



Clinical Practice Guide for the Diagnosis and Management of Open Angle Glaucoma

2020

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1. Introduction

Glaucoma is one of the leading causes of irreversible blindness worldwide¹⁻³. In 2005, the Australian Institute of Health and Welfare reported that 3% of all vision impairment and 16% of blindness caused in Australia in those aged 55 years or over was due to glaucoma⁴. In Australia alone, the number of cases of glaucoma is expected to rise from 208,000 in 2008 to 379,000 in 2025 due to ageing of the population⁵. Over the same period of time, the health system costs are estimated to increase from \$AU355 million to \$AU784 million⁵. Total costs, including indirect costs (falls, aged care, depression, loss of productivity etc.) are estimated to reach up to \$AU4.3 billion in Australia by 2025⁵.

Half of all glaucoma cases are undiagnosed⁶⁻¹².

Optometrists, in their capacity as primary eye health care providers, play a pivotal role in the provision of eye care services to Australians who have been diagnosed with, or are at risk of developing glaucoma. It is important that optometrists are competent in preventing vision loss through early detection and the provision of evidence-based assessment, including diagnosis and referral when indicated, and where the practitioner is therapeutically endorsed; management of the condition in accordance with the Optometry Board of Australia's guidelines.

This clinical practice guide aims to provide an update regarding all aspects of glaucoma care: from the evolving definition of glaucoma, to the diagnostic process, to management and considerations beyond medical treatment. Dependent on level of scope, therapeutic qualification and special interests of practice; collaborative care models of treating glaucoma will vary from practitioner to practitioner.

2. Definition

Currently, a widely accepted, comprehensive definition of glaucoma¹³:

Glaucoma describes a group of ocular disorders of multifactorial aetiology united by a clinically characteristic optic neuropathy with potentially progressive, clinically visible changes at the optic nerve head (ONH), comprising focal or generalised thinning of the neuroretinal rim with excavation and enlargement of the optic cup, representing neurodegeneration of retinal ganglion cell axons and deformation of the lamina cribrosa. Corresponding diffuse and localized nerve-fibre-bundle pattern visual field loss may not be detectable in early stages; while visual acuity is initially spared, progression can lead to complete loss of vision; the constellation of clinical features is diagnostic.

The current definition of glaucoma also recognises different aetiological factors including:

- Mechanical: Intraocular pressure (IOP) related
- Ischaemic: Vascular and oxidative stress
- Neurodegenerative: Degenerative, similar to processes occurring in the brain
- Autoimmune: Own body's cells damaging themselves

Clinical pearl

Due to variability in aetiology and stage of presentation, there is not one single diagnostic test or diagnostic test value for glaucoma diagnosis; rather, a battery of tests must be performed and the sum of the clinical findings will sway a decision between non-glaucoma, glaucoma suspect or manifest glaucoma in an individual.

3. Open Angle Glaucoma

Primary open angle glaucoma (POAG) is the most common form of glaucoma¹ and diagnosis is always made in the presence of an open anterior chamber drainage angle. It is usually associated with elevated IOP, sometimes referred to as high-tension glaucoma. However, glaucoma may also occur with IOPs within the normative range; classified as normal-tension glaucoma⁶. In some ethnicities, such as Asian populations, normal-tension glaucoma is the most prevalent type of open angle glaucoma¹⁴, which has also been noted to be a common form of glaucoma within the Australian population⁹.

The importance of distinguishing between normal-tension glaucoma and high-tension glaucoma stems from large clinical trials that compare the differences in progression rates and natural history¹⁵⁻¹⁷. Treatment paradigms are similar, with IOP reduction being key regardless of baseline IOP.

Open angle glaucoma is also further distinguished between primary and secondary causes. Secondary open angle glaucoma presents with direct causes, that are typically related to IOP. POAG is defined as such when there is no secondary cause of glaucoma present. Note that an initial diagnosis of POAG does not preclude a future change in diagnosis to secondary open angle glaucoma as more clinical information comes to light.

3.1 Secondary Glaucoma

Secondary glaucoma refers to a case of glaucoma in which a source is identifiable. Typically, these sources are referred to as “risk factors for secondary glaucoma,” as these may present in the absence of glaucomatous changes. In such cases, it is not uncommon to frequently review these patients to determine if and when progression has occurred.

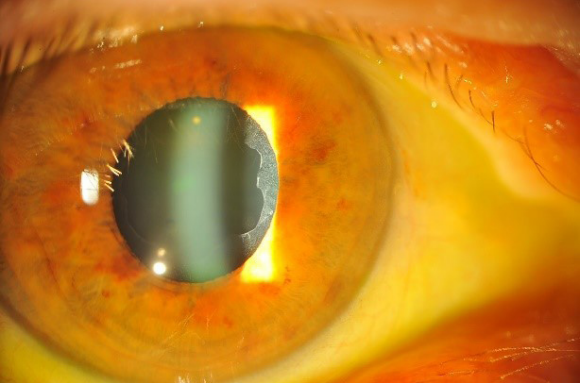

In most of these cases, the course of glaucoma tends to be more aggressive in comparison to primary glaucoma¹⁷⁻¹⁹. Some of the most common causes of secondary open angle glaucoma are pseudoexfoliation and pigment dispersion syndrome (Table 1). Some of the less common causes are angle recession/trauma, uveitis, neovascularisation (Rubeosis Iridis) and lens-related (phacolytic)^{20,21}.

Table 1: Pseudoexfoliation and Pigment Dispersion Syndrome

	Pseudoexfoliation (PXF)	Pigment Dispersion Syndrome (PDS)
Epidemiology	<ul style="list-style-type: none"> PXF represents the single most recognised pathogenic factor leading to a diagnosis of open angle glaucoma²². The Blue Mountains eye study showed PXF was a risk factor for glaucoma independent of the IOP⁹. Ethnicity may play a role in the epidemiology of PXF: Scandinavians and northern Europeans appear to have a greater prevalence of PXF²³. PXF is more prevalent in older age groups²³. Approximately one-third of patients with PXF will progress to pseudoexfoliation glaucoma (PXG)²⁴. 	<ul style="list-style-type: none"> In the United States general population, the estimated incidence is 4.8 per 100,000 for PDS and 1.4 per 100,000 for pigmentary glaucoma (PDG)²⁵. PDS and subsequent glaucoma are primarily encountered in Caucasian populations and are considered to be relatively rare in other races. They are also more prevalent in myopic individuals, who are likely to have deeper anterior chamber depth increasing contact between the iris and the zonules²⁶. Currently, PDG is the most common cause of non-traumatic glaucoma in younger patients, particularly prevalent in Caucasian myopic males between the 3rd and 5th decade of life, making an early diagnosis a crucial part of management²⁷. Conversion rates from PDS to PDG have been reported in the literature, ranging from 18-50%²⁸⁻³⁰. In a more recent study, the risk of developing PDG was 10% at 5 years and 15% at 15 years²⁵, with IOP greater than 21mmHg at initial visit being the only factor associated with increased conversion^{25,31}.
Pathogenesis	<p>PXF is an age-related disease with both ocular and potentially systemic manifestations - abnormal extracellular material is produced and accumulates in a variety of tissues and organs. In the eye, deposition can occur in the trabecular meshwork³², causing impaired outflow of aqueous humour and therefore increased IOP. It has also been associated with angle closure disease, as the deposited material has been suggested to also have sticky qualities that may result in iridotrabecular contact³³.</p>	<p>PDS is due to the mechanical friction of anterior packets of lens zonules and peripheral iris pigment epithelium³⁴ with liberation of the pigment from the posterior iris pigment epithelium and deposition onto various ocular structures, mainly in the anterior chamber, corneal endothelium and subsequently trabecular meshwork.</p> <p>Pigmentation in the trabecular meshwork increases aqueous outflow resistance leading to increased IOP³⁵.</p>

Table continued over page

Table 1: Pseudoexfoliation and Pigment Dispersion Syndrome (continued)

	Pseudoexfoliation (PXF)	Pigment Dispersion Syndrome (PDS)
Diagnosis	<p>Initial signs of PXF may be subtle and pupillary dilation is often required to visualise these changes.</p> <p>The classic signs of PXF are:</p> <ul style="list-style-type: none"> ▪ presence of exfoliative material at the pupil margin³⁶ ▪ iris transillumination defects at or around the pupil margin and markedly reduced pupillary ruff in the involved eye²² ▪ exfoliative rings and frosting on the anterior lens capsule ▪ pigment in the trabecular meshwork on gonioscopy <p>PXF is commonly diagnosed in one eye only in its initial stages³⁷. Long term follow-up reveals 74-82% convert from unilateral to bilateral presentation over approximately 5 years^{38,39}. Pupillary dilation and pupil dynamics are typically reduced in PXF^{40,41}.</p>	<p>The typical triad of clinical signs of PDS are:</p> <ul style="list-style-type: none"> ▪ mid-peripheral iris trans-illumination defects ▪ heavily pigmented trabecular meshwork ▪ presence of Krukenberg spindle (endothelial pigmentation in a vertical spindle-like pattern). <p>Traditionally, patients with PDS and PDG are classified in 4 groups²⁸:</p> <ol style="list-style-type: none"> 1. Inactive pigment dispersion with stable IOP (PDS and burned out PDG*) 2. Active pigment dispersion with stable IOP (early PDS and PDG) 3. Active pigment dispersion with progressive glaucoma and increased IOP (late PDS or PDG which could lead to inactive stage or progress) 4. Inactive pigment dispersion with progressive glaucoma and normal or elevated IOP (likely a permanently damaged trabecular meshwork and hence progressive ONH damage may occur irrespective of normalized IOP). <p>Some patients report experiencing symptoms of blurred vision, headaches, halos due to higher IOP spikes associated with strenuous exercise^{42,43}. A thorough history and IOP measurements before and after exercise can be useful clinical tools to aid PDS and PDG diagnosis.</p>
Images Both images courtesy of Murray Smith		

*It has been shown with increasing age the disease reaches an inactive phase, known as “burn out phase of pigmentary glaucoma” with reduced pigment dispersion and stabilised IOP.

4. Angle Closure Glaucoma

In angle closure disease, the anterior chamber angle is variably narrow or closed. The impairment of drainage of aqueous humour from the eye subsequently leads to elevation of IOP, and eventual glaucomatous damage. Angle closure glaucoma will not be covered in this clinical practice guide – please see Optometry Australia’s ‘Clinical Practice Guide for the diagnosis, treatment and management of anterior eye conditions.’

Textbook symptoms associated with acute angle closure glaucoma of headaches, nausea, haloes around lights and vomiting may not be present in all patients and asking specific questions may be required to identify these patients⁴⁴. This may be especially the case in patients with subtypes of angle closure such as intermittent and chronic forms, and subsequently these subtle symptoms may contribute to why these patients have a poorer prognosis compared to acute angle closure⁴⁵.

