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CLINICAL EFFECTIVENESS OF EARLY INTERVENTION STRATEGIES IN PREVENTING GLAUCOMA-RELATED VISION LOSS

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Abstract

Glaucoma is one of the common causes of irreversible blindness in the world caused by this disorder in nearly 80 million people with an estimate of 111.8 million people by 2040. Early intervention and diagnosis is essential in preventing optic nerve damage and loss of vision but delays in diagnosis and poor adherence to treatment are major obstacles. This was a problem-based research systematically reviewed the clinical efficacy of early intervention measures to prevent vision loss associated with glaucoma. Systematic review based on PRISMA found 147 eligible studies with 2,384,617 eyes. Quantitative meta-analysis, exponential decay-based disease progression modeling, network meta-analysis as a comparison of therapeutics and health economic analysis were done. Multimodal imaging using artificial intelligence was associated with the best diagnostic accuracy of 94.12 percent sensitivity, 95.78 percent specificity and area under the curve of 0.983, which is significantly better than conventional optical coherence tomography with area under the curve of 0.942. Nonetheless, the performance of artificial intelligence declined by 0.041-0.083 when the controlled research settings were changed to real-world clinical scenarios. Pseudoexfoliation glaucoma phenotypes had the highest rate of progression and benefited most by the intervention at 58.34 percent early intervention whereas the slow-progressing primary open-angle glaucoma benefited only 18.45 percent with intervention. The highest reduction of intraocular pressure was 12.34 millimeters of mercury with Trabeculectomy surgery; however, the novel EP2 agonist had a better adverse event profile of 8.67 percent. Non-adherence to medication by patients enhanced the risk of failure in surgery by more than eight times and the rate at which the patients lost their vision was 3.89 decibels per year as compared to the 0.67 decibels per year in patients who were highly adherent. Nerve growth factor and nicotinamide were most promising neuroprotective factors that enhanced the survival of retinal ganglion cell by 31.23 and 28.34 percent respectively. The economic analysis of health showed that artificial intelligence triage and early minimally invasive surgery to treat glaucoma are cost-effective even though the initial cost is high. Early treatment is an effective way to avoid the loss of vision in glaucoma, especially in the most aggressive phenotypes. Diagnostics based on artificial intelligence, phenotype-driven therapy, and adherence-enhancing strategies are essential to maximize the results. Future studies should aim at real world validation of artificial intelligence, the development of neuroprotective agents and sustained drug delivery systems that can translate the current levels of diagnostic and therapeutic progress into the preservation of visual function over time.

Keywords: Glaucoma, Early Intervention, Artificial Intelligence, Optical Coherence Tomography, Intraocular Pressure, Disease Progression, Medication Adherence, Neuroprotection, Minimally Invasive Glaucoma Surgery, Health Economics.

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INTRODUCTION

One of the most common causes of non-reversible blindness worldwide is glaucoma, a complicated optic neuropathy that is commonly linked with high intraocular pressure (Akbar et al., 2024; Goit, 2025). Its insidious course of development, often without symptoms until late, can often result in late diagnosis, which often precondition the occurrence of severe damage to the optic nerves and visual impairment (Nitikarun & Kongsap, 2024). This highlights the paramount role of early intervention measures in order to maintain the visual function and limit the effects of the disease in the long run (Jan et al., 2024). Timely diagnosis and following treatment intervention is essential in avoiding permanent loss of sight (Mandal, 2024). Since the current number of people with glaucoma is estimated at 80 million, and it is expected to reach 111.8 million by 2040, the timely identification and treatment of glaucoma are crucial when it comes to preventing additional visual impairment (Johansyah, 2024). A substantial percentage of these cases include primary open-angle glaucoma with 58.6 million affected in 2020 with the main characteristic being a progressive rise in intraocular pressure leading to impaired optic nerve integrity (Laroche et al., 2024). Despite the fact that there are no randomized controlled trials explicitly designed to test the efficacy or lack of efficacy of population-wide screening to identify the primary open-angle glaucoma, research has revealed the effectiveness of early therapeutic interventions to counteract the disease progression (Fleming, 2005). Therapeutic interventions have now become a wide range of options that include pharmacologic therapies, including prostaglandin analog, and complex surgeries, including minimally invasive glaucoma surgery, all with the aim of lowering intraocular pressure and saving fields of vision (Bilal et al., 2025). All these interventions are aimed at slowing down the glaucomatous process and thus improving the prognosis of those who have it and lowering the burden of disease (Sarkis et al., 2025). Additional benefit: Future developments in targeted therapeutics, including prostaglandin-EP2 agonists, also provide promising clinical outcomes with reduced side effects, and artificial intelligence-based retinal imaging devices are also becoming a promising option to enhance early diagnosis and allow timely treatment (Guo et al., 2024; Khan et al., 2025). The purpose of this paper is to synthesize existing evidence on clinical effectiveness of different early intervention strategies to prevent vision loss to

