International Journal of Scientific Advances
ISSN: 2708-7972
Volume: 7 | Issue: 2 | Mar – Apr 2026 Available Online: www.ijscia.com
DOI: 10.51542/ijscia.v7i2.1

Artificial Intelligence in the Early Detection of Glaucoma: A Systematic Review

Daniel Atnil*, **Gusti Ayu Ning Wikan Sari**, **Maria Valentina Wibawa**

Faculty of Medicine, Universitas of Pelita Harapan, Tangerang, Indonesia

E-mail: daniel_atnil@yahoo.com; wikan.sari9@gmail.com; mwibawa04@gmail.com

*Corresponding author details: Daniel Atnil; daniel_atnil@yahoo.com

ABSTRACT
The application of artificial intelligence (AI), including machine learning and deep learning, demonstrates significant potential in screening, diagnosis, progression monitoring, and personalized management of glaucoma patients. Literature analysis, PICO evaluation, and QUADAS-2 bias assessment reveal that AI improves diagnostic accuracy, sensitivity, and specificity compared to conventional methods, while supporting early detection, progression prediction, and precision therapy decisions. Most studies show low risk of bias in test and flow domains, although several reviews present unclear risk in patient selection and reference standards due to heterogeneous populations and protocols. These findings highlight AI's transformational potential in clinical glaucoma practice, yet broader validation, standardized protocols, algorithm transparency, and consideration of ethical and patient diversity aspects remain necessary.

Keywords: AI; deep learning; glaucoma; machine learning; screening

INTRODUCTION
Glaucoma is one of the leading causes of blindness worldwide. The most common type is open-angle glaucoma. In this condition, intraocular pressure gradually increases, damaging the optic nerve and resulting in a narrowing of the visual field. Treatment for glaucoma may involve both medication and surgical procedures. [1]. Given these challenges in diagnosis and management, recent advances such as artificial intelligence (AI) are increasingly being explored to enhance early detection and improve patient outcomes. Artificial intelligence (AI) has emerged as a critical tool in ophthalmology, particularly for the early detection of glaucoma, a leading cause of preventable blindness worldwide. Because glaucoma is often asymptomatic in its early stages, delayed diagnosis can result in irreversible optic nerve damage [2]. Advances in imaging technologies such as Optical Coherence Tomography (OCT) and fundus photography have enabled AI to analyze data more rapidly and accurately than conventional approaches [3]. Multiple studies have demonstrated that deep learning algorithms can detect subtle retinal changes that may be overlooked during manual examinations [3]. This underscores the potential of AI as a scalable screening tool in clinical practice.

Several investigations report high accuracy rates for AI-based glaucoma diagnosis. For example, Thompson et al. showed that deep learning algorithms could directly analyze OCT images without manual segmentation, significantly reducing the need for clinician-driven image processing [1]. This approach streamlines evaluations, offering faster and more consistent results than traditional methods that rely heavily on clinical expertise [3]. Similarly, Cellini et al. highlighted that training algorithms on mixed datasets-combining publicly available images with expert-labeled data-enhances diagnostic performance [2]. These findings emphasize the importance of integrating multi-source datasets when developing robust AI systems.

One of the key applications of artificial intelligence (AI) in the early detection of glaucoma is machine learning. Through machine learning, computers can be trained to identify complex patterns in medical data, such as fundus images, Optical Coherence Tomography (OCT) scans, and clinical records. These algorithms are capable of learning from existing datasets, adapting as new data are introduced, and improving predictive accuracy over time. In the context of glaucoma, machine learning enables the identification of early signs of optic nerve damage and visual field changes that are often difficult for clinicians to detect manually, thus facilitating earlier and more accurate diagnosis. [4]

AI's applications in glaucoma extend beyond static image analysis. Medeiros et al. stressed the value of combining structural and functional information to improve diagnostic accuracy. The structure-function index, derived from OCT imaging and visual field perimetry, provides deeper insights into optic nerve health and disease progression [5]. This integrative approach allows AI not only to identify glaucoma in its early stages but also to track its progression longitudinally [5], thereby reducing the risk of irreversible vision loss.

Speed is another major advantage of AI in glaucoma screening. Machine learning algorithms can process thousands of images in a short period, enabling large-scale population screening with efficiency [2,3]. Yousefi classified AI applications in ophthalmology into screening, diagnosis, and progression monitoring, reflecting the breadth of its clinical utility [5]. Integrating AI into routine practice could help mitigate workforce shortages, especially in regions with limited access to ophthalmologists [6], thereby improving global eye health equity.

