated from the coded determinants.

Identification of Important domains

The following three criteria were used to identify the important domains influencing glaucoma medication adherence and details are given in Table 2.3.

1. *Frequency*: TDF domains according to number of studies and determinants identified per domain. The highest number of studies (n=70) were mapped to the *Environmental Context and Resources* domain which also generated the greatest number of barriers (n=146) and enablers (n=51). This was followed by *Skills* and *Knowledge* domains, which contained similar numbers of studies (n=45 and n=49 respectively) and total determinants (n=90 and n=81 respectively).
2. *Level of elaboration*: TDF domains according to the number of themes and sub-themes identified. Again, *Environmental Context and Resources* domain generated most themes/sub-themes (n=6/n=7). *Knowledge*, *Skills* and *Beliefs about consequences* were the next highest ranked domains.

3. *Expressed importance*: TDF domains according to the number of times authors/participants expressed a level of importance. Expressed importance was determined either by:

- study authors' comments in discussion sections or throughout the paper e.g. *"another notable finding....."*, *"physicians most often identified....."* or *"an important theme that arose....."*.
- direct quotations from study participants signifying importance e.g. *"the older you get, the more important it is to establish a routine"*
- notable statistically significant findings not reflected in study authors' comments e.g. *"having difficulties in reading the labels and identifying the eyedrop bottles significantly affected adherence"*

Initially, the intention was to only use study authors' comments or participants' direct quotations to define expressed importance, however this strategy was adapted post-hoc and a number of the most notable statistically significant findings were included, reflecting the preponderance of quantitative studies (87%) and relative dearth of qualitative studies (8%). Extracted data items deemed to express a level of importance, using the above criteria, were assigned a point and totals for each domain were calculated to determine the overall level of expressed importance. Again, the *Environmental Context and Resources* domain ranked highest followed by *Knowledge, Skills and Memory, Attention and decision processes*.

Table 2.3 TDF domains by level of frequency, level of elaboration and expressed importance

TDF domain	Frequency			Level of elaboration		Expressed importance
	Number of studies identifying domain	Number of barriers	Number of enablers	Number of themes	Number of sub-themes	
Knowledge	49	37	44	3	6	33
Skills	45	65	25	3	4	30
Social Professional Role and Identity	7	2	5	2	0	5
Beliefs about capabilities	10	2	12	3	0	8
Optimism	1	0	1	1	0	0
Beliefs about consequences	25	25	20	2	4	15
Reinforcement	9	2	10	2	0	8
Intentions	3	1	3	1	0	0
Goals	5	2	4	1	0	4
Memory, Attention and decision processes	38	38	6	2	0	29
Environmental Context and Resources	70	146	51	6	7	57
Social Influences	16	9	18	3	0	12
Emotion	19	12	16	2	0	10
Behavioural Regulation	18	4	19	1	0	0

Combining results from frequency, level of elaboration and expressed importance identified the most important domains influencing glaucoma medication adherence as *Environmental Context and Resources, Knowledge, Skills and Memory, Attention and decision processes* (See Table 2.4). Good convergence between all three importance criteria (frequency, level of elaboration and expressed importance) was demonstrated. Appendix A5 lists all TDF domains in order of importance.

Table 2.4 The four most important TDF domains as identified by frequency, level of elaboration and expressed importance

Frequency	Level of Elaboration	Expressed Importance	Top 4 domains
Environmental Context and Resources	Environmental Context and Resources	Environmental Context and Resources	Environmental Context and Resources
Skills	Knowledge	Knowledge	Knowledge
Knowledge	Skills	Skills	Skills
Memory, Attention and decision processes	Beliefs about consequences	Memory, Attention and decision processes	Memory, Attention and decision processes

The following narrative description documents theoretical domains and themes/sub-themes of high importance that influence glaucoma medication adherence. (A tabular summary can be found in Table 2.5). The remaining themes and corresponding TDF domains can be found in Appendix A6 together with illustrative examples.

Environmental Context and Resources

The main themes within this domain were treatment considerations, financial circumstances, patient-related factors, existence of side effects, eye clinic factors and pharmacy issues.

Treatment considerations, as identified in 46 studies, related to class/type of drug or eyedrop regimen. The type/class of drug prescribed either aided or hindered adherence. Consistently, PGAs were associated with better adherence than other

types of IOP-lowering medication (Castel et al., 2014; Djafari et al., 2009; Reardon et al., 2003). A large study, conducted in the USA with over 1000 participants, evaluated persistency rates with four different classes of glaucoma monotherapy in newly diagnosed patients and found those using PGAs were *“less likely to discontinue therapy than patients receiving β -blockers..., CAIs [Carbonic Anhydrase Inhibitors],...or brimonidine”* (Dasgupta et al., 2002). Unpreserved medications were associated with better adherence levels compared to medications containing preservatives (Wolfram et al., 2019).

Complex eyedrop regimens and issues with dosing schedules were barriers to adherence (Balkrishnan et al., 2003; Day et al., 2006; Dreer et al., 2013). Midday was reported to be the most inconvenient administration time as patients were often too busy to instil eyedrops (Norell, 1981; Spencer et al., 2019; Taylor et al., 2002). The number of glaucoma medications to be administered had a mixed effect on adherence. One study (Gurwitz et al., 1993) reported poorer adherence was associated with fewer eyedrops whereas another study found improved adherence with fewer eyedrops (Shirai et al., 2021). Both patients and practitioners, in a multi-perspective Japanese study, reported a greater number of eyedrops and more frequent instillations negatively affected adherence (Tsumura et al., 2019).

Finance, as identified in 28 studies, was a barrier to adherence. Difficulties paying for eyedrops (Anbesse et al., 2019; Cook et al., 2015; Lai et al., 2020), self-funding (Mehari et al., 2016; Ramesh et al., 2021; Tamrat et al., 2015), high medication co-payments (Newman-Casey et al., 2015a; Stein et al., 2015) or not having health insurance (Osman et al., 2016; Tsai et al., 2003) contributed to poorer adherence. For example, a participant commented *“They told me to use [the drops] for both eyes, but due to lack of money I used only for one [eye]. I used only for left eye; if [I was using it in both eyes] the drops would have run out long back”* (Killeen et al., 2020). Studies conducted in countries where patients had health insurance plans covering all/the majority of their medical expenses (e.g. Japan, South Korea) reported good adherence rates (Kashiwagi & Furuya, 2014; Kim et al., 2017; Mansouri et al., 2011).

Patient-related factors were identified in 28 studies. Competing priorities (e.g. being away on holiday, caring for a family member, work commitments, life stresses) were commonly reported as obstacles to using eyedrops (Carpenter et al., 2015; Effendi & Aulia 2018; Friedman et al., 2009b). Patients not having eyedrops with them was also a barrier. One study revealed that 15.9% of participants reported that sometimes they did not use their drops because they did not have their medication to hand (Tsumura et al., 2019).

Relying on someone else to instil medication had a mixed effect on adherence, depending on carer/family member availability. One participant commented *"When I was living alone I had problems taking my drops, now I live with my daughter and I have no problems"* (Tsai et al., 2003). Whereas authors from a Nigerian study observed that carers were often unavailable for days and as a result patients who had assistance administering their eyedrops were more likely to be nonadherent (Onwubiko et al., 2020).

The existence of side effects, reported in 18 studies, was associated with poorer adherence (Bloch et al., 1977; Schwartz et al., 2009; Stringham et al., 2018) in all but one study. Surprisingly, this study found patients experiencing burning or stinging with their eyedrops had higher objectively measured adherence levels (Friedman et al., 2008).

Eye clinic factors were identified in 12 studies, with the main issue being frequency of follow-up appointments. More regular clinic visits and seeing the same practitioner were found to promote adherence (Gurwitz et al., 1998; Kayode et al., 2019; Khandekar et al., 2005). In one study patients with more frequent follow-ups were found to have better adherence than those with less frequent follow-ups, and this difference in adherence was statistically significant (Tamrat et al., 2015). Both patients and practitioners reported time constraints within clinic as a barrier to adherence (Gelb et al., 2008; McClelland et al., 2019). Busy clinics led to patients feeling reluctant to ask for help or practitioners unable to provide adequate advice due to lack of time. A UK study reported *"unsatisfactory hospital-led education was*

considered to be the direct result of the current NHS system, where doctors appeared too busy clinically to have time to provide adequate education" (Lacey et al., 2009). Another study found clinic size was associated with level of adherence (Tsumura et al., 2019).

Issues obtaining eyedrops from the pharmacy were identified in six studies. One study, investigating adherence patterns over a four-year period, reported that the use of mail order services to receive repeat prescriptions was an important factor in contributing towards better adherence long-term (Newman-Casey et al., 2015a). Difficulties obtaining medications (Gatwood et al., 2022) with eyedrops either being out of stock at the pharmacy, not used commonly enough for the pharmacist to order stocks in, or prescription discrepancies (Gray et al., 2010) were barriers to adherence. In a study from Nigeria, the distance patients had to travel to collect their eyedrops influenced adherence; living more than five km from a pharmacist was reported as a barrier (Onwubiko et al., 2020).

Knowledge

The main themes generated within *Knowledge* were patient understanding, education and role of the HCP.

Patient understanding, as identified in 41 studies, covered awareness of the nature of glaucoma and/or its treatment. Poor understanding of glaucoma was consistently reported by patients and practitioners as a contributing factor to nonadherence (Nordmann et al., 2007; Rees et al., 2010; Tshivhase et al., 2021). One participant commented *"I kind of missed, you know, I, I wasn't, um, taking them the drops as regularly as I probably should have because I didn't know what glaucoma was"* (Gatwood et al., 2022). Another study in the USA that interviewed practitioners involved in the management of glaucoma reported *"Physicians most often identified ... lack of patient understanding about glaucoma ... as a major barrier to compliance"* (Gelb et al., 2008). Good glaucoma knowledge was associated with better adherence (Mowatt et al., 2011; Park et al., 2013; Rees et al., 2014). In one study, with high levels of self-reported and objectively measured adherence, authors

speculated this was due to patients being seen in a specialised glaucoma clinic rather than a general clinic, as a result of which they were more likely to be aware of their condition (Djafari et al., 2009).

Lack of understanding about treatment and its rationale was a barrier to adherence (Boland et al., 2014; Loon et al., 2015; Masoud et al., 2013). In a qualitative USA study one participant remarked *"I stopped taking my drops because I did not understand initially that I need to take them forever"* (Tsai et al., 2003). A 2022 study, in which glaucoma patients in China were interviewed, found higher self-reported adherence in those who better explained *"the side effects of eyedrops,.... understood the side effects.....and rationale for using eyedrops"* (Chen et al., 2022).

The sub-theme of education arose in 17 studies and incorporated lack of/desire for more information and the source of educational information. Lack of education surrounding glaucoma and its treatment was a contributing factor to poor adherence, with patients commenting they wanted more information on glaucoma symptoms (Sanchez et al., 2020), instillation techniques (Olthoff et al., 2009) and emerging treatments (Taylor et al., 2002). A study conducted in Saudi Arabia, found 76.2% of self-reported nonadherent participants lacked background information on glaucoma and treatment (Khaled et al., 2021). Patients who reported not needing any more information were more likely to be adherent (Hoevenaars et al., 2008).

Patients who researched glaucoma themselves, received more education from their provider or obtained additional information from sources such as optometrists, leaflets or the internet were more likely to be adherent (Lunnela et al., 2011; Sleath et al., 2015b). One study that interviewed participants across Europe, noted UK and German patients were more aware of support organisations providing additional information on glaucoma compared to patients from France, Italy or Spain (Stewart et al., 2004). Another study found reasons for nonadherence varied from patient-to-patient, leading authors to recommend patients receive personalised information, either electronically or face to face, depending on their need (Newman-Casey et al., 2015b).

The theme of HCP role emerged from five studies and incorporated the practitioner-patient relationship and HCP awareness of adherence/nonadherence. Good practitioner-patient relationships, which support patient understanding of their condition, were found to facilitate medication adherence (Hwang et al., 2014). In contrast, relationships built on patients passive dependence on their practitioner for information contributed to poorer adherence (Friedman et al., 2008). Better practitioner awareness of the importance of adherence resulted in improved long-term patient adherence (Owen et al., 2009).

Skills

Within *Skills* the themes that emerged were ability to administer eyedrops, practitioner skills and patients' ability to obtain ongoing prescription supplies.

Practical or vision related skills needed to instil eyedrops were identified in 31 studies. Problems with drop administration were associated with poorer adherence, (Kawai-Tsuboi et al., 2015; Kholdebarin et al., 2008; Konstas et al., 2000) the more difficulties a patient reported the less adherent they were likely to be (Sleath et al., 2006, 2009b; 2014). A Canadian study, assessing patient instillation methods, found 33.8% *“demonstrated improper drop administration technique”* (Kholdebarin et al., 2008). HCPs were also aware of the problems patients experienced instilling eyedrops; in one qualitative study ophthalmologists commented *“they [patients] find it hard to put them in themselves”* (Nordmann et al., 2007). The main problems patients described instilling eyedrops were difficulty squeezing the bottle (Mansberger et al., 2013), too many drops coming out or drops falling onto their cheeks (Omolase et al., 2013; Sleath et al., 2009a). Another factor hindering adherence was the ability to see print on the eyedrop bottle (O'Hare et al., 2009). A Malaysian study found adherence was significantly affected by a patient's ability to read the label and identify the eyedrop bottle (Suet Yee et al., 2018).

HCP skills emerged from 22 studies and related to communication and education skills, or the skills required to detect adherence/nonadherence. The ability of HCPs to have meaningful conversations, inquire about adherence issues, discuss the

rationale for treatment, counsel patients, teach administration techniques and provide education on the nature of glaucoma were associated with better adherence. One study interviewing practitioners reported *"Physicians most often identified [their]... inability to communicate why compliance is important (15%)... as a major barrier to compliance"* (Gelb et al., 2008). A multi-perspective study exploring the relationship between practitioner-patient interactions found providers only offered education about treatment and its rationale at 14% and 17.6% of study clinic visits (Sleath et al., 2015a). Several studies found patients struggled to instil their eyedrops, which led authors to recommend practitioners should not only assess patient technique but demonstrate the correct method and offer practical assistance (Olthoff et al., 2009; Sanchez et al., 2020). Practitioners' ability to detect nonadherence was consistently reported to be poor with HCPs remarking that their own ability was limited (Gelb et al., 2008). One study found *"71.1% of patients thought by physicians to be nonadherent were actually adherent"* (Djafari et al., 2009). To help improve practitioner detection skills, authors from another study, conducted in Australia, suggested patients self-complete an adherence assessment questionnaire prior to their clinic visit (McClelland et al., 2019).

The sub-theme based on the skill of obtaining continuous supplies of eyedrops emerged from seven studies, with patient inability to order repeat prescriptions contributing to poorer adherence (Stringham et al., 2018; Tsai et al., 2003). One participant commented *"When I ran out I would think I'm going to get it reordered and then.....it would be like a day or two before I remembered to call"* (Gatwood et al., 2022).

Memory, Attention and decision processes

The main themes within *Memory, Attention and decision processes* were forgetfulness and HCP treatment decision process.

Forgetting to instil eyedrops, as identified in 34 studies, was commonly reported as a major barrier to adherence.(Newman-Casey et al., 2016b; Patel & Spaeth, 1995; Welge-Lussen et al., 2015). In one study over 88% of nonadherent patients admitted

they forgot to use their medication sometimes (Sanchez et al., 2020). HCPs also recognized that patients' inability to remember to instil eyedrops was a contributing factor to poorer adherence (Gelb et al., 2008).

Practitioners' decision-making process in selecting a relevant treatment was identified in six studies. Authors consistently reported that practitioners should consider prescribing simplified regimens, specifically once daily treatments and unpreserved medications to promote better adherence (Wolfram et al., 2019; Zhu et al., 2019).

Table 2.5 An overview of generated themes/sub-themes, with illustrative examples, from the four key TDF domains influencing glaucoma medication adherence

Environmental Context and Resources N=70		
1.1 Theme:	Enabler/Barrier/ Mixed	Illustrative Examples
Treatment considerations N=46		
Sub-theme		
Class/type of drug	Enabler	Persistence with a PGA was <i>“substantially higher than with any of the other classes”</i> (Nordstrom et al., 2005)
Eyedrop regimen	Barrier	<i>“Patients on more glaucoma medications were less likely to take their doses on time”</i> (Sleath et al., 2015b)
1.2 Theme:	Enabler/Barrier/ Mixed	Illustrative Examples
Financial circumstances N=28	Barrier	<i>“Those participants who pay for their medications by themselves were 79% less likely to be adherent to glaucoma topical medications as compared to those who were sponsored by family/employer”</i> (Anbesse et al., 2019)
1.3 Theme:	Enabler/Barrier/ Mixed	Illustrative Examples
Patient-related factors N=28		
Sub-theme		
Dependency on carer/family member to instil eyedrops	Mixed	Lack of carer help was a reason for nonadherence (Gray et al., 2010) <i>“...having someone to help in eyedrops administration was a motivation to adhere to medication regimen...”</i> (Tshivhase et al., 2021)
Competing priorities	Barrier	Busy patient schedule was the second most common reason for non-compliance (Park et al., 2013)
Drops not to hand	Barrier	<i>“Sometimes the drops aren’t with me when it is time to take them [48%]”</i> (Sanchez et al., 2020)

1.4 Theme:	Enabler/Barrier/ Mixed	Illustrative Examples
Existence of side effects N=18	Barrier	<i>"Patients offered unsolicited information about barriers such as ... side effects"</i> (Friedman et al., 2009b)
1.5 Theme:	Enabler/Barrier/ Mixed	Illustrative Examples
Eye clinic factors N=12		
Sub-theme		
Demands during clinic	Barrier	<i>"Physicians most often identified [their]... limited time to spend with patients (12%) as a major barrier to compliance"</i> (Gelb et al., 2008)
Follow-up appointment/continuity of care	Barrier	Second most important factor associated with nonadherence was <i>"longer frequency of follow up"</i> (Kayode et al., 2019)
1.6 Theme:	Enabler/Barrier/ Mixed	Illustrative Examples
Pharmacy issues N=6	Barrier	<i>"[The pharmacists] say 'no one [comes] to buy this medicine except you. If it was for diabetes or blood pressure we could order it, but for [these eyedrops] you have to go to Madurai city"</i> (Killeen et al., 2020)
Knowledge N=49		
2.1 Theme:	Enabler/Barrier/ Mixed	Illustrative Examples
Patient understanding N=41		
Sub-theme		
Awareness of nature of glaucoma	Barrier	Nonadherent patients were <i>"less aware of the permanent nature of glaucoma"</i> (Guyen et al., 2021)

Awareness of treatment rationale/regimen/side effects	Barrier	<i>"Compared with the adherent group, nonadherent participants were less likely to be able to name their glaucoma medications (61.4% vs 82.2%)(P < .05)" (Boland et al., 2014)</i>
2.2 Theme:	Enabler/Barrier/Mixed	Illustrative Examples
Education N=17		
Sub-theme		
Lack of desire/desire for more information	Enabler	<i>"patients had a desire for more individualized information from their health care team to better understand their disease course, especially in the early stages" (Gatwood et al., 2022)</i>
Source of educational information	Enabler	<i>"very adherent people with glaucoma had also received information from other sources (69%, n=81), such as opticians, leaflets, literature and the Internet" (Lunnela et al., 2011)</i>
2.3 Theme:	Enabler/Barrier/Mixed	Illustrative Examples
HCP role N=5		
Sub-theme		
Practitioner-patient relationship	Enabler	<i>Author comment that continuity of care was associated with persistence which "implies better physician-patient relationship and communication, which may help improve patients' knowledge about their disease status and the importance of adherence" (Hwang et al., 2014)</i>
HCP awareness of adherence/nonadherence	Enabler	<i>"Better ... appreciation among healthcare providers of the need for better compliance with treatment may also partly explain the improvements in persistence observed over time" (Owen et al., 2009)</i>
Skills N=45		
3.1 Theme:	Enabler/Barrier/Mixed	Illustrative Examples
Ability to administer drops N=31		
Sub-theme		

Practical skills	Barrier	<i>"difficulty of drop application, [is] ... highly associated with [low] adherence" (Barker & Mansberger, 2019)</i>
Vision related skills	Enabler	<i>"Patients who could read the standard label information were three times more likely to recall their drops accurately compared with patients who were unable to read the standard label" (O'Hare et al., 2009)</i>
3.2 Theme:	Enabler/Barrier/ Mixed	Illustrative Examples
HCP skills N=22		
Sub-theme		
Communication and educational skills	Enabler	<i>"....patients said that they would be encouraged to continue their treatment if their physicians were willing to train them how to administer their medication...." (Nordmann et al., 2007)</i>
Clinical skill to detect adherence/nonadherence	Barrier	<i>"Interviewed physicians ... agreed that ... the ability to detect and address nonadherence is limited" (Gelb et al., 2008)</i>
3.3 Theme:	Enabler/Barrier/ Mixed	Illustrative Examples
Ability to obtain ongoing prescription supplies N=7	Barrier	<i>"Patients who reported forgetting to refill their drops ... were found to be less compliant" (Stringham et al., 2018)</i>
Memory, Attention and decision processes N=38		
4.1 Theme:	Enabler/Barrier/ Mixed	Illustrative Examples
Forgetfulness N=34	Barrier	<i>"Patients who reported difficulty remembering to take their glaucoma medications increased their odds of being less than 100% adherent during the previous week by 12-fold" (Sleath et al., 2006)</i>
4.2 Theme:	Enabler/Barrier/ Mixed	Illustrative Examples

HCP treatment decision making process N=6	Enabler	Authors comment <i>“result stresses the role of the physician’s choice of medication in promoting adherence to glaucoma pharmacotherapy”</i> (Castel et al., 2014)

N= number of studies
 Enabler = facilitates glaucoma medication adherence
 Barrier = hinders glaucoma medication adherence
 Mixed = either facilitates or hinders glaucoma medication adherence

2.5 Discussion

This systematic review aimed to systematically identify modifiable barriers and enablers to glaucoma medication adherence, operating at the patient, HCP and healthcare system levels, through the lens of the TDF. The majority of the identified determinants were reported from the patient perspective and assigned to four key TDF domains *Environmental Context and Resources*, *Knowledge, Skills, and Memory*, *Attention and decision processes*. In contrast, the domains *Goals*, *Intentions* and *Optimism* appeared to have the least impact on adherence behaviour. The large number of barriers and enablers identified reflects the complex nature of medication adherence.

Having identified the modifiable influences on medication adherence, the next step is to translate these insights into the development of evidence-based behaviour change interventions to improve adherence that could operate at either the patient, HCP or organisational level. As outlined in Section 1.15.2 (page 72), the TDF is linked to two frameworks that facilitate the systematic design of theoretically grounded interventions: the Behaviour Change Wheel (BCW) (Michie et al., 2011) and the Behaviour Change (BCT) Taxonomy (Michie et al., 2013). The BCW enables the mapping of relevant TDF domains to IFs and policy categories, thereby identifying appropriate strategies for behaviour change at the patient, practitioner, or organisational level. Complementing this, the BCT Taxonomy provides a standardised language to describe the active components of behaviour change interventions. In addition, the 'Theory and Techniques Tool' offers an interactive resource that links specific BCTs to the TDF domains with which they are theoretically associated (Johnston et al., 2021). This resource supports a systematic and transparent approach to intervention design by ensuring that selected BCTs are conceptually aligned with the identified behavioural determinants. Applying this theoretically informed approach to intervention development offers a means to address the current limitations in adherence interventions, which, as discussed earlier in Section 1.14.2 (page 67), often lack a clear theoretical basis and demonstrate limited efficacy. By targeting the underlying mechanisms of behaviour

identified through the TDF, future interventions can be designed to be both contextually relevant and behaviourally focused, thereby increasing the likelihood of achieving meaningful improvements in glaucoma medication adherence.

2.5.1 Implications for practice

The main barriers influencing glaucoma medication adherence related to; treatment characteristics, lack of patient understanding, forgetfulness and difficulties administering eyedrops. Whereas the main facilitators included simplified treatments, knowledgeable educated patients, and good patient-practitioner relationships. Based on these findings the author proposes three key recommendations are implemented into practice:

- Choice of treatment regimen
- Promotion of glaucoma awareness and education among patients and HCPs
- Promote better patient relationships with HCPs

Choice of treatment regimen

Deciding on a treatment regimen is an important factor influencing patient adherence. In this review, monotherapy (typically with PGAs) was associated with better adherence. Non-PGAs, multiple glaucoma drops and preserved preparations were associated with poorer adherence. Patients found complex regimens requiring multiple daily instillations of one or more glaucoma medications, especially instillations around the middle of the day, disrupted their lifestyle leading to poorer adherence. The existence of side-effects was often a barrier to adherence. Hence, practitioners should consider reducing the burden of instilling eyedrops by simplifying dosing regimens, prescribing fixed combination regimes where possible and preservative free preparations when there are signs of preservative toxicity (Steven et al., 2018). Successful choice of therapy is likely to promote better long-term adherence with fewer medication changes and fewer new prescription collections for patients (Nordstrom et al., 2005).

Practitioners are encouraged to follow recommended guidelines in relation to treatment choices for glaucoma and OHT such as the NICE, EGS, American Academy of Ophthalmology and Asia Pacific Glaucoma guidelines. Up to January 2022, NICE guidance in England and Wales recommended offering patients with OHT, suspect glaucoma or COAG who are at risk of visual loss during their lifetime a generic PGA as first line drug therapy (NICE, 2017). PGAs have good efficacy at reducing IOP, require a convenient once a day dosing regime and are well tolerated with limited systemic side effects (Lee & McCluskey, 2010). Since glaucoma requires long-term treatment, the acceptability of a patient's current eyedrop regimen in terms of side effects, ease of use, and convenience is important for maintaining long-term adherence. Preservative-free prostaglandin preparations, available in single unit or multidose containers, are often associated with greater patient satisfaction and tolerability than preserved versions (Muñoz Negrete et al., 2017) although at increased cost (Steven et al., 2018). Studies have shown patients can use individual unit dose vials just as well as multidose bottles (Aptel et al., 2021; Dietlein et al., 2008; Parkkari et al., 2010) but they can be more difficult to store due to the extra packaging, and they produce more plastic waste.(Safarzadeh et al., 2017).

Another option to consider when deciding on IOP- lowering treatment is selective laser trabeculoplasty (SLT). As discussed in Section 1.3.4 (page 33) SLT is a safe, repeatable, clinically effective and cost-effective treatment for COAG and OHT (excluding pigment dispersion syndrome) (Gazzard et al., 2019, 2023). Since January 2022, NICE recommends offering SLT to newly diagnosed COAG or OHT patients (where IOP is > 23mmHg and they are at risk of visual impairment within their lifetime) as first line treatment (NICE, 2022). Similar recommendations have been advocated by the USA and Europe (EGS, 2021; Gedde et al., 2021). As an initial treatment SLT can delay the need for eyedrops in approximately 69.8%% of patients for up to 6 years (Gazzard et al., 2023). In patients already on treatment but with uncontrolled IOP, SLT can potentially reduce the need for further medications or delay more invasive procedures (e.g. surgery). Difficulties paying for and obtaining medications, particularly in LMICs, were reported as barriers to adherence. In such cases SLT may be a more suitable and cost-effective option. However, SLT may not

be successful in every case, IOP reduction may not be sufficient or sustained (Khawaja et al., 2020) and, whilst uncommon, severe complications can arise (Garg & Gazzard, 2018; Song, 2016).

To overcome patients forgetting instillation times either due to poor memory or competing priorities practitioners can recommend patients develop a routine which becomes habit forming (e.g. instilling eyedrops at the same time as taking other medication), use visual or practical cues as reminders (e.g. placing eyedrops next to their toothbrush) or use reminder aids (e.g. mobile phone alarm, medication reminder apps). Reminder strategies can also be recommended to patients who struggle to remember to order repeat prescriptions (e.g. creating an alert in a mobile phone diary or physically writing on a calendar). Using mail order services to deliver eyedrops should be promoted since this was found to facilitate long-term adherence (Newman-Casey et al., 2015a).

Promotion of glaucoma awareness and education

Poor awareness of glaucoma and its treatment were reported by both patients and HCPs as barriers to adherence. Patients who had good knowledge of glaucoma and its symptoms, an understanding of the rationale for treatment, were aware of the consequences of nonadherence and could accurately describe their medication regimen were more likely to be adherent. To improve glaucoma knowledge the implementation of a structured national group educational programme, similar to the DESMOND (Diabetes Education and Self Management for Ongoing and Newly Diagnosed) scheme, which has proved effective in improving patients' knowledge and behaviours in people with type 2 diabetes (Chatterjee et al., 2018), is recommended.

Educational interventions in the form of tailored counselling sessions, educational videos, the use of illustrative pictures and information leaflets provided by pharmacists, nurses or research assistants have all proved beneficial in improving glaucoma medication adherence (Aleem et al., 2021; Cook et al., 2010; Okeke, 2009b; Sheppard et al., 2003). Providing patients with regular training programmes

reviewing, updating and reinforcing information would be desirable (Nassar et al., 2021). Group educational sessions, tailored to the individual needs of attendees, could also be considered since they have been found to be acceptable to glaucoma patients (Waterman et al., 2018) and may prove more cost effective and time efficient. Utilising the services of charities (e.g. Glaucoma UK <https://glaucoma.uk/>) that are trusted by patients to provide information in a relatable digestible manner is also recommended. Glaucoma UK issues patient information leaflets, educational videos, runs support groups and provides a dedicated telephone helpline for patient queries.

Issues with eyedrop administration were identified by both patients and HCPs as barriers to adherence, with patients reporting they would like more information on how to instil eyedrops correctly. Both hospital and community pharmacists can play a major role in raising awareness of instillation techniques. A UK pharmacist led “#KnowYourDrops” campaign, which delivered informal support events teaching administration techniques, demonstrating the use of compliance aids and addressing adherence issues proved extremely successful with patients, carers and HCPs (Thomas & Chiu, 2017). Community pharmacists are also ideally placed to regularly review patient adherence concerns, reiterate correct instillation techniques and offer further counselling as needed. Utilizing services outside of the eye department addresses the issue of time constraints within clinic. Patients reported busy clinics hindered them being able to ask for help and practitioners felt unable to offer sufficient information due to lack of time. Support staff, such as Eye care liaison officers (ECLOs) in the UK, could also play an integral role in providing this service. ECLOs are able to offer practical and emotional support and provide information about a patient’s condition whilst ensuring continuity of care in busy outpatient clinics (Llewellyn et al., 2019; Menon et al., 2020). However, consideration would need to be given to ensuring there were sufficient numbers of trained support staff to meet the demand.

To effectively manage nonadherence HCPs need to be aware of the magnitude of the problem, need to be able to assess and identify poor adherence, and to

recommend strategies to help. In this review, whilst practitioners appeared to be aware of the importance of adherence, their ability to detect cases of nonadherence was poor. To address this issue, providing training events for those involved in glaucoma care is recommended. Educational meetings can change professional practice (Forsetlund et al., 2021) and whilst they have been effective in supporting practitioners manage nonadherence issues in asthma, training for HCPs involved in medication adherence is generally lacking (Andersson et al., 2014). Arranging educational events at national/international conferences or local study days focussing on best adherence practice, enhancing practitioner communication skills and consolidating up-to-date knowledge relevant to glaucoma management could provide HCPs with practical tools to better address adherence in practice. Practitioners are also encouraged to follow professional body guidelines and recommendations to aid prescribing and management decisions.

Promote better patient-practitioner relationships

Good patient-practitioner relationships supporting patient understanding and effective HCP communication were found to facilitate adherence. Medicines adherence guidance issued by NICE and the Royal Pharmaceutical Society Competency Framework for all prescribers advocates open, honest and non-judgemental conversations encouraging patient participation (NICE, 2009; Royal Pharmaceutical Society, 2021). To promote an environment where patients can be honest about their adherence behaviour without the fear of feeling judged, HCPs need to have good communication skills and employ non-judgemental interview techniques to encourage a healthy patient-practitioner relationship (Hahn et al., 2010). UK practitioners are encouraged to follow NICE recommendations since informed and engaged patients tend to be more involved in shared decision making and hence are likely to be more adherent (Tan et al., 2021).

2.5.2 Implications for future work

As highlighted in Section 1.13 (page 60) improving adherence to glaucoma medication has been identified as a national research priority within the UK (Bourne

et al., 2024). To address this unmet clinical need, future work should focus on the development of theory-informed, scalable, and cost-effective interventions aimed at improving adherence. The findings from this review, which identify modifiable behavioural determinants, provide a foundation for such intervention development. Building on this, subsequent research should follow established frameworks, outlined earlier in this discussion, for translating theoretical determinants into targeted behaviour change interventions. These interventions will then require evaluation to assess their effectiveness, acceptability, and feasibility in real-world clinical settings.

The majority of studies included in this review reported determinants from a patient perspective. While this offers a valuable insight to gain a more comprehensive understanding of what influences medication-taking, future research should concentrate on studying HCPs' and carers' perspectives. HCPs are exposed to clinically diverse environments so will perceive determinants that not only influence themselves but also patients and organisational processes. Similarly, a carer's point of view will add another dimension to understanding influences on medication adherence.

Furthermore, very few of the included studies were qualitative in design. Adherence is a complex multi-faceted behavioural issue so exploring patients', HCPs' and carers' personal experiences with glaucoma medication to capture rich in-depth information would provide a deeper understanding of the problem. Future work addressing this would be recommended.

Existing literature has identified several key predictors of nonadherence, including younger age, lower educational attainment, minority ethnic background, and co-existing depression (Newman-Casey et al., 2020). To enhance the effectiveness of future interventions, it is essential that they are tailored to address the specific needs and challenges faced by populations at higher risk of nonadherence. While it was not a specific objective of this review to identify which theoretical domains were most relevant to these subgroups, future research work should explore this area. Such work could inform the development of more targeted, patient-centred strategies to

improve outcomes among those at risk of sub-optimal medication use. Similarly, research focussing on different healthcare systems, especially those that are not universal, not publicly funded or have poor infrastructure may be needed since factors influencing adherence may be different and more specific to these settings.

2.5.3 Strengths and Limitations

This systematic review is the first to use the TDF within the context of glaucoma medication adherence, hence addressing a gap in the evidence. Only modifiable determinants were reported on, since strategies to improve medication adherence are more likely to be effective if they target those factors that are amenable to change. A strength of using the TDF is that it is linked to evidence-based BCTs through the application of the BCW, hence it provides a theory-driven process for identifying determinants to glaucoma medication-taking that are suitable for targeting with a behaviour change intervention.

A second strength of the study was the extensive systematic reproducible search strategy, which included grey literature and studies of all designs (quantitative, qualitative and mixed methods). Another strength was the robust nature of the data analysis process where all decisions (deductive and inductive) were reviewed and verified by a second reviewer. All data, extracted from the 83 included studies, were able to be coded to a TDF domain, demonstrating the comprehensive nature of the TDF framework in identifying determinants.

There are, however, some limitations of the review which need to be considered. Sixty-eight (82%) of the 83 included studies were conducted in high-income countries. As medication adherence tends to be lower in LMICs due to factors such as limited healthcare access, financial constraints and lower socio-economic status (Castro & Mesquita, 2009; Sabaté, 2003), the findings of this review may not be globally representative.

Secondly, there is no current universally accepted method for defining and

measuring adherence (Waterman et al., 2013). Included studies used a range of definitions and measurement tools to report on adherence. Future work developing a standardised definition and approach to adherence measurement would be advantageous to aid interpretation and application of heterogeneous results.

A further limitation relates to the screening process. Due to time and resource constraints, a pragmatic decision was made for one reviewer to conduct the majority of the title/abstract and full text screening. To assess the reliability of this approach, a second reviewer independently screened a substantial subset of records (25% of abstracts and 28% of full texts), with high levels of agreement observed (Cohen's kappa = 0.89 and 0.78, respectively). This strategy aimed to provide a practical balance between rigour and feasibility; however, it is acknowledged that single screening can introduce the risk of selection bias and result in the inadvertent exclusion of relevant studies (Waffenschmidt et al., 2009). Although the substantial level of agreement provides reassurance regarding the consistency of screening decisions, full dual screening would have further strengthened the reliability of the review.

Finally, although "expressed importance" was part of a pre-established criterion for identifying the most influential TDF domains, applying this criterion required some degree of subjectivity.

2.6 Conclusion

This review presents a comprehensive synthesis of modifiable determinants influencing adherence to glaucoma medication, using the TDF. Multiple factors, from four theoretical domains, were identified as key in influencing adherence behaviour. Interventions targeting these domains are more likely to be effective in improving medication adherence. This review also highlights the impact that treatment characteristics, lack of patient understanding, forgetfulness and administration difficulties have on adherence behaviour. Addressing these issues through multimodal, theory-informed strategies may enhance the overall effectiveness of future interventions.

Importantly, the review identifies gaps in the current literature, particularly the limited exploration of adherence determinants from the perspectives of HCPs, carers and different patient sub-groups. Future work is recommended in these areas in order to encourage behavioural change where necessary.

The insights gained from this review will help form the foundation for the development of a behaviour change intervention, as outlined in the subsequent chapters of this thesis.

2.7 Dissemination of findings

The work presented in this chapter formed the basis of a peer-reviewed publication in *Ophthalmic and Physiological Optics* (Bott et al., 2023), available [here](#). The article was ranked within the top 10% of most-viewed papers published by the journal in 2023 (see Appendix A7).

Chapter 3 Defining Acceptable Medication Adherence in Glaucoma Care: a Delphi consensus survey of UK Eye Care Professionals

3.1 Chapter overview

The previous chapter explored factors influencing glaucoma medication adherence across patients, eye care professionals (ECPs), and the wider healthcare system. These findings will help inform the development of a patient-targeted intervention to support adherence. However, for the intervention to achieve maximum impact, it is important to determine not only how to intervene, but also when the intervention should be introduced.

Currently, no universally accepted definition exists for what constitutes an acceptable level of glaucoma medication adherence. To address this gap, this study seeks to establish a clinically relevant benchmark. Determining this level will help provide a clear standard for identifying patients who may require additional support and will guide the future design and timing of the proposed intervention.

This chapter presents findings from a Delphi consensus survey (Hasson et al., 2000) conducted with UK ECPs to inform the development of a benchmark definition that will guide when and for whom the intervention should be delivered.

3.2 Introduction

Adherence to ocular hypotensive medication is important for effective glaucoma management and preventing vision loss. However, as discussed in Section 1.6 (page 42), nonadherence remains a persistent challenge in everyday clinical practice. As highlighted in Section 2.4.3 (page 93), ECPs often find it difficult to accurately detect nonadherence, while patients frequently overestimate their adherence, further complicating clinical assessment. When nonadherence is not recognised, opportunities for early intervention and the prevention of disease progression are lost.

Although various tools exist to assess medication adherence, as discussed in Section 1.11 (page 53), their use in routine practice is limited by constraints on time, workforce, and resources. Furthermore, there is currently no universally accepted method for measuring adherence in glaucoma care (Waterman et al., 2013), nor is there an agreed benchmark to define what constitutes an acceptable level of adherence (Broadway & Cate, 2015).

In many chronic conditions, an 80% threshold is commonly used to distinguish between adherent and nonadherent patients (Andrade et al., 2006). In glaucoma, research suggests that lower adherence rates are associated with worse clinical outcomes, including progression of visual field loss (Sleath et al., 2011; Newman-Casey et al., 2020; Rossi et al., 2011). However, variability in how adherence is measured, differences in disease severity, and variations in treatment characteristics make it difficult to establish a single threshold suitable for all glaucoma patients.

Given the preventative nature of glaucoma treatment and the long-term risks associated with nonadherence, it is important to develop a clinically meaningful and practical definition of acceptable adherence. Establishing such a benchmark would support clinicians to identify patients who may benefit from targeted support and to guide the timing and targeting of interventions aimed at improving adherence.

3.2.1 Study aim

The aim of this chapter is therefore to develop a clinically relevant benchmark for acceptable glaucoma medication adherence by achieving consensus among UK ECPs with experience in glaucoma care. Specifically, the study seeks to define the percentage of prescribed doses that would constitute an acceptable level of adherence. Establishing this benchmark will provide a foundation for identifying patients who require additional support and will inform the future design and timing of the proposed patient-level adherence intervention.

3.2.2 Delphi methodology

The Delphi method is a structured research technique used to achieve consensus among a panel of experts through a series of iterative survey rounds (Barrett & Heale, 2020). It is particularly useful in healthcare for addressing complex issues where evidence may be limited or conflicting and is also used to develop guidelines, best practices and policy recommendations (Shang, 2023).

Participants are usually selected based on their expertise in a specific field to ensure that responses are well-informed and relevant to the topic in question. Typically, the process involves several rounds of questionnaires, during which participants rate or rank specific items. After each round, anonymised feedback is shared with the group, allowing participants to reconsider their responses in light of the collective results. This iterative process helps refine opinions and supports the gradual convergence towards consensus (Nasa et al., 2021).

A key advantage of the Delphi method is the anonymity it offers, minimising the risk of dominant individuals influencing the group and reducing pressure to conform, which can occur in face-to-face discussions (Hsu & Sandford, 2007). Additionally, the method allows for remote participation, as information is exchanged via email or other electronic means, enhancing accessibility and enabling a wider geographic spread of participants.

In glaucoma research, the Delphi method has been successfully applied to develop standards for virtual glaucoma clinics (Kotecha et al., 2018), establish a practical definition of stable glaucoma among UK ECPs (Lakhani et al., 2020, 2021), and create a competency framework for optometrists with a special interest in glaucoma (Myint et al., 2010).

Given these advantages, the Delphi approach was selected to develop a consensus definition of acceptable glaucoma medication adherence to support the design and implementation of the proposed adherence intervention in this project.

3.3 Materials and methods

3.3.1 Ethical approval

Ethical approval for this consensus study was granted by the Optometry Research and Ethics Committee at City St George's, University of London (Reference number: ETH2324-1874, Appendix B1). All participants provided written informed consent, adhering to the principles outlined in the Declaration of Helsinki.

3.3.2 Design

A modified two-round Delphi survey was conducted via email. A two-round approach was selected because there was sufficient existing literature informing the topic (Hsu & Sanford, 2007). Given that the study sought expert opinions on a straightforward and well-defined issue, two rounds were considered sufficient to achieve consensus. Without this literature base, three or four rounds would have been more appropriate, with the first round exploring the panel's opinions on suggested adherence levels.

The survey was developed using the online tool Qualtrics (<https://www.qualtrics.com/en-gb/>), with each questionnaire designed to take no longer than ten minutes to complete. It included questions on participant demographics and a key clinical question regarding what constitutes an acceptable level of glaucoma medication adherence. The clinical question and associated response options were informed by existing literature and the research team's clinical knowledge in glaucoma management.

3.3.3 Piloting the survey

Before starting the Delphi study, the survey was piloted by the research team, comprising five optometrists, two of whom are specialist practicing glaucoma optometrists. The aim of the pilot was to ensure that the survey was concise, clear, and appropriately structured. Following the pilot minor refinements, such as wording

adjustments, were made to enhance clarity. The revised version was subsequently used in the main study.

3.3.4 Participants and recruitment

The invited panel consisted of 18 practicing UK-registered ECPs from various professions, including ophthalmologists, optometrists working in both hospital and community settings, nurse practitioners and orthoptists, all actively involved in glaucoma care. This multidisciplinary representation aimed to reflect the increasingly team-based nature of glaucoma management in the UK (NICE, 2022; The Royal College of Ophthalmologists, 2020).

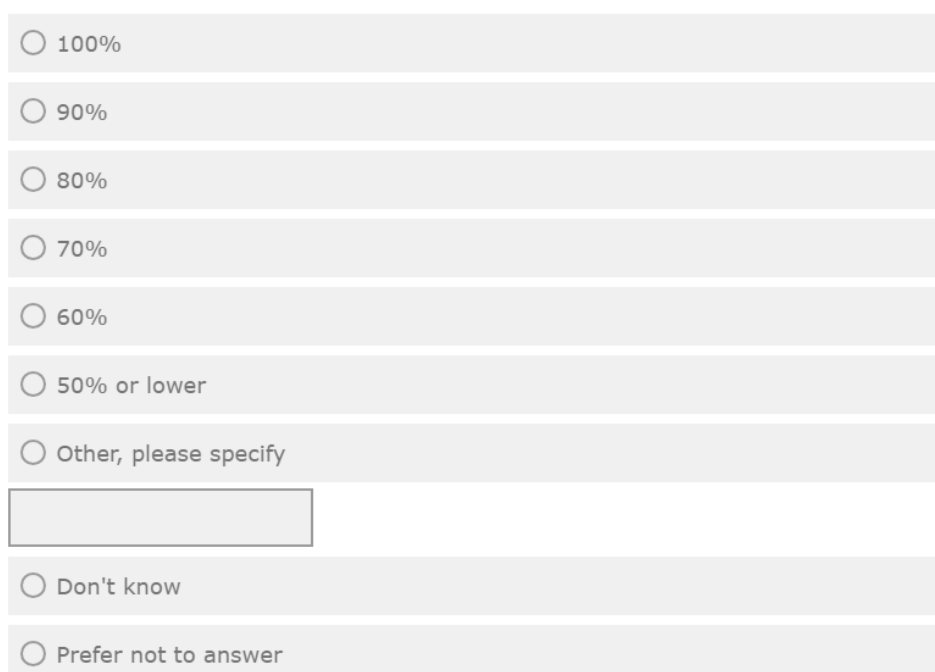
Participants were required to be currently practicing in glaucoma care to ensure relevant and up-to-date expertise. Recruitment used purposive sampling of individuals who either had participated in a previous stage of the project and expressed interest in further involvement, or from ECPs known to the research team. The aim was to recruit a panel that was representative of UK ECPs working in glaucoma care, with variations in age, professional background, work setting, and geographical location. In terms of Delphi methodology, the sample could be described as homogeneous, in that all participants shared specific expertise in glaucoma care, a feature considered desirable for studies focusing on targeted clinical questions such as defining an acceptable level of medication adherence (Nasa et al., 2021). At the same time, within this shared experience, the panel exhibited sufficient diversity to capture a broad range of professional perspectives.

Recruitment was conducted via email invitation, which included a participant information leaflet (see Appendix B2). Out of the 18 participants initially contacted, 16 responded and consented to participate. This sample size was considered suitable, as a minimum of 12 participants is generally recommended to achieve valid and reliable consensus in Delphi studies (Murphy et al., 1998).

3.3.5 Survey administration

Round one: Participants who agreed to take part received an email with instructions on how to access the anonymous online survey. Full details of the Round one survey are provided in Appendix B3. The key clinical question (see Figure 3.1) asked participants to select the percentage of prescribed eyedrops a glaucoma patient needs to take correctly to be considered adherent. Participants could also select 'Other' or 'Don't know,' recognising that medication adherence is a challenging area and that some participants might feel unable to quantify a response. An optional free-text box was provided to allow participants to justify their choice or offer additional comments. Participants were given four weeks to complete the survey, with reminder emails sent one week and two days before the deadline to encourage timely responses and minimise withdrawals.

When managing patients on long-term ocular hypotensive therapy, what percentage of eyedrops would they need to take correctly to define an 'acceptable' level of medication adherence? It is assumed that a value less than this would constitute non-adherence.



The image shows a survey interface with the following elements:

- A list of radio button options: 100%, 90%, 80%, 70%, 60%, 50% or lower, Other, please specify, Don't know, and Prefer not to answer.
- A text input box located below the 'Other, please specify' option.

Figure 3.1 Clinical question asked in Round one of the Delphi survey

Round Two: The median response from Round One was calculated to guide the next stage. The median was chosen because it represents the central tendency of the group and is less influenced by outliers than the mean, making it suitable for this sample size (McKenna et al., 2011). The median is straightforward to determine and interpret, making it easier for participants to understand the feedback provided between rounds.

Based on the median findings and feedback from Round one, the clinical question and options were refined. For example, if the median indicated a strong preference for a particular option, the second-round options focussed more closely around that range. The second-round survey, which can be found in Appendix B4, was then distributed by email and included anonymised feedback from the panel as well as the median percentage identified in Round one. Participants were asked to reconsider their initial responses in light of the panel's feedback and select a response for Round two (See Figure 3.2). They were again invited to provide additional free-text comments if desired. As in Round One, participants had four weeks to complete the survey, with reminder emails sent one week and two days before the deadline.

In the initial survey, we found a median value of 90% adherence to be an acceptable level.

When managing patients on long-term ocular hypotensive therapy, what percentage of eyedrop adherence **for the majority of glaucoma cases** would you define as an 'acceptable' level of medication adherence? It is assumed that a value less than this would constitute non-adherence.



☐ 100%

☐ 90%

☐ 80%

Figure 3.2 Clinical question asked to participants in Round two of the Delphi survey

3.3.6 Data analysis

Descriptive statistics were used to summarise the demographic characteristics of the participants.

Criteria for determining consensus: There is no universally agreed definition for consensus in Delphi studies (Diamond et al., 2014), and a review of consensus measurement approaches has highlighted the lack of a standardised method (von der Gracht, 2012). In this study, consensus was defined as at least 75% agreement among participants on a single medication adherence option. This threshold was selected to ensure robust and reliable results, in line with recommendations suggesting that a 70–80% threshold is appropriate for achieving meaningful and valid outcomes (Shang, 2023).

3.4 Results

In Round one of the survey, 16 of the 18 invited participants responded. However, one questionnaire was incomplete as it did not answer the key question regarding medication adherence. This response was excluded from the analysis, resulting in a response rate of 83% (15/18).

In Round two, 16 participants again submitted responses. However, two questionnaires were incomplete due to missing answers to the clinical question on medication adherence. These were excluded from the analysis, resulting in a final response rate of 78% (14/18).

The demographic characteristics of the participants are presented in Table 3.1.

Table 3.1 Demographic characteristics of Delphi participants

Participant demographics		N (%)
		N=15 total
Gender	Female	11 (73)
	Male	4 (27)
Age (years)	21-30	2 (13)
	31-40	3 (20)
	41-50	6 (40)
	51-60	4 (27)
Profession	Specialist glaucoma optometrist	5 (33)
	Specialist glaucoma ophthalmologist	4 (27)
	Specialist glaucoma orthoptist	4 (27)
	Glaucoma nurse practitioner	2 (13)
Time worked in glaucoma care (years)	2-5	2 (13)
	6-10	4 (27)
	11-15	4 (27)
	16-20	3 (20)
	>20	2 (13)
Work location	Northwest	3 (20)
	London	6 (40)
	Southeast	2 (13)
	Southwest	1 (7)
	Yorkshire	3 (20)

In Round one, the median value for acceptable medication adherence was 90%. Just over half of the respondents (8 out of 15) indicated that 90% adherence was acceptable. However, this did not meet our pre-defined 75% agreement criterion for consensus, as only 53% of respondents agreed on this threshold. Figure 3.3 illustrates the distribution of responses by profession.

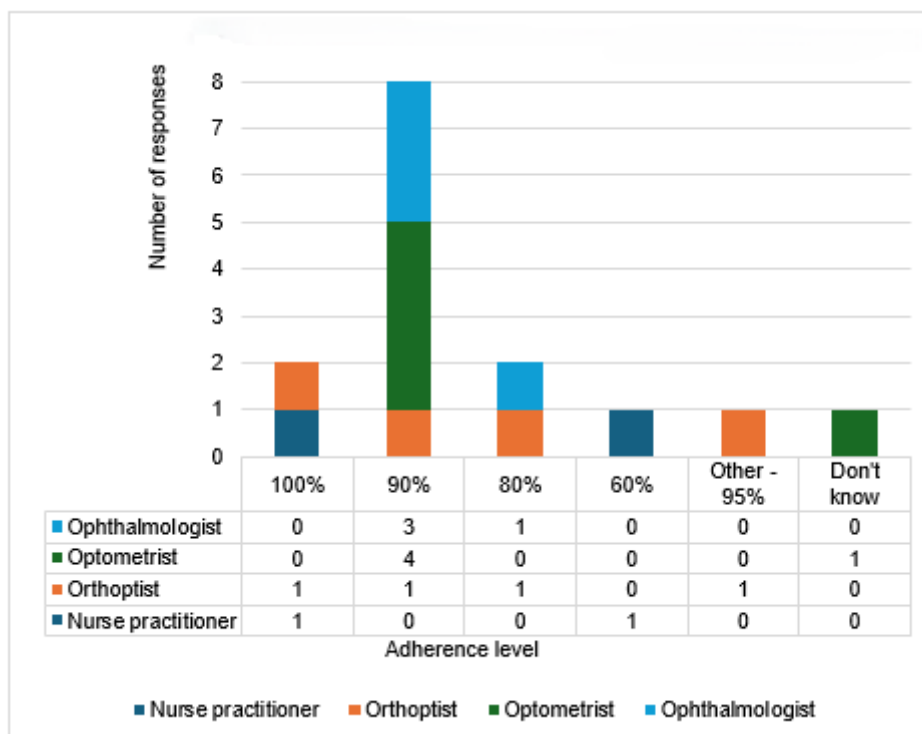


Figure 3.3 Distribution of medication adherence levels selected in Round one of Delphi survey

Participants were given the opportunity to make comments to justify their responses. Four comments were provided, three by optometrists and one from an orthoptist, and these are presented in Table 3.2. In general, the feedback highlighted that defining an acceptable level of adherence should consider individual factors, such as the severity of the disease, the specific treatment regimen and the patient's unique circumstances. This feedback informed the Round two survey.

In response to the feedback from Round one, the question was slightly modified in Round two to reflect that a generic adherence level may not be applicable to all cases. The revised question included the phrase "for the majority of glaucoma cases." Given that 87% of respondents in Round one selected at least 80% as an acceptable level of medication adherence, the options in Round two were adjusted to reflect this trend.

In Round two, the majority of respondents (8 out of 14) selected 90% adherence as the acceptable threshold. However, consensus was still not achieved, with only 57% of respondents agreeing that, in general, glaucoma patients must correctly administer at least 90% of their eyedrops to be considered adherent. Figure 3.4 illustrates the distribution of responses by profession.

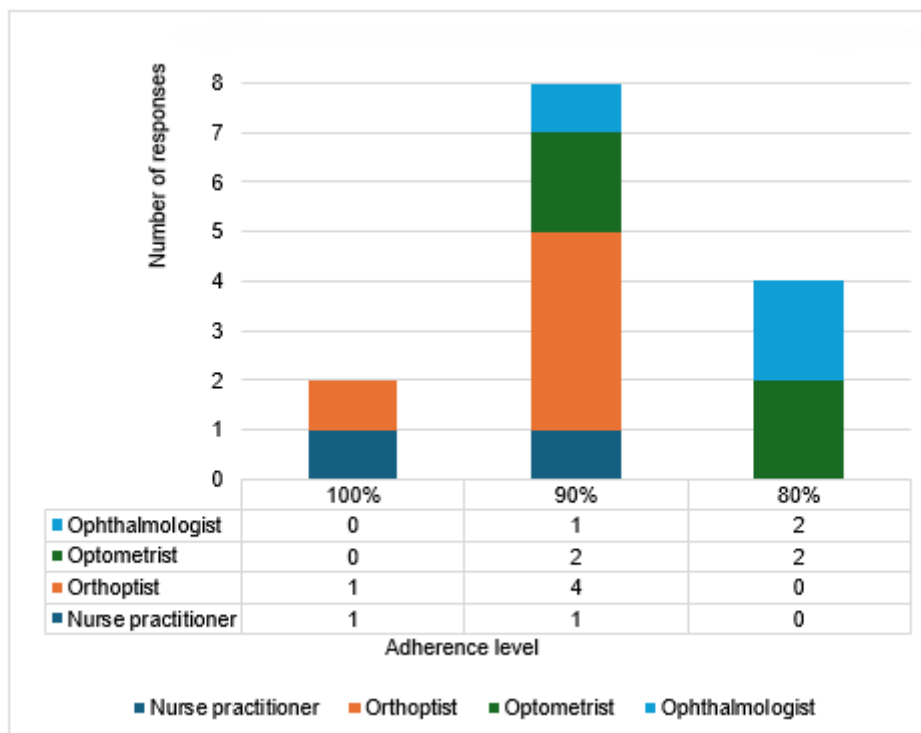


Figure 3.4 Distribution of medication adherence levels selected in Round two of Delphi survey

Two additional comments were provided in Round two, both by optometrists (see Table 3.2). These further emphasised that disease status and IOP need to be considered when determining an acceptable level of medication adherence.

