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PERSPECTIVE

The Finnish current care guideline for open-angle glaucoma

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This article is an English translation of the 4th Finnish Current Care Guideline for diagnostics, treatment and follow-up of primary open-angle glaucoma, normal-tension glaucoma and pseudoexfoliative glaucoma. This guideline is based on systematic literature reviews and expert opinions with Finland's geographical and operational healthcare environment in mind.

KEYWORDS
Current Care Guideline, normal-tension glaucoma, open-angle glaucoma, primary open-angle glaucoma, pseudoexfoliative glaucoma

1 | INTRODUCTION

This article is an English translation of the 4th Finnish Current Care Guideline for diagnostics, treatment and follow-up of primary open-angle glaucoma, normal-tension glaucoma and pseudoexfoliative glaucoma. This guideline is based on systematic literature reviews and expert opinions with Finland's geographical and operational healthcare environment in mind.

A guideline working group was assembled by The Finnish Medical Society Duodecim, the Finnish Association of Ophthalmologists and the Finnish Glaucoma Society. The group consisted of 10 glaucoma specialists representing university and central hospital clinics and private care. The working group worked in cooperation with Duodecim's Current Care Guideline editor-in-chief.

A systematic literature search was supported by Duodecim's Current Care Guidelines team, the Cochrane Eyes and Vision US project and European Glaucoma Society. The evidence was graded following the Grading of Recommendations Assessment, Development and Evaluation Working Group Guideline, GRADE (Guyatt et al., 2008). In Current Care Guidelines, grade A represents high quality of evidence, B moderate quality, C low quality and D very low quality of evidence. The Current Care Guideline process description is available online (Guideline process description, 2022). The applicability of results of the study population was considered, especially when evidence from the Finnish population was not available.

Evidence summaries were written. Summaries from previous guideline versions were utilised where applicable. The evidence summaries, additional background materials in either Finnish or English and references are available online at The Finnish Medical Society Duodecim website for Current Care Guidelines

(Glaucoma. Current Care Guidelines, 2023). The glaucoma working group discussed the evidence in January 2021–February 2022.

The process to reach consensus on the clinical recommendations was conversational and informal. Finnish universal healthcare with limited resources was considered when trying to define adequate care for patients with glaucoma and ocular hypertension. The working group considered what may represent undercare of glaucoma and overproduction of care, so that resources could be sensibly distributed and at-risk patients would receive the treatment they needed. The group summed up the available evidence and limitations in bullet points in the guideline. The pragmatic recommendations for everyday clinical practice are presented in nine tables. Sixty-three stakeholders were requested to review the guidelines, and 16 responded. Reviewers' suggestions were discussed in the working group and the guidelines were edited accordingly. The guideline was published on 28th of March 2023 online at www.kaypahoito.fi.

2 | GOALS AND LIMITATIONS

- In this guideline, the term open-angle glaucoma refers to
  - primary open-angle glaucoma
  - pseudoexfoliative glaucoma, and
  - normal-tension glaucoma.
- In addition, the guideline includes recommendations for ocular hypertension (OHT), which is defined as elevated intraocular pressure (IOP) without structural and functional defects.
- The guideline does not include treatment guidelines for
  - angle-closure glaucoma
  - secondary glaucomas other than pseudoexfoliative glaucoma
  - congenital and
  - juvenile glaucoma.
- The objective of the recommendation is to unify patient care in glaucoma and promote equal and cost-effective treatment practices in Finland by providing answers to the following questions:
  1. What factors increase the risk of glaucoma?
  2. Which tests are needed for the diagnosis of glaucoma?
  3. Is glaucoma screening worthwhile?
  4. What is the effect of lowering intraocular pressure (IOP) in patients with glaucoma or ocular hypertension? Can IOP-lowering treatment prevent disease progression and glaucoma-induced visual disability?
  5. Which treatments lower IOP, and what are their side effects?
  6. What is the goal of glaucoma treatment? Which treatment and monitoring plans should be followed?
  7. Which tests should be selected for glaucoma follow-up, and how frequently should glaucoma patients be monitored?
  8. What treatment and follow-up schemes should be chosen for advanced or aggressive glaucoma?
  9. What policies should be avoided?
- This Current Care Guideline is aimed at both public and private healthcare in Finland.
- The text section is a summary of 13 evidence-based surveys and several additional literature references and data collection summaries.
- The recommendations of the working group for clinical practice policies are presented in 9 Tables (Figures 1–9).
  - 1. Glaucoma treatment goals (Figure 1)
  - 2. Risk factors for open-angle glaucoma (Figure 2)
  - 3. Fundamentals of glaucoma diagnostics (Figure 3)
  - 4. Treatment plan for glaucoma (Figure 4)
  - 5. Evaluation of glaucoma test results (Figure 5)
  - 6. Treatment and monitoring of high-risk glaucoma (Figure 6)
  - 7. 2-year plan for the treatment and monitoring of stable glaucoma: based on earlier follow-up (Figure 7)
  - 8. Follow-up in stable glaucoma (Figure 8)
  - 9. Choosing wisely –recommendations (Figure 9)

3 | KEY POINTS

- Chronic open-angle glaucoma is mostly a slowly progressing disease (Aspberg et al., 2021; Burr et al., 2007; Chan et al., 2017; George et al., 2022; Heijl et al., 2011; Heijl, Bengtsson, & Oskarsdottir, 2013; Heijl, Buchholz, et al., 2013; Leske, 2003; Peters et al., 2013).
  - Exceptions are patients with glaucoma with a very high IOP ≥30 mmHg and patients whose disease progresses rapidly at any, even very low, IOP levels. These patients need more frequent monitoring and more intense treatment than patients with ordinary, slowly progressing glaucoma.
- The primary goal of glaucoma treatment is to prevent glaucoma-induced visual disability.
- Although the goal is to prevent glaucoma-induced visual disability, no randomised trials with visual disability as the endpoint have been published (Burr et al., 2007; Tuulonen, 2011).
- Instead, most studies assess treatments' IOP-lowering efficacy and compare the IOP-lowering effects of different treatments (Boland et al., 2013).
- Lowering IOP is currently the only proven method of treatment for glaucoma (Boland et al., 2013; Burr et al., 2007; Collaborative Normal-Tension Glaucoma Study Group, 1998; Heijl et al., 2002; The AGIS Investigators, 2000).
- When planning treatment, the cost of treatment and potential side effects should also be weighed (Boland et al., 2013; Tuulonen, 2011).
- The effectiveness of treatment is monitored by following IOP and
  - analysing optic disc and retinal nerve fibre layer (RNFL) photographs, and
  - analysing visual field tests.
- If structural or functional glaucoma lesions progress, treatment should be intensified after considering the patient's age, severity of glaucoma in both eyes and their other diseases (Burr et al., 2007; "European

The goal of glaucoma treatment is to prevent visual disability.

Treatment target for IOP
- A level of IOP at which glaucoma does not progress.
- It may take 3-5 years to determine an ideal individual IOP level, because open-angle glaucoma is mostly a slowly progressing disease.
- Target IOP level should be adjusted at each follow-up based on progression in fundus images and visual fields.

Lowering IOP
- If treatment is started, IOP should be lowered by at least 25% of the untreated IOP level.

Target IOP should be lowered more if the patient has
- advanced glaucoma
- fast-progressing glaucoma
- several risk factors for glaucoma
- long life expectancy

IOP, mmHg		
Starting IOP	Minimum target (-25 %)	-35 %
12	9	8
14	10	9
16	12	10
18	14	12
20	15	13
22	16	14
24	18	16
> 26	< 20	< 17

FIGURE 1 Glaucoma treatment goals.

Risk factor[1]	Risk	GRADE
Age	Risk doubles approximately every 10 years	A
IOP 22–29 mmHg > 30–35 mmHg	 10–13-fold 40-fold	A
Pseudoexfoliation with ocular hypertension	5–10-fold compared with ocular hypertension alone	B
Optic nerve head hemorrhage	12-fold	B
Myopia	2–4-fold	C
Family history of glaucoma	3-fold	C
Reduced perfusion pressure with advanced age	3-fold	C

[1] African ancestry is a risk factor for glaucoma (GRADE C).

FIGURE 2 Risk factors for open-angle glaucoma.

When planning a glaucoma test set after a clinical examination, the doctor must consider the following
- the age of the patient
- severity of the disease
- patient's other ocular diseases.