Despite these advances, implementation challenges remain. Algorithm performance can vary across populations due to demographic and clinical differences such as age, ethnicity, and ocular conditions [6,7]. Chaurasia et al. emphasized the need for extensive validation across diverse clinical settings to ensure generalizability [6]. Interpretability also poses a challenge, as clinicians must be able to understand and verify AI-driven decisions [3]. Addressing these issues requires ongoing research with diverse datasets and a focus on explainable AI.

High-quality data are essential for building reliable AI systems in glaucoma care. Expert-labeled datasets are particularly valuable for training algorithms to detect complex pathological patterns [2,3]. Gu et al. noted that visualizing the output of deep learning models can help clinicians better understand algorithmic decision-making, thereby strengthening trust in AI systems [3]. Longitudinal patient data further enhances predictive capabilities, particularly in forecasting disease progression [4]. These observations highlight the central role of data quality and availability in successful AI deployment.

Combining multiple imaging modalities can further enhance diagnostic accuracy. OCT, fundus photography, and visual field testing each provide complementary insights [4,5]. AI can integrate these inputs simultaneously, increasing both sensitivity and specificity [5]. Vemulapalli underscored the importance of standardized diagnostic protocols to ensure consistent data collection and algorithm evaluation [7]. Such multi-modal approaches demonstrate AI's potential to support more precise clinical decision-making and personalized treatment strategies.

Ethical and legal considerations are also critical in the medical application of AI. Algorithms must comply with data privacy regulations and be designed to minimize bias against particular patient groups [6,7]. Transparency in model development-including detailed documentation of datasets and training methods, is essential for independent validation and regulatory approval [3,7]. Ethical governance should therefore be embedded into both research and implementation.

AI also holds promise in risk prediction, identifying patients with elevated susceptibility to glaucoma before irreversible damage occurs. Predictive models based on machine learning can flag high-risk individuals for early intervention [2,4]. Longitudinal studies suggest that AI-assisted early detection can slow vision loss progression and improve long-term patient outcomes [4,5]. This reinforces AI's role not only as a diagnostic tool but also as a preventive instrument in glaucoma management.

Integration of AI into glaucoma screening and diagnosis offers opportunities to enhance accuracy, efficiency, and accessibility in eye care. Leveraging advanced imaging technologies, high-quality datasets, and rigorous clinical validation, AI can enable earlier and more reliable detection of glaucoma [1–7]. With continued research and standardized protocols, AI has the potential to become an integral component of future clinical practice, empowering clinicians to make better-informed decisions and reducing the global burden of glaucoma [6,7].

DISCUSSION

PRISMA

The literature search process was conducted systematically following the PRISMA guidelines. The initial search identified a total of 20 articles considered relevant based on the predefined keywords. These records were screened through title and abstract evaluation, with duplicate articles removed, followed by a full-text review to assess eligibility according to the inclusion and exclusion criteria.

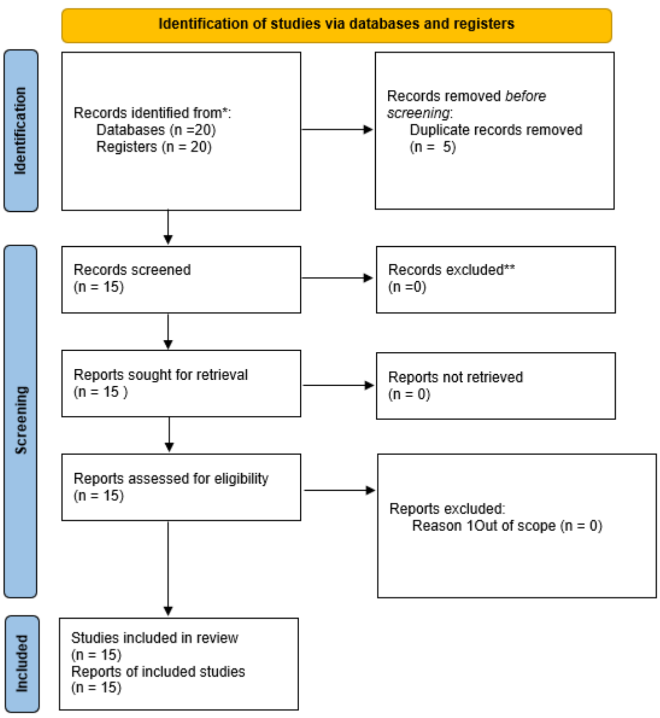

FIGURE 1: PRISMA Flowchart.

After this rigorous selection process, 15 articles were retained for final analysis in this systematic review. These studies were deemed suitable in terms of topic relevance, methodological rigor, and reporting quality, thereby providing a comprehensive overview of the application of artificial intelligence in the early detection of glaucoma.