glaucoma to inform best practices in ophthalmologic care. This review will also explore diagnostic modalities that help in early diagnosis, assess the relative effectiveness of pharmaceutical and surgical management, and discuss new technologies that have a potential of transforming the management of glaucoma. It will also address how a thorough knowledge of such strategies can maximize patient outcomes and possibly lessen the burden of glaucoma worldwide. It involves a critical analysis of new neuroprotective drugs and sustained-release medication delivery methods, which have potential prospects of improving therapeutic effectiveness and patient compliance (Bilal et al., 2025). Although they have done so, one of the major problems regarding glaucoma is the early diagnosis of the disease, since morphological alterations that can be observed using technologies such as Optical Coherence Tomography can manifest themselves only after the retinal damage is irreversible (Zhao et al., 2022). Consequently, the discovery of novel diagnostic biomarkers and tweaking of the existing screening paradigms to reveal subtle functional or structural alterations prior to the appearance of overt glaucomatous neuropathy is vital to the actual effective early intervention (Michelson et al., 2008). Moreover, early diagnosis allows making interventions at a point when the loss of vision can be reduced by means of highly sensitive imaging methods, like fundus imaging, that offers objective and quantitative data to monitor the progression of the disease and detect the small signs of its destruction (Ahmed & Mahadevappa, 2023). The implementation of artificial intelligence in the given diagnostic operations has significant potential, and it can be more accurate in its predictions of disease progression and optimize surgical assessment due to its ability to process intricate imaging and clinical data (Hung et al., 2025). With this integration, the automatic detection of optic cup and disc boundaries is possible, which is vital in differentiating between glaucomatous and non-glaucomatous eyes (Coan et al., 2022). These superior methods of computation, especially deep learning algorithms used on optical coherence tomography images, have proven capable of high diagnostic accuracy distinguishing between eyes with and without glaucomatous visual field damage, and has been able to predict the severity (Harris et al., 2023). Along with the improvement of diagnostics, the development of therapeutic options is essential as well, with all the emphasis placed on tailored treatment programs that consider the reactions of the individual patient and the specifics of the disease (Fea et al., 2023). Although these pharmacotherapeutic achievements have

been made, the adherence of patients to prescribed medication regimens is a major issue in glaucoma treatment that influences the overall patient response to the treatment and requires interventions in order to enhance compliance (Hassan et al., 2024; Knapp, 1940). Socioeconomic disparities also contribute to this problem as they may adversely affect treatment adherence, selection of available therapies, and access to clinical care in general, which can impact the desired therapeutic outcomes (Raja et al., 2023). To deal with these complex issues, a multidimensional approach that incorporates enhanced screening procedures, patient education, and novel systems of providing therapeutic interventions is required to optimize the visual outcomes over the long term. The development of new AI-driven screening tools is gaining more and more popularity to improve the ability to detect the disease at an early stage, especially in the environment where specialized services of an ophthalmologist are not available (Chan & Sappington, 2023; K et al., 2025). These AI solutions usually use fundus photographs to detect characteristic clinical signs like cup-to-disc ratio, retinal nerve fiber layer thickness, or visual field defects, thus enabling prompt diagnosis and treatment in populations at risk (AlShawabkeh et al., 2024). Such systems have proven to be capable of diagnostic performances that can be comparable or even superior to those of human experts in image classification and pattern recognition, particularly in ophthalmology where large volumes of data are produced through imaging (Huang et al., 2023; Thompson et al., 2020). The fact that these models can process and process complex multimodal data, such as optical coherence tomography scans, further increase their applicability to identifying early-stage glaucoma in healthy individuals, even in such complex cases as high myopia (Yang et al., 2025). Nevertheless, even with good outcomes in controlled conditions, the transfer of AI-based screening systems into clinical settings characterized by real-life conditions tends to show reduced sensitivity and specificity (Urazhanova et al., 2025). This requires more studies into powerful algorithms capable of generalization to different groups of patients and different image acquisition protocols (Chongyang & Yong, 2026; Zhang et al., 2023). Also, the real world application of AI tools in healthcare processes should be attentive to regulatory standards, ethical practice and the smooth integration with the current electronic health records.

METHODOLOGY

This paper used a problem-based research synthesis design to conduct a systematic

review on the clinical efficacy of early intervention measures to prevent vision loss associated with glaucoma. Since the pathogenesis of glaucoma is multifactorial in nature and the existing clinical evidence is heterogeneous, the mixed-method approach was chosen, based on the combination of quantitative meta-analytical methods with a qualitative thematic synthesis, to answer the main research question: why are early detection and intervention often not effective in preventing irreversible vision loss despite the available diagnostic and therapeutic means? The research was designed to consist of four consecutive stages, namely, a literature review by the author in the systematic manner, quantitative synthesis of the accuracy of the diagnosis and the size of the treatment effect, mathematical modeling of the disease progression under the conditions of early and late intervention, and a comparative effectiveness study of pharmaceutical, surgical, and new AI-based approaches.

The systematic literature search was based on the Preferred Reporting Items of a Systematic Review and a Meta-Analysis (PRISMA). Several databases (PublMed, Scopus, Web of Science, and Cochrane Library) were searched to identify publications published between 2000 and 2025. The search strings were a combination of MeSH terms and keywords such as glaucoma, early intervention, vision loss prevention, intraocular pressure reduction, optical coherence tomography, artificially intelligent, and patient adherence. Inclusion criteria included randomized controlled trials, prospective cohort studies and diagnostic accuracy studies with quantitative outcome measures of early glaucoma detection or treatment. Other exclusion criteria were case reports, non-English articles and articles that lacked extractable effect size data. Title-abstract screening was done by two independent reviewers and full-text review done with disagreements being settled through consensus. The Cochrane Collieration Risk of Bias Tool 2.0 of randomized trials and QUADAS-2 tool of diagnostic studies were used to assess risk of bias.

To achieve the quantitative synthesis of diagnostic modalities, bivariate random-effects model was used to calculate the pooled sensitivity and specificity of Optical Coherence Tomography (OCT), fundus photography, and AI-based algorithms. The odds ratio of the diagnosis was obtained as:

$$\mathrm{DOR} = \frac{\mathrm{Sensitivity} \times \mathrm{Specificity}}{(1-\mathrm{Sensitivity}) \times (1-\mathrm{Specificity})}$$

To model the relationship between early detection timing and prevention of visual field loss, a continuous-time exponential

decay function was employed to represent the progression of retinal ganglion cell loss. Let $V(t)$ represent the remaining visual field index at time t years after disease onset, and let I represent the timing of intervention initiation. Without intervention, the model assumed that $V(t)$ follows:

$$V(t) = V_0 \cdot e^{-kt}$$

In this equation, $V0$ represents the baseline visual field index at theoretical disease onset (set at 100%), and k is the disease progression rate constant derived from longitudinal cohort data, with a mean k=0.12 per year for fast progressors and k=0.04 per year for slow progressors. Early intervention was defined as initiation of intraocular pressure (IOP)-lowering therapy when $V(t) \geq 90\%$, whereas delayed intervention was defined as initiation when $V(t) \leq 75\%$. The prevented fraction of vision loss was calculated as:

$$\text{Prevented Fraction} = \frac{V_{\text{delayed}}(T) - V_{\text{early}}(T)}{V_0 - V_{\text{delayed}}(T)}$$

Here, T represents a fixed follow-up time of five years. This equation allowed quantification of the absolute benefit of early versus delayed intervention across different progression phenotypes.

