MedPharmRes (MPR) TITLE PAGE

Upload this completed form to website with submission

ARTICLE INFORMATION	Fill in information in each box below
Article Type	Research article
Article Title (within 20 words without abbreviations)	**Cost-effectiveness analysis of the fixed-dose combination of *Dorzolamide* + *Timolol* versus *Brinzolamide+Timolol* in the treatment of ocular hypertension and Primary open-angle glaucoma in Vietnam**
Running Title (within 10 words)	CEA of FDC Dorzolamide+Timolol in treatment of glaucoma in Vietnam
Author	Nguyen Thi Hong Tran 1, Hung Manh Nguyen1, Uyen Le Lan Ngo1, Chau Thi Khanh Le2, Nga Thi Kieu Dang1, Nga Thi Quynh Nguyen1, Tuan Duc Nguyen1, Yen Thi Hai Nguyen1
Affiliation	1Department of Pharmaceutical Administration, University of Medicine and Pharmacy at Ho Chi Minh, Ho Chi Minh City, Viet Nam. 2Department of Pharmacy, Eye Hospital in Ho Chi Minh, Ho Chi Minh City, Viet Nam.
ORCID (for more information, please visit https://orcid.org)	Nguyen Thi Hong Tran (https://orcid.org/0000-0003-1043-6484) Hung Manh Nguyen (https://orcid.org/0000-0001-5610-3234) Uyen Le Lan Ngo (https://orcid.org/0009-0003-3154-5396) Nga Thi Kieu Dang (https://orcid.org/0009-0000-2002-7495) Nga Thi Quynh Nguyen (https://orcid.org/0000-0001-9843-4410) Tuan Duc Nguyen (https://orcid.org/0000-0001-9479-403X) Yen Thi Hai Nguyen (https://orcid.org/0009-0000-4948-4294)
Competing interests	No potential conflict of interest relevant to this article was reported.
Funding sources State funding sources (grants, funding sources, equipment, and supplies). Include name and number of grant if available.	This study was funded by the Saigon Pharmaceutical Science and Technology Center - SAPHARCEN, University of Medicine and Pharmacy at Ho Chi Minh City, and Santen Pharmaceutical Co., Ltd. Vietnam.
Acknowledgements	We would like to show our utmost gratitude towards the clinicians and facilitators from Ho Chi Minh Eye Hospital for their vital supports leading to the success of our research.
Availability of data and material	Upon reasonable request, the datasets of this study can be available from the corresponding author.
Authors' contributions Please specify the authors' role using this form. Authors can't change and add items, but you can delete items that are not applicable.	Conceptualization: Nguyen Thi Hong Tran, Yen Thi Hai Nguyen, Nga Thi Quynh Nguyen Data curation: Nguyen Thi Hong Tran, Nga Thi Quynh Nguyen, Chau Thi Khanh Le Formal analysis: Nguyen Thi Hong Tran, Uyen Le Lan Ngo, Chau Thi Khanh Le Methodology: Nguyen Thi Hong Tran, Yen Thi Hai Nguyen, Nga Thi Quynh Nguyen, Tuan Duc Nguyen Software: Nguyen Thi Hong Tran, Nga Thi Kieu Dang, Nga Thi Quynh Nguyen Validation: Yen Thi Hai Nguyen, Nga Thi Quynh Nguyen, Nga Thi Kieu Dang, Tuan Duc Nguyen Investigation: Nguyen Thi Hong Tran, Uyen Le Lan Ngo, Tuan Duc Nguyen Writing - original draft: Nguyen Thi Hong Tran, Hung Manh Nguyen Writing - review & editing: Nguyen Thi Hong Tran, Hung Manh Nguyen, Uyen Le Lan Ngo, Nga Thi Kieu Dang, Nga Thi Quynh Nguyen, Yen Thi Hai Nguyen.

Ethics approval and consent to participate	The study is exempt from ethics approval and consent to participate. For this research, ethical approval was not required because the study involves secondary data analysis of previously published clinical trial data, cost data, and health outcomes rather than direct patient interactions or clinical trials. No personal identifying information was collected from participants, and the study did not involve any interventions or modifications to treatment plans. Therefore, it falls outside the scope of ethical review requirements typically required for studies involving human subjects or direct interventions.

CORRESPONDING AUTHOR CONTACT INFORMATION

For the corresponding author (responsible for correspondence, proofreading, and reprints)	**Fill in information in each box below**
First name, middle initial, last name	Nguyen Thi Hai Yen
Email address – this is where your proofs will be sent	haiyen@ump.edu.vn
Secondary Email address	
Address	41-43 Dinh Tien Hoang Str., Ben Nghe Ward, District 1, Ho Chi Minh City, Viet Nam
Cell phone number	0938769626
Office phone number	
Fax number	

Abstract

Introduction: This pharmacoeconomic assessment aimed to explore the cost-effectiveness of the fixed-dose combination of *Dorzolamide+Timolol* (DTFC) in ocular hypertension and primary open-angle glaucoma (OH/POAG) in Vietnam. **Methods:** A cost-effectiveness analysis from third-party health payer perspective was designed with mixed modelling technique to simulate the long-term care for OH/POAG patients in Vietnam. With fixed-dose combination of *Brinzolamide+Timolol* (BTFC) as comparator, the treatment process was simulated by the decision-tree model for initial therapy and continued with the Markov model for maintenance therapy. Model parameters were derived from multiple sources, including real-world data, literature reviews and clinician consultations. Sensitivity analysis, including deterministic and probabilistic analyses, was conducted to explore the uncertainty of model outcomes. **Results:** Base case analysis showed that the cost of treatment for each patient by *DTFC* was 42,906,600 VND, and by *BTFC* was 43,864,938 VND, while the comparative effectiveness was not different. Costs for healthcare services and medications were the most influential factors to model outcomes. DTFC demonstrated a 53.51% probability of being cost-effective compared to BTFC at the standard willingness-to-pay threshold. **Conclusion:** From third-party health payer perspective, *DTFC* was the more cost-saving option while maintaining treatment benefits, compared to *BTFC*.