Table 1 summarizes the most recent literature on the use of artificial intelligence (AI), including machine learning (ML) and deep learning (DL), in the diagnosis, screening, monitoring, and management of glaucoma. The included publications, ranging from 2019 to 2025, comprise systematic reviews, meta-analyses, and narrative or comprehensive reviews. The table outlines the authors, study methods, and key findings of each paper, with a particular focus on diagnostic performance, clinical applications, implementation challenges, and the potential of AI to enhance the accuracy, efficiency, and personalization of glaucoma management. AI applications covered in the reviewed studies include retinal imaging, OCT, visual field testing, biomarker analysis, precision therapy management, and patient education.

TABLE 1: Literature Extraction.

No.	Authors (Year)	Methodology	Key Findings
1	Nan-Nan Shi, Jing Li, Guang-Hui Liu, Ming-Fang Cao (2024)	Systematic review and meta-analysis. Literature search across PubMed, Embase, Scopus, ScienceDirect, ProQuest, and Cochrane Library until May 31, 2023. Analysis with Stata 16.0 (meta-analysis, meta-regression, subgroup analysis, publication bias) and RevMan 5.4 (QUADAS-2 for risk of bias).	20 studies (51 models) were analyzed. Pooled sensitivity = 0.91 (95% CI: 0.86–0.94), pooled specificity = 0.90 (95% CI: 0.87–0.92). PLR = 8.79, NLR = 0.11, DOR = 83.58, AUC = 0.95. No significant threshold effects. Conclusion: AI with SD-OCT demonstrates high accuracy for glaucoma detection, supporting "clinician + AI" as a diagnostic strategy.
2	Marco Zeppieri et al. (2024)	Review article. Literature search in Web of Science, PubMed, and Scopus until Aug 2024. Inclusion: peer-reviewed, English-language studies using AI/ML/DL for glaucoma diagnosis/therapy in humans.	CNNs and DL algorithms show high sensitivity and specificity in detecting glaucomatous changes from fundus photographs, OCT, and visual field tests. AI enables automated screening, differentiation between healthy vs. glaucomatous eyes, disease progression prediction, and reduces clinician workload. Challenges: diverse datasets, external validation, decision transparency, and ethical/legal issues. Conclusion: AI holds strong potential for glaucoma management; future work requires robust, cross-population validated, ethical, and clinically integrated models.
3	Yuki Hagiwara et al. (2024)	Comprehensive review of AI, especially DL, in Computer-Aided Diagnosis (CADx) systems for glaucoma detection. Focus on the strengths, limitations, and challenges of AI implementation.	AI, particularly DL, is promising for early glaucoma detection and supports CADx as a clinical aid. Research gaps include safety, reliability, interpretability, and explainability. Conclusion: AI-based CADx is important for early glaucoma diagnosis, but safer and more transparent models are needed.
4	Emanuele Tonti et al. (2024)	Systematic review. Literature search in PubMed, Scopus, and Web of Science until 2024. Inclusion: studies on AI for personalized glaucoma management.	AI applications span early detection, diagnosis, therapy optimization, and prognosis prediction. DL shows high accuracy in OCT and visual field tests. AI-based risk stratification supports personalized therapy decisions. Teleophthalmology improves access and timely intervention. *Challenges:* data heterogeneity, interpretability, and regulation. *Conclusion:* AI integration enhances clinical decision-making, therapy effectiveness, and progression prevention but requires broader validation and real-world integration.