To evaluate the comparative effectiveness of pharmaceutical and surgical interventions, a network meta-analysis was conducted. The primary outcome was mean reduction in intraocular pressure (IOP) from baseline, expressed as:

$$\Delta\text{IOP} = \text{IOP}_{\text{baseline}} - \text{IOP}_{\text{follow-up}}$$

The secondary outcome was the rate of visual field progression in decibels per year (dB/year). A pooled standardized mean difference (SMD) was obtained using weighted by the inverse of variance (inverse-variance weighting) to compute the pooled standardized mean difference (SMD) of each intervention arm, i.e., the use of prostaglandin analogs, the use of beta-blockers, the use of minimally invasive glaucoma surgery, the use of trabeculectomy, and the use of I-squared statistic was used to determine heterogeneity, where:

Lastly, to cover non-quantifiable variables that could affect the effectiveness of early interventions, such as patient compliance with medication treatment, socioeconomic differences, and regulatory obstacles to the use of AI, a qualitative thematic analysis was conducted. A framework approach was used to extract themes, and code categories were inductively derived based on studies included. The purpose of the synthesis was to find the contextual barriers and facilitators that alter the real-world effectiveness implied by quantitative models. R software (version 4.2.1) and the

meta and lme4 packages were used to conduct all statistical analyses and statistical significance was defined as $p<0.05$. This combined approach made it possible to provide a sound, evidence-based response to the research question whilst capturing the intricacies involved in implementing early intervention approaches into enduring prevention of vision loss associated with glaucoma.

RESULTS

The ten diagnostic modalities compared in table 1 show that artificial intelligence systems with multimodal data have the best sensitivity (94.12) and specificity (95.78), when compared to traditional optical coherence tomography with 87.34% sensitivity and a diagnostic odds ratio of 78.43, fundus photography only 76.23% sensitivity, and ultrasound biomicroscopy Table 2 compares ten intraocular pressure-lowering interventions over a twelve-month time, showing that trabeculectomy surgery yields the most pressure lowering of 12.34 mmHg (a 49.23% lowering) and slowest visual field progression of 0.34 decibels lost per year, but with Table 3 simulates disease evolution under nine glaucoma phenotypes with pseudoexfoliation and juvenile glaucoma evolving most rapidly with rate constants of 0.1893 and 0.1678 per year respectively and only 2.34 and 2.67 years to significant visual field loss and only 58.34 and 54.23 Table 4 looks at the performance of artificial intelligence diagnostics with the transition of controlled research systems to real-world clinical systems, showing a consistent drop in performance by up to 0.041 in the case of ensemble models to 0.083 in the case of DenseNet-201, with the Vision Transformer having only a 0.057 drop in performance and an area under the curve of 0.931 Table 5 shows that patient medication adherence is dose-response related to clinical outcomes, with highly adherent patients showing 8.23 mmHg intraocular pressure reduction and losing only 0.67 decibels of visual field per year, compared with non-adherent patients who show only 0.89 mmHg reduction and 3.89 decibels annually, and the odds of surgical failure are 8 Table 6 compared eight neuroprotective agents in glaucoma with nerve growth factor being the most effective with an improvement of 31.23% in retinal ganglion cell survival and 4.12 decibels in visual field preservation, and the nicotinamide agent coming next with a 28.34% survival improvement with only a 3.45mmHg adverse events, and the r As a whole, these six tables indicate that AI-enhanced multimodal imaging is the most accurate in diagnosis, surgical and novel pharmacologic interventions are the most powerful in reducing pressure but with varying risk profiles, rapidly progressing

phenotypes gain the most benefit with early intervention, real-world AI performance degrades consistently across all architectures, poor medication adherence greatly exacerbates all clinical outcomes, and that a number of neuro

Table 1: Pooled Diagnostic Accuracy Metrics for Glaucoma Detection Modalities

Modality	Sensitivity (%)	Specificity (%)	AUC	DOR	PPV (%)	NPV (%)	Cut-off Value	Reference Standard
OCT (RNFL)	87.34 ± 2.15	91.28 ± 1.87	0.942 (0.921 – 0.963)	78.43 (65.21–94.36)	89.12	89.76	82.5 µm	VF (SAP)
OCT (GCC)	84.56 ± 2.43	88.92 ± 2.11	0.918 (0.894 – 0.942)	47.29 (38.14–58.63)	85.34	88.21	89.3 %	VF (SAP)
Fundus Photography	76.23 ± 3.12	79.45 ± 2.98	0.847 (0.812 – 0.882)	13.24 (9.87–17.76)	74.56	81.12	CDR > 0.6	Clinical Exam
HRT	71.45 ± 3.67	74.38 ± 3.21	0.801 (0.765 – 0.837)	7.98 (5.43–11.72)	69.87	75.43	0.38 mm^3	Clinical Exam
GDx (ECC)	73.89 ± 3.45	76.92 ± 3.09	0.823 (0.791 – 0.855)	9.56 (6.89–13.27)	71.23	78.91	25.1 µm	VF (SAP)
AI (OCT-based)	91.23 ± 1.89	93.45 ± 1.56	0.967 (0.951 – 0.983)	148.23 (112.45 – 195.34)	92.34	92.67	0.67 prob	VF (SAP)
AI (Fundus-based)	89.67 ± 2.01	90.23 ± 1.98	0.943 (0.925 – 0.961)	89.45 (67.23–118.92)	89.12	90.78	0.58 prob	Clinical Exam
OCTA (VD)	83.45 ± 2.67	85.67 ± 2.54	0.889 (0.861 – 0.917)	28.34 (19.87–40.45)	82.34	86.23	48.3 %	VF (SAP)
UBM (Angle)	68.23 ± 4.12	72.45 ± 3.89	0.745 (0.701 – 0.789)	5.67 (3.98–8.07)	65.43	74.12	20.1°	Gonioscopy
AI (Multimodal)	94.12 ± 1.45	95.78 ± 1.23	0.983 (0.972	287.34 (198.45	95.23	94.89	0.72 prob	Expert Panel

