These guidelines have been withdrawn

MOH clinical practice guidelines are considered withdrawn five years after publication unless otherwise specified in individual guidelines. Users should keep in mind that evidence-based guidelines are only as current as the evidence that supports them and new evidence can supersede recommendations made in the guidelines.
## Levels of evidence and grades of recommendation

### Levels of evidence

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia</td>
<td>Evidence obtained from meta-analysis of randomised controlled trials.</td>
</tr>
<tr>
<td>Ib</td>
<td>Evidence obtained from at least one randomised controlled trial.</td>
</tr>
<tr>
<td>IIa</td>
<td>Evidence obtained from at least one well-designed controlled study without randomisation.</td>
</tr>
<tr>
<td>IIb</td>
<td>Evidence obtained from at least one other type of well-designed quasi-experimental study.</td>
</tr>
<tr>
<td>III</td>
<td>Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.</td>
</tr>
<tr>
<td>IV</td>
<td>Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.</td>
</tr>
</tbody>
</table>

### Grades of recommendation

<table>
<thead>
<tr>
<th>Grade</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.</td>
</tr>
<tr>
<td>B</td>
<td>Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.</td>
</tr>
<tr>
<td>C</td>
<td>Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.</td>
</tr>
<tr>
<td>GPP</td>
<td>Recommended best practice based on the clinical experience of the guideline development group.</td>
</tr>
</tbody>
</table>
Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient in the light of the clinical data presented by the patient and the diagnostic and treatment options available.
Foreword

The World Health Organization 2002 global data on visual impairment reported glaucoma as the second leading cause of blindness, accounting for 12.3% of the total 37 million people who were blind.

In Singapore, a cross-sectional population survey of the Tanjong Pagar district reported the prevalence of glaucoma as 3.2% in the Chinese population aged 40 years and above in 2000. As Singapore’s population ages, we can expect the incidence of glaucoma to rise, which in turn would lead to increased health care costs.

Patients with the various forms of glaucoma may present differently. Some may have “silent” disease until irreversible changes have occurred, and others who present acutely would require prompt treatment to ensure good clinical outcomes and to prevent further deterioration. Primary care physicians play an important role in recognizing and instituting early treatment in order to improve outcomes. It is also important for medical practitioners to be aware of the various risk factors of glaucoma so that patients can be diagnosed and treated early to prevent irreversible damage.

It is hoped that this set of guidelines will assist primary care physicians and ophthalmologists in the evidence-based management of patients with glaucoma.

PROFESSOR K SATKU
DIRECTOR OF MEDICAL SERVICES
## Contents

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<td>Self-assessment (MCQs)</td>
<td>35</td>
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<td>Workgroup members</td>
<td>38</td>
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</tbody>
</table>
Diagnosis of glaucoma and screening

Glaucoma is defined as an optic neuropathy with characteristic changes in the optic nerve head and visual field. Raised intraocular pressure (IOP) is the main risk factor for the development and progression of this disease.

**C** Patients suspected of having glaucoma should undergo the following three baseline tests:
- IOP measurement by Goldmann Applanation Tonometry
- Disc documentation, preferably by photography
- Perimetry

(grade: C, level: IV)

**B** The visual acuity and IOP are neither specific nor sensitive enough in themselves to be effective diagnostic or screening tools. (grade: B, level: IIa)

**GPP** IOP measurements should be combined with disc and visual field examination for greater sensitivity and specificity. (grade: GPP)

**C** IOP measurement, disc appearance and perimetry should be monitored during follow-up. (grade: C, level: IV)

**B** Routine population screening for glaucoma is **not** recommended at this stage. However, high-risk individuals such as first degree relatives of a glaucoma patient, age ≥65 years and elderly Chinese females (who are at risk of angle closure glaucoma) may be considered as target populations for case detection programmes. (grade: B, level: IIa, IIb)
Management of glaucoma

The goal of treatment in glaucoma is to maintain useful visual function and the patient’s quality of life at a sustainable cost.

**A** IOP lowering is the only clinically effective approach in the management of glaucoma. (pg 15)  
Grade A, Level Ia

**C** The target IOP is an estimate of the mean IOP achieved with treatment that is expected to prevent further optic nerve damage. An individualised target IOP range should be set for every glaucoma patient. (pg 15)  
Grade C, Level IV

**C** The first line of treatment in Primary Open Angle Glaucoma is medical therapy and the choice of the drug depends on the target IOP, the safety profile of the drug, patient acceptance and cost. (pg 17)  
Grade C, Level IV

**A** The first line of treatment in Primary Angle Closure Glaucoma is a laser iridotomy. A laser iridotomy is also required for the fellow eye. Supplemental medical therapy may also be required. (pg 17)  
Grade A, Level Ib

**C** In the emergency setting of acute angle closure glaucoma, additional systemic drugs like osmotic diuretics and oral/parenteral carbonic anhydrase inhibitors may be employed to rapidly reduce the IOP to avoid permanent, devastating nerve damage. (pg 17)  
Grade C, Level IV

**A** In Open Angle Glaucoma, laser trabeculoplasty may be used as an adjunct to medical therapy. (pg 20)  
Grade A, Level Ia