Table 3.2 Free text responses generated during Rounds one and two of Delphi survey

Free text responses generated during Round one of Delphi survey
<i>"The response above is generic - someone with advanced disease is likely to need virtually 100%, whereas someone with OHT may be OK with a lesser rate of adherence - the IOP- lowering is key - we do know this is protective versus an absolute percentage adherence rate, so what is 'acceptable' adherence is only part of the question"</i> [R008 optometrist]
<i>"I may accept less than 90% if the patient was on multiple drop therapies and the lower percentage was only applicable to part of the treatment regimen. For example, they were missing one of their 2 doses of Cospot a few days a week but were taking their PGA 100% of the time"</i> [R009 optometrist]
<i>"I assume that if a patient's condition is stable, adherence is 'acceptable'. If their condition is not stable then either their adherence is an issue or there is progression despite acceptable adherence. I think, 'acceptable' depends on the risk of progression to/in sight loss. More advanced, early onset or rapidly progressing cases require better adherence to reduce the risk of sight loss than 'milder' cases. There are too many variables for me to be able to give a definitive response"</i> [R012 optometrist]
<i>"I have found that patients who are open about their adherence progression has been noted even when using drops about 80% of the time. If patients are admitting to that, they are likely to be using it less therefore I think there needs to be a high cut off as what is acceptable"</i> [R013 orthoptist]
Free text responses generated during Round two of Delphi survey
<i>"As previously mentioned, severity of disease does affect this acceptable level in specific cases"</i> [R101 optometrist]
<i>"It would depend on the starting IOP and the IOP with the treatment at 80% adherence"</i> [R102 optometrist]

3.5 Discussion

The aim of this chapter was to establish a clinically relevant benchmark for acceptable adherence to glaucoma medication through consensus among UK ECPs with experience in glaucoma care. Specifically, the study sought to define the percentage of prescribed doses that would be considered acceptable in routine clinical practice. Establishing such a benchmark is intended to help identify patients

who may benefit from additional support and guide the future development of the proposed adherence intervention.

The panel did not reach consensus on a single adherence value. Although 90% adherence was the most commonly selected option across both rounds, it fell short of the predefined 75% agreement threshold for consensus. Overall, at least 80% adherence was viewed as the minimum acceptable standard for the majority of glaucoma patients. While most ECPs supported a higher benchmark, 80% is considered a more broadly acceptable and realistic target. This threshold offers a pragmatic starting point to guide clinical decision-making and intervention planning.

However, panellist feedback highlighted that a single, fixed adherence threshold may be overly simplistic and not adequately account for individual variation in disease risk. For instance, patients with advanced glaucoma may require near-perfect adherence, while those with OHT might manage with lower adherence rates. The well-established link between IOP reduction and the preservation of visual function supports this (Agis Investigators, 2000; Garway-Heath et al., 2015; Heijl et al., 2002). A longitudinal cohort study found that patients with advanced OAG who achieved a 20% IOP reduction over ten years experienced less progression than those with smaller IOP reductions (Shin et al., 2024), confirming the importance of consistent adherence in high-risk cases.

Treatment complexity was another factor influencing perceptions of acceptable adherence. One panellist noted that a patient on multiple therapies could be viewed as adherent even if they missed doses of one medication but were fully adherent to another. Patients on multiple medications are often those with difficult-to-control IOP and are at greater risk of progression. Yet these regimens are also associated with lower adherence, as increased dosing frequency and regimen complexity are known to reduce adherence (Castel et al., 2014; Dreer et al., 2013; Olthoff et al., 2005). A lower adherence threshold in these scenarios may seem more practical, however, their increased risk profile may in fact require stricter adherence targets and earlier clinical intervention.

Individual variation in drug response, due to pharmacokinetic differences between patients, may also influence what constitutes an acceptable level of adherence. Pharmacokinetics refers to how a drug is absorbed, distributed, metabolised, and excreted by the body, and these processes can vary significantly between individuals (Agrahari et al., 2016). For example, differences in corneal permeability, tear film dynamics and systemic absorption can affect how much of a topically administered drug reaches its target tissue and how long it remains effective (Agrahari et al., 2016; Virani & Rewri, 2024). As a result, two patients with the same level of adherence may experience different therapeutic outcomes. A patient with rapid drug clearance or poor ocular absorption may require stricter adherence to maintain IOP control, while another with slower clearance may achieve stability with lower adherence. This variability suggests that a fixed adherence threshold may not be universally appropriate and supports the need for personalised adherence benchmarks.

A further challenge in defining adherence benchmarks relates to the reliance on self-reporting, which is known to overestimate actual adherence (Ajit et al., 2010; Cate et al., 2014; Sayner et al., 2015). One panel member noted that patients who report using their drops about 80% of the time may be using them even less. As a result, they recommended setting a high threshold for what is considered acceptable adherence. This supports the use of a conservative benchmark and highlights the importance of interpreting self-reported adherence with caution. Establishing a higher minimum standard may help to compensate for overestimation and avoid missing patients who are at risk due to suboptimal medication use.

In addition to the limitations of self-reporting, temporal patterns of nonadherence also warrant consideration when defining adherence thresholds. Some patients may increase their drop use in the days leading up to a clinic appointment, creating a misleading impression of consistent adherence. This behaviour has been observed in electronic monitoring studies, where adherence improves shortly before scheduled visits and declines afterwards (Okeke et al., 2009a; Zaharia et al., 2022). Such patterns may result in IOP readings that appear well-controlled during clinic assessments, despite suboptimal adherence over the longer term. This has

implications for both adherence measurement and threshold setting, as it suggests that clinic-based assessments may overestimate true adherence and risk missing patients who require additional support. A conservative benchmark may help to account for these fluctuations and ensure that patients with inconsistent medication use are not overlooked.

The feedback also highlighted that adherence must be considered in relation to IOP control. Both the initial IOP and the IOP achieved through treatment are important considerations when determining whether adherence is acceptable. This aligns with recommendations from the EGS (2021), which stress the importance of individualised target IOPs tailored to a patient's risk profile. Accordingly, adherence should not be evaluated in isolation but interpreted within the broader clinical context, including disease severity, IOP trends, and treatment complexity.

3.5.1 Risk-based glaucoma care models

The difficulty in establishing a universal adherence threshold in this study highlights a need for personalised adherence targets based on individual patient risk. While an 80% threshold is useful as a general guide, especially in routine care or low-risk cases, it may not be appropriate for all patients. This benchmark can support clinical decision-making, particularly in virtual settings and where non-medical HCPs are increasingly involved in glaucoma management (Nikita et al., 2023). In England, frameworks such as the Clinical Council for Eye Health Commissioning's system assurance model (2018) and the Royal College of Ophthalmologists' Way Forward report (2020) support a stratified approach to glaucoma care. In these systems, non-medical HCPs manage lower-risk patients, while consultant-led clinics focus on more complex or high-risk cases (Harper et al., 2020). In such stratified models, a generic 80% threshold may have utility in routine monitoring but may not be appropriate for high-risk individuals who require tighter control and more tailored goals. Further research is warranted to examine the relationship between specific adherence levels and clinical outcomes across different patient subgroups.

3.5.2 Implications for future intervention design

Future interventions to support adherence may need to be adaptable to account for differences in clinical risk and may benefit from tools that allow individualised assessment. Emerging digital health and AI-based decision support systems offer promising potential in this space (Kanyongo & Ezugwu, 2023). AI-supported models could be explored in glaucoma to help clinicians identify patients most in need of adherence support and ensure that intervention occurs at the right time.

3.5.3 Strengths and limitations

A key strength of this study was the high response rates achieved across both rounds, 83% in Round one and 78% in Round two, which exceed the recommended 70% threshold for maintaining methodological rigour (Sumsion, 1998). These high response rates likely reflect the clarity and brevity of the survey and the convenience of email-based participation, which are important for time-constrained, clinically active ECPs.

Another strength was the composition of the expert panel, which included a multidisciplinary mix of ophthalmologists, optometrists, orthoptists, and nurse practitioners working in both primary and secondary care settings. While orthoptists are not currently authorised to prescribe glaucoma medications, their inclusion was considered important given their increasing involvement in glaucoma monitoring and patient support, particularly in relation to adherence. Additionally, the panel's gender distribution was broadly representative of the UK eye care workforce (Health Education England, 2020; General Optical Council, 2021; Nursing and Midwifery Council, 2022; Shah et al., 2023).

However, several limitations should be acknowledged. First, the use of purposive sampling and recruitment from among those individuals previously involved in the wider research project may have introduced selection bias. Nevertheless, this approach allowed for the inclusion of a clinically diverse and experienced panel.

Second, the clinical question used in the survey did not specify how medication adherence was to be assessed. In routine clinical practice, adherence is typically self-reported, which is known to overestimate true adherence levels. If panel members assumed self-reporting as the default measure, this may have influenced their responses.

A further limitation is that the time period over which adherence was to be assessed was not defined in the survey. Although this issue was carefully considered during the design phase, no consensus exists on an optimal timeframe. A US-based study has suggested a one-month recall period as a practical application in clinical settings (Cho et al., 2022), but this has not yet been validated and was therefore not used. In addition, Round 2 of the survey did not include a “don’t know” or “other” response option which may have constrained participants to select from the provided options even if none fully reflected their views.

Finally, the survey did not explore whether acceptable adherence thresholds should differ between high-risk and low-risk patients. This limitation was reflected in participant feedback, which highlighted that disease severity, IOP and treatment regimen influence what might be considered acceptable adherence. Future work could investigate adherence thresholds stratified by clinical risk profiles to provide more tailored guidance.

3.6 Conclusion

This Delphi study aimed to establish a consensus on what constitutes an acceptable level of medication adherence for patients with glaucoma. Although a single adherence threshold was not universally agreed, the study provides a clear foundation for future work by identifying a minimum benchmark of 80% adherence as acceptable for the majority of patients. It also highlights the complexity of defining a universal adherence threshold and supports the need for individualised targets informed by clinical risk of progression. An 80% benchmark may serve as a useful general guide, particularly in routine care settings, but higher-risk patients may

require more stringent adherence targets and personalised support.

These findings will help inform the development of the proposed patient-targeted intervention to support glaucoma medication adherence in later stages of this research.

Chapter 4 Factors Influencing Glaucoma Medication Adherence: A Qualitative Study of Patients and Eye Care Professionals in the UK Using the Theoretical Domains Framework

4.1 Chapter overview

The previous chapter established a benchmark for acceptable medication adherence in glaucoma, highlighting the importance of identifying patients who may require additional support. To inform the development of an effective patient-targeted intervention, it is important to understand the underlying behavioural factors that influence adherence.

This chapter presents a qualitative exploration of these modifiable behavioural determinants, as reported by patients and eye care professionals (ECPs) in the UK. Guided by the Theoretical Domains Framework (TDF), this study builds on the findings from the systematic review (Chapter 2), providing a deeper insight into the real-world influences on adherence and supports the development of a tailored, evidence-based intervention strategy.

4.2 Introduction

As previously outlined in Section 1.6 (page 42), many individuals are at risk of preventable vision loss due to sub-optimal adherence to glaucoma medication. This presents major clinical, social and economic challenges. With the global population ageing and glaucoma prevalence projected to increase, it is increasingly important to address adherence in order to optimise long-term outcomes. A deeper understanding of the behavioural factors underpinning adherence is essential for developing effective, person-centred support strategies. It is equally important for clinicians to understand the factors influencing patients' medication-taking behaviour in order to provide more tailored strategies for improving adherence.

While much of the focus in adherence research centres on patient behaviour, the role of ECPs in recognising and addressing nonadherence should not be overlooked.

ECPs are often responsible for assessing adherence during routine consultations and guiding patients toward better medication-taking habits. However, evidence suggests that clinicians frequently underestimate or misidentify nonadherence (Djafari et al., 2009; Okeke et al., 2009a), leading to missed opportunities for timely intervention which can contribute to poorer patient outcomes.

To ensure that interventions are grounded in the realities of clinical practice and patient experience, qualitative research provides a complement to literature-based findings. While the systematic review (Chapter 2) identified modifiable determinants of adherence from published studies, it did not capture the richness of first-hand perspectives, particularly in the UK context. Qualitative methods are particularly well suited to exploring the nuanced and context-specific influences on behaviour that may not be fully represented in quantitative data (Sankar et al., 2006). This phase of the research therefore aimed to capture lived experiences and professional insights to strengthen the development of an acceptable and theoretically sound adherence intervention.

The TDF previously used in the systematic review (Chapter 2) provides a 'lens' through which to examine behavioural influences across a range of domains. Although, the TDF has been applied in qualitative research studies relating to other chronic conditions (Aloudah, 2023; Smith et al., 2023; Vallis et al., 2024), it has not yet been used to explore glaucoma medication adherence through direct engagement with patients and ECPs.

4.2.1 Aims and objectives

The aim of this study was to explore the factors influencing glaucoma medication adherence, using the TDF as the guiding theoretical model. The specific objectives were to:

- Identify the barriers and enablers to glaucoma medication adherence from the perspectives of UK-based patients and ECPs

- Identify the key TDF domains most relevant to the target behaviours from the perspective of both patients and ECPs

4.3 Methods

4.3.1 Standards and Ethics

This study was conducted and is reported in accordance with the Standards for Reporting Qualitative Research (SPQR) guidelines (O'Brien et al., 2014). Ethical approval was obtained from the Research Ethics Committee of the Department of Optometry and Visual Sciences at City St George's, University of London (Ethics Approval Number: ETH2122-1657, Appendix C1). Written informed consent was obtained from all participants prior to data collection. The study adhered to the ethical principles set out in the Declaration of Helsinki.

4.3.2 Study design

This qualitative study employed semi-structured interviews, informed by the TDF, to investigate factors influencing glaucoma medication adherence. Interview guides were developed based on the TDF, with questions structured around the 14 TDF domains. Separate interview guides were developed for patients and ECPs, each tailored to their specific experiences. For patients, questions focused on behaviours related to instilling and managing their glaucoma eyedrops. For ECPs, the emphasis was on their approaches to managing medication adherence in clinical practice.

Not every TDF domain was explicitly addressed in the guide; instead, questions were structured to facilitate a natural flow, as rigid adherence to the TDF has been noted to sometimes inhibit participant expression (McGowan et al., 2020).

The development of the interview guides was informed by the research conducted in Chapter 2 and recommendations from researchers within the team (AS, JGL) experienced in qualitative research and behaviour change studies. Prior to data

collection, the interview guide was piloted with one patient and one ECP, and refinements made based on their feedback. Final versions of the interview guides for both participant groups can be found in Appendix C2.

4.3.3 Participants and recruitment

Patients

Eligible patients were English-speaking individuals aged 18 years or older who were currently prescribed, or had previously been prescribed, one or more IOP-lowering eyedrops. Recruitment was carried out through advertisements with the charity Glaucoma UK (via their website, magazine and telephone helpline), as well as through social media platforms (e.g., X formerly Twitter, LinkedIn). Purposive sampling was used to aim for a diverse sample based on age, ethnicity, geographical location, number of prescribed eyedrops, and duration of eyedrop use.

Eye Care Professionals

UK-registered ECPs (ophthalmologists, optometrists, orthoptists, or nurse practitioners) were eligible if they were aged over 18 years old and involved in managing glaucoma care either in primary or secondary care settings. Recruitment strategies included advertisements through professional organizations (e.g., The Royal College of Ophthalmologists, College of Optometrists, British and Irish Orthoptic Society), social media, and the UK and Eire Glaucoma Society (UKEGS) annual conference in 2022. To aim for diversity, practitioners were purposively sampled based on age, gender, ethnicity, location within the UK, experience levels, and professions.

4.3.4 Procedure

One-on-one interviews were conducted online via Zoom (San Jose, CA, Zoom Video Communications Inc) by the same researcher (DB) between September 2022 and February 2023. Both the participant and researcher kept their videos turned on to

facilitate engagement and rapport. Interviews were audio-recorded, transcribed verbatim, and fully anonymised to ensure no individual could be identified.

4.3.5 Sample size

The sample size for each participant group was guided by the principle of data saturation in theory-informed interviews, where interviews continue until no new themes emerge (Francis et al., 2010). Following the 10+3 principle, we aimed to conduct at least 10 interviews per group, with additional interviews performed as necessary until saturation was reached.

4.3.6 Researcher characteristics and reflexivity

The primary researcher conducting the interviews (DB) is an experienced ECP working in glaucoma care. This background provided valuable insights into the clinical aspects of glaucoma management and the challenges related to medication adherence. While this expertise facilitated rapport with participants, it also required ongoing reflexivity to minimise potential biases in data interpretation. Throughout the study, DB remained conscious of how her clinical knowledge and preconceptions could shape both data collection and analysis, always trying to ensure that participants' perspectives were accurately represented.

4.3.7 Data analysis

Data were organised using NVivo 12 software (QST International, Doncaster, Australia). Analysis was conducted separately for patients and ECPs, following a combined content and framework analysis approach. As recommended by Atkins et al (2017) the analysis followed a stepwise process (see Figure 4.1):

(1). **Familiarisation process:** After transcription of the interviews, an in-depth familiarisation process was undertaken, which involved reading and re-reading the transcripts and listening to the audio recordings to gain a comprehensive

understanding of the data.

(2). **Deductive analysis:** Participant responses were coded into one of the TDF domains, categorising each response as either a barrier or enabler to eyedrop adherence. To guide this process a coding framework was collaboratively developed by the researchers (DB, AS, DE, JGL, and PC) after the first two pilot interviews and refined throughout data collection. For example, if a participant mentioned they didn't take their medication due to not understanding its importance, this would be coded as a barrier under the *Knowledge* domain. The coding framework for both participant groups is available in Appendix C3. The primary researcher (DB) deductively coded all transcripts, and a second researcher (PC) independently coded the same data to enhance coding reliability. Any disagreements were resolved through discussion and consensus between DB and PC, or with input from a third reviewer (AS) when necessary.

(3). **Inductive analysis:** Key themes were generated for each participant group based on the data within each domain. These themes, referred to as "belief statements" in TDF literature, were categorised as barriers, enablers, or mixed influences on adherence (i.e., themes that acted as barriers for some participants and enablers for others). The primary researcher (DB) generated and classified the key themes. Two reviewers (PC and AS) independently reviewed the generated themes to ensure they accurately represented the data. Any discrepancies were resolved through discussion until consensus was reached.

(4). **Identifying salient domains:** The most prominent domains representing barriers and enablers to glaucoma medication adherence were identified using established criteria (Prothero et al., 2022; Sethu et al., 2021): (a) frequency of coding (number of participant responses within a TDF domain) (b) elaboration (number of themes per domain) and (c) spontaneity (whether responses arose spontaneously or were prompted by the interview guide).

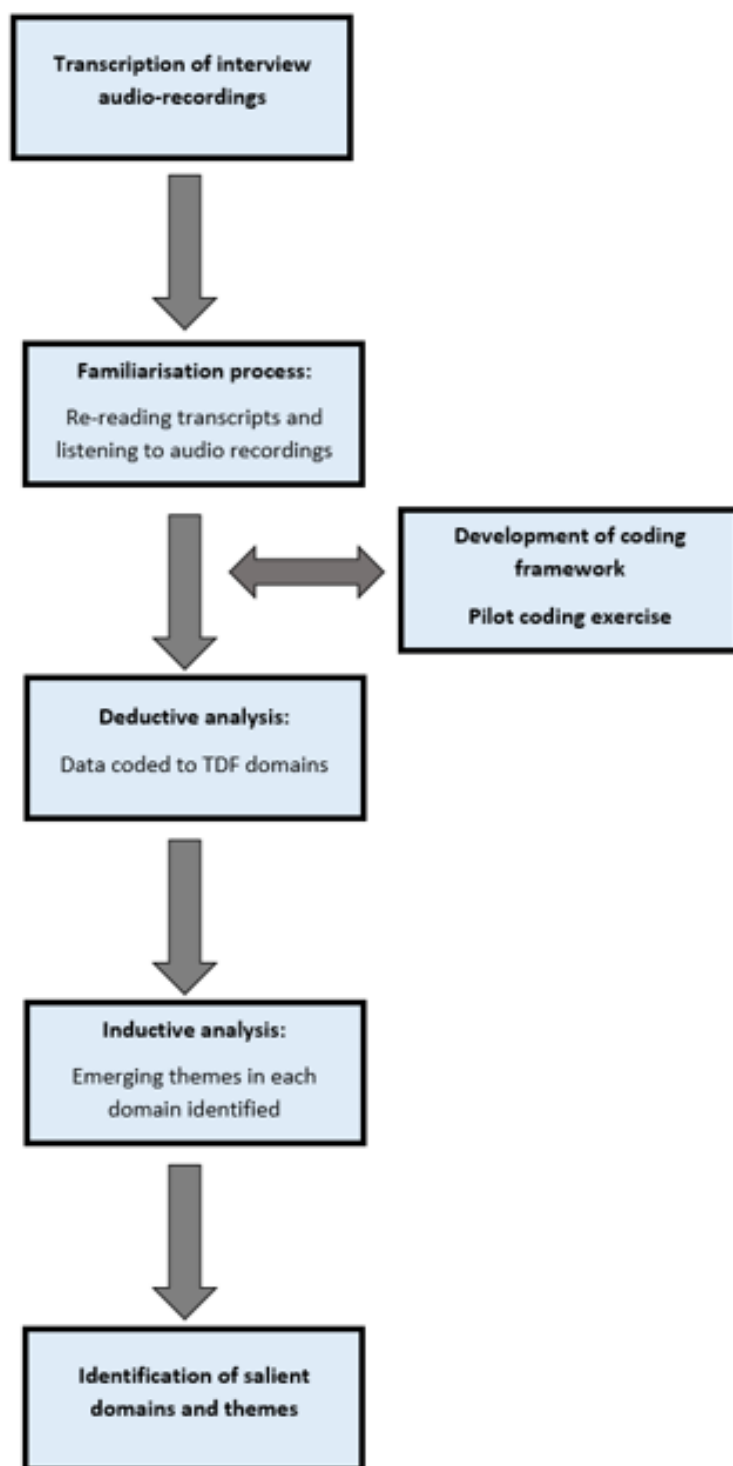


Figure 4.1 Flow chart representing step-by-step process of data analysis. Abbreviation: TDF, Theoretical Domains

4.4 Results

4.4.1 Participant characteristics

A total of 13 patients and 13 ECPs participated in the interviews. Interview duration ranged from 28 to 75 minutes, with an average of 57 minutes for patient interviews and 40 minutes for those with ECPs. Data saturation was reached after 13 interviews in each group.

Among the patient participants, ten were classified as adherent (reporting no missed doses or only one missed dose in the past month), two were unintentionally nonadherent, and one was intentionally nonadherent. Of the 13 ECPs, seven were able to prescribe glaucoma medications. Participant characteristics are detailed in Tables 4.1 and 4.2.

Table 4.1 Patient participant demographics

Patient demographics		N (%) N=13 total
Gender	Female	6 (46)
	Male	7 (54)
Age (years)	31-45	1 (8)
	46-60	4 (31)
	61-74	6 (46)
	75-90	2(15)
Ethnicity	White British	11 (85)
	White Other	1 (8)
	Caribbean British	1 (8)
Location	England	11 (85)
	Wales	1 (8)
	Scotland	1 (8)
Highest level of education	School education (up to 16)	3 (23)
	School education (up to 18)	2 (15)
	Degree or higher	8 (62)
Occupational status	Full-time job	6 (46)
	Part-time job	2 (15)
	Retired	5 (38)

Type of glaucoma (according to patient)	POAG	9 (69)
	PACG	2 (15)
	2° glaucoma	2 (15)
Number of topical glaucoma medications ¹	1	4 (33)
	2	4 (33)
	3	1 (8)
	4	3 (25)
Duration of glaucoma eyedrop usage (years)	<5	4 (31)
	5-10	3 (23)
	11-20	3 (23)
	>30	3 (23)
Number of eyedrop instillations per day ¹	1	4 (33)
	2	2 (17)
	>2	6 (50)
Eyedrop administration ¹	Self-administer	10 (83)
	Dependence on others	2 (17)
¹ P009 currently not using eyedrops since had surgery in 2021 hence N=12		

Table 4.2 ECP participants demographics

ECP demographics		N (%) N=13 total
Gender	Female	11 (85)
	Male	2 (15)
Age (years)	18-30	3 (23)
	31-45	6 (46)
	46-60	4 (31)
Ethnicity	White	6 (46)
	Asian	6 (46)
	Afro-Caribbean	1 (8)
Location in UK	London	7(54)
	Yorkshire	2(15)
	Liverpool	1(8)
	Kent	1(8)
	Birmingham	1(8)
	Cornwall	1(8)
Profession	Optometrist	3 (23)
	Ophthalmologist	4 (31)
	Orthoptist	4 (31)

	Nurse Practitioner	2 (15)
Time worked in glaucoma care (years)	<1	1 (8)
	5-10	6 (46)
	11-20	4 (31)
	>20	2 (15)

4.4.2 Outcomes

Salient domains

Barriers and enablers to medication adherence for patients were identified across 12 of the 14 TDF domains, with the exceptions being *Optimism* and *Reinforcement*. For practitioners, barriers and enablers spanned 11 domains, excluding *Optimism*, *Intentions*, and *Emotion*. Applying the established criteria of frequency, elaboration, and spontaneity, we identified the most salient domains influencing patient adherence behaviour, as well as those relevant to ECPs in managing adherence. Table 4.3 ranks these domains by their relevance to medication adherence. Nine domains emerged as particularly important for patients and seven for ECPs.

Key themes within these domains are described below, with a summary provided in Tables 4.4 and 4.5. Remaining themes and domains are included in Appendix C4.

Table 4.3 Relevance of Theoretical Domains Framework (TDF) domains to medication adherence based on frequency, elaboration, and spontaneity for Patients and Eye Care Professionals (ECPs)

TDF Domain	Patient group			TDF Domain	ECP group		
	Frequency (number of patients reporting barriers/enablers within domain, max N=13)	Elaboration (number of themes per domain)	Spontaneity (frequency of spontaneous response)		Frequency (number of patients reporting barriers/enablers within domain, max N=13)	Elaboration (number of themes per domain)	Spontaneity (frequency of spontaneous response)
Environmental Context and Resources	13	4	0	Environmental Context and Resources	13	5	2
Skills	12	2	0	Social/ Professional Role and Identity	12	1	1
Goals	13	1	0	Beliefs about capabilities	13	1	0
Memory, Attention and decision processes	13	1	0	Knowledge	12	1	0
Social Influences	11	1	2	Skills	12	1	0
Behavioural Regulation	13	1	0	Memory, Attention and decision processes	11	1	0
Knowledge	11	1	1	Behavioural Regulation	6	1	3
Beliefs about capabilities	10	1	0	Reinforcement	6	1	0
Beliefs about consequences	8	1	2	Social Influences	4	1	0

Emotion	5	1	0	Beliefs about consequences	4	1	0
Social/ Professional Role and Identity	3	1	0	Goals	2	1	1
Intentions	2	1	0	Optimism	0	0	0
Optimism	0	0	0	Intentions	0	0	0
Reinforcement	0	0	0	Emotion	0	0	0

Patients (also refer to Table 4.4)

Environmental Context and Resources

Changes in patients' lifestyles, such as going on holiday, visiting family, or working shifts, often posed barriers to adherence. Patients noted that morning doses were generally easier to manage, while doses throughout the day or at night were particularly challenging for those with busy work schedules or evening commitments.

Difficulties obtaining medication, often due to eyedrops being out of stock, were also common barriers to adherence. Several patients mentioned they kept reserve supplies as a precaution to ensure they could maintain adherence in case there were difficulties obtaining repeat prescriptions. On the other hand, the type of eyedrop container played a role in supporting adherence. Many patients found individual unit dose vials more practical, especially when traveling, as they were easier to carry. However, some expressed frustration about the inconsistency in bottle design between different manufacturers, wanting more uniformity to make the bottles easier to use and recognise.

Issues within the healthcare system also hindered adherence. Patients described busy clinics as feeling *'like a cattle market,'* where long waiting times and rushed appointments left them feeling they had insufficient time to ask questions or address concerns about their eyedrops. Difficulties in contacting the eye clinic or reaching the medical secretary for prescription issues further complicated adherence, adding frustration and delays to their treatment.

Skills

Having the necessary skills to order repeat prescriptions was a key enabler of adherence. Patients who had effective systems in place for ordering medication, such as forward planning, electronic prescription ordering (e.g. via the NHS app or website), and home delivery services, were more likely to maintain a consistent supply of eyedrops and adhere to their regimen. Many patients noted that this ability

improved with time.

However, physical limitations such as poor manual dexterity or reduced vision posed barriers to administering eyedrops. Several patients mentioned that their ability to use drops was particularly challenging when they first started treatment but improved over time as they developed better techniques. As one adherent patient explained, *'At one point, my hands were very swollen and weak, and I had trouble opening the bottle, especially when it was new.'*

Goals

Preserving vision and avoiding blindness were strong motivators for all patients to adhere to their medication regimen. Many expressed the view that losing their sight would have a profound impact on their lives. One patient noted, *'It would be pretty disastrous for the lifestyle we lead.'* Patients were motivated by the need to maintain their ability to work, use a computer, drive, and read, understanding that proper use of their eyedrops was important to be able to continue with these activities.

Memory, Attention and decision processes

Forgetting to use eyedrops as prescribed was an important barrier to adherence, with nonadherent patients often mentioning they were forgetful or unaware they had missed a dose. Although adherent patients generally did not forget to use their eyedrops, some noted that when they were particularly tired, it became more challenging to remember to instil them at the correct time.

Social Influences

Social influences impacted medication adherence, with positive support from partners, family members, and HCPs playing a crucial role. Patients expressed appreciation for the resources and support offered by the patient support organisation Glaucoma UK, noting that sharing with and hearing experiences from others who also manage glaucoma and use eyedrops was particularly beneficial. This sense of community not only fostered encouragement but also provided valuable insights into effective strategies for maintaining adherence.

Behavioural Regulation

Establishing a consistent routine and utilising reminder strategies were key factors that facilitated medication adherence among patients. However, two participants noted that over time, they became de-sensitised to the sound of their alarms, rendering them less effective as reminders to instil their eyedrops. One participant remarked, *'to be honest sometimes I would hear the alarm and it's just after a while the alarm becomes less effective.'*

Knowledge

Understanding glaucoma and the rationale behind treatment and the eyedrop regimen served as an important enabler to adherence. Both adherent and nonadherent patients demonstrated a solid awareness that using their eyedrops helped reduce IOP and preserve their vision. However, one unintentionally nonadherent patient mentioned that they lacked sufficient information about the specific timing and proper method of instilling their drops, highlighting a gap in practical knowledge.

Beliefs about capabilities

Patients who had confidence in their ability to consistently administer eyedrops over the long term were more likely to remain adherent. This belief in self-efficacy played a key role in maintaining regular use. In contrast, the intentionally nonadherent patient expressed doubts about their ability to continue using their eyedrops.

Beliefs about consequences

The belief that using eyedrops is crucial for preserving vision was a key motivator for adherence. One patient, who experienced vision difficulties but was not formally registered as sight-impaired, emphasised the importance of this belief, stating, *'I know what the consequences are if I don't [take my eyedrops].'* In contrast, the intentionally nonadherent patient expressed scepticism about the necessity of eyedrops, questioning their *'authenticity.'*

Eye Care Professionals (also refer to Table 4.5)

Environmental Context and Resources

ECPs frequently noted that time constraints greatly hindered their ability to manage adherence effectively, particularly in busy, overbooked clinics. Limited resources, including both staff and support materials, further complicated these challenges. The unavailability of educational resources, such as information leaflets or translations in different languages, was also reported as a barrier to addressing adherence issues effectively.

In contrast, a multidisciplinary team approach and well-structured organisational support proved beneficial in facilitating adherence. Practitioners especially valued the presence of dedicated glaucoma nurses or ECLOs (Royal National Institute of Blind People [RNIB], 2024), as well as specialised glaucoma helplines, which provided essential support for patient adherence.

Issuing a clinic letter directly to patients following their appointments, which outlined their condition and treatment schedule in an understandable format, emerged as an important enabler of adherence. This proactive approach helped prevent confusion about medication regimens, allowing patients to refer back to the letter if questions arose and reducing the risk of important information being lost in the post.

Additionally, ECPs faced challenges related to medication availability, including instances where eyedrops were out of stock at pharmacies. Complications also arose when GPs failed to maintain ongoing prescriptions or did not specify that certain medications were preservative-free. In response to potential short-term medication shortages, some practitioners opted to issue interim hospital prescriptions instead of altering GP prescriptions, ensuring that patients maintained access to their necessary treatments.

Social/Professional Role and Identity

ECPs recognised their professional responsibility to address and effectively manage nonadherence among patients as an enabler. While they acknowledged that everyone involved in a patient's care, including the patients themselves, plays a crucial role, practitioners felt a particular obligation to ensure that patients understood their treatment regimens and received the necessary support to adhere to them. This sense of responsibility was especially pronounced among those practitioners who prescribed eyedrops, highlighting their crucial role in facilitating patient adherence.

Beliefs about capabilities

Beliefs about capabilities had a mixed influence on adherence management among ECPs. While some practitioners expressed confidence in their ability to detect nonadherence, others felt less assured about identifying it. There was no obvious association between age or glaucoma experience and levels of confidence. Interestingly, those who expressed greater confidence in detecting poor adherence in this cohort were typically non-prescribing practitioners. One ophthalmologist remarked *'I think the confidence of the definitions [regarding adherence/nonadherence] I've just given are pretty subjective and open to differences between different practitioners. So I would say I actually have probably a kind of let's call it low confidence in that ultimately'* [in terms of identifying nonadherent patients].

Knowledge

ECPs reported challenges in determining what constitutes an acceptable level of adherence based on patients' self-reported adherence levels. This uncertainty was identified as a barrier to effectively managing adherence. Several practitioners noted that they had *'no set way of classifying it'* leading to confusion about how to interpret patient behaviour. For instance, some practitioners were unsure whether a patient missing doses several times a month could still be considered broadly adherent or if missing just once a week indicated poor adherence.

Skills

The communication and education skills of ECPs facilitated adherence management. Practitioners emphasised the importance of engaging patients in open, honest, and non-judgmental conversations about their adherence. Direct questioning often facilitated more meaningful discussions. To further educate their patients, ECPs employed various aids, including visual representations illustrating how glaucoma affects vision, physical demonstrations on the proper technique for instilling eyedrops, and sharing test results to effectively convey important information. Practitioners noted that their ability to communicate these concepts and support adherence improved with experience.

Memory, Attention and decision processes

ECPs found tailoring their decision-making processes to align with individual patient circumstances enhanced their ability to manage nonadherence. By gaining an understanding of each patient's unique situation, practitioners were better positioned to recommend suitable alternatives. This might involve adjusting the type of eyedrops prescribed, opting for longer-acting formulations that only require once-daily administration, or exploring other options such as SLT or surgical interventions.

Behavioural Regulation

Action planning played a key role in facilitating adherence management among ECPs. For instance, orthoptists were in the process of implementing Patient Group Directives (PGDs) within their departments, enabling them to take a more active role in managing patient adherence (GOV.UK, 2017). Practitioners also highlighted the importance of ongoing professional development, such as attending Continuing Professional Development (CPD) courses or pursuing higher qualifications, which kept them better informed about medication adherence challenges.

Additionally, conducting departmental audits or holding regular meetings to discuss adherence-related issues allowed teams to identify gaps in practice and make necessary adjustments, further improving their ability to support patients in adhering to their treatment regimens.

Table 4.4 summary of key themes and illustrative quotes from patients assigned to Theoretical Domains Framework (TDF) domains identified as relevant to adherence behaviour

Theme	Barrier/Enabler/ Mixed	Illustrative quote(s)
TDF domain: Knowledge		
An understanding of glaucoma and treatment rationale	Enabler	<i>'they're [eyedrops] all aimed at reducing the pressure, is my understanding.....to keep your pressure down to reduce the damage at the back of your eye. Then, ultimately, reducing that damage is going to slow down sight loss'</i> (P003)
TDF domain: Skills		
Skills needed to order ongoing supplies of eyedrops	Enabler	<i>'I signed up with Lloyds Direct....that's a really effective way of me getting my Monopost...I just request them by mail'</i> (P007)
Poor physical skills and/or poor vision required to instil eyedrops	Barrier	<i>'I was not putting my drops in right.... I would always have to look in the mirror. I'd have to go in the mirror, angle my head and put the drops in. I could never do them straight like that, I would always be blinking, I couldn't do it.....I would taste the drops, so they wouldn't go into my eye'</i> (P012)
TDF domain: Beliefs about capabilities		
Believing can continue to use eyedrops long-term	Enabler	<i>'I'm completely confident that I can continue doing it'</i> [instilling eyedrops] (P013)
TDF domain: Beliefs about consequences		

Believing eyedrops are necessary to preserve sight	Enabler	<i>'when I decided I'm stopping medications, I didn't stop my eyedrops. So, I always kept my eyedrops. So, that, to me, has been far more important than all the other tablets and injections, and all the other nonsense that I have to have I suppose it's the preserving of eyesight'</i> (P001)
TDF domain: Goals		
Not wanting to lose sight/go blind	Enabler	<i>'I gave a talk at the Hilton Hotel about 15 years ago..... and there's a lot of people there, and the hand went up to the back, and he said how come you're so compliant? I said tell me how much of your eyesight would you like to lose? Tell me how much you think you'd like to lose? There was a bit of a hush. I said well that answers the question doesn't it – it's quite straightforward'</i> (P002)
TDF domain: Memory, Attention and decision processes		
Forgetting to instil eyedrops as prescribed	Barrier	<i>'I can be quite - not lazy, but I can be quite forgetful about putting my drops in..... So I think at least once a week I forget to put them in'</i> (P102)
TDF domain: Environmental, context and resources		
Change in lifestyle	Barrier	<i>'It's even trickier then when you go away'</i> [instilling eyedrops] (P008)
Difficulties obtaining medication	Barrier	<i>'but that one [Simbrinza eyedrops] repeatedly would be out of stock'</i> (P009)
Issues within the healthcare system	Barrier	<i>'Even when I got the secretary's phone number earlier, left a message. No one has called me back.'</i> [when patient had an issue with eyedrops] (P005)
Nature of eyedrop container	Enabler	<i>'I always carry the pilocarpine.....it's only a little tiny thing. It's a minim..... So, it just fits in the little thing in your jeans'</i> (P010)
TDF domain: Social Influences		

Positive social influence from family/partner/charities/HCPs	Enabler	<i>'One thing that's motivated me to follow the regime more correctly, has been a session I had just by accident – Glaucoma UK did a small workshop thing one morning, and the guy explained about the effectiveness of the eyedrops, and it's not, take this in the morning, take this in the evening, whatever, but he explained about the 12 hours and the 24 hours and trying to be as precise as possible' (P001)</i>
TDF domain: Behavioural Regulation		
Developing a routine and/or reminder strategies	Enabler	<i>'I'm going to bed this is the perfect time. Put my head on the pillow, Brenda then just puts the eyedrops in, gives me a good-night kiss, job done" (P007)</i>

Table 4.5 Summary of key themes and illustrative quotes from Eye Care Professionals assigned to Theoretical Domains Framework (TDF) domains identified as relevant to adherence management behaviour

Theme	Barrier/Enabler/ Mixed	Illustrative quote(s)
TDF domain: Knowledge		
Difficulties classifying an acceptable level of adherence	Barrier	<i>'I think if someone has missed it maybe in - yeah, it's difficult to have an exact cut-off'</i> (ECP009 Ophthalmologist)
TDF domain: Skills		
Practitioner communication, education and clinical skills	Enabler	<i>'I will ask them an open-ended question about their drops.....I try and ask it in a way that they're going to feel comfortable to say, oh, I'm not really using them'</i> (ECP004 Optometrist)
TDF domain: Social Professional role and identity		
Professional role in the management of adherence	Enabler	<i>'I think we have a duty to make sure that we've educated the patient so that they understand why they're on treatment'</i> (ECP005 Orthoptist)
TDF domain: Beliefs about capabilities		
Perceived confidence/lack of confidence in own ability to identify non-adherence	Mixed	<i>'I would feel fairly confident in terms of trying to identify people who are adherent to medication'</i> (ECP008 Ophthalmologist) Enabler <i>'In reality, I've got no idea.....I think as a clinician, you don't really know'</i> [if patient is adherent or not] (ECP004 Optometrist) Barrier
TDF domain: Memory, Attention and decision processes		

Tailoring decision-making process according to patient needs	Enabler	<i>'I'm looking at why they're not compliant, if they're suitable for a selective laser trabeculoplasty, and if they're not suitable, then let's work on the timings. Is it the timings? So, if it's a once-a-day drop, and we prescribed it in the morning, but they can take it at night, then maybe just give it at night'</i> (ECP013 Optometrist)
TDF domain: Environmental, context and resources		
Lack of time	Barrier	<i>'because obviously we've only got a finite amount of time. So, that can be a bit of a barrier sometimes'</i> (ECP005 Orthoptist)
Lack of resources (manpower/materials)	Barrier	<i>'we know that you know there's less resources out there. I mean we used to get District Nurses involved but I mean that's really difficult or near impossible nowadays. So you haven't even really got those options'</i> [to help patients put their eyedrops in] (ECP001 Nurse practitioner)
Multidisciplinary team/organisational structure	Enabler	<i>'I know it works well.....Manchester, they have dedicated ophthalmic nurses just within the glaucoma team and they work very well to communicate levels of questions to their patients. Here in York, we have an optician who again, those kind of queries would be fired to, so that's helpful'</i> (ECP008 Ophthalmologist)
Issuing clinic letters directly to patient after their appointment	Enabler	<i>[I] 'always give them a letter now after they've seen us. So if they get home and then sort of are confused about the regime then they can look at the letter and it's all documented what drops they're to take'</i> (ECP001 Nurse practitioner)
Lack of availability of medications	Barrier	<i>'I've had on more than a few occasions [patients] not being able to get the actual drops from their nominated pharmacies due to GPs not continuing prescribing the drops'</i> (ECP011 Orthoptist)
TDF domain: Behavioural Regulation		

Action planning and/or habit formation	Enabler	[I attended] <i>'a talk about educating patients and sight loss in glaucoma....and so following on from that I then started using it [visual illustrations] in my own practice and encouraged the people that I work with who I train to do the same'</i> (ECP005 Orthoptist)

4.5 Discussion

This study used the TDF framework to identify key barriers and enablers to glaucoma medication adherence, examining modifiable behaviours from the perspectives of both patients and ECPs. The findings contribute to existing knowledge, aligning with and expanding upon prior research in glaucoma care, and underscore the complexity of adherence behaviour shaped by multi-level influences (Bott et al., 2023; Kardas et al., 2013).

For patients, adherence-related factors covered 12 of the 14 TDF domains, with the most influential domains being *Knowledge; Skills; Beliefs about Capabilities; Beliefs about Consequences; Goals; Memory, Attention and decision processes; Environmental Context and Resources; Social Influences; and Behavioural Regulation*. Key enablers included understanding the purpose of glaucoma treatment, the physical ability to administer drops, a belief in the necessity of eyedrops to protect vision, a strong desire to preserve sight, positive social support, and a clear routine. Common barriers included forgetfulness, lifestyle changes, and systemic challenges within the healthcare system.

For ECPs, factors spanned 11 TDF domains, with *Knowledge; Skills; Social/Professional Role and Identity; Beliefs about Capabilities; Memory, Attention and decision processes; Environmental Context and Resources; and Behavioural Regulation* being central. Practitioners reported that challenges in defining acceptable adherence levels complicated their ability to identify nonadherence among patients. Time constraints and limited resources further hindered their capacity to manage adherence effectively. However, ECPs acknowledged their responsibility to promote adherence, noting strong communication, educational skills, and a multidisciplinary approach as valuable strategies for addressing adherence issues.

Both groups reported disruptions in the availability of eyedrops as an important barrier. Patients reported disruptions due to stock shortages which impacted

consistent use, while ECPs highlighted delays or errors in repeat prescriptions, especially from other HCPs, which hindered their management. Eyedrop shortages not only place an additional burden on patients, who have to go to extra lengths to source ongoing supplies but also increase the workload for practitioners and hospital staff as they handle additional patient queries (Shah et al., 2015).

This study used the TDF to systematically explore the behavioural determinants of glaucoma medication adherence from the perspectives of both patients and ECPs in the UK. The TDF offered a robust, theory-driven structure that helped uncover the complex, multi-level barriers and enablers that operate across individual, professional, and systemic levels. These findings provide an evidence base for the development of a behaviour change intervention aimed at improving adherence in clinical practice.

As outlined in Section 1.15.2 (page 72), one of the key strengths of using the TDF is its established integration with broader behaviour change frameworks. Specifically, the Behaviour Change Wheel (BCW) (Michie et al., 2011) and the Behaviour Change Technique (BCT) Taxonomy (Michie et al., 2013) support the translation of theoretical constructs into practical intervention strategies. The BCW enables identified TDF domains to be mapped onto relevant Intervention Functions (IFs), (e.g., *Education, Training and Environmental Restructuring*) and aligned with appropriate policy categories (e.g., *Legislation, Service Provision and Guidelines*). The BCT Taxonomy further strengthens this approach by offering a standardised language to describe the specific, active components of an intervention, including strategies such as *Instructions on how to perform the behaviour, prompts or cues, and behavioural practice/rehearsal*. The recently developed 'Theory and Techniques Tool' builds on this by providing an interactive way to link individual BCTs to their corresponding theoretical domains, helping to ensure that selected strategies directly target the mechanisms underlying adherence behaviour (Johnston et al., 2021).

Importantly, grounding the intervention in a clear theoretical framework not only improves its design and focus but also enhances the ability to evaluate 'why' and

‘*how*’ it works (Michie & Abraham, 2004). This transparency supports both the effectiveness and replicability of the final intervention and aligns with MRC guidance for developing complex interventions (Skivington et al., 2021).

4.5.1 Implications for Practice

Our findings suggest that improving glaucoma medication adherence requires a comprehensive multi-level approach addressing both patient and practitioner needs.

Patient-level Interventions

Patient education is essential, as understanding glaucoma and its treatment significantly impacts adherence (Newman-Casey et al., 2016a; 2016b; Tsai et al., 2003). Studies indicate that adherence improves when HCPs explain treatment rationale, provide drop administration guidance, and discuss glaucoma progression (Bott et al., 2023). This aligns with the TDF domains *Knowledge* and *Beliefs about Consequences* and the corresponding BCW IFs of *Education* and *Training*, which promote understanding and skill development.

Establishing a routine also supports adherence and is consistent with findings from other qualitative studies (Frech et al., 2021; Lacey et al., 2009). Routines draw on the TDF domains of *Behavioural Regulation* and *Memory, Attention, and decision processes*. Developing a routine that aligns with a patient’s lifestyle, rather than requiring substantial lifestyle changes, is likely to encourage automatic, habitual adherence behaviours (Arlinghaus & Johnston, 2019; Gardner et al., 2012). Interventions incorporating BCTs, such as *prompts/cues* and *self-monitoring*, could help facilitate this.

Social and family support, linked to the TDF domain *Social Influences*, plays a key role in adherence. This mirrors findings from other chronic conditions, such as diabetes, where support networks have been shown to improve patients’ ability to manage their condition (Karataş & Bostanoğlu, 2017; Miller & Dimatteo, 2013). Integrating social support systems, personalised education, and behavioural

strategies tailored to promote habit formation could further support adherence and align with the BCW IF *Environmental Restructuring*.

Practitioner-Level Interventions

For ECPs, clearer guidance from professional regulatory bodies regarding adherence and nonadherence definitions and training on strategies for identifying nonadherence may help standardise adherence management practices. Training programs informed by BCTs, such as *Instruction on How to perform the Behaviour* and *Feedback on the Behaviour*, could improve ECP practice. Online, CPD-accredited modules on adherence strategies, effective patient communication, and glaucoma management updates could offer accessible, flexible training solutions. BCW policy categories, such as *Guidelines* and *Service Provision* could help support these initiatives.

Tailored clinic letters providing relevant and accessible information, addressing the TDF domain of *Environmental Context and Resources*, can help manage adherence more effectively. Letters outlining treatment plans and emphasising adherence, align with *Education* and *Training* strategies from the BCW. Providing patients with supportive information in an understandable, digestible and relatable manner follows best practice and encourages patients to take greater responsibility for managing their condition (General Medical Council, 2023; NICE, 2021).

System-Level Interventions

Addressing healthcare system limitations, such as high patient volumes, limited clinic time, and resource shortages could further enhance adherence. These barriers fall under the TDF domain of *Environmental Context and Resources* and can be addressed through structural reforms. A multidisciplinary approach incorporating contributions from allied health professionals (AHPs) utilising each professional's expertise in areas such as patient education, clinical management, and administrative support, aligns with the BCW function of *Environmental Restructuring*. Such strategies could help create a more integrated care environment, streamlining patient management within busy clinics.

Promoting electronic prescribing, linked to the TDF domain of *Environmental Context and Resources*, has the potential to reduce prescription errors, simplify the prescription process, and improve prescription quality (Donyai et al., 2008). A co-ordinated care model that includes pharmacists, primary care providers, and glaucoma specialists could provide patients with a seamless, supportive environment. Pharmacy policies focussed on improving medication access and optimising resource distribution further support consistent adherence and align with *Environmental Restructuring*.

4.5.2 Strengths and Limitations

A key strength of this study is its focus on addressing an important evidence gap by exploring the views and experiences of both patients and practitioners regarding glaucoma medication adherence. While numerous studies have reported barriers and enablers from a patient perspective (Lacey et al., 2009; McClelland et al., 2019; Newman-Casey et al., 2015b), to our knowledge this is the first study to investigate factors influencing adherence from the perspectives of both patients and practitioners.

Another strength is the use of the TDF, which provides a structured, theory-based approach for identifying behavioural influences on adherence. This robust and replicable methodology lays the groundwork for developing evidence-based behaviour change strategies that can be tailored to address modifiable barriers to adherence for both patients and practitioners. Importantly, behaviour change interventions developed with a similar approach have been effective in improving medication adherence among individuals with Type 2 diabetes (Teo et al., 2024).

The inclusion of practitioners from diverse professional backgrounds further enhances our study's relevance, reflecting the increasingly multidisciplinary nature of glaucoma care in the UK, where shared-care models are often adopted to meet rising demand (NHS England, 2019; NICE, 2022; The Royal College of Ophthalmologists, 2020).

However, several limitations should be considered when interpreting the findings. First, while most patients in our sample reported high adherence, self-reported adherence often overestimates true adherence rates (Ajit et al., 2010; Cate et al., 2015). Consequently, actual adherence may be lower than reported, which could affect the generalisability of our findings.

Recruiting participants through Glaucoma UK and social media platforms may have resulted in a sample that included patients who are particularly proactive or engaged in managing their condition. These recruitment methods are more likely to reach individuals who are already connected to support networks or actively seeking information about glaucoma, which could influence the perspectives shared in the study. Although purposive sampling was used to aim for diversity in demographic and clinical characteristics, the recruitment approach may have underrepresented those patients who are less engaged or face barriers to accessing support and information, again potentially limiting the generalisability of our findings.

Our sample included patients from various ethnic backgrounds, but Afro-Caribbean individuals, who have a higher prevalence of glaucoma (Leske et al., 1994) and lower adherence levels (Dreer et al., 2012; Rees et al., 2014) were underrepresented. Additionally, there was a higher percentage of university-educated patients than in the general UK population (Office for National Statistics, 2023). These demographic differences could also limit the generalisability of our findings. Lastly, as all participating ECPs were based in England, our findings may not be directly transferable to other UK countries with different healthcare structures and practices.

4.6 Conclusion

This study emphasises the importance of understanding both patient and practitioner perspectives to address glaucoma medication nonadherence. By identifying the key modifiable behavioural determinants across both groups, it highlights the complexity of adherence behaviours and the need for a comprehensive, multi-level approach.

The findings provide a foundation for designing interventions targeting patients, practitioners, healthcare systems, and the pharmaceutical industry. Such interventions could enhance patient adherence, equip ECPs with effective tools for managing nonadherence, and address systemic barriers. Ultimately, these strategies aim to improve adherence, support long-term patient outcomes, and reduce preventable vision loss in glaucoma care.

In the context of this thesis, these insights provide a crucial evidence-base for the development of an intervention grounded in behavioural theory and real-world experience. These findings will directly inform the next phase of the research, described in Chapters 6 and 7, where they are integrated into the design of a patient-targeted adherence intervention.

4.7 International Research Experience: Study Conducted at LV Prasad Eye Institute, India

As part of an international research opportunity funded by the Turing Programme, I undertook a four-week visit to the LV Prasad Eye Institute in India, a globally recognised centre of excellence in ophthalmic care and research. During this time, an additional study exploring the behavioural determinants of glaucoma medication adherence from the perspectives of both patients and ophthalmologists within a LMIC context was completed.

Although this study does not directly inform the development of the UK-based intervention described in Chapters 6 and 7, it provided a valuable opportunity to investigate adherence behaviours within a contrasting healthcare system. The experience deepened my understanding of how social, cultural, and structural factors influence medication-taking behaviours and highlighted important comparisons with the UK context.

A manuscript reporting this study, currently under peer review, is provided in Appendix C5.

Chapter 5 Developing a Theory-Informed Intervention to Support Glaucoma Medication Adherence Using the Behaviour Change Wheel

5.1 Chapter overview

This chapter presents the initial stage in the development of a theory-informed, patient-centred behavioural change intervention to support glaucoma medication adherence. Building on the findings from Chapters 2 and 4, it describes the structured, theory-driven process used to translate those findings into potential intervention components, using the Behaviour Change Wheel (BCW) framework (Michie et al., 2014).

5.2 Introduction

Nonadherence to glaucoma medication remains a persistent global challenge, contributing to preventable vision loss, reduced quality of life, and increased healthcare costs (Cutler et al., 2018; Newman-Casey et al., 2020; Thompson et al., 2018). As discussed in Section 1.14.2 (page 67), despite numerous efforts to improve adherence, no single intervention has proven universally effective. A common limitation is they lack theoretical underpinning and transparent reporting on how behavioural change is intended to occur (Nieuwlaat et al., 2014). This points to the need for structured, theory-informed approaches that reflect the complexity and individual variation in adherence behaviours.

This chapter outlines the development of a behaviour change intervention to support adherence to glaucoma medication, using a systematic and theory-based approach. The process is guided by the MRC framework for developing complex interventions, which advocates a phased approach encompassing development, feasibility testing, evaluation, and implementation (Skivington et al., 2021). While research often focuses on the feasibility and evaluation phases, the development phase, where the theoretical foundation and intervention components are established, is often underreported. A systematic and transparent approach at this stage enhances

replicability, promotes learning from past findings and increases the likelihood of real-world effectiveness (Bleijenberg et al., 2018).

Although the MRC framework recommends grounding intervention development in theory, it does not specify which theoretical model to use. Given that adherence is a health-related behaviour, the BCW was selected to guide intervention design. The BCW offers a comprehensive and structured methodology for understanding behaviour and designing targeted interventions (Michie et al., 2011). Unlike many other theoretical models, the BCW not only facilitates a behavioural analysis but also links behavioural determinants to evidence-based strategies for change. It has been applied across various healthcare contexts to improve health behaviours (Gould et al., 2017; Murphy et al., 2023; Watson et al., 2023). For example, Murphy et al. (2023) used the BCW to develop an intervention for pregnant women with gestational diabetes, aiming to reduce the risk of progression to type 2 diabetes postpartum and to improve pregnancy outcomes.

The BCW integrates key constructs from 19 behavioural and social science frameworks and comprises four layers (Michie et al., 2011). At its core is the COM-B model, which proposes that for a behaviour to occur, an individual must have the capability (physical and psychological), opportunity (physical and social), and motivation (reflective and automatic) to perform that behaviour (see Figure 5.1). Surrounding the COM-B model is the Theoretical Domains Framework (TDF), which provides a more detailed lens through which to understand the psychological, social, and contextual factors influencing behaviour across 14 domains (Atkins et al., 2017). For instance, the Capability component includes domains such as *Knowledge*, *Skills* and *Behavioural Regulation*.

The next layer outlines nine intervention functions (IFs), such as *Education*, *Enablement*, or *Training*, which are broad strategies used to bring about change. These functions are supported by seven policy categories which represent how interventions can be implemented in real-world settings (the outer layer of the BCW in Figure 5.1). The final component of the BCW involves identifying Behaviour

Change Techniques (BCTs), the active ingredients of an intervention that operationalise the selected IFs. The BCT Taxonomy, which links to the TDF, provides a standardised classification of 93 techniques grouped into 16 categories (Michie et al., 2013).