Clinical pearl:

The anterior chamber angle may be an undervalued aspect of the clinical examination in glaucoma, as evidenced by the proportion of missed narrow or closed angle disease in patients previously diagnosed with cataract or open angle glaucoma. This highlights the importance of anterior chamber assessment as part of a comprehensive glaucoma exam.

Historically, angle closure glaucoma has been considered to occur in low frequency compared to open angle glaucoma, with 0.4% prevalence in Caucasian-European populations over 40. However the condition is more common in those with Asian ancestry, and with increasing population rates and the ageing population in this demographic it is estimated 20 million people could be affected⁴⁷.

5. Detection

As primary eye care practitioners, optometrists are ideally positioned to detect patients who have risk factors for glaucoma during the routine eye examination⁴⁷. It is the responsibility of all optometrists, whether therapeutically endorsed or not, to detect glaucoma suspects and those with glaucoma at routine eye examinations. The major areas of investigation include:

- Risk factors/history and symptoms
- Ocular structure: anterior and posterior eye
- Intraocular pressure
- Functional assessment, i.e. visual acuity and visual fields

5.1 Risk factors/history

Some of the risk factors for glaucoma are summarised in Table 2.

Risk factor	Notes	Approximate relative risk †
Age ¹⁻³	<ul style="list-style-type: none"> ▪ Glaucoma can be considered to be an accelerated age-related process. ▪ Patients are >17 times more likely to be diagnosed with glaucoma at age 80+ years compared to patients aged < 40 years. 	High
Family history ⁴⁸	<ul style="list-style-type: none"> ▪ A positive family history of glaucoma increases the risk by approximately 4 times compared to no family history⁴⁹. ▪ As many as 40-60% of all patients with glaucoma have a positive family history. ▪ The type of glaucoma, age of onset, any surgery and the severity of glaucoma in family members is relevant to a patient’s own risk. ▪ First-degree relatives (parents, siblings, children) are likely to play a predominant role in risk elevation. 	High
Ocular history		
<ul style="list-style-type: none"> ▪ Myopia 	<ul style="list-style-type: none"> ▪ After dividing levels of myopia into low myopia (up to -3D) and higher myopia (greater than or equal to -3D), the odds of having glaucoma are approximately 1.8 and 2.5, respectively⁵⁰. ▪ Myopia and myopic disc configuration can confound interpretation of the ONH and visual field result, mimicking glaucoma^{51,52}. 	Moderate-high*

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Table 2: Historical risk factors (continued)		
Risk factor	Notes	Approximate relative risk †
Ocular history		
▪ Trauma	▪ Assess the seriousness of blunt trauma to determine its additive risk for development of glaucoma (assess for signs of angle recession) ^{53,54} .	Moderate
Vascular disease history		
▪ Diabetes	<ul style="list-style-type: none"> ▪ The Blue Mountains Eye Study found an association between diabetes and glaucoma (relative risk 2.2), independent of IOP⁵⁷. ▪ Overall, although there is evidence that diabetes may be associated with glaucoma, there are confounding issues at play and thus it is likely that the overall risk is attributable to an interplay of other associated factors such as cardiovascular disease and ageing changes⁵⁸. 	Low
▪ Hypertension/hypotension	<ul style="list-style-type: none"> ▪ A recent meta-analysis demonstrated that the overall risk of developing glaucoma was higher in individuals with hypertension (relative risk 1.2), but there were differences between high-tension glaucoma (significant risk) compared to low-tension glaucoma (non-significant risk)⁵⁹. ▪ Either very low diastolic (70 mmHg or lower) or high diastolic (above 90 mmHg) blood pressure were associated with an almost two-fold increased risk of glaucoma⁶⁰. ▪ The effects of anti-hypertensive medications should be considered in patients with glaucoma: dosing medications at night may be detrimental to ocular perfusion pressure⁶¹. ▪ At some point during the disease progression, cardiovascular health may play a role in progression or management⁶². 	Low
▪ Vasospastic disorders/migraine	<ul style="list-style-type: none"> ▪ There is a spectrum of vasospastic disorders (migraine, Raynaud's phenomenon) that may have implications in the risk of developing normal tension glaucoma, as vasospasm can cause chronic or recurrent ischaemic events occurring at the ONH, leading to glaucomatous changes⁶³⁻⁶⁵. ▪ There is a 1.2 times increased risk of glaucoma in those who get migraines⁶⁶. ▪ Younger individuals or those with more frequent migraine attacks may be at greater risk of glaucoma⁶⁷. 	Moderate (in younger individuals)*
▪ Thyroid disease	<ul style="list-style-type: none"> ▪ The link between thyroid disease and glaucoma is arguably less clear compared to other systemic risk factors. Most commonly, hypothyroidism has been considered the stronger association compared to hyperthyroidism and Graves disease⁶⁵. 	None to low*
▪ Sleep apnoea	<ul style="list-style-type: none"> ▪ Ocular disorders associated with obstructive sleep apnoea include floppy eyelid syndrome, papilloedema, anterior segment disease and optic neuropathy^{68,69}. ▪ Sleep apnoea results in nocturnal relative hypoxia, which can lead to ischaemic damage to the ONH. ▪ One large cohort study in Taiwan showed a significantly elevated risk of 1.7 after controlling for a number of confounding factors⁷⁰. ▪ There is weak evidence to suggest that treating the sleep apnoea will result in a lowered risk of glaucoma progression^{71,72}. 	Moderate*

Table continued over page

Table 2: Historical risk factors (continued)		
Risk factor	Notes	Approximate relative risk †
Corticosteroid usage	<ul style="list-style-type: none"> ▪ Steroid responders are classified into low (<6 mmHg compared to baseline, around 2/3 of individuals), moderate (6-15 mmHg increase, <1/3 of individuals) or high response (>15 mmHg, around 3% of individuals) tiers^{73,74}. ▪ Risk factors for steroid response include: myopia, personal ocular history of glaucoma or family history of glaucoma^{75,76}. ▪ An individual who experiences a steroid response is more likely to develop glaucoma in the future^{77,78}. ▪ Topical ocular corticosteroids have the strongest association with increase in IOP and secondary glaucoma⁷⁹ with the response occurring within weeks; evidence for the contribution of topical dermatological, nasal and oral corticosteroids is weaker. 	Moderate to high*
Smoking	<ul style="list-style-type: none"> ▪ There may be a dose-dependent effect of smoking, where heavy smoking (40 pack years or more) is associated with glaucoma, but not anything less than that^{80,81}. ▪ At this stage, although recommendations for cessation of smoking should be provided to patients, there is no evidence for a direct link between smoking and glaucoma⁸²⁻⁸⁴. 	None*
Neurodegenerative coinditions	<ul style="list-style-type: none"> ▪ Questions regarding this may form part of general or specific history ▪ Similar macular VF defects can be seen in Alzheimer's as in glaucoma so practitioners should be cognizant to comorbidity⁸⁶. 	N/A

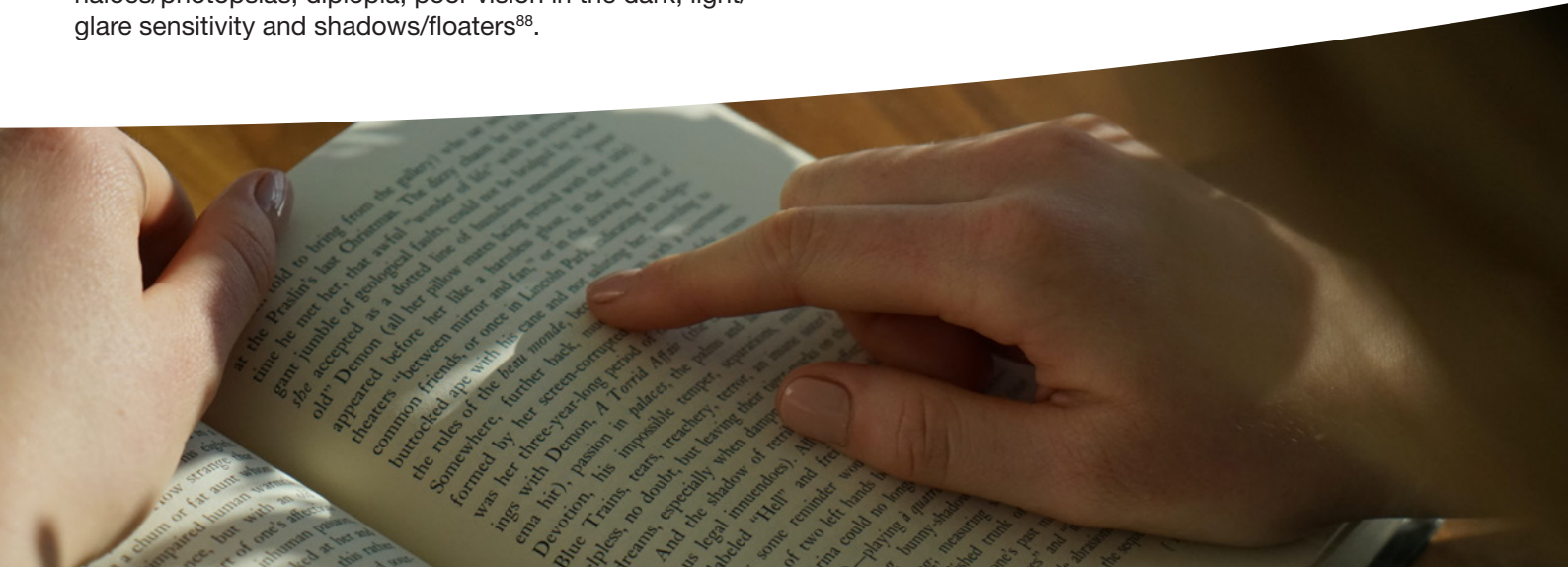
* Although strong evidence (longitudinal cohort studies) are not currently available for these risk factors, it is nonetheless prudent to explore these during history-taking.

† The calculations of risk are an approximate amalgamation of the magnitude of effect, as per the expert and consensus opinion from a review of the literature. A significant increase in risk was deemed as “low” = >1.00 to <1.50; “moderate” = 1.50 to <2.00; “high” > or equal to 2.00 relative risk.

5.2 Symptoms

Contrary to common thought, some patients do experience symptoms in early stages of glaucoma (~4%), but they are more common in advanced stages of glaucoma (~25%) where significant vision loss has already occurred⁸⁷. Such symptoms include: blurry vision, glare/haloes/photopsias, diplopia, poor vision in the dark, light/glare sensitivity and shadows/floaters⁸⁸.