No.	Authors (Year)	Methodology	Key Findings
5	Yan Zhu et al. (2024)	Literature review covering AI across the glaucoma care spectrum: screening, diagnosis, progression monitoring, precision therapy, surgery, and patient education.	AI enhances screening (retinal imaging & ML risk models), diagnosis (DL on OCT, visual field, fundus), progression monitoring (longitudinal data), and precision therapy (patient-specific data). Potential in robotic surgery and adherence tools (chatbots, reminders). Challenges: clinical integration, usability, diversity, and ethics. Conclusion: AI can transform glaucoma care, but clinical adoption must be cautious and inclusive.
6	Yan Zhu et al. (2024)	Literature review on glaucoma spectrum (screening, diagnosis, monitoring, precision therapy, surgery, education).	AI improves screening, diagnosis, progression monitoring, and precision therapy. Promising roles in robotic surgery and patient adherence. Challenges: clinical integration, ethics, population diversity.
7	Yu Jin et al. (2024, est.)	Literature review on ML and DL in glaucoma screening, diagnosis, and monitoring.	AI improves accuracy and efficiency, reduces costs, and supports early detection. Challenges: limited data, difficulty detecting subtle progression, and current clinical limitations. Prospects: AI is promising in glaucoma and other ocular diseases.
8	Patrick Xiang Ji et al. (2024)	Literature review on AI in glaucoma diagnosis, progression monitoring, and management strategies, with focus on ethical, legal, and social aspects.	AI detects subtle changes in early glaucoma, supports detection, monitoring, and therapy optimization. Challenges: clinical limitations, algorithm transparency, ethics, and access. Conclusion: AI is transformative; the future requires interdisciplinary collaboration, explainable algorithms, and equitable access.
9	Douglas R. da Costa, Felipe A. Medeiros (2024)	Narrative review. Focus on big data, AI, and DL in glaucoma screening, diagnosis, and monitoring.	AI + big data improve early detection, progression prediction, and disease mechanism understanding. Strengthens clinical practice and public health via faster diagnosis, reliable monitoring, and innovative technologies. Conclusion: AI + big data represent a critical direction for future glaucoma research and applications.
10	Xiaoqin Huang et al. (2023)	Systematic review of ML and DL techniques applied to retinal data (fundus, visual field) for detection, progression assessment, and staging of glaucoma. Includes taxonomy of AI models.	AI using fundus images achieves high diagnostic performance for glaucoma and other retinal diseases. Opportunities: faster diagnosis, progression prediction, automated staging. Challenges: model design with large imaging datasets, generalizability, interpretability, and validation needs. Conclusion: AI is promising but requires systematic steps, validation, and clinical/technical insight.
11	Aidan Pucchio et al. (2022)	Systematic review. Screened 10,258 studies, included 39 (23 cross-sectional, 9 prospective, 6 retrospective, 1 case-control). Focus: AI/bioinformatics in biofluid biomarker analysis (metabolomics, proteomics).	AI (discriminant analysis, ANNs) differentiates glaucoma vs. controls with high sensitivity /specificity. >175 biomarkers identified, mainly in POAG, but pathogenesis is unclear. Conclusion: AI supports biomarker-based diagnosis and pathogenesis understanding, but clinical application remains limited.
12	Delaram Mirzania et al. (2021)	PRISMA-guided systematic review on DL for glaucoma detection using fundus photos, OCT, and standard automated perimetry (SAP).	DL performance equals or surpasses clinicians for structural/functional tests. Conclusion: High potential for screening/diagnosis, but challenges include cross-population generalization, interpretability, and clinical integration.

No.	Authors (Year)	Methodology	Key Findings
13	Jincy C. Mathew et al. (2023)	Systematic review of >100 ML/DL studies for glaucoma detection/ prediction (methods, performance, pros/cons).	ML/DL automates diagnosis and reduces clinician workload. SVM and fuzzy C-means are widely used with high accuracy. Conclusion: Identifies most promising techniques and future development directions.
14	Chaurasia, Greatbatch, Hewitt (2022)	Meta-analysis of 79 studies (66 quantitative) on AI for glaucoma detection (fundus & OCT). PRISMA-DTA & QUADAS-2 used.	AI shows strong performance: AUC = 96.3%, sensitivity = 92%, specificity = 94%. Challenges: study heterogeneity, weaker performance with mixed datasets, and external validation. Conclusion: Need for standardized protocols, external validation, and cross-ethnic trials before clinical use.
15	Devalla S.K. et al. (2019)	Narrative review on AI in glaucoma diagnosis/prognosis via functional (VF) and structural (OCT, fundus) analysis.	DL methods support classification, segmentation, and ocular image enhancement. Conclusion: AI improves diagnostic/prognostic accuracy but faces challenges in reliability, interpretability, costs, and validation. Authors emphasize AI's future role as integral to glaucoma management.

Based on the extracted literature, the majority of studies demonstrate that AI, particularly deep learning algorithms, achieves high sensitivity and specificity in glaucoma detection using modalities such as OCT, fundus photography, and functional data like visual field testing. Beyond screening and diagnosis, AI contributes to disease progression prediction, patient risk stratification, and optimization of personalized therapy. However, the studies also highlight critical challenges, including limited and heterogeneous datasets, issues of model interpretability, the need for external validation, and concerns related to ethics and regulation. Overall, the literature underscores AI's transformative potential in glaucoma management. Yet, successful clinical implementation requires further validation, standardized diagnostic protocols, and careful integration into real-world practice with emphasis on safety, transparency, and equitable access to eye care.