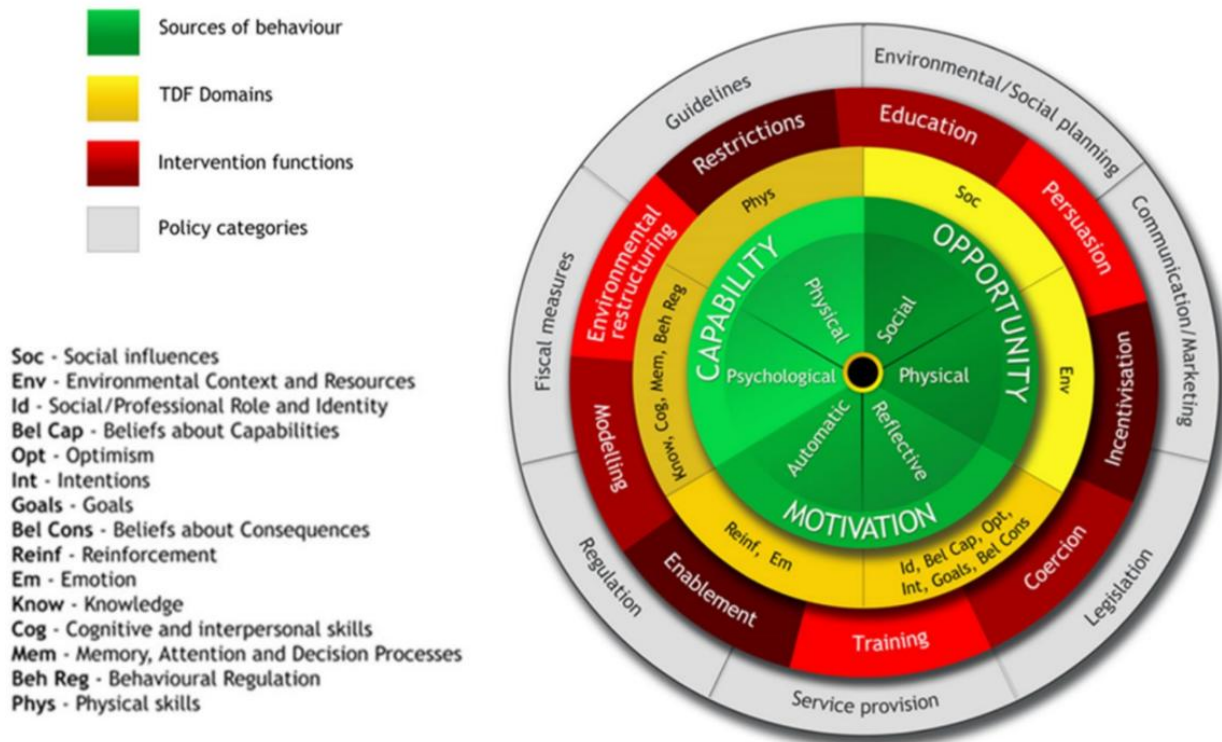


Figure 5.1 The four layers of the Behaviour Change Wheel
 Image courtesy of Michie et al., 2011

The BCW intervention development process is structured into three main stages (see left hand side of Figure 5.2; a flow diagram outlining the design process) (Michie et al., 2014):

- **Stage 1** involves conducting a behavioural diagnosis to understand what needs to change
- **Stage 2** uses this understanding to identify the most appropriate IFs and policy strategies likely to bring about the desired behavioural change
- **Stage 3** focuses on selecting appropriate BCTs and delivery strategies

This structured framework provides a clear pathway from behavioural diagnosis (i.e. understanding the nature of the problem and what specifically needs to change) to the design of tailored, evidence-based interventions with well-defined mechanisms of action (Richardson et al., 2019).

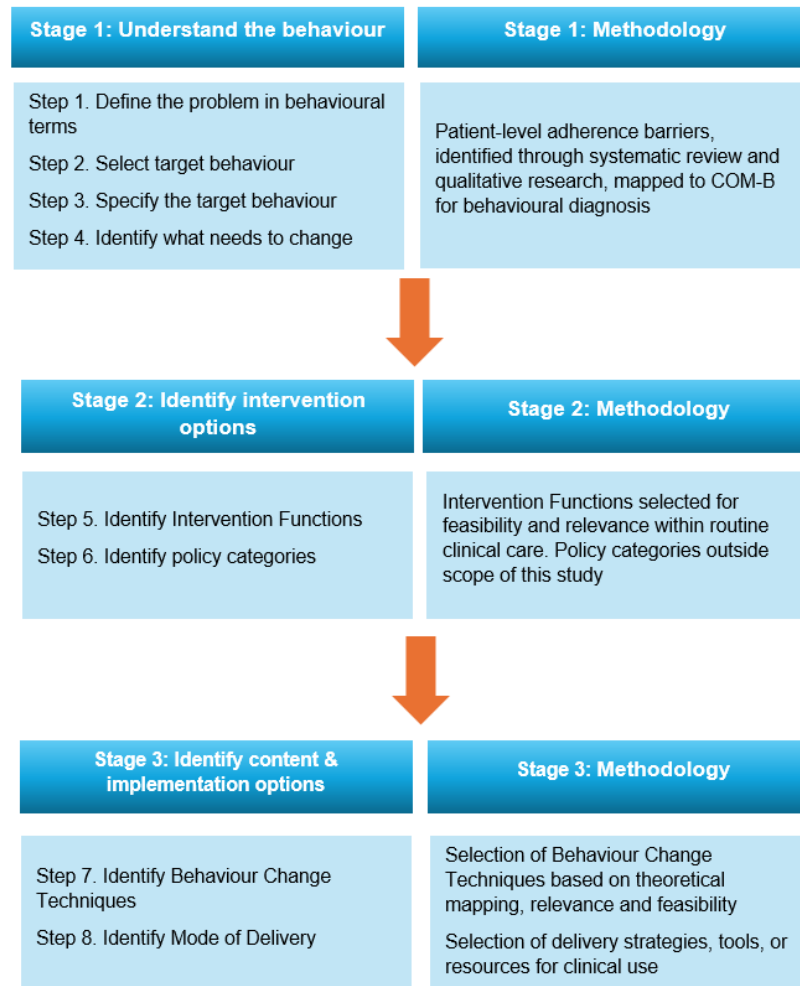


Figure 5.2 Step-by-step process for developing a Behaviour Change Intervention using the Behaviour Change Wheel. Image adapted from Michie et al 2014

5.2.1 Aims and objectives

The aim of this chapter is to begin the development of a patient-centred intervention to support adherence to glaucoma medication, by identifying theory-based and clinically feasible strategies to address modifiable barriers to adherence.

The specific objectives are to:

- Apply behaviour change theory, using the BCW, to identify key modifiable patient-level barriers to glaucoma medication, drawing on findings from previous work (Chapters 2 and 4)
- Select appropriate IFs and BCTs to address these barriers

This iterative process aligns with the Development phase of the MRC framework for developing complex interventions (Skivington et al., 2021), ensuring that each step builds logically on the previous one to support a systematic and evidence-informed approach to intervention design.

5.3 Design

The development of the intervention follows the step-by-step approach as set out by the BCW. It draws on the findings from Chapters 2 and 4, which identified the modifiable determinants of glaucoma medication adherence and provided the foundation for conducting a behavioural diagnosis. These insights were then used to inform the selection of targeted intervention strategies to support the desired behavioural change (See right hand side of Figure 5.2; a flow diagram outlining the design process).

The following sections describe each stage of intervention development process.

5.3.1 Stage 1: Understanding the behaviour

Step 1 - Define the Problem in Behavioural Terms

As outlined in Sections 1.6 (page 42) and 1.7 (page 43), poor adherence to glaucoma medication remains a persistent challenge with clinical, personal, societal, and economic consequences. Accordingly, the behavioural problem was defined as nonadherence to glaucoma medication.

Step 2 - Select the Target Behaviour

In response to this problem, the target behaviour for change was defined as improving patient adherence to glaucoma medication, specifically the correct and consistent use of prescribed ocular hypotensive eyedrops.

Step 3 - Specify the Target Behaviour

To gain a detailed understanding of this target behaviour and its influencing factors, the development process drew on prior empirical work: a systematic review (Chapter 2) and a UK-based qualitative interview study (Chapter 4). These studies identified a range of modifiable influences on adherence, operating across multiple levels, including the patient, HCPs, and the healthcare system.

Using both methodological triangulation (multiple research methods) and data triangulation (multiple data sources), as recommended by Moon (2019), key determinants from these studies were synthesised. For the purposes of this intervention, the focus was narrowed to patient-level barriers to adherence. This decision was based on the premise that addressing challenges to eyedrop use is likely to produce more sustainable improvements in adherence, rather than enhancing existing facilitators. Given that resources are often limited in clinical settings (e.g., money, time, personnel), prioritising barriers helps allocate resources more efficiently and ensures the most pressing issues are addressed first. Additionally, this approach helps ensure that the intervention remains relevant and feasible for real-world implementation (French et al., 2012). Narrowing the focus to the patient-level also streamlines the development process, making it easier to

replicate, implement and evaluate in the future (Kilbourne et al., 2007). System-level factors, such as prescribing practices or pharmacy supply chains, were excluded as they fall beyond the scope of a patient-directed intervention and would require broader service or policy reform.

Step 4 - Identify what needs to change

The identified patient-level barriers were then mapped onto the COM-B model to determine what specifically needs to change to support improved adherence. This mapping process produced a behavioural diagnosis that formed the foundation for the subsequent stages of the intervention development.

Stage 1 was carried out by the primary researcher (DB), with regular discussions and input from the rest of the research team. This collaborative approach ensured that refinements could be made as needed throughout the process.

5.3.2 Stage 2: Identifying Intervention options

Step 6 – Identify Intervention Functions

To determine how best to address the behavioural determinants identified in Stage 1, appropriate IFs were selected using the BCW matrix (Michie et al., 2014). TDF-informed barriers to adherence were mapped to the IFs most likely to promote behaviour change, guided by the COM-B model and using the criteria outlined by Michie et al. (2014). Definitions of the nine BCW IFs are provided in Table 5.1.

Table 5.1 Definitions of BCW Intervention Functions. Image courtesy of Michie et al., 2014.

Intervention Function	Definition
<i>Education</i>	Increasing knowledge or understanding
<i>Persuasion</i>	Using communication to induce positive or negative feelings or stimulate action
<i>Incentivisation</i>	Creating an expectation of reward
<i>Coercion</i>	Creating an expectation of punishment or cost
<i>Training</i>	Imparting skills
<i>Restriction</i>	Using rules to reduce the opportunity to engage in the target behaviour (or to increase the target behaviour by reducing the opportunity to engage in competing behaviours)
<i>Environmental restructuring</i>	Changing the physical or social context
<i>Modelling</i>	Providing an example for people to aspire to or imitate
<i>Enablement</i>	Increasing means/reducing barriers to increase capability (beyond education and training) or opportunity (beyond environmental restructuring)

A group consensus exercise was undertaken by members of the research team, with input from a behavioural scientist specialising in implementation science, to identify the most appropriate IFs based on feasibility and relevance. Decisions were informed by the TDF–COM-B mapping and practical considerations for implementation within clinical settings. For example, *Restriction*, which involves limiting competing behaviours by setting rules, was deemed inappropriate for this context (Michie et al., 2014). Imposing restrictions on patients' daily routines to prioritise medication adherence was considered unrealistic. Instead, adherence support should be flexible and support integration into existing routines, as behaviours are more sustainable when they align with individual lifestyles (Arlinghaus & Johnston, 2019).

Step 6 – Identify Policy Categories

The final step in Stage 2 involves identifying policy categories that could support the delivery of the chosen IFs. However, as this intervention is designed specifically at the patient level, broader policy-level strategies (e.g., legislative) were deemed beyond the scope of this project. The focus remained on developing an intervention that could be implemented seamlessly within routine clinical care without requiring systemic or organisational change.

5.3.3 Stage 3: Identifying content and implementation options

Step 7 – Identify Behaviour Change Techniques

Stage 3 focused on defining the specific content of the intervention by identifying appropriate BCTs. This process was guided by the evidence-based BCT Taxonomy, which provides a standardised language to describe the active components of behavioural interventions (Michie et al., 2013). Each BCT is theoretically linked to mechanisms of action, as captured by domains within the TDF. For example, the domain *Knowledge* may be addressed by BCTs such as *Information about health consequences* and *Instructions on how to perform the behaviour*.

To support the mapping of BCTs to the behavioural determinants identified in Stage 1, the interactive ‘Theory and Techniques Tool’ was used (Johnston et al., 2021). This resource systematically links BCTs to their associated TDF domains, highlighting those most likely to address the specified barriers. Additionally, the tool identifies techniques that have limited or inconclusive evidence for effectiveness in particular domains, allowing for a more refined and targeted selection process.

This mapping exercise produced a preliminary list of BCTs with the potential to address adherence barriers. These were then reviewed in a group consensus exercise involving the research team and a behavioural scientist. Final selections were made based on two key considerations: their relevance to the target population (patients who use glaucoma eyedrops) and their practical feasibility for integration into routine clinical practice. Decisions were informed by the team’s expertise in

glaucoma care and behavioural science, alongside evidence from existing literature supporting the effectiveness of the technique in other chronic health conditions.

Step 8 – Identifying Modes of Delivery

Following the selection of BCTs, the next step involved identifying suitable modes of delivery (MoDs) to operationalise the intervention content. MoDs refer to the formats through which BCTs are delivered, such as face-to-face support, printed materials, or digital platforms (Marques et al., 2021). Their selection was guided by feasibility, alignment with the healthcare context, and the needs of the target population.

A consensus-driven approach was adopted by the research team to match each BCT to an appropriate delivery format, informed by the team's expertise in glaucoma care and relevant literature. Where possible, existing strategies and resources already used in glaucoma services were considered as potential delivery mechanisms. This pragmatic approach aimed to maximise efficiency, avoid unnecessary duplication, and enhance the likelihood of real-world feasibility, reflecting best practice recommendations in the development of complex interventions (French et al., 2012; Cotterill et al., 2018).

To support and inform this decision-making process, a retrospective coding exercise was conducted to assess the theoretical alignment of existing real-world interventions designed to support glaucoma medication adherence.

The objectives of this retrospective review were to:

- Systematically identify and analyse the content of existing UK-based interventions
- Code their behavioural content using the BCW framework (Michie et al., 2014) and BCT Taxonomy (Johnston et al., 2021)
- Determine whether the BCTs in use addressed the key behavioural determinants of nonadherence identified earlier in Section 5.3.1 (page 174)
- Identify any potential 'missed opportunities,' that is, BCTs supported by theory but underused in current practice

Eligible interventions were those in current use within the UK and endorsed or promoted by national organisations such as the NHS, NICE, or patient advocacy charities (e.g. Glaucoma UK, RNIB) and targeted at patients to support their adherence to glaucoma medication (i.e. existing ‘real-world’ interventions). Interventions were identified by searching the internet, directly contacting relevant charities or using the research team’s knowledge of available resources. It was assumed that if an intervention could not be easily identified or accessed by the primary researcher (DB), it was unlikely to be widely available or in routine use.

For each included intervention, the following information was extracted:

- Type of adherence strategy (e.g., educational tools, reminder systems), categorised according to definitions in Section 1.14, page 60)
- MoD, classified using the established Behaviour Change Intervention Ontology (Marques et al., 2021)
- IFs, as per the BCW Framework (Michie et al., 2014)
- BCTs, coded using the BCT Taxonomy (Johnston et al., 2021)

Each BCT was coded only once per intervention to avoid skewing the data for longer or more complex interventions. The coding was led by the primary researcher (DB), with a pilot exercise undertaken alongside a behavioural scientist and another team member (PC) to refine the approach. Any discrepancies during the main coding phase were resolved through consensus.

Once all interventions were coded, the findings were compared with those identified through the theoretical mapping process in Sections 5.3.2 (page 175) and 5.3.3 (page 177). This comparison helped identify delivery strategies that were both theoretically coherent and already in use and informed the development of potential delivery approaches for each included BCT. Where existing delivery strategies aligned well with selected BCTs and behavioural influences, they were considered as candidate formats for the final intervention design.

5.4 Results

5.4.1 Stage 1: Understanding the behaviour

The target behaviour was defined as improving patient adherence to glaucoma medication. To explore the influences on this behaviour, findings from the systematic review and UK-based qualitative interview with patients and ECPs were synthesised. Table 5.2 provides an overview of key TDF domains identified across these studies.

Table 5.2 Key TDF domains influencing glaucoma medication adherence identified in the systematic review and qualitative interviews

Systematic review	Patient interviews	ECP interviews
<i>Knowledge</i>	<i>Knowledge</i>	<i>Knowledge</i>
<i>Skills</i>	<i>Skills</i>	<i>Skills</i>
<i>Memory, Attention and decision processes</i>	<i>Memory, Attention and decision processes</i>	<i>Memory, Attention and decision processes</i>
<i>Environmental Context and Resources</i>	<i>Environmental Context and Resources</i>	<i>Environmental Context and Resources</i>
	<i>Belief about capabilities</i>	<i>Belief about capabilities</i>
	<i>Belief about consequences</i>	<i>Social, Professional Role & Identity</i>
	<i>Goals</i>	
	<i>Social Influences</i>	
	<i>Behavioural Regulation</i>	
Domains are colour-coded to highlight commonalities and differences across data sources. Importance of domains was determined based on criteria outlined in Sections 2.3.4 and 4.3.7.		

These findings highlight both overlapping and different influences. All studies identified *Knowledge* and *Skills* as important, reflecting a shared understanding of the importance of patient education and practical capability in managing glaucoma medication. Additionally, *Memory, Attention and decision processes* and *Environmental Context and Resources* were consistently highlighted, emphasising the role of cognitive processes and contextual factors in adherence behaviours.

However, unique insights were also revealed. *Beliefs about Capabilities* were identified in patient and ECP interviews, while *Beliefs about Consequences* appeared only in patient interviews, suggesting that personal confidence in medication management and perceived risks of nonadherence may be more apparent through direct interactions with patients and ECPs. Patient interviews also revealed *Goals*, *Social Influences* and *Behavioural Regulation* as important domains, highlighting the importance of personal motivation, social support, and self-management. In contrast, *Social Professional Role and Identity* was unique to ECPs, reflecting the professional responsibility clinicians perceive in supporting adherence. These differences highlight the value of drawing on multiple methods and perspectives to gain a comprehensive understanding of behavioural influences (Moon, 2019).

Drawing on these findings, five overarching barrier themes were identified (See Table 5.3).

Table 5.3 Five key barrier themes influencing glaucoma medication adherence identified from the systematic review, patient and ECP interviews

Identified Barrier Themes	Corresponding TDF Domains	Targets
1. Lack of understanding and/or lack of education includes Lack of patient understanding and/or lack of education regarding nature of glaucoma and/or its treatment	<i>Knowledge</i>	Patient
2. Issues administering eyedrops includes Lack of physical skills and/or poor vision, competing priorities, eyedrops not to hand, forgetfulness, complex regimens, inconvenient dosing schedules and lack of education on how to instil eyedrops	<i>Skills</i> <i>Environmental, Context & Resources,</i> <i>Memory, Attention & decision processes</i>	Patient, Carer/family support, HCP
3. Difficulties obtaining eyedrops includes Lack of availability of eyedrops, inability to order repeat prescriptions and financial issues	<i>Skills</i> <i>Environmental, Context & Resources</i>	Patient, Carer/family support, HCP, Healthcare system, Pharmaceutical industry
4. Insufficient HCP knowledge regarding adherence issues includes Lack of confidence in own ability to detect nonadherence, difficulties knowing how to classify adherent/nonadherent patients, clinical skills needed to detect nonadherence, and ability to educate patients	<i>Belief about capabilities, Knowledge,</i> <i>Skills, Environmental, Context & Resources</i>	HCP
5. Impact of organisational structure includes Lack of resources (manpower/material), time constraints, demands within the eye clinic and difficulties contacting the eye clinic	<i>Environmental, Context & Resources</i>	Healthcare system

To focus the intervention at the patient level, three of these were prioritised:

1. Lack of patient understanding and/or education about glaucoma and the rationale for treatment
2. Challenges with administering eyedrops
3. Difficulties obtaining medication

A behavioural diagnosis was then conducted using the COM-B model. This analysis concluded that improved adherence requires change in three behavioural components: psychological capability, physical capability, and physical opportunity (See third column of Table 5.4). Motivation, both reflective and automatic, was not identified as a barrier.

5.4.2 Stage 2: Identifying intervention options

Building on the behavioural diagnosis in Stage 1 (Section 5.4.1, page 180), four key TDF domains: *Knowledge, Skills, Memory, Attention and decision processes*, and *Environmental Context and Resources*, were mapped to IFs using the BCW matrix (Michie et al., 2014).

Following this mapping exercise, the research team considered five COM-B-aligned IFs for their contextual appropriateness and feasibility within a routine clinical care setting. Of these, three IFs were selected as suitable for addressing the identified patient-level barriers: *Education, Training and Environmental Restructuring* (See fourth column of Table 5.4). Two IFs were excluded. *Restriction* was deemed inappropriate as it would involve limiting patients' behaviours or routine, an approach considered unrealistic and potentially counterproductive in supporting long-term adherence. *Enablement* while relevant in broader contexts, typically involves providing resources or systemic changes that extend beyond the scope of a patient-focused intervention. For instance, reducing medication burden (e.g. by prescribing fewer drops) would require practitioner-level changes rather than patient-level strategies.

Table 5.4 Behavioural diagnosis using the COM-B Model, suggested Intervention Functions, associated Behaviour Change Techniques and proposed delivery methods

Identified Barriers	Corresponding TDF domains	COM-B component ¹	Intervention Function ²	BCT (from online tool ³)	Selected BCTs	Proposed delivery strategies, tools or resources
Lack of understanding and/or lack of education regarding nature of glaucoma and/or its treatment	Knowledge	Physiological Capability	Education Training	2.6 4.1 4.2 5.1 5.3	4.1. Instruction on how to perform behaviour 5.1. Information about health consequences	Educational tools: Interactive group workshops or 1-1 training sessions providing information on glaucoma and rationale for treatment, in person or online Online educational glaucoma course Printed poster positively framing benefits of using eyedrops. Displayed in waiting rooms, pharmacies, GPs or community optometrist practices. QR code/web address could be incorporated into poster Printed/electronic information leaflets on glaucoma, rationale for treatment and outlining positive consequences of adhering to treatment. Displayed in waiting rooms, pharmacies, GPs or community optometrist practices. QR code/web address could be incorporated into material. Information could be incorporated into clinic letters Video screens in clinic waiting rooms outlining what glaucoma is, its treatment and benefits of adhering to treatment Patient Information Leaflet included with eyedrops
Issues administering eyedrops	Skills Environmental, Context & Resources Memory, Attention & decision processes	Physical and Physiological Capability Physical Opportunity	Training Education Environmental restructuring	3.2 4.1 7.1 7.5 8.1 8.7 11.3 12.1	3.2. Social support (practical) 4.1. Instruction on how to perform behaviour 8.1. Behavioural practice/rehearsal 7.1. Prompts/cues	Support strategies: Organise/encourage additional support from family/friends/informal carers to help with drop instillation either physically administering drops or providing reminders Consider using an online social community network to provide patient with support Training strategies: In person or online training sessions on instillation technique, periodically revisited and backed up with written material Utilise written resources and/or online videos demonstrating how to use eyedrops correctly and how to overcome common mistakes Memory aids: Set up a reminder system when eyedrops need instilling, alarm, medication reminder app

				12.2	11.3 Conserving mental resources	Use personalised eyedrop chart/calendar, printed or electronic
				12.3		
				12.5	12.1. Restructuring the physical environment	Association strategies: Associate instilling eyedrops with a daily habit e.g. brushing teeth or strategic placement of eyedrop bottle e.g. next to bed. If using multiple bottle place in order of use/size order/colour code
					12.5. Adding objects to the environment	Use eyedrop dispensing aid
Difficulties obtaining eyedrops	Skills Environmental, Context & Resources	Physical and Physiological Capability Physical Opportunity	Training Education Environmental restructuring	3.2 4.1 7.1 7.5 8.1 8.7 12.1 12.2 12.3 12.5	3.2. Social support (practical) 4.1. Instruction on how to perform behaviour 7.1. Prompts/cues 12.1. Restructuring the physical environment 12.5. Adding objects to the environment	Support strategies: Use family members/caregivers to help with ordering and/or collecting repeat prescriptions Planning strategies: Use electronic system for ordering repeat prescriptions e.g. NHS app/online GP system/medication reminder app. Online instructions on how to use electronic ordering system Memory aids: Set up reminders, printed or electronic, when need to order repeat prescription e.g. calendar, partner reminds patient, alarm Medication reminder apps Consider using mail order services for delivery of eyedrops
¹ Michie et al 2014, ² Michie et al 2014, ³ Johnston et al 2021 BCT = Behaviour Change technique						

5.4.3 Stage 3: Identifying content and implementation options

Using the 'Theory and Techniques Tool' described in Section 5.3.3 (page 177), key TDF domains were systematically mapped to BCTs with demonstrated links to the identified barriers. Fourteen candidate BCTs were initially identified and considered for potential inclusion. Following discussions with the research team and a behavioural scientist, seven BCTs were excluded. The final set of BCTs retained for inclusion in the intervention were: 3.2 *Social support (practical)*, 4.1 *Instruction on how to perform behaviour*, 5.1 *Information about health consequences*, 7.1 *Prompts/cues*, 11.3 *Conserving mental resources*, 12.1 *Restructuring the physical environment* and 12.5 *Adding objects to the environment* (see column six in Table 5.4). A more detailed overview of all theoretically derived BCTs, including justifications for inclusion and exclusion, is provided in Appendix D1.

To identify appropriate delivery mechanisms for these BCTs, a retrospective coding exercise was conducted on 21 existing UK-based interventions aimed at supporting glaucoma medication adherence. A detailed summary of each intervention is provided in Appendix D2. Interventions were categorised into four main types:

- **Educational Strategies** (n=9): printed or digital materials providing glaucoma and eyedrop use information
- **Reminder Systems** (n=9): tools such as alarms, calendars, or cues to support memory and habit formation
- **Medication simplification strategies** (n=2): devices or aids to support eyedrop instillation
- **Alternative Engagement Methods** (n=1): remotely delivered support via telephone or online video calls, offering informational and emotional support individually or in groups

Each strategy was considered in relation to the three identified adherence barriers. For example, educational tools primarily addressed lack of understanding and administration difficulties; reminder systems were more relevant to administration issues and difficulties accessing medication; medication simplification strategies

targeted administration barriers; and support-based interventions addressed both knowledge gaps and administration challenges.

Across the interventions, between one and four IFs were identified. The most common were *Environmental Restructuring* and *Education*. In total, 18 BCTs were coded, with the most frequent being: 9.1 *Credible source*, 12.1 *Restructuring the physical environment*, 3.1 *Social Support (unspecified)*, and 7.1 *Prompts/Cues*. A full breakdown of the IFs and BCTs is available in Appendix D2.

The exercise also compared the components of real-world interventions with those identified through the theoretical mapping process (Sections 5.4.2, page 183 and 5.4.3, page 186) to assess theoretical coherence. Tables 5.5 and 5.6 present direct comparisons of the IFs and BCTs respectively, mapped across the three key adherence barriers. Areas of alignment are colour-coded: green for IFs and orange for BCTs.

The IFs identified in real-world interventions generally showed good alignment with those derived theoretically. While *Modelling* was not selected during the theoretical mapping, it was identified in a number of existing interventions. According to Michie et al. (2014), *Modelling* involves providing examples for individuals to emulate. This function was evident in support groups where patients shared their own experiences and strategies for eyedrop use, serving as peer role models. Additionally, visual aids such as informational leaflets or YouTube videos offered relatable demonstrations of correct eyedrop administration.

All seven theoretically selected BCTs were identified in at least one existing intervention, indicating good congruence. Some of the BCTs identified in existing interventions were considered to conceptually overlap with those selected through the theoretical mapping process. For instance, *Social support (unspecified)* was viewed as being encompassed by *Social support (practical)*. Similarly, *Demonstration of the behaviour* was judged to fall under *Instruction on how to perform the behaviour*, which can include visual or practical demonstrations. Other

BCTs such as *Problem solving*, *Action planning* and *Habit formation* were considered theoretically addressed by *Instruction on how to perform the behaviour*, *Prompts/cues*, and *Conserving mental resources*.

Finally, the retrospective review informed the identification of practical delivery strategies and formats for the seven selected BCTs. These proposed delivery modes are presented in the final column of Table 5.4.

Table 5.5 Comparison of Intervention Functions across theoretically selected and real-world interventions for three key adherence barriers

Barrier Theme	Theoretically selected Intervention Functions	Intervention Functions Identified in Real-World Interventions
Lack of understanding regarding nature of glaucoma and/or its treatment	Education Training	Education Training <i>Modelling</i> <i>Environmental Restructuring</i>
Issues administering eyedrops	Education Training Environmental Restructuring	Education Training <i>Modelling</i> Environmental Restructuring
Difficulties obtaining eyedrops	Education Training Environmental Restructuring	Education <i>Modelling</i> Environmental Restructuring
Intervention Functions highlighted green indicate they were both theoretically selected and observed in real-world interventions		

Table 5.6 Comparison of Behaviour Change Techniques across theoretically selected and real-world interventions for three key adherence barriers

Barrier Theme	Theoretically selected Behaviour Change Techniques	Behaviour Change Techniques identified in real-world interventions
Lack of understanding regarding nature of glaucoma and/or its treatment	4.1. Instruction on how to perform behaviour 5.1. Information about health consequences	3.1 Social support (unspecified) 4.1 Instruction on how to perform the behaviour 5.1 Information about health consequences 6.1 Demonstration of the behaviour 6.2 Social comparison 6.3 Information about others approval 7.1 Prompts/cues 9.1 Credible source 12.1 Restructuring the physical environment 12.5 Adding objects to the environment
Issues administering eyedrops	3.2. Social support (practical) 4.1. Instruction on how to perform behaviour 7.1. Prompts/cues 11.3 Conserving mental resources 12.1. Restructuring the physical environment 12.5. Adding objects to the environment	1.2 Problem solving 1.4 Action planning 2.2 Feedback on behaviour 2.3 Self-monitoring of behaviour 3.1 Social support (unspecified) 3.2 Social support (practical) 4.1 Instruction on how to perform the behaviour 5.1 Information about health consequences 5.6 Information about emotional consequences 6.1 Demonstration about the behaviour 6.2 Social comparison 7.1 Prompts/cues 8.3 Habit formation 9.1 Credible source 10.7 Self-reward 11.3 Conserving mental resources

		12.1 Restructuring the physical environment
		12.5. Adding objects to the environment
Difficulties obtaining eyedrops	3.2. Social support (practical)	2.2 Feedback on behaviour
	4.1. Instruction on how to perform behaviour	2.3 Self-monitoring of behaviour
	7.1. Prompts/cues	3.1 Social support (unspecified)
	12.1. Restructuring the physical environment	3.2 Social support (practical)
	12.5. Adding objects to the environment	4.1 Instruction on how to perform the behaviour
		5.1 Information about health consequences
		6.1 Demonstration about the behaviour
		6.2 Social comparison
		7.1 Prompts/cues
		9.1 Credible source
		11.3 Conserving mental resources
		12.1 Restructuring the physical environment
		12.5. Adding objects to the environment
Behaviour Change Techniques highlighted orange indicate they were both theoretically selected and observed in real-world interventions		

5.5 Discussion

This chapter applied the BCW framework to systematically develop a theory-informed, patient-centred intervention to support glaucoma medication adherence. Through the structured, stepwise process outlined by the BCW, this study progressed from identifying the target behaviour, through detailed behavioural analysis and diagnosis, to the selection of appropriate IFs, BCTs, and potential MoDs. This transparent and theory-driven approach ensures a clear rationale for how each component is intended to influence behaviour, aligning with the Development phase of the MRC framework for complex interventions (Skivington et al., 2021).

Drawing on findings from the systematic review and qualitative interviews in Chapters 2 and 4, three key barrier themes were identified and grouped by their relevant TDF domains. This behavioural analysis highlighted the complex and multifactorial nature of glaucoma medication adherence, aligning with and building upon existing literature (Gatwood et al., 2022; Kardas et al., 2013; Tsumura et al., 2019).

A notable strength of this analysis is that it conceptualises adherence not as a single act, but as a sequence of interrelated behaviours (as described in Section 1.4.1.1, page 37), including obtaining repeat prescriptions, instilling drops correctly, maintaining a daily routine, and remembering to administer drops at appropriate times (Muir & Lee, 2011). The resultant intervention therefore aims to address the full adherence pathway, rather than focusing narrowly on administration alone, increasing the likelihood of achieving and sustaining long-term adherence.

The behavioural diagnosis identified that nonadherence was primarily influenced by limitations in patients' physical and psychological capability, as well as physical opportunity. Informed by this, three IFs were selected and operationalised through seven targeted BCTs. These components were carefully matched to the specific

behavioural challenges identified and designed to enhance patients' capability and opportunity for adherence.

The use of BCTs in health interventions is well-established (Michie et al., 2008), and tailoring BCTs to the behavioural determinants identified through theoretical models has been shown to increase the likelihood of intervention effectiveness (Michie & Abraham, 2004; Teo et al., 2024). For example, a systematic review of diabetes self-management interventions found that those grounded in behaviour change theory were more effective in improving adherence (Teo et al., 2024). In this study, BCT selection was grounded in the results of the behavioural diagnosis and supported by evidence of their application across other chronic conditions (Bond et al., 2021; Kassavou & Sutton, 2018; Teo et al., 2024).

Evidence further supports the relevance of the selected BCTs, with several having demonstrated effectiveness in supporting medication adherence in both glaucoma care and other chronic health conditions. For example, *Social Support (practical)* has been associated with improved adherence when delivered by family members, carers, or peer networks (Hollenhorst et al., 2020; Mair et al., 2023). *Instruction on how to perform behaviour* and *Information about health consequences* have been shown to be effective strategies for improving adherence to statin and diabetes medication (Bond et al., 2021; Teo et al., 2024). *Conserving mental resources* using *prompting* strategies to make the behaviour less cognitively demanding have demonstrated effectiveness across diverse patient groups (Thakkar et al., 2016). while simplifying routines through *Restructuring the Physical Environment* and *Adding Objects to the Environment* can reduce the cognitive burden of adherence, particularly in older adults (Choudhry et al., 2011; Gualtieri et al., 2022).

The retrospective review of existing UK-based interventions revealed the use of several BCTs that were not identified through the theoretical mapping process. This may indicate a degree of unnecessary complexity in current practice, evidence suggests that multifaceted interventions are not always more effective than those

with fewer components (Squires et al., 2014).

One of the most commonly used BCTs in existing interventions was *Credible source*, which was not among those theoretically selected. Research supports its effectiveness in improving adherence, by ensuring information is seen as trustworthy and authoritative it can improve patient trust and engagement (Bond et al., 2021; Carman et al., 2013). Conversely, poor-quality web-based content can reduce trust and lead to confusion (Stellefson et al., 2018). Materials produced by reputable organisations have been shown to improve health knowledge (Daraz et al., 2019; Win et al., 2016). NICE (2022) also recommends that health information be clear, reliable, and evidence-based to support effective patient decision-making. Studies also indicate that patients are more likely to follow advice from recognised HCPs or validated educational materials (Gatwood et al., 2022). For example, in a study evaluating an app to support hypertension medication adherence, participants suggested incorporating logos from trusted institutions such as the NHS to enhance credibility and uptake (Kassavou et al., 2020a).

Another BCT not selected during theoretical mapping but observed in some digital interventions was *Feedback on behaviour*. This BCT has demonstrated effectiveness in improving treatment engagement across other long-term conditions, such as diabetes and cardiovascular disease (Bond et al., 2021; Eisele et al., 2019; Wilson et al., 2020). For example, a systematic review of RCTs evaluating mobile health interventions for statin adherence found that including behavioural feedback improved outcomes (Bond et al., 2021). It has also been found to promote engagement and reinforce positive behaviours in diabetes care (Vallis et al., 2023). Effective use of this BCT typically requires prior self-monitoring and works best when integrated into interactive digital platforms or through direct interaction with a HCP.

The review also identified existing interventions that demonstrated strong theoretical congruence with the selected BCTs and underlying behavioural determinants. These were considered potential candidates for inclusion in the final intervention design. Two such examples were MyGlaucoma, a mobile app developed by Glaucoma UK

and Santen, and its paper-based version, My Personal Glaucoma Monitoring Record. The MyGlaucoma app includes features such as medication and prescription reminders, educational content, eyedrop instillation tips, and access to additional support via the Glaucoma UK website. It also enables patients to track IOP readings and add personal notes or photographs. Screenshots of the app are provided in Figure 5.3.

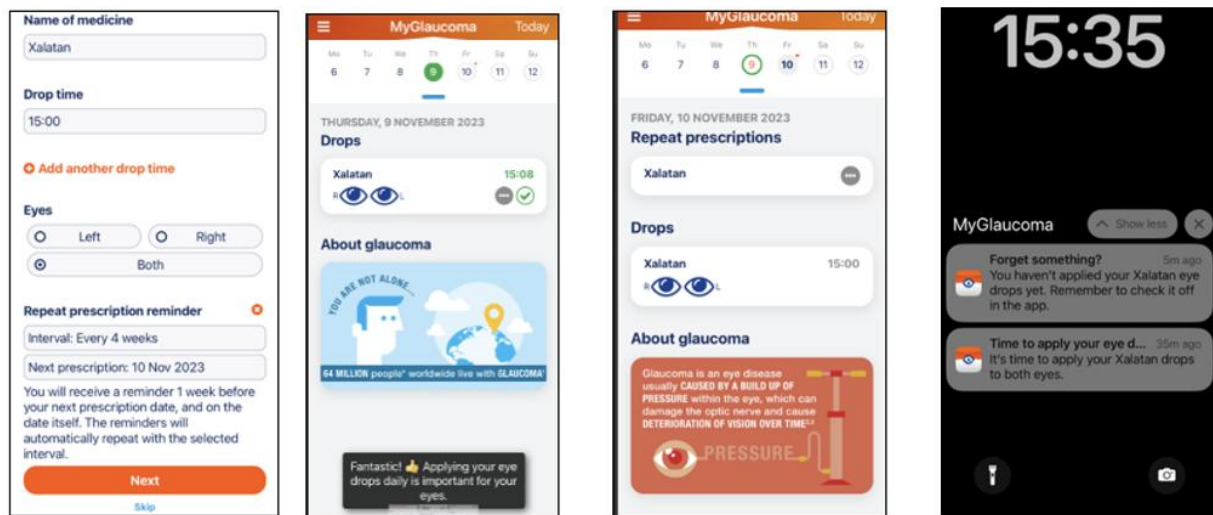


Figure 5.3 Screenshots of content from MyGlaucoma app

The final intervention design reflects a comprehensive, behaviourally informed approach that integrates cognitive, environmental, and motivational strategies to support medication adherence without increasing the perceived burden on patients. It aims to provide patients with the capability and opportunity to adhere to their treatment regimen. This approach aligns with evidence indicating that reducing patient effort and tailoring interventions to real-world behaviour are important for sustaining long-term change (Kwasnicka et al., 2016).

5.5.1 Strengths and limitations

A key strength of the work undertaken in this chapter lies in the systematic and theory-informed development of a glaucoma medication adherence intervention using the BCW Framework. By integrating insights from earlier empirical work,

including a systematic review and qualitative study, with behavioural theory, this chapter provides a transparent and replicable account of the intervention development process. Each stage, from behavioural diagnosis through to the selection of IFs and BCTs is clearly described, highlighting the rationale behind key decision-making processes.

Another strength is the collaborative nature of the development process. Decisions were informed by a research team with expertise in clinical glaucoma care and behavioural intervention design, alongside consultation with a behavioural scientist specialising in implementation science. This helped strike a balance between clinical relevance and theoretical fidelity.

However, several limitations should be acknowledged. While the BCW provides structured guidance, its application can involve a degree of interpretation. Despite efforts to ensure consensus among the research team, some decisions may have been influenced by subjective judgement.

In addition, although the mapping process offers a structured evidence-based approach to selecting BCTs and IFs, it does not guarantee real-world effectiveness. The success of the chosen intervention components will ultimately depend on their delivery, context, and acceptability within clinical practice. Another consideration is the generalisability of the qualitative findings (from Chapter 4) that helped inform the behavioural analysis. The sample, while purposively selected, may not fully reflect the diversity of glaucoma patients and ECPs across the UK. However, this limitation was mitigated by triangulating findings with those from the systematic review, thereby enhancing the robustness of the behavioural diagnosis.

5.6 Conclusion

This chapter presented a systematic, theory-informed approach to initiating the development of a patient-centred intervention aimed at improving adherence to glaucoma medication, consistent with MRC guidance for developing complex

interventions (Skivington et al., 2021). The BCW was successfully applied to identify the behavioural drivers influencing patient adherence and to guide the design of an intervention tailored to address these challenges.

Through the integration of theory-led mapping, empirical evidence from earlier chapters, and insights from real-world interventions, a refined set of potentially active intervention components was developed. This included three IFs and seven BCTs, selected for their theoretical justification and practical feasibility. These components are designed to enhance patients' psychological and physical capability, as well as their physical opportunity, to support sustained medication-taking behaviours. This work lays the foundation for the next stages of intervention development and evaluation, which are explored in Chapter 6, ensuring the intervention remains grounded in both behavioural science and the realities of day-to-day glaucoma care.

Chapter 6 The Adherence Resources Toolkit (ART): Design and Preliminary Evaluation of Acceptability

6.1 Chapter overview

This chapter presents the development of a theory-informed, patient-centred intervention to support glaucoma medication adherence. It builds on the behavioural components identified in Chapter 5, combining them into a cohesive conceptual model, the Adherence Resources Toolkit (ART), grounded in established behaviour change theory. The chapter also reports preliminary stakeholder feedback on the ART's acceptability, providing insights for future refinement and evaluation.

6.1 Introduction

This chapter presents the next stage in intervention development: the conceptualisation of the Adherence Resources Toolkit (ART), a practical, patient-focused model aimed at improving glaucoma medication adherence. Drawing on the behavioural strategies identified in Chapter 5, the ART integrates seven Behaviour Change Techniques (BCTs) and three Intervention Functions (IFs), mapped to the behavioural determinants identified through the BCW Framework.

To provide a theoretical foundation, a logic model (Figure 6.1) was developed to illustrate the hypothesised pathways through which each intervention component is expected to influence adherence behaviour. The model maps how BCTs are intended to address specific barriers, trigger patient-level changes (e.g. increased knowledge or consistent eyedrop administration), and ultimately lead to improved long-term medication use.

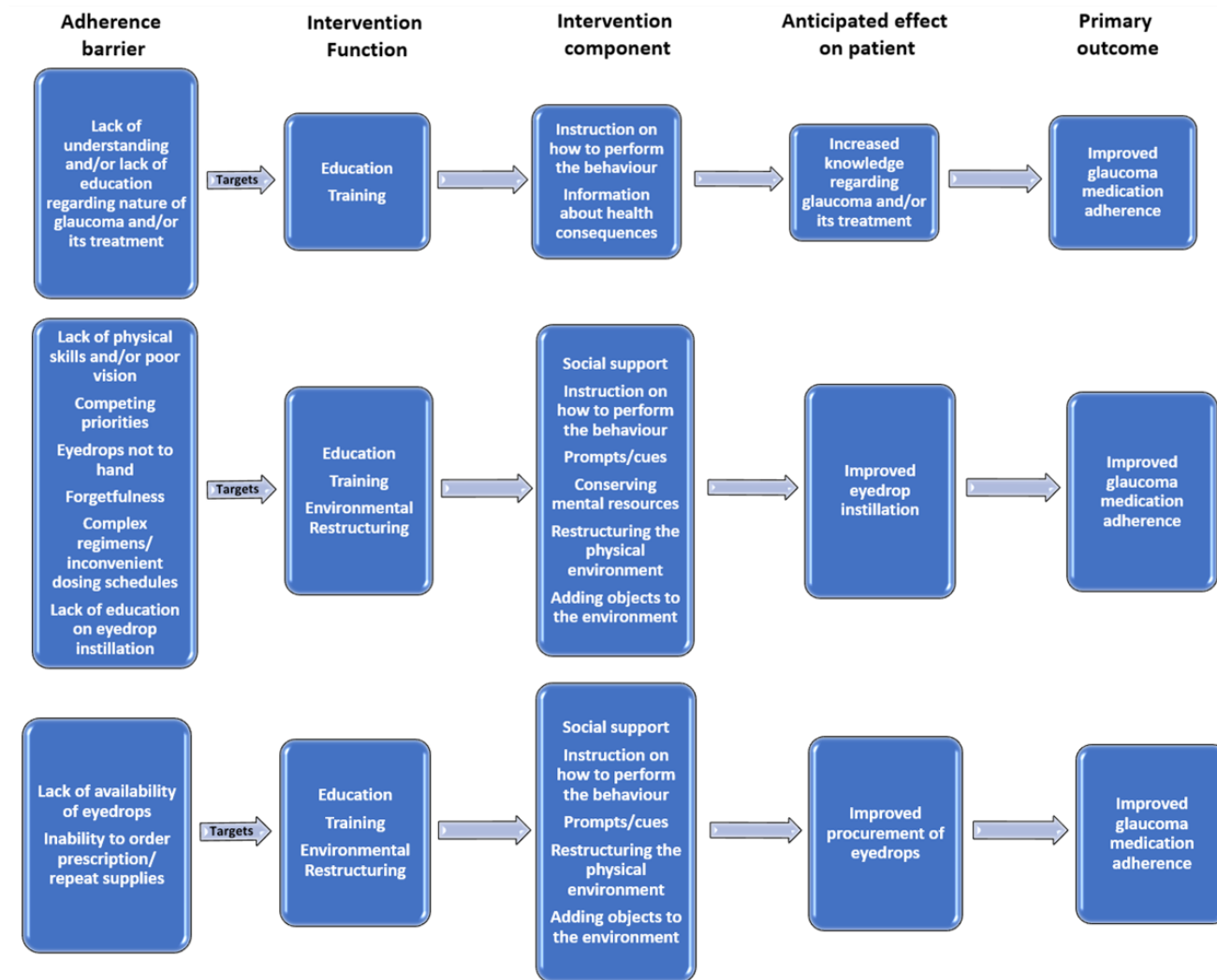


Figure 6.1 Logic model illustrating the hypothesised pathways through which intervention components are expected to improve glaucoma medication adherence

Once the conceptual model was developed, attention turned to how the ART could be implemented within current glaucoma care pathways. This included consideration of when, where, and by whom the intervention could be delivered and how best to package the selected BCTs into a deliverable and accessible format. Given the increasing integration of digital technologies into healthcare, a flexible, potentially digital format for the ART was considered.

Smartphone ownership and internet access in the UK are high and continue to rise (Office for National Statistics, 2020; Uswitch, 2024). Research suggests that ophthalmic patients are both capable of and receptive to using digital tools (Ali et al., 2019; Lee et al., 2014). Digital health interventions offer a scalable and accessible solution and have been successfully implemented in other chronic health conditions (Mikulski et al., 2022; Soobiah et al., 2020). As such, digital delivery may provide a practical and cost-effective route for implementation. However, digital delivery alone may not be suitable for all patients. Barriers to technology adoption exist, particularly among older adults and certain socio-economic or cultural groups (Bertolazzi et al., 2024; Nittas et al., 2024). A flexible, inclusive approach to delivery will therefore be required to ensure equitable access and engagement.

A core principle underpinning the ART's development is the active engagement of end-users, both those who will use the intervention and those who may deliver it. In line with the MRC framework for complex intervention development (Skivington et al., 2021), this user-centred approach is intended to enhance the relevance, acceptability, and feasibility of the intervention. Involving diverse stakeholders early in the development process, including patients, healthcare professionals, and advocacy organisations, helps ensure that the intervention is practical, engaging, and aligned with real-world contexts (Dopp et al., 2019; Yardley et al., 2015). Such collaboration can also support integration into routine practice (O'Cathain et al., 2019). Many complex interventions encounter barriers to implementation and sustainability, but early stakeholder engagement can improve long-term uptake and ultimately enhance patient outcomes (Cowdell et al., 2022).

To explore initial perceptions of the ART's acceptability for supporting glaucoma medication adherence, a stakeholder engagement activity will be conducted. Feedback from this process will inform further refinement of the intervention and support planning for subsequent feasibility and pilot testing, in line with the MRC framework (Skivington et al., 2021). This iterative process ensures that each stage builds logically on the last, supporting a systematic and evidence-informed approach to intervention design.

6.2.1 Aims and objectives

This chapter has two aims. The first is to integrate the theory-informed behavioural components identified in Chapter 5 into a conceptual model for a patient-centred intervention, the ART. This includes consideration of the ART's format, delivery, and potential integration into the existing glaucoma care pathway. The second aim is to explore the prospective acceptability of the ART through engagement with key stakeholders.

The following sections will first detail how the ART was developed, then use this conceptual model to guide the stakeholder engagement activity.

6.3 Adherence Resources Toolkit Development

Given the complexity of glaucoma medication adherence, an effective intervention must address the diverse challenges that patients encounter. As discussed in Section 5.4.1 (page 180) reasons for nonadherence are multifactorial, requiring an approach that first identifies individual barriers before recommending targeted strategies. To meet this need, the ART was developed by integrating the seven selected BCTs and three IFs into a comprehensive, multifaceted, patient-centred intervention.

The ART uses a structured process that begins with the assessment of personal barriers, followed by the delivery of tailored BCTs to address those challenges.

Figure 6.2 provides an overview of the conceptual model underpinning the ART. The following sections describe its key components in more detail.

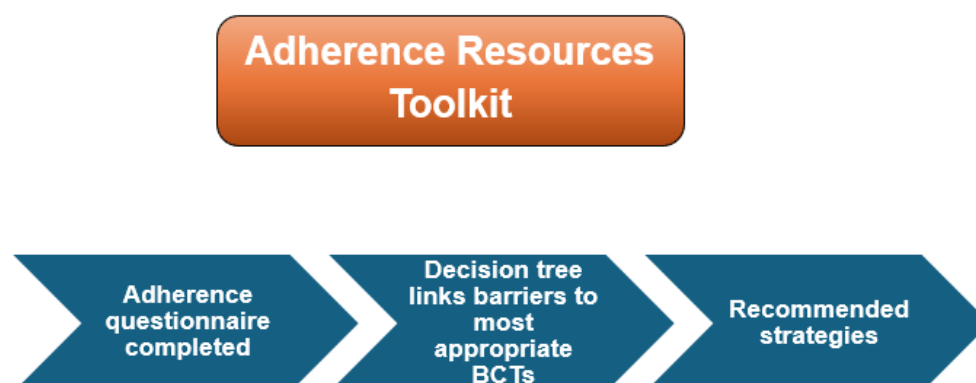


Figure 6.2 Overview of the Adherence Resources Toolkit (ART)

6.3.1 Identifying reasons for nonadherence: The questionnaire

At the core of the ART is a structured questionnaire designed to identify a patient's specific adherence barriers. The questionnaire is organised into three key themes:

- **Knowledge:** Assesses the patient's understanding of their condition, treatment goals, and medication regimen.
- **Administration Difficulties:** Explores challenges with instilling eyedrops, following the dosing schedule, or remembering to take medication.
- **Obtaining Medication:** Focuses on logistical barriers such as prescription refills, pharmacy access, or availability of supplies.

Questions within each category were informed by earlier evidence-based, theoretically driven research (Chapters 2 and 4) and further refined through input from the research team's clinical expertise.

6.3.2 Tailoring Behaviour Change Techniques to individual needs

The questionnaire operates as a decision-support tool, guiding patients through a simple series of yes/no questions about their adherence behaviour. Based on

responses, relevant BCTs are selected to offer personalised solutions. For example, if forgetfulness is identified as an issue, BCTs like *Prompts/cues* may be suggested as a reminder strategy. If difficulty obtaining medication is noted, BCTs like *Social support* or *Restructuring the physical environment* (e.g., arranging home delivery) might be recommended.

Each BCT is selected based on its alignment with the identified barrier and is supported by evidence demonstrating its potential to promote behaviour change. The ART presents these BCTs in a flexible, user-friendly and integrated toolkit, ensuring that patients receive tailored recommendations appropriate to their individual challenges.

Figure 6.3 illustrates an example from the first theme, Knowledge, with sample questions and corresponding intervention suggestions. A full overview of the ART content can be found in Appendix E1.

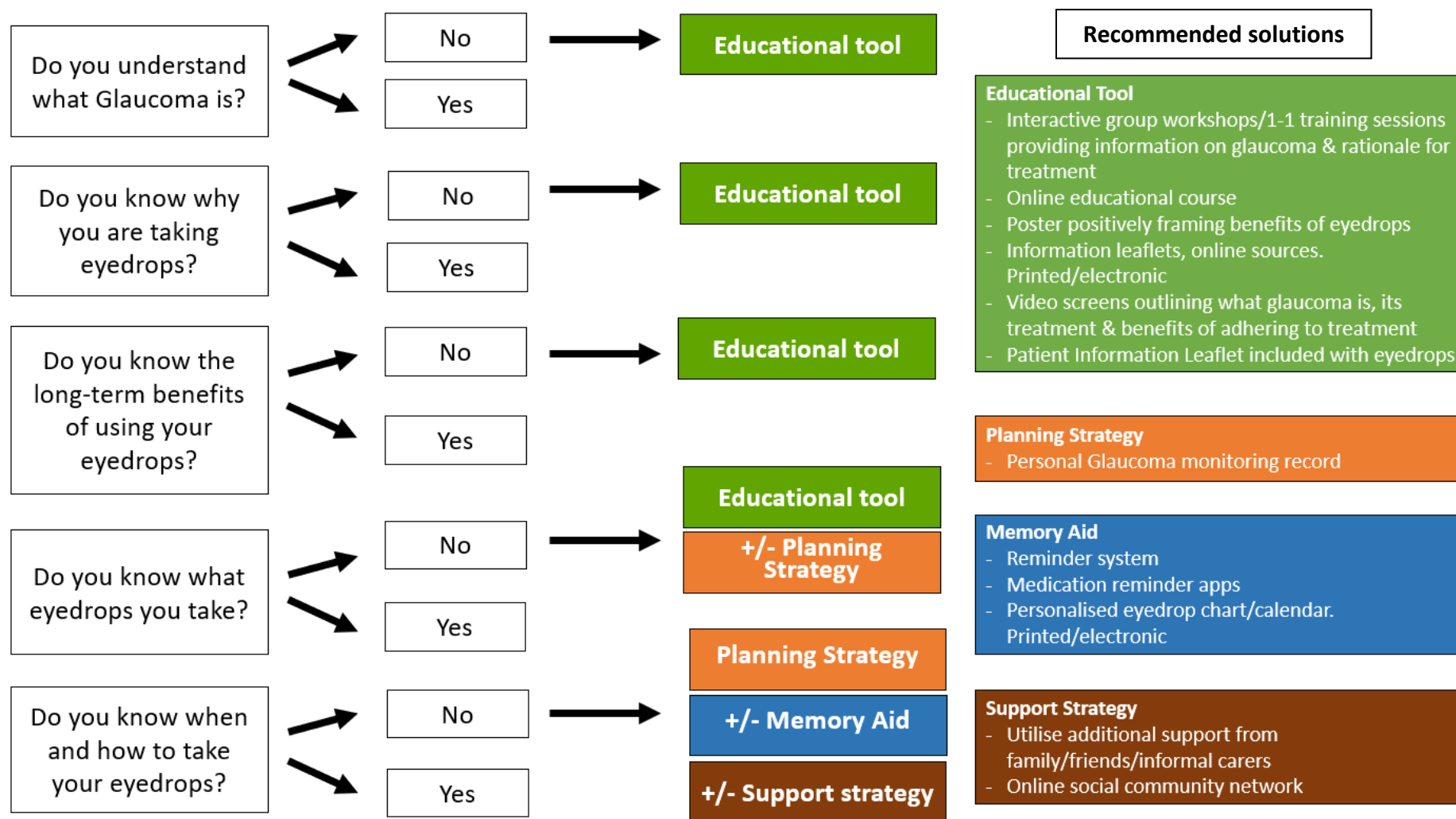


Figure 6.3 Adherence Resources Toolkit example. Knowledge theme with sample questions and recommended solutions

6.3.3 Implementing the ART: Delivery and integration

Having proposed a conceptual model for the ART, the next step involves how it can be effectively delivered and integrated into existing care pathways. Given that glaucoma is a chronic condition requiring long-term use of topical medication, any adherence intervention must support sustained use to create lasting behavioural change. This aligns with NICE guidance on behaviour change, which emphasises that for chronic conditions, ongoing support and reinforcement are necessary rather than one-off, brief interventions (NICE, 2014). Another key consideration is identifying how and where to embed the ART within the glaucoma care pathway to maximise feasibility and patient engagement.

6.3.3.1 Mode of Delivery

To ensure scalability, the ART's initial step, identifying reasons for nonadherence, must be rapid and easy to administer. This assessment could be delivered via human interaction (either face-to-face or remotely via telephone/video call) or through technology-driven solutions. As discussed in Section 6.1 (page 198), digital technology is increasingly integrated into healthcare, making smartphone-based interventions a scalable and accessible option.

An Artificial Intelligence (AI) conversational agent presents a promising delivery method, enabling interactive, two-way communication through text or speech (Car et al., 2020). This format is adaptable to diverse patient populations and easily accessible via smartphone applications. AI-driven interventions can deliver personalised, targeted adherence support (Alowais et al., 2023), an important component for managing glaucoma (see Section 1.14.2, page 67). Conversational agents are generally well accepted, scalable, and effective in supporting behaviour change (Aggarwal et al., 2023). Additionally, a meta-analysis has shown that multi-component mobile interventions are particularly effective for improving long-term medication adherence and addressing the complex nature of nonadherence (Wiecek et al., 2019).

For patients comfortable using technology, the ART could be delivered electronically via an AI-driven smartphone application. For those preferring human interaction, HCPs could facilitate delivery during remote or in-person consultations.

Once the overall delivery mode is selected, the specific format and method of delivery for each BCT will need to be determined.

