Indonesian Journal of Public Health
Volume.3 Issue.2, (July, 2026) Pages 122-130
E-ISSN:3048-1139
DOI : https://doi.org/10.62872/40bnns73
https://ejournal-nawalaedu.com/index.php/JHH/index

Intensive Intraocular Pressure-Lowering Treatment in Open-Angle Glaucoma Patients: Critical Review

Mega Ayu Naily Rahmatika[1], Hilmy Fawwas Al Hakim[2]
Puskesmas Guntur 1, Demak, Indonesia[1]

Received: July 01, 2026
Revised: July 24, 2026
Accepted: July 30, 2026
Published: July 31, 2026

Corresponding Author:
Author Name: Mega Ayu Naily Rahmatika
E-mail: megameg1612@gmail.com

Abstract**:** *Glaucoma is a progressive optic neuropathy and one of the leading causes of irreversible visual field loss and blindness worldwide, with intraocular pressure (IOP) representing the most important modifiable risk factor. The Glaucoma Intensive Treatment Study (GITS) evaluated the effectiveness of intensive IOP-lowering therapy compared with standard treatment in patients with newly diagnosed open-angle glaucoma. This critical review aimed to evaluate the study's methodology, findings, validity, strengths, limitations, and clinical implications for determining initial therapeutic strategies in open-angle glaucoma. A critical appraisal was conducted of the randomized controlled trial by Bengtsson et al. (2024), published in the American Journal of Ophthalmology, involving 242 treatment-naïve patients. Participants in the intensive treatment group received a combination of IOP-lowering medications and laser trabeculoplasty, whereas the standard treatment group received monotherapy. Intensive therapy achieved a significantly lower median IOP (14 mmHg vs. 17 mmHg) and reduced glaucoma progression (11% vs. 21%; p = 0.03). However, the primary endpoint, predicted lifetime Visual Field Index (VFI), showed no statistically significant difference (87.1% vs. 79.3%; p = 0.15), and the reduction in visual field deterioration was also not significant (p = 0.09). Moreover, adverse events occurred more frequently in the intensive treatment group (36% vs. 25%). Overall, GITS demonstrates that intensive IOP-lowering therapy improves IOP control and reduces glaucoma progression; however, its routine implementation cannot yet be universally recommended because of the absence of significant benefit in the primary outcome and the higher incidence of treatment-related adverse effects. Therapeutic decisions should therefore be individualized according to baseline IOP, disease severity, risk of progression, patient age, and the balance between potential benefits and harms.*

Keywords: glaucoma, open-angle glaucoma, intraocular pressure, visual field, intensive therapy, randomized controlled trial, critical review

How to cite:
Rahmatika, M. A. N., & Al Hakim, H. F. (2026). Intensive intraocular pressure-lowering treatment in open-angle glaucoma patients: Critical review. *Indonesian Journal of Public Health, 3*(2), 122–130. DOI: https://doi.org/10.62872/40bnns73

Indonesian Journal of Public Health
Volume.3 Issue.2, (July, 2026) Pages 122-130
E-ISSN:3048-1139
DOI : https://doi.org/10.62872/40bnns73
https://ejournal-nawalaedu.com/index.php/JHH/index

INTRODUCTION

Glaucoma is a group of chronic neurodegenerative diseases characterized by progressive optic neuropathy, including degeneration of retinal ganglion cells (RGCs) and their axons, characteristic changes in the optic nerve head, and progressive visual field loss. Optic nerve damage from glaucoma is irreversible, making early detection and treatment crucial to prevent or slow visual loss. In its early stages, glaucoma often causes no noticeable symptoms because visual field loss generally occurs slowly and begins in the peripheral areas. This condition causes some patients to only become aware of their visual impairment after the disease has reached an advanced stage (Weinreb et al., 2014).