Keywords: Dorzolamide+Timolol, primary open-angle glaucoma, ocular hypertension, fixed-dosed combination, cost-effectiveness analysis.

1. INTRODUCTION

According to the World Health Organization, around 7.7 million cases of glaucoma led to moderate-to-severe vision impairment and blindness in 2020 [1]. This disease is categorized into two subtypes, namely open-angle glaucoma and angle-closure glaucoma, with the latest global prevalence of 3.05% and 0.5%, respectively [2]. The number of glaucoma cases in the 40–80-year-old age group was predicted to reach 111.8 million by 2040, among which approximately 79.76 million would suffer from primary open-angle glaucoma (POAG) [2]. Presenting the highest number of POAG and angle-closure glaucoma cases (23.54 million and 15.47 million respectively), Asia, followed by Africa, plays a significant role in the global management of glaucoma, and poses the urging necessity for the development healthcare system in glaucoma screening and treatment [2].

The current consensus guideline offers three approaches for glaucoma therapy including medication therapy, laser procedures and surgery, with the treatment objectives of preventing or deferring disease progression and complications on optic nerve system, maintaining vision and quality of life for patients [3–6]. The most common treatment option is medication therapy, in which fixed-dosed combination (FDC) eye-drop products gain fondness for the benefits of simplifying treatment regimen and improving patient adherence. According to the 4th Guideline by Asia Pacific Glaucoma Society in 2024, FDC formulation enhances the ease of use for patients since it is only required one drop each use, instead of multiple drops from different packages, which lowers the risk of improper regimen use [5]. In their systematic review and meta-analysis publication, Wei et al showed that FDC therapy significantly improved the medication compliance of patients by 1.29 times (95% CI: 1.23-1.35, $p<0.001$) comparing to free-equivalent combination therapy [7].

In Vietnam, according to Circular No. 20/2022/TT-BYT, only two FDC regimens for glaucoma, namely *prostaglandin analogues* (PGA) + Timolol and *carbonic anhydrase inhibitors* (CAI) + Timolol, are reimbursed by health insurance. Based on clinical practice, expert consultations, and treatment guidelines, the CAI + Timolol group is frequently used for patients who require additional IOP reduction after monotherapy with β-blockers or who do not tolerate PGA therapy. Although PGA + Timolol combinations are also reimbursed, they differ significantly in the mechanism of action, clinical indication, and patient profile, and are often reserved for cases requiring more aggressive IOP-lowering effects. In addition, free-equivalent combinations (FECs) were excluded due to lower adherence and inferior cost-effectiveness compared to FDCs [5,7]. As such, BTFC was selected as the most clinically relevant and appropriate comparator for DTFC in this context. The two popular

FDCs of *CAI* and Timolol are *Dorzolamide + Timolol (DTFC)* and *Brinzolamide + Timolol (BTFC)*. Though evidence on the comparative clinical efficacy of *DTFC* and *BTFC* are available, there are lack of publication in Vietnam on the pharmacoeconomic comparison of the two in treatment for glaucoma and ocular hypertension (OH), which raises the question of their offering in economic benefits for patients [8–10]. Thus, this study aimed to analyse the cost-effectiveness of *DTFC* versus *BTFC* in the treatments of OH/POAG in Vietnam. The results can provide insights on the economic efficiency of *DTFC*, which aid the health policy development and the glaucoma-therapy indication for optimal treatment effectiveness.

2. MATERIALS AND METHODS

2.1. Research population

In this pharmacoeconomic assessment of Dorzolamide + Timolol Fixed-Dose Combination (DTFC) versus Brinzolamide + Timolol Fixed-Dose Combination (BTFC), the target population was defined as adult patients diagnosed with ocular hypertension (OH) or primary open-angle glaucoma (POAG), according to the ICD-10 diagnosis code H40.11. The population included patients with mild-to-moderate OH, encompassing both treatment-naïve and previously treated individuals. Disease severity was classified based on the POAG severity stages in the Markov model, reflecting the progression from ocular hypertension to early-stage POAG. Patients were included in the model if they had OH or POAG, with or without optic atrophy or related complications, such as visual field loss. Importantly, patients without other concurrent ocular pathologies were considered for inclusion, and it was assumed that those with OH would enter the Markov model through the 'early POAG' stage once treatment criteria were met.

2.2. Research design

This pharmacoeconomic study applied modelling techniques, using real-world data from Ho Chi Minh Eye Hospital for the cost-effectiveness analysis of *DTFC* versus *BTFC* in the treatment of OH/POAG. Model parameters such as response rates, treatment switching, and resource use frequencies were determined through structured consultations with ophthalmologists at Ho Chi Minh Eye Hospital, and triangulated with evidence from published clinical trials and systematic reviews. This study was conducted in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 guidelines [11]. A completed checklist is provided as Supplementary Table 1.

2.2.1. Comparator

BTFC was chosen as research comparator for the usual clinical practice and choice of treatment in Vietnamese settings, as priorly presented in the Introduction section.

2.2.2. Costing perspective

Perspective of third-party payer in healthcare (Vietnam Health Insurance Fund in particular) was adopted in this analysis, accounting for direct medical costs for medication and health services incurred from laser procedures, diagnostic examinations (including visual field test, tonometry, optic disc photography, retinal-optic disc tomography), hospital stays, and physical examinations. Societal costs, such as productivity loss or informal care, were not included. All cost data were collected and reported in Vietnamese Dong (VND) in 2024, reflecting the local healthcare payer's perspective.

2.2.3. Assessment outcome

Incremental cost-effectiveness ratio (ICER) per quality-adjusted life year (QALY) was calculated for cost-effectiveness conclusions, which was derived from treatment effectiveness by QALY and costing estimation in 2024. This indicator is widely used for its universal implication but features a limitation in disease-specific willingness to pay threshold, which can lead to misinterpretation if not carefully examined.