6.3.3.2 Who delivers the ART?

If the ART assessment is conducted in person, it could be integrated into existing healthcare roles. Evidence supports the use of nurses and allied health professionals, such as pharmacists or trained non-medical staff, in delivering adherence interventions (Kim et al., 2023; Marcum et al., 2021; Singh et al., 2021; Tolley et al., 2023). In the UK, Eye care liaison officers (ECLOs) could also play a key role. ECLOs in Northern Ireland already provide eyedrop training as part of the ECLO Glaucoma Good Practice Guidelines (RNIB, 2022). However, this is not yet routine practice in England, Scotland, or Wales, presenting an opportunity to expand their role. With 120 ECLOs employed by RNIB and a further 40 by other sight loss charities, there may be potential for ECLOs to become involved in providing eyedrop training across the UK.

Utilising services outside of the hospital setting could address the issue of limited time within busy outpatient clinics. Community pharmacists also present an opportunity to deliver adherence support. For example, the UK-based ‘#KnowYourDrops’ campaign demonstrated success with pharmacist-led informal training, including hands-on demonstrations and adherence counselling (Thomas & Chiu, 2017). However, resource availability and cost considerations would need to be addressed in future planning.

Due to clinical time constraints, it is unlikely that the treating clinician would be able to deliver the intervention. If the ART is delivered electronically via AI, a virtual glaucoma assistant could be utilised. Studies have demonstrated that virtual

assistants can improve medication adherence in chronic conditions and are generally well accepted by patients (Babel et al., 2021; Roca et al., 2021).

6.3.3.3 Target population for the ART

As discussed in Section 1.17 (page 77), the ART is designed to support adherence in patients prescribed IOP-lowering eyedrops. The intervention targets individuals without moderate or severe cognitive impairment, as those with significant cognitive impairment were excluded from the qualitative work that informed its design (Chapter 4). However, patients with cognitive impairment may still benefit from the ART if supported by caregivers or family members.

6.3.3.4 Timing and implementation of the ART

A key consideration is when to introduce the ART to maximise its effectiveness. One potential trigger is when sub-optimal adherence is identified at a follow-up appointment, and it cannot be resolved by adjusting the treatment regimen. Defining what constitutes sub-optimal adherence is essential. Findings from the Delphi study (Chapter 3) suggest that a threshold of 80% adherence is generally accepted by ECPs, though this may vary depending on clinical context. Based on these findings, it is recommended that the ART be introduced when adherence falls below 80% or at the clinician's discretion.

Furthermore, introducing the ART at treatment initiation may help establish good habits from the outset. Research highlights high rates of early treatment discontinuation: only 10% of newly diagnosed patients consistently collect prescriptions throughout the first year (Erras et al., 2021) and nearly 50% stop treatment within six months (Bansal & Tsai, 2008). Proactively supporting adherence from the beginning of treatment may therefore improve long-term outcomes.

Following initial ART delivery, a follow-up session is recommended approximately six

weeks later, allowing sufficient time for patients to implement behavioural changes and assess progress. This follow-up could be delivered via the same mode as the initial session (AI or human). Additional sessions can be scheduled if needed. Patients should also have ongoing access to the ART for continued support and reinforcement.

Figure 6.4 provides an overview of the proposed ART pathway.

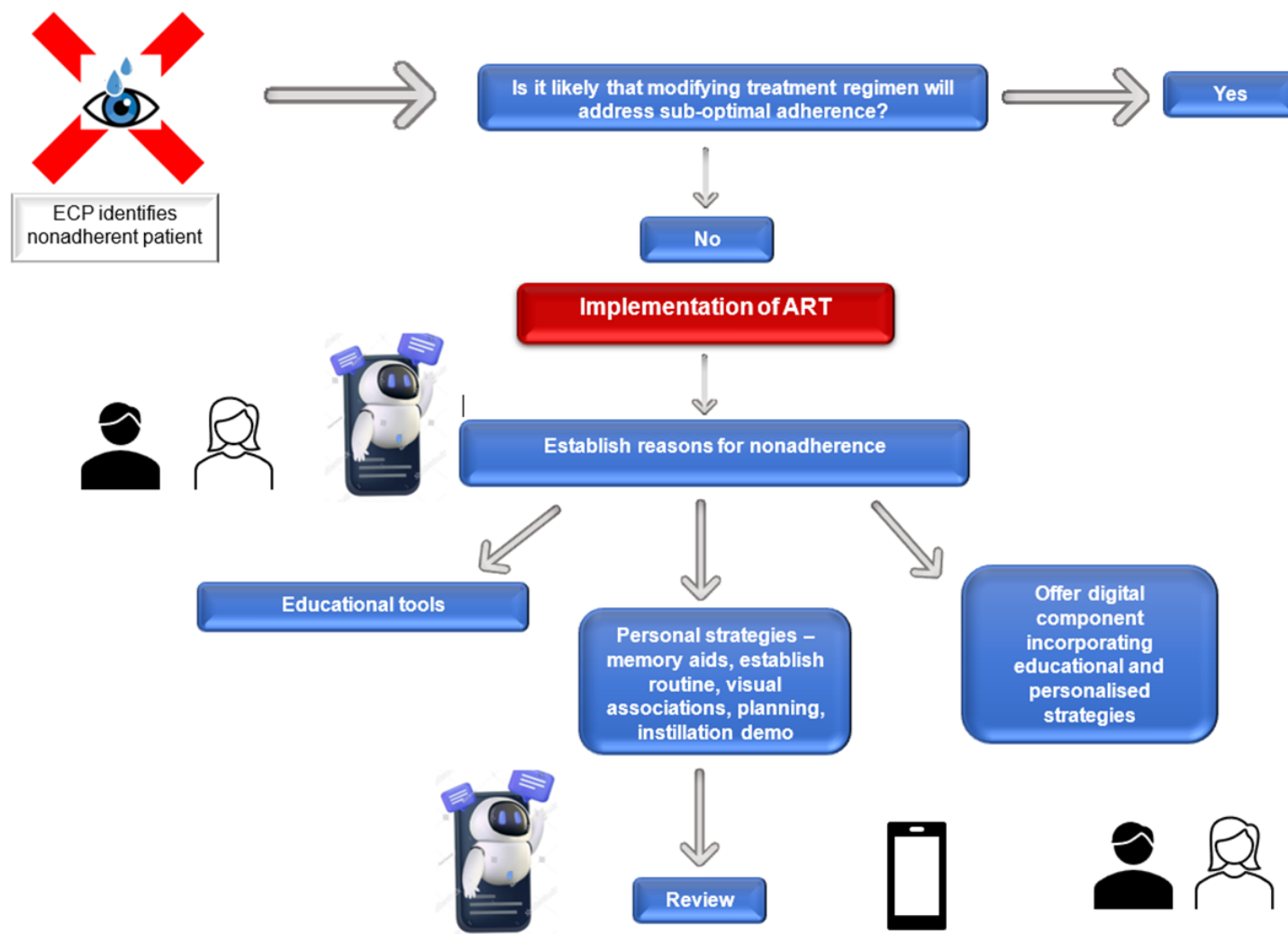


Figure 6.4 Overview of proposed Adherence Resources Toolkit (ART) pathway

Having proposed a conceptual model for the design, delivery and integration of the ART within the glaucoma care pathway, the next step was to evaluate its prospective acceptability among end-users prior to further development. Understanding how acceptable it is to potential users is important to ensure that necessary refinements can be made to enhance its likelihood of real-world success. The following sections provide a detailed account of this evaluation process.

6.4 Evaluating the ART: Assessing prospective acceptability with key stakeholders

6.4.1 Overview

Acceptability is a complex concept that encompasses individuals' cognitive and emotional responses to an intervention, whether anticipated or experienced (Sekhon et al., 2017). The Theoretical Framework of Acceptability (TFA) was developed to assess the acceptability of healthcare interventions by providing a structured approach to evaluation from the perspectives of both those delivering and receiving the intervention (Sekhon et al., 2017). It considers acceptability at different time points: before engagement (prospective), during engagement (concurrent) and after engagement (retrospective). The framework comprises seven key constructs that capture various aspects of acceptability, which are outlined in Figure 6.5.

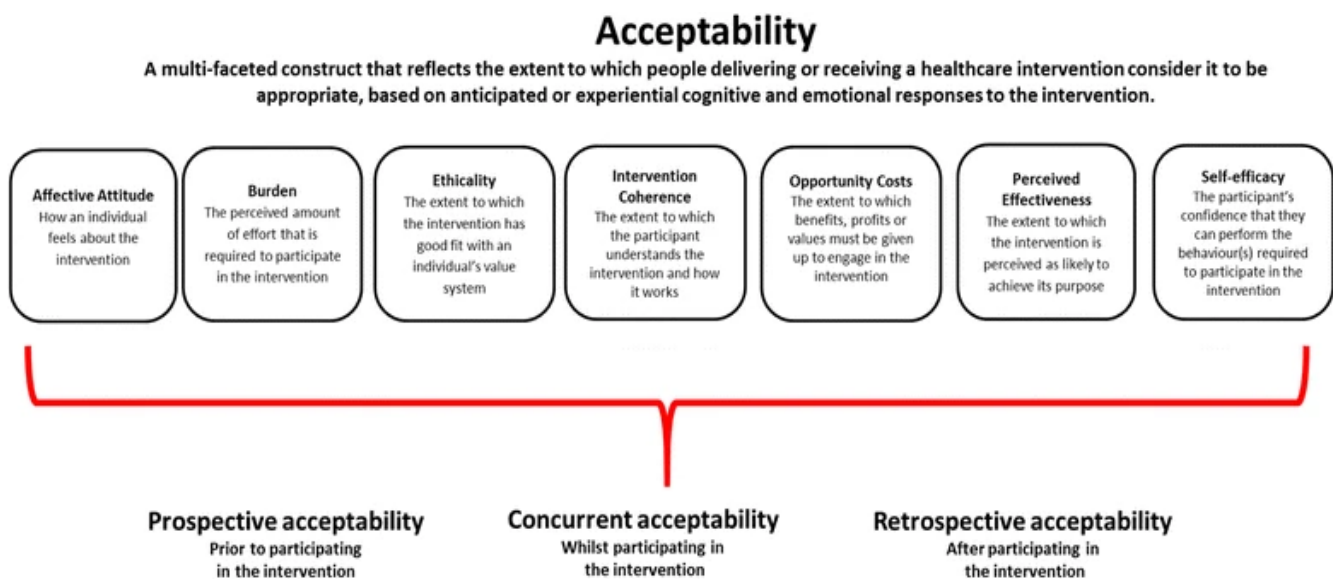


Figure 6.5 The Theoretical Framework of Acceptability: seven constructs and their definitions.

Image courtesy of Sekhon et al., 2017

The TFA has been applied in ophthalmic research, including the assessment of patient acceptability of emerging therapies for geographic atrophy (Enoch et al., 2023). However, to the author's knowledge, it has not yet been used in the context of glaucoma care.

This aim of this study was to use the TFA to explore the overall perceived acceptability of the ART, in its conceptual form, to support medication adherence from the perspective of potential end-users, including both those who might use it and those who might administer it. At this stage, the ART was a conceptual model rather than a working prototype, allowing participants to respond to its structure and intent rather than interact with a functional version. The study also examined whether the ART questionnaire was perceived as effective in identifying reasons for nonadherence and gathered feedback on ways to refine and improve the toolkit. Importantly, the study did not evaluate the acceptability of the specific intervention components i.e. the proposed strategies, their format, content and delivery mode. This decision was made because, if participants did not find the ART effective in identifying reasons for nonadherence, design modifications might be necessary.

Such changes could, in turn, impact the proposed intervention strategies, since they are directly linked to the questionnaire via a decision tree.

6.5 Methods

6.5.1 Study design and procedure

This study employed a mixed methods research design to assess the acceptability of the ART using the TFA. In line with the development phase of the MRC guidance on developing complex interventions, Sekhon et al. (2017) recommend applying the TFA both qualitatively and quantitatively to evaluate prospective intervention acceptability.

To explore perceptions of the ART, a co-development activity was carried out through a knowledge exchange event involving potential end-users. This interactive session used qualitative methods to facilitate group discussion, enabling participants to share experiences, generate ideas collaboratively, and reflect on the toolkit's relevance and usability. Additionally, a post-event poll was also conducted to gather quantitative feedback on the perceived effectiveness of the toolkit in identifying reasons for nonadherence.

6.5.2 Participant recruitment

Potential end-users

Recruitment for the study targeted individuals who were aged 18 years or older and either used or had used one or more IOP-lowering eyedrops or lived with or cared for someone with glaucoma who used such medication. Purposive sampling was employed (Sandelowski, 1995) to aim for a diverse sample, considering factors such as age, ethnicity, geographical location, number of prescribed eyedrops and duration of use.

Participants were recruited through various channels, including advertisements placed on the Glaucoma UK website, in their magazine and via their telephone helpline, as well as social media platforms such as X (formerly Twitter) and LinkedIn. Additionally, individuals who had previously taken part in qualitative interviews (Chapter 4) and expressed an interest in further participation were invited to join the study. An example of the recruitment materials is provided in Appendix E2.

Potential Administrators

The study also sought participation from individuals who could potentially be involved in administering or implementing the ART. They included HCPs working in primary or secondary care settings, such as optometrists, ophthalmologists, orthoptists and ECLOs, as well as key stakeholders involved in glaucoma care, including representatives from Glaucoma UK and the RNIB.

Recruitment followed a similar approach, with advertisements shared via social media platforms, postings on professional organisation websites (e.g., the British and Irish Orthoptic Society) and direct invitations to previous research participants who had expressed interest in continued involvement. Additionally, snowball sampling was used (Marshall, 1996), allowing existing participants to suggest colleagues who met the eligibility criteria, such as pharmacists working in glaucoma care. To aim for diversity among administrators, purposive sampling was again employed, considering variables such as age, gender, ethnicity, geographical location within the UK and professional role.

All participants were provided with an information sheet about the study in their preferred format (electronic or hardcopy): a copy of which is provided in Appendix E3.

6.5.3 Data collection

A two-hour online knowledge exchange event was conducted via Microsoft Teams in June 2024 and was audio-recorded for transcription and analysis. Before the

session, each participant received written information about the ART, including a visual representation and a hard copy for reference during the discussion. Participants were also asked to complete a demographic questionnaire and provide written consent, with materials sent in their preferred format (email or post).

To ensure participants were comfortable with the format of the event, the primary researcher (DB) personally contacted all patient participants before the session. This provided an opportunity to confirm their understanding of the session structure and offer a practice run with Teams to build confidence and facilitate engagement. Professionals expressed familiarity with Teams and were contacted via email only. On the day of the event, a designated IT facilitator was also available to assist with any technical issues.

The session began with introductions and an overview of the study's objectives, led by the primary researcher (DB). The group comprised 15 participants, who were then divided into three virtual breakout rooms, each discussing one of the ART's three themes. Discussions were led by trained academic facilitators, with a researcher observing in each group. Each breakout group included five participants, with a mix of patients, HCPs and key stakeholders (Ayala & Elder, 2011). The research team decided to keep the groups mixed to ensure that the patient voice remained central in each discussion, reflecting the patient-targeted nature of the ART. This approach also allowed practitioners to hear directly from patients, while enabling patients to address any concerns raised by practitioners, facilitating a more balanced and insightful discussion.

A structured topic guide was used to explore each of the seven TFA constructs, as outlined in Section 6.4.1 (page 210), ensuring a comprehensive evaluation of anticipated acceptability. This guide was developed by the primary researcher (DB), drawing on Sekhon et al.'s recommendations (2017, 2022), along with input from the research team and a behavioural scientist. The full topic guide is available in Appendix E4.

Each group focused on a specific theme of the ART:

- Group 1 explored issues related to patients' lack of knowledge and education about glaucoma and the rationale for treatment
- Group 2 examined challenges in administering eyedrops
- Group 3 discussed difficulties in obtaining eyedrop medication

Before the session, facilitators were briefed on the intervention and provided with a visual representation of the ART (identical to that given to participants) and a detailed topic guide with prompts. During the breakout discussions, the relevant section of the toolkit was also displayed on screen to facilitate engagement.

The session concluded with participants reconvening in the main group to share key insights and allow for further discussion.

Following the knowledge exchange event, participants were sent an anonymous online poll to obtain a snapshot of their views on the ART's potential effectiveness in identifying reasons for nonadherence. They were asked whether they believed the ART could effectively determine why an individual does not use their eyedrops correctly. The poll question was adapted from guidance on using a generic questionnaire to assess the acceptability of healthcare interventions using the TFA (Sekhon et al., 2022). Participants rated the ARTs potential effectiveness on a scale from 1* (not very effective) to 5* (extremely effective).

6.5.4 Data analysis

Qualitative Analysis

All discussions were transcribed verbatim and anonymised, supplemented by field notes taken by observing researchers. A content and framework analysis approach was used, with both deductive and inductive coding. Deductive coding, conducted by the primary researcher (DB), initially categorised data according to the seven TFA constructs. Inductive coding was then applied to generate emerging themes within each construct, offering deeper insight into participants' perspectives. Throughout the analysis, findings were reviewed iteratively by the research team and the

behavioural scientist to ensure alignment with the TFA framework and accurate interpretation of the data. Any discrepancies were resolved through consensus agreement.

To capture additional insights beyond the TFA constructs, any data that did not fit within the predefined framework were separately coded using an inductive approach. This ensured that valuable findings outside the TFA model were not overlooked.

Quantitative Analysis

Data from the post-event poll were analysed using descriptive statistics to assess participants' overall perceptions of the ART's perceived effectiveness in identifying reasons for nonadherence.

6.5.5 Ethical considerations

Ethical approval for the study was granted by the Research Ethics Committee of the Department of Optometry and Visual Sciences at City St George's, University of London (Ethics Approval Number: ETH2122-1657), as detailed in Appendix E5. All participants provided written informed consent, and the study adhered to the ethical principles outlined in the Declaration of Helsinki.

6.6 Results

A total of 16 participants initially agreed to take part in the study, comprising seven patients, seven HCPs and two key stakeholders. However, on the morning of the event, one patient was unable to attend due to a family illness, resulting in a final sample of 15 participants.

Among the six participating patients, all were female and self-administered their eyedrops. The group included individuals with varying levels of education, employment status and durations of glaucoma treatment. The majority of HCPs had over six years of experience in glaucoma care, with 33% having worked in the field

for more than 20 years. Participant demographics are detailed in Tables 6.1 and 6.2, with patient data presented separately from HCPs and key stakeholders.

Table 6.1 Patient demographics

Participant demographics		N (%) N=6 total
Gender	Female	6 (100)
	Male	0
Ethnicity	White British	4 (67)
	White – other	1 (17)
	Asian	1 (17)
Age (years)	51-60	1 (17)
	61-70	3 (50)
	>70	2 (33)
Location	England	5 (83)
	Scotland	1 (17)
Highest level of education	School (up to 16)	2 (33)
	School (up to 18)	1 (17)
	Diploma	1 (17)
	Degree or higher	2 (33)
Occupational status	Full/part time employment	2 (33)
	Retired	3 (50)
	Housewife	1 (17)
Duration of glaucoma eyedrop usage (years)	<5	1 (17)
	5-10	2 (33)
	11-20	3 (50)
Self-administer eyedrops	Yes	6 (100)
Visual ability	No visual difficulties reported	4 (67)
	Visual difficulties but not formally registered	2 (33)

Table 6.2 Healthcare professional and key stake holder demographics

Participant demographics		N (%) N=9 total
Gender	Female	5 (56)
	Male	4 (44)
Age (years)	31-40	2 (22)
	41-50	3 (33)
	51-60	1 (11)

	61-70	2 (22)
	>70	1 (11)
Ethnicity	Caucasian	6 (67)
	Asian	2 (22)
	Other white	1 (11)
Location in UK	Southeast England	4(44)
	Yorkshire	1(11)
	Northwest England	2(22)
	South Wales	1(11)
	Northern Ireland	1(11)
Role within glaucoma	Optometrist	2 (22)
	Ophthalmologist	1 (11)
	Orthoptist	2 (22)
	ECLO	1 (11)
	Pharmacist	1 (11)
	Glaucoma UK engagement team	2 (22)
Work setting ¹	Hospital Eye Service	6 (55)
	Community optometry practice	1 (9)
	Charity organisation	4 (36)
Time worked in glaucoma care (years)	2-5	1 (11)
	6-10	2 (22)
	11-15	2 (22)
	16-20	1 (11)
	>20	3 (33)
¹ 2 participants work in the Hospital Eye Service and for a charity hence N=11		

6.6.1 Findings from the TFA analysis

The following section presents a narrative description of each TFA domain, structured around the perceived acceptability of using the ART to support glaucoma medication adherence. To enhance understanding and interpretation, the framework's domains have been organised into three categories: the nature of the intervention (affective attitude and ethicality), the implementation of the intervention (intervention coherence, self-efficacy, burden and opportunity costs) and the outcomes of the intervention (perceived effectiveness) (Sekhon et al., 2016). Insights from HCPs and patient advocacy groups are described separately from those of

patients. This separation ensures a clear understanding of the perspectives of both groups.

6.6.1.1 Nature of the Intervention

Affective attitude

This theme explores how participants feel about the ART and whether they perceive it positively or negatively. Three sub-themes emerged: Likes and Dislikes, Output Options, and Format and Delivery.

Likes and Dislikes

Professionals had a largely positive response to the ART, particularly appreciating its structured approach to addressing nonadherence. They found it a useful tool for identifying patients who may not be suitable for eyedrops, allowing clinicians to suggest alternative treatments. E105, an optometrist, commented *'I think going through a process where you have a structured support system to improve adherence for the variety of different reasons there may be seems very, very sensible to me.'*

The ARTs straightforward design, particularly its colour-coding and flowchart, was well received. However, some noted that the knowledge section appeared overly complex and cluttered, suggesting that simplifying this part could improve clarity and ease of use. E101, an ophthalmologist noted, *'The flow looks a little bit too busy, especially the green tables. There's loads of subcategories outlined which makes it a little bit difficult to follow.'*

Patients were also receptive to the ART, appreciating its proactive approach to addressing nonadherence. P104 said, *'I think anything of any sort is a way forward, is better, isn't it.'*

Output Options

Both participant groups appreciated the ability to be able to generate a final report summarising the adherence strategies discussed. This report was seen as a helpful

reminder of next steps and a form of positive reinforcement for maintaining adherence. The idea of sharing this report with other HCPs, such as pharmacists, social prescribers and GP practice nurses, was particularly well-received. P106, a patient commented, *'It would be good with involvement of your GP...most GP's have a pharmacy person on their books as well, I think that might be better.'*

Participants believed it could enhance integrated care, streamline communication between providers and improve patient access to essential resources and support.

Format and Delivery

Both participant groups highlighted the benefits of an interactive process for working through the flowchart, though they were flexible about who should administer it. Involving family members or caregivers was suggested as a way to improve patient support and raise awareness of glaucoma and correct eyedrop use. P107, a glaucoma patient, commented *'I wouldn't mind [who went through the toolkit with me] as long as someone knew how it operates and....they can explain that to me clearly.'*

While participants had no strong preference between paper or digital formats of the ART, they appreciated having both options available. Some patients favoured a paper version, although concerns were raised about its compatibility with technology-dependent features. The use of QR codes was suggested as a way to provide additional information and bridge the gap between paper and digital formats. E101 remarked, *"If you're going to develop an app, I'm assuming there would be lots of pictures and videos, and if it was more interactive, it would be even better."*

Ethicality

This domain explores whether the ART aligns with participants' values and addresses the challenge of glaucoma medication adherence. One practitioner highlighted that nonadherence is a major issue, made more challenging by the lack of practical guidelines for its management. They emphasised the need for developing effective solutions to address this gap. E105 stated *'It's a problem area*

[glaucoma medication adherence] of course. So I think all clinicians would recognise from their interface with patients regularly that this continues to be problematic and a really important area of research. So in that sense, you know, this tool is to be welcomed.'

Coding for this theme proved challenging, as individuals are not accustomed to considering whether an intervention fits with their values. However, two key sub-themes emerged: Accessibility and Equity of care.

Accessibility

Both participant groups highlighted that if the ART were developed in a digital format to be fairly accessible to all, it would need to account for individuals who may be less familiar with technology, lack access to devices or have inadequate technological resources. Patients expressed concerns about ensuring networks are in place to support them in using any technological features of the toolkit. P102 remarked *'Keep in mind all age groups if it's going to be a technology thing, is it going to be something that's going to be easily accessible by people who maybe have difficulties with technology?'*

Equity of care

Equity of care was another issue raised, with both patients and clinicians emphasising that those receiving community-based care should have equal access to the same support services as those treated in hospital eye care settings. E105 stated *'I do feel she [P104] was on to something when she referred to concerns she has about her care in the different clinic setting in the future..... I'm all for primary care, optometry engaging but whatever services we've got to support patients in terms of adherence in a hospital setting...that's got to be replicated there in a community setting where we can't create a cohort of patients who are denied the opportunity for this important intervention.'*

6.6.1.2 Implementation of the Intervention

Intervention Coherence

This theme explores participants' understanding of the ART's purpose and its overall functionality. Two sub-themes emerged: Clarity of Objectives and Usefulness in Practice.

Clarity of Objectives and Usefulness in Practice

Both clinicians and patients recognised the importance of developing the ART and found its objectives clear and purposeful. HCPs appreciated the structured guidance it offers for addressing nonadherence in clinical settings. E106, an ECLO, commented *'I can see [the need for developing a tool] I mean this is my daily bread and butter.....I could see your questions are the questions I would ask pretty much on a daily basis. I can see the need for it [developing tool] and I can see the clear guidance around like you know what, what happens if this is the answer, what are the possible solutions. So yeah, I can see how the toolkit would work.'*

Patients also found the toolkit easy to follow and its purpose understandable. P104 stated *'As for you know, you're laid out plan [tool] I can understand it.'*

Self-efficacy

This theme explores participants' confidence in being able to use the ART. Three sub-themes emerged: Perceived usability, Need for support, and Technology concerns.

Perceived Usability

HCPs generally found the toolkit user-friendly but believed that real-world testing would provide a more accurate assessment of its practical usability. They anticipated that certain aspects, such as recommending strategies to address nonadherence, could be more complex, with the level of difficulty varying depending on how these solutions are integrated into the ART. One practitioner E105 commented, *'the*

questions are quite straightforward...but it is then about the subsequent steps in the process and how they're implemented and how easy that is and so that ease of use, you know, I think I think that could be variable.'

Need for Support

Both professionals and patients felt that patients might feel more confident in using the toolkit if there was someone available in the clinic to guide them through the process. This support, they emphasised, would need to be consistently available, especially for first-time users. P105, a patient, reflected '*I think I'd feel more reassured if someone went through it [using the toolkit] with me, yeah,*' highlighting the importance of in-person assistance to reinforce patient confidence.

Technology Concerns

Concerns were raised that incorporating technology-based elements into the toolkit, could reduce an older person's confidence in using it. Both groups noted that while technical skill was not necessarily the issue, patients' confidence could be undermined by the instability and unreliability of technology. E105 remarked '*I just hope any toolkit that had.... [technology-based elements] was actually robust and wasn't subject to fragility as opposed to an elderly person with glaucoma believing it's their fault because they can't manage the technology.*'

Burden

This theme explores the perceived additional effort participants felt was needed to either administer or personally use the ART. Three sub-themes were generated: Time and resource demands, Delegation and support structures, and Patient ease of use and accessibility.

Time and Resource Demands

Practitioners noted that administering the toolkit in clinical settings could be time-consuming, especially in already busy and under-resourced clinics. While asking the questions themselves might not significantly add to their workload, addressing the issues identified by the toolkit would place extra demands on both time and

resources. Clinicians expressed concern that without additional support, the process of managing nonadherence could become overwhelming. E106, an orthoptist, remarked *'if it's going to be a clinical person that's using this toolkit.... something that has to be quick and easy to use.....straightforward and simple.....that doesn't take up a lot of time because we know that clinicians time is finite and they only have a certain amount of time.'*

Delegation and Support Structures

It was suggested that having a designated individual, such as a trained assistant or coordinator, to guide patients or carers through the ART would be more beneficial and lessen the burden on clinicians. This would allow practitioners to focus on more pressing clinical tasks while ensuring the toolkit's proper use. E106 commented *'It was the view of the clinician in the group that could be an issue depending on how well resourced the clinic is in terms of nursing support or ECLO support....versus placing another demand onto the clinician.'*

Both patients and practitioners noted that in community settings, new support structures would need to be developed to mirror the processes introduced in specialist hospital clinics, ensuring consistent engagement with the ART across all care environments. This would require additional time, money, effort and resources.

Patient ease of use and accessibility

From the patient's perspective, it was thought that developing a quick, easy-to-use, accessible and straightforward ART would minimise the effort required on their part. P104 commented *'I'm quite lazy, especially if I get something from like the dentist or what not, I'll just put it on the side and then it will never get looked at ever again. Whereas if you've got something that you can access more easily right at the time, it might be something, even if you're in the waiting room, perhaps...it just makes it a little bit easier.....to just [use] there and then.'*

Opportunity costs

This theme explores the perceived costs or sacrifices associated with engaging with the ART. A key sub-theme that emerged was Integration into Clinical Workflow vs. Additional Demands.

Integration into Clinical Workflow vs. Additional Demands

Professionals within the group believed that the toolkit could be seamlessly integrated into the existing eye care pathway and administered by non-medical staff (e.g., ECLOs, Glaucoma UK helpline staff, ophthalmic technicians). This approach was seen as a way to streamline the process without overburdening clinical professionals. E108, an optometrist, commented, [the patient] *'sees the HCA or the nurse prior to coming into clinic or the technician.....I think [they] probably would help just to identify the area where things are falling apart, the reason for that nonadherence, so yes, absolutely'* [using toolkit can be incorporated into clinic flow].

However, some concerns were raised about the additional demands that might arise from the issues identified by the ART. While asking the questions themselves might not significantly increase workload, the process of addressing nonadherence could create extra challenges for practitioners. E105 highlighted, *'if you as a clinician identify a problem area, there might be nobody else around. You might have to be doing quite a bit of scrambling around, making some note to contact somebody else subsequently.'*

Participants acknowledged the need for proper training and operational planning to ensure that the ART is effectively implemented without overloading clinical staff, making it a sustainable addition to the care pathway.

6.6.1.3 Outcomes of the Intervention

Perceived effectiveness

This theme explores participants' views on the ARTs potential to effectively identify reasons for nonadherence and assist both patients and clinicians in addressing

these challenges. A sub-theme that emerged was Effectiveness Dependent on Implementation and Case Complexity.

Effectiveness Dependent on Implementation and Case Complexity

Both patients and HCPs generally agreed that the ART could be valuable in highlighting the underlying causes of nonadherence. Patients felt the toolkit could encourage more reflection on their difficulties. P107, a glaucoma patient remarked *'it [the tool] makes people think about it [why you are not using eyedrops correctly] 'cause I think when people just live their day-to-day lives they don't give it much thought. But when you're actually asked to think about it and answer, I think it can be useful.'*

However, professionals noted that the toolkit's success would largely depend on its implementation and integration into practice. While they saw its potential, they cautioned that its effectiveness might be limited in more complex cases. Despite this, practitioners noted that the ART could be especially valuable for patients who may feel uncomfortable discussing difficulties with their HCP. It could enable patients to independently identify their reasons for nonadherence and explore possible solutions on their own. E106, an ECLO remarked *'if the patient [did] not have the confidence to say they, you know, were having difficulties with this [instilling drops] and didn't have the confidence to say to someone, something like this toolkit where they could go through themselves on their own individually where they could go this is what I'm having difficulties with. And then there's like almost like a guidance around what to do in that instance would be great.'*

Both participant groups saw potential in the toolkit's ability to encourage self-awareness in patients while supporting HCPs in delivering targeted solutions, particularly in less complex cases.

Themes Generated Outside the TFA Framework: Considerations for Further Development

Although some themes emerged outside the formal constructs of the TFA, they were deemed important to the overall acceptability and usability of the ART. One such theme focused on considerations and recommendations for further development.

Potential Improvements

Patients noted that certain scenarios, particularly within the knowledge section, may not be relevant to everyone, potentially affecting engagement with the toolkit. To address this, participants suggested replacing binary response options with an additional choice such as “would like to know/learn more” to enhance patient education and increase engagement. Another recommendation was to include clear guidance on proper eyedrop storage, given the confusion patients often face regarding refrigeration requirements. As one patient, P107, remarked *‘I think there... needs to be more clarity around consultants or pharmacies telling patients how do you actually store your medication if it has to be kept in a fridge or not.’*

Encouraging Ongoing Care and Support

Patient advocacy group representatives emphasised the importance of using the toolkit to encourage regular eye check-ups and ongoing glaucoma care. They suggested the addition of features guiding patients toward support services and additional resources, which could offer ongoing assistance. These enhancements were seen as beneficial for improving patient outcomes and warranting further development. E104 remarked *‘it’s really important to keep stressing to people that they do need to go for regular eye health checks...I think somewhere that needs to be in there.’*

Flexibility and Accessibility

Participants generally agreed that while the toolkit was well-suited for a broad audience, it needed to be adaptable to meet diverse user needs. One HCP proposed developing a hybrid version that blends paper-based elements with technological features. This approach would allow supportive family members or caregivers to use

the toolkit alongside the patient ensuring that key resources remain accessible to everyone. To improve inclusivity, it was suggested that a digital version incorporate audio commands, making it easier for individuals with visual impairments to navigate. Additionally, some patients recommended that a paper version be available in large print to further support those with vision problems. Both groups also emphasised the need to accommodate different language requirements, with E109, a clinical pharmacist, commenting, *'you've got a huge ethnic population and you'll see that again the language problem also causes quite a number of issues there as well.'*

Refining Questions for Clarity

To enhance the ART's overall effectiveness, patient advocacy representatives suggested revising certain questions and adding new ones. For example, in the knowledge section, they recommended separating the question *"Do you know when and how to take your eyedrops?"* into two separate questions, as each addresses different aspects of adherence that require different approaches. Additionally, one patient proposed including a question about side effects or long-term frustrations with eyedrops to better identify reasons for nonadherence.

In the section addressing difficulties obtaining medication, both patients and clinicians felt that the existing questions did not fully capture issues like pharmacy supply problems, patients not recognising their medication or running out of eyedrops before their next prescription. They recommended adding specific questions to address these challenges and improve the toolkit's comprehensiveness.

6.6.1.4 Post-event poll responses

Participants rated the ART's perceived effectiveness in identifying reasons for nonadherence using a 5-point scale (1* = not very effective, 5* = extremely effective). The majority of respondents (80%) considered the ART to be potentially effective. A more detailed breakdown of responses is provided in Figure 6.6.

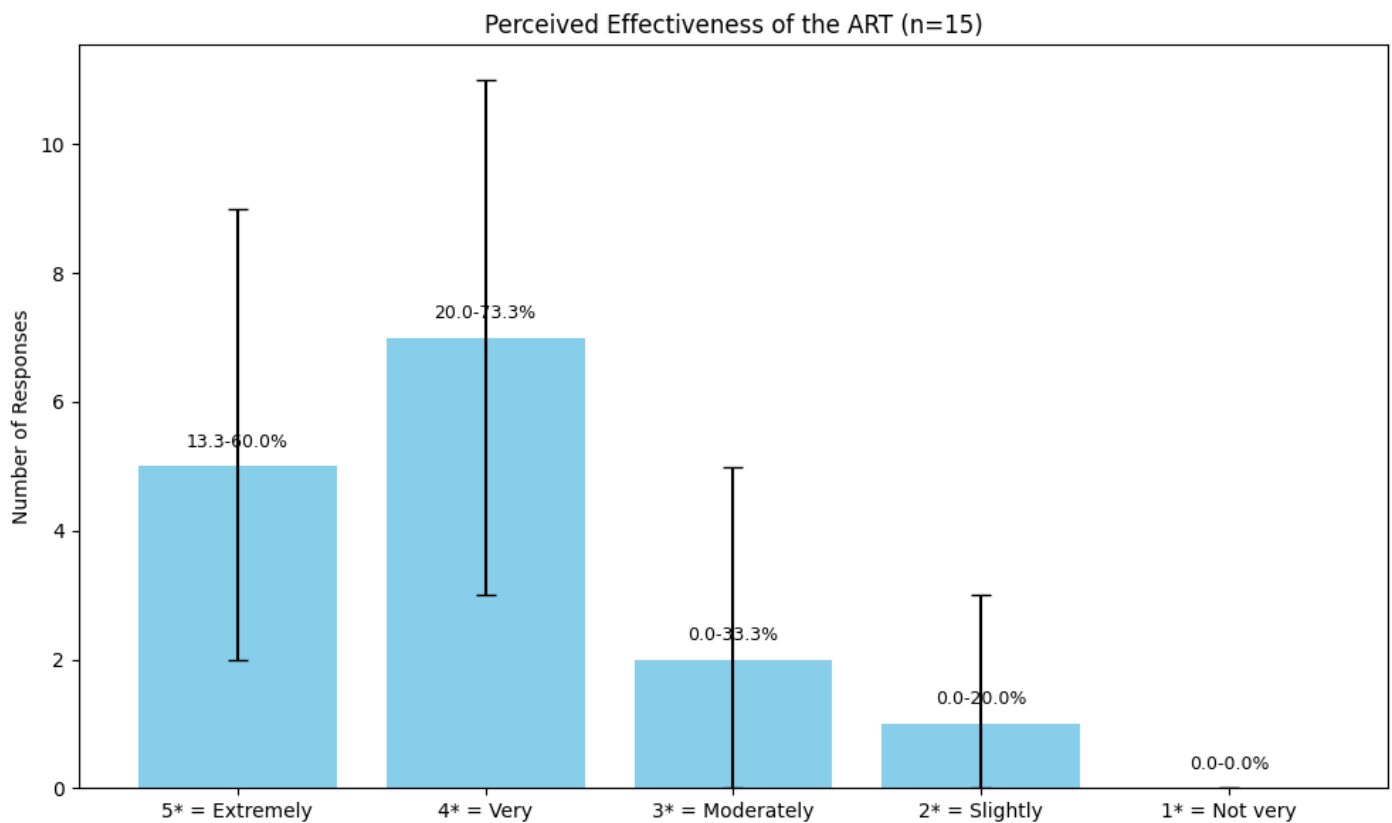


Figure 6.6 Post-event poll responses on the perceived effectiveness of the ART (n=15), with 95% Confidence Intervals

6.7 Discussion

This chapter presents how previously identified theoretically selected intervention components were combined into a cohesive, patient-centred intervention designed to support glaucoma medication adherence. The resulting ART was developed as a conceptual model and evaluated by potential end-users to assess its prospective acceptability.

A key design priority was ensuring the ART could be systematically tailored to individual patients. This was important because research highlights that nonadherence arises from a variety of patient-specific barriers and interventions that offer personalised solutions show the greatest promise in improving adherence (Gatwood et al., 2022; Ha et al., 2022; Waterman et al., 2013). To achieve this, a

structured questionnaire was developed to align with the theoretically identified barrier themes. This tool enables a personalised assessment of each patient's adherence challenges and recommends appropriate BCT-based solutions, ensuring the intervention is tailored rather than one-size-fits-all.

By tailoring adherence support, the ART adopts a patient-centred approach that increases engagement and promotes self-management. This aligns with existing evidence that self-management support is the most common and effective intervention for improving outcomes in chronic health conditions (Reynolds et al., 2018). Additionally, the structured format also enhances consistency across different users and increases the potential for replicability in clinical practice. Given the practical constraints of healthcare settings, the questionnaire needed to be easy to administer and efficient. For example, a 30-item questionnaire developed to assess adherence barriers in cardiovascular patients, was later reduced to 10 items due to feasibility concerns in routine practice (Bhattacharya et al., 2023; Brown et al., 2017). These considerations influenced the final design of the ART questionnaire.

Evaluating acceptability

The ART's prospective acceptability was assessed through a knowledge exchange event involving potential end-users, using the TFA. Data from the event mapped onto all seven TFA constructs, though ethicality proved more challenging to code. These findings provide key insights into how the ART could be refined and implemented to maximise its acceptability and effectiveness in real-world settings.

Perceived strengths of the ART

Overall, the ART was well received, with participants recognising its value in addressing nonadherence. HCPs found its systematic design particularly beneficial, as it provided a clear process for understanding patients' adherence barriers and delivering targeted solutions. Patients also viewed the ART as a valuable tool, particularly as it could encourage self-reflection on medication use. This finding aligns with research from Kassavou et al. (2020a), who reported that participants in

their study found the *Feedback on behaviour* functionality in their adherence app prompted reflection on medication-taking patterns.

Clinicians highlighted the ART's potential for patients who struggle to articulate their adherence challenges. Research suggests that patients may not always feel comfortable disclosing their medication-taking behaviours to clinicians (Martin et al., 2005). Therefore, a structured yet non-judgmental assessment tool like the ART is more likely to elicit honest responses about nonadherence.

The post-event poll further supports the ART's potential as an effective tool for improving medication adherence, with 80% of participants rating it potentially very effective in identifying adherence barriers. However, it is important to note that the poll included only 15 participants, which may limit the generalisability of this finding. While the responses provide useful initial insights, they may not reflect the views of a broader or more diverse population of potential end-users.

Enhancing communication and collaboration

Both patients and clinicians valued the ART's ability to generate a summary report outlining recommended adherence strategies. Patients saw this as a useful reference to reinforce adherence behaviours, while HCPs viewed it as a structured overview that could be shared among those involved in the patient's care, enhancing communication and continuity. The potential for multidisciplinary collaboration through shared documentation is well-supported in the literature, with research indicating that coordinated care improves intervention efficacy (Lammila-Escalera et al., 2024; Tandan et al., 2024).

Format preferences and accessibility considerations

Participants highlighted the importance of an interactive and flexible approach to using the ART, with many expressing a preference for both paper-based and digital formats to ensure accessibility across diverse patient populations. The importance of flexibility in adherence support tools has been highlighted in other research. For instance, Sumner et al. (2023) found that an AI-driven nudge tool was considered

acceptable by users provided it was adaptable to their individual needs, reinforcing the necessity for personalised and user-centred approaches in adherence interventions. Concerns were raised about digital accessibility, particularly for those with limited technological skills or resources, reflecting broader challenges reported in the implementation of digital health interventions (Brewer et al., 2020; Madanian et al., 2023).

Equitable access to adherence support was another key consideration. Participants emphasised that patients receiving community-based care should have the same access to adherence interventions as those in hospital settings. Without careful implementation, there is a risk of exacerbating existing disparities in healthcare provision. This concern aligns with existing literature on healthcare equity, which highlights how structural inequalities can lead to variations in service availability and inconsistent levels of care (Williams et al., 2020).

Implementation challenges and practical considerations

Participants demonstrated a clear understanding of the ART's purpose and functionality. Clinicians expressed confidence in its structured guidance, while patients found it easy to follow and its objectives clear, indicating strong potential for patient engagement. However, discussions around self-efficacy revealed varying levels of confidence in using the ART. While clinicians generally considered it user-friendly, they emphasised the need for real-world testing to assess its practical implementation. Patients were expected to benefit from in-person guidance when first using the ART. This finding is consistent with research on digital adherence interventions. For instance, a study assessing the acceptability of a smartphone app and text messaging service for hypertension medication adherence found that participants recommended an introductory help guide to explain all features upon installation, which was expected to improve accessibility and engagement (Kassavou et al., 2020a).

Concerns were raised about the burden of implementation, particularly in busy clinical environments. While administering the ART's questions was not seen as

time-consuming, addressing the issues it identified could place additional strain on healthcare resources. Clinicians suggested that non-medical staff could support the administration of the ART. This recommendation aligns with the multidisciplinary approach to glaucoma care in the UK (NICE, 2022; The Royal College of Ophthalmologists, 2020). It also supports previous research showing that interventions facilitated by HCPs can improve adherence and clinical outcomes but often require frequent and lengthy consultations, making them resource-intensive and challenging to sustain (Glynn et al., 2010; Kassavou et al., 2018; Schroeder et al., 2004).

A potential solution to address this challenge could be digital implementation using AI-driven chatbots, which have been shown to effectively mimic human support and improve engagement with digital health interventions (Aggarwal et al., 2023). AI-assisted technology has demonstrated effectiveness in improving medication adherence, offering a scalable and cost-efficient approach to supporting patient self-management (Aggarwal et al., 2023; Labovitz et al., 2017; Pouls et al., 2021).

6.7.1 Future refinements

Several refinements were suggested to enhance the ART's usability and potential effectiveness. One key recommendation was simplifying the knowledge section to make it more user-friendly. Additionally, modifications to the response formats were proposed, allowing patients to indicate areas where they would like further information rather than relying solely on binary responses. This supports NICE (2017) guidance in providing patients with ongoing support and mirrors previous research that found glaucoma patients have a desire for more educational information (Olthoff et al., 2009; Sanchez et al., 2020; Taylor et al., 2002). Participants also emphasised the need to address common adherence challenges, such as medication storage concerns, within the ART's content. Refinements to questionnaire wording were suggested to improve clarity, including rephrasing certain questions to capture more nuanced information. Finally, ensuring digital

accessibility while maintaining paper-based alternatives was considered essential for equitable implementation.

The knowledge exchange findings highlight the ART's strong potential as a structured intervention for addressing glaucoma medication nonadherence. Participants valued its clear objectives, structured format and ability to generate adherence strategies, while also identifying key areas for improvement. Addressing these refinements will support the transition of the ART from a conceptual model to a functional prototype, paving the way for feasibility testing and further development.

Although participants at the knowledge exchange event recommended developing an updated version of the ART incorporating these refinements, this was not undertaken within the current study. Due to time and resource constraints, producing a fully revised toolkit was beyond the scope of this thesis. However, future work is planned to build on these recommendations, with a focus on co-developing and testing an updated, user-informed version of the ART.

6.7.2 Strengths and limitations

One of the key strengths of this study is that the intervention was developed in line with the MRC guidance for designing complex interventions (Skivington et al., 2021). This framework advocates for thorough documentation of the intervention development process, making it easier for others to replicate and build upon. This study has carefully outlined the systematic decision-making process and provided a clear rationale behind the design of the overall intervention toolkit.

Another strength was the use of the TFA, which provided a recognised and structured framework for assessing the intervention's prospective acceptability (Sekhon et al., 2016). By incorporating both patients and key stakeholders in the process, the study provided a diverse mix of perspectives on the perceived acceptability of the ART, ensuring that the needs and concerns of both users and administrators were captured.

However, while the sample was diverse in terms of patients and professionals, there is room for improvement in the representation of underrepresented groups. Future research should aim to include a more balanced gender distribution and greater ethnic diversity within the patient cohort and the inclusion of carers or family members. These factors would further enhance the generalisability of the findings.

It is also important to acknowledge that the ART was a conceptual model. As a result, some of the constructs within the TFA framework may have been difficult for participants to assess, given that the intervention components were still in the formative stages of development. At the time of the knowledge exchange event, the full details of the intervention were not yet determined, and only potential applications had been suggested. Once refinements are made to the ART, future studies should further investigate the acceptability of the proposed strategies and formats to assess their real-world feasibility.

6.8 Conclusion

This chapter has detailed the development of a theory and evidence-based intervention toolkit designed to support glaucoma medication adherence at the patient level. It describes how seven theory-driven BCTs and three IFs were integrated into the intervention and outlines the key decision-making processes involved in its complex design.

Initial feedback from both potential users and administrators was highly positive, indicating strong potential for the intervention's acceptability. However, to enhance its applicability in real-world settings, further refinements and feasibility trials are necessary. These modifications identified through this feedback will guide the next stages of development and testing, helping to optimise the intervention for wider implementation.

Chapter 7 Summary of Findings, Key Insights and Future Directions

7.1 General discussion

This thesis adopted a behaviour change approach to explore how to improve medication adherence in glaucoma, with a focus on developing a theory-informed, patient-centred intervention to support use of ocular hypotensive eyedrops.

Glaucoma is a leading cause of preventable vision loss worldwide, and with increasing life expectancy, its prevalence is rising (Tham et al., 2014). The only proven method, to date, to slow disease progression is lowering IOP, making sustained and effective treatment essential. While various treatment options exist, topical eyedrops remain the first-line therapy globally (Radcliffe et al., 2023; Virani & Rewri, 2024; Wagner et al., 2022). Yet adherence to these medications is often poor, with some estimates as low as 30% (Olthoff et al., 2005). Given that over 76 million people are affected globally, nonadherence represents a major global health challenge, putting millions at risk of avoidable vision loss.

Despite considerable research, sustained improvements in adherence have been difficult to achieve (Waterman et al., 2013). Complex interventions, those that combine patient education with personalised behavioural strategies show the greatest promise (Kuntz et al., 2014; Nieuwlaat et al., 2014; Waterman et al., 2013). However, a key limitation of many existing interventions is the lack of a clear theoretical foundation, which limits an understanding of how they work and how they might be optimised.

Behavioural theory provides a structured lens through which to explore these mechanisms. By applying established theoretical models, researchers can identify the determinants of behaviour, select appropriate intervention strategies, and evaluate how and why interventions work (Cadogan et al., 2017; Gorman et al., 2022). This approach is advocated by the MRC framework for developing and evaluating complex interventions (Skivington et al., 2021).

To address these gaps, this thesis developed a conceptual model for a theory-based complex intervention toolkit, the ART, to support patients in adhering to their prescribed glaucoma eyedrops. Informed by the Behaviour Change Wheel (BCW) and aligned with NICE and WHO guidelines promoting shared decision-making and patient engagement (NICE, 2009; World Health Organization, 2017) the ART was designed using behavioural theory, empirical research, and stakeholder perspectives. This work represents the initial Development phase of the MRC framework, creating a strong foundation for future feasibility testing and refinement.

The following sections summarise the key findings of the thesis in the context of the wider literature, and outline implications for future research, clinical practice, and policy.

7.2 Research approach

A clear understanding of the behavioural drivers of nonadherence was essential to guide effective intervention design. This thesis adopted the BCW framework to provide a systematic, theory-informed structure for identifying behavioural determinants and designing appropriate intervention strategies.

At the core of the BCW is the COM-B model, which defines behaviour as arising from Capability, Opportunity, and Motivation. The COM-B model was used to frame the behavioural diagnosis, while the Theoretical Domains Framework (TDF) was applied to organise qualitative and systematic review findings into specific personal, sociocultural and environmental domains.

These TDF domains were then mapped to relevant Intervention Functions (IFs) and Behaviour Change Techniques (BCTs), using the BCW's structured linking processes. In doing so, the BCW provided a practical framework to move from behavioural understanding to intervention design, ensuring that selected strategies directly addressed the most salient and modifiable barriers to adherence. This

approach reflects evidence suggesting that adherence interventions are more effective when they explicitly target the underlying mechanisms of behaviour change (Rahman et al., 2022).

This research followed a multi-stage process, as described in Section 1.15 (page 68). The first stage involved identifying the modifiable determinants of glaucoma medication adherence through a systematic review and qualitative studies (Chapters 2 and 4).

7.3 Identifying modifiable determinants of adherence

A comprehensive approach was taken to examine modifiable behavioural determinants from multiple perspectives: patients, ECPs and the healthcare system. Chapter 2 presented a systematic review synthesising existing evidence on these determinants using the TDF. While this provided valuable insights, further exploration was necessary in real-world settings. To build on these findings, qualitative interviews were conducted with patients and ECPs in the UK (Chapter 4) providing a deeper understanding of the specific and universal barriers and enablers influencing adherence.

Using the TDF across both studies (the systematic review and qualitative research) allowed for a consistent and structured analysis of the behavioural influences on adherence. Previous research has highlighted the importance of identifying modifiable rather than unmodifiable factors, as only modifiable determinants can guide development of effective targeted interventions (Horne, 2011). In contrast, unmodifiable factors may help identify ‘at-risk’ groups but do not explain why nonadherence occurs or how it can be improved.

7.3.1 Systematic review findings (Chapter 2)

The systematic review identified key modifiable adherence barriers and enablers across patient, practitioner and system levels. Common barriers included complex

medication regimens, limited patient understanding of glaucoma, forgetfulness and difficulties with eyedrop administration. These challenges align with previous research, which consistently highlights poor knowledge, forgetfulness and administration difficulties as major obstacles to adherence (Newman-Casey et al., 2015; Olthoff et al., 2009; Tsai et al., 2003).

Conversely, adherence was facilitated by simplified treatment regimens, well-informed and educated patients and strong patient-practitioner relationships. Less complex regimens and positive patient-practitioner interactions have been shown to improve adherence outcomes (Barnebey & Robin, 2017; Friedman et al., 2008). These findings reinforce the idea that adherence is shaped by a complex interplay of individual, systemic and environmental factors, aligning with previous literature (Brown & Bussell, 2011; Gast & Mathes, 2019; Kardas et al., 2013).

The review also identified a notable gap in research on practitioner and system-level influences, as most studies predominantly focused on patient-related determinants. This highlights the need to explore how these broader influences shape patient adherence behaviours, which is essential for developing effective system-wide interventions.

7.3.2 Qualitative research findings (Chapter 4)

Chapters 4 presented findings from qualitative interviews conducted with patients and ECPs in the UK to identify the key modifiable determinants of medication adherence. A key strength of this research was its dual focus on both patient and ECP perspectives, revealing distinct yet interrelated behavioural challenges. While patients provided insight into their personal experiences of taking glaucoma medication, ECPs discussed their role in supporting adherence and the difficulties of managing nonadherence in practice. Understanding adherence from both perspectives is essential, as patient behaviour is shaped not only by individual factors but also by their interactions with HCPs. It is recognised that facilitating behaviour change in one group of individuals often requires understanding and

addressing the behaviours of another group (Huston, 2015; Stewart et al., 2023).

ECPs play a key role in identifying and addressing nonadherence, yet many struggle to accurately detect it (Djafari et al., 2009; Okeke et al., 2009a) leading to missed intervention opportunities. The WHO has emphasised the need for targeted training to equip HCPs with the skills to assess adherence risk and deliver effective interventions (Sabaté, 2003). This raises an important consideration: while adherence interventions often target patient behaviour, there is also a need to provide structured support for practitioners.

For patients, key facilitators of adherence included: sufficient understanding of glaucoma, ability to obtain ongoing supplies of medication, confidence in eyedrop administration, strong belief in the necessity of treatment, a desire to prevent vision loss, positive social influences and the establishment of a routine. In contrast, barriers included forgetfulness, poor administration skills, competing lifestyle demands, prescription delays, stock shortages and systemic healthcare challenges. These findings align with previous research, which highlights the multifaceted nature of adherence, encompassing both intentional and unintentional barriers (Newman-Casey et al., 2015b; Rees et al., 2010).

From the perspective of ECPs, adherence management was influenced by their professional responsibility to address nonadherence, their ability to tailor decision-making to individual patients, a multidisciplinary team approach and structured action planning. However, key challenges included time and resource constraints, difficulties in identifying nonadherence and issues with medication availability. While ECPs recognised their role in promoting adherence, many felt limited in their ability to provide tailored support due to pressures within the healthcare system. These findings reflect previous research, where practitioners have reported persistent challenges in supporting patient self-management in routine clinical care (Hind et al., 2020; Kvarnström et al., 2018; Weiss et al., 2015).

While previous studies have primarily focused on patient-reported adherence barriers, the research presented in Chapter 4 highlights the important role of practitioners in shaping patient behaviour and acknowledges the behavioural constraints they themselves face. These findings emphasise the need to address challenges experienced by both patients and HCPs. Future interventions should go beyond targeting patient behaviour alone; they must also equip HCPs with the tools to identify and manage nonadherence effectively. Additionally, broader systemic challenges within the healthcare system and pharmaceutical industry must be considered to create a more supportive environment for both patients and practitioners.

7.4 Selection of components for a conceptual model of a complex intervention to support patient medication adherence in glaucoma

Having established the key modifiable behavioural determinants of adherence, Chapter 5 described the process of developing a patient-centred intervention using the BCW framework.

7.4.1 Stage 1 Selecting components for the intervention

The first stage involved synthesising the findings from the systematic review (Chapter 2) and UK-based qualitative research (Chapter 4) to identify the key behavioural determinants of glaucoma medication adherence at the patient level. Using the TDF, three overarching barrier themes were identified, mapped to four modifiable TDF domains.

These domains were then linked to corresponding components of the COM-B model. The behavioural diagnosis indicated that nonadherence was primarily influenced by limitations in psychological and physical capability, as well as physical opportunity. These COM-B components shaped the direction of the intervention, ensuring that selected strategies directly targeted the most influential drivers of behaviour. Each of the four TDF domains was systematically mapped to relevant BCTs using the Theory

and Techniques Tool (Johnston et al., 2021). This process ensured that BCT selection was theory-informed and evidence-based, rather than arbitrarily chosen. A key strength of using the TDF is its linkage to evidence-based BCTs, ensuring that behaviour change strategies are theoretically grounded rather than arbitrarily chosen (Michie et al., 2008).

In total, seven BCTs were selected, addressing the key COM-B drivers through intervention strategies that enhance patients' capability and opportunity to take their medication as prescribed. This number aligns with findings from a systematic review of cystic fibrosis interventions, which reported an average of 9.6 BCTs per intervention (Dawson et al., 2023). Furthermore, many of these techniques are consistently identified in reviews of effective adherence interventions across other chronic conditions (Douma et al., 2024; Fujii et al., 2022; Teo et al., 2024).