Systematic glaucoma screening is not recommended, because evidence of its effectiveness is lacking.

Very good level	IOP +	Gonioscopy +	Visual fields +	ONH imaging +	RNFL imaging
Good level	IOP +	Gonioscopy +	Visual fields +	ONH or RNFL imaging	
Fair level	IOP +	Gonioscopy +	Visual fields +		
Insufficient level	IOP				

IOP, intraocular pressure; ONH, optic nerve head; RNFL, retinal nerve fiber layer

* Gonioscopy should not be replaced by automated imaging.
** Visual fields should be recorded with a standard automated perimetry. The same instrument and protocol should be used in the follow-up.
*** Clinical examination or fundus images taken with a digital camera should not be replaced by optical coherence tomography (OCT).

FIGURE 3 Fundamentals of glaucoma diagnostics.

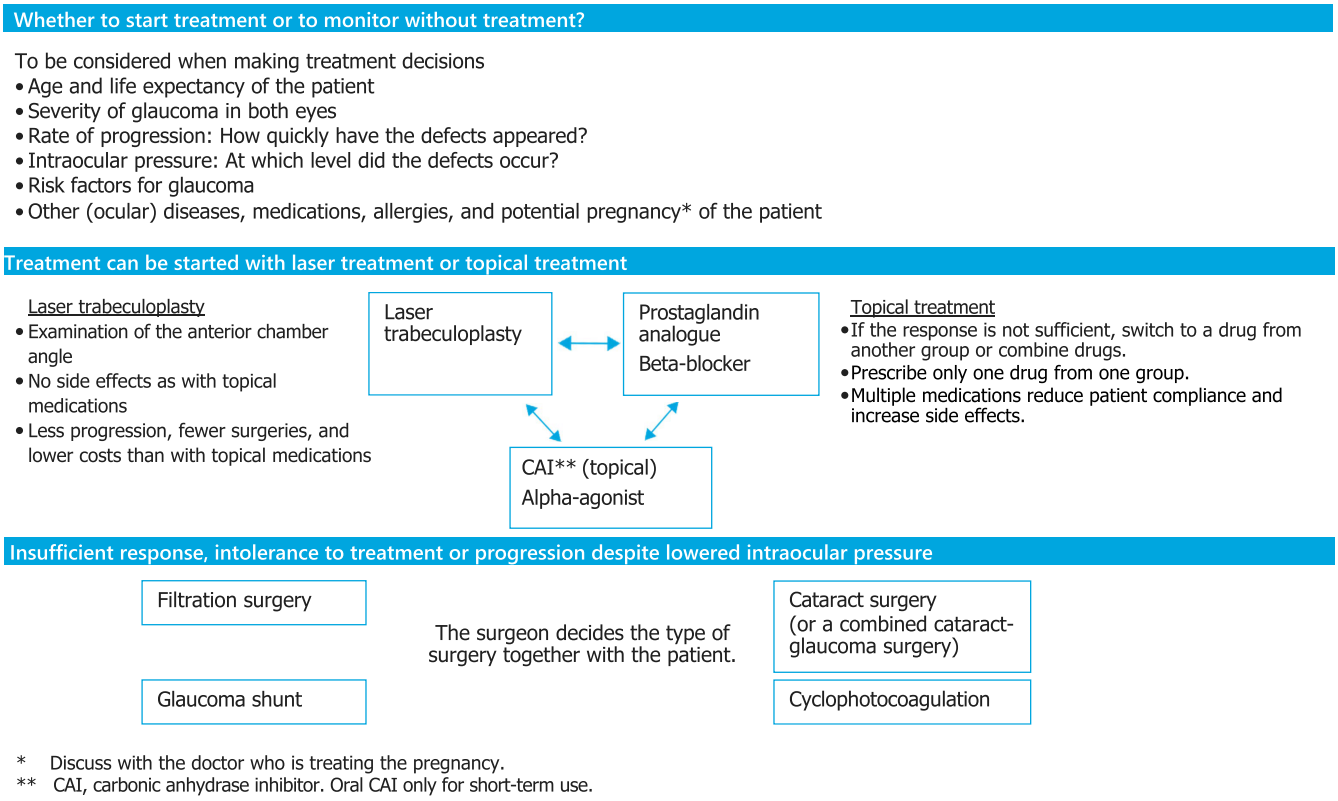

FIGURE 4 Treatment plan for glaucoma.

2 out of 3 abnormal findings suggests glaucoma

Abnormal	Normal	Diagnosis	Comments	Actions
Retinal nerve fiber layer (RNFL) Optic nerve head (ONH) Visual field		Glaucoma	Clear glaucoma diagnosis	Consider starting treatment
RNFL Visual field	ONH	Glaucoma	Probably a small ONH	
RNFL ONH	Visual field	Preperimetric glaucoma	10-degree visual field may be abnormal	
ONH Visual field	RNFL	Possibly a disease other than glaucoma	Rare in glaucoma, if RNFL image is of high quality	The need of treatment is unlikely
RNFL	ONH Visual field	Preperimetric glaucoma	Wait and see if progression occurs. 10-degree visual field may be abnormal	The need of treatment is likely
ONH	RNFL Visual field	Glaucoma suspect	A big or anomalous optic disc Wait and see if progression occurs.	Monitoring without treatment is possible, unless the IOP is >30 mmHg.
Visual field	RNFL ONH	Other than glaucoma or glaucoma suspect	Retest the visual field. Another cause for the visual field defect?	

FIGURE 5 Evaluation of glaucoma test results.

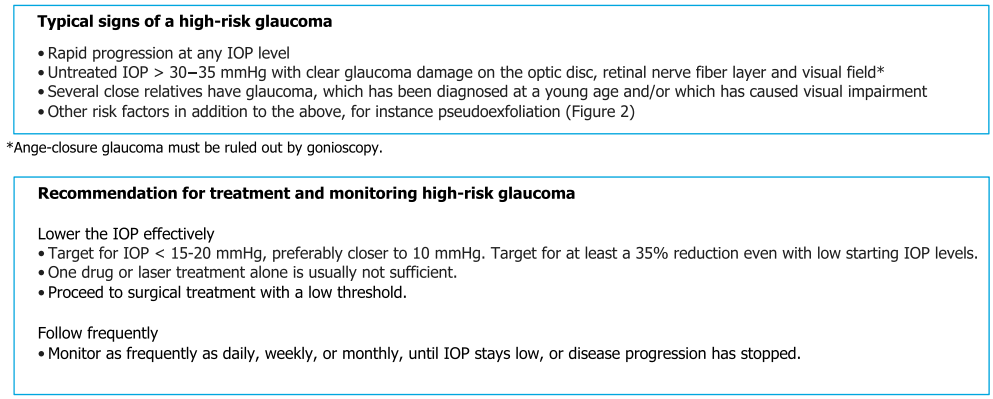

FIGURE 6 Treatment and monitoring of high-risk glaucoma.

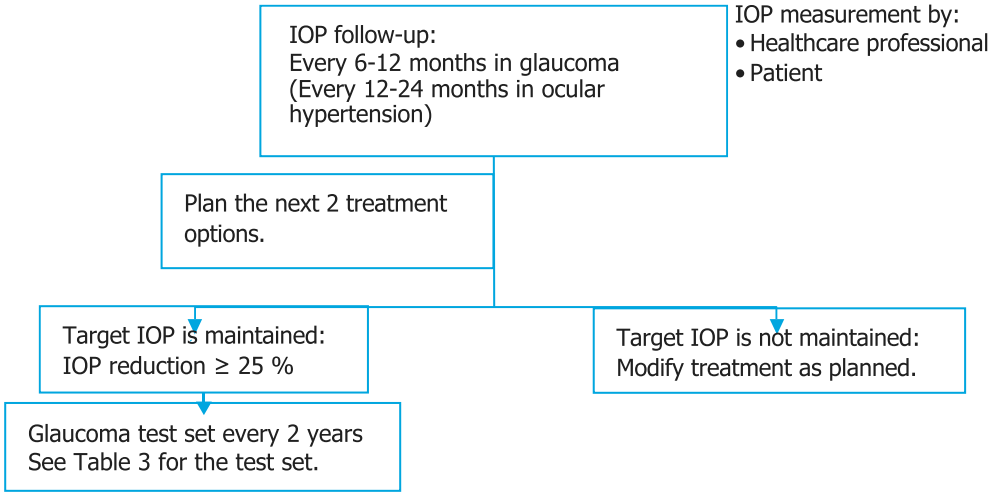

FIGURE 7 2-year plan for the treatment and monitoring of stable glaucoma: based on earlier follow-up.