2.3. Modelling technique

A decision-tree model and a Markov model were combined to simulate treatment pathways and long-term disease progression, developed by consensus treatment guideline and validated by expert consultation. The decision-tree model captured short-term therapeutic decisions (e.g., treatment response and switching) during the initial year, which are often nonlinear and require discrete branching logic. The Markov model then simulated long-term disease progression across health states with annual cycles, which was deemed appropriate for chronic conditions like POAG. This mixed modelling approach is widely recommended in pharmacoeconomic modelling of chronic diseases and aligns with prior studies. [12,13]

2.3.1. Decision-tree model

In the decision-tree model, a hypothetical cohort of 10,000 patients with OH or POAG, refractory to monotherapy, were assigned to either the DTFC or BTFC treatment arms. Patients were evaluated under two scenarios: Scenario 1 assumed treatment success with FDC, maintaining the therapy throughout the analysis period. In Scenario 2, patients unresponsive to FDC were reassigned to alternative strategies, including switching to the counterpart treatment arm, adding prostaglandin analogues, or proceeding directly to laser surgery if no response was observed. (Figure 1)

[Place Figure 1 here]

2.3.2. Markov model

The model was designed to simulate long-term disease progression following the acute treatment. Hither, patients were put under the assumptions of continuing previously responsive treatment until the end of observation, and of absolute treatment adherence. The health states of the model were early POAG (MD < -6dB), moderate POAG (MD < -12dB), advance POAG (MD > -12dB), blindness and death.

[Place Figure 2 here]

2.3.3. Timeframe of analysis and discount rate

The timeframe of decision tree model was twelve months with 3-month cycle, while Markov model applied lifetime timeframe with cycle duration of one year.

The value of discount rate for both cost and effectiveness parameters was 5% per year. The discount rate followed the consensus recommendation in health economics and was suitable for economic context in Vietnam [14].

2.4. Model parameters

2.4.1. Transitional probability

In the decision-tree model, the transition probabilities for each treatment arm were determined based on IOP reduction achieved by the respective treatments. These values were derived from a meta-analysis of randomized controlled trials (RCTs) and reflect treatment-specific efficacy. To simulate treatment pathways accurately, the proportions of patients requiring treatment reassignment or escalation after becoming refractory to first-line therapy were informed by clinical expert consultation at Ho Chi Minh Eye Hospital, ensuring the model closely reflects real-world clinical practices.

In the Markov model, transition probabilities between health states were determined based on disease progression data and adjusted according to treatment effectiveness reflected by IOP reduction. The IOP levels achieved in the decision-tree model were used to estimate changes in visual field (VF), which defined each patient's health state (e.g., early, moderate, or advanced POAG) at the start of the Markov phase. These health states then guided the transition frequencies over time. This approach allowed the model to dynamically simulate disease progression as influenced by treatment response. The transitional probability to the "death" health state was extracted from Vietnamese age- and sex-standardized mortality statistics by World Health Organization [15].

Information on transitional probability and proportion for both models are provided in Table 1.

[Insert Table 1 here]

2.4.2. Effectiveness parameter

The vital clinical indicators based on the conclusion from literature reviews and clinical expert opinions were "the mean reduction of IOP", "visual field damage" and "quality-adjusted life years". These indicators were included to the models as effectiveness parameters.

The mean reduction of IOP: Data on IOP reduction from each treatment phase were derived from meta-analysis of randomized controlled trials of respective treatment [16].

Visual field damage: The severity of visual field damage was based on the visual field mean deviation (MD), following the approach of Canadian Agency for Drugs and Technologies in Health in effectiveness assessment of glaucoma treatments in health economic assessment [17]. Accordingly, the change of MD was calculated as follows, using the natural disease progression (NP) of untreated glaucoma patient and the standardized reduction (SR) derived from visual field damage and IOP reduction [13].

$$\text{Change of MD} = NP \times SR^{(\text{annual IOP reduction})} = 0.6 \text{ dB} \times 0.905 \text{ dB}^{(\text{annual IOP reduction})}$$

In the above formula, the annual IOP reduction in each treatment arm was calculated as the sum of the IOP reduction in one year of treatment wherein multiple interventions were implemented as simulated by the decision-tree model.

Quality-adjusted life years (QALYs): Data on the treatment effectiveness based on QALYs were derived from the systematic reviews results on utility values in respective health state representing the severity of disease. Data of utility value in each health state and their respective probability distribution are presented in Table 2.

[Insert Table 2 here]

2.4.3. Costing parameter

Costs of medication were extracted from the latest "Summarized drug bidding reports of distribution facilities" of the Department of Pharmaceutical Management-Vietnam Ministry of Health by the time of research completion.

[Insert Table 3 near this point]

The clinical consultation was implemented in 2024 to simulate the most updated the clinical practice of OH/POAG treatment in Vietnamese medical settings. Costs incurred for health services were calculated in Vietnam Dong before converting to USD using the exchange rate in 2024. The calculation was derived from clinician consultation and official costs of health services promulgated in Circular no. 22/2022/TT-BYT by the Vietnam Ministry of Health [18].

[Insert Table 4 near this point]

2.5. Statistical method

2.5.1. Base case analysis

The total costs and QALYs were calculated for *DTFC* and *BTFC* over two models with respective timeframe as presented. From a payer perspective, total costs included direct medical costs (covered by third-party payers). The primary outcome was ICER defined as the difference in costs divided by the difference in QALYs of the two treatment arms. Willingness-to-pay threshold was set at 3-time of GDP per capita in Vietnam, published by the General Statistics Office of Vietnam [19].