Despite growing recognition of the importance of theory-based interventions, many adherence strategies are still poorly described in the literature (Dawson et al., 2023; Morrissey et al., 2017; Screti et al., 2024). To address this issue, researchers recommend explicitly detailing the methodology behind intervention development to clarify the underlying mechanisms of action and facilitate replication in clinical practice. This thesis contributes to bridging that gap by clearly outlining the COM-B components and TDF domains targeted, the rationale for selected IFs and BCTs, and the process used to finalise intervention content. In doing so, it supports the development of transparent, evidence-based, and replicable strategies to address glaucoma medication nonadherence.

7.4.2 Developing a comprehensive intervention toolkit

Following the identification and selection of theoretically grounded intervention components, Chapter 6 focused on integrating these into a structured, patient-centred adherence support toolkit, the ART. The ART was designed to help identify an individual's specific reasons for nonadherence and provide tailored strategies targeting both intentional and unintentional barriers to correct eyedrop use. By

addressing both perceptual and practical factors, the ART aims to enhance patient understanding, build routines, and increase motivation. This approach aligns with NICE guidance (NICE, 2009), which recommends supporting adherence through a dual focus on perceptual and practical influences.

Central to the ART is a structured questionnaire developed using insights from the systematic review (Chapter 2) and qualitative research (Chapter 4). This questionnaire serves as a tool for identifying patient-specific adherence barriers and was designed to be quick to administer, user-friendly, and non-judgemental. This focus on practical feasibility is consistent with guidance on the real-world implementation of complex interventions (Skivington et al., 2021) and mirrors recommendations from NICE and other health behaviour research (Chan et al., 2020), which emphasise the importance of open, non-confrontational patient engagement.

A key strength of the ART lies in its personalised and structured approach. Rather than applying a one-size-fits-all strategy, the toolkit provides support that is tailored to individual needs, enhancing both relevance and acceptability. Personalised interventions have been shown in RCTs to be effective in improving adherence (Kibbons et al., 2023; Nguyen et al., 2016; Xavier et al., 2016). However, as highlighted in a systematic review and meta-analysis of 771 adherence interventions, individual tailoring remains underreported, with only nine studies explicitly describing this approach (Conn & Ruppar, 2017). Moreover, Conn & Ruppar (2017) found that the most effective interventions prioritised behavioural strategies, particularly those that promote habit formation, a principle that is central to the ART's design. By combining individual tailoring with evidence-based behavioural techniques, the ART addresses key gaps in intervention design and offers a replicable, transparent pathway for delivering personalised adherence support in glaucoma care that is both theoretically grounded and practically feasible.

7.4.3 Assessing prospective acceptability of the ART

Following the development of the ART, Chapter 6 then focused on evaluating its perceived acceptability among potential end-users. The findings from a mixed-methods acceptability study, conducted with both patients and professionals, are outlined in the final part of Chapter 6. Overall, the ART was perceived as highly promising, with participants valuing its structured format, clear objectives and ability to generate tailored adherence strategies. Both patients and practitioners recognised its potential as a practical and systematic tool for improving glaucoma medication adherence.

Despite the positive findings, the study also highlighted key refinements needed to optimise the intervention. Patients suggested improvements to the questionnaire's wording and delivery, emphasising the need for both paper-based and digital formats to enhance accessibility. Previous research has shown that younger adults are more likely to adopt digital technology than older adults, however, this age disparity can be mitigated by individuals' existing baseline technology skills (Czaja et al., 2006). A similar trend was observed in a UK study with ophthalmic patients, where individuals over 80 years old had greater difficulty using technology and were less likely to engage with digital tools (Ali et al., 2019).

When implementing a digital health intervention, a patient's baseline technology skills may play a crucial role in their ability and willingness to engage with it. This factor must be carefully considered to ensure accessibility. Careful planning is required in how the intervention is introduced and supported to accommodate varying levels of digital literacy. To prevent exclusion, offering a paper-based version of the ART remains essential for individuals who may struggle with digital engagement. A similar model has been proposed for a pharmacist-delivered, individually tailored intervention aimed at improving medication adherence in patients with hypertension, asthma or chronic obstructive pulmonary disease. This approach combines a reduced number of in-person pharmacist sessions with a supporting tool available in both digital and paper-based formats (Garfield & Judah, 2022).

An alternative approach, as suggested by a HCP (Section 6.6.1.2, page 222), is to develop a hybrid version of the ART that blends paper-based elements with technological features. Adopting a hybrid strategy for the ART could enhance accessibility while utilising the benefits of digital tools for those who can engage with them.

Professionals provided insights on integrating the intervention into existing workflows and refining its design to ensure ease of implementation. Additionally, both patients and key stakeholders emphasised the importance of equitable access, advocating for the intervention to be available not only in hospital settings but also in community healthcare environments. Addressing these refinements will support the transition of the ART from a conceptual model to a functional prototype, paving the way for feasibility testing and further development.

This study reinforces the value of assessing acceptability before progressing to large-scale evaluation, aligning with MRC guidance on complex intervention development (Skivington et al., 2021). Similar approaches have been successfully applied in other adherence-focused interventions. For example, researchers developing a tailored intervention for hypertensive medication adherence first conducted a qualitative acceptability study (Kassavou et al., 2020a) which then informed a feasibility RCT (Kassavou et al., 2020b) that demonstrated its effectiveness in improving adherence behaviour. By following this structured approach, the ART toolkit is positioned for further refinement and feasibility testing, ensuring it is both user-friendly and effective in real-world settings.

7.4.4 Implementation considerations

An important aspect of developing the ART intervention was determining the optimal timing for introducing adherence support. Chapter 3 addressed this by establishing a benchmark for acceptable adherence among UK ECPs, helping to define when the intervention should be initiated. Findings from the Delphi survey presented in Chapter 3 suggest that ECPs generally consider an adherence rate of 80%

acceptable for most glaucoma patients. However, this threshold was not absolute and may vary based on factors such as disease severity, risk of progression, individual patient characteristics and treatment complexity. Given these nuances, it was proposed that the ART should be introduced when adherence falls below 80% or at the clinician's discretion, allowing for a more flexible and patient-centred approach.

The complexity of defining acceptable adherence, as highlighted in Chapter 3, highlights the limitations of a single, universal threshold. Several factors influence the level of adherence needed to optimise patient outcomes and this research highlights the potential for establishing individualised adherence benchmarks rather than a standardised cut-off. Future research should explore personalised adherence thresholds tailored to individual risk profiles, which would help ensure support is delivered when clinically necessary rather than based on an arbitrary percentage.

In addition to deciding when to introduce the ART, practical aspects of intervention implementation were explored in Chapter 6, including optimal delivery method, the appropriate personnel to administer the intervention and strategies for its integration into the existing eye care pathway. The aim was to develop an intervention that could be seamlessly embedded into routine clinical practice, ensuring feasibility and sustainability. A key challenge in adherence interventions is that, while many are theoretically effective, they often fail in real-world implementation due to practical constraints (Skivington et al., 2021). By addressing these considerations early, this research aims to enhance the ART's potential to be successfully adopted in clinical settings.

7.5 Future research, practice and policy recommendations

Based on the findings and insights presented throughout this thesis, the following recommendations are proposed to guide future research, clinical practice, and policy development in the area of glaucoma medication adherence.

1. Advancing the ART Intervention

Given the ART intervention was positively received by potential end-users, further development is justified. The next step is to refine the conceptual model into a practical prototype suitable for use in clinical settings. This process should continue to involve patients and key stakeholders to ensure the final intervention is both clinically feasible and patient-centred. Once the ART prototype has been finalised, the next step will be to conduct pilot studies to evaluate its feasibility, usability, and effectiveness. In accordance with the MRC framework, this stage is essential to ensure the intervention is practical and acceptable before proceeding to wider implementation. To determine the ART's effectiveness a cluster randomised control trial or a stepped-wedge trial could be conducted (Hooper, 2021).

2. Refinement and adaption of the ART intervention

Given that adherence to glaucoma medication is shaped by various contextual and cultural factors, as outlined in Chapters 2 and 4, further research should investigate how the ART intervention can be refined and adapted to meet the needs of diverse patient populations. Future research could explore ways to personalise the intervention based on key patient characteristics, such as visual impairment, health literacy, language preferences and socio-cultural contexts.

Intervention adaptation has been successfully applied in other areas of healthcare. For example, an evidence-based adherence intervention for HIV treatment in sub-Saharan Africa was modified by researchers to suit different regional contexts, improving its relevance and effectiveness (Audet et al., 2017). Similar approaches could be applied to the ART intervention, ensuring it remains flexible and applicable across different healthcare environments to increase its reach, effectiveness and accessibility.

3. Exploring the role of technology in supporting adherence

A key area for further research is the potential for digital tools, such as an AI-driven app, to enhance the ART intervention. AI-based interventions have the potential to

personalise adherence support, provide real-time feedback to both patients and clinicians and facilitate remote monitoring of medication use (Aggarwal et al., 2023). For example, the AI-driven app, Medisafe, not only delivers reminders but also tracks patient adherence and shares these data with HCPs. A RCT demonstrated that the app significantly improved adherence in medically underserved patients with chronic illnesses compared to standard care (Hartch et al., 2024).

Future research should investigate how digital health technologies can be seamlessly integrated into the ART framework to enhance accessibility, engagement and effectiveness. This may be particularly valuable in settings where patients face barriers to attending in-person appointments or require more frequent adherence monitoring. A systematic review found that interactive digital interventions can improve medication adherence by facilitating communication and decision-making between patients and HCPs (Pouls et al., 2021).

4. Integrating the ART intervention into clinical practice

Although the ART intervention was developed as a stand-alone tool for ease of development, its long-term success will depend on its integration into existing eye care pathways. Future research should examine how the ART intervention can be embedded within hospital eye services, community optometry settings, and primary care, such as GP practices or pharmacies. Understanding how the intervention can complement current care structures will be critical for its scalability and sustainability.

5. Developing training materials for delivery

For the ART intervention to be effectively delivered in clinical settings, appropriate training materials and resources must be developed. Future research should focus on developing training materials and resources for those administering the ART. These resources would ensure that the intervention is delivered consistently (Horner et al., 2006), provide clear instructions on how to integrate it into clinical practice and ensure that those administering it are equipped to use the intervention to its fullest potential with their patients. Additionally, research should assess the effectiveness of these training materials in enhancing HCPs' skills and confidence in implementing

the ART intervention.

6. Long-term sustainability and impact of the ART intervention

While the ART intervention has been designed to initiate behaviour change, ensuring its long-term effectiveness and sustainability will be an area for future research. Longitudinal studies will be needed to assess whether improvements in medication adherence persist over time. Research could also explore whether periodic reinforcement strategies, such as follow-up support or refresher sessions, are necessary to sustain adherence over extended periods. Additionally, understanding how patient engagement with the intervention evolves over time will help identify potential drop-off points and inform strategies to maintain continued use.

7. Establishing personalised adherence thresholds

One of the key insights from the Delphi study (Chapter 3) is that a generic adherence cut-off, such as the 80% threshold commonly used, may not be appropriate for all patients. Future research should focus on developing personalised adherence targets that account for individual patient characteristics, including disease severity, risk of progression, and treatment regimen. Such an approach could ensure that adherence goals are clinically meaningful and tailored to patient needs rather than arbitrarily defined.

Advancements in digital health and AI-driven clinical tools offer promising avenues for advancing this concept. AI-based models could integrate patient-specific data, such as disease severity, clinical findings and treatment regimens, to calculate personalised adherence thresholds (Kanyongo & Ezugwu, 2023). Such tools could enhance risk stratification, allowing clinicians to identify patients most vulnerable to disease progression and provide targeted adherence support at the right time. Similar approaches have been explored in other chronic disease management areas. For example, a retrospective cohort study using machine learning found that adherence thresholds predictive of hospitalisation risk in diabetic patients varied based on individual and treatment characteristics, rather than conforming to a uniform 80% benchmark (Lo-Ciganic et al., 2015). This reinforces the idea that

adherence targets should be tailored rather than generalised, and future research could further investigate how digital tools can assist with this.

8. Practitioner-level interventions

As highlighted in Chapter 4, addressing medication adherence in glaucoma requires a multi-level approach that considers both patient and practitioner needs. Further research should explore targeted interventions aimed at improving the knowledge, confidence and skills of ECPs in identifying and addressing medication nonadherence. Evidence suggests interventions designed to support HCPs can have an impact on improving patient adherence by enhancing the quality of care provided and fostering better communication between practitioners and patients (Conn et al., 2015).

9. System-level interventions

As highlighted in Chapters 2 and 4, barriers to adherence are often experienced at a systemic level. While providing patients with the necessary tools and equipping ECPs to identify and address nonadherence are critical, system-wide reforms are also needed to create an environment that supports adherence. Further research should explore the development of system-level strategies that address structural barriers through policy changes or reforms aimed at alleviating these obstacles. These could include improving access to medications, reducing prescription delays, and addressing financial barriers that patients face in obtaining necessary treatments.

For instance, pharmacy policies aimed at improving medication access and optimising resource distribution have the potential to support consistent adherence. The NHS's "New Medicines Service" in the UK, which provides support for individuals newly prescribed medication for long-term conditions, has proven effective in improving adherence through community pharmacies (Elliott et al., 2016) and is considered cost-effective (Elliott et al., 2017). Additionally, structural healthcare reforms that integrate care and streamline processes between HCPs could be explored. The integration of advanced IT tools and software into healthcare

systems could help streamline current processes and address systemic inefficiencies. However, considerations regarding IT infrastructure and the associated cost implications would need to be considered.

10. Public awareness campaigns

Public awareness campaigns focusing on medication adherence for chronic conditions like glaucoma could be another valuable area for future research. Such campaigns should aim to educate patients, families, and the wider public about the risks associated with nonadherence, as well as the long-term benefits of consistent medication use. Research could explore how these campaigns are best structured, the most effective communication strategies, and the potential role of community engagement in driving behavioural change.

For example, the DESMOND (Diabetes Education and Self-Management for Ongoing and Newly Diagnosed) programme in the UK has proven to be effective in improving patient knowledge and behaviour in individuals with type 2 diabetes (Chatterjee et al., 2018). Future research could adopt similar educational approaches for glaucoma patients to increase awareness and encourage adherence behaviours, potentially improving clinical outcomes in the process.

7.6 General limitations of the work conducted in this thesis

Despite the strengths of this research, several limitations should be acknowledged. Much of the qualitative data relied on self-reported adherence and participant experiences, which are subject to recall bias and social desirability influences. This may have limited the accuracy of reported behaviours and outcomes. There was also some degree of selection bias in participant recruitment. The qualitative studies largely involved motivated glaucoma patients with relatively high digital literacy, as shown by their ability to participate via online platforms such as Zoom. This may have excluded individuals who are less engaged, digitally excluded, or face other barriers to participation. Additionally, the perspectives of carers were not captured in any of the studies, representing a gap in understanding real-world adherence

challenges for individuals who rely on support with medication management. Future research should address this gap by involving more integrated Public and Patient Involvement and Engagement (PPIE), with particular attention to carers and those from underserved communities, in line with the UK Standards for Public Involvement (<https://sites.google.com/nihr.ac.uk/pi-standards/home>).

The Theoretical Domains Framework (TDF) and the Theoretical Framework of Acceptability (TFA) provided structured approaches for analysing the data; however, their application can be subject to researcher interpretation, introducing a degree of subjectivity into the analysis.

In relation to the ART development specifically, the research focused primarily on a UK-based glaucoma population. As such, the findings and implications for intervention design may not be fully transferable to other healthcare systems, social contexts, or cultural settings.

Although there is a substantial body of adherence research in glaucoma, no studies have applied behavioural science frameworks to guide data collection and intervention development. This limited the opportunity for direct comparison with similar behaviourally-informed work in ophthalmology, particularly during the design and refinement of the ART.

7.7 General conclusion

This thesis has taken a behavioural approach to glaucoma medication adherence, addressing an important gap in the literature by developing a complex, theory-based, and personalised intervention toolkit to support patients in adhering to their IOP-lowering eyedrops. By integrating behavioural science, theoretical insights, empirical findings, and stakeholder input, this research has systematically developed a patient-centred, evidence-informed intervention aligned with the MRC guidance for complex intervention development.

The work began by identifying modifiable determinants of adherence through a systematic review and qualitative studies, underpinned by the TDF. These findings informed a behavioural diagnosis, which guided the mapping of behavioural determinants to appropriate IFs and BCTs. This process led to the development of a conceptual intervention model designed to address key adherence barriers. The selected BCTs were justified, not only by theory and evidence but also by practical considerations around delivery and patient needs. These components were then integrated into a flexible, multifaceted toolkit, the ART, designed to address individual patient-specific barriers. This represents the first time such a theoretically grounded and patient-centred toolkit has been developed to support adherence to IOP-lowering eyedrops. The ART's conceptual model was positively received by both patients and key stakeholders, supporting its potential for further development.

This research contributes to the growing body of literature focused on applying behavioural approaches to improving adherence outcomes and enhancing patient care in chronic disease management. As glaucoma prevalence continues to rise with an ageing population, nonadherence remains a major challenge in eye care. Future research should focus on further refining and developing the ART into a practical, sustainable, and cost-effective intervention. The ultimate goal is to improve adherence, support long-term patient outcomes, and reduce preventable vision loss in glaucoma care.

Peer reviewed publications, conference abstracts and prizes

This section presents peer-reviewed manuscripts and conference abstracts that were developed as part of the research conducted in this thesis.

Publications:

Bott D, Subramanian A, Edgar D, Lawrenson JG, Campbell P. Barriers and enablers to medication adherence in glaucoma: A systematic review of modifiable factors using the Theoretical Domains Framework. *Ophthalmic Physiol Opt.* 2024 Jan;44(1):96-114. doi: 10.1111/opo.13245. Epub 2023 Nov 20. PMID: 37985237.

This article was ranked within the top 10% of most-viewed papers published by the journal in 2023.

Conference Abstracts:

City, University of London Annual Doctoral Researchers Conference, 2021 – **Oral presentation**

Investigating the feasibility and acceptability of using a chatbot to improve adherence to glaucoma medication

Bott D, Subramanian A, Edgar D, Lawrenson JG, Campbell P

Women in Vision UK annual conference, 2022 – **Poster presentation**

Feasibility and Acceptability of using a chatbot to aid glaucoma medication adherence

Bott D, Subramanian A, Edgar D, Lawrenson JG, Campbell P

British Congress of Optometry and Vision Sciences conference, 2022 – **Poster presentation**

Investigating the feasibility and acceptability of using technology to improve adherence to glaucoma medication

Bott D, Subramanian A, Edgar D, Lawrenson JG, Campbell P

EAOO Annual Conference, Poland, 2023 – **Oral presentation**

Eye care practitioner experiences managing glaucoma medication adherence and recommending technology: A qualitative study using the Theoretical Domains Framework.

Bott D, Subramanian A, Edgar D, Lawrenson JG, Campbell P

City, University of London Annual Doctoral Conference, 2023 – **Poster presentation**
Practitioner experiences in managing glaucoma medication adherence and recommending technology-based aids.

Bott D, Subramanian A, Edgar D, Lawrenson JG, Campbell P

College of Optometrists Annual Conference, **2024 - Poster presentation: Awarded Best Early Career Researcher Poster Prize**

Barriers and Enablers to managing glaucoma medication adherence: An interview study with UK specialist Eye Care Practitioners.

Bott D, Subramanian A, Edgar D, Lawrenson JG, Campbell P

Association for Research in Vision and Ophthalmology, 2024 – **Poster presentation**
Determinants of medication adherence in UK glaucoma patients: An interview study.

Bott D, Subramanian A, Edgar D, Lawrenson JG, Campbell P

British Congress of Optometry and Vision Sciences Conference, 2024 – **Oral presentation**

Factors influencing glaucoma medication adherence in patients from the UK and India: A qualitative study.

Bott D, Subramanian A, Edgar D, Lawrenson JG, Campbell P

UK and Éire Glaucoma Society Annual Conference, 2024 – **Poster presentation**
Determinants of medication adherence in glaucoma patients from the UK and India: An interview study.

Bott D, Subramanian A, Edgar D, Lawrenson JG, Campbell P

Research Dissemination and Engagement Activities:

City, University of London School of Health and Psychological Sciences 3-minute thesis competition, 2022 – **Oral presentation and winner**

How to help glaucoma patients use eyedrops as prescribed

City, University of London School of Health and Psychological Sciences

Glaucoma UK event, 2023 – Oral presentation showcasing research to members of Glaucoma UK, patients and university colleagues

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Appendices

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Appendix A1

Search strategy for Medline database

Determinants concept

S6	 S1 OR S2 OR S3 OR S4 OR S5	
S5	 AB barrier* OR obstacle* OR hinder* OR influence* OR determin* OR difficult* OR inhibit* OR discourage* OR prevent* OR factor* OR predictor* OR indicator* OR facilitat* OR promote* OR enable* OR motivate* OR encourage* OR self-efficacy OR "self efficacy" OR belief* OR attitude* OR acceptance OR support OR behaviour N3 change* OR behavior N3 change* OR behaviour* OR behavior* OR knowledge OR communicat* OR "patient N3 educat"	
S4	 (MH "Patient Medication Knowledge")	
S3	 (MH "Patient Education as Topic")	
S2	 (MH "Health Knowledge, Attitudes, Practice")	
S1	 (MH "Health Behavior")	

Adherence concept

S12	 S7 OR S8 OR S9 OR S10 OR S11	
S11	 AB nonadherence OR non-adherence OR noncompliant* OR non-compliant* OR nonpersist* OR non-persist* OR noncooperat* OR non-cooperat* OR "secondary nonadhere*" OR "secondary non-adhere*" OR "secondary noncompliant*" OR "secondary non-compliant*" OR "treatment N3 non-persist*" OR "treatment N3 non-persist*" OR "medication N3 non-persist*" OR "medication N3 non-persist*" OR "treatment N3 discontinu*" OR "medication N3 discontinu"	
S10	 AB adhere* OR compliant* OR concordance OR persist* OR cooperat* OR co-operat* OR "secondary adhere*" OR "secondary compliant*" OR "treatment N3 persist*" OR "medication N3 persist"	
S9	 (MH "Treatment Adherence and Compliance") OR (MH "Treatment Refusal")	
S8	 (MH "Medication Adherence")	
S7	 (MH "Patient Compliance")	

Medication concept

S15  S13 OR S14

S14  AB "glaucoma medication" OR "ocular hypotensive drop*" OR "glaucoma N3 eyedrop*" OR "glaucoma N3 eye-drop*" OR "glaucoma N3 eye drop*" OR "glaucoma treatment"

S13  (MH "Glaucoma/DT") OR (MH "Ocular Hypertension/DT") OR (MH "Glaucoma, Open-Angle/DT") OR (MH "Glaucoma, Angle-Closure/DT")

S12  S7 OR S8 OR S9 OR S10 OR S11

Overall search

S16  S6 AND S12 AND S15

Appendix A2

Codebook including definitions for each domain to aid mapping decisions for extracted data in systematic review

Theoretical Domains Framework: definitions and examples for glaucoma medication adherence. Adapted from Cane et al (2012)

TDF domain and definition	Determinants (i.e. enablers/barriers) of adherence
Knowledge: awareness of the existence of something	Patient's knowledge or HCP/carer referring to patient's knowledge of: • Glaucoma • Rationale for using eyedrops • Consequences of adherence/non-adherence • Treatment application and regimen • Side effects of eyedrops Knowledge can be either extent of (enabler) or lack of (barrier) HCP awareness/lack of awareness regarding adherence/nonadherence in practice (enabler/barrier)
Skills: ability or proficiency acquired through practice	Physical skills needed by patient/carer to instil eyedrops correctly e.g. poor manual dexterity prevents opening or squeezing bottle or poor VA prevents being able to use drops References made by HCP regarding patient's ability to instil eyedrops correctly (enabler/barrier) Ability to order ongoing supplies of eyedrops by patient (enabler) HCP competence may include skills needed to inquire about/assess adherence/educate patients on nature of glaucoma and/or treatment and/or treatment application techniques Skills can be present (enabler) or absent (barrier)
Social/professional role and identity: a coherent set of behaviours and displayed personal qualities of an individual in a social or work setting	Professional role relates to extent HCPs feel providing education regarding glaucoma, treatment, medication adherence and instillation advice is part of their professional role

	Personal identity relates to how patients identify with having glaucoma and whether they take ownership of their behaviour (instilling eyedrops correctly) or see it as someone else's responsibility
Beliefs about capabilities: acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to a constructive use	How confident a patient feels about their ability to instil eyedrops as prescribed and/or manage their glaucoma (enabler/barrier) References made by HCP relating to how confident a patient feels about their ability to instil eyedrops as prescribed and/or manage their glaucoma (enabler/barrier)
Optimism: confidence that things will happen for the best or that desired goals will be attained	Patient's judgement regarding the likelihood instilling eyedrops correctly will prevent sight loss/control glaucoma. Includes optimism (enabler), unrealistic optimism or pessimism (barrier)
Beliefs about consequences: acceptance of the truth, reality or validity of outcomes of a behaviour in a given situation	Patient's perceptions about the outcomes of instilling/not instilling eyedrops as prescribed. Includes beliefs regarding benefits and concerns about unwanted side-effects/future side-effects (enabler/barrier) References from HCP/carer relating to patient's perceptions about the outcomes of instilling/not instilling eyedrops as prescribed. Includes beliefs regarding benefits and concerns about unwanted side-effects (enabler/barrier) Perceptions about the nature of glaucoma and/or outcomes of treatment. Includes how glaucoma or eyedrops may affect patients' life or cause symptoms (enabler/barrier)
Reinforcement: increasing the probability of a response by arranging a dependant relationship, or contingency, between the response and a given stimulus	Patient's response to: - receiving praise/encouragement for instilling eyedrops as prescribed (enabler) - receiving negative feedback for not instilling eyedrops correctly (barrier/enabler) - receiving feedback (either positive or negative) about nature of glaucoma and/or treatment e.g. from family members/HCP (enabler/barrier) HCP's perception that praising/providing negative feedback on compliance/nature of glaucoma/treatment influences patient instilling their eyedrops (enabler/barrier)
Intentions: conscious decision to perform a behaviour or to resolve to act in a certain way	Patient's referring to their intentions to: - instil/not instil their eyedrops as prescribed (enabler/barrier) - continue/discontinue instilling their eyedrops (enabler/barrier)

	HCP referring to patients' intentions to instil/not instil their eyedrops (enabler/barrier) or continue/discontinue instilling their eyedrops (enabler/barrier)
Goals: mental representation of outcomes or end states that an individual wants to achieve	Patient's referring to/HCPs referring to patients: • high/low motivation to adhere to their eyedrop regimen (enabler) • desire to retain as much sight as possible (enabler)
Memory, Attention and Decision Processes: ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives	Whether patients/ carers: • have the ability to remember to instil eyedrops (enabler) • occasionally miss or take longer breaks from instilling their eyedrops due to forgetfulness (barrier) • have the ability to decide whether they instil their eyedrops, whether they decide to take occasional breaks from using eyedrops (enabler/barrier) HCP referring to patients forgetting to instil their eyedrops (either occasionally or more frequently) or lacking the ability to decide whether or not to instil eyedrops (barrier) HCP making treatment decisions and/or what influences these regimen decisions e.g. HCP decides on combination therapy instead of multiple monotherapies as more likely to improve adherence
Environmental Context and Resources: any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behaviour	Any resource that encourages/discourages the instillation of eyedrops e.g. dropper aid may assist/hinder instillation (enabler/barrier) Comorbidities/concurrent medication Financial resources, healthcare issues (e.g. time constraints in clinic, obtaining timely follow up appointments or prescription errors) or accessibility problems (e.g. in acquiring repeat prescriptions from GP/pharmacy) (barrier) Circumstantial factors that influence adhering to eyedrop regimen (e.g. inconvenient administration times, away on holiday, working patterns, time limitations, dosing frequency, existence of side-effects, being dependent on a carer/family member to instil eyedrops and/or collect prescriptions) (barrier)

Social Influences: interpersonal processes that can cause an individual to change their thoughts, feeling or behaviours	Patients referring to the social support/pressure from others on them to instil or not instil their eyedrops (e.g. from family, friends, carers, HCPs, experiences with glaucoma community groups (enabler/barrier) Patients referring to their trust/respect in HCPs (enabler) The influence, either positive or negative, clinician-patient relationships have on patient adherence behaviour (enabler/barrier) Whether a patient takes their eyedrops as prescribed either because they are told to (e.g. by HCP) or because of previous experiences with family members/friends (enabler)
Emotion: complex reaction pattern, involving experiential, behavioural and physiological elements, by which the individual attempts to deal with a personally significant matter or event	Patient's expression of, or references from HCP/carers regarding patient's expression of: • feelings/emotional state/reaction to having to instil eyedrops • feelings/emotional state/reaction to not instilling eyedrops correctly • feelings/emotional state/reaction to loss of vision/sight • Feelings/emotional state/reaction to living with glaucoma (Feelings/emotional state/lack of emotion/reaction can be positive or negative, so enabler or barrier respectively)
Behavioural Regulation: anything aimed at managing or changing observed or measured actions	References from either patient / HCP in using/providing techniques/habits/processes to remember to instil eyedrops e.g. placement of medicine in a prominent place/ personalised routine (enabler/barrier)

Appendix A3

Characteristics of 83 studies included in the systematic review

Study details (1st author, date)	Study aims	Participant characteristics – patient/ HCP Sample size	Adherence rate	Country	Study design	Data collection methods	Data analysis
Anbesse (2019)	To evaluate glaucoma medication adherence and associated factors amongst patients in Northwest Ethiopia	Patients aged 19+ years, diagnosed with glaucoma, using eyedrops, attending a tertiary medical centre outpatient clinic N=360	Self-reported (>60% on questionnaire) 61.4% (95% CI: 56.1-66.7)	Ethiopia	Quantitative - cross sectional	Questionnaire	Multivariate logistic regression
Balkrishnan (2003)	To examine associations between HRQL and patient identified medication adherence, self-belief in eyedrops, administration issues and treatment schedule difficulty among older adults with glaucoma	Patients aged 65-89 years, diagnosed with POAG using glaucoma eyedrops N=375	Self-reported regular use of eyedrops 82%	USA, South-eastern states	Quantitative - cross sectional	Questionnaire	Percentages
Barker (2019)	To assess the psychometric properties of the GTCAT, reduced version Report barriers and enablers to adherence	Patients diagnosed with OAG or OHT, with a recent VF test, self-administering 1 glaucoma eyedrop daily, attending tertiary eye clinic N=183	Objectively measured average adherence ¹ 79.5%	USA	Quantitative - prospective	Electronic monitoring system (MEMS)	Narrative description
Bloch (1977)	To assess glaucoma medication nonadherence and examine how it differs from adherent patients	Patients diagnosed with COAG using topical therapy, attending hospital glaucoma clinic N=40	Self-reported medication missed ≤ once a week 72.5%	USA	Quantitative – cross sectional	Questionnaire – researcher administered	Chi-squared test

Boland (2014)	To assess adherence with once daily glaucoma medication	Patients aged 18+ years, diagnosed with POAG, POAG suspect, PACG or OHT, using a PGA once daily, attending university-based glaucoma clinic N=491	Objectively measured ¹ (>75% of study period) 82.8%	USA	Quantitative – prospective cohort	Electronic monitoring system (MEMS)	Percentages, Fisher's exact test, Wilcoxon rank sum test, Mann-Whitney test
Carpenter (2015)	To examine whether patient-provider communication influences medication adherence, IOP control and drop instillation technique	English speaking patients aged 18+ years, diagnosed with glaucoma or suspect glaucoma, attending 1 of 6 specified ophthalmology clinics N=279	Objectively measured mean adherence ¹ 76.30 (SD = 23.2)	USA	Quantitative – prospective cohort Quantitative – cross sectional	Electronic monitoring system (MEMS) Questionnaire	Generalized estimating equations
Castel (2014)	To explore factors associated with glaucoma medication adherence within primary care and the influence of practitioner dynamics	Patients aged 40+ years, diagnosed with unspecified glaucoma in electronic health database, using ≥ 2 eyedrops attending a primary care clinic N=738	Mean MPR ² objectively measured 1.1 ± 0.51, range 0.11-3.81	Israel	Quantitative - retrospective database analysis Quantitative – cross sectional	Pharmacy claims database Questionnaire – by telephone	Descriptive statistics, t-test, chi-squared test, multivariate logistic regression
Chen (2022)	To examine glaucoma understanding, patient beliefs, experiences with eyedrops and associated factors amongst adults with primary glaucoma in China	Chinese speaking patients aged 18+ years diagnosed with primary glaucoma attending hospital eye clinic N=93	79.1% self-reported using eyedrops on time 69.4% never stop using eyedrops of own accord	China	Quantitative – cross sectional	Questionnaire – interviewer administered	Descriptive statistics, chi-squared, Multivariate logistic regression

Cook (2015)	To identify predictors of glaucoma medication adherence using 2 separate measures of adherence in a multisite study	English speaking patients aged 18+ years, diagnosed with POAG or OHT using 1 eyedrop, recent VF test, attending speciality glaucoma clinic N=201	MEMS median adherence ¹ 81% Self-reported median adherence (eyedrops taken correctly on day + previous 2 days) 100%	USA	Quantitative – prospective cohort	Electronic monitoring system (MEMS) Questionnaires	Nonparametric univariate Spearman correlations, multiple Poisson analysis
Dasgupta (2002)	To evaluate persistency rates with 4 different classes of glaucoma monotherapy, when started as initial treatment	Newly treated glaucoma patients < 65 years, started on monotherapy, enrolled in 1 of 3 specified healthcare plans N=1330	Persistency ³ PGA 43% Persistency ³ BB 53% Persistency ³ CAI 64% Persistency ³ AA 69%	USA	Quantitative - retrospective cohort	Insurance claims database	Cox regression analysis, hazard rate ratios, CIs
Day (2006)	To assess the validity of the TSS-IOP. Report factors associated with medication adherence, patient satisfaction and perception of glaucoma	Patients aged 18+ years, diagnosed with POAG or OHT using ≥ 1 eyedrop, attending a hospital eye clinic N=250	Not reported Participants questioned on their unwillingness to use their eyedrops	USA	Quantitative – prospective cohort	Questionnaire	Spearman's Rho correlation
Djafari (2009)	To assess glaucoma medication adherence comparing patient and practitioner estimates and explore factors	Patients diagnosed with POAG, OHT or suspect glaucoma for ≥ 2 years who were covered by pharmaceutical insurance program, under the care of 1	Patient self-reported adherence ⁴ 88.3%	Canada	Quantitative – cross sectional	Patient questionnaire	Chi-squared tests, univariate analysis

	associated with nonadherence	of 3 specified ophthalmologists at hospital glaucoma clinic N=181	Practitioner estimated adherence (considered patient $\geq 75\%$ adherent) 74.6% Insurance claim adherence ($\geq 75\%$ of Rxs filled) 71.8%		Quantitative - prospective database analysis Multi perspective	Practitioner questionnaire Insurance claims database	
Dreer (2013)	To identify factors related to glaucoma medication adherence among African Americans and develop a community-based program for improving adherence amongst these patients	English speaking, self-identifying African American patients aged 21+ years, diagnosed with POAG or OHT for ≥ 1 year, using a PGA, attending university eye clinic N=98	Not reported	USA	Qualitative - descriptive	Focus groups - NGT	Themes
Effendi (2018)	To assess medication adherence in NTG patients and identify factors related to nonadherence	Patients aged 18+ years, ability to answer questionnaire, diagnosed with NTG, using glaucoma eyedrops for ≥ 1 month and carrying with themselves, attending hospital glaucoma clinic N=40	Therapeutic compliance (weight of eyedrop bottle + contents) 40%	Indonesia	Quantitative – cross sectional	Questionnaire Weighing of eyedrop bottles and contents	Correlations, regression tests
Friedman (2008)	To identify factors related to glaucoma medication adherence using numerous information sources	Patients aged 40+ years diagnosed with POAG, prescribed a PGA as initial therapy, enrolled in a healthcare plan	High adherence 25% (MPR ² 0.89-2.18)	USA	Quantitative - retrospective database analysis	Pharmacy claims database	Percentages, Wilcoxon rank-sum test, Kruskal-Wallis test, chi-squared test, multivariate analysis, Spearman correlation

		N=300	Moderate adherence 49% (MPR ² 0.37-0.88)		Quantitative – cross sectional	Questionnaire	
			Low adherence 26% (MPR ² 0-0.36)				
Friedman (2009)	To examine practitioner- patient communication in community glaucoma clinics	Patients diagnosed with OAG or OHT on treatment for ≥ 1 year, attending a community ophthalmologist glaucoma clinic N=50 Ophthalmologists working in community glaucoma clinics N=23	Missed doses based on researchers' criteria 26% Patient self-reported missed doses 22% Missed doses as detected by practitioner 8%	USA	Quantitative – cross sectional Observational cohort Multi perspective	Questionnaire (practitioner and patients) Semi-structured interviews (patients) Audio and videotaping	Frequencies, percentages, Fisher's exact test
Gatwood (2022)	To identify the determinants of medication nonadherence in glaucoma patients > 18 years old	Patients aged 18+ years, diagnosed with unspecified glaucoma, using ≥ 1 eyedrop attending eye clinic N=15 (interview) N=55 (questionnaire)	Self-reported mean adherence ⁵ 17.2	USA	Mixed methods Qualitative - descriptive Quantitative – cross sectional	Interview – face to face Questionnaire – tablet based	Thematic analysis Descriptive statistics, inferential statistics, Pearson correlations
Gelb (2008)	To explore how practitioner demographics, attitudes, experiences and	Practitioners involved in the management of glaucoma	Not reported	USA	Quantitative – cross sectional	Interview -structured by telephone	Percentages

	behaviours surrounding glaucoma medication adherence correlate with patient adherence levels	N=103					
Gray (2010)	To explore the influence of educational support on patient understanding of glaucoma and medication adherence. Findings used to guide an intervention study	Patients diagnosed with OHT, OAG or suspect glaucoma attending hospital outpatient clinic N=174	Missed drops self-reported to practitioner 6% Missed drops self-reported to researcher 94%	UK	Quantitative – cross sectional	Interview	Descriptive statistics, percentages, Mann-Whitney test, Kendall's tau correlation coefficient
Gurwitz (1993)	To assess the level of glaucoma medication nonadherence in patients ≥ 65 years	Patients newly diagnosed with unspecified glaucoma, aged 65+ years, treated with eyedrops, continuously enrolled in national health insurance plan for 15 months N=2440	Total nonadherence (after 1 st Rx subsequent Rxs unfilled during 12-month period) 76.7% After 1 st Rx mean number of days without therapy during 12-month period 112.0±111.6	USA	Quantitative - retrospective cohort	Pharmacy claims database	Chi-squared test, t tests, multivariate logistic models
Gurwitz (1998)	To assess factors associated with nonadherence in newly diagnosed glaucoma patients who are covered by a healthcare plan	Patients newly diagnosed with POAG, treated with topical therapy, continuously enrolled in healthcare insurance plan for 4 months prior to and 15 months post initial Rx N=616	Compliance (eyedrop coverage > 80% of study days) 75.3% Mean number of days without therapy during 12-month period 30.7±57.0	USA	Quantitative - retrospective cohort	Pharmacy claims database	Chi-squared test, t tests, logistic regression analyses

Güven (2021)	To identify level of medication adherence amongst glaucoma patients in Turkey and the association with attitudes and disease perceptions	Patients aged 18+ years, able to complete questionnaire, diagnosed with glaucoma ≥ 6 months, using ≥ 1 eyedrop attending hospital eye clinic N=317	Self-reported fully adherent ⁶ 40% Mean RAM score 27.5 $\pm$ 3.3	Turkey	Quantitative - cross sectional	Questionnaire	Descriptive statistics, Mann–Whitney U test, Kruskal–Wallis test, chi-square test, multiple linear regression analysis
Hoevenaars (2008)	To assess level of glaucoma and treatment knowledge and their impact on medication adherence	Patients with unspecified glaucoma, attending hospital clinic at 1 of the randomly selected doctors from the Dutch Ophthalmology Society N=166	Self-reported adherence ⁷ 72.7%	Netherlands	Quantitative - cross sectional	Questionnaire – self administered	Descriptive statistics, Pearson chi-squared, logistic regression analysis
Hwang (2014)	To determine the level of persistence with glaucoma treatment in POAG or OHT patients in Taiwan 2 years post diagnosis and identify factors associated with non-persistence	Patients diagnosed with POAG or OHT, prescribed long term topical glaucoma therapy, continuously enrolled with the National Health Insurance program during 2-year study period N=3134	Persistence ⁸ at 2 years 24.2%	Taiwan	Quantitative - retrospective cohort	National Health Insurance database	Chi-squared test, cox regression analysis
Kashiwagi (2014)	To assess the level of persistence with glaucoma treatment in newly diagnosed patients in Japan and identify factors associated with non-persistence	Patients newly diagnosed with unspecified glaucoma, prescribed topical glaucoma therapy, enrolled in the Japanese Health insurance database > 6 months prior to diagnosis and for length of study N=2483	Persistence ⁸ at 3 years 52% (95 % CI: 49.7–55.2 %)	Japan	Quantitative - retrospective cohort	Health Insurance database	Kaplan-Meier method, logistic regression analysis
Kawai-Tsuboi (2015)	To evaluate the influence of prescribing	Patients using topical glaucoma therapy including a PGA in both eyes for > 6	Not reported	Japan	Quantitative - cross sectional	Questionnaire	Mann-Whitney U test

	habits on the taking of eyedrops in glaucoma	months, attending hospital eye clinic N=70					
Kayode (2019)	To assess glaucoma medication adherence and factors associated with nonadherence in patients at a Nigerian hospital	Patients aged 18+ years, diagnosed with unspecified glaucoma, using ≥ 1 eyedrop for ≥ 6 months, attending hospital clinic N=338	Self-reported adherence ⁹ (score 6-8) 72.5%	Nigeria	Quantitative - cross sectional	Questionnaire	Descriptive statistics, chi-squared tests
Khaled (2021)	To evaluate glaucoma medication adherence and factors associated with nonadherence among patients in the Aseer area of Saudi Arabia	Patients aged 30+ years, diagnosed with unspecified glaucoma, using eyedrops for ≥ 1 month but < 2 years with IOP > 20mmHg, attending hospital eye clinic N=102	Self-reported high adherence ¹⁰ 38.2%	Saudi Arabia	Quantitative - cross sectional	Questionnaire	Descriptive statistics, multivariate binary logistic regression analysis
Khandekar (2005)	To assess glaucoma medication adherence among patients in Oman and factors related to nonadherence. Using this information recommendations to care were suggested	Omani patients with unspecified glaucoma, using topical therapy, attending Ministry of Health eye clinics N=105	Excellent compliance (questionnaire scores >75%) 24.8% (95% CI: 16.5–33.1) Intermediate compliance (questionnaire scores 50-75%) 68.6%	Oman	Quantitative - cross sectional	Questionnaire – administered by health professional	Relative risk, 95% CIs
Kholdebarin (2008)	To determine extent of poor medication adherence, poor eyedrop instillation technique and associated factors	Patients aged 18+ years, with unspecified glaucoma, using topical therapy, attending an eye clinic at 1 of 10 centers across Canada	Overall compliance (no self-reported missed doses per week and accurately explained drop regimen) 72.1%	Canada	Quantitative - cross sectional	Questionnaire	Chi-squared test, univariate logistic regression

	among Canadian glaucoma patients	N=500					
Killeen (2020)	To explore factors related to glaucoma medication nonadherence in Southern India and use information to guide possible interventions	English or Tamil speaking patients aged 18+ years, diagnosed with any form of glaucoma, using ≥ 1 eyedrop, attending either the fee paying or free hospital eye clinic N=167 (questionnaire) N=45 (interview)	Based on interview adherence 47% (21/45) Based on questionnaire self-reported adherence 58% (97/167)	India	Mixed methods Qualitative Quantitative – cross sectional	Interview – semi-structured Questionnaire – administered by researcher not involved in patient clinical care	Grounded theory Descriptive statistics, paired t-tests
Kim (2017)	To assess glaucoma medication adherence and associated factors among patients in South Korea	Patients aged 20+ years diagnosed with unspecified glaucoma, using topical therapy for ≥ 1 month but < 2 years attending 1 of 15 eye centres in South Korea N=1042	Self-reported ≥ 80% of doses taken in past 7 days 72.6%	South Korea	Quantitative - cross sectional	Questionnaire	Descriptive statistics, chi-squared test, t-test, Mann-Whitney tests, logistic regression analysis
Konstas (2000)	To evaluate glaucoma medication nonadherence among patients in Greece and explore their views about glaucoma	Patients diagnosed with POAG or PXE glaucoma using topical therapy, attending hospital eye clinic N=100	Self-reported compliance ⁴ 56% Capable of instilling eyedrops correctly 53%	Greece	Quantitative - cross sectional	Questionnaire – administered by medical student Assessment of eyedrop instillation technique	Descriptive statistics, Student's t-test, chi-square test, Fisher's exact test
Lacey (2009)	To investigate facilitators and barriers to glaucoma medication adherence and consider	English speaking patients aged 18+ years, diagnosed with moderate/severe POAG for ≥ 1 year, using ≥ 2	Majority of participants reported rarely missing their eyedrops	UK	Qualitative	Focus group/	Framework analysis, themes

	possible strategies to aid taking eyedrops	eyedrops, seen ≥ 2 NHS ophthalmologists, attending either a teaching or district general hospital N=24 in total N=14 focus group N=10 interviews				Home-based semi-structured interview	
Lai (2020)	An RCT to assess factors related to glaucoma medication nonadherence among patients in Asia and evaluate the effect of individualised drug charts or medication phone reminder messages on adherence levels	Patients aged 30-90 years, diagnosed with unspecified glaucoma for ≥ 3 months, using ≥ 2 IOP lowering eyedrops with VA $\geq 6/60$, attending routine hospital eye appointment N=59	Self-reported adherence ⁹ (score > 6) 76.3%	Singapore	Quantitative - cross sectional	Questionnaire (conducted before RCT began) – interviewer administered	Logistic regression analysis
Loon (2015)	To investigate glaucoma medication adherence, QoL and factors associated with nonadherence among patients in Singapore	Chinese or English-speaking patients aged 18+ years, diagnosed with chronic glaucoma, using topical therapy for > 3 months, attending regular hospital follow up N=314	Self-reported fully adherent ⁶ 19.7%	Singapore	Quantitative - cross sectional	Questionnaire	Descriptive statistics, multivariate analysis
Lunnala (2011)	To assess the level of glaucoma medication adherence and factors related to nonadherence among patients in Finland. Using this information develop	Patients aged 18+ years, diagnosed with unspecified glaucoma using topical therapy, attending an ophthalmologist either at the hospital or privately, able to respond in Finnish	Good adherence (based on ACIDI scores) 97%	Finland	Quantitative - cross sectional	Questionnaire (by mail)	Factor analysis, chi-squared test

	strategies to improve adherence	N=249					
Mansberger (2013)	To use focus group methodology to assess validity of a new glaucoma adherence questionnaire, GTCAT, and whether it captures elements associated with glaucoma adherence	Patients with a VF test in the past 12 months using ≥ 1 IOP lowering eyedrop, attending tertiary care glaucoma centre N=20	Not reported	USA	Qualitative	Focus groups	Themes
Mansouri (2011)	To investigate self-reported medication adherence, knowledge of glaucoma and factors associated with nonadherence among glaucoma patients in Switzerland	Patients diagnosed with POAG, using topical therapy for > 6 months, attending 1 of 2 tertiary care glaucoma centres N=200	Self-reported compliance (missing ≤ 2 doses in any given week) 81%	Switzerland	Quantitative - cross sectional	Questionnaire Assessment of eyedrop instillation technique	Descriptive statistics, bivariate and multivariable logistic regression
Masoud (2013)	To assess glaucoma medication adherence in POAG and factors related to nonadherence among Arabic patients living in Israel	Patients of Arabic ethnicity, with cognitive and physical capacity, diagnosed with POAG for > 3 months on topical therapy, attending routine appointment at 1 of 3 glaucoma clinics in Israel N=400	Overall compliance (no self-reported missed doses per week and/or could accurately explain drop schedule) 50%	Israel	Quantitative - cross sectional	Questionnaire – doctor administered	Chi-squared test, t-tests, multiple logistic regression analysis
McClelland (2019)	To assess the effect of glaucoma prescription changes due to disease progression and self-reported medication adherence in POAG patients	Patients diagnosed with POAG, on topical therapy for > 3 months, aged < 85 years, attending specialist glaucoma clinic, able to read English N=138	Self-reported high adherence ¹⁰ 41.4%	Australia	Quantitative - cross sectional	Questionnaire – administered by researcher not involved in patient clinical care	Chi-squared tests

Mehari (2016)	To evaluate glaucoma medication adherence and associated factors amongst Ethiopian patients in tertiary care	Patients aged 18+ years, diagnosed with glaucoma or OHT using topical therapy unilaterally/bilaterally for > 6 months, attending glaucoma clinic at a tertiary care hospital N=359	Self-reported adherence ⁹ 42.6%	Ethiopia	Quantitative - cross sectional	Questionnaire – interviewer administered	Descriptive statistics, multivariate binary logistic regression analysis
Mowatt (2011)	To evaluate glaucoma medication adherence and factors associated with nonadherence in Jamaican patients	Any patient capable of giving consent, diagnosed with unspecified glaucoma attending hospital eye clinic N=100	Full compliance (self-reported no missed doses since last appointment) 50% Partial compliance (self-reported >1 missed dose per week) 43%	Jamaica	Quantitative - cross sectional	Questionnaire – doctor administered	Descriptive statistics, cross-tabulation, chi-squared test, ORs
Newman-Casey (2015a)	To identify patterns of glaucoma medication adherence over a 4-year period and determine whether habits created in year 1 continue during the following 3 years	Patients newly diagnosed with OAG, using topical therapy, continuously enrolled in insurance plan for 3 years prior to start of study and for the 4-year study period N=1234	Year 1 f/u: - persistently very poor adherence group mean MPR ² 16.9% - persistently moderate adherence group mean MPR ² 42.2% MPR ² was > 70% over 4-year study period for persistently good adherence group	USA	Quantitative - retrospective cohort	Insurance claims database	Regression analysis

Newman-Casey (2015b)	To assess factors associated with poor glaucoma medication adherence and evaluate the likelihood of 11 commonly cited difficulties to achieving optimum adherence	English speaking patients, attending a specified university or private practice glaucoma clinic, using ≥ 1 IOP lowering eyedrop N=185	Based on self-reported MAS (score ≤ 2) 73.5%	USA	Quantitative - cross sectional	Questionnaire	Chi-square test, two-sample t-test, Fisher's exact test, Logistic regression analyses
Newman-Casey (2016)	To investigate patient views about glaucoma causing sight loss and what obstacles patients face in receiving optimum care	Patients with glaucoma from a range of socio-economic backgrounds and varied visual abilities, attending 1 of 3 tertiary care medical centres. Family members or friends of patients also participated N=56	Not reported	USA	Qualitative	Focus groups	Content analysis to identify themes, semi-quantitative analysis measuring frequency of each theme
Nordmann (2007)	To create a questionnaire evaluating adherence and patient satisfaction with glaucoma eyedrops	POAG or OHT patients aged 50-75 years, using ≥ 1 IOP lowering eyedrop, attending follow up appointment at either a hospital outpatient department in the UK or a private practice in France N=15 Unclear with respect to ophthalmologists N=5	Not reported	France, UK	Qualitative – descriptive Multi perspective	Structured Interview (patients) Unclear for ophthalmologists	Concepts (themes)
Nordstrom (2005)	To identify patterns of medication adherence and persistence in glaucoma or glaucoma suspects and determine	Newly diagnosed POAG or glaucoma suspect patients, aged ≥ 30 years using topical therapy, continually enrolled in health insurance	Adherence ^a at 3 years 37%	USA	Quantitative - retrospective cohort	Insurance claims database	Cox proportional hazard models, Generalized estimating equations

	factors related to nonadherence and poor persistence	program for ≥ 1 year prior to diagnosis N=5300	Persistence ⁸ -majority of patients stopped using initial Rx by median follow up of 1.2 years				
Norrell (1981)	To assess adherence to pilocarpine eyedrops when used three times daily	Patients diagnosed with POAG (VFD, OD cupping and raised IOP), VA $\geq 2/60$, using pilocarpine eyedrops 3x daily, under the care of hospital eye clinic N=82	No doses missed in past 20 days 25.6%	Sweden	Quantitative - prospective analysis	Medication recording monitor	Chi-squared test, linear regression analysis
O'Hare (2009)	To determine whether the ability of glaucoma patients to read eyedrop bottle labels influences whether they accurately recall their medication regimen	English speaking patients diagnosed with OHT, primary or secondary glaucoma, using topical therapy, attending outpatient clinic at hospital N=200	68% of patients able to correctly recall eyedrop regimen (name, dose and frequency of instillation)	Australia	Quantitative - cross sectional	Survey	Descriptive statistics, Pearson's chi-squared test, multivariate logistic regression analysis
Olthoff (2009)	To evaluate glaucoma medication adherence and determine factors causing nonadherence to help guide interventions for improving adherence	Patients diagnosed with POAG using topical therapy, attending clinic of 1 of 60 randomly selected ophthalmologists N=166	Self-reported adherence ⁷ 72.7%	Netherlands	Quantitative - cross sectional	Questionnaire	Chi-squared test, univariate logistic models
Omolase (2013)	To evaluate glaucoma medication adherence and identify any eyedrop administration issues among Nigerian patients at a hospital eye clinic	Patients diagnosed with unspecified glaucoma using topical therapy, attending hospital eye clinic N=100	Self-reported compliance ⁴ 66%	Nigeria	Quantitative - cross sectional	Semi-structured questionnaire	Chi-squared test

Onwubiko (2020)	To assess glaucoma medication adherence and factors associated with nonadherence among patients at a tertiary hospital in Southern Eastern Nigeria	Patients diagnosed with unspecified glaucoma using topical therapy, attending eye clinic at a tertiary hospital N=114	Self-reported adherence ¹¹ 63.2%	Nigeria	Quantitative - cross sectional	Questionnaire – interviewer administered	Descriptive statistics, bivariate analysis
Osman (2016)	To determine reasons for glaucoma medication nonadherence	Patients with unspecified glaucoma using topical therapy, attending a specialised morning glaucoma clinic at the hospital N=105	Self-reported compliance (administer eyedrops correctly +/- < 1 missed dose per week) 80.6%	Saudi Arabia	Quantitative - cross sectional	Questionnaire – administered by doctor	Descriptive statistics, chi-squared test, Mann-Whitney U test
Owen (2009)	To assess patterns and variables influencing the taking of glaucoma eyedrops from 1994, when PGAs were unavailable, until 2004, when they were in widespread use	Patients initially started on topical therapy for glaucoma or OHT between 1994-2004, registered with 1 of 94 UK GPs using an electronic primary care database with patient records enrolled in the system N=5670	Persistence ⁸ at 1-year pre-PGA introduction 61% Persistence ⁸ 1 year post PGA introduction 70%	UK	Quantitative - retrospective database analysis	Electronic primary care database	Hazard ratios
Park (2013)	To assess factors associated with medication adherence, the impact of herbal medicines and frequently occurring treatment side effects among glaucoma patients in South Korea	Patients aged 19+ years, with cognitive capacity, living in Korea, diagnosed with unspecified glaucoma (OD changes and VFD) for > 1 month, using and able to self-administer topical therapy unilaterally/bilaterally, attending 1 of 5 health institutions	Self-reported total compliance (always attend f/u, take drops on time + never stop using of own accord) 60.2%	South Korea	Qualitative	Questionnaire – structured, included 2 open questions administered by trained field staff	Frequency of response analysed, descriptive statistics, ANOVA