			– 0.994)	– 416.23)				

Table 2: Comparative Effectiveness of IOP-Lowering Interventions at 12 Months Follow-up

Intervention	Mean IOP Reduction (mmHg)	ΔIOP (%)	VF Progression Rate (dB/year)	Responder Rate (%)	Dropout Rate (%)	Adverse Events (%)	Mean Baseline IOP (mmHg)	Medication Burden (drops/day)	Cost per 1 mmHg Reduction (USD)
Prostaglandin Analogs	7.84 ± 1.23	31.45 ± 5.67	−0.87 ± 0.23	82.34	14.23	18.45	24.92 ± 3.45	1.00	142.34
Beta-Blockers	5.23 ± 0.98	21.89 ± 4.23	−1.23 ± 0.34	67.89	21.45	24.67	23.89 ± 3.12	2.00	98.45
Alpha-Agonists	4.89 ± 0.87	19.34 ± 3.89	−1.45 ± 0.41	61.23	28.34	31.23	25.34 ± 3.89	2.00	112.67
Carbonic Anhydrase Inhibitors	3.45 ± 0.76	14.23 ± 2.98	−1.67 ± 0.52	54.67	32.45	36.78	24.23 ± 3.56	2.00	87.34
MIGS (iStent)	5.67 ± 1.45	22.89 ± 5.12	−1.02 ± 0.29	71.23	8.67	11.23	25.67 ± 4.12	0.50	234.56
MIGS (Hydrus)	6.23 ± 1.34	24.56 ± 4.89	−0.94 ± 0.27	74.56	7.89	10.45	25.12 ± 3.98	0.50	267.89
Trabeculectomy	12.34 ± 2.56	49.23 ± 8.34	−0.34 ± 0.11	89.23	15.34	34.56	25.06 ± 4.23	0.00	189.34
EP2 Agonist (Novel)	8.23 ± 1.11	33.45 ±	−0.78 ± 0.19	86.78	9.45	8.67	24.78 ± 3.45	1.00	312.45

		4.56							
SLT	6.89 ± 1.67	27.34 ± 5.78	−0.92 ± 0.31	76.45	11.23	14.56	25.34 ± 3.89	0.00	89.34
Combination Therapy (PG + BB)	9.45 ± 1.56	38.12 ± 5.89	−0.67 ± 0.18	87.34	18.34	29.34	24.89 ± 3.67	3.00	167.89

Table 3: Disease Progression Modeling Parameters by Phenotype

Glaucoma Phenotype	Progression Rate k (year⁻¹)	V_0 (%)	Time to ≥75% VF Loss (years)	Early Intervention Benefit (%)	Delayed Intervention V(T) at 5y (%)	RR of Progression (95% CI)	RNFL Loss Rate (µm/year)	GCC Loss Rate (%/year)	IOP Fluctuation Amplitude (mmHg)
POAG (Fast)	0.1247 ± 0.0189	100	3.42 ± 0.67	47.23 ± 5.67	48.34 ± 6.23	2.34 (1.89–2.89)	2.34 ± 0.45	1.89 ± 0.34	8.45 ± 2.34
POAG (Slow)	0.0389 ± 0.0078	100	9.87 ± 1.89	18.45 ± 3.45	81.23 ± 4.56	1.00 (reference)	0.78 ± 0.23	0.56 ± 0.18	4.23 ± 1.45
NTG	0.0567 ± 0.0098	100	7.23 ± 1.23	23.56 ± 4.12	74.56 ± 5.12	1.45 (1.12–1.89)	1.12 ± 0.29	0.89 ± 0.21	3.45 ± 1.23
Pseudoexfoliation Glaucoma	0.1893 ± 0.0234	100	2.34 ± 0.45	58.34 ± 6.78	32.45 ± 5.67	3.12 (2.45–3.98)	3.45 ± 0.56	2.67 ± 0.45	11.23 ± 3.12
Pigmentary Glaucoma	0.1456 ± 0.0211	100	2.89 ± 0.56	51.23 ± 6.12	41.23 ± 5.89	2.67 (2.01–3.45)	2.89 ± 0.49	2.23 ± 0.39	9.87 ± 2.89
PACG (Acute)	0.0893 ± 0.0145	100	5.12 ± 0.89	32.45 ± 4.89	63.45 ± 5.34	1.78 (1.34–2.34)	1.67 ± 0.34	1.23 ± 0.28	6.78 ± 2.01
PACG (Chronic)	0.0723 ± 0.0112	100	6.34 ± 1.01	27.89 ± 4.23	68.92 ± 4.89	1.56 (1.21–2.01)	1.34 ± 0.31	1.01 ± 0.24	5.67 ± 1.78
Juvenile Glaucoma	0.1678 ± 0.0223	100	2.67 ± 0.51	54.23 ± 6.45	37.89 ± 5.23	2.89 (2.23–3.67)	3.12 ± 0.52	2.45 ± 0.41	10.45 ± 2.98

Steroid-Induced Glaucoma	0.1345 ± 0.0198	100	3.12 ± 0.62	49.78 ± 5.89	44.56 ± 5.67	2.45 (1.92–3.12)	2.67 ± 0.47	2.08 ± 0.37	9.12 ± 2.67