2.5.2. Uncertainty analysis

Deterministic sensitivity analysis (DSA) served to assess the uncertainty of the models and explore the parameters to which the models were most sensitive. Each parameter, one at a time, was adjusted between corresponding 95% confidence intervals, or 20% deviation, or standard upper and lower values (such as 0% and 6% for discounting parameter of cost and effectiveness). For the probabilistic sensitivity analysis (PSA), Monte Carlo simulation method was applied with 10,000 iterations. In each of which, the model parameters were assigned value randomly drew from corresponding probability distributions to explore the robustness of the results to variations of multiple parameters at once.

2.6. Patient and public involvement and engagement

The development of research objectives and design went through a thorough process of consultation from relevant stakeholders to answer the most critical question for the best choice of OH/POAG treatment that addressed the interest of both clinical practitioner and health policy makers. Furthermore, the estimation of cost and effectiveness parameters were performed by using real-world data from Ho Chi Minh Eye Hospital and offered the most relatable and applicable scenario for the implication and suggestion in Vietnamese medical setting. The results were then simplified and translated in the mutual, and less field-specific, context that can extend the coverage in the use of findings to the most relevant population possible.

3. RESULTS

3.1. Base case analysis

The results from base case analysis of the hypothetical population showed that the total cost of treatment by *DTFC* was 429,066,001,437 VND, and by *BTFC* was 438,649,383,016 VND. The cost difference of the two arms was -9,583,381,579 VND. Regarding treatment effectiveness, *DTFC* arm yielded 94,955.41 QALYs at the end of analysis timeframe, higher than *BTFC* with 94,943.59 QALYs, offering an additional benefit of 11.82 QALYs.

Consequently, regarding the comparative analysis for each patient, cost of treatment by *DTFC* was 42,906,600 VND, lower than the cost of treatment by *BTFC* (43,864,938 VND), differed by -958,338 VND (for one year in the decision-tree model and 40 years in the Markov model). *DTFC* offered 9.5 QALYs for each patient, higher than *BTFC* (9.49 QALYs). However, the difference in quality-of-life benefits from *DTFC* and *BTFC* was insignificant with only 0.001182 QALY. While the QALY difference per patient was small (0.001182), the cost savings observed and the potential for improved adherence justify consideration in treatment policy. This indicated the lower treatment cost of *DTFC* compared to *BTFC*, while their comparative effectiveness is almost equal.

Table 5 shows the results of base-case analysis on the hypothesis population and for each patient.

[Insert Table 5 here]

3.2. Deterministic sensitivity analysis

The results of DSA are presented as a tornado diagram in Figure 5, designed to depict the change intensity of ICER as each parameter deviates. Accordingly, the models were most influenced by variation of the costs incurred for health services. The second- and third-most influencing parameters were costs for *DTFC* treatment, and costs for *BTFC* treatment in each health state in Markov model.

[Place Figure 3 near this point]

3.3. Probabilistic sensitivity analysis

Results of PSA using Monte-Carlo 10,000-iteration simulation are presented in Figure 4 and 5. At the willingness-to-pay of 3-time Vietnam GDP per capita in 2023 (approximately 305,7 million VND per QALY gained), DTFC demonstrated a 53.51% probability of being cost-effective compared to BTFC at the standard willingness-to-pay threshold.

[Place Figure 4 and 5 near this point]

4. DISCUSSION

Results from base case analysis showed that *DTFC* was more cost savings than *BTFC*, while guaranteed treatment effectiveness since the difference was insignificant. Costs incurred for

health services and medication costs were the parameters that had the most influence on the model outcome. PSA results showed that at the willingness-to-pay threshold of 3-time GDP per capital in Vietnam, *DTFC* had a probability of 51.53% of being cost-effective compared to BTFC. Our findings indicated the cost-saving potential of glaucoma treatment by *DTFC*, but the treatment selection should be carefully considered based on other associated factors and cost-effectiveness probability under the influence of abovementioned factors in Markov model.

The models applied in our pharmacoeconomic assessment were developed using literature reviews on disease progression, pharmacoeconomic models on the treatment for OH/POAG and clinician consultation [12,13]. The objectives were to propose the model with proper structure that can reflect the clinical practices in two phases: (1) the initial treatment phase depicted through the decision-tree model, and (2) the maintenance treatment phase depicted through the Markov model. This approach not only offers the compatibility with practical treatment procedure, but also simulates the natural disease progression, enabling the monitoring of unrecovered disease progression through different health states as follows: "early POAG", "moderate POAG", "advance POAG", "blindness" and "death". The analysis timeframe, including the first year in decision-tree model and the lifetime timeframe in the Markov model, offers strength in analysis, since it reflects the chronic characteristics of the disease, and yields more accurate prediction in costs for long-term care. Moreover, the real-world data for pharmacoeconomic analysis retrieved from Ho Chi Minh Eye Hospital were used to optimize the input data that can address the practical situation in Vietnam.

Comparing to our assessment, the cost-effectiveness evidence of *DTFC* versus *BTFC* from Rouland et al in 2003 and Jothi et al in 2010 were analysed in shorter timeframes (3 months and 8 months, respectively) which raised the question of their ability to reflect the long-term treatment process of the disease [20,21]. Hence, it further emphasizes the strength of our research, being one of the first studies to evaluate the cost-effectiveness of two interventions with a long-term timeframe, using input data sources that reflect clinical practice and appropriate to the treatment context in Vietnam [22].

However, there are some potential risks of bias from the data validation, hypothesis probability distribution and long analysis timeframe. This study has several limitations. First, due to the lack of large-scale clinical trials in Vietnam, treatment efficacy data were primarily sourced from international literature [23–25]. While model inputs were adjusted through expert consultation and real-world cost data from Vietnamese hospitals,

generalizability may still be limited. Second, the model assumed perfect adherence, which may overestimate real-world effectiveness and cost-efficiency. Third, comorbidities were not included as covariates due to unavailable data, which may affect transition probabilities. Besides, the exclusion of indirect costs, such as management, monitoring, and patient follow-up, limited the comprehensiveness of our economic evaluation. Lastly, although the QALY difference per patient was minimal, it could lead to meaningful implications at the population level, supporting the value of cost-saving strategies like DTFC.