		N=581					
Patel (1995)	To evaluate glaucoma medication nonadherence and associated factors	Patients with unspecified glaucoma using eyedrops being seen in private practice N=100	Self-reported compliance ⁴ 59%	USA	Quantitative – cross sectional	Questionnaire – interviewer administered	Descriptive statistics, chi-squared
Ramesh (2021)	To assess factors related to adherence, administration and acquisition of glaucoma medication among literate patients in Southern India	Literate patients aged 30+ years, diagnosed with either POAG or PACG using topical therapy for > 1 month, attending an urban tertiary eye institute N=101	Self-reported adherence ⁷ 49.5%	India	Quantitative – cross sectional	Questionnaire – interviewer administered	Descriptive statistics, chi-squared, discriminant analysis
Reardon (2003)	To assess persistency with a single eyedrop in newly diagnosed glaucoma patients	Patients aged 20+ years, newly diagnosed with glaucoma, started on monotherapy, continuously enrolled in insurance claims database between May 1999-Jan 2001 N=2850	Persistency ³ for 21 months 61.2%	USA	Quantitative–retrospective cohort	Insurance claim database	Chi-squared, Cox regression models
Rees (2010)	To assess the level of glaucoma medication nonadherence and whether patient beliefs about glaucoma and its treatment influence adherence	English conversing patients with reasonable hearing diagnosed with glaucoma or suspect glaucoma, using ≥ 1 eyedrop for > 6 months attending specialist glaucoma clinic at a tertiary eye hospital N=131	Self-reported fully adherent ⁶ 55%	Australia	Quantitative – cross sectional	Questionnaire – interviewer administered	Percentages, t-tests, Chi squared tests, Pearsons correlation, multiple linear regression
Rees (2014)	To evaluate glaucoma medication adherence in different patient	White Americans, White Australians, AAs or Chinese Singaporeans diagnosed	Self-reported fully adherent ⁶	Australia, USA, Singapore	Quantitative – cross sectional	Questionnaire – by telephone	Correlation and multivariate analysis

	populations – White Americans, White Australians, AAs and Chinese Singaporeans and assess opinions about glaucoma and its management	with glaucoma or OHT, using ≥ 1 eyedrop for > 6 months, capacity to respond to questionnaire, attending glaucoma clinic at tertiary eye hospital in each country N=133 White Americans N=58 AA N=107 White Australians N=177 Chinese Singaporeans	White Americans 65.4% AAs 56.9% White Australians 61.7% Chinese Singaporeans 47.5%				
Sanchez (2020)	To assess factors associated with glaucoma medication adherence, as measured electronically, among self-reported nonadherent patients	English speaking patients aged 40+ years with cognitive and mental capacity, diagnosed with glaucoma, suspect glaucoma or OHT, self-administering ≥ 1 glaucoma eyedrop and self-reported as poorly adherent in the past 1 month N=100	Average adherence measured objectively (based on 3-month period) 73.8% (SD 21.04, range 3-10)	USA	Quantitative – prospective cohort	Electronic monitoring system Questionnaire – interviewer administered	Percentages
Schwartz (2009)	To establish a tool for assessing patient willingness to change and improve adherence behaviour amongst poorly adherent patients from 2 different settings	Patients diagnosed with POAG, PACG, suspect glaucoma or OHT using ≥ 1 IOP lowering eyedrop, attending either a tertiary specialist glaucoma practice or a rural multi-speciality practice N=203 in total	Mean adherence score (range 5-25) Glaucoma practice - 23.98 $\pm$ 1.29 (range, 20–25) Multi-speciality practice - 23.77 $\pm$ 2.54 (range, 5–25)	USA	Quantitative – cross sectional	Questionnaire	Descriptive statistics, χ^2 test, Kruskal–Wallis tests, t-tests, Pearsons correlation

Shirai (2021)	To assess medication adherence, using pharmacy claims database, in Japanese glaucoma patients prescribed either fixed or unfixed combination eyedrops and determine factors associated with nonadherence	Patients diagnosed with POAG, OAG, NTG or unspecified glaucoma, using fixed or unfixed combination eyedrops for ≥ 12 months, enrolled in database between April 2011 and March 2016 with evidence of Rx claims for monotherapy for ≥ 12 months prior to changing to combination eyedrops N=638	PDC over 12-month period 70.4% in total 79.1% in fixed combination 62.2% in unfixed combination	Japan	Quantitative - retrospective cohort	Pharmacy claims database	T-test, Pearson's χ^2 test, Multivariate analyses, Kaplan-Meier
Sleath (2006)	To determine what problems glaucoma patients report using ≥ 2 different IOP lowering eyedrops and how these factors influence medication adherence	Patients with unspecified glaucoma, using ≥ 2 different eyedrops unilaterally or bilaterally, attending 1 of 4 specified private eye centres during 2004 N=324	Self-reported adherence ¹¹ 86%	USA	Quantitative – cross sectional	Questionnaire	Descriptive statistics, logistic regression analysis
Sleath (2009a)	To establish what issues glaucoma patients in Southern India report when using eyedrops and how these factors influence self-reported medication adherence	Adult patients with unspecified glaucoma using topical therapy for ≥ 1 month, attending specialised glaucoma clinic at a medical centre in Southern India during 2006 N=243	Self-reported adherence ¹¹ 94.2%	India	Quantitative – cross sectional	Questionnaire	Descriptive statistics, Fisher's exact tests, t-test
Sleath (2009b)	To assess medication adherence and factors related to nonadherence, as reported by veteran glaucoma patients	Patients with unspecified glaucoma using ≥ 1 eyedrop, attending eye clinic at Veteran Affairs hospital N=141	Self-reported adherence ¹¹ 79.4%	USA	Quantitative – cross sectional	Questionnaire	Logistic regression analysis

	attending an outpatient clinic						
Sleath (2014)	To investigate the influence of patient demographics, health literacy, symptoms of depression, self-perceived issues using eyedrops and self-identified medication adherence in glaucoma	English speaking, adult POAG patients self-administering IOP lowering eyedrops, attending 1 of 6 specified eye centres in 4 different US states N=228	Not reported	USA	Quantitative – cross sectional	Questionnaire – administered by research assistant	Percentages, Chi-squared test, t-test, Pearson correlation, multivariable linear regression
Sleath (2015a)	To explore the relationship between practitioner-patient interactions, patient self-belief in using eyedrops, consequences of using incorrectly and electronically measured medication adherence in glaucoma	English reading and writing patients, aged 18+ years, diagnosed with unspecified glaucoma attending 1 of 6 eye centres N=279 Physicians working in eye clinic at 1 of 6 specified eye centres N=15	Not reported	USA	Quantitative – prospective observational cohort Multi perspective	Electronic monitoring system (MEMS) Questionnaire	Pearson correlation, chi-squared, t-tests, multiple logistic regression analysis
Sleath (2015b)	To explore how practitioners use resources to communicate and activate patients to self-manage glaucoma and its influence on medication adherence, as measured electronically over 8 months	English speaking adult patients diagnosed with unspecified glaucoma attending 1 of 6 eye centres (2 private practice, 4 affiliated with academic departments) N=279	Not reported	USA	Quantitative – prospective longitudinal cohort Multi perspective	Electronic monitoring system (MEMS) Questionnaire	Generalized estimating equations

		Unclear with respect to practitioners N=15					
Spencer (2019)	To determine factors associated with glaucoma medication adherence in an urban Australian cohort	Patients diagnosed with unspecified glaucoma using IOP lowering eyedrops for ≥ 2 weeks attending public or private eye clinics N=150	Self-reported missed doses in last 2 days 8.3% Self-reported missed doses in past 2 weeks 30.3%	Australia	Mixed methods Quantitative – cross sectional Qualitative	Questionnaire – interviewer administered Free text response to 1 question	Descriptive statistics, Percentages, Binary logistic regression analysis
Stein (2015)	To establish if changing to a non-branded PGA, when they became available, improves patient medication adherence compared to remaining on a generic PGA. Factors associated with adherence/nonadherence also investigated	Patients aged 40+ years, continuously enrolled in health insurance program from 2009-2012, diagnosed with OAG, and prescribed a branded PGA prior to September 2009 N=8427	Mean adherence (PDC) branded PGA 2009-2011 ranged from 0.43-0.65 Mean adherence (PDC) non-branded PGA 2011-2012 ranged from 0.54-0.65	USA	Quantitative – longitudinal cohort	Insurance claims database	Descriptive statistics, t-test, Wilcoxon-Mann-Whitney test, multivariable logistic regression analysis
Stewart (2004)	To explore practitioner and patient views on medication adherence in glaucoma, with a view to using findings to implement changes in	Practising ophthalmologists prescribing > 2 IOP lowering eyedrops N=250	Patient reported noncompliance (self-interpretation) 34% Approximately half of self-reported	France, UK, Spain, Italy, Germany	Quantitative – cross sectional Multi perspective	Questionnaire – by telephone	Percentages

	practice which will improve adherence	Unclear with respect to patients N=250	noncompliant patients reported missing 2 doses in past 30 days				
Stringham (2018)	To investigate reasons for glaucoma medication nonadherence in veterans	Patients using IOP lowering eyedrops attending veterans eye clinic N=74	Self-reported compliance (administered doses > 75% of the time) 80%	USA	Quantitative – cross sectional	Questionnaire	Chi-squared test, logistic regression analysis
Suet (2018)	To assess glaucoma medication adherence and factors related to nonadherence in a Malaysian cohort	English speaking patients, aged 18+ years diagnosed with unspecified glaucoma, using eyedrops unilaterally/bilaterally for > 2 months, attending hospital eye clinic N=100	Good adherence based on BMQ score (0/1) 75%	Malaysia	Quantitative – cross sectional	Questionnaire	Multiple logistic regression analysis
Tamrat (2015)	To assess extent of glaucoma medication adherence and associated factors among Ethiopian patients with glaucoma or OHT	Patients aged 18+ years diagnosed with unspecified glaucoma or OHT, using eyedrops for > 6 months attending hospital eye clinic N=200	No missed doses in past week/clinic appointments in past year 32.5%	Ethiopia	Quantitative – cross sectional	Questionnaire – doctor administered Medical chart review	Cross-tabulations, Fisher's exact tests
Taylor (2002)	To explore factors related to medication nonadherence in glaucoma patients	Patients with unspecified glaucoma having previously seen ≥ 2 glaucoma practitioners, using ≥ 2 eyedrops, attending a specialised university glaucoma clinic or a general private practice N=28 in total	Overall most patients admitted some form of nonadherence	USA	Qualitative	Focus group/interview conducted by research firm Audio/videotaping	Summary of observations

		N=21 focus groups N=11 interviews (4 also participated in focus group)					
Tsai (2003)	To determine and develop a systematic classification of common barriers to glaucoma medication adherence	Patients with a diagnosis of POAG attending an academic based specialist glaucoma clinic N=48	Overall self-reported compliance deemed high 3% reported not using drops for ≥ 1 week 8% reported missing a dose in past 14 days	USA	Qualitative - descriptive	Interviews	Identification of categories
Tshivhase (2021)	To determine self-reported medication adherence rates, as part of a study to improve glaucoma f/u care utilising the IMBSM in patients from Limpopo	Patients with unspecified glaucoma, using topical therapy attending a specialised eye hospital and been under review for ≥ 3 years N=429	45% of patients self-reported adherence ⁹ $\geq 95\%$	South Africa (Limpopo province)	Quantitative – cross sectional	Questionnaire	Percentages
Tsumura (2019)	To assess glaucoma medication adherence and associated factors from a patient and ophthalmologist perspective	Patients aged 20+ years using IOP lowering eyedrops, whose ophthalmologist had been recruited and proposed to prescribe a fixed combination eyedrop due to clinical findings N=4430	Patient reported good adherence ⁴ 72.4% Adherence (frequency of missing a dose in past week) as assumed by ophthalmologist 78.5%	Japan	Quantitative – cross sectional Multi perspective	Questionnaire	Multivariate logistic regression analysis

		Ophthalmologists who were members of the Japanese Ophthalmologist Association N=1358					
Welge-Lussen (2015)	To assess level of self-reported glaucoma medication adherence and associated factors	Patients with POAG using IOP lowering eyedrops for ≥ 4 weeks attending university eye clinic, with no dementia or cognitive capacity issues N=196	Mean ARMS2 score ¹² At start 3.38 At 2 months 2.8 Drops taken as recommended ¹³ At start 9.03 At 2 months 9.08 Missed doses in past 14 days At start 77.9% At 2 months 74.2%	Germany	Quantitative - prospective	Questionnaire	Descriptive statistics, bivariate correlations, regression models
Wolfram (2019)	To determine level of self-reported glaucoma medication adherence and establish reasons for nonadherence	Patients with unspecified glaucoma using topical therapy for ≥ 1 year, with adequate understanding of German language, attending eye clinic at university health centre N=201	Self-reported adherence (taking > 95% of prescribed therapy) 69.7%	Germany	Quantitative – cross sectional	Questionnaire	Descriptive statistics, multivariable logistic regression analysis
Zhu (2019)	To assess glaucoma medication persistence, as measured by	Patients diagnosed with unspecified glaucoma using long-term topical therapy	Persistence ⁸ at 2 years 69.9%	Australia	Quantitative – prospective cohort	Pharmacy claims database	Descriptive statistics, multiple logistic regression analysis

	pharmacy claims data and identify factors associated with persistence among Australian patients over the age of 45 years	and continuously enrolled in universal insurance scheme for 2-year study period N=12,899				Questionnaire	
¹ calculated as percentage of doses taken correctly, determined by timing of bottle opening ² defined as number of days of eyedrop cover ÷ days between Rx refills during study period ³ calculated as time from 1 st Rx to discontinuation/change of Rx ⁴ defined as strictly complying with eyedrop regimen ⁵ based on ARMS score, range 4-48, lower scores indicate greater adherence ⁶ based on RAM score of 30, range 5-30, higher scores indicate greater adherence ⁷ defined as no missed doses in past 4 weeks ⁸ defined as continuous filling of Rx with < 90 days gap between Rx's ⁹ based on 8-MMAS score, range 0-8, higher scores indicate greater adherence ¹⁰ based on MGL score, range 0-4, lower scores indicate greater adherence ¹¹ defined as using eyedrops correctly in past week ¹² ARMS2 score range 1-99, lower scores indicate greater adherence ¹³ based on VAS-AD score, 0=never, 10=always							

Abbreviations

CI – confidence interval
 HRQL - health related quality of life
 POAG - primary open angle glaucoma
 GTCAT - glaucoma treatment compliance assessment tool
 MEMS - medication event monitoring system
 OAG - open angle glaucoma
 OHT - ocular hypertension
 VF - visual field
 PACG - primary angle closure glaucoma
 MPR – medication possession rate
 TSS-IOP – treatment satisfaction survey-Intraocular pressure
 NGT – nominal group technique
 PGA – prostaglandin analogue

NTG – normal tension glaucoma
 BB – beta-blocker
 CAI – carbonic anhydrase inhibitor
 AA- alpha agonist
 ARMS - adherence to refills and medications scale
 RAM – reported adherence to medication
 MMAS-8 – 8 item Morisky Medication Adherence Scale
 PXE – pseudo exfoliation
 MGL - Morisky, Green and Levine Medications Adherence Questionnaire
 ACIDI – Adherence of people with chronic disease instrument
 IOP – Intra ocular pressure
 MAS – Morisky adherence score

Rx – prescription
 VFD – visual field defect
 OD – optic disc
 PDC – proportion of days covered
 BMQ – brief medication questionnaire
 IMBSM - information-motivation and behavioural skills model
 ARMS2 - Adherence to Refills and Medication Scale 2
 VAS-AD - visual analog scale for adherence
 AA – African American
 HCP – health care professional

Appendix A4

Quality assessment for 83 included studies using Mixed Methods Appraisal Tool (Hong et al 2018)

Studies were initially assessed using 2 screening questions:

S1. Are there clear research questions? Yes, No, Can't tell

S2. Do the collected data allow to address the research questions? Yes, No, Can't tell

Responses to screening questions were "yes" for all studies.

Depending on study design the appropriate category was then chosen to appraise study.

Qualitative study design

Study	1.1	1.2	1.3	1.4	1.5
Dreer et al (2013)	Yes	Yes	Yes	Yes	Yes
Lacey et al (2009)	Yes	Yes	Yes	Yes	Yes
Mansberger et al (2013)	Yes	Yes	Yes	Yes	Yes
Newman-Casey et al (2016b)	Yes	Yes	Yes	Yes	Yes
Nordmann et al (2007)	Yes	Yes	Yes	Yes	Yes
Park et al (2013)	Yes	Yes	Yes	Yes	Yes
Taylor et al (2002)	Yes	Yes	Yes	Yes	Yes
Tsai et al (2013)	Yes	Yes	Yes	Yes	Yes
1.1. Is the qualitative approach appropriate to answer the research question? 1.2. Are the qualitative data collection methods adequate to address the research question? 1.3. Are the findings adequately derived from the data? 1.4. Is the interpretation of results sufficiently substantiated by data? 1.5. Is there coherence between qualitative data sources, collection, analysis and interpretation?					

Qualitative non-randomised studies

Study	3.1	3.2	3.3	3.4	3.5
Barker et al (2019)	No	Yes	Yes	Yes	Yes
Boland et al (2014)	Yes	Yes, for MEMs cap No, for questionnaire	Yes	Yes	Yes
Carpenter et al (2015)	No	Yes	Yes	Yes	Yes
Castel et al (2014)	Yes	Yes	Yes	Yes	Yes
Cook et al (2015)	No	Can't tell	Yes	Yes	Yes
Dasgupta et al (2002)	No	Yes	Yes	Yes	Yes
Djafari et al (2009)	No	Can't tell	Yes	Yes	Yes
Friedman et al (2008)	Can't tell	No	Yes	Yes	Yes
Gurwitz et al (1993)	Can't tell	Yes	Yes	Yes	Yes
Gurwitz et al (1998)	Yes	Yes	Yes	Yes	Yes
Hwang et al (2014)	Yes	Yes	Yes	Yes	Yes
Kashiwagi et al (2014)	No	Yes	Yes	Yes	Yes
Newman-Casey et al (2015a)	Yes	Yes	Yes	Yes	Yes
Nordstrom et al (2005)	Yes	Yes	Yes	Yes	Yes
Norell et al (1981)	Can't tell	Yes	Yes	Yes	Yes
Owen et al (2008)	Yes	Yes	Yes	Yes	Yes
Reardon et al (2003)	Yes	Yes	Yes	Yes	Yes
Sanchez et al (2020)	No	Yes	Yes	Yes	Yes
Shirai et al (2021)	No	Yes	Yes	Yes	Yes
Sleath et al (2015a)	Can't tell	Yes	Yes	Yes	Yes

Sleath et al (2015b)	Can't tell	Yes	Yes	Yes	Yes
Stein et al (2015)	Yes	Yes	Yes	Yes	Yes
Welge-Lussen et al (2015)	No	Yes	No	Yes	Yes
Zhu et al (2019)	No	Yes	Yes	Yes	Yes
3.1. Are the participants representative of the target population? 3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)? 3.3. Are there complete outcome data? 3.4. Are the confounders accounted for in the design and analysis? 3.5. During the study period, is the intervention administered (or exposure occurred) as intended?					

Quantitative descriptive studies

Study	4.1	4.2	4.3	4.4	4.5
Anbesse et al (2019)	Yes	Yes	No	Yes	Yes
Balkrishnan et al (2003)	Yes	Yes	No	Yes	Yes
Bloch et al (1977)	Yes	Yes	No	Yes	Yes
Chen et al (2022)	Can't tell	Yes	Can't tell	Yes	Yes
Day et al (2006)	Yes	Yes	Yes	Yes	Yes
Effendi et al (2018)	Yes	No	Can't tell	Can't tell	Yes
Friedmann et al (2009)	Yes	No	No, for questionnaires Yes, for video phase of study	Yes	Yes
Gelb et al (2008)	Yes	Can't tell	Yes	No	Yes
Gray et al (2010)	Yes	Yes	Yes	Yes	Yes
Guven et al (2021)	Yes	Can't tell	Yes	Yes	Yes
Hoevenaars et al (2008)	Yes	Can't tell	Yes	Yes	Yes

Kawai-Tsuboi et al (2015)	Yes	No	No	Yes	Yes
Kayode et al (2019)	Yes	Yes	Yes	Can't tell	Yes
Khaled et al (2021)	Can't tell	No	Yes	Can't tell	Yes
Khandekar et al (2005)	Yes	Yes	Yes	Yes	Yes
Kholdebarin et al (2008)	Yes	Yes	No	Yes	Yes
Kim et al (2017)	No	Yes	No	Yes	Yes
Konstas et al (2000)	Yes	Yes	No	Can't tell	Yes
Lai et al (2020) [†]	Can't tell	No	Can't tell	Yes	Yes
Loon et al (2015)	Can't tell	Yes	Yes	Can't tell	Yes
Lunnela et al (2011)	No	Yes	Yes	Yes	Yes
Mansouri et al (2011)	Yes	No	Yes	Yes	Yes
Masoud et al (2013)	Can't tell	Yes	No	Can't tell	Yes
McClelland et al (2019)	Yes	No	Yes	Yes	Yes
Mehari et al (2016)	Yes	Yes	Yes	Yes	Yes
Mowatt et al (2011)	Yes	Yes	No	Can't tell	Yes
Newman-Casey et al (2015b)	Yes	Yes	Yes	Yes	Yes
O'Hare et al (2009)	Yes	Can't tell	No	Yes	Yes
Olthoff et al (2009)	Yes	Yes	Yes	Yes	Yes
Omolase et al (2013)	Yes	Can't tell	Yes survey	Can't tell	Yes
Onwubiko et al (2020)	Yes	Yes	Can't tell	Can't tell	Yes
Osman et al (2016)	Yes	Can't tell	Can't tell	Yes	Yes
Patel et al (1995)	Can't tell	Can't tell	No	Can't tell	Yes
Ramesh et al (2010)	Yes	Yes	No	Can't tell	Yes

Rees et al (2010)	Yes	Can't tell	Yes	Yes	Yes
Rees et al (2014)	Yes	No	Yes	Yes	Yes
Schwartz et al (2009)	Yes	Yes	No	Yes	Yes
Sleath et al (2006)	Can't tell	Yes	Yes	Can't tell	Yes
Sleath et al (2009a)	Yes	Yes	Yes	Can't tell	Yes
Sleath et al (2009b)	Can't tell	Yes	Yes	Can't tell	Yes
Sleath et al (2014)	Can't tell	Can't tell	No	Yes	Yes
Stewart et al (2004)	Yes, for physicians Can't tell for patients	Yes, for physicians Can't tell for patients	Yes	Yes	Yes
Suet et al (2018)	Yes	No	Yes	Yes	Yes
Stringham et al (2018)	Yes	Yes	No	Yes	Yes
Tamrat et al (2015)	Yes	Yes	No	Can't tell	Yes
Tshivhase et al (2021)	Yes	Yes	Yes	Yes	Yes
Tsumura et al (2019)	Can't tell	Yes	No	Yes	Yes
Wolfram et al (2019)	Can't tell	Yes	No	Can't tell	Yes

† study is a randomized control trial but for this review relevant part classified as quantitative descriptive

4.1. Is the sampling strategy relevant to address the research question?

4.2. Is the sample representative of the target population?

4.3. Are the measurements appropriate?

4.4. Is the risk of nonresponse bias low?

4.5. Is the statistical analysis appropriate to answer the research question?

Mixed Methods studies

Study	5.1	5.2	5.3	5.4	5.5
Gatwood et al (2022)	Yes	Yes	Yes	Yes	No
Kileen et al (2020)	Yes	Yes	Yes	Yes	Yes
Spencer et al (2019)	Yes	Yes	Yes	Yes	Yes
5.1. Is there an adequate rationale for using a mixed methods design to address the research question? 5.2. Are the different components of the study effectively integrated to answer the research question? 5.3. Are the outputs of the integration of qualitative and quantitative components adequately interpreted? 5.4. Are divergences and inconsistencies between quantitative and qualitative results adequately addressed? 5.5. Do the different components of the study adhere to the quality criteria of each tradition of the methods involved?					

Appendix A5

TDF domains in order of importance in influencing glaucoma medication adherence

1. Environmental Context and Resources
2. Knowledge
3. Skills
4. Memory, Attention and decision processes
5. Beliefs about consequences
6. Emotion
7. Social Influences
8. Behavioural Regulation
9. Beliefs about capabilities
10. Reinforcement
11. Social professional role and identity
12. Goals
13. Intentions
14. Optimism

Appendix A6

An overview of generated themes/sub-themes, with illustrative examples, from the TDF domains deemed less important in influencing glaucoma medication adherence

1. Beliefs about consequences N=25		
Theme:	Enabler/Barrier/ Mixed	Illustrative Examples
1.1 Beliefs about medicines N=22 Sub-theme		
Beliefs about treatment outcomes	Enabler	The most common facilitator to medication adherence was patients thinking about the consequences of not using their eyedrops (Dreer et al 2013)
Concerns about eyedrops +/- unwanted side effects	Barrier	Nonadherent patients had greater concerns about their glaucoma medication than adherent patients, which was significant $p < 0.001$ (Loon et al 2015)
1.2 Beliefs about illness N=9 Sub-theme		
Beliefs about nature of glaucoma	Barrier	Beliefs about glaucoma was the third most commonly cited barrier to taking eyedrops from nonadherent participants (Newman-Casey et al 2015b)
Beliefs about impact of glaucoma on life	Barrier	Non adherent patients perceived glaucoma to affect their life more than adherent patients did, which was significant $p = 0.001$ (Guvén et al 2021)
2. Emotion N=19		
2.1 Fear or denial N=18	Mixed	Author comment <i>"most patients had fears of vision loss, and this may have been sufficient motivation to use eyedrops as recommended"</i> (Lunnala et al 2011) Patients reporting <i>"a fear of blindness were less likely to be adherent"</i> (Wolfram et al 2019)
2.2 Emotional burden of glaucoma/sight loss N=5	Barrier	<i>"I love my babysitting. I think if there was a day when I couldn't do that, that would be awful"</i> (Lacey et al 2009)
3. Social Influences N=16		
3.1 Presence of support from HCP/family/friends/support groups N=11	Enabler	<i>"...one-third (39%) of participants indicated that forming support groups with other patients with glaucoma disease were also an important motivating factor to strengthen adherence"</i> (Tshivhase et al 2021)
3.2 Lack of trust in health service/pharmacy/HCP N=7	Barrier	<i>"I quit taking my drops because I was dissatisfied with my doctor's care"</i> (Tsai et al 2003)

3.3 Past experiences N=3	Enabler	<i>"A friend or family member's experience with eyedrops has encouraged me to use my eyedrops"</i> (Sanchez et al 2020)

4. Behavioural Regulation N=18		
Developing routines/habits/reminder systems N=18	Mixed	<i>"on the other hand, these...routines might be perceived as a constraint"</i> ³³ (Nordmann et al 2007) <i>"I keep my medication(s) in a special place to remind me to take it"</i> (Schwartz et al 2009)

5. Beliefs about capabilities N=10		
5.1 Patient self-efficacy N=8	Enabler	<i>"The majority of participants reported that they were "always" confident inserting their drops (73.4%)"</i> (McClelland et al 2019)
5.2 Treatment satisfaction N=3	Barrier	<i>"very adherent people with glaucoma experienced positive results from treatments"</i> (Lunnala et al 2011)

6. Reinforcement N=9		
6.1 Reinforcement regarding adherence and treatment N=6	Enabler	<i>"If providers gave positive reinforcement about the patient's medication-taking at one or more visits, patients were significantly more likely to be adherent"</i> ⁵⁷ (Sleath et al 2015b)
6.2 Reinforcement regarding glaucoma education N=6	Enabler	Author comment high adherence rate in this study can be <i>"explained by the periodically repeated glaucoma awareness programs in our institute"</i> (Osman et al 2016)

7. Social professional role and identity N=7		
7.1 Lack of personal identification with glaucoma N=2	Barrier	Denial (my eyes are ok) was a reason for non-adherence (Stewart et al 2004)
7.2 HCP role in providing information N=5	Enabler	Author comment "Consequently, clinicians play a major role by supplying this [educational and training] information" (Nordmann et al 2007)

9. Goals N=5		

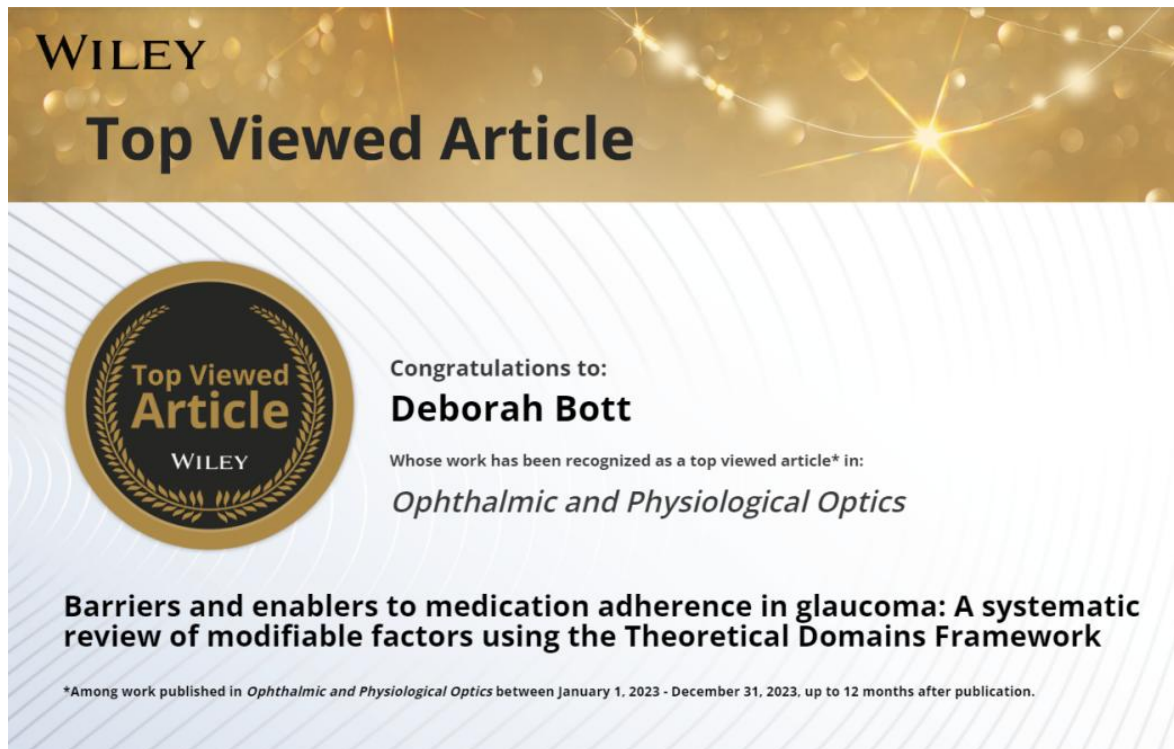
Motivation N=5	Enabler	<i>"Other psychological predictors of adherence including ... motivation for treatment...were significant in univariate analyses"</i> (Cook et al 2015)

10. Intentions N=3		
Intention to adhere to treatment N=3	Enabler	<i>"I tell myself that I can figure out a way to not miss doses"</i> (Schwartz et al 2009)

10. Optimism N=1		
Confidence all will be fine N=1	Enabler	<i>"I consulted a specialist who cheered me up, he told me that if the pathology is treated early enough, it couldn't go badly"</i> (Nordmann et al 2007)
N= number of studies, Enabler = facilitates glaucoma medication adherence, Barrier = hinders glaucoma medication adherence Mixed = either facilitates or hinders glaucoma medication adherence		

Appendix A7

Systematic review was published in *Ophthalmic and Physiological Optics*, and ranked among the top 10% of most-viewed papers in the journal in 2023.



Appendix B1

Ethics approval for Delphi study



Dear Deborah

Reference: ETH2324-1874

Project title: Investigating the feasibility and acceptability of using a chatbot to improve adherence to glaucoma medication

Start date: 23 Aug 2022

End date: 1 Oct 2024

I am writing to you to confirm that the research proposal detailed above has been granted formal approval from the Optometry Proportionate Review Committee. The Committee's response is based on the protocol described in the application form and supporting documentation. Approval has been given for the submitted application only and the research must be conducted accordingly. You are now free to start recruitment.

Please ensure that you are familiar with [City's Framework for Good Practice in Research](#) and any appropriate Departmental/School guidelines, as well as applicable external relevant policies.

Please note the following:

Project amendments/extension

You will need to submit an amendment or request an extension if you wish to make any of the following changes to your research project:

- Change or add a new category of participants;
- Change or add researchers involved in the project, including PI and supervisor;
- Change to the sponsorship/collaboration;
- Add a new or change a territory for international projects;
- Change the procedures undertaken by participants, including any change relating to the safety or physical or mental integrity of research participants, or to the risk/benefit assessment for the project or collecting additional types of data from research participants;
- Change the design and/or methodology of the study, including changing or adding a new research method and/or research instrument;
- Change project documentation such as protocol, participant information sheets, consent forms, questionnaires, letters of invitation, information sheets for relatives or carers;
- Change to the insurance or indemnity arrangements for the project;
- Change the end date of the project.

Adverse events or untoward incidents

You will need to submit an Adverse Events or Untoward Incidents report in the event of any of the following:

- a) Adverse events
- b) Breaches of confidentiality
- c) Safeguarding issues relating to children or vulnerable adults
- d) Incidents that affect the personal safety of a participant or researcher

Issues a) and b) should be reported as soon as possible and no later than five days after the event. Issues c) and d) should be reported immediately. Where appropriate, the researcher should also report adverse events to other relevant institutions, such as the police or social services.

Should you have any further queries relating to this matter, please do not hesitate to contact me. On behalf of the Optometry Proportionate Review Committee, I do hope that the project meets with success.

Kind regards

Michael Powner

Optometry Proportionate Review Committee

City, University of London

Appendix B2

Participant Information Sheet for Delphi study



**Department of Optometry and Visual Sciences,
School of Health and Psychological Sciences,
City, University of London**

Can technology help with eyedrop compliance in glaucoma?

Name of principal researcher: Deborah Bott

Reference number: ETH2324-1874, Version 2.1 04/04/2024

Participant Information Sheet

Background

Glaucoma is characterized by a group of optic neuropathies which if left untreated lead to progressive irreversible blindness. In 2020, glaucoma was the second most common cause of global blindness. The only proven treatment to slow down or halt progression is by lowering intraocular pressure (IOP) and therapy is frequently achieved by instillation of lifelong daily eyedrops. However, adherence to long-term medication (the extent to which a patient's behaviour corresponds to the prescribed medication regime) is known to be poor. Non-adherence reduces treatment effectiveness and increases the social and economic burden on both patient and society. Current strategies to aid adherence are of limited success lacking a robust theoretical underpinning. To address this issue a study to develop a new theory-informed intervention which seeks to improve patient adherence is being undertaken. This research forms the basis of my PhD project.

By reviewing existing literature, interviewing patients and eye care practitioners the key factors that influence glaucoma medication adherence have been identified. Using this information a list of potential strategies, which incorporate technology-based solutions, has been developed and will form the basis of an overall

intervention to improve glaucoma medication adherence. Sub-optimal patient adherence will trigger implementation of this intervention. However, defining what level of adherence is acceptable to maintain therapeutic efficacy is difficult since no standardised threshold exists in glaucoma. Different definitions have been used in the literature, with some studies using a cut-off point of 80% to signify acceptable adherence (i.e. a patient receives at least 80% of a prescribed medication over a specified time interval), whilst others more strictly define non-adherence as missing a single dose.

Aim of the survey:

The aim of this short survey is to achieve a consensus agreement, amongst UK glaucoma specialists, as to what level of glaucoma medication adherence is considered acceptable. This will help inform the next stage of the study which seeks to establish individual reasons for non-adherence with subsequent implementation of a suitable intervention.

Establishing a universal cut-off point at which non-adherence becomes clinically significant is challenging, with factors such as drug, patient and disease characteristics influencing the definition. However, your responses will help decide upon an agreed threshold for determining non-adherence to glaucoma medication that can be used in routine clinical practice.

Why have I been invited to take part?

You have been invited to take part because you are a registered UK eye care professional specialising in glaucoma management. You may also have been involved in an earlier stage of my research and expressed an interest in further involvement.

Content of survey

The survey consists of questions relating to:

- demographic information

and

- your views on what constitutes an acceptable level of glaucoma medication adherence

There are six questions in total, which are either tick box or one-word answers and should take no more than 10 minutes to complete. All answers will be anonymised and no individual will be identifiable.

Do I have to take part?

Participation in the survey is voluntary. By completing the survey it is assumed you are consenting to take part, however you are free to withdraw at any stage.

What will happen to the results from the survey?

Data collected will be analysed, using Delphi methodology, to provide a consensus view on what level of glaucoma medication adherence is deemed acceptable. This result will help to inform the next stage of my PhD, which seeks to establish individual reasons for non-adherence and subsequent implementation of a suitable intervention.

The results of this survey may also be reported in a peer review journal and at relevant health/research conferences. The information we report will be completely anonymous and will not identify you in anyway.

Who has reviewed this study?

This survey forms part of a study “Can technology help with eyedrop compliance” which has been approved by City, University of London, Department of Optometry and Visual Sciences Research Ethics Committee.

Data privacy statement

City, University of London is the sponsor and the data controller of this study based in the United Kingdom. This means that we are responsible for looking after your information and using it properly. The legal basis under which your data will be processed is City’s public task.

Your right to access, change or move your information are limited, as we need to manage your information in a specific way in order for the research to be reliable and accurate. To safeguard your rights, we will use the minimum personal-identifiable information possible (for further information please see <https://ico.org.uk/for-organisations/guide-to-data-protection/guide-to-the-general-data-protection-regulation-gdpr/lawful-basis-for-processing/public-task/>). City will use your name and contact details to contact you about the research study as necessary.

You can find out more about how City handles data by visiting <https://www.city.ac.uk/about/governance/legal>. If you are concerned about how we have processed your personal data, you can contact the Information Commissioner’s Office (IOC) <https://ico.org.uk/>.

What if there is a problem?

If you have any problems, concerns or questions about this study, you should ask to speak to a member of the research team. If you remain unhappy and wish to complain formally, you can do this through City’s complaints procedure. To complain about the study, you need to phone 020 7040 3040. You can then ask to speak to the Secretary to Senate Research Ethics Committee and inform them that the name of the project is: “Can technology help with eyedrop compliance”.

You can also write to the Secretary at: Annah Whyton, Research Integrity Manager, City, University of London, Northampton Square, London, EC1V 0HB Email:

[REDACTED]

Insurance

City, University of London holds insurance policies which apply to this study, subject to the terms and conditions of the policy. If you feel you have been harmed or injured

by taking part in this study you may be eligible to claim compensation. This does not affect your legal rights to seek compensation. If you are harmed due to someone's negligence, then you may have grounds for legal action. Thank you for taking the time to read this information sheet.

If you would like any further information, please contact **Deborah Bott**

([REDACTED])

Appendix B3

Delphi survey Round 1 questionnaire



Background

Adherence to long-term ocular hypotensive medication is known to be poor. Current strategies to aid adherence are of limited success lacking a robust theoretical underpinning. To address this issue a study to develop a new theory-informed intervention which seeks to improve patient adherence is being undertaken. This research forms the basis of my PhD project.

By reviewing existing literature, interviewing patients and eye care practitioners the key factors that influence glaucoma medication adherence have been identified. Using this information a list of potential strategies, which incorporate technology-based solutions, has been developed and will form the basis of an overall intervention to improve glaucoma medication adherence. Sub-optimal patient adherence will trigger implementation of this intervention. However, defining what level of adherence is acceptable to maintain therapeutic efficacy is difficult since no standardised threshold exists in glaucoma. Different definitions have been used in the literature.

Aim of the survey: The aim of this short survey is to achieve a consensus agreement, amongst UK glaucoma specialists, as to what level of glaucoma medication adherence is considered acceptable. This will help inform the next stage of the study which seeks to establish individual reasons for non-adherence with subsequent implementation of a suitable intervention.

Establishing a universal cut-off point at which non-adherence becomes clinically significant is challenging, with factors such as drug, patient and disease characteristics influencing the definition. However, your responses will help decide upon an agreed threshold for determining non-adherence to glaucoma medication that can be used in routine clinical practice.

For further information please follow this [link](#) to read the Participant Information Leaflet

Content of survey

The survey consists of questions relating to:

- demographic information
- and
- your views on what constitutes an acceptable level of glaucoma medication adherence

There are six questions in total, which are either tick box or one-word answers and should take no more than 10 minutes to complete. All answers will be anonymised and no individual will be identifiable.

I confirm I am over 18 years old, have read the participant information leaflet and consent to taking part in the survey.

☐ Yes

☐ No

Which age range are you in?

☐ 21-30

☐ 31-40

☐ 41-50

☐ 51-60

☐ >60

What is your gender?

☐ Male

☐ Female

☐ Other

☐ Prefer not to say

Which country in the UK do you practice in?

Your profession

Are you:

☐ An ophthalmologist specialising in glaucoma

☐ A specialist glaucoma optometrist

☐ A specialist glaucoma orthoptist

☐ A glaucoma nurse practitioner

How long have you been working in glaucoma care?

☐ <2 years

☐ 2-5 years

☐ 6-10 years

☐ 11-15 years

☐ 16-20 years

☐ >20 years

When managing patients on long-term ocular hypotensive therapy, what percentage of eyedrops would they need to take correctly to define an 'acceptable' level of medication adherence? It is assumed that a value less than this would constitute non-adherence.

☐ 100%

☐ 90%

☐ 80%

☐ 70%

☐ 60%

☐ 50% or lower

☐ Other, please specify

☐ Don't know

☐ Prefer not to answer

Please add any additional comments you would like to make

We thank you for your time spent taking this survey.
Your response has been recorded.

Appendix B4

Delphi survey Round two questionnaire



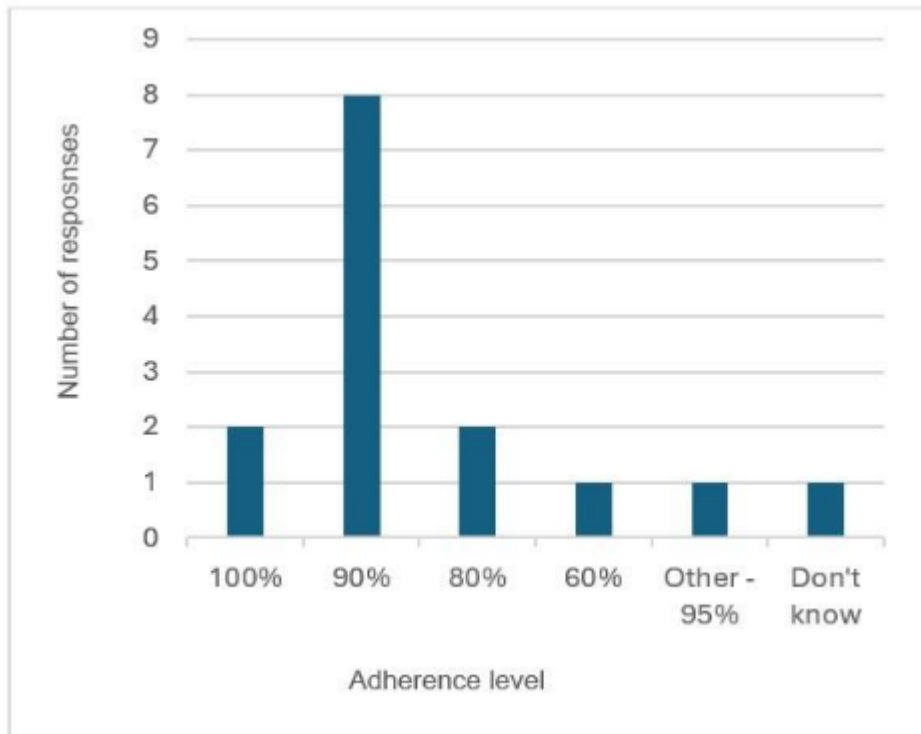
Glaucoma medication adherence threshold survey - Round 2

Thank you for participating in the first round of the survey. We received an extremely good response to the questionnaire and some informative comments which were supported by personal and professional knowledge.

We have analysed your responses to the question we asked and found a median value of 90% was considered to be an acceptable generic level of adherence.

Below is a summary of the results:

Adherence level	Number of responses
100%	2
90%	8
80%	2
60%	1
Other - 95%	1
Don't know	1



In light of the comments we received, we recognise that an 'acceptable' level of adherence is likely to vary between patients depending on their risk of progression. Comments received are summarised below:

- more advanced, rapidly progressing or earlier onset disease require better adherence levels than stable disease or OHT
- lower levels of adherence may be acceptable if a patient is using multiple IOP-lowering medications
- patients who report a certain level of adherence are likely to have a level lower than they report

All these and other caveats are valid, nevertheless we are seeking to establish an agreed consensus that can be used in most cases in routine clinical practice. Based on the results from Round 1 we have narrowed the choices for an acceptable level of glaucoma adherence down to the three options that were selected by two or more respondents. We are now embarking on Round 2 and again would be most grateful if you could complete the second survey.

For a reminder on the study please follow this [link](#) to read the Participant Information Leaflet.

Content of survey, Round 2

The survey consists of questions relating to:

- demographic information
- and
- your views on what constitutes an acceptable level of glaucoma medication adherence

There are six questions in total, which are either tick box or one-word answers and should take no more than 10 minutes to complete. All answers will be anonymised and no individual will be identifiable.

I confirm I am over 18 years old, have read the participant information leaflet and consent to taking part in the survey.

☐ Yes

☐ No

Which age range are you in?

☐ 21-30

☐ 31-40

☐ 41-50

☐ 51-60

☐ >60

What is your gender?

☐ Male

☐ Female

☐ Other

☐ Prefer not to say

Which country in the UK do you practice in?

Your profession

Are you:

- ☐ An ophthalmologist specialising in glaucoma
- ☐ A specialist glaucoma optometrist
- ☐ A specialist glaucoma orthoptist
- ☐ A glaucoma nurse practitioner

How long have you been working in glaucoma care?

- ☐ <2 years
- ☐ 2-5 years
- ☐ 6-10 years
- ☐ 11-15 years
- ☐ 16-20 years
- ☐ >20 years

In the initial survey, we found a median value of 90% adherence to be an acceptable level.

When managing patients on long-term ocular hypotensive therapy, what percentage of eyedrop adherence **for the majority of glaucoma cases** would you define as an 'acceptable' level of medication adherence? It is assumed that a value less than this would constitute non-adherence.

- ☐ 100%
- ☐ 90%
- ☐ 80%

Please add any additional comments you would like to make

We thank you for your time spent taking this survey.
Your response has been recorded.

Appendix C1

Ethics approval for UK-based interview study



Dear Deborah

Reference: ETH2122-1657

Project title: Investigating the feasibility and acceptability of using a chatbot to improve adherence to glaucoma medication

Start date: 23 Aug 2022

End date: 31 Aug 2023

I am writing to you to confirm that the research proposal detailed above has been granted formal approval from the Optometry Proportionate Review Committee. The Committee's response is based on the protocol described in the application form and supporting documentation. Approval has been given for the submitted application only and the research must be conducted accordingly. You are now free to start recruitment.

Please ensure that you are familiar with [City's Framework for Good Practice in Research](#) and any appropriate Departmental/School guidelines, as well as applicable external relevant policies.

Please note the following:

Project amendments/extension

You will need to submit an amendment or request an extension if you wish to make any of the following changes to your research project:

- Change or add a new category of participants;
- Change or add researchers involved in the project, including PI and supervisor;
- Change to the sponsorship/collaboration;
- Add a new or change a territory for international projects;
- Change the procedures undertaken by participants, including any change relating to the safety or physical or mental integrity of research participants, or to the risk/benefit assessment for the project or collecting additional types of data from research participants;
- Change the design and/or methodology of the study, including changing or adding a new research method and/or research instrument;
- Change project documentation such as protocol, participant information sheets, consent forms, questionnaires, letters of invitation, information sheets for relatives or carers;
- Change to the insurance or indemnity arrangements for the project;
- Change the end date of the project.

Adverse events or untoward incidents

You will need to submit an Adverse Events or Untoward Incidents report in the event of any of the following:

- a) Adverse events
- b) Breaches of confidentiality
- c) Safeguarding issues relating to children or vulnerable adults
- d) Incidents that affect the personal safety of a participant or researcher

Issues a) and b) should be reported as soon as possible and no later than five days after the event. Issues c) and d) should be reported immediately. Where appropriate, the researcher should also report adverse events to other relevant institutions, such as the police or social services.

Should you have any further queries relating to this matter, please do not hesitate to contact me. On behalf of the Optometry Proportionate Review Committee, I do hope that the project meets with success.

Kind regards

Michael Powner

Optometry Proportionate Review Committee

City, University of London

Appendix C2

Interview topic guide

Patient Interviews

Introduction

“My name is _____, a researcher at City, University of London. The main purpose of this interview is to understand your experiences using eyedrops in glaucoma.”

“I will also be interviewing eye care practitioners to understand their experiences of eyedrop compliance in practice and how they manage it. I plan to use the information gained from these interviews to help me develop some form of technology-based solution to help patients use their eyedrops correctly. ”

“Have you read the participant information sheet that you have been provided with?”

“I will just re-cap some information. The interview should last about 45 minutes. Everything you say will be kept strictly confidential. You are free to stop participating at any time with no consequences. You do not need to answer any questions that you do not wish to. I will be audio recording the interview so that I don't have to take too many notes and can listen to what you are saying. After the interview any identifiable information, such as your name, will be removed.”

“Please feel free to be open and honest about your experiences using eyedrops. There are no right or wrong answers, we are keen to learn from your experiences both positive and negative.”

“Are you happy to take part in this interview? Before we start do you have any questions?”

Complete consent form.

“I'm going to start recording now.”

Demographic Information

“I'd like to ask some questions about yourself first. This information will be used to describe the people who took part in our study, all your responses will be combined so you will not be identified.”

Please can you confirm:

- your gender, ethnicity, where you live in the country – first part of your postcode
- what age range you fall into (18-30, 31-45, 46-60, 61-74, 76-90, 91+)
- what is your highest level of education (e.g. school/college -up to 18 yrs. old, graduate, postgraduate)

- your employment status
- if you live alone/with family members (if yes ask which members)
- what type of glaucoma do you have (if known)
- how long approximately have you been using eyedrops for glaucoma
- is this the first type of eyedrop you have used/have you been changed to a different type? If yes do you know how many times they been changed?
- what drops are you currently taking – how many times a day do they go in? Don't worry if you don't remember the names of the drops
- do you instil your eyedrops yourself/family member/carer?
- do you pay for your prescriptions?
- how often do you have check-ups for your glaucoma?
- you have no visual difficulties/have visual difficulties but not formally registered as sight impaired/registered as sight impaired/registered severely sight impaired

Questions aligned with domains of Theoretical Domains Framework (TDF)

1. Do you know why you take your eyedrops? **(Knowledge domain)**
Prompts – explore understanding of glaucoma and rationale for using eyedrops and possibility of losing vision
2. On a daily basis do you have any problems putting your eyedrops in? **(Skills domain)**
Prompts – if yes explore why, maybe have problems with opening bottle due to arthritis in hands/unable to see to put your drops in/drops keep running down cheek
3. If answer yes to above question– even though you have some difficulties putting your drops in, how confident are you that you can continue using your drops as prescribed (i.e. once/twice a day) on a long-term basis? **(Beliefs about capabilities)**
If answer no to above question – as you don't experience any difficulties putting your drops in on a daily basis, how confident are you that you can continue to use your drops as prescribed (i.e. once/twice a day) on a long-term basis? **(Beliefs about capabilities)**
4. Is it important to you to use your eyedrops as instructed? **(Goals domain)**
Prompt – explore why
5. What do you think the benefits of using your eyedrops correctly are?
What do you think the disadvantages of not using your eyedrops correctly are? **(Beliefs about consequences)**

6. Who do you think is responsible for making sure your eyedrops are used correctly every day? (**Social/professional role and identity domain**)

Prompt – your eye practitioner, your GP, you, your family/carer

7. Is there anything/anyone that would make you more likely to use/not use your eyedrops as you should? (**Reinforcement domain**)

Prompt – praise from your eye care practitioner/family or receiving negative feedback from your practitioner

8. If you use your eyedrops correctly, how likely do you think it is that this will help you maintain your vision/stop your glaucoma from getting worse? (**Optimism domain**)

9. If you think about how you use your eyedrops each day, is there anything that makes it easier for you, anything that makes it harder? (**Environmental context and resources domain**)

Prompts- being away on holiday, being dependant on a carer/family member to instil drops/ not obtaining repeat prescriptions from pharmacy/GP in time

10. Is there anything that you do/or could do to overcome these problems? (**Behavioural regulation domain**)

Prompt – habits/techniques or practical strategies employed

11. Does anyone else influence your decision to take your eyedrops? (**Social influences domain**)

Prompt – family members/carers/support groups/healthcare professionals (HCPs)

12. Do you ever forget or deliberately not use your eyedrops? If yes how often have you not used your eyedrops? Is there any reason that would lead to this decision? Have you forgotten to use your eyedrops in the past month? (**Memory, Attention and decision processes domain**)

Prompt – forgetting when go away on holiday, side effects using drops so purposefully don't use

“Thank you for your time today, I really appreciate you sharing your views and experiences. Is there anything else you would like to add that I haven't covered? Do you have any questions?”

Eye Care Practitioner Interviews

Introduction

“My name is _____, a researcher at City, University of London. The main purpose of this interview is to hear about your experiences managing glaucoma medication adherence in practice.”

“I will also be interviewing patients to learn about their experiences with glaucoma medication. We will use the information from both practitioner and patient interviews to guide the development of a potential intervention to help with glaucoma medication adherence.”

“Have you read the participant information sheet that you have been provided with?”

“I will just re-cap some information. The interview should last about 45 minutes. Everything you say will be kept strictly confidential. You are free to stop participating at any time with no consequences. You do not need to answer any questions that you do not wish to. I will be audio recording the interview so that I don't have to take too many notes and can listen to what you are saying. After the interview any identifiable information, such as your name, will be removed.”

“Please feel free to be open and honest about how you feel. There are no right or wrong answers, we are keen to hear your views and learn from your experiences both positive and negative.”

“Are you happy to take part in this interview? Before we start do you have any questions?”

Complete consent form.

“I'm going to start recording now.”

Demographic Information

“I'd like to ask some questions about yourself first. This information will be used to describe the people who took part in our study, all your responses will be combined so you will not be identified.”

Please can you confirm:

- your gender, ethnicity, where you practise in the country – first part of postcode
- what age range you fall into (18-30, 31-45, 46-60, 61-74, 76-90, 91+)
- your job title and role within glaucoma care
- how long have you been qualified as an eye care practitioner? How long have you been involved in glaucoma care?

- do you work in hospital, community practice or both?
- on average how many glaucoma sessional clinics a week are you involved in?
- only for non-ophthalmologists - do you issue prescriptions to glaucoma patients? Are you an independent prescriber or do you issue by other means e.g. PGD?

Questions aligned with domains of Theoretical Domains Framework (TDF)

1. In practice how do you usually assess whether a patient is taking their eyedrops as prescribed? **(Skills domain)**
 Prompt – subjectively ask patient/family member about adherence, what questions would you ask, use a questionnaire, what questionnaire would you use?
 Do you provide education regarding glaucoma/treatment/ adherence/advice on how to instil eyedrops? How do you do this?
2. How do you classify a patient as nonadherent? Do you think nonadherence is a problem in your clinic? Why? **(Knowledge domain)**
 Prompt – is missing once/twice a week/month etc nonadherent
3. Whose role do you think it is to ensure patients comply with their treatment? Why do you think this? **(Social/professional role and identity)**
4. How important do you feel it is to actively manage patient adherence to treatment? What influences your approach? What are the main outcomes you aim for when supporting a patient's adherence? **(Beliefs about consequences)**
5. How confident do you feel in your ability to identify if a patient is adherent or nonadherent to their medication? Why do you feel that? **(Beliefs about capabilities)**
6. When a patient is having difficulty using their eyedrops correctly, how do you determine the most appropriate adjustments to their treatment or select an alternative approach? **(Memory, Attention and decision processes domain)**
 Prompt – if developing side effects how do you manage, do you consider SLT or surgical intervention as an alternative, if patient struggling with dosing regimen due to hectic lifestyle how do you amend treatment to suit patient?

7. In clinic, are there any resources, tools, or colleagues that make it easier for you to manage non-adherence? Conversely, are there any factors that make it more challenging to support patients who struggle to adhere to their treatment? **(Environmental context and resources domain)**
Prompt - dedicated glaucoma nurses, dedicated adherence clinics, educational resources, not enough time, too many patients to see, not enough staff to support smooth running of clinic
8. How do you keep up to date/remain consistently aware of glaucoma medication adherence and its management? **(Behavioural regulation domain)**
Prompt – use of guidelines/recommendations, CPD, courses, conferences
9. When it comes to managing patient adherence what are your main goals or priorities in clinic? How do these goals guide your actions or interactions with patients? **(Goals)**

“Thank you for your time today, I really appreciate you sharing your views and experiences. Is there anything else you would like to add that I haven’t covered? Do you have any questions?”