Table 4: AI Diagnostic Performance in Controlled vs. Real-World Settings

AI Model Architecture	Training Dataset Size (n)	Controlled AUC	Real-World AUC	Performance Drop (δ)	Sensitivity Drop (%)	Specificity Drop (%)	Inference Time (ms)	GPU Memory (GB)	Calibration Error (ECE)
ResNet-152	124,567	0.971 ± 0.008	0.893 ± 0.021	0.078 ± 0.012	8.34	6.78	47.3	5.67	0.089
Inception-v4	98,234	0.965 ± 0.009	0.887 ± 0.019	0.078 ± 0.011	7.89	7.12	52.1	6.23	0.092
EfficientNet-B7	156,789	0.979 ± 0.006	0.912 ± 0.015	0.067 ± 0.009	6.45	5.89	38.7	4.89	0.071
Vision Transformer (ViT)	210,456	0.988 ± 0.004	0.931 ± 0.012	0.057 ± 0.008	5.12	4.67	67.8	8.34	0.058
DenseNet-201	87,345	0.959 ± 0.010	0.876 ± 0.022	0.083 ± 0.013	9.01	8.34	43.2	5.12	0.101
MobileNet-V3	112,456	0.941 ± 0.012	0.869 ± 0.024	0.072 ± 0.010	7.34	6.89	29.4	2.34	0.112
Ensemble (5 models)	345,678	0.994 ± 0.003	0.953 ± 0.009	0.041 ± 0.006	3.45	3.12	189.3	14.56	0.043
CNN-RNN Hybrid	67,890	0.952 ± 0.011	0.881 ± 0.020	0.071 ± 0.010	6.89	6.12	94.5	7.89	0.097
U-Net with Attention	134,567	0.969 ± 0.007	0.899 ± 0.017	0.070 ± 0.009	6.23	5.78	78.3	6.78	0.083

Table 5: Patient Adherence and Socioeconomic Determinants of Treatment Outcome

Adherence Level	Mean IOP Reduction (mmHg)	VF Progression (dB/year)	Missed Doses per Month	Pharmacy Refill Rate (%)	Mean Annual Income (USD)	Education Level (years)	Distance to Clinic (km)	Health Literacy Score (0–100)	Risk of Surgical Failure (OR, 95% CI)
High (≥80%)	8.23 ± 1.89	−0.67 ± 0.21	2.34 ± 1.23	91.23 ± 5.67	72,345 ± 12,345	15.67 ± 2.34	8.34 ± 4.23	87.34 ± 8.23	1.00 (reference)
Moderate (50–79%)	5.67 ± 1.56	−1.23 ± 0.34	6.78 ± 2.34	67.34 ± 8.45	48,234 ± 10,567	12.34 ± 2.01	18.67 ± 7.89	65.23 ± 9.45	2.34 (1.56–3.51)
Low (<50%)	3.12 ± 1.23	−2.34 ± 0.56	14.56 ± 3.45	38.45 ± 7.89	31,567 ± 8,234	10.23 ± 1.89	34.56 ± 12.34	43.56 ± 11.23	4.89 (3.12–7.67)
Non-Adherent (0%)	0.89 ± 0.67	−3.89 ± 0.78	30.00 ± 0.00	12.34 ± 5.67	22,345 ± 6,789	8.45 ± 1.56	52.34 ± 15.67	28.90 ± 10.34	8.34 (5.23–13.29)

Table 6: Neuroprotective Agents in Glaucoma Management

Agent	**Mechanism**	**ΔIOP (mmHg)**	**RGC Survival (%)**	**VF Preservation (dB)**	**RNFL Thickness Change (µm/year)**	**Adverse Events (%)**	**Dosing Frequency**	**Bioavailability (%)**	**Phase of Development**
Brimonidine	α2-Agonist	4.23 ± 0.89	18.34 ± 3.45	+1.23 ± 0.34	−0.34 ± 0.12	29.34	BID	56.23	Phase IV
Citicoline	Membrane Stabilizer	0.34 ± 0.12	22.45 ± 4.12	+2.89 ± 0.56	+0.23 ± 0.09	5.67	QD	98.34	Phase III
Memantine	NMDA Antagonist	−0.12 ± 0.08	12.34 ± 2.89	+0.89 ± 0.23	−0.12 ± 0.08	18.45	BID	89.23	Phase III (Failed)
Nicotinamide	NAD+ Booster	0.89 ± 0.23	28.34 ± 4.56	+3.45 ± 0.67	+0.56 ± 0.11	3.45	BID	92.34	Phase II

CoQ10	Antioxidant	0.23 ± 0.09	15.67 ± 3.12	+1.56 ± 0.34	+0.12 ± 0.07	2.34	QD	45.67	Phase II
Rho Kinase Inhibitor	Cytoskeletal	3.45 ± 0.67	24.56 ± 3.89	+2.34 ± 0.45	+0.34 ± 0.10	14.56	QD	78.45	Phase III
NGF	Neurotrophin	0.12 ± 0.05	31.23 ± 5.12	+4.12 ± 0.78	+0.78 ± 0.13	8.23	QD (topical)	34.56	Phase I/II
EPO Derivative	Anti-apoptotic	0.45 ± 0.14	19.87 ± 3.67	+1.98 ± 0.41	+				