A specific visual task that can be impaired in glaucoma is visual search⁸⁹⁻⁹¹. As a symptom, it can manifest as more difficulties in searching for objects within a visual scene, with extended time and more scanning eye movements required. This is a task that has many practical implications, such as reading and navigation.



6. Ocular structure: anterior and posterior eye

6.1 Anterior segment

Pathologies affecting the anterior segment may contribute to the development of glaucoma.

6.1.1 Slit lamp biomicroscopy

Slit lamp biomicroscopy needs to be conducted thoroughly to examine the anterior segment for the following reasons:

- Indications of risk factors for secondary glaucoma: PDS, PXF, angle recession, uveitis and evidence of trauma.
- Angle closure spectrum disease
- Concurrent anterior segment diseases that may affect management paradigms for glaucoma

The limbal anterior chamber depth measurement (van Herick) has very high inter-observer reproducibility⁹²⁻⁹⁴ and is best documented as a numerical ratio. The technique involves:

- Offsetting illumination arm by 60° to the temporal side
- Bright, narrow beam of light directly perpendicularly to the ocular surface at the limbus
- Limbal anterior chamber depth measured by comparing the depth of the peripheral anterior chamber depth to the thickness of the cornea.
- A cut-off value of less than or equal to 25% on van Herick has excellent specificity but poor sensitivity, and so therefore should lead to gonioscopy being performed⁹⁵.

Clinical pearl

Van Herick is an appropriate screening tool, however all those with narrow angles (less than or equal to 25%) require gonioscopy, as do all glaucoma suspects⁹⁵.

6.2 Posterior segment (optic disc assessment)

Stereoscopic examination of the optic disc and retinal nerve fibre layer (RNFL) allows the practitioner to exclude other retinal pathology which may contribute to optic disc changes or visual field loss. Thus, when possible, dilated fundus examination⁹⁶ is recommended to enhance the stereoscopic view and to rule out other pathologies. Furthermore, use of the red-free filter during funduscopy allows assessment of the RNFL integrity⁹⁷.

Several features of the ONH come together to be diagnostic of glaucoma, such as focal or generalised thinning of the neuroretinal rim with excavation and enlargement of the optic cup (note: there is no cut-off cup-to-disc ratio specified here) and deformation of the lamina cribrosa, but individual signs should not be considered in isolation. Retinal nerve fibre layer loss in the absence of ONH changes should have other diagnoses systematically investigated before considering glaucoma (diagnosis of exclusion), especially given that some other optic neuropathies have potentially sinister compressive aetiologies⁹⁸.

The features of a glaucomatous optic disc include (Table 3):

Table 3: Glaucomatous optic disc features

Enlargement of the optic disc cup	Disc size and insertion should be assessed. Discs of a smaller size of 1.5mm diameter are less likely to have cupping and larger discs >2.0mm far more likely ⁹⁹ with some studies reporting an increase of 0.21 in VCDR for each 1mm ² in disc area ¹⁰⁰ .
Cup-disc ratio asymmetry	Asymmetric cup-disc ratio >0.2 ^{9,101}
Neuroretinal rim (NRR) thinning and/or notching	Thinning, focal narrowing or notching of the NRR typically in the superior and inferior poles of the optic nerve head. The Inferior Superior Nasal Temporal (ISNT) rule is not obeyed in up to 80% of patients with glaucomatous damage, as the cup enlarges vertically ^{102,103} . However, it is not recommended as a diagnostic tool due to a poor trade-off for sensitivity and specificity, especially in the context of atypical disc configurations, such as large discs or small discs ^{104,105} .
Presence of an optic disc haemorrhage	Sometimes referred to as a Drance haemorrhage. See further information below.
Retinal nerve fibre layer thinning	In cases of NRR thinning or notching, there is often adjacent RNFL thinning which may be visible as reduced reflectivity or a defined wedge defect ¹⁰⁶ , particularly in the superior and inferior bundles. In the absence of NRR changes, RNFL loss in isolation should not be considered to be a glaucomatous sign; rather a potential sign of previous ischaemic episodes (such as in diabetes) or consecutive optic atrophy ^{52,107} .
Blood vessels at the optic disc	Nasalisation of central ONH vessels, barring of the circumferential vessels and bayoneting of vessels in cupping where they emerge at the disk margin making a sharp bend, more common in advanced glaucoma ¹⁰⁸ .
Peripapillary atrophy	Zone-beta PPA – represents loss of retinal pigment epithelium and choriocapillaris leaving intact choroid vasculature ¹⁰⁹ . Can also occur in normal eyes.

Clinical pearl

The Inferior Superior Nasal Temporal (ISNT) rule is not obeyed in up to 80% of patients with glaucomatous damage, as the cup enlarges vertically however it is a poor diagnostic tool, with false positive and false negative rates as high as 30%^{104,105}. Perform a comprehensive examination of the disc on all patients, followed by the application of risk factors to guide review and management and document findings.

6.2.1 Disc haemorrhage

Presence of a disc haemorrhage, sometimes referred to as a Drance haemorrhage, can precede RNFL loss or disc damage and may represent progression¹¹⁰⁻¹¹⁴. In those with glaucoma, a new Drance haemorrhage can indicate the onset of more rapid visual field deterioration¹¹⁵. By definition, a disc haemorrhage involved in glaucoma should meet the following criteria¹¹⁶:

- Linear in shape and perpendicular to the disc margin
- Appear within the prelaminar region (though may be more “blotchy” if within the cup)
- Length can be variable, but typically from NRR to extent of the peripapillary atrophy
- Should be within one disc diameter of the disc margin

It is important to remember that the only true indices of glaucoma progression are structural and functional metrics of progression: a disc haemorrhage alone and in isolation is insufficient for a diagnosis of glaucoma progression and can be found infrequently in patients without glaucoma¹¹⁷. Thus, increasing aggressiveness of treatment should not be done prematurely: like most retinal haemorrhages, it would be expected to take 6-8 weeks to resolve, after which re-examination would reveal if any significant structural and functional change has occurred.

6.3 Intraocular pressure

It is well established from major clinical trials that elevated IOP is a strong risk factor for glaucoma conversion and progression¹¹⁸⁻¹²¹ and measurement of IOP is an essential part of glaucoma diagnosis and management¹²². However, it is important to note that IOP is not diagnostic of glaucoma, as glaucoma can develop at any IOP level, including at normal or low IOP¹²³.

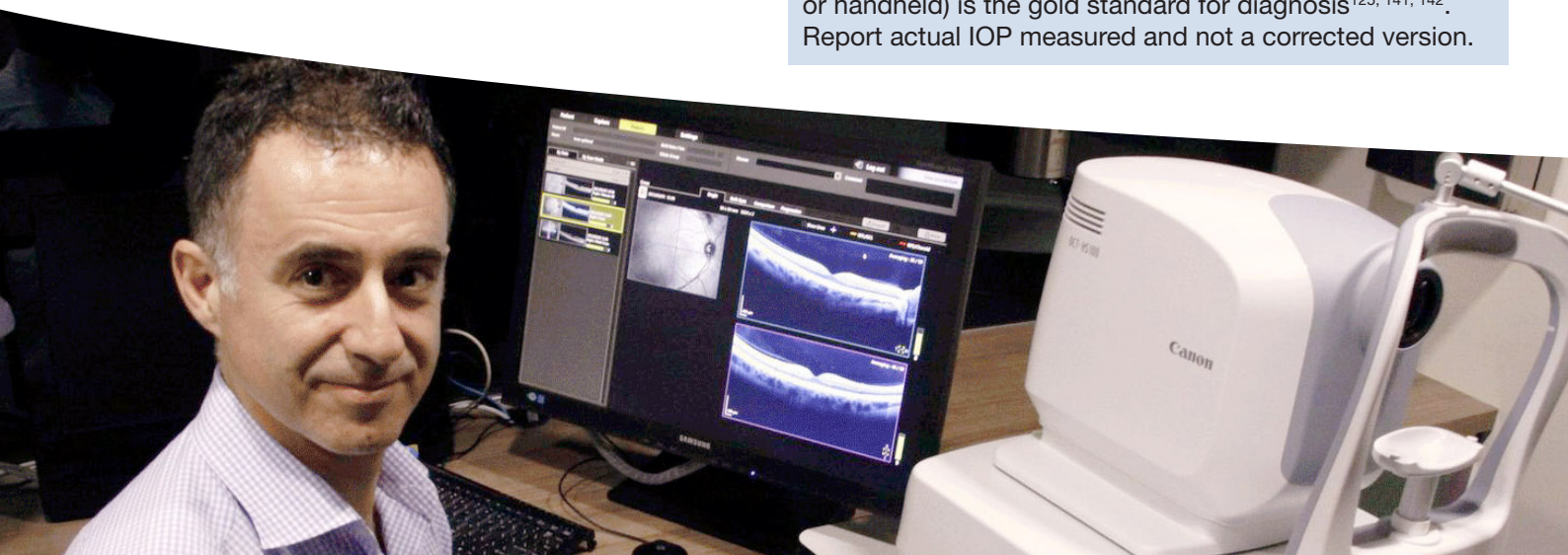
A number of devices for measuring IOP are currently available for clinical use; each with their own advantages and disadvantages¹²⁴. Current World Glaucoma Association Consensus Statements and National Health Medical Research Council (NHMRC) Guidelines recommend the use of Goldmann applanation tonometry (GAT)^{125,126}. The hand-held versions of GAT (Kowa HA-2 and Perkins) have been shown to demonstrate similar measurements^{127,128}. When measuring IOP with GAT, thinner corneas can result in underestimation of IOP and thicker corneas cause overestimation¹²⁹. However, there currently exists no widely accepted, single correction factor for altering intraocular pressures by corneal thickness. Thus, it is more important that clinicians document pressures by the reading plus the measurement technique used, and not report on “corrected” measurements.

Alternative methods for measuring IOP are also in widespread clinical use, but are comparable to GAT in different ways:

- **Non-contact tonometry** shows good agreement with GAT, however there is a tendency to overestimate IOP, particularly at higher IOPs^{128,130,131}. NHMRC recommends non-contact tonometry only where GAT is not suitable such as for young children, patients unable to tolerate GAT, physically unable to reach a slit lamp due to disability and with corneal diseases that precludes its use¹³².
- **Tono-Pen** has a poorer level of agreement with GAT compared to other techniques, though the direction of bias is unclear^{133,134}. Due to the small area of contact with the corneal surface, it may be useful in obtaining IOP measurements for eyes with irregular corneas or with the use of therapeutic contact lenses¹³⁵⁻¹³⁷.
- **Rebound tonometry (iCare)** has shown good agreement with GAT, typically within 3mmHg but with a tendency to underestimate when compared to GAT measurements¹³⁸⁻¹⁴⁰. Additionally, iCare measurements seem to be more affected by the extremely high or extremely low central corneal thickness¹³⁹.