Epidemiologically, glaucoma is one of the leading causes of irreversible blindness worldwide. The disease burden is expected to continue to increase with global population growth and aging. A meta-analysis by Tham et al. (2014) estimated the global prevalence of glaucoma in the 40–80 year old population at 3.54%. The number of glaucoma sufferers worldwide is projected to reach approximately 111.8 million by 2040, with a large burden of the disease particularly in Asia and Africa (Tham et al., 2014).

Clinically, glaucoma consists of several types, one of which is primary open-angle glaucoma (POAG), which is the most common form of primary glaucoma. Under physiological conditions, aqueous humor is produced by the ciliary body, then flows through the pupil to the anterior chamber and then out primarily through the trabecular meshwork to Schlemm's canal. The balance between aqueous humor production and outflow plays a crucial role in maintaining intraocular pressure (IOP). In POAG, the anterior chamber angle remains open, but there is increased resistance to aqueous humor outflow through the trabecular system, which can lead to increased IOP (Weinreb et al., 2014).

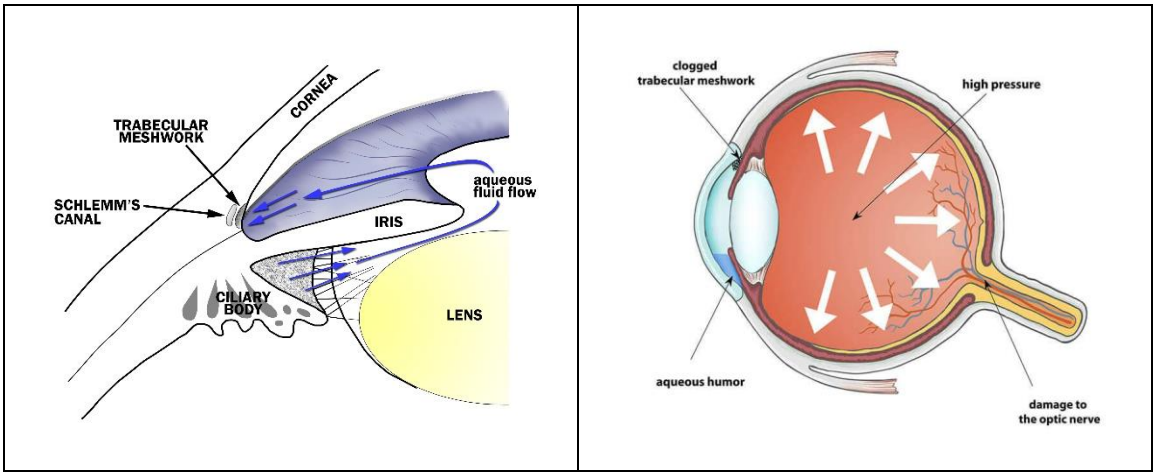


Figure 1. Mechanism of aqueous humor outflow and increased intraocular pressure in glaucoma (*Alward, WLM A new angle on ocular development, 2003*)

Indonesian Journal of Public Health
Volume.3 Issue.2, (July, 2026) Pages 122-130
E-ISSN:3048-1139
DOI : https://doi.org/10.62872/40bnns73
https://ejournal-nawalaedu.com/index.php/JHH/index

Figure 1:Studies have shown that aqueous humor produced by the ciliary body drains into the anterior chamber and exits through the trabecular meshwork. Increased resistance in this drainage pathway can lead to increased IOP and subsequently contribute to optic nerve damage. However, elevated IOP is not a prerequisite for glaucoma. Some patients can develop glaucomatous optic neuropathy even when their IOP is within the normal range, while individuals with elevated intraocular pressure do not necessarily experience optic nerve damage. This indicates differences in the susceptibility of optic nerve tissue to intraocular pressure in each individual.

Elevated IOP can exert biomechanical pressure on the optic nerve head structures, particularly the lamina cribrosa, the area where retinal ganglion cell axons leave the eyeball to form the optic nerve. Pressure and tissue deformation in this area can disrupt axonal transport, tissue perfusion, and cellular homeostasis, further contributing to axonal degeneration and retinal ganglion cell death. In addition to biomechanical mechanisms resulting from IOP, the pathogenesis of glaucoma is multifactorial and involves various other mechanisms, including impaired ocular perfusion, oxidative stress, mitochondrial dysfunction, neuroinflammation, excitotoxicity, aging, and genetic factors (Weinreb et al., 2014).