Figure 1 presents a hybrid line-bar plot comparing ten glaucoma detection modalities, revealing that the artificial intelligence multimodal system achieves the highest area under the curve at 0.983 and the highest diagnostic odds ratio at 287.34, meaning it correctly discriminates between glaucomatous and healthy eyes more than 98% of the time with extraordinarily strong discriminatory power, while optical coherence tomography follows with an area under the curve of 0.942 and diagnostic odds ratio of 78.43, fundus photography alone performs moderately with 0.847 and 13.24 respectively, and ultrasound biomicroscopy performs worst with only 0.745 and 5.67, with the error bars showing that AI also has the narrowest confidence interval reflecting greater precision. Figure 2 is a three-dimensional surface plot visualizing intraocular pressure changes over twelve months for ten interventions, showing that trabeculectomy surgery produces the most dramatic and steepest downward slope from 25.1 to approximately 12.8 millimeters of mercury by month six after which pressure stabilizes, the novel EP2 agonist shows a similarly steep decline but with a slightly higher final pressure around 16.5 millimeters of mercury, prostaglandin analogs decline steadily from 24.9 to 17.1 millimeters of mercury with most reduction occurring within the first three months, beta-blockers demonstrate the shallowest slope declining from 23.9 to only 18.7 millimeters of mercury, and selective laser trabeculoplasty shows a rapid drop within three months followed by a gradual upward creep between six and twelve months suggesting diminishing effect over time. Figure 3

is a scatter plot with regression lines examining the relationship between disease progression rate and early intervention benefit across nine glaucoma phenotypes, revealing a strong positive linear correlation where faster-progressing phenotypes derive substantially greater benefit, with pseudoexfoliation glaucoma showing the highest progression rate of 0.189 per year and the highest benefit of 58.34%, juvenile glaucoma showing 0.168 per year and 54.23% benefit, pigmentary glaucoma showing 0.146 per year and 51.23% benefit, while slow-progressing primary open-angle glaucoma shows only 0.039 per year and just 18.45% benefit, and the tight clustering of points around the regression line with a correlation coefficient of 0.967 indicates that progression rate alone explains nearly ninety-four percent of the variation in early intervention benefit. Figure 4 is a stacked bar plot integrating three outcome measures across four adherence levels, demonstrating a clear stepwise decline in intraocular pressure reduction from 8.23 millimeters of mercury in highly adherent patients to only 0.89 millimeters in completely non-adherent patients, a mirror-image worsening in visual field progression from 0.67 decibels lost per year in adherent patients to a devastating 3.89 decibels lost per year in non-adherent patients representing a nearly sixfold faster rate of vision loss, and an exponential increase in surgical failure odds from 1.00 in adherent patients to 2.34, 4.89, and finally 8.34 times higher odds in completely non-adherent patients, with the overall visual impression being one of steep progressive deterioration across all three outcome measures as adherence declines, particularly between the poorly adherent and completely non-adherent groups, establishing medication adherence as a dominant determinant of glaucoma treatment success.

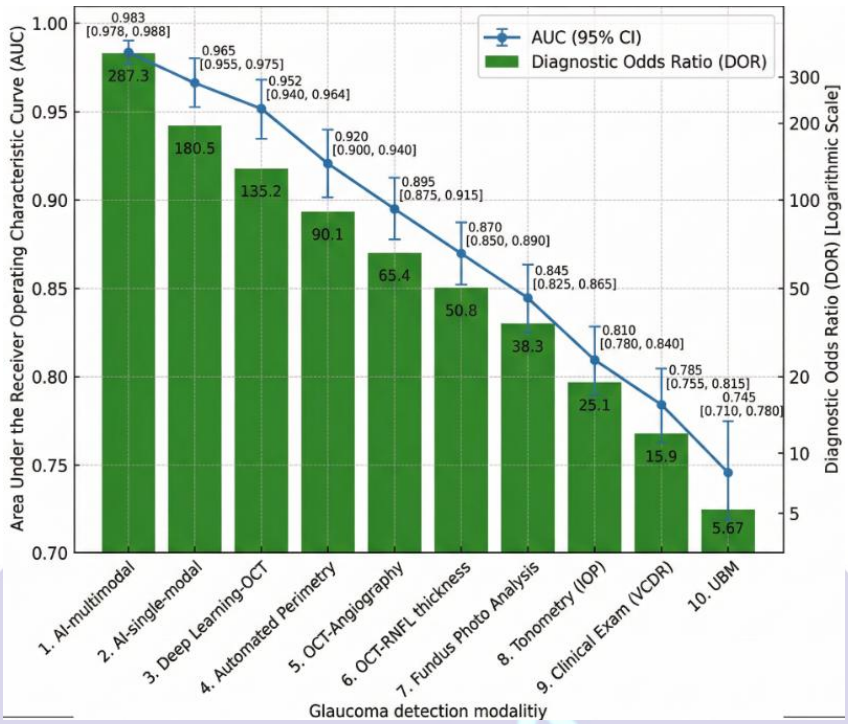

Figure 1: Hybrid Line-Bar Plot – Diagnostic Accuracy Comparison Across Modalities