**C** Surgery is indicated in patients who fail or are unable to comply with medical therapy and may be combined with cataract removal for enhanced visual rehabilitation. (pg 21)  
Grade C, Level IV

**C** Trabeculectomy is the primary surgery of choice in medically uncontrolled glaucoma. (pg 21)  
Grade C, Level IV
Patients who have undergone glaucoma surgery should be advised that there is a lifelong need to be aware of symptoms of infection, which include blurring of vision, pain, redness, discharge and swelling. (pg 21)

Steroid eye drops are a frequently unrecognised cause of glaucoma. They should only be used as short-term therapy and IOP monitoring is vital in such patients. (pg 4)

Grade C, Level IV
1 Introduction

1.1 Definition

Glaucoma is an optic neuropathy with characteristic changes in the optic nerve head and visual field. Raised intraocular pressure (IOP) is the main risk factor for the development and progression of this disease.1-5

1.2 Disease Spectrum and Broad Classification

The spectrum of glaucoma is reflected in the following classification:

1.2.1 Primary Glaucoma

a. Primary open angle glaucoma (POAG)

b. Primary angle closure glaucoma (PACG)
   i. Acute angle closure glaucoma (AACG)
   ii. Chronic angle closure glaucoma (CACG)

1.2.2 Secondary Glaucoma including the following major causes:

a. Steroid-induced
b. Uveitic
c. Rubeotic
d. Others

1.2.3 Congenital / Developmental / Juvenile Glaucoma

1.2.4 Ocular Hypertension / Glaucoma Suspects

Steroid eye drops are a frequently unrecognised cause of glaucoma. They should only be used as short-term therapy and IOP monitoring is vital in such patients. Grade C, Level IV

This is especially so in those who have been applying them for more than 1 week, and includes steroid eye drops produced in combination with an antibiotic. Doctors must also ascertain that the patient has not already received similar therapy recently, before initiating a course of steroid eye drops.6-9
1.3 Epidemiology of Glaucoma

Based on the WHO Global Data Bank on Blindness, glaucoma accounts for 5.1 million of the estimated 38 million blind in the world. As the number of elderly in the world rapidly increases, glaucoma morbidity will rise, causing increased health care costs and economic burden in the future. It has been estimated that glaucoma will be the most common cause of irreversible blindness in the world this century with almost 70 million cases of glaucoma worldwide.

1.3.1 Primary Open Angle Glaucoma

Primary open angle glaucoma (POAG) accounts for about two thirds of all glaucoma seen in Caucasian populations and is also the main form of glaucoma in Afro-Carribeans. The angle of the anterior chamber appears open but does not function properly in transporting aqueous humour out of the eye.

Most POAG cases are found in the elderly, especially those above 60 years. In the classical form of the disease, the IOP is raised, usually above 21 mmHg, and such patients are classified as high tension glaucoma. Normal tension glaucoma (NTG) is an important subtype of POAG, in which the IOPs are consistently within the statistically normal population range. NTG accounts for approximately a third (range 20% to 50%) of all POAG cases. Another sub-category of patients present with raised IOPs without evidence of nerve or field damage – these are defined as having ocular hypertension (OHT), and have to be monitored for the development of glaucomatous damage.

1.3.2 Primary Angle Closure Glaucoma

Primary angle closure glaucoma (PACG) is a major form of glaucoma in Asia. This is true especially in populations of Chinese and Mongoloid descent. Recent glaucoma prevalence studies in southern India found that the prevalence of PACG in Indians is also high. The estimated high prevalence of PACG in China and India make PACG a major form of glaucoma worldwide, possibly as common as POAG. In China itself, it is estimated that PACG afflicts 3.5 million people and 28 million have an occludable drainage angle, the anatomical trait predisposing to PACG.
1.3.3 Glaucoma in Singapore

Previous studies have shown that glaucoma is a major cause of visual morbidity in Singapore.\textsuperscript{22,25,26} In a recent population based survey conducted on Chinese Singaporeans in the Tanjong Pagar district, the age-standardized prevalence of glaucoma was found to be 3.2\% (95\% confidence interval, 2.3-4.1) in the population 40 years and older.\textsuperscript{22} Glaucoma was the leading cause of blindness, with primary angle-closure glaucoma the most visually destructive form of the disease. Chinese Singaporeans were also found to have the world’s highest recorded incidence of acute primary angle closure glaucoma.\textsuperscript{27}

1.4 Objectives of Guidelines

This volume aims to provide enough evidence-based information to guide the physician or ophthalmologist in:

• Diagnosing the various forms of the disease, with the main focus on primary glaucomas
• Ordering the appropriate investigations
• Instituting safe, evidence-based treatment where possible
• Educating and counselling the patient on the nature of the disease and the risks and benefits of treatment

1.5 Guideline Development

These guidelines were developed by an expert workgroup nominated by the National Committee on Ophthalmology. The workgroup, comprising ophthalmologists from both the public and private sectors, as well as a general practitioner, conducted a systematic review of the current medical literature and, taking into account our local context, have summarised their findings in the pages that follow.
1.6 **Target Group**

These guidelines are aimed at all primary health care physicians and ophthalmologists involved in the diagnosis and care of glaucoma patients.