Progressive damage to retinal ganglion cells and their axons causes structural changes in the form of thinning of the retinal nerve fiber layer (RNFL), a reduction in the neuroretinal rim, and increased optic disc cupping. These structural changes are subsequently associated with functional impairment in the form of glaucomatous visual field defects. The relationship between structural changes in the optic nerve and visual impairment is an important characteristic of glaucoma progression (Weinreb et al., 2014).

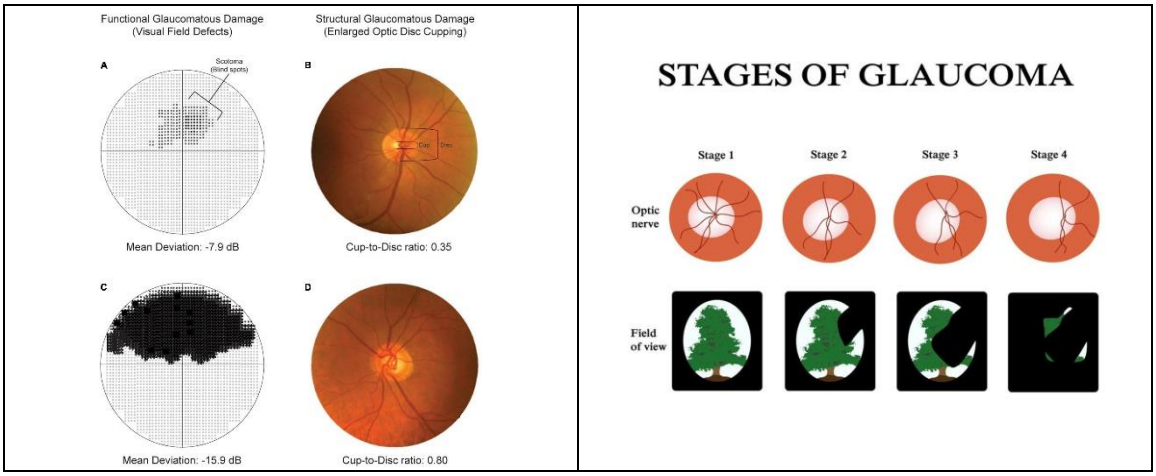


Figure 2.Progression of optic nerve damage and visual field in glaucoma (Weinreb, RN, Aung, T., & Medeiros, FAThe pathophysiology and treatment of glaucoma, 2014)

Figure 2:shows a comparison between a normal optic nerve head and a glaucomatous optic nerve head. Glaucomatous damage is characterized by a reduction in the neuroretinal rim and increased optic disc cupping, which is associated with the development of visual field defects. In

Indonesian Journal of Public Health
Volume.3 Issue.2, (July, 2026) Pages 122-130
E-ISSN:3048-1139
DOI : https://doi.org/10.62872/40bnns73
https://ejournal-nawalaedu.com/index.php/JHH/index

the early stages, visual field defects may include a paracentral scotoma, nasal step, or arcuate scotoma. As the disease progresses, these defects can become more extensive and, in later stages, can cause severe visual field narrowing and significant visual loss.

Although the pathogenesis of glaucoma is multifactorial, IOP is the primary risk factor that can be modified through therapeutic intervention. Other factors associated with the risk of glaucoma development and progression include age, family history, genetic predisposition, central corneal thickness, myopia, optic disc characteristics, and vascular factors. However, compared to these factors, IOP plays a special role because it can be modified through pharmacological therapy, laser therapy, or surgery (Weinreb et al., 2014).