- Glaucoma is considered stable when there is no progression of glaucoma defects or when the progression is very slow in relation to the patient's life expectancy.
- When ordering glaucoma follow-up tests, the doctor must consider the patient's age, severity of glaucoma and other ocular diseases.
- A treatment plan is written up and made available to the patient and primary care.
- Possible side effects of the treatment and follow-up, and compliance to treatment must also to be evaluated during the follow-up.

IOP measurement (with the same instrument)

- Follow-up interval is determent on a patient-by-patient basis. Typical interval is 6-12 months in stable glaucoma.
- In ocular hypertension without glaucoma damage: Every 12-24 months
- The treatment plan must record at which IOP level the glaucoma damage occurred or progressed, and what is the patient's target IOP and threshold IOP.

Clinical examination

- Refractive error is determined to examine visual acuity and visual fields.
- Gonioscopy is performed at diagnosis and repeated during follow-up. Gonioscopy cannot be replaced by automated imaging.
- The fundus is thoroughly examined.

Imaging and visual field examinations (with the same protocol and instrument)

	1st year of follow-up		2nd year	3rd year		4th year
Very good level	ONH and RNFL imaging*	and VF	X	ONH and RNFL imaging*	and VF	X
Good level	ONH or RNFL imaging*	and VF	X	ONF or RNFL imaging*	and VF	X
Fair level		VF	X		VF	X
Insufficient level	IOP follow-up only					

* Optical coherence tomography (OCT) does not replace a clinical examination or ONH and RNFL imaging.
X: If a more instable disease is suspected, additional examinations are considered on a case-by-case basis with the patient.
ONH, optic nerve head; RNFL, retinal nerve fiber layer; VF, visual field

FIGURE 8 Follow-up in stable glaucoma: What tests should be performed and how often?

Glaucoma Society Terminology and Guidelines for Glaucoma, 5th Edition," 2021).

- During follow-up, structural and functional defects typically occur and progress at different rates. The delay from structural to functional damage can be up to several years (Karvonen et al., 2022; Leaney et al., 2012; Quigley et al., 1992).
- Different test methods and diagnostic equipment may give different results in glaucoma diagnostics and progression analysis (Azuara-Blanco et al., 2016; Caprioli et al., 1996; Karvonen et al., 2022; Leaney et al., 2012; Quigley et al., 1992).
- The specificity and sensitivity of different tests vary considerably across studies (Azuara-Blanco et al., 2016; Caprioli et al., 1996; Girkin, 2000; Katz et al., 1997; Leaney et al., 2012; Quigley et al., 1992).
- There are no randomised studies in glaucoma screening, diagnostics, or follow-up that have evaluated which tests can be cost-effective or reduce visual impairment in glaucoma (Aspberg et al., 2021; Burr et al., 2007; Ervin et al., 2012; Tarride et al., 2011).
- The evaluation and comparison of different diagnostic and follow-up tests is hampered by missing gold standards for reference, and a potentially high risk of bias in study designs (Azuara-Blanco et al., 2016; Burr et al., 2007; Ervin et al., 2012; Karvonen et al., 2020; Tarride et al., 2011; Tuulonen, 2011).
- Since confirmation of a glaucoma diagnosis requires verified progression of glaucomatous defects, the best-suited gold standard for glaucoma diagnosis is progression in long-term monitoring.

Choosing wisely recommendations

Do not make a glaucoma diagnosis or assess progression based on optical coherence tomography (OCT) alone.
- Clinical examination or digital photographs cannot be replaced by OCT.
- OCT compares measurements to a reference population, which is not age-corrected in most devices.
- Examinations performed with different OCT devices are not comparable.
- Artefacts and software issues are not rare.
- An abnormal result can be a false positive, especially when clinical findings and visual fields are normal, and the subject has no risk factors.

Do not screen the general population for glaucoma.
- There are no good-quality studies that show which screening tests are cost-effective and can reduce visual disability in glaucoma.
- A significant portion of subjects who could benefit from glaucoma treatment may go unnoticed due to insufficient sensitivity of screening tests.
- Due to insufficient specificity of screening tests, screening produces false positives in a low-risk population. False positive results cause unnecessary worry, costs and further examinations to the examinees and burden the healthcare.

Do not routinely measure diurnal IOP.
- Benefits of diurnal IOP measurements are uncertain when evaluating prognosis for glaucoma.

FIGURE 9 Choosing wisely recommendations.

- Major risk factors for glaucoma are
  - elevated IOP (even though in half of glaucoma patients, the IOP may be within the normal range) (A)
  - advanced age (A) (Burr et al., 2007; Hollands et al., 2013; Medical Advisory Secretariat, 2006)
  - pseudoexfoliation together with an increased IOP (B) (Ekström, 2012; Mitchell et al., 1996)
  - optic disc haemorrhages (B) (Hollands et al., 2013)
- In addition, the risk of glaucoma may increase with
  - myopia (C) (Burr et al., 2007; Hollands et al., 2013; Medical Advisory Secretariat, 2006)
  - family history of glaucoma (C) (Burr et al., 2007; Hollands et al., 2013; Medical Advisory Secretariat, 2006)
  - African ancestry (C) (Burr et al., 2007; Hollands et al., 2013; Medical Advisory Secretariat, 2006)
  - reduced perfusion pressure (C) (Kim et al., 2020)

4 | CLINICAL PRESENTATION AND EPIDEMIOLOGY

- Glaucoma is a progressive neuropathy of the optic nerve that causes typical structural and functional defects in
  - optic disc
  - retinal nerve fibre layer, and
  - visual field (Burr et al., 2007; "European Glaucoma Society Terminology and Guidelines for Glaucoma, 5th Edition," 2021)
- In most patients, glaucomatous defects progress slowly over years (Aspberg et al., 2021; Burr et al., 2007; George et al., 2022; Heijl et al., 2011; Heijl, Bengtsson, & Oskarsdottir, 2013; Heijl, Buchholz, et al., 2013; Leske, 2003; Peters et al., 2013).
- However, for some patients, glaucoma may lead to serious functional and structural damage in as little as a few months (Chan et al., 2017; Heijl, Buchholz, et al., 2013).
  - It is important to organise glaucoma care in such a way that high-risk patients are identified early.
  - High-risk patients are discussed separately in this recommendation (Figure 6)
- The risk of glaucoma increases significantly with advancing age.
  - The prevalence of glaucoma is 2% among people over 50 years of age (B), and even more than 5% among people >75 years of age (Hirvelä et al., 1994; Mukesh et al., 2002; Sommer et al., 1991).
- Even in developed countries, less than half of the patients with glaucoma know that they have glaucoma (Klein et al., 1992; Sommer et al., 1991; Weih et al., 2001).
- Open-angle glaucoma is the second most common cause of visual disability registered in Finland following age-related macular degeneration.
- In 2019, 84% of patients treated for glaucoma in Finland were ≥65 years of age (The Annals of Finnish Register of Visual Impairment, 2019).
- At the end of 2020, 101 000 people were treated with glaucoma medications compensated by the Medication statistics in Finland (2021).
  - Outside these statistics, there are people who have risk factors for glaucoma or are suspected for glaucoma. These people may also need monitoring because some of them may develop glaucoma.

5 | RISK FACTORS

- Risk factors for open-angle glaucoma are presented in Table 2 (Figure 2)
- Half of glaucoma patients may have a 'normal' intraocular pressure within a statistically defined reference range 10–21 mmHg (Karvonen et al., 2019; Medical Advisory Secretariat, 2006).
- Risk of developing glaucomatous defects increases with increasing IOP, especially when IOP is ≥30 mmHg (A) (Burr et al., 2007; Hollands et al., 2013).
- If IOP is <30 mmHg, conversion from ocular hypertension to glaucoma is best predicted by age of the patient. The older the patient, the greater the risk (A) (Burr, Botello-Pinzon, et al., 2012; Kass et al., 2002; Mitchell et al., 1996; Sommer et al., 1991).