5. CONCLUSION

DTFC was the more cost-saving option while maintaining treatment benefits, compared to *BTFC*, from third-party health payer perspective. The management of OH/POAG, treatment adherence, disease progression and patient's quality-of-life are vital in the treatment of glaucoma and ocular hypertension.

6. COMPETING INTERESTS

The authors declare that they have no competing interests related to the content of this article.

7. SUPPLEMENTARY INFORMATION

The project was funded by the Saigon Pharmaceutical Science and Technology Center - SAPHARCEN, University of Medicine and Pharmacy at Ho Chi Minh City, and Santen Pharmaceutical Co., Ltd. The authors confirmed that there was no potential conflict of interest relevant to this article.

8. Author's Contributions

Conceptualization: Nguyen Thi Hong Tran, Yen Thi Hai Nguyen, Nga Thi Quynh Nguyen

Data curation: Nguyen Thi Hong Tran, Nga Thi Quynh Nguyen, Chau Thi Khanh Le

Formal analysis: Nguyen Thi Hong Tran, Uyen Le Lan Ngo, Chau Thi Khanh Le

Methodology: Nguyen Thi Hong Tran, Yen Thi Hai Nguyen, Nga Thi Quynh Nguyen, Tuan Duc Nguyen

Software: Nguyen Thi Hong Tran, Nga Thi Kieu Dang, Nga Thi Quynh Nguyen

Validation: Yen Thi Hai Nguyen, Nga Thi Quynh Nguyen, Nga Thi Kieu Dang, Tuan Duc Nguyen

Investigation: Nguyen Thi Hong Tran, Uyen Le Lan Ngo, Tuan Duc Nguyen

Writing - original draft: Nguyen Thi Hong Tran, Hung Manh Nguyen

Writing - review & editing: Nguyen Thi Hong Tran, Hung Manh Nguyen, Uyen Le Lan Ngo, Nga Thi Kieu Dang, Nga Thi Quynh Nguyen, Yen Thi Hai Nguyen.

Supplementary Materials

Supplementary materials are only available online from:

https://doi.org/10.32895/UMP.MPR.9.3.x

9. REFERENCE

1. Bourne RRA, Steinmetz JD, Saylan M, Mersha AM, Weldemariam AH, Wondmeneh TG, et al. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. Lancet Glob Health. 2021;9(2):e144–60.
2. Tham YC, Li X, Wong TY, Quigley HA, Aung T, Cheng CY. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology. 2014;121(11):2081–90.
3. Vietnam Ministry of Health. Decision No. 40/QD-BYT promulgating the medical specialized document on Guideline for diagnosis and treatment of eye diseases. 2015. Available from: https://thuvienphapluat.vn/van-ban/The-thao-Y-te/Quyet-dinh-40-QD-BYT-tai-lieu-chuyen-mon-Huong-dan-chan-doan-va-dieu-tri-cac-benh-ve-mat-263803.aspx
4. National Institute for Health and Care Excellence (NICE). *Glaucoma: diagnosis and management. NICE guideline [NG81]*. London: NICE; 2017. Available from: https://www.nice.org.uk/guidance/ng81
5. APGG - Asia Pacific Glaucoma Guidelines | Asia Pacific Glaucoma Society. Available from: https://www.apglaucomasociety.org/apgg-asia-pacific-glaucoma-guidelines
6. European Glaucoma Society Terminology and Guidelines for Glaucoma, 4th Edition - Chapter 3: Treatment principles and options Supported by the EGS Foundation: Part 1: Foreword; Introduction; Glossary; Chapter 3 Treatment principles and options. Br J Ophthalmol. 2017;101(6):130–91.

7. Wei Q, Zhou J, Li H, Wang L, Wu Y, Ma A, et al. Medication adherence with fixed-dose versus free-equivalent combination therapies: Systematic review and meta-analysis. Front Pharmacol. 2023;14:1156081.
8. Agarwal P, Tayal S, Gautum A. Comparative study to assess efficacy and safety of brinzolamide1% and timolol0.5% fixed combination eye drops versus dorzolamide2% and timolol0.5% fixed combination eye drops in management of open-angle glaucoma. J Family Med Prim Care. 2022;11(5):2167–71.
9. Galose MS, Elsaied HM, Macky TA, Fouad PH. Brinzolamide/timolol versus dorzolamide/timolol fixed combinations: A hospital-based, prospective, randomized study. Indian J Ophthalmol. 2016;64(2):127–31.
10. Aihara M, Adachi M, Matsuo H, Togano T, Fukuchi T, Sasaki N, et al. Additive effects and safety of fixed combination therapy with 1% brinzolamide and 0.5% timolol versus 1% dorzolamide and 0.5% timolol in prostaglandin-treated glaucoma patients. Acta Ophthalmol. 2017;95(8):e720–6.
11. Husereau D, Drummond M, Augustovski F, de Bekker-Grob E, Briggs AH, Carswell C, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations. Value in Health. 2022;25(1).
12. Reviewer Worksheets - Pharmacoeconomic Review Report: Latanoprostene Bunod (Vyzulta) - NCBI Bookshelf. Available from: https://www.ncbi.nlm.nih.gov/books/NBK549687/
13. Bartelt-Hofer J, Ben-Debba L, Flessa S. Systematic Review of Economic Evaluations in Primary Open-Angle Glaucoma: Decision Analytic Modeling Insights. Pharmacoecon Open. 2020;4(1):5–12.
14. Attema AE, Brouwer WBF, Claxton K. Discounting in economic evaluations. Pharmacoeconomics. 2018;36:745–58.
15. World Health Organization. Data of Viet Nam. Available from: https://data.who.int/countries/704, Accessed: February 10, 2025
16. Peeters A, Schouten JSAG, Severens JL, Hendrikse F, Prins MH, Webers CAB. Latanoprost versus timolol as first choice therapy in patients with ocular hypertension. A cost-effectiveness analysis. Acta Ophthalmol. 2012;90(2):146–54.
17. Lund UH, Bidonde J, Kornør H, Reinar LMB, Kvist BCF, Nguyen L, et al. Minimally Invasive Glaucoma Surgery (MIGS) for individuals with glaucoma. A health technology assessment. 2021;
18. Vietnam Ministry of Health. Circular no. 22/2022/TT-BYT on the promulgation of uniform prices for health insurance medical examination and treatment services among hospitals of the same class nationwide, and guidance on applying prices and payment of medical examination and treatment costs in some cases. 2022;