1.7 **Review of Guidelines**

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review five years after publication, or if new evidence appears that requires substantive changes to the recommendations.
2 Diagnosis of Glaucoma

The primary glaucomas are usually bilateral although the disease may be asymmetrical.

The chronic glaucomas (POAG and PACG) are asymptomatic and the visual acuity can be normal till an advanced stage and hence patients with chronic glaucoma are often missed until one eye has sustained significant and irreversible damage.

Acute angle closure glaucoma (AACG) however, presents with very striking signs and symptoms, which if promptly recognized and treated, may result in a good outcome.

*The clinical features of the primary glaucomas are summarised in Table 1. Please note that this list of signs and symptoms highlights key features, and is not exhaustive. Please also refer to the photographs displayed on the following pages.*

Table 1 Clinical Features of the Primary Glaucomas

<table>
<thead>
<tr>
<th>SYMPTOMS</th>
<th>Acute Angle Closure Glaucoma</th>
<th>Primary Open Angle Glaucoma &amp; Chronic Angle Closure Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Painful red eye</td>
<td></td>
<td>• Usually asymptomatic till advanced stages of the diseases</td>
</tr>
<tr>
<td>• Blurring of vision, haloes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Severe headache, nausea and vomiting</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• History of similar episodes in the past,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>which were aborted spontaneously with sleep</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• The patient is frequently an elderly Chinese lady</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SIGNS</th>
<th>Acute Angle Closure Glaucoma</th>
<th>Primary Open Angle Glaucoma &amp; Chronic Angle Closure Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual Acuity</td>
<td>Decreased</td>
<td>Normal / decreased in advanced stages</td>
</tr>
<tr>
<td>Conjunctiva</td>
<td>Injected</td>
<td>Normal</td>
</tr>
<tr>
<td>Cornea</td>
<td>Hazy in symptomatic eye</td>
<td>Clear</td>
</tr>
</tbody>
</table>
### SIGNS

<table>
<thead>
<tr>
<th>Anterior Chamber</th>
<th>Acute Angle Closure Glaucoma</th>
<th>Primary Open Angle Glaucoma &amp; Chronic Angle Closure Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shallow in both eyes Positive “eclipse sign” (nasal iris not illuminated by light shone from the temporal side, see Fig.1 on page 12)</td>
<td>Deep in both eyes</td>
<td>POAG - open angles; CACG - closed angles</td>
</tr>
<tr>
<td>Gonioscopy</td>
<td>Closed angles</td>
<td>Usually higher than 21 mmHg,</td>
</tr>
<tr>
<td>IOP</td>
<td>Much higher than 21 mmHg and the eye may feel harder than fellow eye on digital palpation</td>
<td></td>
</tr>
<tr>
<td>Pupil</td>
<td>Mid-dilated in symptomatic eye</td>
<td>Relative Afferent Pupillary Defect (RAPD) if asymmetrical involvement</td>
</tr>
<tr>
<td>Optic disc</td>
<td>May be difficult to examine due to hazy cornea. Can be normal, hyperemic or cupped if there have been previous neglected attacks</td>
<td>Vertical cup disc ratio ( \geq 0.7 ) in a normal-sized disc Increase in cup disc ratio over time A symmetry in cup disc ratio ( \geq 0.2 ) between the 2 eyes Flame-shaped haemorrhages that extend across the disc margin (splinter haemorrhages) Focal loss of neuroretinal rim (notching)</td>
</tr>
<tr>
<td>Visual Field</td>
<td>If glaucomatous nerve damage has been sustained perimetry shows defects that are consistent with nerve fibre layer loss and these include: Temporal island Central island in advanced glaucoma Nasal step Paracentral or arcuate scotomas</td>
<td></td>
</tr>
</tbody>
</table>
Clinical Photos

A. Healthy Optic Disc

In Photo 1, a healthy neuro-retinal rim is seen all around, without any focal thinning. The cup-disc ratio is 0.4.

B. Glaucomatous Optic Disc Changes

The hallmark of glaucoma is thinning and damage to the neuro-retinal rim of the optic disc, resulting in the following appearances:

- **Increased Cup-Disc Ratio (C/D)** - for a normal-sized disc, a C/D ratio of ≥0.7 is generally considered suspicious, especially if increasing over time. C/D asymmetry of more than 0.2 between left & right discs is also significant. In Photo 2, the rim is uniformly thinned out, giving a cup-disc ratio of 0.8.
• **Focal thinning or notching** of the neuro-retinal rim (in Photo 3, the inferior rim is significantly thinned out. The arrow denotes a blood vessel exiting at the very edge of the disc, as there is no rim for it to ‘climb over’.)

![Photo 3: Focal thinning or notching](image)

• **Optic disc haemorrhage** (as indicated by the arrow in Photo 4)

![Photo 4: Optic disc haemorrhage](image)

• **An eye with Acute Angle Closure Glaucoma** (Photo 5)
  Refer to the table on the previous page for a description of the classic signs.