6 | GLAUCOMA DIAGNOSTICS

- The diagnosis and subclassification of glaucoma are based on examining the following:
  - optic disc

- retinal nerve fibre layer
- visual fields
- intraocular pressure, and
- anterior chamber angle with gonioscopy ("European Glaucoma Society Terminology and Guidelines for Glaucoma, 5th Edition," 2021)

- However, there are no unambiguous and generally accepted diagnostic criteria for glaucoma (Azuara-Blanco et al., 2016; Burr et al., 2007; Ervin et al., 2012; Michelessi et al., 2015).
- Table 3 provides a recommendation for diagnostic tests for glaucoma (Figure 3).

6.1 | Intraocular pressure

- In measuring IOP, intra-device variability is great, even when using Goldmann applanation tonometer, which is considered the gold standard (Burr, Botello-Pinzon, et al., 2012; Tonnu et al., 2005).
  - A more complete evaluation of these data is hindered by inaccuracies in reporting.
- The role of diurnal IOP variation and the usefulness of its monitoring in the context of glaucoma progression are uncertain (de Moraes et al., 2018; Medical Advisory Secretariat, 2006).
- Although a thick cornea increases the IOP reading and a thin cornea reduces it, there is no generally accepted conversion table for the effect of corneal thickness on IOP (Brandt et al., 2020; Doughty & Zaman, 2000; Shimmyo et al., 2003; Tonnu et al., 2005).
  - Additionally, different devices for measuring central corneal thickness use different technologies and yield different, poorly comparable results.
- In ocular hypertension, risk prediction for development of glaucoma does not improve after correcting IOP readings for corneal thickness (Brandt et al., 2012).
- The relevance of corneal thickness as an independent risk factor for glaucoma is unclear, but a thin cornea, together with ocular hypertension, associates with an elevated risk for glaucoma (Brandt et al., 2020; Burr, Botello-Pinzon et al., 2012).
- There is no evidence that measuring corneal thickness as part of glaucoma diagnostics has any effect on preventing glaucoma-induced visual impairment.

6.2 | Gonioscopy

- Evaluation of the anterior chamber angle by gonioscopy is a critical diagnostic study to distinguish open-angle glaucoma from angle-closure glaucoma ("European Glaucoma Society Terminology and Guidelines for Glaucoma, 5th Edition," 2021).
- There are several-chamber angle classifications. The Schaffer classification is used in Finland (Shaffer, 1973).
- Results from anterior chamber angle imaging devices seem inconsistent (Araie, 2013; Karvonen et al., 2022) and there is inadequate evidence on their clinical significance as a supplement to gonioscopy (Smith et al., 2013).

7 | DIAGNOSTICS OF STRUCTURAL AND FUNCTIONAL GLAUCOMA TEST FINDINGS

- There have been no published randomised screening or diagnostic trials that compare different glaucoma tests that report their cost-effectiveness or clinical effectiveness in preventing glaucoma-induced visual disability.
- It is challenging to evaluate different diagnostic tests in glaucoma because there is no gold standard for reference (Azuara-Blanco et al., 2016; Burr et al., 2007; Ervin et al., 2012; Karvonen et al., 2020; Tarride et al., 2011).
  - Also, there may be a high risk of bias in the published studies.
- Since confirmation of a glaucoma diagnosis requires verified progression of glaucomatous defects, the best-suited gold standard for glaucoma is long-term monitoring.
- The variability of studies that describe ocular structure and function is affected by the chosen
  - test methods
  - reference materials
  - examinees
  - observers, and
  - severity of the studied disease.
- Although diagnostic accuracy may improve when results from different tests are combined, optimal test combinations are not known (Azuara-Blanco et al., 2016; Caprioli et al., 1996; Karvonen et al., 2022; Zhu et al., 2010).
- The following evidence is available regarding the application of different test methods and the need for method combining:
  - No single parameter of the optic disc (e.g. cup to disc ratio, which is the ratio between central depression and disc diameter) seems to distinguish patients with glaucoma from healthy individuals (Klein et al., 1992; Leske, 2003; Tielsch et al., 1991).
  - Mean inter-observer reliability, kappa coefficient, is 0.7 (range, 0.5–0.9) in qualitative evaluation of glaucoma from the optic disc images (Hadwin et al., 2013; Reus et al., 2010; Tielsch et al., 1991; Varma et al., 1992).
  - Also, automated evaluations by automated imaging devices differ from each other both in diagnostics and follow-up (Yang et al., 2012).
  - The mean agreement rate is 72%, range 54%–92%, between clinicians when assessing progression from the optic disc photographs (Chee et al., 2013; Coleman et al., 1996; Heijl et al., 2002; Heijl & Bengtsson, 1989).
  - During follow-up, clinically detectable defects in the optic disc, RNFL and visual field typically appear and progress at different times with a delay of 1–6 years. Their inter-correlation is poor at a single

follow-up (Caprioli et al., 1996; Girkin, 2000; Heijl & Bengtsson, 1989; Karvonen et al., 2022; Katz et al., 1997; Leaney et al., 2012; Quigley et al., 1992; van der Schoot et al., 2013).
- The sensitivity and specificity of visual field tests vary considerably in different comparative studies. There is a significant risk of bias in some of these study designs (Burr et al., 2007; Ervin et al., 2012).
- The significance of one abnormal visual field is weak (Glaucoma Laser Trial Research Group, 1995; Keltner, 2000; Schulzer et al., 1994). See Table 5, Evaluation of glaucoma test results (Figure 5).
- Because optic disc and RNFL damage usually precede visual field loss, visual fields may be normal even if there is structural damage (Caprioli et al., 1996; Heijl & Bengtsson, 1989; Karvonen et al., 2020; Katz et al., 1997; Leaney et al., 2012; van der Schoot et al., 2013).
- Variation in the selected start time and length of follow-up in trials and at the clinic may define which defects, structural or functional, can be detected first (Caprioli et al., 1996; Girkin, 2000; Karvonen et al., 2019; Katz et al., 1997; Leaney et al., 2012; Quigley et al., 1992; van der Schoot et al., 2013; Zeyen, 1993).
  - Table 5 presents a proposal for the application of test results in glaucoma diagnostics (Figure 5).

7.1 | Evaluation of structural defects

- Sensitivity and specificity of both clinical evaluation and automated evaluations performed with automated imaging devices vary in different studies (Azuara-Blanco et al., 2016; Burr et al., 2007; Ervin et al., 2012; Karvonen et al., 2020).
  - High risk of bias in some of the study designs is of concern.

7.2 | Optic disc

- In clinical diagnostics and follow-up, verbal descriptions of the optic disc, estimations of the cup to disc ratio, or drawings are not as accurate test methods as optic disc photography (Coleman et al., 1996; Heijl & Bengtsson, 1989; Odberg & Riise, 2009; Tielsch et al., 1988).
  - For example, >80% of optic disc splinter haemorrhages detected in fundus photographs are not discovered in clinical examination (Budenz et al., 2006).
- Even though extensive experience is required for optimal evaluation of fundus photographs, photographs cannot be replaced by constructed images and their printouts from automated imaging devices, in which for example disc haemorrhages are not visible (Chauhan & Burgoyne, 2013).
- Appearance of a healthy optic disc varies greatly due to varying optic disc sizes among healthy individuals (Heijl & Mölder, 2009; Jonas et al., 1988; Varma et al., 1992).
- Cup to disc ratio varies from 0 to 0.9 in the normal population (Jonas et al., 1988), which limits its diagnostic capacity in distinguishing the healthy from the sick (Heijl & Mölder, 2009).
  - A large cup in a large optic disc can easily raise unnecessary suspicion of glaucoma (Burk et al., 1992).
  - A small optic disc is more insidious because early disc defects may go unnoticed in a thick rim (Heijl & Mölder, 2009; Jonas et al., 1990).
- Optic disc and RNFL haemorrhages may precede new glaucomatous defects and progression of existing defects (Airaksinen & Heijl, 2009; Budenz et al., 2006; Rasker, 1997).
- Haemorrhages are more prevalent in normal-tension glaucoma than in high-tension glaucoma (Budenz et al., 2006; Healey et al., 1998; Rasker, 1997; Tezel et al., 1996).
- The role of IOP-lowering treatment in preventing disc haemorrhages is unclear in normal-tension glaucoma (Hendrickx et al., 1994).
- Peripapillary atrophy is more prevalent in glaucoma than in the normal population, but it cannot distinguish the sick from the healthy. Its relevance in the aetiology and progression of the glaucoma is unclear (Jonas, 1992; Jonas et al., 2000; Quigley, 1994; Tuulonen et al., 1996).