Thus, the primary principle of glaucoma management is to lower IOP to a level deemed safe enough to slow the progression of optic nerve damage and preserve the patient's visual function for as long as possible. However, the target IOP reduction and optimal therapy intensity need to be tailored to each patient's individual characteristics and risk of progression. This is crucial in determining whether a patient with newly diagnosed glaucoma requires intensive IOP-lowering therapy from the outset or whether a stepwise approach can be successfully managed.

METHODOLOGY

The Glaucoma Intensive Treatment Study (GITS) is a prospective, randomized, controlled, open-label, two-center clinical trial that aims to compare the effectiveness of an intensive, early-stage intraocular pressure (IOP) lowering strategy with standard therapy in patients with newly diagnosed open-angle glaucoma. The study was conducted at two university hospitals in Sweden: Skåne University Hospital, Malmö, and Umeå University Hospital, Umeå (Bengtsson et al., 2024).

An open-label design means that both patients and clinicians know which treatment group they are receiving. However, using a randomized controlled trial design allows for prospective comparison of the two treatment strategies and reduces the potential for selection bias through the randomization process.

Research Population and Sample

The study involved 242 patients with newly diagnosed open-angle glaucoma who had not previously received IOP-lowering therapy. The recruited patients had early-to-moderate glaucomatous visual field loss (Bengtsson et al., 2024).

Participants were then randomly allocated in a 1:1 ratio into two treatment groups: standard monotherapy and intensive therapy. This randomization was intended to ensure that each group had relatively comparable baseline characteristics, making it more likely that any differences in outcomes emerging during the study were related to the treatment strategy administered.

Standard Therapy Group

In the standard therapy group, patients started treatment with a single topical IOP-lowering medication (monotherapy). This approach mirrors conventional therapy strategies, where

Indonesian Journal of Public Health
Volume.3 Issue.2, (July, 2026) Pages 122-130
E-ISSN:3048-1139
DOI : https://doi.org/10.62872/40bnns73
https://ejournal-nawalaedu.com/index.php/JHH/index

treatment is initiated with a single agent and then increased if IOP control is deemed inadequate or if other clinical indications for therapy intensification arise (Bengtsson et al., 2024).

Thus, this group does not mean that patients receive only one drug throughout the entire study period. Therapy can be modified or increased according to the patient's clinical progress during follow-up.

Intensive Therapy Group

In the intensive therapy group, patients received a more aggressive IOP-lowering strategy from the outset. Based on the GITS protocol and the study's interim report, patients in this group received IOP-lowering medications from three different drug classes, followed by 360-degree laser trabeculoplasty (Bengtsson et al., 2021).

This strategy is designed to produce greater and more rapid IOP reductions than conventional monotherapy approaches. By intensively lowering IOP early, researchers wanted to determine whether exposing the optic nerve to lower pressures throughout the disease course could provide greater protection against progressive visual field loss.

Follow-up and Examination

Participants were followed longitudinally for five years. During this period, regular clinical examinations were performed to evaluate intraocular pressure and visual function development. IOP was evaluated using tonometry, while visual field function was repeatedly assessed using standard automated perimetry (SAP). Serial visual field examinations were a crucial component of the study because they allowed researchers to assess changes in visual function over time and quantify the rate of progression of visual field loss (Bengtsson et al., 2024).

In addition, longitudinal monitoring allows researchers to compare the achieved IOP levels, the incidence of glaucoma progression, and the side effects that occur with both therapy strategies.

Research Outcomes

The primary outcome of the study was the prediction of the remaining Visual Field Index (VFI) at the end of the patient's life. This prediction was based on the development of VFI during the observation period and took into account the patient's age and estimated life expectancy (Bengtsson et al., 2024). In addition to the primary outcome, several other outcomes were also evaluated, including:

1. IOP levels during the follow-up period;
2. rate of change or loss of VFI per year;
3. glaucoma progression events;
4. differences in visual field development between the intensive therapy and monotherapy groups; and
5. occurrence of adverse events in each therapy group.