Clinical pearl

IOP should be measured before gonioscopy to avoid artificially modifying IOP. Applanation tonometry (GAT or handheld) is the gold standard for diagnosis^{125, 141, 142}. Report actual IOP measured and not a corrected version.



7. Assessment

People with glaucoma risk factors that have been identified during the routine eye examination are recommended to undergo further clinical investigations to determine if glaucoma is present. The glaucoma assessment can be made by all optometrists, whether therapeutically endorsed or not. If certain equipment is not available to the practitioner, a referral can be made to a colleague for specialised testing with interpretation and a report returned back. It may be prudent to conduct the glaucoma assessment over several visits and at different times of the day to reduce patient fatigue and assist in determining any diurnal fluctuations in IOP.

7.1 Equipment

In order to comply with the Optometry Board of Australia guidelines¹⁴³ to competently review glaucoma patients within their practice, optometrists must have the following equipment available, or alternatively, refer to another optometrist or an ophthalmologist for these assessments (Table 4):

Area of assessment	Equipment required
Intraocular Pressures	Tonometer; Goldmann applanation gold standard ¹²⁵
Central corneal thickness	Pachymeter or anterior optical coherence tomography (OCT) (for diagnosis)
Anterior chamber angle	Slit lamp and gonioscope
Optic nerve head and retinal nerve fibre layer	Slit lamp and fundus lens; fundus photography and/or posterior OCT
Threshold Visual Fields	Automated threshold perimetry tailored to the patient and degree of visual field loss

Detection of glaucoma has undergone a recent paradigm shift to address the multifactorial aetiology of the disease. Clinical diagnosis requires a comprehensive examination including the following¹³²:

- Thorough personal and medical history including establishment of risk factors (Table 2)
- Full eye examination including (but not limited to);
 - Measurement of vision, pupil reactions and other screening/entrance tests
 - Anterior chamber angle assessment (gonioscopy)
 - Intraocular pressures and corneal thickness measurement
 - Stereoscopic optic nerve head and retinal nerve fibre layer assessment

- Visual field
- Imaging (when available)

Further supplementary tests that can aide in glaucoma diagnosis and assessment include monocular colour vision assessment and contrast sensitivity assessment^{144, 145}.

7.2 Anterior chamber angle assessment

In order for a diagnosis of glaucoma to be made, the anterior chamber angle must be assessed using gonioscopy - the 'gold standard' technique¹⁴⁶. The normal anterior chamber angle features are outlined below¹⁴⁷:

- The superior angle tends to be the narrowest
- Angles tend to be narrower in females and older individuals
- Interestingly, there is no consistent evidence of racial differences in gonioscopic grades, however, the rate of anterior chamber angle narrowing tends to be more rapid amongst Chinese individuals¹⁴⁸

Anterior segment imaging devices such as optical coherence tomography, Scheimpflug photography and ultrasound biomicroscopy should be used only as complementary techniques to the gonioscopic examination. They may be particularly useful for visualizing the iris contour and retroiridal pathologies. As technology improves these devices may become more mainstream however gonioscopy is gold standard¹⁴⁶. With current technology, none of these imaging modalities can provide enough information to replace Goldman e.g. visualizing angle neovascularization and pigmentation of the angle¹⁴⁶.

Grade	Definition
Open angles	Posterior trabecular meshwork or deeper visible in all quadrants*
Primary angle closure suspect	Posterior trabecular meshwork not visible in three or more quadrants
Primary angle closure	Posterior trabecular meshwork not visible in three or more quadrants potentially with raised intraocular pressure (>21 mmHg) AND/OR presence of synechiae
Primary angle closure glaucoma	Primary angle closure glaucoma: posterior trabecular meshwork not visible in three or more quadrants AND glaucomatous optic nerve AND/OR visual field changes

*Posterior trabecular meshwork non-visibility implies the presence of iridotrabecular contact, which is the analogous grading method used by some other authoritative bodies, and the anatomical appearance visible on imaging modalities such as anterior segment OCT.

Clinical pearl

The features seen on gonioscopy should be recorded systematically: the deepest visible structure, the amount of trabecular pigmentation and the iris contour, plus the presence or absence of pertinent features.

7.3 Intraocular pressures and diurnal variation

Currently, evidence for IOP fluctuations being associated with glaucoma conversion and progression is inconclusive, though higher fluctuations may be associated with greater likelihood of disease progression¹⁵⁰⁻¹⁵³. To estimate the extent and patterns of diurnal IOP fluctuations, the clinician can perform IOP phasing. By taking measurements of IOP at different times of the day, the clinician can appreciate the profile of the IOP across the day, including the presence of any IOP spikes. This is supported by current NHMRC Guidelines¹³².

For treated patients who progress despite apparently adequate IOP control according to in-office measurements, 24-hour IOP monitoring may reveal poor IOP control outside normal office hours; up to 69% of patients exhibit their peak IOP outside office hours¹⁵⁴.

An alternative to IOP phasing is the water drinking test as peak IOP obtained from the water drinking test is highly correlated with those obtained from diurnal IOP phasing^{155, 156}. It is used as a stress test to establish the patient's ability to recover from a transient rise in IOP, however the mechanisms are not fully understood¹⁵⁵. The water drinking test cannot be used for diagnosis of glaucoma¹⁵⁷.

Clinical pearl

Understanding the patient's IOP profile is important for establishing risk of conversion or progression, treatment targets and identifying potential reasons for uncontrolled disease. Similar to IOP fluctuations, there are no standardized cut-offs for significant results, but high fluctuations and disparate peaks should be treated as suspicious.

7.4 Intraocular pressures and corneal thickness

In patients with ocular hypertension, a thinner central corneal thickness (CCT) was shown to be an independent risk factor for conversion to POAG¹²⁰. This is in part due to thinner central corneal thicknesses resulting in an underestimation of the IOP, and is more likely to be associated with normal tension glaucoma^{158,159}.

However, population-based studies in Asia and West Africa have shown an association between higher CCT and ocular hypertension but no increased risk of glaucoma associated with thinner CCT¹⁵⁹⁻¹⁶¹. Several correction factors have been proposed for adjusting IOP measurements based on CCT, however as these methods introduce other errors, they are of limited clinical value^{142, 162-164} and are not recommended for widespread clinical use. Note that once pachymetry has been performed, it does not typically need to be repeated unless there is a co-existing condition likely to change the corneal thickness. The finding that corneal thickness (and other biochemical factors such as corneal hysteresis) contribute to glaucoma risk independently to IOP measurement suggest there are other factors at play^{142,165} such as weakened collagen in the eye.

Clinical pearl

Using CCT and IOP adjustment formulas can introduce errors and are of limited clinical value^{142,162-164} and are not recommended for widespread clinical use. CCT is still a valuable clinical test however, as it is a risk factor to glaucoma independent to IOP¹⁶⁵ and still has some impact on the interpretation on pressure readings^{158,159}.

7.5 Visual field

Standard automated perimetry (SAP) is the current recommended procedure for assessment of the visual field in glaucoma¹⁶⁶. Recommended test grids for automated perimetry glaucoma encompass up to 24-30° from fixation (up to 60° along each meridian). Note, the 30-2 test grid is sometimes used assessment of other neurological conditions, however 24-2 is usually the preferred strategy.¹⁶⁷ There are a number of instruments available for performing SAP. However, it is important to ensure that results are comparable over time, thus it is best to use an equivalent perimeter instrument to measure thresholds.

In order to assess the reliability of the visual field data; fixation losses, false positives and false negatives should be considered. Furthermore, the global indices including mean deviation, pattern standard deviation and hemifield asymmetry should be reviewed.

Due to issues with the learning effect for perimetry¹⁶⁸, some practitioners may "frontload" if the initial visual field isn't satisfactory, where more visual fields are performed closer together at baseline, whereas other practitioners repeat fields after weeks or months. Consider emergent repetition of visual fields when results do not show a relationship between structure and function, if reliability is good the urgency to repeat is reduced. Excessive repetition is not necessary and patient fatigue should be balanced with patient familiarity with testing.

Clinical pearl

In general, it is recommended that a visual field be conducted¹⁶⁹ more than twice a year. A minimum of three would be reasonable to overcome an average amount of patient test variability¹⁷⁰ as practitioners should be looking at progression analysis for long term fluctuations and loss of visual field over time.

Visual field defects in glaucoma are retinotopic (follow the anatomy of the optic nerve head and retinal nerve fibre layer). Typical patterns of defects include: nasal step, arcuate, paracentral and centrocaecal¹⁷¹. Enlarged blind spots and temporal defects are possible, but rare. Some examples of glaucomatous visual field defects are shown in Figure 1¹⁷².