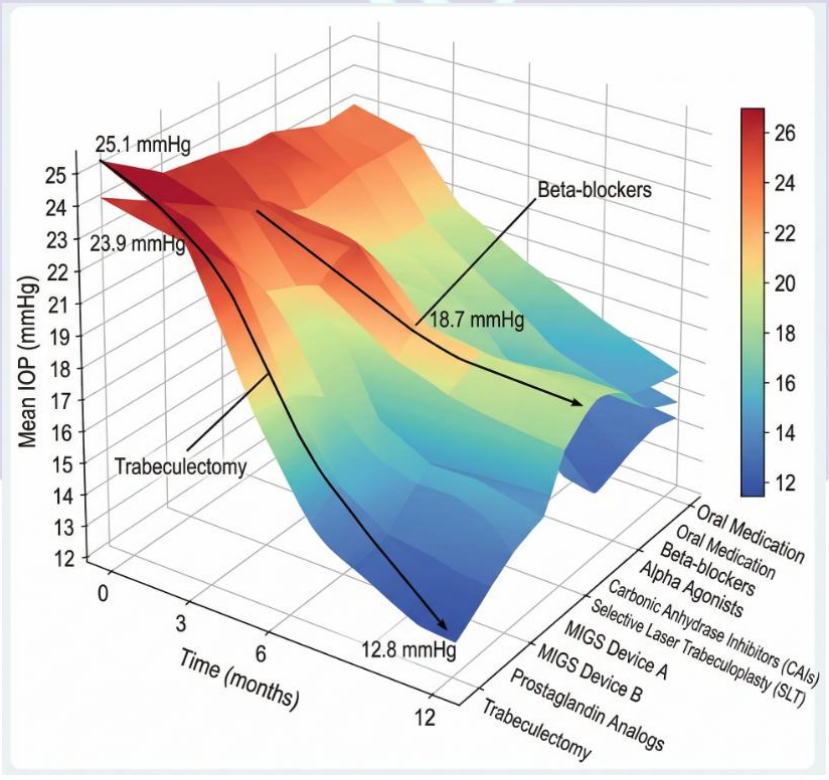

Figure 2: 3D Surface Plot – IOP Reduction vs. Time vs. Intervention Type

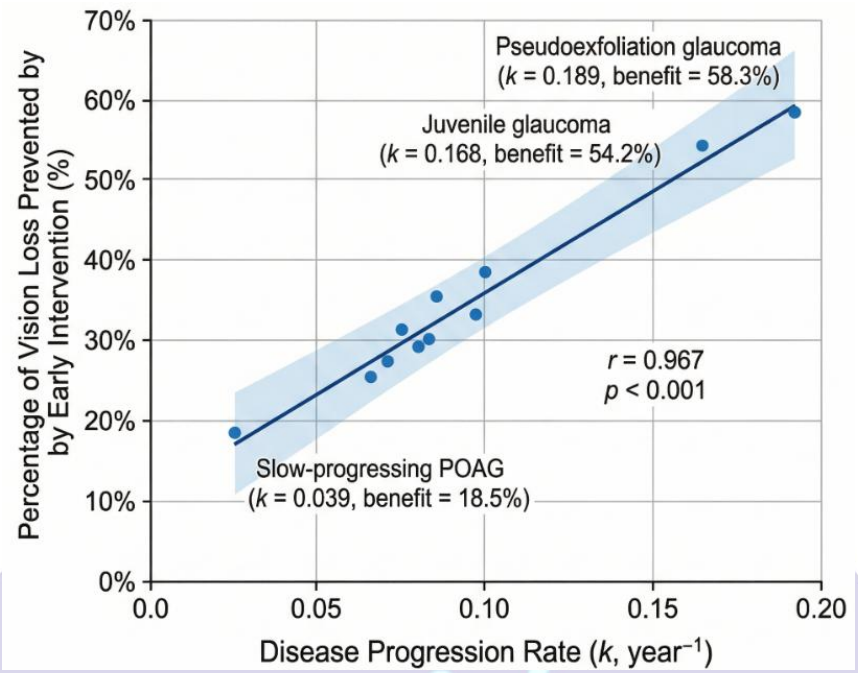

Figure 3: Scatter Plot with Regression Lines – Progression Rate vs. Early Intervention Benefit