The use of visual field parameters as outcomes has clinical relevance because the primary goal of glaucoma therapy is not only to produce a reduction in IOP, but to maintain the patient's visual function for as long as possible.

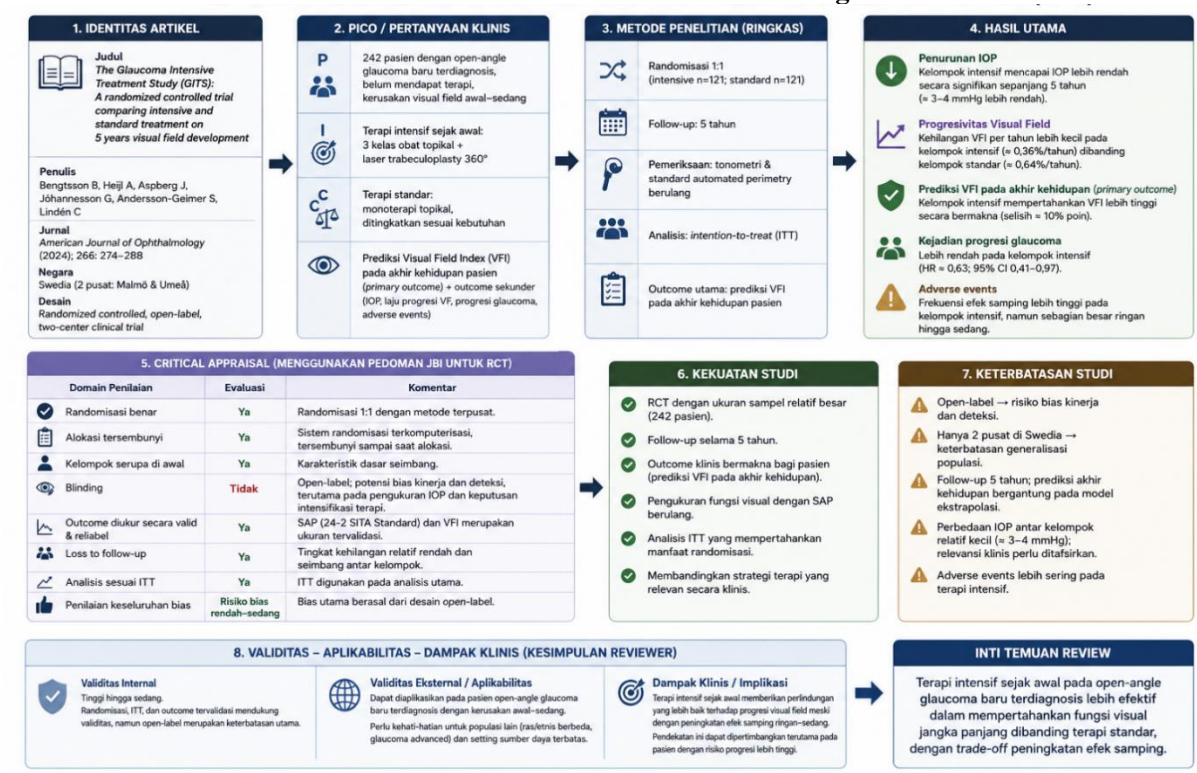
Indonesian Journal of Public Health
Volume.3 Issue.2, (July, 2026) Pages 122-130
E-ISSN:3048-1139
DOI : https://doi.org/10.62872/40bnns73
https://ejournal-nawalaedu.com/index.php/JHH/index

Data analysis

The primary analysis of the study was conducted based on the intention-to-treat (ITT) principle. In this approach, patients remain analyzed according to their initial randomization group, regardless of any changes or intensifications in therapy that may occur during the study period. The ITT principle is important in randomized controlled trials because it helps maintain the benefits of randomization and reduces bias that can arise from crossover, therapy changes, or non-adherence to the protocol (Bengtsson et al., 2021; Bengtsson et al., 2024).