7.3 | Photography of the retinal nerve fibre layer

- RNFL photography with a digital camera can help in glaucoma diagnostics, especially when the optic disc is larger or smaller than average.
- Glaucomatous defects may be visible in RNFL photographs before defects in the optic disc or visual field are detectable (Caprioli et al., 1996; Karvonen et al., 2019; Klein et al., 1992; Paczka et al., 2001; Tielsch et al., 1991; Tuulonen et al., 1993; Ugurlu et al., 2000). Congruence of RNFL defects, optic disc and visual field defects is further discussed on the Finnish Medical Society Duodecim website (Glaucoma. Current Care Guidelines, 2023) (Caprioli et al., 1996; Girkin, 2000; Heijl & Bengtsson, 1989; Karvonen et al., 2020; Katz et al., 1997; Leaney et al., 2012; Quigley et al., 1992; van der Schoot et al., 2013; Zeyen, 1993).
- There is limited evidence on the specificity and sensitivity of digital RNFL photographs both in screening (Karvonen et al., 2019; Komulainen et al., 1992; Niessen et al., 1997; Wang, 1994) and diagnostics of glaucoma (Caprioli et al., 1996; Jonas et al., 1989; Paczka et al., 2001; Tuulonen & Airaksinen, 1991).

7.4 | Automated imaging devices

- No randomised screening or diagnostic trials using automated imaging devices have been published reporting their cost-effectiveness or clinical

effectiveness in preventing glaucoma-induced visual disability, including their use to supplement or replace existing diagnostic methods (Azuara-Blanco et al., 2016; Burr et al., 2007; Ervin et al., 2012; Karvonen et al., 2020; Michelessi et al., 2015; Tarride et al., 2011; Tuulonen, 2011).
- Although evidence is limited, one of the currently available instruments, optical coherence tomography, may complement the diagnostics and follow-up of glaucoma alongside digital photography of the optic disc and RNFL (Araie, 2013; Leaney et al., 2012).
- Along with automated imaging results interpretation skills, the development and maintenance of traditional clinical evaluation skills are essential in glaucoma diagnostics and follow-up.
  - Glaucoma diagnostics should not be based solely on colours indicative of pathology or normal in automated imaging (Chong & Lee, 2012; "European Glaucoma Society Terminology and Guidelines for Glaucoma, 5th Edition," 2021).
  - Clinicians must be able to distinguish automated imaging artefacts from clinically significant findings (Araie, 2013; Chong & Lee, 2012).
  - Normative databases for automated imaging devices are not comprehensive enough for automated evaluation (Chong & Lee, 2012).
  - It is not yet known what findings observed in automated imaging are clinically significant in the diagnosis or follow-up of glaucoma (Azuara-Blanco et al., 2016; Chong & Lee, 2012; Karvonen et al., 2020).
- In terms of life-long disease monitoring, rapid development of these devices and their outputs pose a challenge because the results of the most up-to-date imaging modalities may not be comparable to previous ones. For this reason, optic disc and RNFL photography are still indispensable in glaucoma diagnostics and follow-up (Chauhan & Burgoyne, 2013).

7.5 | Visual field examination

- Sensitivity and specificity of visual field tests vary between different test strategies and devices (Burr et al., 2007; Ervin et al., 2012; Vesti et al., 2003).
  - When evaluating individual studies, a significant risk of bias associated with the study designs should be considered.
- Visual field defects and progression have been defined in several different ways (Collaborative Normal-Tension Glaucoma Study Group, 1998; Glaucoma Laser Trial Research Group, 1995; Keltner, 2000; Schulzer et al., 1994; "The Advanced Glaucoma Intervention Study (AGIS)," 1994; The AGIS Investigators, 2000; Vesti et al., 2003).
- A reproducible and reliable visual field test method should be chosen for the diagnostics and follow-up of glaucoma.
- Visual field examination is a patient-dependent test, in which variability both during one test and between tests is common (Bengtsson & Heijl, 1999; Birt et al., 1997).
  - Visual field outcomes may improve by practice during follow-up, which must be considered when interpreting the test results.
- Patients should be monitored with the same instrument and protocol because the visual field test strategy affects the final result (Thulasidas & Patyal, 2020; Vesti et al., 2003).
- Several randomised long-term studies such as Early Manifest Glaucoma Trial, Ocular Hypertension Treatment Study and Collaborative Initial Glaucoma Treatment Study used lower threshold strategies compared to currently used strategies (Collaborative Normal-Tension Glaucoma Study Group, 1998; Gordon, 1999; Heijl, Bengtsson, & Oskarsdottir, 2013).
- Current faster test strategies (e.g. SITA Faster) improve treatment access and patient experience, and are considered sufficiently accurate (Heijl et al., 2019).
- The effect of faster test strategies on the number of visual fields needed to detect visual field progression is not yet known.
- Kinetic visual field examination may still be useful for measuring peripheral vision for example when issuing a driver's licence (Goldmann II/4 isopter) in advanced glaucoma.
- In advanced glaucoma, it is recommended to monitor visual field progression with a 10-degree visual field protocol that tests several points of the remaining central field.

8 | GLAUCOMA SCREENING

- The glaucoma working group does not recommend non-targeted screening for glaucoma.
- There is no data showing the effectiveness of cost-effectiveness of systematic population screening (Burr et al., 2007; Ervin et al., 2012; Vaahtoranta-Lehtonen et al., 2007).
- The lack of suitable screening methods has been an obstacle to general population screening.
  - Sensitivity and specificity of fundus photographs, automated imaging studies and visual fields vary widely in screening (Azuara-Blanco et al., 2016; Burr et al., 2007; Ervin et al., 2012; Karvonen et al., 2020).
- Population-based studies show that at least half of patients with open-angle glaucoma go undetected (Burr et al., 2007; Medical Advisory Secretariat, 2006).
- In general, the purpose of screening general population is
  - to detect a disease early enough to treat it most effectively.
  - to identify individuals with a high susceptibility to the disease to prevent the disease onset (Pelkonen, 2000).
- There are no systematic reviews that prove a direct or indirect association between glaucoma screening and glaucoma-related visual impairment, structural, or functional damage, or patient-important outcomes (Burr et al., 2007; Ervin et al., 2012).

- In addition, conclusions from studies simulating screening-related cost-effectiveness are inconsistent (Tuulonen, 2011).

8.1 | Measuring intraocular pressure in screening

- Measuring IOP is an insufficient screening method for glaucoma (Founti et al., 2021; Heijl, Bengtsson, & Oskarsdottir, 2013; Karvonen et al., 2019; Klein et al., 1992; Mukesh et al., 2002; Sommer et al., 1991).
- In glaucoma screening, IOP is normal in more than half of adults with glaucoma.
  - For instance, in the Northern Finland Birth Cohort and Thessaloniki Eye study, IOP was normal in 89% of new glaucoma patients found in screening (Founti et al., 2021; Karvonen et al., 2019).

8.2 | Fundoscopic examination in screening

- In population screening, fundoscopic examination has proven to be an unreliable screening method (Burr et al., 2007; Ervin et al., 2012).
- There may be considerable variability in the evaluation of glaucomatous defects in slit lamp examination, even among experienced ophthalmologists (Hadwin et al., 2013; Reus et al., 2010; Tielsch et al., 1988; Varma et al., 1992).
- In clinical examination, majority of disc haemorrhages may be overlooked (Chauhan & Burgoyne, 2013).

8.3 | Optic disc imaging with a digital camera in screening

- Population-based studies show that there are no distinct features in the optic disc that would sufficiently distinguish glaucoma patients from healthy individuals (Klein et al., 1992; Leske, 2003; Tielsch et al., 1991).

8.4 | RNFL imaging with a digital camera in screening

- In the Northern Finland Birth Cohort Eye Study, abnormal RNFL was the most common structural damage in the 43 eyes diagnosed with glaucoma (Karvonen et al., 2019). Age-related clouding of the lens decreases the visibility of RNFL (Niessen et al., 1995).
- Early glaucomatous defects have been found in RNFL photographs also in screening more selected populations (Komulainen et al., 1992; Niessen et al., 1997; Wang, 1994).