19. General Statistics Office of Vietnam. Statistics of Vietnam. 2025. Available from: https://www.gso.gov.vn/so-lieu-thong-ke/
20. Jothi R, Ismail AM, Senthamarai R, Pal S. A comparative study on the efficacy, safety, and cost-effectiveness of bimatoprost/timolol and dorzolamide/timolol combinations in glaucoma patients. Indian J Pharmacol. 2010;42(6):362–5.
21. Rouland JF, Le Pen C, Pinto CG, Berto P, Berdeaux G. Cost-minimisation study of dorzolamide versus brinzolamide in the treatment of ocular hypertension and primary open-angle glaucoma: in four European countries. Pharmacoeconomics. 2003;21(3):201–13.
22. Ministry of Health. Decision no. 1315/QD-BYT in 2024 on the guideline for reporting pharmacoeconomic assessment promulgated by Ministry of Health. 2024;
23. Halawa OA, Jin Q, Pasquale LR, Kang JH, Lorch AC, Sobrin L, et al. Race and Ethnicity Differences in Disease Severity and Visual Field Progression Among Glaucoma Patients. Am J Ophthalmol. 2022;242:69–76.
24. Le Thi Khanh Chau. Analysis of Outpatient Treatment Costs for Glaucoma in the Period of 2017-2019 and Open-Angle Glaucoma in the Period of 2020 at Ho Chi Minh City Eye Hospital. University of Medicine and Pharmacy at Ho Chi Minh; 2020.
25. Heijl A, Leske MC, Bengtsson B, Hyman L, Bengtsson B, Hussein M. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. Arch Ophthalmol. 2002;120(10):1268–79

426 **Table 1.** Baseline Parameters and Transitional Probabilities

Parameter	Value	Distribution	Source
Years of age, mean (SD)	57 (17)	Lognormal	[12,13]
Sex ratio (Female/Male)	49/51	Beta	[14]
Baseline MD (dB), mean (SD)	-6,2 (7,6)	Lognormal	[13]
Monthly MD natural reduction (dB), mean (SD)	0,05 (0,07)	Lognormal	[15]
IOP reduction, % (SD)			
Latanoprost	29,5 (13,4)	Normal	[16]
Timolol+Dorzolamide (concomitant)	18 (12)	Normal	[16,17]
1 active ingredient + 1 active ingredient or laser surgery (concomitant)	18 (12)	Normal	[16,17]
2 active ingredients + 1 active ingredient or laser surgery (concomitant)	10 (5)	Normal	[16,17]
3 active ingredients and laser surgery (concomitant)	8 (4)	Normal	[16,17]
Laser surgery	30 (12)	Normal	[18–22]
Comparative efficacy ratio of DTFC and BTFC, mean (SD)	1,03 (0,153)	Normal	[23]
Proportion of treatment transition after refractory to first-line therapy, % (SD)			
Transition to FDC	67,14% (14,85%)		Clinician consultation, real-world data
Third concomitant drug prescription	17,86% (9,95%)		
Laser surgery	15,00% (10,35%)		

427

428 **Table 2.** Utility value in health states

Health state	Utility value	Parameter distribution	Source
Early POAG	0,847	Beta (251, 45)	[24,25]
Moderate POAG	0,781	Beta (231, 65)	
Advance POAG	0,704	Beta (208, 88)	
Blindness	0,594	Beta (176, 120)	
Death	0		

429

430

Table 3. Medication Costs for Base Case Analysis

Medication	Volume (ml)	Unit price	Dose/day	Drops/day (both eyes)	Daily costs (VND)
Dozolamid + Timolol (Cosopt)	5	210,000	1 drop, twice a day	4	7,000
Brinzolamid + Timolol	5	310,800	1 drop, twice a day	4	10,360
PGA (BDG+Generic)*					6,681

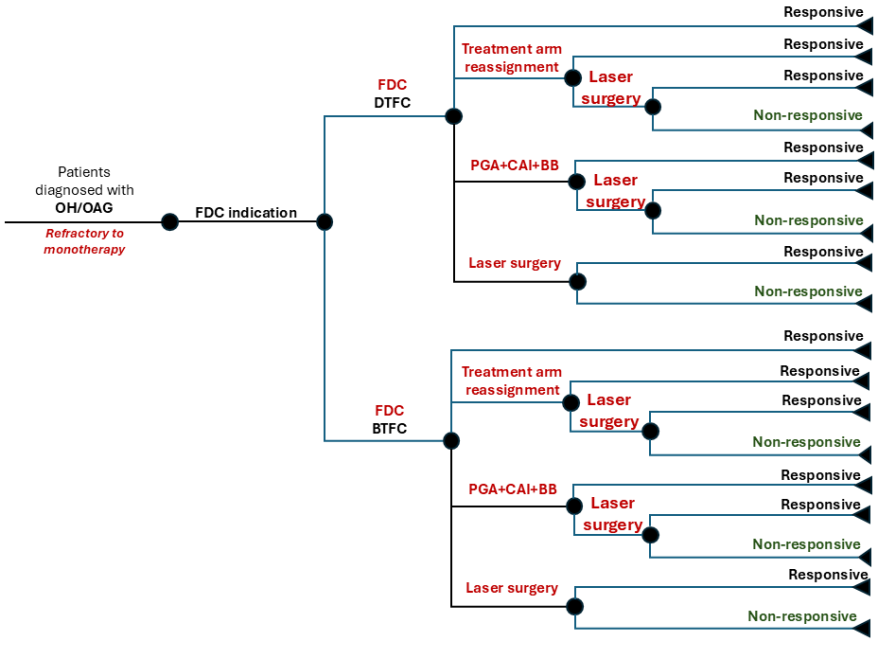
**The cost of PGA drugs is estimated on average based on brand name and generic drugs on the market*