Longitudinal data from visual field examinations were used to estimate the rate of change in visual function during follow-up. The results of the two groups were then compared to determine whether the intensive therapy strategy resulted in improvement. greater protection against glaucoma progression than standard therapeutic strategies.

Table 1. Framework of Thought



Analysis Results, 2026

RESULTS AND DISCUSSION

Based on the results of the Glaucoma Intensive Treatment Study (GITS) by Bengtsson et al. (2024), the median intraocular pressure (IOP) before therapy was 24 mmHg in both groups. During the follow-up period, the median IOP in the monotherapy group reached 17 mmHg, while

Indonesian Journal of Public Health
Volume.3 Issue.2, (July, 2026) Pages 122-130
E-ISSN:3048-1139
DOI : https://doi.org/10.62872/40bnns73
https://ejournal-nawalaedu.com/index.php/JHH/index

in the intensive therapy group it reached 14 mmHg. These results indicate that the intensive therapy strategy is able to produce lower IOP control than monotherapy.

In the primary outcome, which predicted the remaining visual field function at the end of life, the median Visual Field Index (VFI) in the monotherapy group was 79.3%, while the median VFI in the intensive therapy group was 87.1%. Although numerically, the intensive therapy group demonstrated better visual field preservation, the difference did not reach statistical significance ($p = 0.15$).

The annual rate of visual field loss also tended to be lower in the intensive therapy group. The median VFI loss in the monotherapy group was 0.65 percentage points/year, compared to 0.25 percentage points/year in the intensive therapy group. However, this difference did not reach statistical significance ($p = 0.09$).

A significant difference was found in the incidence of glaucoma progression. Progression occurred in 21% of patients in the monotherapy group compared to 11% of patients in the intensive therapy group, a statistically significant difference ($p = 0.03$). These findings indicate that intensive therapy is associated with a lower incidence of glaucoma progression during the study period.

On the other hand, adverse events were more common in the intensive therapy group. Side effects were reported in 25% of patients in the monotherapy group compared to 36% in the intensive therapy group, although most of the side effects were mild.

Further analysis showed that the difference in visual field outcomes between the two groups was more pronounced in patients with higher baseline IOP. This finding suggests that the benefits of intensive therapy may not be uniform across all patients and may be greater in the group with higher baseline IOP.

Table 2. Research Results

Parameter	Monotherapy	Intensive Therapy	p-value
Median IOP before therapy	24 mmHg	24 mmHg	-
Median IOP during follow-up	17 mmHg	14 mmHg	-
Predicted VFI at end of life	79.3%	87.1%	0.15
Loss of VFI per year	0.25 percentage points/year	0.25 percentage points/year	0.09
Progression events	21%	11%	0.03
Adverse events	25%	36%	-

Analysis Results, 2026

CONCLUSIONS

Based on the Glaucoma Intensive Treatment Study (GITS) by Bengtsson et al. (2024), a randomized controlled trial provides important evidence regarding the effectiveness of an intensive intraocular pressure (IOP) lowering strategy from the outset compared to standard therapy in patients with newly diagnosed open-angle glaucoma. This study has several methodological strengths, particularly its randomized design, five-year follow-up period, the use of standardized

Indonesian Journal of Public Health
Volume.3 Issue.2, (July, 2026) Pages 122-130
E-ISSN:3048-1139
DOI : https://doi.org/10.62872/40bnns73
https://ejournal-nawalaedu.com/index.php/JHH/index

serial automated perimetry, and an intention-to-treat analysis. The use of visual field function as an outcome measure also enhances the clinical relevance of the study because the primary goal of glaucoma therapy is to maintain patients' visual function in the long term.

The results showed that intensive therapy achieved lower IOP and resulted in fewer glaucoma progression events compared to monotherapy. However, the primary outcome, predicted Visual Field Index (VFI) at the end of life, did not show a statistically significant difference. Similarly, the difference in annual visual field loss rates did not reach statistical significance. Furthermore, intensive therapy was associated with a higher frequency of adverse events. Therefore, the results cannot be interpreted as evidence that intensive therapy is universally superior for all patients with open-angle glaucoma.