8.5 | Automated imaging devices in screening

- No randomised screening or diagnostic trials using automated imaging devices have been published that report their clinical effectiveness or cost-effectiveness in preventing glaucoma-induced visual disability, including their use to supplement or replace existing diagnostic methods (Azuara-Blanco et al., 2016; Ervin et al., 2012; Karvonen et al., 2020; Michelessi et al., 2015; Tarride et al., 2011).

8.6 | Visual field examination in screening

- Sensitivity and specificity vary depending on the selected reference standard.
- The risk of bias is significant in these study designs.
- Sensitivity and specificity of visual field examinations vary between different test strategies and devices (Burr et al., 2007; Ervin et al., 2012).

9 | CLINICAL EFFECTIVENESS AND COST-EFFECTIVENESS OF GLAUCOMA TREATMENT

- Although there is high-quality evidence indicating that medications, laser and surgical treatments reduce IOP and the risk of structural and functional disease progression, there is no evidence on direct effects of such treatments on visual impairment (Boland et al., 2013; Takwoingi et al., 2014; Tuulonen, 2011; van Gestel, 2012).
- To date, evidence of cost-effectiveness in glaucoma treatment is available in a few population-specific economic simulation models.
- According to health-economic **simulation models**, treatment of glaucoma is more cost-effective compared with no treatment in, for example the United States, the United Kingdom and the Netherlands (Boland et al., 2013; Burr et al., 2007; van Gestel, 2012).
- In contrast, models that simulate treatment of OHT produce varying results that depend on the country and estimates that were used to define glaucoma and visual impairment (Burr, Botello-Pinzon et al., 2012; Takwoingi et al., 2014; Tuulonen, 2011).
- Simulation models are based on optimal clinical data from randomised controlled trials (RCTs), which may not agree with everyday clinical practice due to, for example stricter inclusion and exclusion criteria and more frequent monitoring in RCTs (Tuulonen, 2011).
  - In RCTs, both patient compliance and clinicians' adherence to treatment protocols are better than in clinical practice.
  - In RCTs, data are reported for only one eye, which means that data of the other eye are simulated or left unreported. Studies do not always publish whether the reported eye is the patient's worse or better-seeing eye.
  - Different studies have used different estimates of visual disability and clinical effectiveness because information on glaucoma-induced visual disability and clinical effectiveness in preventing visual disability is limited.
  - In addition, little is known about the effect of the severity of glaucoma on quality of life.

10 | VISUAL DISABILITY

- The goal of glaucoma treatment is to prevent visual disability.
- However, no longitudinal glaucoma or ocular hypertension trials have been published in which prevention of visual disability was an endpoint (Boland et al., 2013; Burr, Botello-Pinzon, et al., 2012; Li et al., 2013; Tuulonen, 2011).
- In population-based cross-sectional studies, prevalence of visual disability or blindness in one or both eyes vary between 3% and 12% in glaucoma (George et al., 2022). Prevalence of visual disability due to glaucoma among screened populations ranges from 0.03% to 2.4% (Dielemans et al., 1994; Heijl, Bengtsson, & Oskarsdottir, 2013).
- Due to varying criteria for visual disability and inaccuracies in reporting, data regarding visual disability in glaucoma should be assessed with caution (George et al., 2022).

According to a cross-sectional registry study from the Finnish Register of Visual Impairment, 1.5% of patients receiving glaucoma medications were visually impaired due to glaucoma in 2019 (Vaajanen et al., 2022).

  - The relative rate of visual impairment in glaucoma may also be higher because the study includes patients treated for OHT.
- Some registry-based and retrospective studies report much higher rates of visual disability compared with cross-sectional studies: visual disability rate of 6% in both eyes in 15 years and 22% in 20 years, and 9% in one eye in 10 years and 54% in 20 years (Forsman et al., 2007; Peters et al., 2013).

11 | TREATMENT OF GLAUCOMA

- Most clinical trials focus on treatments' IOP-lowering efficacy, monitoring and comparing them with other treatment options because lowering IOP is currently the only proven treatment strategy for glaucoma (Boland et al., 2013; Collaborative Normal-Tension Glaucoma Study Group, 1998; Leske, 2003; The AGIS Investigators, 2000).

11.1 | Efficacy of treatment of glaucoma

- Lowering IOP appears to reduce progression of structural and functional defects in glaucoma (Boland et al., 2013; Collaborative Normal-Tension Glaucoma Study Group, 1998; Heijl et al., 2002; Leske, 2003; The AGIS Investigators, 2000).

11.2 | Efficacy of treatment of ocular hypertension

- The glaucoma working group does not recommend routine treatment of OHT. However, treatment should be considered for IOP levels ≥30 mmHg (Burr, Botello-Pinzon, et al., 2012; Kass et al., 2002; Takwoingi et al., 2014).
- Greater variation in IOP does not seem to increase the risk of glaucoma in ocular hypertension (Bengtsson & Heijl, 2005).

12 | METHODS FOR LOWERING INTRAOCULAR PRESSURE IN GLAUCOMA

- Target IOP levels for the treatment of glaucoma are presented in Table 1 and glaucoma treatment chart is presented in Table 4.
  - Additional information in Tables 6 and 7.

12.1 | Medication

- Lowering IOP is currently the only method of treatment for glaucoma.
- Although it has been suggested that some medications may protect against degeneration of ganglion cells, adequate evidence for neuroprotection is missing (Sena & Lindsley, 2017).
- In systematic reviews, prostaglandin analogues lower IOP more than other monotherapies. (GRADE B) (Boland et al., 2013; Li et al., 2016; van der Valk et al., 2009).
  - There are no clinically meaningful differences between different prostaglandin analogues in their IOP-lowering effect.
- Timolol is the second most effective IOP-lowering drug following prostaglandin analogues. (GRADE B) (Boland et al., 2013; Li et al., 2016; van der Valk et al., 2009)

12.1.1 | Fixed combination drugs

- Only minor differences have been detected between different fixed combinations in their IOP-lowering effect (Aptel et al., 2012; Li et al., 2016).
  - However, a fixed combination of a prostaglandin analogue and a beta-blocker seems to reduce IOP more than other combinations.
- Combinations of prostaglandin analogue and timolol may be more effective when administered in the evening than in the morning without a clinically meaningful difference (Quaranta et al., 2013).

12.1.2 | Compliance

- Treatment compliance to glaucoma medication is poor (Olthoff et al., 2005; Waterman et al., 2013).
- According to studies that report patients' medication use, 5%–80% of patients do not follow their medication plan (Waterman et al., 2013).
- It is unclear whether patient education improves their compliance (Waterman et al., 2013).