Appendix C3

Coding framework for patient group

Determinants (enablers/barriers) influencing patient glaucoma medication adherence as categorised by TDF domains together with illustrative quotes

TDF Domain and definition	Component constructs	Examples may include	Illustrative quotes
Knowledge – an awareness of the existence of something	Knowledge about condition/scientific rationale Knowledge of task environment Procedural knowledge	Discussions around patient's knowledge of: - Glaucoma progression through poor adherence - Rationale for using eyedrops - Consequences of adherence/non-adherence - Treatment application and regimen - Side effects of eyedrops Knowledge can be either extent of (enabler) or lack of (barrier)	<i>"the idea of the drops is to reduce the pressure, or keep the pressure down, so that there's no squashing of the optic nerve, and that some of the drops work by controlling the flow of liquid out of the eyeball. Some of the drops work by controlling the flow of the liquid into the eyeball" (P001)</i>
Skills – an ability or proficiency acquired through practice	Skills Skills development Competence Ability Practice Skill assessment Interpersonal skills	Discussions around patient physical and/visual skills needed to correctly administer eyedrops (enabler/barrier) Discussions around skills needed to order ongoing supplies of eyedrops (enabler/barrier)	<i>"One thing that is a challenge though.....is knowing which one [bottle] is which. The tiny little label on here, I couldn't tell you without going and getting the magnifiers if that's my Monopost or my Tiopex" (P006)</i> <i>"But I learnt from that that I need to do things with weeks of notice basically to order the next one"</i>

			[ordering repeat prescriptions] (P006)
Social/Professional Role and Identity – a coherent set of behaviours and displayed personal qualities of an individual in a social or work setting	Professional role and identity Social identity Identity Professional boundaries Professional confidence Group identity Leadership Organisational commitment	Discussions around how patients relate to people without glaucoma when they have to use their eyedrops (e.g. in a social/group setting) and take personal responsibility for adhering to treatment (enabler/barrier)	<i>"It doesn't worry me [having to instil drops]. I've done it a couple of times when I've been out on a date or something like that."</i> [instil drops] (P002)
Beliefs about capabilities - acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use	Self-confidence Perceived competence Self-efficacy Perceived behavioural control Beliefs Self-esteem Empowerment	Discussions about how confident patients feel about their ability to instil eyedrops correctly and/or manage their glaucoma (enabler/barrier) Also consider coding references about how confident a patient feels about admitting not having used their eyedrops to others to Social influences	<i>"I'm completely confident that I can continue doing it"</i> [instilling eyedrops] (P013)
Optimism - The confidence that things will happen for the best or that desired goals will be attained	Optimism Pessimism Unrealistic optimism Identity	Discussions about how likely patients think adhering to treatment will prevent sight loss/control glaucoma. Includes optimism (enabler), unrealistic optimism or pessimism (barrier)	<i>"Well, I always think if my eyesight took a bit of a nosedive, then technology is out of the question"</i> (P005)
Beliefs about consequences - acceptance of the truth, reality, or	Beliefs Outcome expectations	Discussions about patients accepting they have glaucoma (enabler/barrier)	[follows regime more correctly now because of] <i>"the fact that I have lost the quadrant, and that I've had these</i>

validity about outcomes of a behaviour in a given situation	Characteristics of outcome expectancies Anticipated regret Consequents	Discussions regarding patient perceptions about the nature of glaucoma and/or outcomes of treatment (enabler/barrier). Includes beliefs regarding benefits and concerns about unwanted side-effects/future side effects, how glaucoma or eyedrops may affect patients' life or cause symptoms	<i>two operations. So, I realise, just winging the drops in morning and evening clearly hasn't been adequate" (P001)</i> <i>"I think it's that thing about resistance, it's a bit more resistance.....I think when I read about things, I read about alternative health a lot, so I read up on things that can help strengthen the optic nerve beside taking drops. How diet can help with my eyesight as well. I read up on things like that and I just think do I need to take these [eyedrops]?" (P012)</i>
Reinforcement - increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus	Inventives Punishment Consequents Reinforcement Contingences Sanctions	Discussions surrounding patient's response to: • receiving praise/encouragement for instilling eyedrops as prescribed (enabler) • receiving negative feedback for not instilling eyedrops correctly (barrier/enabler) • receiving feedback (either positive or negative) about nature of glaucoma and/or treatment e.g. from family members/carers/ECP (enabler/barrier)	

		Consider coding discussions about support rather than reinforcement from ECP/family/carer to Social Influences	
Intentions – a conscious decision to perform a behaviour or a resolve to act in a certain way	Stability of intentions Stages of change model Transtheoretical model and stages of change	References from patients referring to their intentions to: • instil/not instil their eyedrops as prescribed (enabler/barrier) • continue/discontinue instilling their eyedrops (enabler/barrier)	<i>"I always think how would I remember if I was older or how do older people remember, does someone do it for them"</i> (P005)
Goals - mental representations of outcomes or end states that an individual wants to achieve	Goals (distal / proximal) Goal priority Goal / target setting Goals (autonomous / controlled) Action planning Implementation intention	Discussions about patient motivation to adhere to treatment (enabler) Discussions regarding patient desire to retain as much sight as possible (enabler)	<i>"why was it so important to you to keep using your eyedrops, even if you developed a side effect?"</i> <i>P001: I suppose it's the preserving of eyesight"</i> (P001) <i>"You know, I'm doing this to help - well, to hopefully preserve what sight I've got"</i> (P006)
Memory, Attention and Decision Processes -the ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives	Memory Attention Attention control Decision making Cognitive overload/tiredness	Discussions around whether patients forget to instil their eyedrops (either occasionally or more frequently) (barrier) Discussions around patients' ability to decide whether they instil their eyedrops or whether they decide to take occasional breaks from using eyedrops (enabler/barrier)	<i>"There's never really been an issue for me remembering to take them"</i> (P006) <i>"I can be quite..... forgetful about putting my drops in"</i> (P012)
Environmental Context and Resources - any circumstance of a person's situation or environment that discourages or encourages the	Enviromental stressors Resources / material resources	Discussions around issues with health care system influencing patient adherence e.g. busy eye clinics, time constraints in clinic, difficulties	<i>"watch the times, but then when you're doing shift work, you can't"</i> [instil eyedrops at the correct times] (P001)

development of skills and abilities, independence, social competence, and adaptive behaviour	Organisational culture /climate Salient events / critical incidents Person x environment interaction Barriers and facilitators	obtaining follow up appointments, limited staff, issues obtaining prescriptions (barrier) Discussions around circumstantial factors influencing patient adherence e.g. complexity of eyedrop regimen, work patterns, away on holiday, existence of side effects, financial issues, being dependent on a carer/family member to instil eyedrops and/or collect prescriptions (barrier) Discussions around obtaining medication e.g. availability of eyedrops, access to chemist, financial implications of purchasing medication (enabler/barrier) Discussions around organisational structure to support patient if they have a problem using their eyedrops (e.g. provision of helpline) (enabler) Discussions around resources that encourage/discourage patient adherence e.g. dropper aid (enabler/barrier)	<i>“when I used to travel for work, I managed very well. I had the little Frio bag, I kept it cool”</i> [in terms of managing to instil drops when travelling] (P001) <i>“it's easier I think..... having the individual cuvettes that I kind of have, you know, I've got some in front of my desk at the moment”</i> [individual vials easier to remember to instil than multi-dose bottle] (P006)
Social Influences - those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviours	Social pressure Social norms Group conformity Social comparisons Group norms Social support Power	Discussions referring to influences, either positive or negative, patients/family/carers/other HCPs/support groups have in aiding patient adherence (enabler/barrier)	<i>“One thing that's motivated me to follow the regime more correctly, has been a session I had just by accident – Glaucoma UK did a small workshop thing one morning, and the guy explained about the effectiveness of the eyedrops, and it's not, take this in</i>

	Intergroup conflict Alienation Group identity Modelling	Discussions around the influence clinician-patient relationships have on patient adherence behaviour (enabler/barrier) Discussions around trust/respect or lack of trust/respect patients have in HCPs and/medical institution (enabler/barrier) Discussions around previous experiences with family members/friends influencing adherence behaviour (enabler)	<i>the morning, take this in the evening, whatever, but he explained about the 12 hours and the 24 hours and trying to be as precise as possible</i> (P001) <i>"So I was fortunate enough actually to have a relationship with my consultant where we'd exchanged email addresses. So I was able to email her"</i> [when patient had an issue with their eyedrops] (P006)
Emotion – a complex reaction pattern, involving experiential, behavioural, and physiological elements, by which the individual attempts to deal with a personally significant matter or event	Fear Anxiety Affect Stress Depression Positive/negative effect Burn-out	Discussions about how patients feel (could be positive or negative): • having to instil eyedrops • losing sight as a result of non-adherence • when eyedrops are unavailable (Enabler/barrier) Discussions about patient feelings/emotions/reaction when having to admit they have not used their eyedrops (barrier)	<i>"Because you get panicky. It's scary"</i> [when eyedrops are unavailable] (P003)
Behavioural Regulation - anything aimed at managing or changing objectively observed or measured actions	Self-monitoring Breaking habit Action planning	Discussions about strategies/techniques patient uses to help with adherence (enabler)	<i>"at one point, and partly because I had a lot of other medications to take, I set up an alarm on my phone"</i> (P001)

Coding framework for Eye Care Professionals

Determinants (enablers/barriers) influencing ECP management of glaucoma medication adherence as categorised by TDF domains together with illustrative quotes

TDF Domain and definition	Component constructs	Examples may include	Illustrative quotes
Knowledge – an awareness of existence of something	Knowledge about condition/scientific rationale Knowledge of task environment Procedural knowledge	References from ECP demonstrating their knowledge/lack of knowledge of medication adherence and consequences of non-adherence (enabler/barrier) Understanding of patient factors e.g. socioeconomic background, ethnicity, general health status and factors which influence adherence behaviour (enabler) Discussions around knowing how to classify/define patient as adherent/non-adherent (enabler)	<i>"No set way of classifying it"</i> [in terms of classifying patient as adherent/non-adherent] (ECP007)
Skills – an ability or proficiency acquired through practice	Skills Skills development Competence Ability Practice Skill assessment Interpersonal skills	Discussions demonstrating ECP skills in educating patients on nature of glaucoma and/or treatment and/or treatment application techniques (enabler/barrier) Discussions around skills needed to inquire about/assess adherence (e.g. listening, questioning, relationship building) (enabler)	<i>"I will ask them an open-ended question about their drops. What drops are you using at the moment? I won't say what drops they're using.....I try and ask it in a way that they're going to feel comfortable to say, oh I'm not really using them"</i> (ECP004)

Social/Professional Role and Identity – a coherent set of behaviours and displayed personal qualities of an individual in a social or work setting	Professional role and identity Social identity Identity Professional boundaries Professional confidence Group identity Leadership Organisational commitment	Discussions around ECP role or professional responsibility to ensure patient adheres to treatment (enabler) ECP referring to integrating their role with other HCPs/patients to encourage adherence (enabler) Consider coding references about support provided by ECP to Social Influences	<i>“To some extent, it’s my role because if I’m prescribing them and I’m explaining to the patient why they need to use them”</i> (ECP004)
Beliefs about capabilities - acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use	Self-confidence Perceived competence Self-efficacy Perceived behavioural control Beliefs Self-esteem Empowerment Professional Confidence	Discussions about how confident an ECP feels identifying or managing non-adherence (enabler/barrier) ECP referring to how difficult it is to influence medication adherence behaviours (barrier)	<i>“In reality, I’ve got no idea. How can I know”</i> [in terms of ECP confidence in identifying non-adherence] (E004) <i>“I would feel fairly confident in terms of trying to identify people who are adherent to medication”</i> (ECP008)
Optimism - The confidence that things will happen for the best or that desired goals will be attained	Optimism Pessimism Unrealistic optimism Identity	References to being optimistic/pessimistic about how to manage medication adherence	
Beliefs about consequences - acceptance of the truth, reality, or	Beliefs Outcome expectations	ECP beliefs about the positive outcomes of patients adhering to treatment (e.g. saves sight, reduces unnecessary	<i>“But I do believe it’s worth investing in that from the point of view that if you haven’t got that compliance or that [adherence from] as</i>

validity about outcomes of a behaviour in a given situation	Characteristics of outcome expectancies Anticipated regret Consequents	changes to medications, less follow ups, reduces burden and cost to NHS) (enabler) Discussions about ECP accepting if patient decides not to use treatment (enabler/barrier)	<i>you go along with the treatment then they're more likely to need more invasive procedures anyway" (ECP006)</i>
Reinforcement - increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus	Incentives Punishment Consequents Reinforcement Contingencies Sanctions	Discussions about ECPs reiterating importance of adherence (enabler) Discussions about ECPs repeating education surrounding nature of glaucoma, rationale for treatment and instillation technique to promote patient adherence (enabler/barrier) Consider coding discussions about support rather than reinforcement from ECP/family/carer to Social Influences	<i>"but I think that reinforcement needs to happen across the board, more so than probably it does" [in terms of demonstrating eyedrop instillation technique] (ECP008)</i>
Intentions – a conscious decision to perform a behaviour or a resolve to act in a certain way	Stability of intentions Stages of change model Transtheoretical model and stages of change	Discussions around ECP intentions to aid patients' adhering to treatment	
Goals - mental representations of outcomes or end states that an individual wants to achieve	Goals (distal / proximal) Goal priority Goal / target setting	Discussions about how important it is to ECPs to ensure patients adhere to treatment (enabler/barrier)	<i>"you know I think it's great and you are actually looking into these kind of issues. Because I think they're very important" [in terms of doing this research into non-adherence] (ECP001)</i>

	Goals (autonomous / controlled) Action planning Implementation intention	Discussions about how important it is for ECP to address adherence issues (enabler)	
Memory, Attention and Decision Processes -the ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives	Memory Attention Attention control Decision making Cognitive overload/tiredness	Discussions about ECPs tailoring treatment or management decisions to suit individual patient needs or clinical findings (enabler) Discussions about using clinical information to decide if patient adherent/non-adherent (enabler)	"I sort of try and elucidate why they're struggling to take their drops. If there's something like ocular surface irritation, I sort of suggest, you know, maybe we can use lubricants or switch to preservative-free or something like that to try and help" (ECP009)
Environmental Context and Resources - any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behaviour	Environmental stressors Resources / material resources Organisational culture /climate Salient events / critical incidents Person x environment interaction Barriers and facilitators	Discussions about challenges working in busy clinics, time constraints, issues with appointment systems, type of clinic or limited staff (barrier) Discussions around organisational structure to support ECP management of non-adherence (e.g. provision of helpline or specific clinics set up) (enabler) Discussions around integration/lack of integration of systems within NHS (enabler/barrier) Discussions around ECP issuing prescriptions e.g. manufacturing issues, eyedrops out of stock, GP not prescribed on repeat (barrier)	<i>"I don't tend to show people things online, I don't really have time in clinic to be looking through things"</i> (ECP004) <i>"We also have a helpline that patients can call in if they are having any side effects, allergies. Or if they are confused by the regime then they can ring us. That kind of helps with compliance as well"</i> (ECP001) <i>"Also we always give them a letter now after they've seen us. So if they get home and then sort of are confused about the regime then they can look at the letter and it's all documented what drops they're to take"</i> (ECP001)

		Discussions around availability of physical resources e.g. leaflets, dropper aids, patient websites (enabler/barrier)	
		Discussions around issuing clinic letters to patient and/or GP (enabler/barrier)	
Social Influences - those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviours	Social pressure Social norms Group conformity Social comparisons Group norms Social support Power Intergroup conflict Alienation Group identity Modelling	ECPs referring to their influence, either positive or negative, on HCPs/support groups/family members/carers on how they aid adherence (enabler/barrier) Discussions around the influence clinician-patient relationships have on patient adherence behaviour and admitting non-adherence (enabler/barrier) Discussions around overall team approach and support from HCPs (enabler)	<i>"I think that if the patient trusts you as a clinician, they're more likely to go ahead with it"</i> (ECP002) <i>"I don't want to say I'm intimidating, but they may feel less intimidated by a nurse to talk to"</i> (ECP003)
Emotion – a complex reaction pattern, involving experiential, behavioural, and physiological elements, by which the individual attempts to deal with a personally significant matter or event	Fear Anxiety Affect Stress Depression Positive/negative effect Burn-out	Discussions about stress experienced when managing adherence issues e.g. due to time constraints or recommending new technology-based strategies (barrier)	
Behavioural Regulation - anything aimed at managing or	Self-monitoring Breaking habit	Discussions around ECPs developing strategies so they are consistently	<i>"That was also based on some Royal College of Medicine guidance that came out</i>

changing objectively observed or measured actions	Action planning	aware/up to date with glaucoma medication adherence and its management (e.g. the use of guidelines/recommendations) (enabler)	<i>several years ago to say that we should direct our communicating to patients as opposed to GP” (ECP008)</i>

Appendix C4

Themes identified in non-salient TDF domains and illustrative quotes from patients

Theme	Barrier/Enabler/ Mixed	Illustrative quote(s)
TDF domain: Social professional role and identity		
Patient autonomy (patient regards taking eyedrops as their responsibility regardless of setting)	Enabler	<i>'It doesn't worry me [having to instil drops]. I've done it a couple of times when I've been out on a date or something like that'</i> (P002)
TDF domain: Intention		
Intention to maintain consistent eyedrop use	Enabler	<i>'if there's something where I thought, do you know what, perhaps now, a knot in the handkerchief no longer suffices [to help remember needs to instil eyedrops]....if it gets to the point that one needs to find other ways of doing this, I would like to think that I wouldn't be so proud, or is it stupid?' [to find other ways to act as a reminder to instil eyedrops]</i> (P004)
TDF domain: Emotion		
Fear of non-adherence/consequences of non-adherence	Barrier	<i>'it worries me when Chris [husband] doesn't do it' [instil eyedrops]</i> (P008)

Themes identified in non-salient TDF domains and illustrative quotes from Eye Care Professionals

Theme	Barrier/Enabler/ Mixed	Illustrative quote(s)
TDF domain: Beliefs about consequences		
Accepted outcomes of non-adherence	Barrier	<i>'you can't force someone to do it. That's the person's eyes. They have to make that decision, and if that patient decides to say, no, or say, yes, sorry, when they mean no,</i>

		<i>you have to just accept that, and that's not really anything you can do about it'</i> (ECP002 Orthoptist)
TDF domain: Reinforcement		
Reinforcing adherence	Enabler	<i>'You've just got to keep reiterating, they need to take it.....I think each time they come in, it's important for us to say, look, this is – things are changing..... I think that's important, and why they should be taking the drops. We should do that each time'</i> (ECP004 Optometrist)
TDF domain: Goals		
Prioritising adherence	Enabler	<i>'Because I always think – my thing is better to be proactive [in terms of ensuring patient is adherent]</i> (ECP002 Orthoptist)
TDF domain: Social Influences		
Positive influence of integrated healthcare team approach in managing adherence	Enabler	<i>'This is where the team really does matter because if I can knuckle down and try and convince a patient to take their drops'</i> (ECP008 Ophthalmologist)

Appendix C5

Manuscript: Factors Influencing Glaucoma Medication Adherence: A Qualitative Study of Patients and Ophthalmologists in India

This appendix presents the manuscript of a qualitative study conducted at the LV Prasad Eye Institute, India. The study explores the behavioural determinants of glaucoma medication adherence from the perspectives of patients and ophthalmologists. The manuscript is currently under peer review.

Abstract

Purpose: Adherence to glaucoma medication helps prevent disease progression. Barriers to adherence exist, particularly in low- and middle-income countries. We explored factors influencing medication adherence from the perspectives of patients and ophthalmologists in India.

Design: Cross-sectional, qualitative study.

Methods: Semi-structured interviews with a purposive patient sample prescribed intraocular pressure (IOP)-lowering eyedrops and ophthalmologists involved in glaucoma care at a tertiary centre. The Theoretical Domains Framework (TDF) of behaviour change guided deductive and inductive thematic analysis of interview transcripts to identify personal, sociocultural, and environmental influences on adherence.

Results: Twenty-two participants (n=11 patients, n=11 ophthalmologists) were recruited. Seven TDF domains were key to patient adherence and practitioner management. Patient barriers mapped to TDF domains: *Environmental, Context and Resources* (difficulties obtaining medication, lifestyle changes, hospital system issues), *Memory, Attention and decision processes* (forgetfulness), and *Skills* (difficulty administering drops). Practitioner barriers related to *Environmental, Context and Resources* (time constraints and medication availability). Patient enablers mapped to *Social Influences* (family support), *Knowledge* (understanding

glaucoma and treatments), *Beliefs about consequences* (perceived treatment necessity) and *Behavioural Regulation* (establishing routines). Ophthalmologist enablers included *Environmental, Context and Resources* (organisational infrastructure), *Knowledge* (knowing how to classify adherence, awareness of non-adherence), *Skills* (effective communication), *Memory, Attention and decision processes* (tailoring patient care), *Social Professional Role/Identity* (professional responsibility), and *Social Influences* (practitioner influence).

Conclusions: A complex interplay of factors influence adherence. Identifying modifiable behaviours provides a basis for developing culturally-sensitive interventions to reduce barriers, enhance patient and family support and equip practitioners with tools to manage non-adherence effectively.

Key-words: glaucoma medication adherence, Theoretical Domains Framework, patient and practitioner perspectives, India

Key Messages:

- An understanding of both patient and practitioner perspectives is required to identify factors influencing glaucoma medication adherence
- We applied a theoretical framework of behaviour change to identify modifiable barriers and enablers to medication adherence, operating across patients, practitioners and the healthcare system
- The theory-driven influences identified can inform the development of evidence-based behaviour change interventions that seek to improve glaucoma medication adherence

Introduction

Glaucoma, the second leading cause of blindness worldwide,^[1] causes irreversible vision loss if untreated.^[2] In low- and middle-income countries (LMICs) patients often present later with more advanced disease, increasing their risk of blindness.^[3] India, with its high population, contributes to the highest regional burden of global blindness.^[4]

Glaucoma management focuses on lowering intraocular pressure (IOP), typically through daily, long-term eyedrops use.^[5] Adherence, which involves patients modifying their health-related behaviours and following an agreed treatment plan,^[6] is crucial for treatment success.

Unfortunately, non-adherence poses a global health challenge, with LMICs facing greater barriers.^[7] In India, non-adherence rates range from 18% to 58%, depending on how adherence is defined and measured.^[8] Sub-optimal adherence compromises treatment outcomes, accelerates disease progression and increases societal and economic costs.^[9,10]

Understanding the behavioural determinants of adherence (i.e. what facilitates or hinders medication-taking) is crucial for developing effective interventions to address non-adherence. Adherence involves complex behavioural patterns influenced by personal, sociocultural, and environmental factors. Interventions targeting these underlying drivers of behaviour are more likely to be effective.^[11] While strategies often focus solely on patient behaviour, practitioners play a key role in identifying and managing non-adherence. However, many practitioners struggle to accurately detect non-adherence,^[12] missing intervention opportunities.

The Theoretical Domains Framework (TDF) synthesises 33 theories grouped into 14 domains, providing a structured approach to understanding and addressing determinants of behaviour.^[13] The TDF is linked to two key behaviour change frameworks: the Behaviour Change Wheel (BCW)^[14] and Behaviour Change Technique Taxonomy (BCTT).^[15] The BCW maps key TDF domains to intervention functions (e.g. *Education, Training and Environmental Restructuring*) and policy categories (e.g. *Legislation, Service Provision and Guidelines*) to guide intervention development. The BCTT complements this by providing standardised language describing the components or 'active ingredients' of interventions, e.g. *Instructions on how to perform the behaviour, prompts or cues, and behavioural practice/rehearsal*. Together these frameworks ensure adherence strategies are designed to address root causes of non-adherence (i.e. identify and overcome barriers to eyedrop use).

While the TDF has been applied to studies in India,^[16] to our knowledge, none have explored glaucoma medication adherence. However, the TDF was used in a systematic review on glaucoma medication adherence.^[12]

This study uses the TDF to:

1. Identify barriers and enablers to glaucoma medication adherence among patients and ophthalmologists in India
2. Identify the salient TDF domains most relevant to target behaviours from the perspectives of patients and ophthalmologists

Methods

Standards, Ethics and Informed consent

The study reporting follows the Consolidated Criteria for Reporting Qualitative Research (COREQ).^[17] Prospective ethical approval was granted by the institutional ethical committee and adheres to the principles of the Declaration of Helsinki. All participants provided informed consent.

Study design

This qualitative study used semi-structured interviews, informed by the TDF, to investigate factors influencing glaucoma medication adherence. The interview guide was based around the 14 TDF domains^[13] (see Table 2). For patients, questions focussed on behaviours related to eyedrop use, for ophthalmologists, they centred on approaches to managing adherence in clinical practice.

Not all TDF domains were explicitly addressed; instead, questions were structured to allow a natural flow, as rigid adherence to the TDF can limit participant expression in qualitative settings.^[18] Both interview guides were informed by previous research^[12] and recommendations from the team's experienced qualitative and behaviour change researchers. Guides were piloted and refinements made based on patient and ophthalmologist feedback (see Supplementary Material S1 for interview guides).

Participants and recruitment

Patients

Patients, ≥ 18 years of age, prescribed one or more IOP-lowering eyedrops for any glaucoma type were recruited from a glaucoma service at a tertiary eye care institute in Southern India. Participants were from higher and lower socioeconomic strata (SES) and conversed in English, Telugu, or Hindi, with interpreters when needed. Purposive sampling was used seeking diversity in age, geographic location, number of prescribed eyedrops, and duration of eyedrop use.

Ophthalmologists

Ophthalmologists managing glaucoma at tertiary centres were recruited via email invitations. Purposive sampling aimed to capture diversity in age, gender, geographic location, and experience.

Procedure

Patient interviews were conducted one-on-one in private, led by an English-speaking researcher with interpreters as needed. Ophthalmologist interviews were conducted in-person or online via Zoom (San Jose, CA, Zoom Video Communications Inc). Interviews occurred in February/March 2024, were audio-recorded, transcribed verbatim, and anonymised.

Sample size

Sample sizes were guided by data saturation in theory-informed interviews, with an initial analysis sample of 10.^[19]

Researcher characteristics and reflexivity

The primary researcher is an experienced United Kingdom (UK) based practitioner specialising in glaucoma care; this background provided valuable insights into challenges associated with medication adherence. However, they consulted with local qualitative researchers to adopt culturally sensitive approaches, and shadowed hospital staff to understand India's healthcare system, aiming to build rapport with participants, minimise the sense of being an 'outsider' and enhance their

communication methods.

Data Analysis

Data analysis was conducted using NVivo 12 software (QST International, Doncaster, Australia), following a combined content and framework analysis approach,^[20] outlined in Figure 1 and detailed in Supplementary Material S2 and S3. The key domains representing adherence barriers and enablers were identified using established criteria: frequency, elaboration and spontaneity^[21] (see Figure 1).

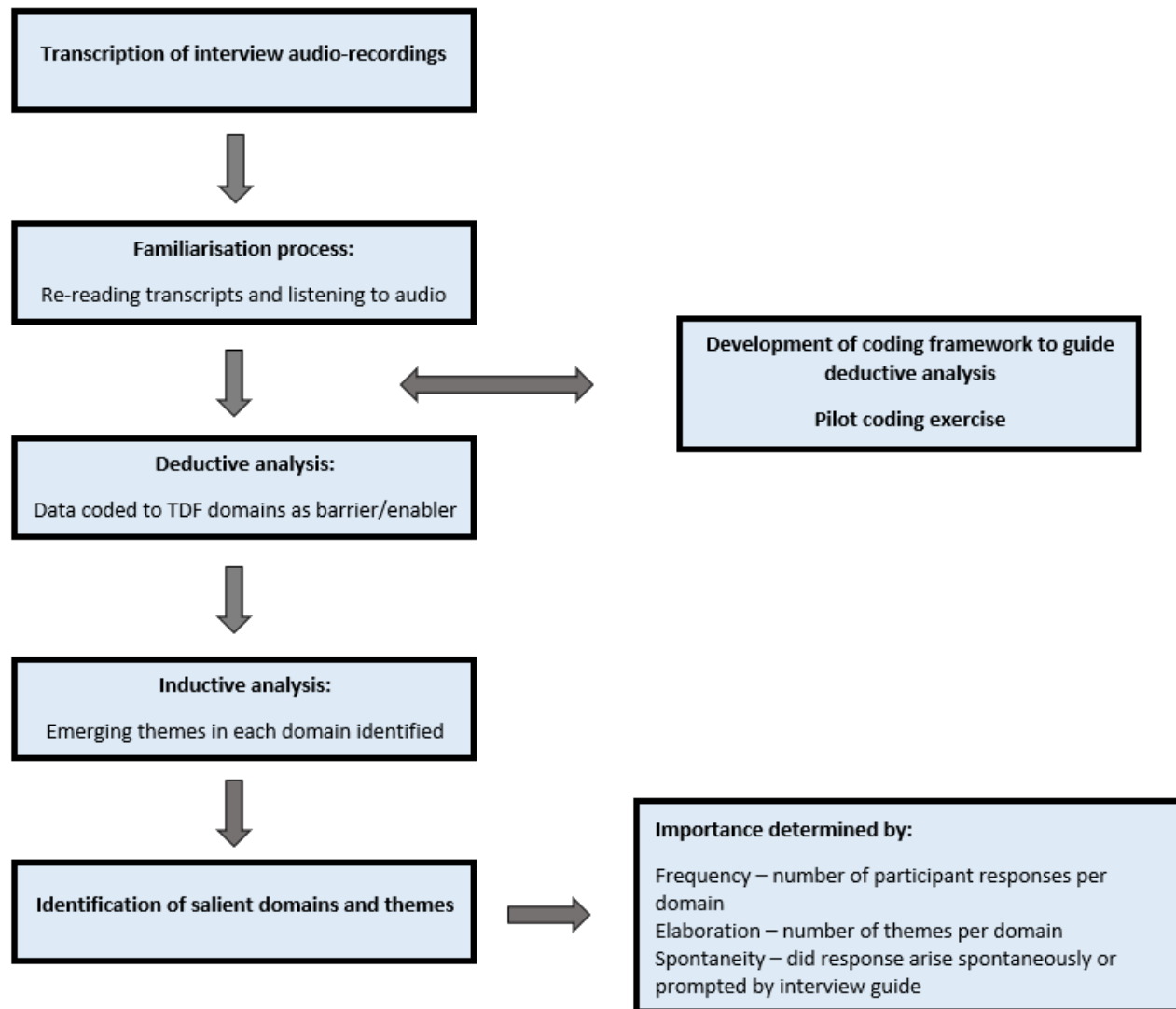


Figure 2 Flow chart representing stepwise process of data analysis.
Abbreviation TDF, Theoretical Domains Framework

Results

Participant characteristics

Eleven patients and 11 ophthalmologists participated. Interviews lasted between 16 and 44 minutes, averaging 19 minutes for patients and 28 minutes for ophthalmologists.

Nine patients were adherent, reporting no missed doses since treatment started. Two were non-adherent. One intentionally missed doses two to three times weekly, while the other reported both intentionally and unintentionally missing doses. Fifty-five percent of patients self-administered their eyedrops. Three interviews required an interpreter: (Telugu=2, Hindi=1). Participant characteristics are in Table 1.

Table 1 Participant characteristics

Patient demographics		N (%) N= 11 total
Gender	Female	3 (27)
	Male	8 (73)
Age (years)	31-45	2 (18)
	46-60	3 (27)
	61-74	6 (55)
Location in India (state)	West Bengal	1 (9)
	Telangana	5 (45)
	Andhra Pradesh	3 (27)
	Gujarat	1 (9)
	Maharashtra	1 (9)
Highest level of education	School education (up to 11 years)	1 (9)
	School education (11 to 18 years)	2 (18)
	Degree or higher	8 (73)
Occupational status	Full-time employment	4 (36)
	Retired	5 (45)
	Housewife	2 (18)
Type of glaucoma (according to patient)	POAG	1 (9)
	PACG	5 (45)
	2° glaucoma	2 (18)
	Does not know	3 (27)

Number of glaucoma medications	1	9 (82)
	2	2 (18)
Duration of glaucoma eyedrop usage (years)	<5	4 (36)
	5-10	5 (45)
	11-20	2 (18)
Number of eyedrop instillations per day	1	7 (64)
	2	3 (27)
	4	1 (9)
Ophthalmologist demographics		N (%) N=11 total
Gender	Female	3 (27)
	Male	8 (73)
Age (years)	33-45	7 (64)
	46-60	3 (27)
	>60	1 (9)
Location of hospital (state)	Telangana	9 (82)
	Andhra Pradesh	1 (9)
	Odisha	1 (9)
Time worked in glaucoma care (years)	4-10	5 (45)
	11-20	3 (27)
	>20	3 (27)

Salient domains

Barriers and enablers to medication adherence were identified across 13 of the 14 TDF domains, excluding *Reinforcement* for patients, and *Optimism* for ophthalmologists. The most salient domains influencing patient adherence and practitioner management were identified and ranked (Table 2). Seven domains were particularly relevant for both groups. Key themes within these domains are described below, and summarised in Table 3a and b. Remaining themes and domains are in Supplementary Material S4.

Table 2 Relevance of Theoretical Domains Framework (TDF) domains to medication adherence based on frequency, elaboration, and spontaneity for Patients (left hand table) and Ophthalmologists (right hand table)

TDF Domain	Patient group		
	Frequency (number of patients reporting barriers/enablers within domain, max N=11)	Elaboration (number of themes per domain)	Spontaneity (frequency of spontaneous response)
Environmental Context and Resources	10	5	2
Social Influences	10	1	5
Memory Attention and decision processes	11	1	0
Knowledge	10	1	0
Skills	10	1	0
Beliefs about consequences	9	1	1
Behavioural Regulation	10	1	0
Social Professional Role/Identity	8	1	0
Beliefs about capabilities	6	1	0
Goals	5	1	0
Emotion	4	1	0
Intentions	3	1	0
Optimism	1	1	0
Reinforcement	0	0	0

TDF Domain	Ophthalmologist group		
	Frequency (number of patients reporting barriers/enablers within domain, max N=11)	Elaboration (number of themes per domain)	Spontaneity (frequency of spontaneous response)
Environmental Context and Resources	11	3	2
Knowledge	10	2	0
Skills	10	1	0
Memory Attention and decision processes	10	1	0
Social Professional Role/Identity	8	1	1
Beliefs about capabilities	9	1	0
Social Influences	7	1	0
Beliefs about consequences	4	1	0
Reinforcement	4	1	0
Intentions	2	1	0
Goals	2	1	0
Behavioural Regulation	2	1	0
Emotion	1	1	0
Optimism	0	0	0

Patients (Refer to Table 3a)

Environmental Context and Resources

Cost and difficulty obtaining medications were major barriers to adherence. Both adherent and non-adherent patients expressed concerns about eyedrops' cost, suggesting companies producing medications should not increase prices for LMICs. Additionally, some patients reported medications were not always available at pharmacies and could only be found in a '*wholesale market*.'

Changes in lifestyles, e.g. visiting family or work commitments, often caused patients to delay scheduled eyedrop instillations. Regimens involving multiple instillations throughout the day were particularly challenging. Drops needing refrigeration posed issues, especially for the unintentionally non-adherent patient who lacked easy access to drops at instillation time.

Issues with the hospital system, e.g. rescheduling appointments hindered adherence. One patient intentionally did not purchase eyedrops when her follow-up appointment was postponed, leading to a 15-day period of non-adherence.

Relying on family members to instil eyedrops facilitated adherence. All participants lived with a spouse or other family members who could assist.

Social Influences

Having trust in the doctor was an important enabler; all patients expressed strong faith in advice received regarding eyedrop use. Family support also played a crucial role in facilitating adherence. Patients frequently mentioned that family members accompanied them to hospital consultations and also believed in the doctor's recommendations.

Memory, Attention and decision processes

Forgetting to take medication was an important barrier. While some adherent patients admitted they may forget to instil eyedrops at the recommended time, they did administer them within two hours of this time. Conversely, non-adherent patients who missed a dose would typically wait until the following day's dosing schedule to instil.

Knowledge

Patients who understood their medication purpose and its importance for preserving vision were more likely to adhere. One non-adherent patient was unaware of the purpose of their specific eyedrops.

Skills

Limited physical skills posed barriers to administering eyedrops. Several patients reported difficulties with eyedrops falling down their cheek or spilling from the eye leading to frequent waste. Many patients felt family assistance was crucial because of their greater ability at instilling drops.

Beliefs about consequences

The belief that adhering to the eyedrop regimen would preserve vision was a key motivator for most patients. However, one intentionally non-adherent patient expressed scepticism about the necessity of eyedrops believing '*nature*' would take its course and '*what will be will be.*'

Behavioural Regulation

Establishing a consistent routine and using reminder strategies were key to adherence. Some patients set alarms to prompt themselves, whilst others relied on family members to act as reminders. One patient used the anticipated discomfort associated with administering her eyedrops as a reminder to instil them.

Ophthalmologists (Refer to Table 3b)

Environmental Context and Resources

Ophthalmologists frequently noted that time constraints greatly hindered their ability to manage adherence effectively, particularly with large caseloads. High patient volumes limited the time available for in-depth discussions about adherence.

In contrast, good organisational infrastructure and sufficient resources facilitated adherence management. Ophthalmology fellows and optometrists in clinic provided valuable support for managing adherence. One ophthalmologist suggested clinic

counsellors, who could provide one-to-one support for patients with their eyedrops, would be beneficial and help their *'job a lot.'* However, resource limitations meant this role was not currently filled. Practitioners especially appreciated teleconsultations' benefits, feeling they could manage many concerns about eyedrops remotely, reducing clinic demand. Additionally, instructional videos in local languages providing demonstrations of eyedrop instillation techniques were a welcome assistance in supporting adherence.

Ophthalmologists encountered challenges due to disruptions in availability of eyedrops, particularly in rural areas where stock shortages were more common. To overcome this, practitioners often prescribed more widely available branded or generic medications.

Knowledge

Understanding what constitutes an acceptable level of patient adherence was identified as a facilitator to managing adherence. Most practitioners considered missing even one dose as non-adherent behaviour regardless of disease stability and were especially clear that missing a scheduled dose on the morning of a hospital visit was unacceptable. Two ophthalmologists, however, interpreted adherence levels based on the patient's glaucoma status, demonstrating some flexibility in their approach.

Understanding issues of non-adherence and recognising patient risk factors within the clinical setting were identified as enablers. Ophthalmologists were particularly mindful of patients' socio-demographic backgrounds and the extra challenges these factors could place on adherence.

Skills

Effective communication and educational skills from ophthalmologists improved adherence management. Practitioners recognised the importance of asking patients direct leading questions about their adherence. With experience they found asking whether eyedrops had been used on the hospital consultation day helped identify non-adherence. To further support patient education, practitioners frequently demonstrated eyedrop instillation techniques to the patient and their attendant.

Memory, Attention and decision processes

Ophthalmologists found tailoring their decision-making processes to align with individual patient circumstances enhanced their ability to manage non-adherence. By understanding each patient's specific challenges, practitioners were better able to recommend suitable alternatives, e.g. reducing the number of daily instillations, prescribing more affordable eyedrops, offering free samples to patients with financial difficulties or recommending surgery.

Social Professional Role/Identity

Ophthalmologists recognised their professional responsibility to address and effectively manage non-adherence among patients as an enabler. They felt a strong duty to ensure patients understood their treatment and received the necessary adherence support.

Beliefs about capabilities

Beliefs about capabilities had a mixed influence on adherence management. Some practitioners expressed confidence in their ability to detect non-adherence, with others less certain. There was no obvious association between age or glaucoma experience and levels of confidence. Male practitioners were more likely to report lower confidence. The more confident credited this to establishing good relationships with and understanding their patients.

Social Influences

Practitioners recognised the positive influence they had on managing adherence, noting their influence was greater than other staff, largely attributable to the continuity of care they provided by consistently seeing their own patients and building lasting relationships, unlike other staff who frequently changed.

Table 3a Summary of key themes and illustrative quotes from patients assigned to Theoretical Domains Framework (TDF) domains identified as relevant to adherence behaviour

Theme	Barrier/Enabler/ Mixed	Illustrative quote(s)
TDF domain: Environmental, Context and Resources		
Difficulties obtaining medication	Barrier	<i>'[I] "will not find [eyedrops in] any medical stores' (P018)</i>
Nature of eyedrops	Barrier	<i>'I travel from [City 1] to [City 2]. It takes 2 1/2 hours by flight...How can I carry [my Latanoprost eyedrops] from [City 1] to [City 2]? They remain [at home] in my refrigerator' (P017)</i>
Changes in lifestyle	Barrier	<i>'Sometimes I'm working on the [computer] system and the time runs out' (P021)</i>
Issues within the hospital system	Barrier	<i>'getting an appointment is a very tedious job...They gave me appointment on 1st week of this February and after that they told me that Dr... is not available in 1st week as Dr. is travelling so [changed my appointment] to come on 23rd' (P020)</i>
Relying on others to instil eyedrops	Enabler	<i>'somebody is there in....family.... so some....other person will be doing it' [instilling eyedrops] (P022)</i>
TDF domain: Social Influences		
Positive social influence from family or eye care practitioner	Enabler	<i>'I trust my doctor because without trust, nothing will work. I absolutely trust her' (P020)</i>
TDF domain: Memory, Attention and decision processes		
Forgetting to instil eyedrops as prescribed	Barrier	<i>'So many days so many days [I forget to use my eyedrops]' (P017)</i>
TDF domain: Knowledge		
An understanding of glaucoma and treatment rationale	Enabler	<i>'Main thing is to control the ocular pressure.....using eyedrop controls the ocular pressure.....it may lead to blindness if the pressure keeps on increasing' (P024)</i>
TDF domain: Skills		

Poor physical skills	Barrier	<i>'if I put one drop more than 10 drops come out' (P020)</i>

TDF domain: Beliefs about consequences

Believing eyedrops are necessary to preserve sight	Enabler	<i>'I realise that drops is more important than my job' (P024)</i>

TDF domain: Behavioural Regulation

Developing a routine and/or reminder strategies	Enabler	<i>'You should keep...your drops out. So you see it.....[next to] bed.... that reminds us.....Because right beside the bed side table.....we'll be keeping our mobiles.....we won't forget to charge our phone' (P016)</i>

Table 3b Summary of key themes and illustrative quotes from Ophthalmologists assigned to Theoretical Domains Framework (TDF) domains identified as relevant to adherence management behaviour

Theme	Barrier/Enabler/ Mixed	Illustrative quote(s)
TDF domain: Environmental, Context and Resources		
Lack of time	Barrier	<i>'As practitioners, the problem is that we have just too many patients and one of us has to do this..... it's not easy...we don't have so much time to be able to spend [with patient] even though you would like it to be that way' (ECP014)</i>
Organisational structure and/ available resources	Enabler	<i>'We have a telephone consult...we can say you can book a teleconference and call me...Many things I manage on the phone' (ECP020)</i>
Unavailability of medications	Barrier	<i>'what happens is many times we write a prescription and that is not available in their hometown' (ECP020)</i>
TDF domain: Knowledge		
An awareness of how to classify adherence/non-adherence behaviour	Enabler	<i>'If the patients are missing even a single drop on the day of the morning [of consultation] or even yesterday I will take it as non-compliant' (ECP024)</i>

An understanding of non-adherence issues and patient risk factors	Enabler	<i>'it is definitely a big problem in any medications. Non-compliance is like one of the major problems for you'</i> (ECP023)

TDF domain: Skills

Practitioner communication, education and interpersonal skills	Enabler	<i>'we speak to them [patient], we find out...what their problem is....what we do is ask them a leading question'</i> (ECP0014)

TDF domain: Memory, Attention and decision processes

Tailoring decision-making process according to patient needs	Enabler	<i>'what I do in such a scenario is first...give them a medication which is of low cost...we give them an alternative which is within their living standards...and the second thing is to advise them surgery...over a shorter period of time it is more cost effective than being on long term glaucoma treatment'</i> (ECP019)

TDF domain: Social Professional Role/Identity

Professional role in the management of adherence	Enabler	<i>'I believe that since I am the one who is treating them... I should tell them'</i> (ECP019)

TDF domain: Beliefs about capabilities

Perceived confidence/lack of confidence in own ability to identify non-adherence	Mixed	<i>'I feel it is very difficult to really make out whether the patient is compliant to medications or not....it's a very subjective way of accessing'</i> (ECP018) Barrier [From the] <i>'two to three....questions I ask them, the way they answer I can make out...whether they are compliant or not'</i> (ECP017) Enabler

TDF domain: Social Influences

Positive influence from practitioner	Enabler	<i>'If I speak to them personally, if I take the time out, and....try to make them understand definitely that will have a better impact than making an optometrist speak [to the patient] or giving them a leaflet...if the doctor really takes the time out to speak to the patient, I think that will have a greater impact'</i> (ECP023)

Discussion

This study identified important factors influencing glaucoma medication adherence in India from patient and practitioner perspectives. It expands upon existing research highlighting the complexity of adherence behaviours shaped by individual, systemic and environmental factors.^[12] Using the TDF, we systematically identified modifiable key domains for developing targeted behaviour change interventions at multiple levels; the patient, the practitioner and healthcare system. These domains can be mapped to evidence-based BCTs,^[22] which represent the ‘active’ components of an intervention and guide its development. Linking intervention components to theoretical domains provides insights into ‘why’ and ‘how’ the intervention works, improving its chances of being effective and replicable.^[23]

Implications for Practice and future work

Both patients and ophthalmologists identified systemic challenges, e.g. medication procurement, as important adherence barriers. Challenges included high medication cost and inconsistent availability, issues previously noted in India.^[24,25] Complex treatment regimens, with multiple daily instillations or medications requiring refrigeration, further compounded these difficulties. Linking these barriers from the *Environmental Context and Resources* domain to the BCW suggests policy-driven solutions including:

1. Subsidising medication costs to improve affordability
2. Improving supply chains to ensure consistent availability in rural and underserved areas
3. Promoting cost-effective alternatives to medication, such as surgery or Selective Laser Trabeculoplasty (SLT). Surgery is often considered a cost-effective first-line option in LMIC countries.^[3] However, possible post-operative complications and accessibility to follow-up care must be considered, as these can increase indirect costs.^[3] SLT is a safe, effective, repeatable treatment for open angle glaucoma, reducing reliance on long-term medication.^[26] Its integration into Indian glaucoma guidelines, similar to those advocated in other countries,^[27] could benefit patients who face barriers to medication access. However, SLT may only be beneficial as an adjunctive treatment for

patients with angle closure glaucoma,^[28] the more prevalent form in India and Southeast Asian countries.^[29] For primary angle closure, clear lens extraction is a proven, effective, safe, and cost-effective initial treatment, especially in LMICs.^[30]

Within the healthcare system, delayed follow-up appointments, time constraints and limited workforce resources were additional barriers. Structural reorganisation, such as optimising clinic workflows and improving scheduling systems, could address these issues. These improvements, part of *Environmental Restructuring* within the BCW, provide opportunities for more effective treatment adherence. For example, introducing stable/low risk glaucoma clinics run by general ophthalmologists or optometrists could reduce the clinic burden. Similar models were acceptable to patients without compromising care in other countries.^[31]

Family support and trust in healthcare providers, linked to the TDF domain *Social Influences*, emerged as important enablers, mirroring findings from other chronic conditions, e.g. diabetes, where family involvement supports patients' ability to manage their condition.^[32] Interventions integrating family support into treatment plans or educating family members could enhance adherence, aligning with the intervention function *Environmental Restructuring*. Trust and rapport between practitioners and patients was also important. Ophthalmologists emphasised the importance of strong patient-provider relationships in promoting adherence. Good communication skills with non-judgemental interview techniques encourage healthy patient–practitioner relationships,^[33] and could be incorporated into training programmes.

Patients' knowledge about glaucoma and consequences of non-adherence was an important enabler. Patient education is essential, as understanding glaucoma and its treatment significantly impacts adherence.^[34] However, in India, awareness and educational programmes are often one-time events rather than ongoing initiatives.^[35] This could be addressed through:

1. Establishing support roles where trained team members provide ongoing education, reinforce ophthalmologist recommendations, offer practical and emotional support, and ensure continuity of care in busy outpatient clinics.

However, staff numbers and training resources should be sufficient to meet demand.

2. A patient advocacy group. Establishing a national patient organisation, similar to Glaucoma UK (<https://glaucoma.uk/>), and utilising resources from organisations such as The World Glaucoma Patient Association (<https://glaucomafoundation.org/get-involved/world-glaucoma-patient-association/>) and Sightsavers India (<https://www.sightsaversindia.org/>), can help disseminate accessible information in relatable and digestible formats through leaflets, videos, support groups and telephone helplines.
3. Digital technology. Mobile phone applications offering educational resources, reminders and adherence tracking could improve adherence. India's expanding IT infrastructure and increasing smartphone user base means digital solutions could offer scalable, cost-effective solutions. Mobile health interventions have proved effective in improving medication adherence in various LMICs.^[36]

These solutions align with the *Knowledge* and *Behavioural Regulation* domains, supported by the BCW intervention functions *Enablement* and *Education*.

Patients who lacked the physical ability to administer eyedrops or struggled with complex regimens faced adherence barriers. Ophthalmologists noted that demonstrating instillation techniques during consultations often helped. Training interventions that include *Behavioural practice/rehearsal* could provide patients with the capability to overcome these challenges.

Practitioner confidence in managing adherence varied, highlighting a need for training to enhance their ability to identify and address non-adherence. Training programs informed by BCTs, such as *Instruction on How to perform the Behaviour* and *Feedback on the Behaviour*, could improve ophthalmologist practice. Online, Continuing Professional Development-accredited modules on adherence strategies, effective patient communication, and glaucoma management updates could offer accessible, flexible training solutions. BCW policy categories, such as *Guidelines* and *Service Provision* could support these initiatives.

Strengths and Limitations

This study addresses an evidence gap by exploring glaucoma medication adherence in India from patients' and practitioners' perspectives, an approach, to our knowledge, not previously undertaken. While existing research often highlights patient reported barriers and enablers,^[37] this dual perspective provides a more comprehensive understanding of adherence challenges.

Use of the TDF is another strength, providing a structured, theory-based methodology for identifying behavioural influences on adherence. This approach supports development of tailored evidence-based behaviour change strategies addressing modifiable barriers for both patients and practitioners. Similarly developed interventions were effective in improving medication adherence in Type 2 diabetes.^[38]

Our study has limitations. Most patients reported high adherence, potentially limiting our findings' generalisability, although self-reported adherence often overestimates actual adherence.^[39] Recruitment from a tertiary centre may not fully represent the broader Indian glaucoma population, restricting applicability of our findings to other settings. The percentage of university-educated patients was higher than in the general Indian population,^[40] which could bias findings. The underrepresentation of female participants may have led to missed factors specific to women.

Conclusions and Recommendations

It is important to target glaucoma medication adherence in India through a multilevel approach informed by a theoretical framework. Based on the identified key TDF domains and associated BCTs, we proposed several potential intervention components that could be implemented as part of a multicomponent strategy to enhance medication adherence. Future research should focus on piloting these components, assessing acceptability, feasibility, and evaluating their effectiveness in improving adherence. Implementing these strategies could significantly reduce glaucoma-related vision loss, enhancing patients' quality of life and easing the burden on India's healthcare system.

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Supplementary Material for India-based manuscript

S1: Interview topic guide

Patient Interviews

Introduction

“My name is _____, a researcher at..... The main purpose of this interview is to understand your experiences using eyedrops in glaucoma.”

“I will also be interviewing doctors to understand their experiences of eyedrop compliance in practice and how they manage it. I plan to use the information gained from these interviews to help me develop some form of technology-based solution to help patients use their eyedrops correctly.”

“Have you read the participant information sheet that you have been provided with?”

“I will just re-cap some information. The interview should last about 45 minutes. Everything you say will be kept strictly confidential. You are free to stop participating at any time with no consequences. You do not need to answer any questions that you do not wish to. I will be audio recording the interview so that I don't have to take too many notes and can listen to what you are saying. After the interview any identifiable information, such as your name, will be removed.”

“Please feel free to be open and honest about your experiences using eyedrops. There are no right or wrong answers, we are keen to learn from your experiences both positive and negative.”

“Are you happy to take part in this interview? Before we start do you have any questions?”

Complete consent form.

“I'm going to start recording now.”

Demographic Information

“I'd like to ask some questions about yourself first. This information will be used to describe the people who took part in our study, all your responses will be combined so you will not be identified.”

Please can you confirm:

- your gender, where you live in the country e.g. which state
- what age range you fall into (18-30, 31-45, 46-60, 61-74, 76-90, 91+)

- what is your highest level of education (e.g. school/college -up to 18 yrs. old, graduate, postgraduate)
- your employment status
- if you live alone/with family members (if yes ask which members)
- what type of glaucoma do you have (if known)
- how long approximately have you been using eyedrops for glaucoma
- is this the first type of eyedrop you have used/have you been changed to a different type? If yes do you know how many times they been changed?
- what drops are you currently taking – how many times a day do they go in? Don't worry if you don't remember the names of the drops
- do you instil your eyedrops yourself/family member/carer?
- do you pay for your medications or healthcare?
- how often do you have check-ups for your glaucoma?
- you have no visual difficulties/have visual difficulties but not formally registered as sight impaired/registered as sight impaired/registered severely sight impaired

Questions aligned with domains of Theoretical Domains Framework (TDF)

13. Do you know why you take your eyedrops? **(Knowledge domain)**

Prompts – explore understanding of glaucoma and rationale for using eyedrops and possibility of losing vision

14. On a daily basis do you have any problems putting your eyedrops in? **(Skills domain)**

Prompts – if yes explore why, maybe have problems with opening bottle due to arthritis in hands/unable to see to put your drops in/drops keep running down cheek

15. If answer yes to above question– even though you have some difficulties putting your drops in, how confident are you that you can continue using your drops as prescribed (i.e. once/twice a day) on a long-term basis? **(Beliefs about capabilities)**

If answer no to above question – as you don't experience any difficulties putting your drops in on a daily basis, how confident are you that you can continue to use your drops as prescribed (i.e. once/twice a day) on a long-term basis? **(Beliefs about capabilities)**

16. Is it important to you to use your eyedrops as instructed? **(Goals domain)**

Prompt – explore why

17. What do you think the benefits of using your eyedrops correctly are?

What do you think the disadvantages of not using your eyedrops correctly are?

(Beliefs about consequences)

18. Who do you think is responsible for making sure your eyedrops are used correctly every day? **(Social/professional role and identity domain)**

Prompt – your doctor, you, your family/carer

19. Is there anything/anyone that would make you more likely to use/not use your eyedrops as you should? **(Reinforcement domain)**

Prompt – praise from your doctor/family or receiving negative feedback from your doctor

20. If you use your eyedrops correctly, how likely do you think it is that this will help you maintain your vision/stop your glaucoma from getting worse? **(Optimism domain)**

21. If you think about how you use your eyedrops each day, is there anything that makes it easier for you, anything that makes it harder? **(Environmental context and resources domain)**

Prompts- being away on holiday, being dependant on a carer/family member to instil drops/ not being able to obtain/afford medications

22. Is there anything that you do/or could do to overcome these problems? **(Behavioural regulation domain)**

Prompt – habits/techniques or practical strategies employed

23. Does anyone else influence your decision to take your eyedrops? **(Social influences domain)**

Prompt – family members/carers/support groups/healthcare professionals (HCPs)

24. Do you ever forget or deliberately not use your eyedrops? If yes how often have you not used your eyedrops? Is there any reason that would lead to this decision? **(Memory, Attention and decision processes domain)**

Prompt – forgetting, away on holiday, side effects using drops so purposefully don't use
"Thank you for your time today, I really appreciate you sharing your views and experiences. Is there anything else you would like to add that I haven't covered?"

Ophthalmologist Interviews

Introduction

"My name is _____, a researcher at The main purpose of this interview is to hear about your experiences managing glaucoma medication adherence in practice."

"I will also be interviewing patients to learn about their experiences with glaucoma medication. We will use the information from both practitioner and patient interviews to guide the development of a potential intervention to help with glaucoma medication adherence."

"Have you read the participant information sheet that you have been provided with?"

"I will just re-cap some information. The interview should last about 45 minutes. Everything you say will be kept strictly confidential. You are free to stop participating at any time with no consequences. You do not need to answer any questions that you do not wish to. I will be audio recording the interview so that I don't have to take too many notes and can listen to what you are saying. After the interview any identifiable information, such as your name, will be removed."

"Please feel free to be open and honest about how you feel. There are no right or wrong answers, we are keen to hear your views and learn from your experiences both positive and negative."

"Are you happy to take part in this interview? Before we start do you have any questions?"

Complete consent form.

"I'm going to start recording now."

Demographic Information

"I'd like to ask some questions about yourself first. This information will be used to describe the people who took part in our study, all your responses will be combined so you will not be identified."

Please can you confirm:

- your gender, where/which state do you work in
- what age range you fall into (18-30, 31-45, 46-60, 61-74, 76-90, 91+)
- your job title and role within glaucoma care
- how long have you been qualified as an ophthalmologist? How long have you been involved in glaucoma care?
- on average how many glaucoma sessional clinics a week are you involved in?

Questions aligned with domains of Theoretical Domains Framework (TDF)

10. In practice how do you usually assess whether a patient is taking their eyedrops as prescribed? **(Skills domain)**

Prompt – subjectively ask patient/family member about adherence, what questions would you ask, use a questionnaire, what questionnaire would you use?

Do you provide education regarding glaucoma/treatment/ adherence/advice on how to instil eyedrops? How do you do this?

11. How do you classify a patient as nonadherent? Do you think nonadherence is a problem in your clinic? **(Knowledge domain)**

Prompt – is missing once/twice a week/month etc nonadherent

12. Whose role do you think it is to ensure patients comply with their treatment? Why do you think this? **(Social/professional role and identity)**

13. How important do you feel it is to actively manage patient adherence to treatment? What influences your approach? What are the main outcomes you aim for when supporting a patient's adherence? **(Beliefs about consequences)**

14. How confident do you feel in your ability to identify if a patient is adherent or nonadherent to their medication? Why do you feel that? **(Beliefs about capabilities)**

15. If a patient is having difficulty using their eyedrops correctly, how do you determine the most appropriate adjustments to their treatment or select an alternative approach? **(Memory, Attention and decision processes domain)**

Prompt – if developing side effects how do you manage, do you consider SLT or surgical intervention as an alternative, if patient struggling with dosing regimen due to hectic lifestyle how do you amend treatment to suit patient?