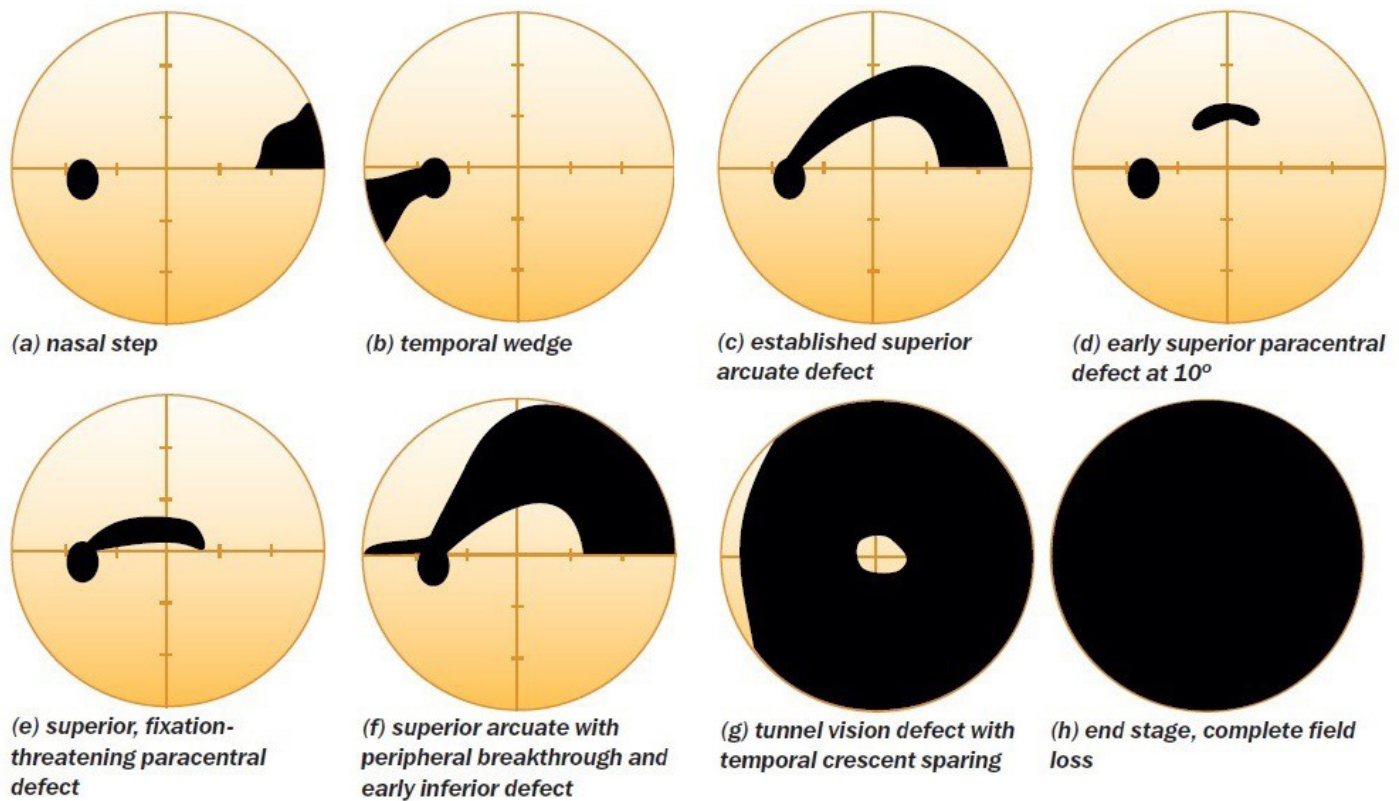


Figure 1: Examples of glaucomatous visual field defects from the *Community Eye Health Journal** Broadway, D. C. (2012). "Visual field testing for glaucoma - a practical guide." *Community eye health* 25⁷⁹⁻⁸⁰: 66-70.

N.B. Visual field defects as depicted in Figure 1 are only a graphical representation of visual field defects and it is important to note that many patients present with less classical signs.

The 10-2 test grid is an important complementary test to the routine 24-2, and may reveal additional central visual field defects. Indications for performing a 10-2 alongside a 24-2 include any of the following:

- Defects seen within the central 10o on the 24-2
- Structural losses in the papillomacular bundle (seen on fundus examination)
- End-stage disease

The 24-2C test, recently clinically available, includes additional points centrally and has been shown to be as effective in detecting field loss as doing a 10-2 and a 24-2 test in conjunction¹⁷³. Several static automated perimetry instruments are available on the market, and each have a proprietary algorithm for obtaining sensitivity measurements across the visual field.

Modern test algorithms may offer significantly reduced test times whilst largely preserving the integrity of sensitivity measurements (such as SITA-Faster, which more than halves the test time compared to SITA-Standard, available on the Humphrey Field Analyzer), which could be considered in a busy clinic^{174,175}.

There are suggestions the glaucoma phenotypes may differ according to their visual field defects: high-tension glaucoma may have more diffuse defects while low-tension glaucoma may have more focal, central loss¹⁷⁶⁻¹⁷⁸. The Early Manifest Glaucoma Trial showed that patients with PXG tended to progress much faster compared to high-tension glaucoma, whereas normal-tension glaucoma tended to progress the slowest^{15,16}.

Clinical Pearl

Scotomas appearing in glaucoma tend to be focal in the early stages, and deepen and widen gradually as the disease progresses¹⁷⁹. In some cases of acute or transient spikes in IOP, the pattern of visual field defect may be more diffuse, but this is typically the exception rather than the rule^{180,181}. There may be some asymmetry, but this is typically not gross^{142,182,183}.

7.6 Standard automated perimetry versus selective perimetry

Other forms of “selective” perimetry (in which non-standard stimuli are presented instead of the regular achromatic circular stimuli) have experienced popularity in clinical use. Examples of these techniques include:

- Frequency doubling technology perimetry
- Short wavelength automated perimetry (blue on yellow)
- Flicker perimetry

Clinical pearl

The recommendations of authoritative guidelines from the available evidence do not recommend the use of alternative perimetric methods¹⁶⁶. Instead, the current recommendations are to continue with SAP – the ‘gold standard’.

8. Imaging

Imaging technologies have been in part responsible for the paradigm shift towards early diagnosis of glaucoma (pre-perimetric glaucoma)^{184,185}. Some of the imaging modalities available to optometrists include fundus photography, posterior optical coherence tomography (OCT) and scanning lasers (HRT, GDx).

The role of posterior OCT in glaucoma is summarised below¹⁸⁶:

- If not already performed during the comprehensive eye examination, OCT can be performed at the diagnosis stage^{187,188} to confirm suspected structural NRR loss visible on fundoscopic examination.
- Quantification of structural information (such as RNFL thickness and ganglion cell layer thickness)^{185,189}.
- Longitudinal analysis to determine significance of change over time¹⁹⁰.
- There are limitations of OCT with “red and green disease”, with false positive and false negatives, when traffic light signals are applied to the instrument’s underlying normative database. Because of this limitation, clinicians should carefully and critically scrutinise the output from the instrument and question the integrity of the data, to determine if the results make sense. The raw data (Heat map and TSNIT curves) are more useful than the deviation maps¹⁸⁶.

Clinical pearl

Diagnosis or referral to an ophthalmologist based solely on imaging or with poor knowledge of imaging instrumentation analysis potentially leads to increased false positive or false negative rates^{191,192}. Thus, these instruments should be utilised as adjunct tools in glaucoma diagnosis^{193,194}.

9. Diagnosis

Upon completion of the glaucoma assessment and with reference to the results of the glaucoma specific testing, a decision can be made regarding the clinical diagnosis of glaucoma.

The complete glaucoma testing and assessment process is vital not only for the diagnosis of glaucoma, but allows the clinician to grade the severity of the disease, determine any underlying aetiology such as secondary causes of glaucoma, and set target intraocular pressures for treatment. This includes consideration of anatomical factors such as tilted discs, or neurodegenerative conditions that can also cause visual field defects such as Alzheimer’s, Parkinson’s and dementia.

Clinical pearl

Exclude other causes of optic atrophy and investigate different subtypes of glaucoma before diagnosing primary open angle glaucoma

Upon completion of all specific testing for glaucoma, a decision can then be made regarding a clinical diagnosis. Three potential outcomes typically occur:

1. The patient is normal in all glaucoma testing and can be returned to routine optometric care;
2. The patient has consistent defects in multiple tests that are characteristic of glaucomatous ocular damage. A definitive diagnosis of glaucoma can then be made;
3. The glaucoma testing is equivocal or ambiguous due to for example poor subjective reliability on visual field testing, reduced signal strength or artefacts on structural scans, and/or defects that are non-matching (e.g. severe superior RNFL thinning that is not present on ganglion cell complex analysis). They may also have results that are consistent with either physiological variation or glaucomatous disease without sufficient evidence of presence or absence of disease. A definitive diagnosis as to normality or glaucoma cannot be made at this stage. The patient remains a glaucoma suspect.

9.1 Glaucoma suspect

A glaucoma suspect status refers to a non-specific interval between normal non-glaucoma and manifest glaucoma, and represents arguably one of the greatest challenges in the diagnostic process. The notion of “conversion” from glaucoma suspect is heavily debated in the literature, with no clear cut-off values for when an individual has met criteria for glaucoma, repeated testing to detect progression over time is required. Glaucoma suspect status or non-glaucomatous causes of optic neuropathy should be considered in cases where the diagnosis of glaucoma is equivocal.

Considering the current availability of technologies and the current understanding of glaucoma, features characterising the glaucoma suspect individual include, typically in isolation and to varying degrees:

- Suspicious features of the optic nerve head: enlarged and/or asymmetric cup-to-disc ratio, NRR thinning, presence of disc haemorrhage, presence of peripapillary atrophy, deep cup with visible lamina cribrosa pores, loss of adjacent RNFL reflectivity.
- Suspicious visual field result: clusters of points of reduced sensitivity resembling glaucomatous-type loss, but not repeatable or concordant with structural defects, or unreliable.

It is important to note that although there are a number of established historical, ocular and medical risk factors for glaucoma, the diagnosis and plan to treat should be based on the structural and functional losses that correlate. These include: ethnicity, positive family history, high IOP (>21mmHg) and/or IOP fluctuations, myopia, ocular history (previous blunt force trauma) and/or medical history (diabetes, hypertension, hypotension, migraine).

Management of a patient with glaucoma suspect status requires repeated administration of structural and functional testing over time, with the aim of increasing reliability and building evidence of progression/to determine the risk of progression. The frequency of follow-up should be based on the suspicion of the practitioner, the severity of the initially detected defects and the number of associated risk factors but will most likely be between 6-24 months¹³² depending on the number of glaucoma risk factors.

9.2 Glaucoma - decision to treat

The Ocular Hypertension Treatment Study¹⁹⁵ showed that 10% of patients with untreated elevated IOP progressed to glaucoma over a 5-year follow-up. The Early Manifest Glaucoma Trial¹⁶ showed that 38% of patients with early perimetric glaucoma did not have progressive visual field loss over the course of the study when left untreated. The Collaborative Normal Tension Glaucoma Study¹⁹⁶ showed that 50% of untreated study participants did not progress over 7 years of follow-up.

Depending on the individual’s circumstances, the diverse range of treatments means that management plans can be tailored.

Patients with early disease and older patients aged >80 years may be monitored closely to assess the rate of progression prior to initiating therapy. Therapy may be delayed if the burden of treatment is high and the risk of significant symptomatic visual field loss is low in the patient’s estimated lifespan. Patient preference or suitability for different treatment modalities should be considered. It may also be worth considering referring the patient for laser trabeculoplasty where appropriate for first line therapy for patients where medical therapy may be difficult¹⁹⁷.

Some groups, such as the Ocular Hypertension Treatment Study Group and the European Glaucoma Prevention Study Group have developed calculators that attempt to estimate the 5-year risk that an individual with high intra-ocular pressure will go on to develop primary open-angle glaucoma. These calculators are validated and can be used as part of a decision to treat.¹⁹⁸ Where these calculators are used and a patient has a risk score estimated, it is important there is a dialogue with patients regarding the best care available to them. Optometry plays an important role in counselling, decision to treat and consent in the beginning of treatment, treatment modality and continuing treatment.