12.1.3 | Adverse effects and allergic reactions

- All glaucoma medications may cause local and systemic adverse effects (Boland et al., 2013).
- The most common adverse reaction to topical glaucoma medications is topical irritation. A toxic reaction is also possible. These local allergic reactions are rare except for brimonidine (Boland et al., 2013).
- When intolerance occurs, the suspected irritant drug should be replaced. There are no suitable or practical tests for drug hypersensitivity.
- Prostaglandin analogues and topical carbonic anhydrase inhibitors have the most favourable systemic side effect profiles (Boland et al., 2013).
- Systemic side effects are more common for beta-blockers and brimonidine (Boland et al., 2013).
- Conjunctival hyperaemia occurs most commonly with prostaglandin analogues and least commonly with beta-blockers (Boland et al., 2013).
- In eyes that have undergone intraocular surgery, prostaglandin analogue treatment may slightly elevate the risk of uveitis (0.2%) and macular oedema (0.1%) (Hu et al., 2020).
    - In eyes without intraocular surgery, no such risk has been identified.
- Benzalkonium chloride, a preservative, may cause both allergic and toxic reactions (Rasmussen et al., 2014).
- Temporary or permanent nasolacrimal duct occlusion may reduce systemic absorption of topical glaucoma medications (Aritürk et al., 2009).
- Glaucoma medications may cause local and systemic adverse effects, some of which may be severe (Boland et al., 2013; Vaajanen & Vapaatalo, 2017).
    - alpha-agonists
        - decreased heart rate and blood pressure, fatigue, central nervous system depression that may affect performance and driving ability, interactions with drugs that affect the central nervous system
        - dry mouth and nose, disturbances in the sense of taste
        - follicular conjunctivitis (Boland et al., 2013; Vaajanen & Vapaatalo, 2017)
    - beta-blockers
        - decreased heart rate and blood pressure, asthma exacerbation, dizziness, nausea, depression, sleep disorders
            - Beta-blockers should not be prescribed to patients with asthma, slow heart rate, low blood pressure, untreated heart failure, or 2nd or 3rd degree AV block (Boland et al., 2013; Vaajanen & Vapaatalo, 2017).
        - allergic reactions, dryness and irritation of mucous membranes
    - systemic carbonic anhydrase inhibitors
        - fatigue, dizziness, gastrointestinal disorders, metabolic acidosis, depression, limb tingling, hypersensitivity reactions, hypokalaemia, kidney stones, gout, allergic reactions, anaphylaxis (Pfeiffer, 1997; Vaajanen & Vapaatalo, 2017)
    - topical carbonic anhydrase inhibitors
        - disturbances in the sense of taste, dry mouth (Vaajanen & Vapaatalo, 2017)
    - prostaglandin analogues
        - Systemic adverse effects are rare. There may be adverse effects on the gastrointestinal tract (Boland et al., 2013; Papachristou, 2008).
        - eyelash growth, contact allergy, skin and iris hyperpigmentation, conjunctival hyperaemia (Boland et al., 2013)
        - corneal thinning and ulceration (Birt et al., 2012)
        - orbital fat atrophy (Kucukevcilioglu et al., 2014)
    - parasympathomimetics
        - Headache at the start of treatment may occur but other systemic side effects are rare (Vaajanen & Vapaatalo, 2017).
        - accommodative dysfunction in young patients, blurring of vision (Pfeiffer, 1997)

12.2 | Laser trabeculoplasty

- Laser trabeculoplasty and medications cause similar reduction in IOP. (A) (Chi et al., 2020; Gazzard et al., 2019)
    - As first-line treatment, selective laser trabeculoplasty (SLT) is more cost-effective than eye drops. In the Laser in Glaucoma and Ocular Hypertension Trial, 74% of patients did not need any medication to control their IOP during 3 years following SLT (Gazzard et al., 2019).
    - The IOP-lowering effect of laser trabeculoplasty decreases with time. SLT treatment can be repeated (Gazzard et al., 2019).
- Eyes treated first with laser trabeculoplasty usually require less medication than eyes treated first with medication (Chi et al., 2020; Gazzard et al., 2019).
- Argon, diode and selective laser trabeculoplasty may produce similar IOP-lowering results (Chi et al., 2020; Chung et al., 1998; Gazzard et al., 2019).

12.3 | Cyclodestructive procedures

- In short-term follow-up studies, cyclophotocoagulation is for the most part an effective and safe procedure in difficult-to-treat glaucoma, but repeated treatments are often required (Chen et al., 2019; Michelessi et al., 2018).

12.4 | Surgical treatment

12.4.1 | The efficacy of surgical treatment

- In advanced glaucoma, primary surgical treatment seems to reduce IOP and rate of visual field progression more than medication or laser treatment. (B) In contrast, surgical treatment does not improve treatment results in early-stage glaucoma compared to other treatments (Burr, Azuara-Blanco, et al., 2012).
- Compared to glaucoma medication, surgical treatment associates with more frequent ocular symptoms

in early postsurgical follow-up than medication. (B) Cataract development is faster following glaucoma surgery. However, after 5 years, cataract surgery rates do not seem to differ between the two treatment groups (Burr, Azuara-Blanco, et al., 2012).
- Surgical treatment lowers IOP more than laser treatment (B) (Boland et al., 2013; Rolim de Moura et al., 2007).
- Visual field defects may continue progressing despite the decreased IOP after surgery (The AGIS Investigators, 2000; Watson et al., 1990). It has not been possible to determine a clear IOP limit, which would prevent glaucomatous progression (The AGIS Investigators, 2000).

12.4.2 | Trabeculectomy

- Trabeculectomy success rates range from 26% to 98% for attaining target IOP over 5 years (Burr, Azuara-Blanco, et al., 2012; Chen et al., 1997; Molteno, 2004; The AGIS Investigators, 2000; Watson et al., 1990).
- Long-term results in 10–15 years of follow-up have only been published in retrospective series where data has been incomplete in most patients (Molteno, 2004; Watson et al., 1990).

12.4.3 | Antimetabolites

- Intraoperative mitomycin C (MMC) may associate with better success rates 1 year after trabeculectomy in eyes with a high risk for scarring and in eyes without previous surgery (Wilkins et al., 2005).
- MMC augmentation may lead to lower IOPs also in combined cataract and glaucoma surgeries (Wilkins et al., 2005). However, its use does not improve success rate in glaucoma shunt surgery (Foo et al., 2019).
- In nonpenetrating glaucoma surgery, MMC may improve surgical success without increasing the complication rate (Cheng et al., 2011).
- MMC may accelerate cataract formation following trabeculectomy (Wilkins et al., 2005).
- Postoperative injections with 5-fluorouracil may associate with lower surgical failure rates and lower IOP levels 1 year after trabeculectomy in eyes with a high risk of scarring and in eyes without previous intraocular surgery (Green et al., 2014).

12.4.4 | Glaucoma shunts

- In eyes with previous intraocular surgery, an aqueous shunt procedure seems to have a higher success rate than trabeculectomy, although IOP reduction is similar for both procedures (Tseng et al., 2017).
  - Ocular hypotony is more common after trabeculectomy than after a shunt procedure. Nevertheless, postoperative visual acuity does not appear to differ between the two groups.
  - Additional surgeries may be required more often after MMC-augmented trabeculectomies than after glaucoma shunts.
- In eyes without previous intraocular surgery, lower IOP and lower medication rates were achieved with trabeculectomies compared to glaucoma shunt procedures during 3 years of follow-up (Gedde et al., 2020).
  - Cumulative probability for failure was 33% for the glaucoma shunt and 28% for trabeculectomy.
- Different shunt procedures appear to be equally effective during 1–5 years of follow-up (Christakis et al., 2013; Nassiri et al., 2010; Tseng et al., 2017).
- When comparing aqueous shunts with and without valves in 1 year of follow-up, postoperative IOP is lower and ocular hypotony-related, sometimes severe, complications are more common in shunts without valves (Christakis et al., 2013; Nassiri et al., 2010; Tseng et al., 2017).

12.4.5 | Non-penetrating surgery

- Trabeculectomy is more effective in reducing IOP than deep sclerectomy, viscocanalostomy or canaloplasty (Eldaly et al., 2014; Gabai et al., 2019; Rulli et al., 2013). There are no differences in the IOP-lowering effect of deep sclerectomy and trabeculectomy when MMC is being used (Gabai et al., 2019).
- Complications, including ocular hypotony, shallow anterior chamber, hyphema, choroidal effusion and cataract formation, may be more common after trabeculectomy than after deep sclerectomy (Gabai et al., 2019).

12.4.6 | Mini-invasive glaucoma surgery

- There is no consensus on the definition of mini-invasive glaucoma surgery (MIGS).
- Various MIGS procedures have been reported to lower IOP and to reduce the number of medications needed (King et al., 2018; Le et al., 2019).
- There is no evidence of the efficacy of MIGS compared to traditional glaucoma surgery and cataract surgery (Elhusseiny et al., 2021).
  - Small sample sizes, narrow eligibility criteria, inconsistently selected endpoints and success criteria, and affiliations complicate the evaluation of MIGS studies.

12.4.7 | Cataract surgery

- Phacoemulsification with intraocular lens implantation decreases the IOP by 2–4 mmHg in patients without or with glaucoma with low to moderately increased preoperative IOP (Mansberger et al., 2012; Masis et al., 2018).
- In eyes with pseudoexfoliation, IOP may decrease more, 4–6 mmHg. IOP also decreases more in eyes with a higher preoperative IOP (Masis et al., 2018).
- In glaucoma, the risk of postoperative IOP spiking is high after cataract surgery, especially in pseudoexfoliative glaucoma (Chen et al., 2015).

- Even an uneventful cataract surgery might impair the filtration of a previously performed glaucoma surgery and cause long-term IOP-elevation (Husain, 2012; Longo et al., 2015; Shingleton et al., 2003).
  - This risk may be lower if the time between surgeries is more than 12 months.