16. In clinic, are there any resources, tools, or colleagues that make it easier for you to manage non-adherence? Conversely, are there any factors that make it more challenging to support patients who struggle to adhere to their treatment? **(Environmental context and resources domain)**

Prompt - dedicated glaucoma nurses, dedicated adherence clinics, educational resources, not enough time, too many patients to see, not enough staff to support smooth running of clinic

8. How do you keep up to date/remain consistently aware of glaucoma medication adherence and its management? **(Behavioural regulation domain)**

Prompt – use of guidelines/recommendations, CPD, courses, conferences

9. When it comes to managing patient adherence what are your main goals or priorities in clinic? How do these goals guide your actions or interactions with patients?
(Goals)

“Thank you for your time today, I really appreciate you sharing your views and experiences. Is there anything else you would like to add that I haven’t covered?”

S2: Description of content and framework analysis for data analysis

The analysis followed a stepwise process:

(1). **Familiarisation process:** After transcribing the interviews, an in-depth familiarisation process was undertaken, which involved reading and re-reading the transcripts and listening to the audio recordings to gain a comprehensive understanding of the data.

(2). **Deductive analysis:** Participant responses were coded into one of the TDF domains, categorising each response as either a barrier or enabler to eyedrop adherence. To guide this process a coding framework was collaboratively developed by the researchers (DB/AS/DE/JGL/PC) after the first two pilot interviews and refined throughout data collection. For example, if a participant mentioned they didn't take their medication due to not understanding its importance, this would be coded as a barrier under the *Knowledge* domain. The coding framework for both participant groups is available in Appendix S3. The primary researcher (DB) deductively coded all transcripts, and a second researcher (PC) independently coded the same data to enhance coding reliability. Any disagreements were resolved through discussion and consensus between DB and PC, or with input from a third reviewer (AS) when necessary.

(3). **Inductive analysis:** Key themes were generated for each participant group based on the data within each domain. These themes, referred to as "belief statements" in TDF literature, were categorised as barriers, enablers, or mixed influences on adherence (i.e., themes that acted as barriers for some participants and enablers for others). The primary researcher (DB) generated and classified the key themes. Two reviewers (PC and AS) independently reviewed the generated themes to ensure they accurately represented the data. Any discrepancies were resolved through discussion until consensus was reached.

(4). **Identifying salient domains:** The most prominent domains representing barriers and enablers to glaucoma medication adherence were identified using established criteria: (a) frequency of coding (number of participant responses within a TDF domain) (b) elaboration (number of themes per domain) (c) spontaneity (whether responses arose spontaneously or were prompted by the interview guide).

S3: Coding framework

Coding framework for patient group

Determinants (enablers/barriers) influencing patient glaucoma medication adherence as categorised by TDF domains together with illustrative quotes

TDF Domain and definition	Component constructs	Examples may include	Illustrative quotes
Knowledge – an awareness of the existence of something	Knowledge about condition/scientific rationale Knowledge of task environment Procedural knowledge	Discussions around patient's knowledge of: • Glaucoma progression through poor adherence • Rationale for using eyedrops • Consequences of adherence/non-adherence • Treatment application and regimen • Side effects of eyedrops Knowledge can be either extent of (enabler) or lack of (barrier)	<i>"it [eyedrops] controls the pressure so that the eyesight will not be affected" (P016)</i>
Skills – an ability or proficiency acquired through practice	Skills Skills development Competence	Discussions around patient physical and/visual skills needed to correctly administer eyedrops (enabler/barrier)	<i>"if I put one drop more than 10 drops used to come out as tears" (P020)</i>

	Ability Practice Skill assessment Interpersonal skills		
Social/Professional Role and Identity – a coherent set of behaviours and displayed personal qualities of an individual in a social or work setting	Professional role and identity Social identity Identity Professional boundaries Professional confidence Group identity Leadership Organisational commitment	Discussions around how patients relate to people without glaucoma when they have to use their eyedrops (e.g. in a social/group setting) and take personal responsibility for adhering to treatment (enabler/barrier)	<i>"This is my responsibility [to keep using drops] because because I am an adult man.....I should take my responsibility"</i> (P015)
Beliefs about capabilities - acceptance of the truth, reality, or validity about an ability, talent,	Self-confidence Perceived competence	Discussions about how confident patients feel about their ability to instil eyedrops correctly and/or manage their glaucoma (enabler/barrier)	<i>"independently putting the drop [in myself] will be difficult"</i> (P016)

or facility that a person can put to constructive use	Self-efficacy Perceived behavioural control Beliefs Self-esteem Empowerment	Also consider coding references about how confident a patient feels about admitting not having used their eyedrops to others to Social influences	
Optimism - The confidence that things will happen for the best or that desired goals will be attained	Optimism Pessimism Unrealistic optimism Identity	Discussions about how likely patients think adhering to treatment will prevent sight loss/control glaucoma. Includes optimism (enabler), unrealistic optimism or pessimism (barrier)	<i>"Technology if [I] use it in a proper way it can be helpful particularly to remember [to instil eyedrops] in the future" (P016)</i>
Beliefs about consequences - acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation	Beliefs Outcome expectations Characteristics of outcome expectancies Anticipated regret	Discussions about patients accepting they have glaucoma (enabler/barrier) Discussions regarding patient perceptions about the nature of glaucoma and/or outcomes of treatment (enabler/barrier). Includes beliefs regarding benefits and concerns about unwanted side-effects/future side effects, how	<i>"I realise that drops is more important than my job so I started putting it [drops] regularly after one month, one month or so" [in 1st month of using drops patient regularly missed as workday was so hectic but after 1 month he realised how important it was to use correctly] (P024)</i>

	Consequents	glaucoma or eyedrops may affect patients' life or cause symptoms	
Reinforcement - increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus	Incentives Punishment Consequents Reinforcement Contingences Sanctions	Discussions surrounding patient's response to: - receiving praise/encouragement for instilling eyedrops as prescribed (enabler) - receiving negative feedback for not instilling eyedrops correctly (barrier/enabler) - receiving feedback (either positive or negative) about nature of glaucoma and/or treatment e.g. from family members/carers/practitioner (enabler/barrier) Consider coding discussions about support rather than reinforcement from to Social Influences	
Intentions – a conscious decision to perform a behaviour or a resolve to act in a certain way	Stability of intentions Stages of change model	References from patients referring to their intentions to: instil/not instil their eyedrops as prescribed (enabler/barrier)	<i>"if nobody is there [to put drops in] obviously I will learn and I will do it for myself" (P020)</i>

	Transtheoretical model and stages of change	continue/discontinue instilling their eyedrops (enabler/barrier)	
Goals - mental representations of outcomes or end states that an individual wants to achieve	Goals (distal / proximal) Goal priority Goal / target setting Goals (autonomous / controlled) Action planning Implementation intention	Discussions about patient motivation to adhere to treatment (enabler) Discussions regarding patient desire to retain as much sight as possible (enabler)	<i>[importance of using eyedrops] "I want to do much more. I mean, I think little research and then maybe I have to write some book and lot of my PhD material. So I wish I have some good sight for some more years" (P021)</i>
Memory, Attention and Decision Processes -the ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives	Memory Attention Attention control Decision making Cognitive overload/tiredness	Discussions around whether patients forget to instil their eyedrops (either occasionally or more frequently) (barrier) Discussions around patients' ability to decide whether they instil their eyedrops or whether they decide to take occasional breaks from using eyedrops (enabler/barrier)	<i>"never forgot since the beginning. Whatever time it will be I will have it" (P018)</i> <i>"So many days so many days [forgotten to use drops]....two to three days in a week" (P017)</i>

Environmental Context and Resources - any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behaviour	Environmental stressors Resources / material resources Organisational culture /climate Salient events / critical incidents Person x environment interaction Barriers and facilitators	Discussions around issues with health care system influencing patient adherence e.g. busy eye clinics, time constraints in clinic, difficulties obtaining follow up appointments, limited staff Discussions around circumstantial factors influencing patient adherence e.g. complexity of eyedrop regimen, work patterns, away on holiday, existence of side effects, financial issues, being dependent on a carer/family member to instil eyedrops and/or collect medications (barrier) Discussions around obtaining medication e.g. availability of eyedrops, access to chemist, financial implications of purchasing medication (enabler/barrier) Discussions around organisational structure to support patient if they have a problem using their eyedrops (e.g. provision of helpline) (enabler)	<i>"It's only one drop then it is not a problem"</i> (P018) <i>"The price is actually expensive. I don't know how the prices are in other countries, but at least for Indian people, right, the price is expensive"</i> (P022)

		Discussions around resources that encourage/discourage patient adherence e.g. YouTube videos (enabler/barrier)	
Social Influences - those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviours	Social pressure Social norms Group conformity Social comparisons Group norms Social support Power Intergroup conflict Alienation Group identity Modelling	Discussions referring to influences, either positive or negative, patients/family/carers/other HCPs/support groups have in aiding patient adherence (enabler/barrier) Discussions around the influence clinician-patient relationships have on patient adherence behaviour (enabler/barrier) Discussions around trust/respect or lack of trust/respect patients have in doctors and/medical institution (enabler/barrier) Discussions around previous experiences with family members/friends influencing adherence behaviour (enabler)	<i>"it's doctor advise.....don't stop your putting your eyedrop....continue until your death.....because we obey the doctor's advice always" (P015)</i> <i>"I trust my doctor because without trust, nothing will work. I absolutely trust her" [when Doctor says I need to use the drops] (P020)</i>

Emotion – a complex reaction pattern, involving experiential, behavioural, and physiological elements, by which the individual attempts to deal with a personally significant matter or event	Fear Anxiety Affect Stress Depression Positive/negative effect Burn-out	Discussions about how patients feel (could be positive or negative): • having to instil eyedrops • losing sight as a result of non-adherence • when eyedrops are unavailable (Enabler/barrier) Discussions about patient feelings/emotions/reaction when having to admit they have not used their eyedrops (barrier)	<i>"He's worried about that"</i> [losing his sight if he does not use his eyedrops] (P023)
Behavioural Regulation - anything aimed at managing or changing objectively observed or measured actions	Self-monitoring Breaking habit Action planning	Discussions about strategies/techniques patient uses to help with adherence (enabler)	<i>"Yeah, yeah. Alarm is also there. Yeah, I use from my mobile"</i> (P014)

Coding framework for Ophthalmologists

Determinants (enablers/barriers) influencing ophthalmologists management of glaucoma medication adherence as categorised by TDF domains together with illustrative quotes

TDF Domain and definition	Component constructs	Examples may include	Illustrative quotes
Knowledge – an awareness of existence of something	Knowledge about condition/scientific rationale Knowledge of task environment Procedural knowledge	References from ophthalmologist demonstrating their knowledge/lack of knowledge of medication adherence and consequences of non-adherence (enabler/barrier) Understanding of patient factors e.g. socioeconomic background, ethnicity, general health status and factors which influence adherence behaviour (enabler) Discussions around knowing how to classify/define patient as adherent/non-adherent (enabler)	<i>“Personally, I don't have a clear-cut answer” [in terms of classifying patient as adherent/nonadherent] (E016)</i>
Skills – an ability or proficiency acquired through practice	Skills Skills development Competence	Discussions demonstrating ophthalmologist skills in educating patients on nature of glaucoma and/or treatment and/or	<i>“what we do is we ask them a leading question and find out as to why the. If they are non-compliant, we need to understand why the</i>

	Ability Practice Skill assessment Interpersonal skills	treatment application techniques (enabler/barrier) Discussions around skills needed to inquire about/assess adherence (e.g. listening, questioning, relationship building) (enabler)	<i>non-compliance is and if it is just problem with understanding we try and explain it” (E014)</i>
Social/Professional Role and Identity – a coherent set of behaviours and displayed personal qualities of an individual in a social or work setting	Professional role and identity Social identity Identity Professional boundaries Professional confidence Group identity Leadership Organisational commitment	Discussions around ophthalmologist role or professional responsibility to ensure patient adheres to treatment (enabler) Ophthalmologists referring to integrating their role with other HCPs/patients to encourage adherence (enabler) Consider coding references about support provided by ophthalmologists to Social Influences	<i>“I believe that only since I am the one who is treating them I tell them” [about the importance of adherence] (E019)</i>
Beliefs about capabilities - acceptance of the truth, reality, or validity about an ability, talent, or facility that a	Self-confidence Perceived competence Self-efficacy	Discussions about how confident an ophthalmologist feels identifying or managing non-adherence (enabler/barrier)	<i>“I think I'm reasonably confident enough to identify the patient” [who is non-adherent](E023)</i>

person can put to constructive use	Perceived behavioural control Beliefs Self-esteem Empowerment Professional Confidence	Ophthalmologist referring to how difficult it is to influence medication adherence behaviours (barrier)	
Optimism - The confidence that things will happen for the best or that desired goals will be attained	Optimism Pessimism Unrealistic optimism Identity	References to being optimistic/pessimistic about how to manage medication adherence	
Beliefs about consequences - acceptance of the truth, reality, or validity about outcomes of a behaviour in a given situation	Beliefs Outcome expectations Characteristics of outcome expectancies Anticipated regret Consequents	Ophthalmologist beliefs about the positive outcomes of patients adhering to treatment (e.g. saves sight, reduces unnecessary changes to medications, less follow ups, reduces burden on health system) (enabler)	<i>"what I feel that if I don't give that 2 minutes extra time today, I have to spend half an hour, one-hour extra time on some other day convincing to have surgery and having also explaining the complications of the surgery...so it's better to spend 2 minutes extra today rather than having to spend one hour and some other extra times later on" (E016)</i>

Reinforcement - increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus	Incentives Punishment Consequents Reinforcement Contingencies Sanctions	Discussions about ophthalmologists reiterating importance of adherence (enabler) Discussions about ophthalmologists repeating education surrounding nature of glaucoma, rationale for treatment and instillation technique to promote patient adherence (enabler/barrier) Consider coding discussions about support rather than reinforcement from to Social Influences	<i>"I keep counselling them as much as possible"</i> [in terms of being adherent] (E023)
Intentions – a conscious decision to perform a behaviour or a resolve to act in a certain way	Stability of intentions Stages of change model Transtheoretical model and stages of change	Discussions around ophthalmologist intentions to aid patients' adhering to treatment	<i>"you know, working towards the goal of getting full 100% compliance we have to try to help them [non adherent patients] so like, we recommend"</i> [solutions to help] (E023)
Goals - mental representations of outcomes or end states that an individual wants to achieve	Goals (distal / proximal) Goal priority Goal / target setting	Discussions about how important it is to ophthalmologists to ensure patients adhere to treatment (enabler/barrier)	<i>"It is very important [to try and ensure patient is adherent to treatment] and that is the sole thing in getting the glaucoma</i>

	Goals (autonomous / controlled) Action planning Implementation intention	Discussions about how important it is for ophthalmologists to address adherence issues (enabler)	[controlled]... <i>I feel that is very important</i> " (E018)
Memory, Attention and Decision Processes -the ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives	Memory Attention Attention control Decision making Cognitive overload/tiredness	Discussions about ophthalmologists tailoring treatment or management decisions to suit individual patient needs or clinical findings (enabler) Discussions about using clinical information to decide if patient adherent/non-adherent (enabler)	<i>"what I do in such a scenario is give, first the first possible alternative is giving them a medication which is of low cost...we give them an alternative which is within their living standards..and the second thing is to advise them surgery...over a shorter period of time is more cost effective than being on long term glaucoma treatment"</i> (E019)
Environmental Context and Resources - any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social	Environmental stressors Resources / material resources Organisational culture /climate	Discussions about challenges working in busy clinics, time constraints, issues with appointment systems, type of clinic or limited staff (barrier) Discussions around organisational structure to support ophthalmologist management of	<i>"that personal talk so I think that's the big challenge also because we have the time time problem. Yeah. So so many patients in a day, we really don't have time to we really have problem in finding time"</i> [to fully educate patient] (E016)

competence, and adaptive behaviour	Salient events / critical incidents Person x environment interaction Barriers and facilitators	non-adherence (e.g. provision of emergency service/teleconsultations) (enabler) Discussions around issuing prescriptions e.g. manufacturing issues, non-availability (barrier) Discussions around availability of physical resources e.g. leaflets, patient websites (enabler/barrier)	<i>"teleconsultations, we do have that as well. So each of us on a day like tomorrow, I have telecom calls like on the day that I do the clinic, I also have a teleconsultations where...my own patient, can get in touch. They can book an online teleconsultations....also be a video consult like I can see the person...and usually medication related and things like that"</i> (E014)
Social Influences - those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviours	Social pressure Social norms Group conformity Social comparisons Group norms Social support Power Intergroup conflict Alienation	Ophthalmologists referring to their influence, either positive or negative, on how they aid adherence (enabler/barrier) Discussions around the influence clinician-patient relationships have on patient adherence behaviour and admitting non-adherence (enabler/barrier) Discussions around overall team approach	<i>"if we see each other a couple of times then obviously the relationship builds up"</i> (E016) <i>"And the optometrist keep changing and the doctor is the same person who's seeing them...then we realise that what they tell the optometrist versus what they tell the doctor different.....[because] I guess the doctor knows that person"</i> (E014)

	Group identity Modelling		
Emotion – a complex reaction pattern, involving experiential, behavioural, and physiological elements, by which the individual attempts to deal with a personally significant matter or event	Fear Anxiety Affect Stress Depression Positive/negative effect Burn-out	Discussions about stress experienced when managing adherence issues e.g. due to time constraints (barrier)	<i>"it's heartbreaking to see a patient after years of care coming and showing that they can't put the drugs" [in correctly] (E021)</i>
Behavioural Regulation - anything aimed at managing or changing objectively observed or measured actions	Self-monitoring Breaking habit Action planning	Discussions around ophthalmologists developing strategies so they are consistently aware/up to date with glaucoma medication adherence and its management (e.g. the use of guidelines/recommendations) (enabler)	<i>"we have something called as a medical audit that we do. So we do the audits.....So when there are issues related to the, everything starting from history to evaluation to management to referral, everything is looked at and if there are any problems that is noted and will be presented and that will be, you know, discussed with the person" [doing monthly departmental audits helps to some</i>

			extent with keeping up to date with adherence issues] (E014)

S4: Supplementary Table

Themes identified in non-salient TDF domains and illustrative quotes from patients

Theme	Barrier/Enabler/ Mixed	Illustrative quote(s)
TDF domain: Social professional role and identity		
Patient autonomy (patient regards taking eyedrops as their responsibility regardless of setting)	Enabler	<i>"I am the sufferer. I am responsible for this I use the drops"</i> (P014)
TDF domain: Beliefs about capabilities		
Belief in own capability to use eyedrops long-term	Barrier	<i>"If someone else will put [the drops in], it'll be better rather than we administering on ourselves"</i> [not confident with own ability to instil drops] (P020)
TDF domain: Goals		
Not wanting to lose sight/go blind	Enabler	<i>"I have glaucoma, I have to see the world for a long time. That's why"</i> [I take the drops] (P017)
TDF domain: Emotion		
Fear of nonadherence and/or consequences of nonadherence	Enabler	<i>"Fortunately, it is only one medication now. That's why I'm a little relieved and a little comfortable"</i> (P021)
TDF domain: Intentions		
Intention will continue to instil eyedrops	Enabler	<i>"if nobody is there [to put drops in] obviously I will learn and I will do it for myself"</i> (P020)
TDF domain: Optimism		

Optimistic using technology can help with adherence	Barrier	<i>"Technology if [I] use it in a proper way it can be helpful particularly to remember [to instil eyedrops] in the future" (P016)</i>

Themes identified in non-salient TDF domains and illustrative quotes from Ophthalmologists

Theme	Barrier/Enabler/ Mixed	Illustrative quote(s)
TDF domain: Beliefs about consequences		
Belief in the positive outcomes of patient adherence	Enabler	<i>"when you try and explain things to them, do it the right way.... if you spend that extra 5 minutes it's going to help them for the rest of their life" (ECP014)</i>
TDF domain: Reinforcement		
Reinforcing adherence	Enabler	<i>"I keep telling them that even on the day of the examination you have to put the drops...I keep counselling them as much as possible" (ECP023)</i>
TDF domain: Intentions		
Ophthalmologist intentions to aid adherence	Enabler	<i>"you know, working towards the goal of getting full 100% compliance we have to try to help them [non adherent patients]So like, we recommend" [solutions to help] (ECP023)</i>
TDF domain: Goals		
Prioritising patient adherence	Enabler	<i>"It is very important [to ensure patient is adherent] and that is the sole thing in getting the glaucoma" [controlled] (ECP018)</i>
TDF domain: Behavioural Regulation		
Facilitating adherence management through action planning and habit formation	Enabler	<i>"they're supposed to tick mark, which means that they have explained it to the patient. So we even audit that have they really explained the medications to the to the patients?" (ECP014)</i>

TDF domain: Emotion		
Negative emotions associated with managing nonadherence	Barrier	<i>"it's heartbreaking to see a patient after years of care coming and showing that they can't put the drugs" [in correctly] (E021)</i>

Appendix D1

Detailed summary of the theoretically identified Behaviour Change Techniques (BCTs), outlining reasons for their inclusion or exclusion from the intervention

Identified Barrier Themes	Corresponding TDF domains	BCTs (from online tool ¹)	BCT definition ¹	BCT selected ✓ = YES ✗ = NO	Proposed operationalised strategy (intervention components)
Lack of understanding and/or lack of education regarding nature of glaucoma and/or its treatment	Knowledge	2.6 <i>Biofeedback</i>	Advise or agree on how to perform the behaviour, includes Skills training	✗	Providing feedback about the body's physiological or biochemical state (e.g. IOP measurement) using external monitoring would be challenging to incorporate into a patient-level intervention
		4.1 <i>Instruction on how to perform behaviour</i>	Advise or agree on how to perform the behaviour, includes Skills training	✓	Could provide educational materials (leaflets, training sessions, digital resources) informing patients about glaucoma, medication use and adherence strategies

		5.1 <i>Information about health consequences</i>	Provide information about health consequences of performing behaviour	✓	Could provide verbal, visual or written information positively framing benefits of using eyedrops
		5.3 <i>Information about social and environmental consequences</i>	Provide information about social and environmental consequences of performing behaviour	✗	The intervention aims to emphasise the health consequences of nonadherence, rather than focusing on social and environmental consequences
Issues administering eyedrops	Skills Environmental, Context & Resources, Memory, Attention & decision processes	3.2 <i>Social support (practical)</i>	Advise on, arrange or provide practical help for performance of behaviour	✓	Patients could be encouraged to seek support from family/friends/carers for help with eyedrop instillation either through physical assistance or practical reminders
		4.1 <i>Instruction on how to perform behaviour</i>	As above	✓	Offer guidance on instillation techniques through in-person training, written instructions or visual demonstrations (e.g., videos) to support correct medication use
		7.1. <i>Prompts/cues</i>	Introduce or define environmental or social stimulus with the purpose of prompting or cueing the behaviour. Prompt or cue would normally occur at	✓	Patients could use reminder strategies such as reminder notes/alarms/voice alerts/text messages, medication reminder app or association strategies such as placing eyedrops in a

			time or place of performance		visually prominent location to prompt medication use
		7.5. <i>Remove aversive stimulus</i>	Advise or arrange for the removal of an aversive stimulus to facilitate behaviour change	✗	Identifying and managing unpleasant/unwanted effects of instilling eyedrops is beyond the scope of a patient-level intervention and is more suited to an intervention at the ECP level
		8.1. <i>Behavioural practice/rehearsal</i>	Prompt practice or rehearsal of the performance of the behaviour one or more times in a context or at a time when the performance may not be necessary, in order to increase habit and skill	✗	It is impractical to recommend patients practice instilling their eyedrops when a dose is not needed to improve technique or develop habit formation. Instillation technique is addressed under 4.1 <i>Instruction on how to perform behaviour</i>
		8.7 <i>Graded tasks</i>	Set east to perform tasks, making them increasingly difficult, but achievable, until behaviour is performed	✗	Implementing an incremental approach to instilling eyedrops is not appropriate, this method does not suit the nature of the intervention
		11.3 <i>Conserving mental resources</i>	Advise on ways of minimising demands on mental resources to facilitate behaviour change	✓	Patients could use marked eyedrop bottles for easy medication identification or follow clear, simple, visually accessible step-by-step

					instructions, reducing the mental effort required to adhere to the eyedrop regimen
		12.1. <i>Restructuring the physical environment</i>	Change, or advise to change the physical environment in order to facilitate performance of the wanted behaviour or create barriers to the unwanted behaviour	✓	Patients could store eyedrops in an easily accessible location (e.g., near a mirror or bedside table) or have an extra supply at work to remove barriers to use, making it more convenient for patients to follow their regimen
		12.2. <i>Restructuring the social environment</i>	Change, or advise to change the social environment in order to facilitate performance of the wanted behaviour or create barriers to the unwanted behaviour	✗	Restructuring the social environment is beyond the scope of this intervention and project
		12.3. <i>Avoidance/reducing exposure to cues for the behaviour</i>	Advise on how to avoid exposure to specific social and contextual/physical cues for the behaviour, including changing daily or weekly routines	✗	Was not considered appropriate to include, as the current intervention aims to be conducive to patients' lifestyles rather than restricting or changing their way of life
		12.5. <i>Adding objects to the environment</i>	Add objects to the environment in order to facilitate performance of the behaviour	✓	Patients could use an eyedrop dispenser as an external tool to facilitate eyedrop use

Difficulties obtaining eyedrops	Skills Environmental, Context & Resources	3.2 <i>Social support (practical)</i>	As above	✓	Patients could seek support from family/friends/carers for help with ordering and/or collecting repeat prescriptions
		4.1 <i>Instruction on how to perform the behaviour</i>	As above	✓	Provide patients with clear, step-by-step written or video instructions on how to order their eyedrops from the pharmacy or arrange for repeat prescriptions
		7.1 <i>Prompts/cues</i>	As above	✓	Patients could use reminder strategies such as reminder notes/alarms/voice alerts/text messages as prompts to reorder their eyedrops
		7.5. <i>Remove aversive stimulus</i>	As above	✗	As above
		8.1. <i>Behavioural practice/rehearsal</i>	As above	✗	Recommending patients practise ordering supplies of eyedrops when they are not needed is impractical
		8.7. <i>Graded tasks</i>	As above	✗	Was not considered appropriate to include since breaking down the process of ordering

					eyedrops is not feasible in practice
		12.1. <i>Restructuring the physical environment</i>	As above	✓	Patients could use to use mail order services for delivery of eyedrops
		12.2. <i>Restructuring the social environment</i>	As above	✗	As above
		12.3. <i>Avoidance/reducing exposure to cues for the behaviour</i>	As above	✗	As above
		12.5. <i>Adding objects to the environment</i>	As above	✓	Patients could use NHS app/online GP system for ordering repeat prescriptions

¹ BCT coded using The Theory and Techniques online tool (Johnston et al., 2021)

Appendix D2

Summary of real-world interventions designed to support glaucoma medication adherence, including their delivery methods and intervention content. The analysis is categorised into different intervention strategies: educational approaches, reminder systems, medication simplification strategies and alternative engagement methods.

Table 1a Identified real-world educational interventions to enhance medication adherence, their delivery methods and content.

Boxes highlighted in dark grey denote BCT included in intervention strategy

Intervention	Educational strategies								
	Glaucoma A guide Leaflet Example here	Understanding Glaucoma Leaflet Example here	NHS conditions – Glaucoma online information Example here	NHS England Decision support tool: making a decision about open-angle glaucoma Example here	Ramadan information Poster Example here	Easy read putting in your eyedrops Leaflet Example here	Eyedrops information Online See here	How to administer eyedrops YouTube See here	Moorfields #KnowYourDrops YouTube See here
Endorsed/promoted by	Glaucoma UK	RNIB	NHS	NHS	Glaucoma UK	Glaucoma UK	Glaucoma UK	Glaucoma UK	Moorfields NHS Trust
Mode of delivery ¹	Informational Visual & Textual	Informational Visual & Textual Printed publication	Informational Textual Electronic Website	Informational Textual Electronic	Informational Visual & Textual Public notice	Informational Visual & Textual Printed publication	Informational Visual & Textual Electronic	Informational Visual & Textual Electronic	Informational Visual & Textual Electronic

	Printed publication Uni-directional	Uni-directional	Uni-directional	Website Uni-directional	Uni-directional	Uni-directional	Website Uni-directional	Website Uni-directional	Website Uni-directional
Intervention Function²	<i>Education</i> <i>Training</i> <i>Environmental restructuring</i> <i>Modelling</i>	<i>Education</i> <i>Environmental restructuring</i>	<i>Education</i> <i>Training</i>	<i>Education</i>	<i>Education</i> <i>Modelling</i>	<i>Training</i> <i>Modelling</i> <i>Education</i> <i>Environmental restructuring</i>	<i>Training</i> <i>Modelling</i> <i>Education</i> <i>Environmental restructuring</i>	<i>Training</i> <i>Modelling</i> <i>Education</i>	<i>Training</i> <i>Modelling</i> <i>Education</i>
Behaviour Change Technique (BCT)³									
2. Feedback and monitoring									
2.3 Self-monitoring of behaviour									
3. Social support									
3.1 Social support (unspecified)									
3.2 Social support (practical)									
4. Shaping knowledge									
4.1 Instruction on how to perform the behaviour									

5. Natural consequences									
5.1 Information about health consequences									
6. Comparison of behaviour									
6.1 Demonstration of the behaviour									
6.2 Social comparison									
6.3 Information about others approval									
7. Associations									
7.1 Prompts/cues									
9. Comparison of outcomes									
9.1 Credible source									
12. Antecedents									
12.1 Restructuring the physical environment									
12.5 Adding objects to the environment									
¹ Mode of delivery classified using a recognised ontology for behaviour change interventions (Marques et al., 2021)									

² Intervention Function identified using Behaviour Change Wheel matrix (Michie et al., 2014)

³ BCT coded using The Theory and Techniques online tool (Johnston et al., 2021)

Table 1b Identified real-world reminder strategies to enhance medication adherence, their delivery methods and content.
Boxes highlighted in dark grey denote BCT included in intervention strategy.

Intervention	Reminder systems								
	Eyedrop calendar Example here	MyGlaucoma mobile phone app Information here	Audio medication reminder pocket clock/ Setting alarm Example here	Healthera mobile phone app See here	My personal Glaucoma monitoring record Example here	Association strategies	Patient access website or mobile phone app for accessing health records and ordering repeat prescriptions See here	NHS mobile phone app for accessing health records and ordering repeat prescriptions See here	Pharmacy2U mobile phone app for ordering repeat prescriptions See here
Endorsed/promoted by	Glaucoma UK	Glaucoma UK	RNIB Glaucoma UK NHS	NHS	Glaucoma UK	Glaucoma UK RNIB	NHS	NHS	NHS
Mode of delivery ¹	Informational Visual Printed material/Electronic Pull	Informational Electronic Mobile application Visual & Textual Pull	Informational Electronic Audio Uni-directional	Informational Electronic Mobile application Visual & Textual Pull	Informational Visual & Textual Printed publication Pull	Environmental change	Electronic Mobile application/website Textual Pull Interactional	Electronic Mobile application Textual Pull	Electronic Mobile application Visual Informational Textual Pull

		Interactional		Interactional					Interactional
Intervention Function²	<i>Environmental restructuring</i>	<i>Modelling</i> <i>Education</i> <i>Environmental restructuring</i>	<i>Environmental restructuring</i>	<i>Environmental restructuring</i>	<i>Education</i> <i>Modelling</i> <i>Environmental restructuring</i>	<i>Environmental restructuring</i>	<i>Environmental restructuring</i>	<i>Environmental restructuring</i>	<i>Environmental restructuring</i>
Behaviour Change Technique (BCT)³									
1. Goals and planning									
1.2 problem solving									
1.4 Action planning									
2. Feedback and monitoring									
2.2 Feedback on behaviour									
2.3 Self-monitoring of behaviour									
3. Social support									
3.1 Social support (unspecified)									

3.2 Social support (practical)									
4. Shaping knowledge									
4.1 Instruction on how to perform the behaviour									
5. Natural consequences									
5.1 Information about health consequences									
5.6 Information about emotional consequences									
6. Comparison of behaviour									
6.1 Demonstration of the behaviour									
6.2 Social comparison									
7. Associations									
7.1 Prompts/cues									
8. Repetition and substitution									

8.3 Habit formation									
9. Comparison of outcomes									
9.1 Credible source									
10. Reward and threat									
10.7 Self-reward									
11. Regulation									
11.3 Conserving mental resources									
12. Antecedents									
12.1 Restructuring the physical environment									
12.5 Adding objects to the environment									
¹ Mode of delivery classified using a recognised ontology for behaviour change interventions (Marques et al., 2021) ² Intervention Function identified using Behaviour Change Wheel matrix (Michie et al., 2014) ³ BCT coded using The Theory and Techniques online tool (Johnston et al., 2021)									

Table 1c Identified real-world interventions to enhance medication by simplifying medication-taking or engagement strategies, their delivery methods and content.
Boxes highlighted in dark grey denote BCT included in intervention strategy.

Intervention	Medication Simplification Strategies		Alternative Engagement Methods
	Eyedrops and dispensing aids A guide	Eyedrop dispensers	Support groups
	Leaflet and aid	Example here	Example here
	Example here		
Endorsed/promoted by	Glaucoma UK	RNIB Glaucoma UK	Glaucoma UK
Mode of delivery ¹	Informational Visual & Textual Printed publication Uni-directional Environmental change	Environmental change Uni-directional	Informational Audio & Visual Human interactional Face to face/ at a-distance Electronic Video call Group-based
Intervention Function ²	<i>Education</i> <i>Training</i> <i>Environmental restructuring</i>	<i>Environmental restructuring</i>	<i>Education</i> <i>Modelling</i> <i>Training</i>
Behaviour Change Technique (BCT) ³			
2. Feedback and monitoring			
2.3 Self-monitoring of behaviour			

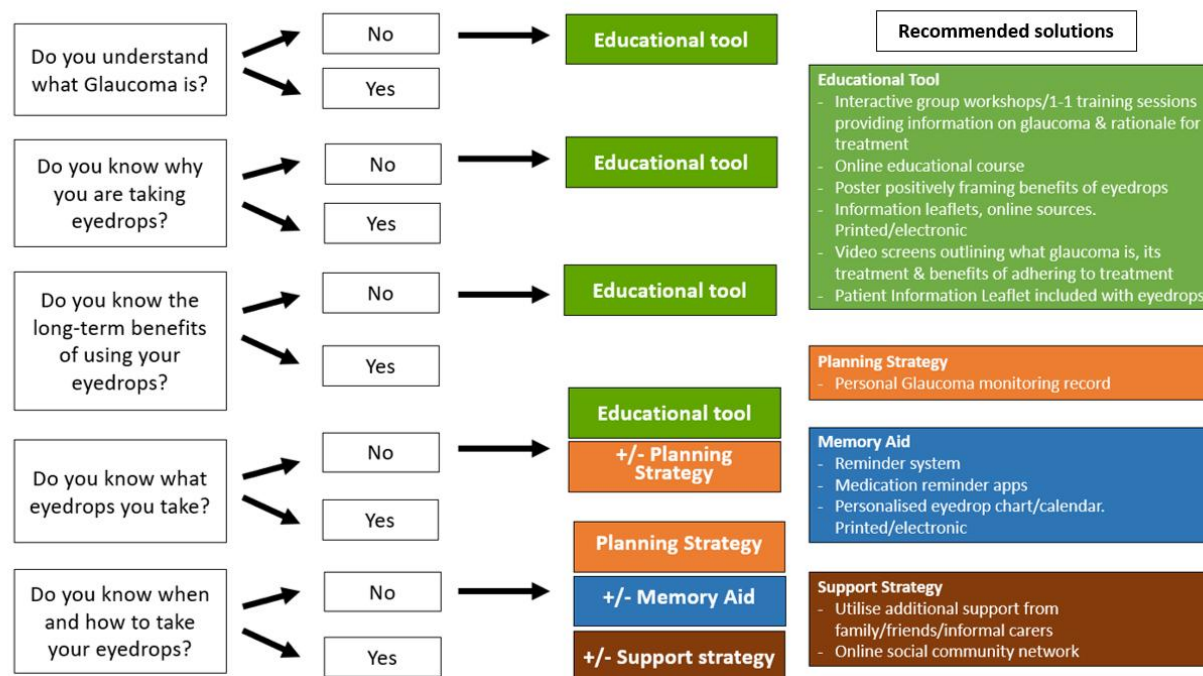
3. Social support			
3.1 Social support (unspecified)			
4. Shaping knowledge			
4.1 Instruction on how to perform the behaviour			
5. Natural consequences			
5.1 Information about health consequences			
6. Comparison of behaviour			
6.1 Demonstration of the behaviour			
6.2 Social comparison			
7. Associations			
7.1 Prompts/cues			
8. Repetition and substitution			
8.3 Habit formation			
9. Comparison of outcomes			
9.1 Credible source			
12. Antecedents			
12.1 Restructuring the physical environment			

12.5 Adding objects to the environment			
¹ Mode of delivery classified using a recognised ontology for behaviour change interventions (Marques et al., 2021) ² Intervention Function identified using Behaviour Change Wheel matrix (Michie et al., 2014) ³ BCT coded using The Theory and Techniques online tool (Johnston et al., 2021)			

Appendix E1

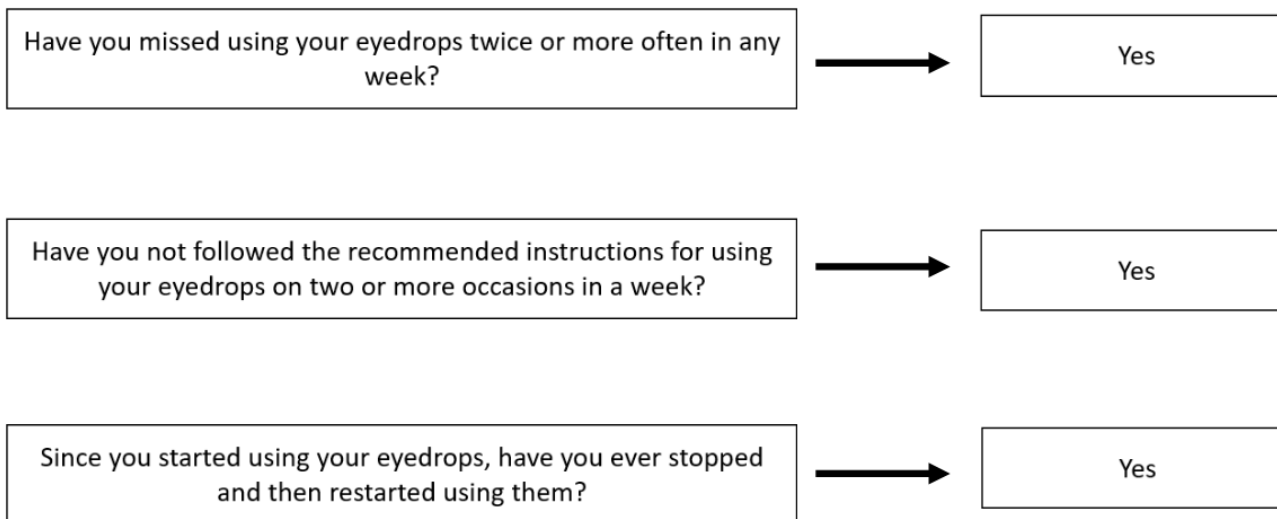
An overview of the Adherence Resources Toolkit (ART), detailing the questions linked to each barrier theme and associated recommended solutions

Theme 1 – lack of understanding regarding nature of glaucoma and/or its treatment



Theme 2 – issues administering eyedrops

It is quite normal for people to miss taking their eyedrops



If you answered Yes to any of the previous 3 questions, did you miss/alter how you used your eyedrops because:

- you forgot?
- you were busy? e.g.. doing other activities/chores/tasks
- you were not at home e.g. on holiday, visiting family?



+/- Memory aid

+/- Association strategy

- you experienced side effects or are worried about developing side effects?
- you noticed no benefit/improvement from using the eyedrops?
- it is ok to miss using your eyedrops from time to time?



Educational tool

+/- Support strategy

Support strategy

- no one was there to remind you?



+/- Memory aid

+/- Association strategy

Support strategy

+/- Memory aid

+/- Association strategy

+/- Planning strategy

- the eyedrop timetable was too difficult to follow?



Consider referral back to practitioner to simplify treatment

Support strategy

+/- Training strategy

Do you have difficulties putting your eyedrops in? E.g. squeezing bottle, making sure drop goes in eye



Support strategy

+/- Association strategy

Can you identify your eyedrop bottle or read print on the bottle?



Solutions

Educational Tool

- Interactive group workshops/1-1 training sessions providing information on glaucoma & rationale for treatment
- Online educational course
- Poster positively framing benefits of eyedrops
- Information leaflets, online sources. Printed/electronic
- Video screens outlining what glaucoma is, its treatment & benefits of adhering to treatment
- Patient Information Leaflet included with eyedrops

Support Strategy

- Utilise additional support from family/friends/informal carers
- Online social community network

Training Strategy

- Training sessions on instillation technique, backed up with written material.
- Written resources +/- online videos demonstrating how to use eyedrops correctly & how to overcome common mistakes

Memory Aid

- Reminder system
- Medication reminder apps
- Personalised eyedrop chart/calendar. Printed/electronic

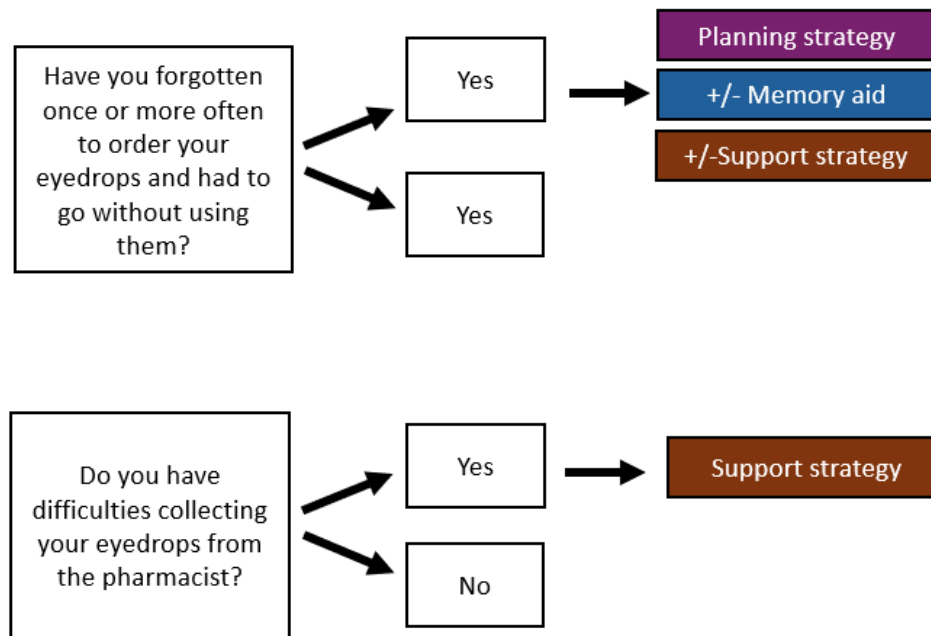
Planning Strategy

- Personal Glaucoma monitoring record

Association strategy

- Associate instilling eyedrops with a daily habit
- Strategic placement of eyedrop bottle
- If using multiple eyedrops place bottles in order of use/ size order/colour code

Theme 3 - difficulties obtaining eyedrops



Solutions

Support Strategy

- Utilise additional support from family/friends/informal carers
- Consider using mail order services for home delivery of eyedrops

Memory Aid

- Reminder system
- Medication reminder apps
- Personalised eyedrop chart/calendar. Printed/electronic

Planning Strategy

- Use electronic system for ordering repeat prescriptions. Practise ordering process with family member/Health Care Practitioner

Appendix E2

Examples of the recruitment advertisements for the knowledge exchange event

Advertisement on Glaucoma UK website

Glaucoma UK Celebrating **50 years** 1974 - 2024

[Search](#) [Donate](#) [About glaucoma](#) [Care & support](#) [Research](#)

help improve diagnosis, care and treatment opportunities. [Research](#) we've funded and experiences of others.

Have you ever thought about taking part in research? Research volunteers in research studies can be found below.

Experiences of glaucoma and visual field testing

If you're over 40 years of age with a diagnosis of primary open angle glaucoma (POAG)? Can you share your experiences of the visual field test? The test may be familiar to you by one of its various names, including the 'fields test', 'Humphrey test', 'visual analysis test', 'perimetry test', or 'VF test'. The main purpose of this survey is to hear your thoughts about the visual field test, and to develop your views on how it might be improved to be more patient-friendly.

City, University of London

Do you ever struggle to put your drops in, or forget? Do you need help from a partner with your eye drops? Researchers are looking at developing new ways to help people with their eye drops. If you ever find your eye drops a problem, your views and experiences will be invaluable! There will be a focus group on Wednesday 12 June where you can share your thoughts.

For more information, read [this document](#). If you would like to take part, contact Deborah Bott on deborah.bott.1@city.ac.uk.

Patient advert



Department of Optometry and Visual Sciences,
School of Health and Psychological Sciences,
City, University of London

Do you use eyedrops for glaucoma? Do you struggle to use them correctly? Have you ever forgotten to put them in? Do you have problems getting supplies from your chemist?
Do you care for or live with someone who uses glaucoma eyedrops?

If yes and you are aged 18+ would you help us with some research?

Would you be willing to take part in an online group discussion reviewing potential strategies to help people use their eyedrops correctly.

The session will be held via Zoom, last approximately 120 minutes and is likely to be held in the last week of May.

To participate or for more information please contact me, Deborah Bott via Email: Deborah.Bott.1@city.ac.uk

In appreciation of your time, you will have the opportunity to be entered into a prize draw to win a £50 Love to Shop voucher.

This study, which is funded by a scholarship from The College of Optometrists, has been reviewed by and received ethics clearance through the Department of Optometry and Visual Sciences Research Ethics Committee City, University of London (ETH2122-1657)

If you would like to complain about any aspect of the study, please contact Annah Whyton at Research & Enterprise Office, City, University of London, Northampton Square, London, EC1V 0HB or via Email: senaterec@city.ac.uk

City, University of London is the data controller for the personal data collected for this research project. If you have any data protection concerns about this research project, please contact City's Information Compliance Team at dataprotection@city.ac.uk

HCP or key stake holder advert



**Department of Optometry and Visual Sciences,
School of Health and Psychological Sciences,
City, University of London**

**PARTICIPANTS NEEDED FOR RESEARCH
INVESTIGATING POTENTIAL STRATEGIES TO
IMPROVE EYEDROP ADHERENCE IN GLAUCOMA**

We are looking for **UK based healthcare professionals** (ophthalmologists, optometrists, orthoptists, nurse practitioners or pharmacists) who are involved in glaucoma management or **key stake holders in glaucoma** to take part in a group meeting discussing whether potential strategies are suitable to address medication nonadherence issues in glaucoma.

As a participant in this study, you would be asked to take part in an online focus group meeting, held via Zoom.

Your participation would involve only 1 session, which is expected to take approximately 120 minutes.

In appreciation for your time, you will be offered the opportunity to be entered into a prize draw to win a £50 Love to Shop voucher.

For more information about this study, or to volunteer for this study, please contact: Deborah Bott Deborah.Bott.1@city.ac.uk

This study, which is funded by a scholarship from The College of Optometrists, has been reviewed by and received ethics clearance through the Department of Optometry and Visual Sciences Research Ethics Committee City, University of London (ETH2122-1657)

If you would like to complain about any aspect of the study, please contact Annah Whyton at Research & Enterprise Office, City, University of London, Northampton Square, London, EC1V 0HB Email: senaterec@city.ac.uk

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Appendix E3

Participant Information Sheet for the knowledge exchange event



**Department of Optometry and Visual Sciences, School of
Health and Psychological Sciences,
City, University of London**

Can technology help with glaucoma medication adherence?

Name of principal researcher: Deborah Bott **Reference number:** ETH2122-1657, Version 2 01/02/2024

Participant Information Sheet

We would like to invite you to take part in a research study. Before you decide whether you would like to take part it is important that you understand why the research is being done and what it would involve for you. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of this study?

Glaucoma, an eye disease, can cause blindness if left untreated. Globally, it is the second most common cause of sight loss and the leading cause of preventable blindness within the UK. Treatment with lifelong instillation of eyedrops can prevent visual loss but we know adherence to treatment is poor.

Technology is becoming more widespread especially within healthcare, more and more people own a smartphone. Smartphone technology is successfully being used in other diseases to help people take their medications. Could a similar form of technology be used in glaucoma to help people take their eyedrops correctly?

By reviewing existing literature, interviewing patients and eye care practitioners we have identified the key factors that influence glaucoma medication adherence. Using

this information we have developed a list of potential strategies, incorporating technology-based elements, which will form the basis of an overall intervention to improve glaucoma medication adherence. We aim to use a co-development process, involving patients, people involved in glaucoma management and key stake holders to help inform the content of this intervention.

This study is expected to take place between March to October 2024 and forms part of my PhD studies.

Why have I been invited?

We are inviting you to take part in this study because you currently use or have used eyedrops for glaucoma, live with someone or care for someone who uses eyedrops for glaucoma, are a healthcare professional involved in glaucoma care or are a key stake holder in glaucoma. Additionally you are aged over 18.

Do I have to take part?

Participation in the study is voluntary. It is up to you to decide whether or not to take part. If you do decide to take part you will be asked to sign a consent form. If you do agree to take part and then you change your mind, you can withdraw at any stage without being penalised or disadvantaged in any way. If you decide to withdraw from this study, with your permission, we would like to keep and use all your previously collected data. This information will remain anonymised and will not be used for any other purpose. To safeguard your rights we will use the minimum personally identifiable information possible.

What will happen if I take part?

After having read this Participant Information Sheet if you decide to take part in the study you will be invited to an online focus group meeting to discuss and hear your opinions on the potential strategies we have proposed for addressing nonadherence. The discussion will be via Teams and should last no more than 2 hours. The discussion will be recorded. All information which is collected about you during the course of this study will be kept strictly confidential and your comments will be anonymised. Before you participate in the discussion you will be given an opportunity to ask any additional questions and be asked to provide verbal consent to participate, which will be recorded.

After the focus group meeting you will be asked if you would like to be entered into a prize draw to win a £50 Love to Shop gift voucher. If you would like to do so, you will need to provide your name and contact details. These details will be securely stored on a database separate from any information from the interviews. It will only be accessible to the research team and will be used solely to contact you for the purposes you have indicated. Your name and contact details will not appear in information from the interview.

What are the benefits and disadvantages of taking part in this study?

There is limited research investigating the effectiveness of using a technology-based intervention to aid glaucoma medication adherence. By taking part in this study you will be contributing to our understanding of this and helping to inform the development of a potential technological development to aid adherence. We do not anticipate there will be any risks associated with participating in this study apart from giving up your time to take part.

What will happen to the results from the focus group meeting?

The anonymised information collected from the focus group meeting will be analysed to understand which potential strategies are feasible to address individual nonadherence barriers and will guide development of an overall intervention which seeks to improve glaucoma medication adherence.

The results of this project may also be reported in a scientific journal and at a relevant health conference. The information we report will be completely anonymous and would not identify you in any way.

Who has reviewed the study?

This study has been approved by City, University of London, Department of Optometry and Visual Sciences Research Ethics Committee.

Data privacy statement

City, University of London is the sponsor and the data controller of this study based in the United Kingdom. This means that we are responsible for looking after your information and using it properly. The legal basis under which your data will be processed is City's public task.

Your right to access, change or move your information are limited, as we need to manage your information in a specific way in order for the research to be reliable and accurate. To safeguard your rights, we will use the minimum personal-identifiable information possible (for further information please see <https://ico.org.uk/for-organisations/guide-to-data-protection/guide-to-the-general-data-protection-regulation-gdpr/lawful-basis-for-processing/public-task/>). City will use your name and contact details to contact you about the research study as necessary.

You can find out more about how City handles data by visiting <https://www.city.ac.uk/about/governance/legal>. If you are concerned about how we have processed your personal data, you can contact the Information Commissioner's Office (IOC) <https://ico.org.uk/>.

Who is funding this study?

This study is part of my PhD project which is sponsored by a scholarship from The College of Optometrists.

What if there is a problem?

If you have any problems, concerns or questions about this study, you should ask to speak to a member of the research team. If you remain unhappy and wish to complain formally, you can do this through City's complaints procedure. To complain about the study please contact:

Annah Whyton

Research & Enterprise Office

City, University of London

Northampton Square

London, EC1V 0HB

Email: senaterec@city.ac.uk

and inform them that the name of the project is: **Can technology help with eyedrop compliance in glaucoma?**

Insurance

City, University of London holds insurance policies which apply to this study, subject to the terms and conditions of the policy. If you feel you have been harmed or injured by taking part in this study you may be eligible to claim compensation. This does not affect your legal rights to seek compensation. If you are harmed due to someone's negligence, then you may have grounds for legal action.

Thank you for taking the time to read this information sheet. If you would like any further information, please contact Deborah Bott, [REDACTED]

Appendix E4

Topic guide issued to the facilitators for the knowledge exchange event

Facilitators to remind participants everyone to be given an opportunity to voice their opinions, everyone's opinions are valid and there are no right and wrong answers we are keen to learn from their experiences. Facilitator to encourage selecting one person to write notes so they can share the groups ideas when reunite with rest of participants.

Is adherence tool acceptable for identifying reasons for non-adherence?

They should discuss:

- Do they like/dislike adherence toolkit
- do they understand reason for developing toolkit and how it would work
- do they think it would be effective i.e. do the questions actually establish reasons for non-adherence
- is it easy to use and intuitive, either to administer or self-use
- is it up-scalable, could it be incorporated easily into eye care pathway
- is tool easy to use for everyone e.g. if visually impaired or digital exclusion
- Preference for Mode of delivery – in person and by who or virtually? If electronically delivered voice activated or written text?
- Any improvements?

Prompts from facilitator - think what would work in practice and why. Explain participants should consider which solutions could actually improve adherence and why, is solution easy for patients to use/understand, would it be feasible to implement strategy into the care pathway taking into consideration time constraints, financial issues and limited manpower resources. Think how you would like to be introduced to strategy or how best would you like to introduce strategy to a patient.

Appendix E5

Ethics approval for the knowledge exchange event



Dear Deborah

Reference: ETH2324-1298

Project title: Investigating the feasibility and acceptability of using a chatbot to improve adherence to glaucoma medication

Start date: 23 Aug 2022

End date: 31 Aug 2023

Amendments granted subject to secretary to senate research detail changes listed below.

I am writing to you to confirm that the research proposal detailed above has been granted formal approval from the Optometry Proportionate Review Committee. The Committee's response is based on the protocol described in the application form and supporting documentation. Approval has been given for the submitted application only and the research must be conducted accordingly. You are now free to start recruitment.

The approval was given with the following conditions:

- **Please amend the research ethics secretary details from J Montgomery, to the below details; on the PIS, Flyers, All social media adverts, and any other material where it is mentioned. Please remove the telephone contact for the Secretary to Senate research on all of these documents.**

New contact details:

Annah Whyton

Research & Enterprise Office

City, University of London

Northampton Square

London, EC1V 0HB

Email:

senaterec@city.ac.uk

Please note the following:

Project amendments/extension

You will need to submit an amendment or request an extension if you wish to make any of the following changes to your research project:

- Change or add a new category of participants;
- Change or add researchers involved in the project, including PI and supervisor;
- Change to the sponsorship/collaboration;
- Add a new or change a territory for international projects;
- Change the procedures undertaken by participants, including any change relating to the safety or physical or mental integrity of research participants, or to the risk/benefit assessment for the project or collecting additional types of data from research participants;
- Change the design and/or methodology of the study, including changing or adding a new research method and/or research instrument;
- Change project documentation such as protocol, participant information sheets, consent forms, questionnaires, letters of invitation, information sheets for relatives or carers;
- Change to the insurance or indemnity arrangements for the project;
- Change the end date of the project.

Adverse events or untoward incidents

You will need to submit an Adverse Events or Untoward Incidents report in the event of any of the following:

- a) Adverse events
- b) Breaches of confidentiality
- c) Safeguarding issues relating to children or vulnerable adults
- d) Incidents that affect the personal safety of a participant or researcher

Issues a) and b) should be reported as soon as possible and no later than five days after the event. Issues c) and d) should be reported immediately. Where appropriate, the researcher should also report adverse events to other relevant institutions, such as the police or social services.

Should you have any further queries relating to this matter, please do not hesitate to contact me. On behalf of the Optometry Proportionate Review Committee, I do hope that the project meets with success.

Kind regards

Michael Powner

Optometry Proportionate Review Committee

City, University of London