Table 4. Unit costs and frequency of health service utilization used in the cost calculations

Health service	Unit price (VND)	For diagnosis		For follow-up care		
		Rate of indication	Cost (VND)	Indication frequency per year	Rate of indication *	Cost per year (VND)
Physical checkup	38.700	100%	38.700	3		
Costs of paraclinical examination						
OCT/GDX3 (funduscopy)	52.500	95%	51.188	5	73%	191.625
Tonometry	25.900	100%	25.900	9	100%	233.100
Visual field test	28.800	80%	21.600	2	73%	42.048
Gonioscopy	52.500	90%	50.768	4	10%	21.000
Vision test	73.000	100%	73.000	10	100%	730.000
Glaucoma screening test	107.000	100%	107.000			
Corneal thickness measurement	133.000	50%	110.789			
Costs for laser surgery	323.000	Based on the proportion of patients indicated laser surgery in the models				

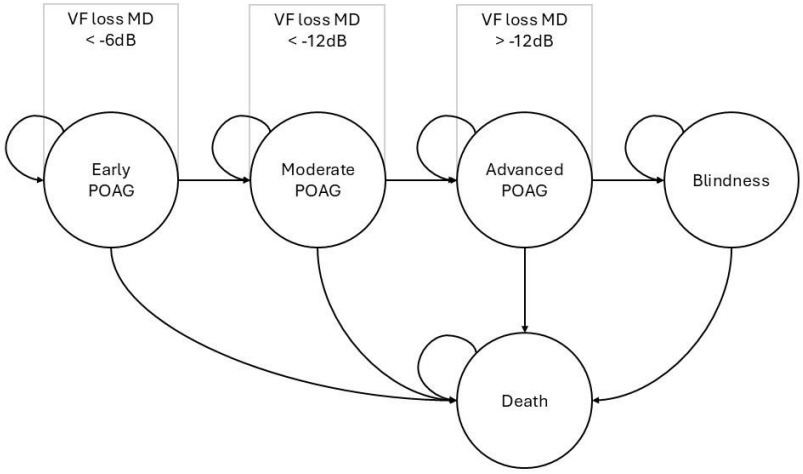
Table 5. Results of the Base Case Analysis

	DTFC	BTFC	Difference
Base case analysis of the hypothesis population			
Decision-tree model			
Cost of treatment (VND)	107.727.010.407	114.008.113.509	-6.281.103.102
QALYs	8.791,16	8.785,44	5,72
Markov model (40 cycles)			
Cost of treatment (VND)	321.338.991.030	324.641.269.507	-3.302.278.477
QALYs	86.164,25	86.158,15	6,10
Base case result			
Cost of treatment (VND)	429.066.001.437	438.649.383.016	-9.583.381.579
QALYs	94.955,41	94.943,59	11,82
Base case analysis of 1 patient			
Cost of treatment (VND)	42.906.600	43.864.938	- 958.338,1579
QALYs	9,50	9,49	0,001182
ICER	DTFC is **dominant** over BTFC *ICER is not applicable (N/A)*		



[Abbreviation: FDC: Fixed Dose Combination, DTFC: Dorzolamid + Timolol fixed-dosed combination, BTFC: Brinzolamid + Timolol fixed-dosed combination, PGA: Prostaglandin analogues, BB: β-blocker, CAI: Carbonic Anhydrase inhibitors]

Figure 1. Decision-tree model on glaucoma-therapy selection based on treatment guidelines from European Glaucoma Society (EGS)[6]



.

Figure 2. Markov model simulating disease progression in POAG treatment by EGS

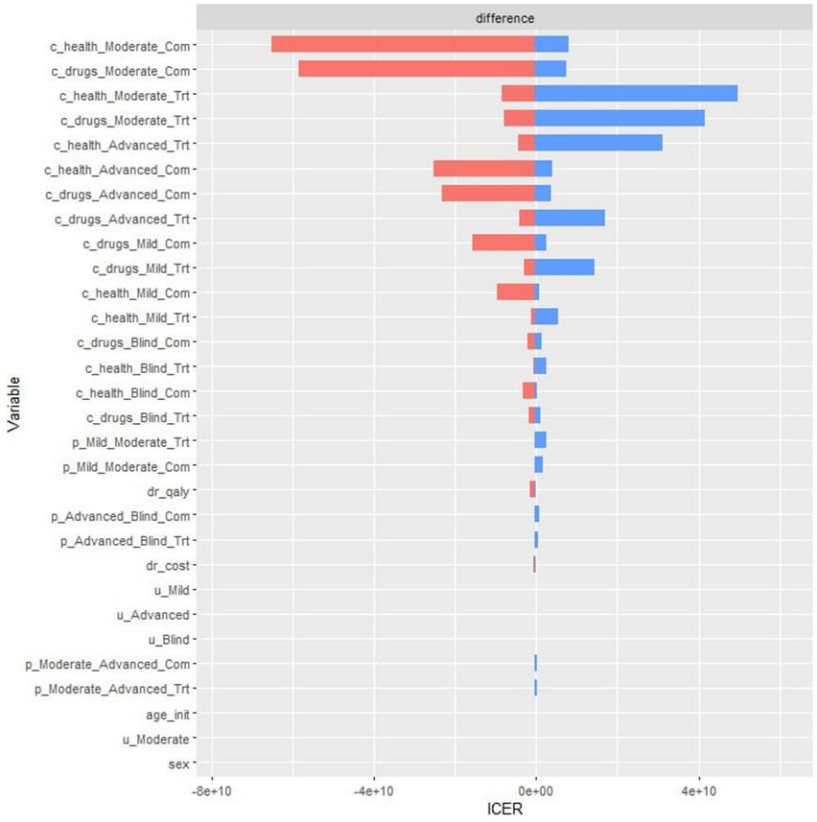


Figure 3. Tornado diagram on the change intensity of ICER by the variation of each parameter based on DSA results