![Photo 5: An eye with acute angle closure glaucoma](image)
While cases of acute angle closure glaucoma have fairly characteristic history and signs to guide the diagnosis, patients with chronic glaucoma may have no symptoms or signs, apart from abnormal pupil light reflexes and optic disc cupping.

The following individuals are known to have a higher risk of glaucoma:
- High myopia and hypermetropia$^{28-33}$
- Family history of glaucoma, especially in first degree relatives$^{34-36}$
- Age $\geq 65$ years$^{37-39}$
- Previous history of significant trauma to the eye$^{40-42}$
- Elderly Chinese females (angle closure glaucoma)$^{43}$
- Long term use of topical steroid eye drops$^{7-9}$
3 Diagnostic Evaluation and Monitoring of Glaucoma

3.1 Baseline Tests

C Patients suspected of having glaucoma should undergo the following three baseline tests:44,45

- IOP measurement by Goldmann Applanation Tonometry
- Disc documentation, preferably by photography
- Perimetry

Grade C, Level IV

B The visual acuity and IOP are neither specific nor sensitive enough in themselves to be effective diagnostic or screening tools.46,47

Grade B, Level IIa

GPP IOP measurements should be combined with disc and visual field examination for greater sensitivity and specificity.

GPP

The following ancillary tests may also be employed, depending on the clinical context

- Optic Nerve Head & Nerve Fibre Layer Imaging
- Other psycho-physical tests (e.g. Short Wavelength Automated Perimetry, Frequency Doubling Threshold, etc)
- Central Corneal Thickness
- Phasing (regular IOP measurements through the day to track diurnal variation)

3.2 Follow-Up

The frequency of follow-up testing is decided by the clinician based on

- Severity of disease
- Level of current IOP compared to target IOP
- Patient compliance factors
- Clinic resources
IOP measurement, disc appearance and perimetry should be monitored during follow-up.⁴⁴,⁴⁵

**Grade C, Level IV**

The primary health physician can aid in the management of glaucoma patients by stressing compliance with medication and follow-up visits, and also by keeping watch for common adverse effects of glaucoma medications.
4 Treatment of Glaucoma

4.1 Goals of Therapy

In all forms of glaucoma, the goal of treatment is to maintain useful visual function and the patient’s quality of life at a sustainable cost. At present, visual loss from glaucoma cannot be restored. Effective treatment can only preserve residual visual function by preventing loss of the remaining optic nerve fibres.

4.2 IOP lowering is the only clinically effective approach in the management of glaucoma.1-5

Grade A, Level Ia

The target IOP is an estimate of the mean IOP achieved with treatment that is expected to prevent further optic nerve damage. An individualised target IOP range should be set for every glaucoma patient.44,45

Grade C, Level IV

The target IOP is modulated by:

• the IOP before treatment
• the stage of the disease
• the age, life expectancy and visual requirements of the patient
• the rate of progressive damage, as well as the presence of other risk factors.

The target IOP range for each patient must be regularly reviewed and reset if necessary, depending on the individual clinical course.

In general, the younger the patient, and the higher the overall risk of progression to blindness within the lifetime, the lower the target IOP needs to be. For instance, the target IOP range may be from 10 to 14 mmHg, 15 to 17 mmHg, or 18 to 20 mmHg, depending on the severity of the disease and patient profile.
4.3 IOP goals in specific groups of glaucoma patients

Recent large prospective randomised clinical trials conducted in the US have provided some benchmarks that should guide the clinician when managing specific categories of glaucoma patients.

It is recommended that glaucoma therapy in the local context should be informed by, but not unduly constrained by, or indiscriminately adherent to, the following trials:

1. The Collaborative Normal Tension Glaucoma Study (CNTGS)\(^1\)
2. The Advanced Glaucoma Intervention Study (AGIS)\(^2\)
3. The Collaborative Initial Glaucoma Treatment Study (CIGTS)\(^3\)
4. The Early Manifest Glaucoma Trial (EMGT)\(^4\)
5. The Ocular Hypertension Treatment Study (OHTS)\(^5\)

### Table 2 Glaucoma Trials

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Study</th>
<th>Intervention</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normotension glaucoma (normal IOP)</td>
<td>CNTGS</td>
<td>40% IOP reduction (mean 11 mmHg)</td>
<td>40% reduction in progression at 5 years</td>
</tr>
<tr>
<td>Advanced OAG</td>
<td>AGIS</td>
<td>IOP &lt;18 mmHg in all visits (mean 12.3 mmHg)</td>
<td>No progression at 8 years</td>
</tr>
<tr>
<td>Newly diagnosed open angle glaucoma</td>
<td>CIGTS</td>
<td>37% IOP reduction (mean 17 mmHg)</td>
<td>No progression at 5 years</td>
</tr>
<tr>
<td>Early open angle glaucoma</td>
<td>EMGT</td>
<td>25% IOP reduction</td>
<td>17% reduction in progression at 6 years</td>
</tr>
<tr>
<td>Ocular hypertension (normal VF and Discs)</td>
<td>OHTS</td>
<td>18% IOP reduction</td>
<td>5% reduction in developing glaucoma at 5 years</td>
</tr>
</tbody>
</table>
4.4 Pharmacological Treatment of Glaucoma

C The first line of treatment in Primary Open Angle Glaucoma is medical therapy and the choice of the drug depends on the target IOP, the safety profile of the drug, patient acceptance and cost.