10. Management

The overall goal of treatment is not only to preserve vision and visual function, but also to maintain quality of life. IOP lowering remains the mainstay of preventing glaucoma progression, and is the only currently established treatment paradigm. The management plan can include topical anti-glaucoma therapy (within the optometric scope of practice), laser treatment, surgical treatment or watchful waiting. Amongst these strategies is a need to balance the aggression of treatment required to preserve ocular structure and function with the potential impact of therapy upon the patient’s quality of life.

10.1 Severity grading

Once a diagnosis of glaucoma is made, the severity of glaucoma should be determined by the degree of structural optic nerve damage and/or functional loss. Once the severity of glaucoma is established, this helps in setting the appropriate target IOP, selecting the best form of treatment (topical, laser or surgical), and guiding the follow-up and/or referral plan.

There are multiple different staging systems that are available for grading the severity of glaucoma, with their own advantages and disadvantages¹⁹⁹. One example is the Enhanced Glaucoma Staging System (GSS 2) which provides a standardized, repeatable classification of functional visual field loss in patients when using the Humphrey Field Analyzer or Octopus results²⁰⁰. Another grading scale is the Hodapp-Parrish-Anderson (H-P-A) criteria, which is commonly used by glaucoma researchers¹⁹⁹. It combines both the overall damage in respect to the mean deviation (or mean defect) value and the defect’s location relative to the macula.

This system however can sometimes be time consuming and overestimate the functional loss¹⁹⁹ but is very sensitive to early glaucoma and subtle nerve damage²⁰¹.

The recent prolific use of imaging modalities have reinforced and popularised the concept of pre-perimetric glaucoma, or glaucoma in which observable structural defects are present in the absence of statistically significant functional loss^{202, 203}. This paradigm shift has manifested in the most recent glaucoma guidelines by the American Academy of Ophthalmology, which lists mild glaucoma – glaucoma in the absence of visual field defects – as the earliest stage of glaucoma²⁰⁴ (Table 6).

This remains a point of contention; as the next stage moderate glaucoma, represents patients with any visual field defect, which is notably more severe compared to other grading schemes^{205, 206}.

The Royal Australian and New Zealand College of Ophthalmologists (RANZCO) mainly make note to the stability of the glaucoma when discussing classifications. Their classifications refer to patients with or without treatment; are also graded on disc, RNFL and VF changes over time²⁰⁷.

Table 6: Stages of glaucoma from the American Academy Preferred Practice Pattern 2021: one example of a staging system

Stage of glaucoma	Structural changes	Functional changes
Mild or 'pre-perimetric'	Definite optic disc, nerve fibre layer or macular imaging abnormalities consistent with glaucomatous damage	Normal visual field
Moderate	Definite optic disc, nerve fibre layer or macular imaging abnormalities consistent with glaucomatous damage	Visual field abnormalities in one hemifield that are not within 5 degrees of fixation
Severe	Definite optic disc, nerve fibre layer or macular imaging abnormalities consistent with glaucomatous damage	Visual field abnormalities in both hemifields and/or loss within 5 degrees of fixation in at least one hemifield
Indeterminate	Definite optic disc, nerve fibre layer or macular imaging abnormalities consistent with glaucomatous damage	Inability of patient to perform visual field testing, unreliable/uninterpretable visual field test results, or visual fields not performed yet

10.2 Target intraocular pressure

Target IOP is the estimated intraocular pressure required to slow or stop glaucomatous optic neuropathy and needs to be individualised for each patient. Target IOP is an estimate derived from glaucoma clinical trials and depends on a number of factors including the severity of the disease, and other ocular and systemic risk factors, including baselines IOP at which damage occurred, age of patient, life expectancy etc.

In patients with newly diagnosed glaucoma, regardless of the level of baseline IOP, treatment reduced the risk of progression, with each mmHg of IOP reduction approximately equal to a 10% risk reduction^{17, 121}. Long-term follow up of patients showed that maintaining a low IOP was associated with reduced progression of visual field defects²⁰⁸.

A reasonable initial treatment in a primary open angle glaucoma patient is to reduce IOP by 20-30% below baseline and to adjust up or down as indicated by disease course and severity²⁰⁹.

A higher percentage reduction in IOP may be chosen if:

- There is more severe optic nerve head damage
- Optic nerve head damage is progressing rapidly
- There are other risk factors present (e.g. family history, age, disc haemorrhage)

A lower percentage reduction in IOP may be chosen if:

- The risk of aggressive treatment outweighs the benefit (e.g. if the patient does not tolerate medical/laser treatment or has high risks to surgical intervention)
- Patient has very mild disease/ if the patient's life expectancy is limited

No practitioner can know the true target IOP for any particular patient prior to initiating glaucoma therapy. The appropriateness of the target is only revealed once structural and function stability is assessed over a number of years. If the patient continues to progress even at their target pressure, the target IOP needs to be lowered further until stability of structure and function occurs. Target IOP should be reviewed at follow up visits and reset and documented if required.

Clinical pearl

Strategies for reducing of intraocular pressure should be tailored for each patient and a target IOP determined and documented

A summary flow chart for treatment recommendations in glaucoma is presented in Figure 2 below.

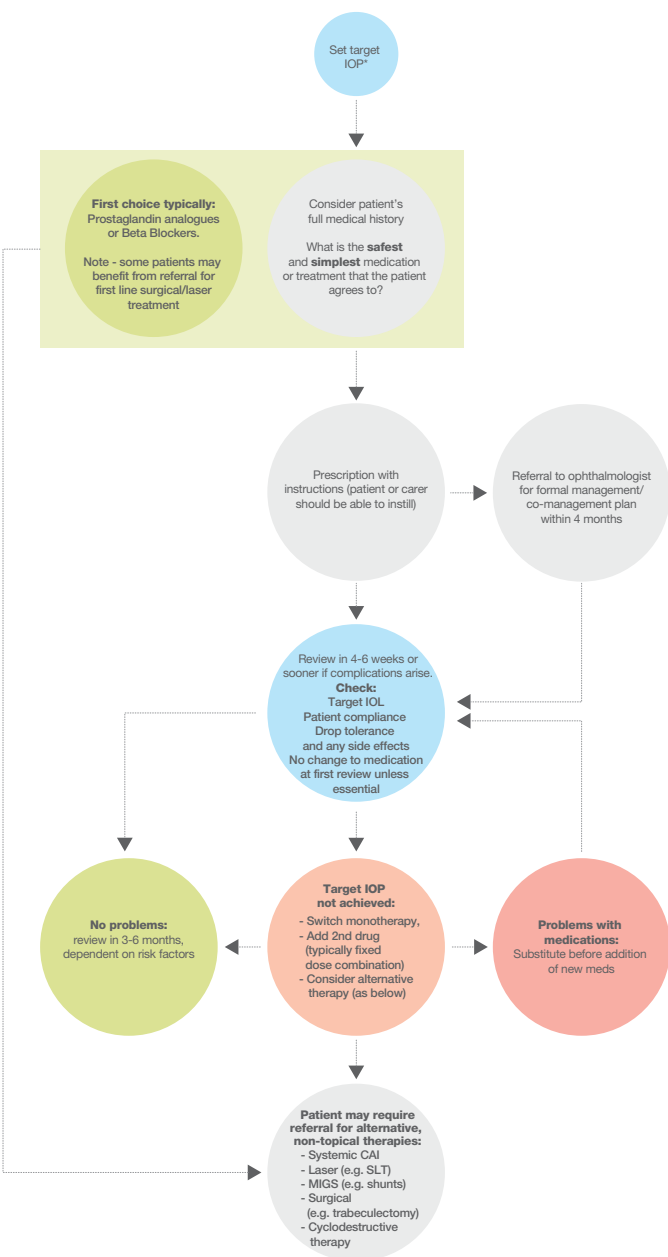


Figure 2: Recommended management protocol for glaucoma patients

10.3 LiGHT trial

The results from a large multicentre study (LiGHT) examining laser versus medications as first line therapy for primary open angle glaucoma and ocular hypertension suggests some benefit in offering selective laser trabeculoplasty to patients first.²¹⁰ Selective laser trabeculoplasty is a safe procedure and has been suggested to be similar in its cost-effectiveness compared to first-line prostaglandin therapy. Clinicians should recognise though that the LiGHT study included patients with high baseline intraocular pressure (on average 24 mmHg), and many studies have shown that selective laser trabeculoplasty works best on patients with higher pressures, compared to those with lower pressures (such as low or normal tension glaucoma). Clinicians should also recognise that many patients still required topical medications due to pressure spikes or increases. Therefore, whilst selective laser trabeculoplasty may be an effective option, clinicians should maintain close follow up of their ocular hypertensive or primary open angle glaucoma patients.

10.3.1 Examination for ocular surface disease

Ocular surface disease can be complicated by the use of topical anti-glaucoma medications, especially the preserved forms. Furthermore, there have also been some suggestions that severe ocular surface disease can affect the efficacy of topical anti-glaucoma medications. In such studies, the IOP measured in patients with severe ocular surface disease appears to be elevated and not at target. Treatment of the ocular surface disease subsequently led to a reduction in IOP to target levels.

Clinical pearl

Assessing the integrity of the ocular surface and addressing ocular surface disease should be part of the routine glaucoma examination.

10.4 Topical therapy

Topical pharmacotherapy is generally considered the mainstay of glaucoma treatment, particularly for optometrists. Medications for treating glaucoma are divided into several classes, depending on their mechanisms of action. Currently, these include:

- Prostaglandin analogues
- Beta-blockers
- Alpha2-agonists
- Carbonic anhydrase inhibitors
- Parasympathomimetics

These medications are summarised in Table 7 (over page).