From a critical appraisal perspective, the study's internal validity was generally good, but its open-label design, its implementation at only two centers in Sweden, and its use of end-of-life VFI prediction as the primary outcome are some limitations that need to be considered. The finding that the benefit of intensive therapy appears to be greater in patients with high baseline IOP also stems from further analysis and requires confirmation in prospective studies specifically designed for this patient group.

Overall, the GITS study supports the importance of optimal IOP control from the time of diagnosis, but does not yet provide a sufficient basis for routinely implementing intensive therapy for all open-angle glaucoma patients. The choice of treatment strategy should be individualized, taking into account baseline IOP, the degree of visual field loss, the risk and rate of progression, the patient's age and life expectancy, tolerance to therapy, and the risk of side effects. Therefore, the primary contribution of the GITS study is to strengthen the individualized, risk-based approach to glaucoma management, where therapy intensity is tailored to the risk of progression and the clinical needs of each patient.

REFERENCES

Alward, W. L. M. (2003). A new angle on ocular development. Science, 299(5612), 1527–1528. https://doi.org/10.1126/science.1082259

Bengtsson, B., Heijl, A., Aspberg, J., Jóhannesson, G., Andersson-Geimer, S., & Lindén, C. (2024). The Glaucoma Intensive Treatment Study (GITS): A randomized controlled trial comparing intensive and standard treatment on 5 years visual field development. American Journal of Ophthalmology, 266, 274–288. https://doi.org/10.1016/j.ajo.2024.06.017

Bengtsson, B., Heijl, A., Johannesson, G., Andersson-Geimer, S., Aspberg, J., & Lindén, C. (2021). The Glaucoma Intensive Treatment Study (GITS), a randomized clinical trial: Design, methodology and baseline data. Acta Ophthalmologica, 99(4), 436–443.

Bengtsson, B., Leske, M. C., Hyman, L., & Heijl, A. (2007). Fluctuation of intraocular pressure and glaucoma progression in the Early Manifest Glaucoma Trial. Ophthalmology, 114(2), 205–209. https://doi.org/10.1016/j.ophtha.2006.07.060

Gazzard, G., Konstantakopoulou, E., Garway-Heath, D., Barton, K., Wormald, R., Morris, S., Hunter, R., Rubin, G., Buszewicz, M., Ambler, G., & LiGHT Trial Study Group. (2023).

Indonesian Journal of Public Health
Volume.3 Issue.2, (July, 2026) Pages 122-130
E-ISSN:3048-1139
DOI : https://doi.org/10.62872/40bnns73
https://ejournal-nawalaedu.com/index.php/JHH/index

Laser in Glaucoma and Ocular Hypertension (LiGHT) Trial: Six-year results of primary selective laser trabeculoplasty versus eye drops for the treatment of glaucoma and ocular hypertension. Ophthalmology, 130(2), 139–151. https://doi.org/10.1016/j.ophtha.2022.09.009

Heijl, A., Leske, M. C., Bengtsson, B., Hyman, L., Bengtsson, B., Hussein, M., & Early Manifest Glaucoma Trial Group. (2002). Reduction of intraocular pressure and glaucoma progression: Results from the Early Manifest Glaucoma Trial. Archives of Ophthalmology, 120(10), 1268–1279. https://doi.org/10.1001/archopht.120.10.1268

Tham, Y. C., Li, X., Wong, T. Y., Quigley, H. A., Aung, T., & Cheng, C. Y. (2014). Global prevalence of glaucoma and projections of glaucoma burden through 2040: A systematic review and meta-analysis. Ophthalmology, 121(11), 2081–2090. https://doi.org/10.1016/j.ophtha.2014.05.013

Weinreb, R. N., Aung, T., & Medeiros, F. A. (2014). The pathophysiology and treatment of glaucoma: A review. JAMA, 311(18), 1901–1911. https://doi.org/10.1001/jama.2014.3192