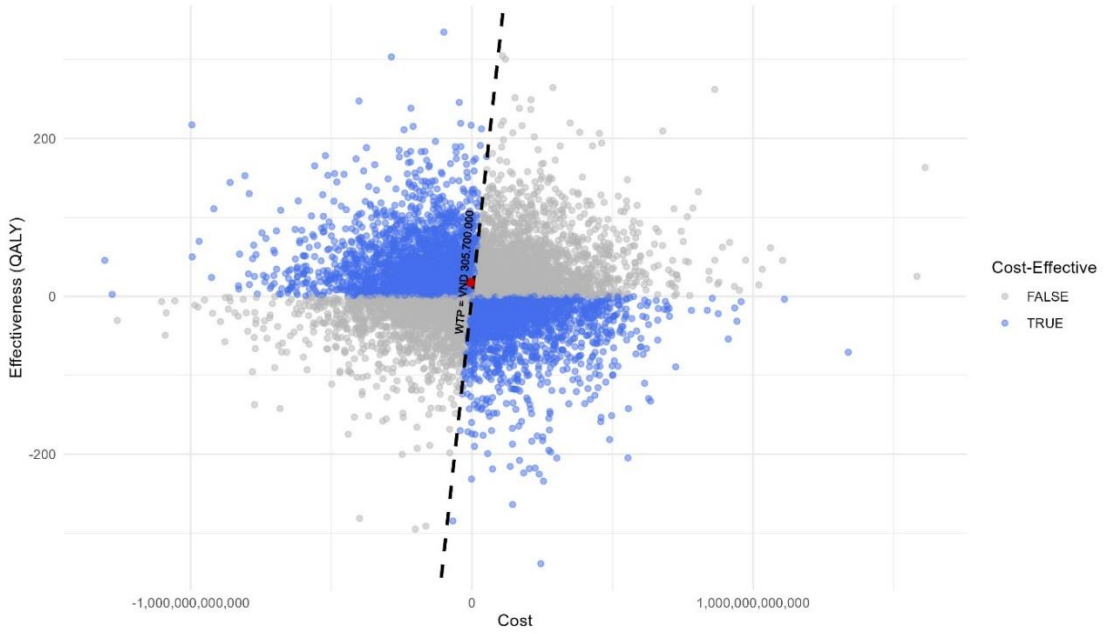


Figure 4. Cost-effectiveness plane of PSA results

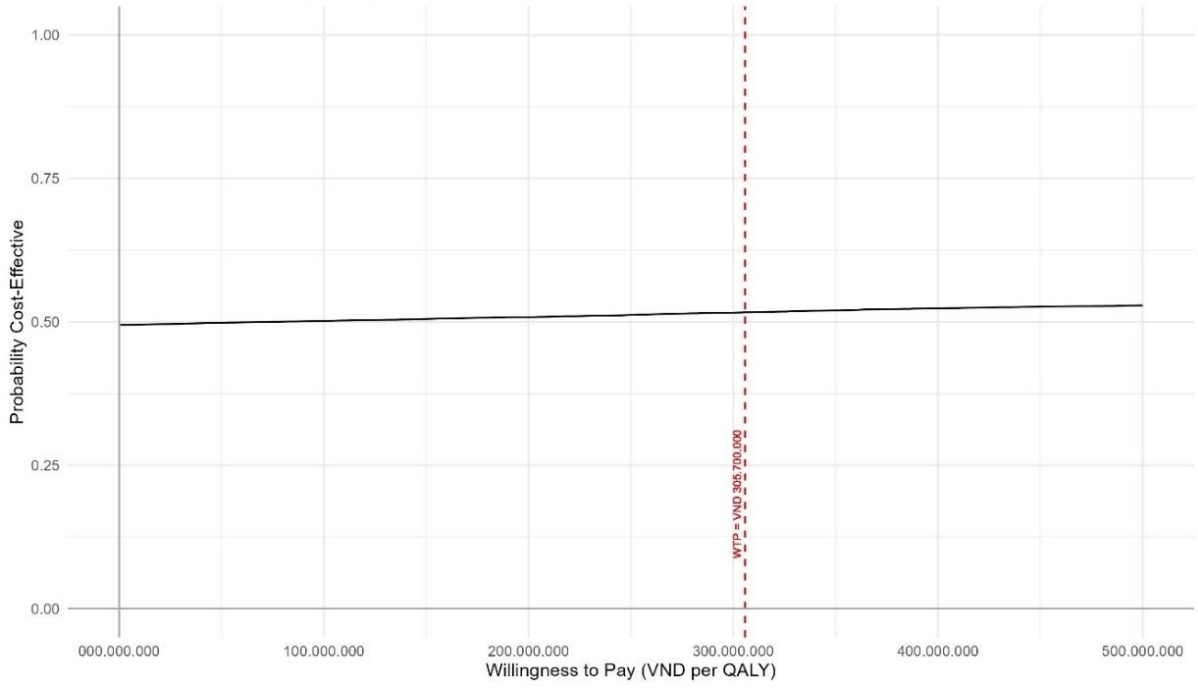


Figure 5. Cost-effectiveness acceptability curve of DTFC versus BTFC in OH/POAG treatment