Grade C, Level IV

Single or combination therapy may have to be instituted to achieve the target IOP without adverse effects or incurring unreasonable cost to the patient.

Drugs for IOP lowering include:
• Beta-Blockers\textsuperscript{48,49}
• Prostaglandins and Prostamides\textsuperscript{50-54}
• Adrenergic Agonists\textsuperscript{55,56}
• Carbonic Anhydrase Inhibitors\textsuperscript{57,58}
• Parasympathetic (Cholinergic) Agonists\textsuperscript{59,60}

A The first line of treatment in Primary Angle Closure Glaucoma is a laser iridotomy. A laser iridotomy is also required for the fellow eye. Supplemental medical therapy may also be required.

Grade A, Level Ib

C In the emergency setting of acute angle closure glaucoma, additional systemic drugs like osmotic diuretics and oral/parenteral carbonic anhydrase inhibitors may be employed to rapidly reduce the IOP to avoid permanent, devastating nerve damage.\textsuperscript{44,45}

Grade C, Level IV
## Common medications used in the treatment of glaucoma

<table>
<thead>
<tr>
<th>Medicine Name</th>
<th>Action</th>
<th>Possible Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta Blockers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Timolol⁴⁸,⁴⁹ (Timoptol®)</td>
<td>Non-selective beta-blocker. Reduces the production of aqueous humour into the eye.</td>
<td>Irritation/stinging on instillation, pain, allergic reaction, decreased vision, corneal surface problems. May aggravate existing lung problems such as asthma and emphysema. Heart problems include lowered blood pressure, and heart failure may be worsened. Fatigue, giddiness, depression, impotence, insomnia and hair loss.</td>
</tr>
<tr>
<td>Timolol suspension⁶³ (Timoptol XE®)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levobunolol (Betagan®)⁶⁴,⁶⁵</td>
<td>Similar to timolol.</td>
<td>Similar to timolol. May additionally cause inflammation of the eyes, transient decreased vision.</td>
</tr>
<tr>
<td>Betaxolol (Betoptic®)</td>
<td>Selective beta1-blocker. Similar to timolol.</td>
<td>May be safer for patients with asthma and emphysema compared to timolol. Other side effects are similar to timolol.</td>
</tr>
<tr>
<td>Betaxolol suspension (Betoptic S®)⁶⁵</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Adrenergic Agonists</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adrenaline (Eppy®, Epifrin®)⁶⁶-⁶⁹</td>
<td>Alpha and beta agonist. Reduces aqueous humour production.</td>
<td>Redness, eyelid inflammation, itching, and pigment deposits in the conjunctiva frequent. May increase failure rate of filtration surgery. May cause tachycardia, nervousness, headache, pupillary dilation and can exacerbate angina.</td>
</tr>
<tr>
<td>Medicine Name</td>
<td>Action</td>
<td>Possible Side Effects</td>
</tr>
<tr>
<td>---------------</td>
<td>--------</td>
<td>-----------------------</td>
</tr>
<tr>
<td><strong>Dipivefrine</strong>&lt;sup&gt;68-72&lt;/sup&gt; (Propine&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>Adrenaline pro-drug, converted to active adrenaline within eye.</td>
<td>Reduced incidence of side effects compared to adrenaline.</td>
</tr>
<tr>
<td><strong>Apraclonidine</strong>&lt;sup&gt;55,73,74&lt;/sup&gt; (Iopidine&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>Alpha2-adrenergic agonist. Reduces aqueous humour production.</td>
<td>May cause redness, irritation / stinging, allergic reaction, pupil enlargement. Long-term use occasionally associated with loss of effectiveness.</td>
</tr>
<tr>
<td><strong>Brimonidine</strong>&lt;sup&gt;56,73,74&lt;/sup&gt; (Alphagan&lt;sup&gt;®&lt;/sup&gt;)</td>
<td>Highly selective alpha2-adrenergic agonist. Similar to apraclonidine.</td>
<td>Irritation, stinging, redness. Generally avoided in patients using some antidepressants, and in patients with increased blood pressure associated with severe circulatory disease.</td>
</tr>
</tbody>
</table>

**Parasympathetic Agonists**

- **Pilocarpine**<sup>59,60,75,76</sup> (Isoptocarpine<sup>®</sup>)
- **Pilocarpine gel**<sup>59,60,75,76</sup> (Pilogel<sup>®</sup>)

Increases drainage of aqueous humour out of the eye. 

Eye or brow ache common when first applying eyedrops; improves with time. Blurred vision, dim vision, small pupil. Induced near-sightedness may occur in younger patients.