12.5 | Glaucoma follow-up

- No randomised trials have been published that have shown which follow-up tests can be cost-effective or clinically effective in preventing visual impairment in glaucoma (Boland et al., 2013).
  - Evaluating diagnostic tests for glaucoma is challenging because of the lack of a gold reference standard and a high risk of bias associated with the study designs.

12.5.1 | Rate of progression

- Open-angle glaucoma is mostly a slowly progressing disease in which the rate of progression in the RNFL, optic disc and visual fields varies from patient to patient, and it may take several years to detect progression (Collaborative Normal-Tension Glaucoma Study Group, 1998; Heijl et al., 2002; Zeyen, 1993).
  - Majority of glaucoma patients do not become blind. It may take an average of 30–40 years for open-angle glaucoma to progress from the first detectable visual field defect to blindness with treatment (Jay & Murdoch, 1993; Peters et al., 2013; Quigley et al., 1996). According to a Swedish study, 5%–6% of patients become bilaterally blind despite treatment in 10 years, 13%–14% in 20 years (Peters et al., 2013).
- Combining multiple medications with laser treatment may slow the progression compared to monotherapy over a 3-year period (Bengtsson et al., 2022).

12.5.2 | Risk factors associated with progression

- Glaucomatous defects tend to progress in a significant proportion of patients (Chan et al., 2017; Collaborative Normal-Tension Glaucoma Study Group, 1998; Ernest et al., 2013; Heijl et al., 2002; Heijl, Buchholz, et al., 2013; Leske, 2003; Quigley et al., 1996; Tuulonen & Airaksinen, 1991; Zeyen, 1993).
- The incidence of progression is more common with
  - advanced age
  - optic disc haemorrhages
  - high IOP at diagnosis
  - significant visual field defects at diagnosis
  - pseudoexfoliation (Ernest et al., 2013).
- The incidence of visual field progression varies considerably across studies. Variation depends largely (80%) on the varying methods used in these studies (Ernest et al., 2013).
- The relevance of diurnal IOP and its monitoring in glaucoma follow-up is unclear (de Moraes et al., 2018; Medical Advisory Secretariat, 2011).

12.5.3 | Clinical structure–function relationship and progression

- During follow-up, clinically detectable lesions in the optic disc, RNFL and visual fields typically appear and progress at different times. The delay may be 1–6 years. Their correlation is poor at a single follow-up (Caprioli et al., 1996; Karvonen et al., 2022; Leaney et al., 2012; van der Schoot et al., 2013; Zeyen, 1993).
- A visual field may appear normal despite structural damage to the optic disc and RNFL.
- The starting moment and length for follow-up in studies and at clinic determine which defects, structural or functional, appear to progress first.

12.5.4 | Automated imaging devices and progression

- When confirming progression, careful evaluation is required to distinguish true clinically meaningful defects from lesions that represent variances related to the patient's anatomy, other eye diseases and the imaging technique.
- Given the need for life-long glaucoma monitoring, rapidly evolving imaging technologies pose a clinical challenge when the most recent test results may not be comparable with earlier examinations.
- In terms of long-term comparability, documentation of optic discs and RNFL with a digital camera will continue to play an important role in glaucoma diagnostics and monitoring (Azuara-Blanco et al., 2016; Chauhan & Burgoyne, 2013).
- It is not possible to consider numerous different metrics and their detailed repeatability in automated image outputs in everyday work, although the reproducibility of measurements has an important role in long-term monitoring.
- The results from different automated imaging methods and devices differ in both diagnostics and follow-up (Azuara-Blanco et al., 2016; Karvonen et al., 2020; Michelessi et al., 2015, 2021).
- It is essential to continuously assess not only which actions represent underdiagnosis and undertreatment, overtesting and overtreatment, but also which actions can unnecessarily increase the number of false positive results and even reduce the patient's quality of life (Caverly et al., 2014; Öhnell et al., 2021).

12.5.5 | Frequency of VF testing

- If glaucoma was monitored only with VFs, 2–6 re-tests may be needed to confirm progression, even if the VF has been examined with the same strategy and the same instrument (Glaucoma Laser Trial Research

Group, 1995; Keltner, 2000; Schulzer et al., 1994; Smith et al., 1996).
  - When the VF examination was repeated 1–2 times to confirm progression, progression could not be verified in more than half of the patients (Glaucoma Laser Trial Research Group, 1995; Keltner, 2000; Schulzer et al., 1994).
- When analysing disease progression, both event and trend-based analysis may be used.
- In ocular hypertension, very few VFs turn out to be abnormal during 5 years of follow-up (Kass et al., 2002; Keltner, 2000).
- If glaucoma was monitored only with yearly VFs, it may take up to 5 years to detect progression (Smith et al., 1996).
- It is worth noticing that these estimates are based on conventional threshold strategies, and the impact of faster VF strategies on adequate testing frequency is unclear (Thulasidas & Patyal, 2020).

12.5.6 | Evaluation and incidence of VF defect progression

- Although several qualitative and quantitative methods have been developed to define VF progression, no method has been proven to be superior in maintaining the quality of life of glaucoma patients (Ernest, Schouten, et al., 2012).
- Optimal VF test methods should be both highly sensitive and specific, provide very little test–retest variation and help detect progression using few retests.
- Incidence of VF progression varies considerably. Variation depends largely on the varying test methods (Ernest, Viechtbauer, et al., 2012).
- Some automated evaluation methods, such as Mean Defect (MD) and VF Index (VFI), and Glaucoma Change Probability (GCPC), can help assess progression (Ernest, Schouten, et al., 2012; Ernest, Viechtbauer, et al., 2012).
- VFI has been developed to predict the future rate of progression. Compared to the estimated progression based on the first 3 years of follow-up, the correlation with the actual VFI after 8 years of follow-up has been 0.78 (Ernest, Schouten, et al., 2012; Ernest, Viechtbauer, et al., 2012).
- Recommendations for glaucoma follow-up are presented in Figures 7 and 8.
- Recommendation for the treatment and follow-up of high-risk glaucoma patients is presented in Figure 6.
- If VF testing and fundus imaging cannot be done due to the patient's poor general health, the follow-up can consist of IOP measurements following to the ophthalmologist's instructions.

12.5.7 | Quality of life

- Although glaucoma seemingly affects quality of life, the effect is not necessarily substantial unless the patient's better eye has a severe VF loss. However, the more severe the VF damage, the greater the impact on quality life (Hagman, 2013; Odberg et al., 2001; Purola et al., 2022).
- Even in earlier stages of glaucoma, quality of life may be affected also by
  - fear of future vision loss
  - burdening related to commitments to life-long treatments
  - monitoring; intense monitoring does not improve quality of life (Hagman, 2013).
- The impact of any disease and its treatments on quality of life should be assessed in cost-effectiveness studies based on real-world data. As far as glaucoma is concerned, such information is limited (Crane et al., 2013; Tuulonen, 2011)
- Glaucoma does not appear to affect mortality (Borger et al., 2003; Grødum et al., 2004).

12.6 | Summary for primary health care

- General practitioners (GPs) should be able to
  - identify an acute angle-closure glaucoma and
  - manage its diagnostics and first aid.
- The diagnosis and treatment of open-angle glaucoma, as discussed in this recommendation, require specialised equipment and expertise.
- It is important to note that a normal visual acuity and intraocular pressure of 10–21 mmHg do not rule out glaucoma.
- A rebound tonometer is suitable for measuring intraocular pressure in primary care.
- Only very advanced glaucomatous visual field defects can be detected in a confrontational visual field test.
- Topical glaucoma medications can cause systemic adverse effects. More on this topic in the chapter *Adverse effects and allergic reactions*.
- General practitioners should remember the possibility of glaucoma, especially in high-risk patients (Table 1) and refer them to an ophthalmological examination as necessary.
- General practitioners should ensure that the patient's glaucoma prescriptions are up to date and that the patient is monitored regularly by an ophthalmologist.
- If the patient experiences glaucoma medication-related side effects or their IOP is over the maximum tolerated IOP and they have not contacted their eye care, GPs should consult an ophthalmologist. This also applies to situations where the patient is no longer under an eye clinic's care.
  - If the patient has a treatment plan with an eye clinic, GP can guide the patient to contact the eye clinic if he or she judges the patient is able to do so.

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