Table 7: IOP medications available in Australia for the management of glaucoma

Preparations by Class	Mechanism of action	Efficacy	Daily dosage	Order of treatment choices	Ocular side effects	Systemic side effects	Contraindications
Prostaglandin analogues <ul style="list-style-type: none"> Latanoprost 0.005% (e.g. Xalatan) Travoprost 0.004% (e.g. Travatan) Bimatoprost 0.03% (e.g. Lumigan[†]) Tafluprost 0.0015% (e.g. Saflutan[‡]) 	Increase aqueous outflow	25-35% Maximum effect: 8-12 hours	Once daily (night)	First	<ul style="list-style-type: none"> Increase in iris pigmentation Darkening Thickening & lengthening of eyelashes Conjunctival hyperaemia Periorbital pigmentation 	Uncommon - may cause respiratory symptoms in susceptible individuals	No contraindications Precautions: <ul style="list-style-type: none"> Intraocular inflammation (iritis, uveitis) History of herpetic keratitis Aphakia or pseudophakia (potential for macular oedema)
Beta-blockers Non-selective agents: <ul style="list-style-type: none"> Timolol 0.25%, 0.5%, 1% (e.g. Timoptol, Nyogel, Timoptic[†]) Selective agents: <ul style="list-style-type: none"> Betaxolol 0.25%, 0.5% (e.g. Betoptic) 	Decrease aqueous production	20-25% Maximum effect: 2 hours	One to two times daily	First	<ul style="list-style-type: none"> Transient ocular discomfort Blurred vision Increased lacrimation Foreign body (FB) sensation 	<ul style="list-style-type: none"> Headache Bradycardia Decreased libido Bronchospasm Nausea 	<ul style="list-style-type: none"> Sinus bradycardia Overt cardiac failure history Cardiogenic shock Precautions: <ul style="list-style-type: none"> Asthma Severe COPD (selective agents, i.e. betaxolol preferred)
Alpha2-agonists <ul style="list-style-type: none"> Brimonidine 0.2%, 0.15% (e.g. Alphagan) Apraclonidine* 0.5% (e.g. Iopidine) 	Increase aqueous outflow and decrease aqueous production	10-25% Maximum effect: 1-4 hours	Two to three times daily	Second	<ul style="list-style-type: none"> Allergic reactions Hyperaemia Burning/stinging Foreign body (FB) sensation Blurring 	<ul style="list-style-type: none"> Headache Bradycardia Decreased libido Bronchospasm Nausea 	Patients receiving MAOIs Precautions: <ul style="list-style-type: none"> Severe cardiovascular disease May have loss of effect over time
Carbonic anhydrase inhibitors Topical: <ul style="list-style-type: none"> Dorzolamide 2% (e.g. Trusopt) Brinzolamide 1% (e.g. Azopt) 	Decrease aqueous production	15-25% Maximum effect: 2 hours	Two to three times daily	Second	<ul style="list-style-type: none"> Allergic reactions Burning/stinging 	<ul style="list-style-type: none"> Headache Bitter taste Dry mouth Nausea Fatigue 	<ul style="list-style-type: none"> Allergy to sulfonamides Severe renal impairment Precautions: <ul style="list-style-type: none"> Corneal grafts Endothelial dystrophy (may cause corneal oedema)
Systemic: <ul style="list-style-type: none"> Acetazolamide 250mg (e.g. Diamox) 	Decrease aqueous production	25-30%	Two to four times daily	Third		<ul style="list-style-type: none"> CNS depression Lactic acidosis (N.B. Up to 50% of patients do not tolerate acetazolamide) 	<ul style="list-style-type: none"> Adrenal or respiratory failure Sodium or potassium depletion
Cholinergics (miotics) <ul style="list-style-type: none"> Pilocarpine 1%, 2% (e.g. Isopto Carpine, Pilocarpine minims[†]) 	Increase aqueous outflow	15-20% Maximum effect: 3-4 hours	Three to four times daily	Third	<ul style="list-style-type: none"> Eye ache/pain Blurred vision Myopic shift Miosis Rare - retinal detachment 	<ul style="list-style-type: none"> Headache Nausea Dizziness 	<ul style="list-style-type: none"> Uveitis Iritis Secondary glaucoma
Combination therapies <ul style="list-style-type: none"> Combigan (brimonidine 0.2%/timolol 0.5%) Cosopt (dorzolamide 2%/timolol 0.5%) DuoTrav (travoprost 0.004%/timolol 0.5%) Xalacom (latanoprost 0.005%/timolol 0.5%) Ganfort (bimatoprost 0.03%/timolol 0.5%) Azarga (brinzolamide 1%/timolol 0.5%) Simbrinza (brinzolamide 1%/brimonidine 0.2%) 	As for individual components	20-35%	Combigan: Twice daily Cosopt: Twice daily DuoTrav: Once daily Xalacom: Once daily Ganfort: Once daily Azarga: Twice daily Simbrinza: Twice daily	Second	As for individual components		As for individual components

Preservative-free option

†Currently not available on the PBS

‡Restrictive benefit: the condition must have been inadequately controlled with monotherapy

1. NHMRC. Guidelines for the Screening, Prognosis, Diagnosis, Management and Prevention of Glaucoma. Canberra, Australia; 2010.

2. MIMS Online [Internet]. Medical Information Management System. [cited 2018 December 12]. Available from <https://www.mimsonline.com.au>.

10.4.1 Prostaglandin analogues

There are a number of reasons why prostaglandin analogues are considered a first-line therapy for glaucoma²¹¹. As monotherapy, it is generally the most efficacious at reducing IOP²¹² and also flattening the diurnal variation curve (i.e. controlling IOP fluctuations). The IOP lowering effect is also sustained over time, unlike some alternatives that may result in development of tachyphylaxis. Adverse effects of prostaglandin analogues are primarily cosmetic in nature. However, this may be a source of non-compliance, so patients need to be appropriately warned prior to treatment initiation.

If the initial prostaglandin is partially effective but does not reach target IOP, consider switching within the prostaglandin analogue class, as individual patients may respond to each medication differently^{213,214}. There is some evidence that prostaglandins may thin corneas over time, which should be considered when reviewing for effective glaucoma control. Repeat CCT on patients undergoing prostaglandin therapy long term, usually the corneal thinning stabilises after 2-3 years and is a reversible change^{215,216}.

10.4.2 Beta blockers

Prior to the discovery of prostaglandin analogue therapy, beta-blockers were the first-line therapy for topical glaucoma therapy. Beta-blockers still have a role as a first-line topical therapy particularly in the following cases:

- Intolerance to prostaglandin analogues (including its cosmetic effects)
- Unilateral treatment (to avoid unilateral cosmetic effects of prostaglandin analogues)
- Concerns regarding the presence or potential presence of ocular inflammation

Beta-blockers in gel-forming solutions may be best suited for therapy, due to the maintenance of efficacy (25% reduction) at only once daily dosing. Specifically, timolol gel-forming solution is a commonly prescribed and well-studied beta-blocker and its once daily dosing is an attractive clinical choice^{217,218}.

Beta-blockers are unlikely to be the first line treatment for most patients, even the cardio-selective medications, given the availability of alternative, safer medications²¹⁹. Beta-blockers should not be used in early or mid-pregnancy periods or in asthma and COPD^{220,221}, or if already taken systemically.

10.4.3 Alpha-2 agonists

Alpha-2 agonists are primarily considered to be second-line therapy or adjunctive medication in the management of glaucoma. Indications for monotherapy using an alpha-2 agonist include: intolerance to prostaglandin analogues plus contraindication to beta-blocker use, short-term use in the presence of inflammation of the eye (such as uveitis) or as an interim treatment prior to undergoing laser or surgical glaucoma treatment. Although aqueous production is also reduced by beta-blockers, the alpha-2 agonist acts on a different receptor and should therefore be considered to be complementary to a beta-blocker.

Alpha-2 agonist use is often limited in long-term glaucoma management due to the frequent development of follicular conjunctivitis, lower efficacy than prostaglandin analogues and more frequent dosing schedule²²². The frequency of ocular allergy varies but can be in up to one-third of patients²²³. Allergy appears to be less frequent with the alpha-2 agonist is used in fixed dose combination with timolol (Combigan).

One of the key studies that claimed to demonstrate a neuroprotective effect of brimonidine compared it to timolol in patients with low-tension glaucoma^{224,225}. Brimonidine has arguably enjoyed some popularity in glaucoma management since, but clinicians should be aware that subsequent studies have failed to demonstrate a true neuroprotective effect for the medication²²⁶.

In pregnancy, brimonidine may be used in the first and second trimesters, but should be avoided in the third trimester²²⁷.

10.4.4 Carbonic anhydrase inhibitors

Carbonic anhydrase inhibitors, like alpha-2 agonists, are also considered to be second-line therapy for glaucoma. Carbonic anhydrase is an enzyme that catalyses the hydration of carbon dioxide and thus inhibition decreases aqueous production from active filtration in the non-pigmented epithelium of the pars plicata. As it decreases aqueous production via an alternative pathway to beta-blockers, it acts synergistically with other antiglaucoma medications.

Brinzolamide is typically recommended over dorzolamide due to better efficacy and tolerability^{228,229}.

10.4.5 Parasympathomimetics

Pilocarpine is the only sympathomimetic available for use by optometrists in Australia and is rarely used in modern glaucoma management.

10.4.6 Combination drops

There are a number of combination drops currently available on the Australian market. These are considered second line therapy and are summarised in Table 6. If considering using combination drops that the side effects and mechanism of action of each active ingredient should be considered, also that if combination medications are to be used in combination with other topical IOP lowering medications that it should be done to avoid double up in a class of drug.

10.5 Laser therapy

Argon laser trabeculoplasty is an older technique that is no longer used, being largely replaced by selective laser trabeculoplasty (SLT). The mechanism of SLT is thought to be an increase in aqueous outflow^{230,231}. Practically, the procedure is short, typically performed as an in-office, out-patient procedure, has a quick recovery and excellent safety profile. Complications are typically transient and self-limiting.

These can include: mild anterior chamber inflammation and IOP spikes following treatments, with IOP spikes observed more commonly in eyes with heavily pigmented trabecular meshwork or in those with PXG^{232,233,234}.

Although topical therapies are usually considered a first line treatment, SLT may be considered a first line treatment in open angle glaucoma (either primary or, less commonly, secondary). Some indications include²³⁵:

- Young patients
- Medication-sparing therapy (avoiding adverse effects), either as monotherapy or medication-reducing treatment
- Medication non-compliance or intolerance (less reduction in quality of life)
- Additive/adjunctive treatment on top of existing topical therapy

The ability of SLT to achieve an IOP reduction of at least 20% has been reported in the literature to be generally quite high (approximately 85%), and comparable to topical therapy when compared head-to-head^{236,237}. SLT also appears to reduce IOP fluctuations but perhaps not as well as a prostaglandin analogues, which may be important for the risk of glaucoma progression^{237,238}.

One of the issues with SLT is the diminishing effect over time. For example, one study showed that only 11-31% of patients will achieve an IOP reduction of >20% at 5 years^{239,240}.

Another study showed that only 50% will achieve target pressure at 2 years²⁴¹. Studies that have examined re-treatment using laser trabeculoplasty have shown that repeat laser can be performed irrespective of prior treatment success²⁴²⁻²⁴⁴. The success of subsequent SLT tends to be lower, but this is generally not statistically significant. The LiGHT trial (Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma), a large multicentre trial published in 2019, suggested that there was a 97% probability of selective laser trabeculoplasty as first treatment being more cost-effective and provided greater quality of life in avoiding patients avoiding drops²¹⁰. Each patient's circumstance and best options should be considered on an individual basis.