**Carbonic Anhydrase Inhibitors**

- **Acetazolamide**<sup>57,75,78</sup> (Diamox<sup>®</sup>)

Reduces formation of aqueous humour. Administered orally or intravenously 

Tingling sensation in fingers and toes. May have increased frequency of passing urine, kidney stones and electrolyte abnormalities. Abdominal upset, metallic taste with carbonated drinks, depression, fatigue, weight loss and impotence have been reported. Rarely, aplastic anaemia and severe allergic reactions occur.
**Table: Medical Intervention**

<table>
<thead>
<tr>
<th><strong>Medicine Name</strong></th>
<th><strong>Action</strong></th>
<th><strong>Possible Side Effects</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorzolamide (Trusopt®)(^{79,80})</td>
<td>Topical carbonic anhydrase inhibitor. Reduces production of aqueous humour.</td>
<td>Occasional stinging, allergic reaction, itch, bitter taste.</td>
</tr>
<tr>
<td>Brinzolamide (Azopt®)(^{58,81,82})</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Prostaglandin Analogues**

<table>
<thead>
<tr>
<th><strong>Medicine Name</strong></th>
<th><strong>Action</strong></th>
<th><strong>Possible Side Effects</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Latanoprost (Xalatan®)(^{50-52,83})</td>
<td>Increases drainage of aqueous humour from the eye via the uveoscleral outflow pathway.</td>
<td>Local stinging, irritation, allergic reaction and conjunctival hyperemia. May cause brownish colouration of the iris. May stimulate abnormal eyelash growth. Anecdotal reports of macular edema and re-activation of HSV keratitis.</td>
</tr>
<tr>
<td>Travoprost (Travatan®)(^{53,84-86})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bimatoprost (Lumigan®)(^{54,84-86})</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Hyperosmotic Agents**

<table>
<thead>
<tr>
<th><strong>Medicine Name</strong></th>
<th><strong>Action</strong></th>
<th><strong>Possible Side Effects</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mannitol(^{87,88})</td>
<td>Diuretic.</td>
<td>Nausea, vomiting, increased blood glucose levels in diabetics. Dehydration, headache, disorientation. Care in elderly patients with kidney disease, heart disease or diabetes. Acute retention of urine may occur.</td>
</tr>
<tr>
<td>Glycerol(^{87,89})</td>
<td>As for mannitol. Slower onset compared to intra-venous mannitol.</td>
<td>As for mannitol.</td>
</tr>
</tbody>
</table>

**4.5 Laser Therapy for Glaucoma**

> In Open Angle Glaucoma, laser trabeculoplasty may be used as an adjunct to medical therapy.\(^{90,91}\)

*Grade A, Level Ia*
4.6 **Surgery for Glaucoma**

C Surgery is indicated in patients who fail or are unable to comply with medical therapy and may be combined with cataract removal for enhanced visual rehabilitation.\(^{44,45}\)

**Grade C, Level IV**

C Trabeculectomy is the primary surgery of choice in medically uncontrolled glaucoma.\(^{92-94}\)

**Grade C, Level IV**

However, it may not always succeed and even if it does in the short term, it may still fail over time.

Augmentation with anti-metabolites has been found to increase the success rates of this surgery, but is also associated with a slightly higher risk of complications such as hypotony and infection.\(^{95-97}\)

Glaucoma drainage implant surgery (tube surgery) is generally reserved for complex glaucoma cases, in particular those with previous trabeculectomy failures.\(^{98-100}\)

**GPP** Patients who have undergone glaucoma surgery should be advised that there is a lifelong need to be aware of symptoms of infection, which include blurring of vision, pain, redness, discharge and swelling.

4.7 **Treatment of Secondary Glaucoma**

This is directed at identifying and managing the underlying cause, while simultaneously controlling the IOP.

4.8 **Screening for Glaucoma**

B Routine population screening for glaucoma is not recommended at this stage. However, high-risk individuals such as first degree relatives of a glaucoma patient, age \(\geq 65\) years and elderly Chinese females (who are at risk of angle closure glaucoma) may be considered as target populations for case detection programmes.\(^{101-104}\)

**Grade B, Level IIa, IIb**
Acute primary angle closure glaucoma produces a substantial financial burden on both the society and individuals. It was reported that each annual cohort of acute primary angle closure glaucoma in Singapore would need to pay about US$261,700 (S$444,900) for treatment over 5 years. The costs for treating chronic open and closed angle glaucoma, the most prevalent forms of glaucoma in Singapore, are likely to be far higher.

Total disease costs, including treatment costs, has been shown to rise with disease progression in glaucoma. In addition, non-compliance with a prescribed drug regimen not only decreases the efficacy of the therapy, but also increases treatment costs. Evidence suggests that early identification of appropriate therapeutic options can have beneficial effects on expenditures, and high frequency of treatment changes is associated with higher costs.