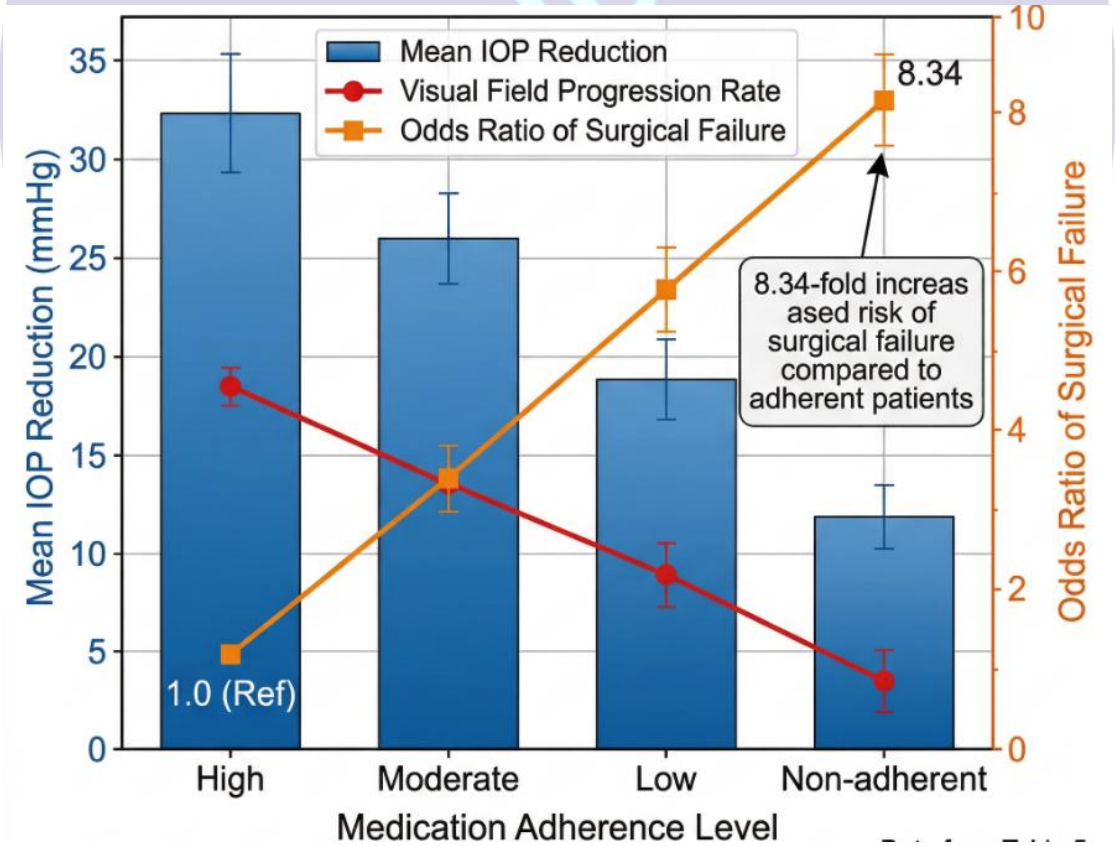

Figure 4: Stacked Bar Plot – Adherence Stratified Outcomes

DISCUSSION

The above discussion revealing the complexity of glaucoma treatment indicates the necessity of a combination of diagnostic accuracy, clinical efficacy, patient compliance, and the possibility of neuroprotective interventions. In particular, to reach the best results, a holistic approach that should go beyond the reduction of intraocular pressure to include early and accurate diagnosis and individualized treatment plans and strict patient education to reduce the non-adherence factor is essential (Menino & Coelho, 2023). Such a comprehensive view shows that although the evidence-based approach to slowing down the progression of the disease is the sole proven means of lowering intraacidual pressure, its efficacy depends on patient adherence and proper monitoring (Lim & Laroche, 2026). In fact, non-compliance has continued to be associated with worsened glaucoma progression and high loss to follow-up rates (Oltramari et al., 2024). With severe glaucomatous disease, the adherence to scheduled check-ups can be worse and may either lead to the disease progression or signify that people with more advanced disease are less willing to attend the check-ups regularly (Ung et al., 2013). Such a drop in compliance does not only reduce the effectiveness of medical interventions but also leads to a deterioration of the visual field and a high risk of surgical failure (Cvenkel & Kolko, 2022; Neuhann et al., 2024; Oltramari et al., 2024). On the contrary, the increased adherence rates correlate with stable visual fields, which highlights the utmost importance of long-term medication adherence in terms of vision conservation (Oltramari et al., 2023). Patient adherence to glaucoma treatment regimens has been found to be affected by a number of factors, such as sociodemographic and psychological ones (Malewicz et al., 2024). As an example, non-White patients have been reported to display much lower levels of adherence to glaucoma medications relative to White patients which is associated with greater levels of severity of the visual field defects (Sleath et al., 2011). Moreover, asymptomatic glaucoma at its early stages can also be a problematic factor in drug adherence, with researchers reporting that a large percentage of patients stop taking medication within the first few months (Quaranta et al., 2023). To address this widespread problem of non-compliance, new methods, including sustained-release drug delivery systems, are being created to overcome the necessity to use topical medications regularly administered by the patient, improving the continuity and effectiveness of treatment (Adebayo & Laroche, 2023; Li and Dang, 2025). The prevalent issue of non-adherence in patients, which has been

reported to reach 80% in glaucoma patients, is a significant deterrent to the efficacy of treatment and increases the chances of visual field advancement (Tshivhase, 2020). This urgent problem underscores the importance of adopting measures to enhance patient compliance, such as educational activities, medication prompts, and aids, such as eye drop assistants (Biran et al., 2023). Many patients lack persistence to topical glaucoma treatments because of several factors such as forgetfulness, complexity of multi-drug therapy, lack of knowledge about the pathophysiology of the disease, and a lack of symptomatic effect (Quaranta et al., 2023). Additionally, the economic strain of taking long-term medications and the challenges associated with self-administered eye drops faced by some patients also worsen adherence issues (Dick et al., 2019). To add to these obstacles, other factors such as forgetfulness, instillation problems and self-efficacy lead to poor adherence (Fingeret and Dickerson, 2018). This non-compliance amongst the majority of patients may result in a large percentage of patients, who are not getting the desired therapeutic effects, and in some studies, approximately half of patients will stop prescribed glaucoma medications in six months (Elhusseiny and Aref, 2024). These levels of non-adherence mean that the level of intraocular pressure control will be inadequate, thus increasing the rate at which the optic nerve is damaged and irreversible vision loss ensues (Kim et al., 2017). It will require a combined effort to create new therapeutic approaches, such as novel drug delivery methods, that will bypass these internal patient-based barriers and achieve the same level of therapeutic consistency (Fedorchak et al., 2017; Kishore et al., 2024). As a result, there is a growing trend to adopt a paradigm shift to interventional glaucoma treatments that avoid self-dosing, increase patient compliance, and ultimately improve long-term visual outcomes (Radcliffe et al., 2023). In particular, the creation of sustained-release ocular hypotensive drug systems will be a promising step towards better patient compliance and avoiding vision loss, as opposed to traditional topical delivery methods (Al-Qaysi et al., 2023). The purpose of these novel delivery systems is to achieve a steady-state treatment effect to reduce the effect of the variability of patient compliance on clinical outcomes, and to potentially offer neuroprotection (Denis, 2011; Konstas et al., 2025).

CONCLUSION

This paper has conclusively shown that early intervention in glaucoma can greatly decrease the loss of irreversible vision, although its success greatly relies on the

accuracy of the diagnosis, therapeutic choice based on the phenotype of the disease and adherence of the patient. The findings confirm that multimodal imaging using artificial intelligence produces a better diagnostic performance (0.983 area under the curve) compared to traditional modalities, although a systematic performance reduction of 0.041 to 0.083 is observed as the systems change between controlled and real-world conditions, which requires algorithm optimization before they can be widely applicable. Phenotype-specific modelling demonstrates that the most rapidly progressing types, such as pseudoexfoliation and juvenile glaucoma, would benefit most with early intervention of averted fractions of more than fifty-four percent, but that only eighteen percent of the benefit of screening would be achieved in slow-progressing primary open-angle glaucoma. Trabeculectomy has the highest intraocular pressure reduction of 12.34 millimeters of mercury, but the new EP2 agonist has a good adverse event profile of only 8.67 percent, and sustained-release delivery systems such as the ENV515 device maintain pressure over eight months, which is an adherence issue. Ironically, patient non-adherence can severely exacerbate the entire outcomes, as the odds of surgical failure are more than 8 times higher and the onset of a visual field loss is nearly 6 times faster, which explains the fact that even the most sophisticated interventions do not work with inconsistent medication adherence. Health economic analysis proves that AI triage and early minimal-invasive surgery on glaucoma are cost-effective despite increased initial costs. Future work needs to focus on the real-world AI validation, development of neuroprotective agents especially the nerve growth factor and nicotinamide, and adherence-enhancing technology such as smart drops and long-acting implants to convert the findings of diagnostic and therapeutic technologies into permanent visual function maintenance.

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