Normal-tension glaucoma cases tend not to have as much success compared to high-tension glaucoma^{245,246}. It has also been suggested that patients with intraocular pressure < 14 mmHg might not benefit from trabeculoplasty at all²⁴⁷ however the cost to the patient of drops is reduced and potential improvement to health-related quality of life due to longer drop-free intervals²¹⁰, so should be considered on a case by case basis.

10.6 Surgical treatment options

Although not performed by optometrists, it is imperative that optometrists understand the various surgical treatment options available to glaucoma patients (Table 8, over page).



Table 8: surgical treatment options for glaucoma

Technique	Notes
Lens extraction	<p>IOP reduction following lens extraction is debated in the literature, but may be associated with higher preoperative IOP and narrow angles.</p> <p>As it is still a surgical procedure, it is typically used as a surgical treatment of convenience, when it will be performed anyway, rather than as a first-line treatment for glaucoma.</p>
Minimally invasive glaucoma surgery (MIGS)	<p>The aim of MIGS is to enhance aqueous outflow and can be further classified into trabecular, suprachoroidal or subconjunctival.</p> <p>MIGS may be beneficial in a subset of patients who require concurrent cataract surgery or top-up for IOP reduction; there is insufficient evidence at this stage for its use as a first-line treatment option.</p> <p>The current role of the optometrist is primarily for identifying individuals suitable for this type of intervention. Indications include: issues with medical therapy (adverse effects, quality of life, compliance)^{248,249}, a less invasive alternative to incisional surgery²⁵⁰ and/or concurrent cataract surgery²⁵¹.</p> <p>Most commonly, IOP spikes following the procedure have been reported²⁵⁰ and mild transient hyphema²⁵².</p>
Filtration/incisional surgery	<p>It is currently the gold standard for glaucoma surgery, especially when a low IOP is required²⁵³ and is typically reserved for advanced cases of glaucoma.</p> <p>Essentially, the surgical procedure creates a new channel (fistula) between the anterior chamber and subconjunctival space. Thus, the IOP reduction obtained using filtration surgery tends to be dramatic and much higher compared to other treatment modalities.</p> <p>The current role of the optometrist is primarily in identification of complications from filtration surgery (e.g. wound leak or separation, bleb failure, hypotony, haemorrhage, blebitis, endophthalmitis, over or under filtration, pupillary block, and cataract formation/progression). These should be promptly referred to the operating surgeon for review^{254,255}, as some complications may be sight-threatening.</p>
Tube shunts	<p>Growing in popularity in the surgical management of glaucoma</p> <p>Tube, with a valve, is inserted in the eye and shunts aqueous</p> <p>The current role of the optometrist is to identify complications from the surgery, such as; infection or hypotony, diplopia, tube shunt erosion or tube failure²⁵⁶.</p>

10.7 Emerging therapies

The role of agents to support neural health or provide neuroprotection to the retinal ganglion cells has been a topic of interest complementing conventional intraocular pressure lowering therapies. Dietary supplementation with vitamin B3 (nicotinamide) has been shown by a variety of animal studies to reduce vulnerability to glaucoma by supporting the neural elements of the eye²⁵⁷. Studies in humans have identified the possible role of mitochondrial health in glaucoma^{258,259}. More recently, inner retinal functional has been shown to be improved through administration of nicotinamide supplementation²⁶⁰.

Nitric oxide is thought to directly trigger relaxation of the trabecular meshwork¹. Nitric oxide is also suggested to relax the vessel within the canal of Schlemm²⁶¹. A topical medication that is available overseas, latanoprostene bunod, incorporates nitric oxide by being a nitric oxide donor, releasing it to the trabecular meshwork upon metabolism²⁶².

By adding another mechanism of action to reduce intraocular pressure, nitric oxide may complement existing anti-glaucoma medications, thereby further lowering intraocular pressure²⁶³.

Netarsudil 0.02% (Rhopressa) is a new antiglaucoma medication in the new rho kinase class. It primarily acts on trabecular meshwork cells, preventing assembly and stabilisation of actin fibres, to increase the pore size and outflow and subsequently reduce IOP. However they also increases blood vessel diameter reducing resistance to aqueous outflow, and inhibit norepinephrine (which is thought to mimic alpha 2 agonists) and reduce aqueous production²⁶⁴. There is potential research that they may have neuroprotective elements with more investigation to come²⁶⁵.

11. Patient compliance and review

Compliance and adherence, terms used interchangeably, are universal issues for practitioners involved in glaucoma management²⁶⁶⁻²⁷⁰. In glaucoma management, compliance refers to the patient's behaviours relating to use of topical medications in accordance to the healthcare providers' prescribed instructions.

Patients naturally want to be thought of positively and will try to conceal non-compliance from their clinicians²⁷¹. Hence, it is important for clinicians to be aware of the reasons for non-compliance and strategies to that can be used to improve patient compliance.

The most commonly reported barriers to glaucoma medication compliance are listed in Table 9²⁷². Most patients (61%) reported multiple barriers. Of the patients who admitted to non-compliance, the barriers they felt were of greatest importance were poor self-efficacy to carry out the treatment strategy, difficulty instilling drops, forgetfulness and difficulties with medication schedule.

Table 9: Adapted from Newman-Casey et al, The Most Common Barriers to Glaucoma Medication Adherence- A Cross-Sectional Survey, Ophthalmology 2015; 122:1308-1316

Scepticism that glaucoma will cause vision loss
Scepticism that glaucoma medications will mitigate vision loss
Poor self-efficacy
Poor knowledge about glaucoma
Mistrust of Physician
Life stress
Forgetfulness
Difficulties with medication schedule
Medication cost
Medication-linked side effects
Difficulty with eye drop administration

Barriers to compliance can be attributable to a number of different factors:

- Disease-related factors: mild to moderate glaucoma less compliant compared to those with severe disease²⁷³.
- Treatment-related factors: more than two doses per day^{248,274}, lack of perceived effectiveness and unwanted side-effects²⁷⁵.
- Patient demographic and social factors: male gender²⁴⁸, ethnic minority^{270, 276, 277}, below average socioeconomic status²⁷⁸.
- Knowledge, attitude and health behaviour-related factors: self-reported poor health²⁷⁶, less knowledge of glaucoma^{248,275} and a poor relationship with treating clinician²⁷⁹.

Clinical pearl

As a greater understanding of glaucoma and better patient-practitioner relationships can influence patient compliance, clinicians can directly impact the rate of vision loss in glaucoma patients^{126,279}. Good communication between patients and their treating clinicians facilitate early identification of patients who have suboptimal compliance and encourage positive behaviour change.

12. Progression analysis and periodic review

Once treatment is initiated, regular review is mandatory to ensure optimal treatment outcomes. Routine review serves several purposes:

- To assess structure and function for any progressive change over time. Progression analysis software on OCT and visual field are useful for this purpose.
 - There is debate regarding the progression rates of visual fields whilst a patient is on treatment, and will be different for each patient depending on age, level of glaucoma control and starting values/amount of vision loss²⁸⁰. A numerical value for the significance of structural change in OCT scans cannot be given as it will vary depending on the precision and repeatability of the instrument, the OCT test type (ganglion cell or RNFL), and the nature of the instruments normative database. OCT progression analysis software is required to flag statistically significant rates of progression²⁸¹. Not all glaucoma progresses structurally and functionally at the same time, and function-form tests are not always linear. Confirmed repeatable structural or functional progression on one test alone would generally require an escalation in therapy and lower target IOP.
- To adjust pharmacotherapy if target IOP is no longer met
 - The target intraocular pressure required to stabilise glaucoma is unknown for each individual optic nerve. Periodic review of ocular structure and function is required, and if the patient's glaucoma is progressively deteriorating then a lower intraocular pressure may be required.
- To assess patient adherence and explicitly discuss compliance with prescribed therapy
- To detect the development of side effects or intolerance to therapy
- To determine whether laser or surgery is now a more effective treatment option
 - Regular review allows the practitioner to determine if initial topical therapy may no longer be the best treatment alternative. If glaucoma cannot be stabilised on maximum medical therapy, the patient is allergic or intolerant to a number of glaucoma drug classes, patient is not compliant to dosing regime or pharmacotherapy is contraindicated due to systemic side effects, then referral for laser or surgical intervention may be indicated.

Once target IOP is met and structural and functional stability is achieved, the review schedule can be extended to every 6 months, which coincides with the maximum number of drug repeats that can be prescribed to patients. Review schedules however should always be titrated to the level of practitioner concern and the risk of progression. Review should also be practical for the patient; e.g. a patient living far away or whom may be unable to financially afford care should provide additional considerations for the plan.

13. Collaborative eye care in glaucoma

Collaborative care between optometry and ophthalmology in order to provide optimal, patient-centric care is encouraged. Optometrists should follow the guidelines of the Optometry Board of Australia (OBA) with regard to glaucoma management. The current OBA guidelines stipulate that in cases where glaucoma is diagnosed, “the optometrist must provide the patient with a referral to an ophthalmologist or ophthalmology service within four months of starting treatment for chronic glaucoma”. Other triggers for referral include “if the anti-glaucoma treatment does not stabilise the patient’s condition, if a patient needs assessment by an ophthalmologist or ophthalmology service for possible surgical intervention or laser treatment or if a patient experiences side effects of initial treatment”. The role of the ophthalmologist is to formulate an ongoing collaborative care management plan agreed upon parties involved (patient, optometrist and ophthalmologist).

Review periods are then dependent on the patient’s condition: if their glaucoma is unstable, or if assessment for potential laser treatment or surgical intervention is indicated, or if a patient experiences side effects to the initial treatment, then referral back to the ophthalmologist is indicated¹⁴³.

These guidelines, provided the optometrist is therapeutically endorsed, prevent overloading the ophthalmology system so that limited ophthalmology resources can be utilised in more advanced disease²⁸².

Collaborative care needs to be planned. The scope of care needs to be understood by all parties and communication needs to be clear to ensure follow-up and minimise medico-legal risks. The patient needs to consent to the care arrangement and to be advised whom they can turn to at various stages of their care. Communication is the linchpin of effective shared care and clearly defined and agreed roles and responsibilities are essential for each health-care practitioner.

Additional considerations include involving the general practitioner or other physicians in the care of the patient. Given that glaucoma is a chronic disease and that prescription of medications may interact with other systemic drugs, it is important to ensure that all team members in the care of the patient are aware of the management plan. Communication of the results should be in a form that is readable to all practitioners. It is advisable to use electronic proformas that make communications more consistent. This principle should be applied to referrals and reports^{283,284}. Consider centralisation of records, such as in My Health Record or similar, so information is available to all of the healthcare team.

Glaucoma Australia is another useful resource for glaucoma patients and their relatives. They encourage regular eye examinations, provide patient support and aim to improve treatment compliance.



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