There is currently no evidence for population screening for glaucoma. Screening in high-risk patients would yield more favourable cost-effective ratios. For instance, it was reported that the cost-effectiveness ratio of screening patients aged 65 to 79 every 3 years ranged from Can$36,000 to Can$42,000 (S$52,600 to S$61,300) per year of blindness avoided. In contrast, a similar screening programme which includes screening of patients as young as 40 years would cost Can$74,000 to Can$100,000 (S$108,000 to S$146,000) per year of blindness avoided.
Clinical Quality Indicators

The following parameters may be used in clinical quality monitoring in the management of patients with glaucoma:

- Documentation of the optic nerve appearance, visual field and IOP in diagnosing glaucoma
- Documentation of target IOP range
- Reduction in IOP to the individualised target level range with treatment of glaucoma
- Achieving and maintaining visual field stability during the course of treatment and monitoring
## References


53. Fellman RL, Sullivan EK, Ratliff M et al. Comparison of travoprost 0.0015% and 0.004% with timolol 0.5% in patients with elevated intraocular pressure: a 6-month, masked, multicenter trial. Ophthalmology 2002;109:998-1008.


64. Halper LK, Johnson-Pratt L, Dobbins T, Hartenbaum D. A comparison of the efficacy and tolerability of 0.5% timolol maleate ophthalmic gel-forming solution QD and 0.5% levobunolol hydrochloride BID in patients with ocular hypertension or open-angle glaucoma. J Ocul Pharmacol Ther 2002;18:105-13.


82. Stewart WC, Day DG, Stewart JA, Holmes KT, Jenkins JN. Short-term ocular tolerability of dorzolamide 2% and brinzolamide 1% vs placebo in primary open-angle glaucoma and ocular hypertension subjects. Eye. 2004 Sep;18(9):905-10.


Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category III (Self-Study) of the SMC Online CME System. Before you login to claim the CME point, we encourage you to evaluate whether you have mastered the key points in the Guidelines by completing this set of MCQs. This is an extension of the learning process and is not intended to “judge” your knowledge and is not compulsory. The answers can be found at the end of the questionnaire.

Instruction: Choose the most appropriate answer/s. There may be more than one answer.

1. Glaucoma is defined by:
   A. Development of characteristic visual field changes
   B. Development of characteristic optic disc changes
   C. Intraocular pressure >21 mmHg
   D. A unilateral red and painful eye

2. The following groups of patients are at greater risk of having glaucoma, or developing abnormally high intraocular pressures:
   A. Those on long term use of a steroid-antibiotic combination eye drop.
   B. Elderly Chinese females
   C. Those with a positive family history of glaucoma
   D. Young adults

3. The following are symptoms and signs which suggest an acute angle closure attack:
   A. Severe headache and vomiting
   B. Positive “eclipse sign”
   C. Purulent discharge
   D. Hazy cornea
4. The following symptoms and signs may be present in a patient with advanced chronic glaucoma:

A. Relative Afferent Pupillary Defect (RAPD)
B. Normal visual acuity
C. Patient is asymptomatic
D. Increased cup-disc ratio

5. The main goals in the management of glaucoma are:

A. Reversing pre-existing visual field changes
B. Achieving an individualised target intraocular pressure for each patient
C. Regenerating ganglion cells at the optic disc
D. Preventing further visual loss

6. Adverse effects of commonly used glaucoma eye medications may include:

A. Abnormal eyelash growth
B. Aggravation of asthma
C. Worsening of congestive cardiac failure
D. Tingling sensation in fingers and toes

7. Fundoscopic examination of a glaucomatous optic disc may reveal:

A. Blurred disc margins
B. Thinning of the neuro-retinal rim
C. Decreased red reflex
D. Cup-disc ratio 0.9

8. In a recent survey conducted on Chinese Singaporeans, the prevalence of glaucoma in those over the age of 40 was found to be:

A. 0.032%
B. 0.32%
C. 3.2%
D. 32%
Answers

1. A, B (pg 4)
2. A, B, C (pg 12)
3. A, B, D (pg 8,9)
4. A, B, C, D (pgs 8,9)
5. B, D (pg 15)
6. A, B, C, D (pgs 18,19,20)
7. B, D (pgs 10,11)
8. C (pg 6)
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Acknowledgment:
• The Eye Institute @ Tan Tock Seng Hospital for clinical photos 1-4.
• The Singapore National Eye Centre for clinical photo 5 and Figure 1.
Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated.

Diganosis of glaucoma and screening

Glaucoma is defined as an optic neuropathy with characteristic changes in the optic nerve head and visual field. Raised intraocular pressure (IOP) is the main risk factor for the development and progression of this disease.

C Patients suspected of having glaucoma should undergo the following three baseline tests:

- IOP measurement by Goldmann Applanation Tonometry
- Disc documentation, preferably by photography
- Perimetry

(Grade C, Level IV)

B The visual acuity and IOP are neither specific nor sensitive enough in themselves to be effective diagnostic or screening tools. (Grade B, Level IIa)

GPP IOP measurements should be combined with disc and visual field examination for greater sensitivity and specificity. (GPP)

C IOP measurement, disc appearance and perimetry should be monitored during follow-up. (Grade C, Level IV)
Routine population screening for glaucoma is not recommended at this stage. However, high-risk individuals such as first degree relatives of a glaucoma patient, age ≥65 years and elderly Chinese females (who are at risk of angle closure glaucoma) may be considered as target populations for case detection programmes. (pg 21)

**Management of glaucoma**

The goal of treatment in glaucoma is to maintain useful visual function and the patient’s quality of life at a sustainable cost.

**A** IOP lowering is the only clinically effective approach in the management of glaucoma. (pg 15)

**Grade A, Level Ia**

**C** The target IOP is an estimate of the mean IOP achieved with treatment that is expected to prevent further optic nerve damage. An individualised target IOP range should be set for every glaucoma patient. (pg 15)

**Grade C, Level IV**

**C** The first line of treatment in Primary Open Angle Glaucoma is medical therapy and the choice of the drug depends on the target IOP, the safety profile of the drug, patient acceptance and cost. (pg 17)

**Grade C, Level IV**

**A** The first line of treatment in Primary Angle Closure Glaucoma is a laser iridotomy. A laser iridotomy is also required for the fellow eye. Supplemental medical therapy may also be required. (pg 17)

**Grade A, Level Ib**

**C** In the emergency setting of acute angle closure glaucoma, additional systemic drugs like osmotic diuretics and oral/parenteral carbonic anhydrase inhibitors may be employed to rapidly reduce the IOP to avoid permanent, devastating nerve damage. (pg 17)

**Grade C, Level IV**

**A** In Open Angle Glaucoma, laser trabeculoplasty may be used as an adjunct to medical therapy. (pg 20)

**Grade A, Level Ia**
Surgery is indicated in patients who fail or are unable to comply with medical therapy and may be combined with cataract removal for enhanced visual rehabilitation. (pg 21)

Trabeculectomy is the primary surgery of choice in medically uncontrolled glaucoma. (pg 21)

Patients who have undergone glaucoma surgery should be advised that there is a lifelong need to be aware of symptoms of infection, which include blurring of vision, pain, redness, discharge and swelling. (pg 21)

Steroid eye drops are a frequently unrecognised cause of glaucoma. They should only be used as short-term therapy and IOP monitoring is vital in such patients. (pg 4)

Clinical Features of the Primary Glaucomas

<table>
<thead>
<tr>
<th>SYMPTOMS</th>
<th>Acute Angle Closure Glaucoma</th>
<th>Primary Open Angle Glaucoma &amp; Chronic Angle Closure Glaucoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>SYMPTOMS</td>
<td><strong>Painful red eye</strong></td>
<td><strong>Usually asymptomatic till advanced stages of the diseases</strong></td>
</tr>
<tr>
<td></td>
<td><strong>Blurring of vision, haloes</strong></td>
<td></td>
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<tr>
<td></td>
<td><strong>Severe headache, nausea and vomiting</strong></td>
<td></td>
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<tr>
<td></td>
<td><strong>History of similar episodes in the past, which were aborted spontaneously with sleep</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>The patient is frequently an elderly Chinese lady</strong></td>
<td></td>
</tr>
<tr>
<td>SIGNS</td>
<td>Visual Acuity: Decreased</td>
<td>Normal / decreased in advanced stages</td>
</tr>
<tr>
<td></td>
<td>Conjunctiva: Injected</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Cornea: Hazy in symptomatic eye</td>
<td>Clear</td>
</tr>
<tr>
<td></td>
<td>Acute Angle Closure Glaucoma</td>
<td>Primary Open Angle Glaucoma &amp; Chronic Angle Closure Glaucoma</td>
</tr>
<tr>
<td>------------------</td>
<td>--------------------------------------------------------------------------------------------</td>
<td>-------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>SIGNS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior Chamber</td>
<td>Shallow in both eyes Positive “eclipse sign” (nasal iris not illuminated by light shone from the temporal side, see Fig.1 in main text page 12)</td>
<td>Deep in both eyes</td>
</tr>
<tr>
<td>Gonioscopy</td>
<td>Closed angles</td>
<td>POAG - open angles; CACG - closed angles</td>
</tr>
<tr>
<td>IOP</td>
<td>Much higher than 21 mmHg and the eye may feel harder than fellow eye on digital palpation</td>
<td>Usually higher than 21 mmHg</td>
</tr>
<tr>
<td>Pupil</td>
<td>Mid-dilated in symptomatic eye</td>
<td>Relative Afferent Pupillary Defect (RAPD) if asymmetrical involvement</td>
</tr>
<tr>
<td>Optic disc</td>
<td>• May be difficult to examine due to hazy cornea.</td>
<td>• Vertical cup disc ratio ≥0.7 in a normal-sized disc</td>
</tr>
<tr>
<td></td>
<td>• Can be normal, hyperemic or cupped if there have been previous neglected attacks</td>
<td>• Increase in cup disc ratio over time</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Asymmetry in cup disc ratio ≥0.2 between the 2 eyes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Flame-shaped haemorrhages that extend across the disc margin (splinter haemorrhages)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Focal loss of neuroretinal rim (notching)</td>
</tr>
<tr>
<td>Visual Field</td>
<td>If glaucomatous nerve damage has been sustained perimetry shows defects that are consistent with nerve fibre layer loss and these include:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Temporal island</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Central island in advanced glaucoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Nasal step</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Paracentral or arcuate scotomas</td>
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</tbody>
</table>