PICO

Table 2 presents a PICO (Population, Intervention, Comparison, Outcome) analysis of 15 studies examining the application of artificial intelligence (AI) in glaucoma diagnosis, screening, and management. This framework highlights the characteristics of patient populations, the types of AI interventions employed, comparisons with conventional or manual diagnostic methods, and the key outcomes measured, such as sensitivity, specificity, accuracy, disease progression prediction, and precision therapy implementation. By applying the PICO approach, the table facilitates a clearer understanding of AI's effectiveness in clinical contexts while also drawing attention to the existing gaps and challenges. These include limited dataset diversity, model interpretability, external validation requirements, and ethical or regulatory considerations. Overall, the PICO analysis underscores both the significant potential of AI to transform glaucoma management and the need for further rigorous evaluation before safe and equitable integration into real-world practice.

TABLE 2: PICO Analysis of Included Studies.

No	Population	Intervention	Comparison	Outcome
1	Patients with glaucoma assessed via OCT imaging	AI models (ML/DL) applied to SD-OCT	Conventional/manual diagnosis	Pooled sensitivity 0.91, specificity 0.90, AUC 0.95; high diagnostic accuracy
2	Human subjects with suspected/confirmed glaucoma	CNNs and DL algorithms applied to fundus, OCT, and VF	Clinician assessment/manual methods	High sensitivity and specificity; supports screening, progression prediction
3	Patients undergoing CADx for glaucoma	DL-based CADx systems	Traditional CADx/clinical judgment	Promising diagnostic aid; challenges in reliability, interpretability

No	Population	Intervention	Comparison	Outcome
4	Glaucoma patients requiring personalized management	AI-driven DL models for OCT, VF, risk stratification	Standard care without AI support	Accurate diagnosis, optimized therapy decisions, improved teleophthalmology access
5	Glaucoma patients across the care spectrum	AI applied to screening, OCT, VF, fundus, and precision therapy	Manual clinician diagnosis/standard therapy	Enhanced screening, monitoring, and personalized treatment
6	Glaucoma patients across different care stages	AI applied to multimodal data	Clinician-only diagnosis	Improved accuracy, progression monitoring, and adherence support
7	Patients screened/monitored for glaucoma	ML/DL for fundus, OCT, VF	Standard diagnostic tests	Improved efficiency, accuracy, and reduced costs; challenges in subtle progression
8	Patients at risk or early-stage glaucoma	AI applied to multimodal clinical data	Conventional diagnosis	Detected subtle changes, supported progression monitoring, and therapy optimization
9	Glaucoma patients with large-scale datasets	Big data + AI/DL models	Traditional diagnostic/monitoring methods	Early detection, reliable monitoring, and enhanced disease understanding
10	Patients with glaucoma and retinal data (fundus, VF)	ML/DL taxonomy models	Standard interpretation of retinal imaging	High diagnostic performance; opportunities for staging and progression prediction
11	Glaucoma patients vs. controls with biofluid samples	AI (ANN, discriminant analysis) for metabolomic/proteomic biomarkers	Traditional biomarker analysis	High sensitivity /specificity; >175 biomarkers identified
12	Patients with glaucoma assessed via fundus, OCT, and SAP	DL models	Human expert assessment	DL matched or exceeded clinician accuracy; challenges in generalization
13	Patients in >100 ML/DL studies on glaucoma	SVM, fuzzy C-means, DL models	Manual/standard diagnosis	Automated diagnosis; reduced clinician workload with high accuracy
14	Patients with glaucoma across 79 studies	AI models applied to OCT, fundus	Standard clinician interpretation	AUC 96.3%, sensitivity 92%, specificity 94%; heterogeneity noted
15	Glaucoma patients with VF, OCT, and fundus data	DL models for classification and segmentation	Manual interpretation	Improved accuracy for diagnosis and prognosis; reliability and cost remain concerns

Most studies involved glaucoma patients assessed through OCT, fundus photography, visual field testing, or biomarkers. AI interventions (ML, DL, CNN, big data integration) were compared to manual or conventional diagnostic methods. Across studies, AI consistently achieved high sensitivity, specificity, and AUC (>90%), supporting early detection, risk stratification, disease monitoring, and personalized therapy. Challenges included dataset heterogeneity, model interpretability, external validation, ethical considerations, and equitable clinical integration.

Bias Test

The following table summarizes the risk of bias evaluation for 15 studies investigating the application of AI in glaucoma diagnosis and management, assessed using the QUADAS-2 instrument. The assessment focuses on four key domains: Patient Selection, Index Test (AI method applied), Reference Standard (comparative diagnostic benchmark), and Flow & Timing (sequence and interval between tests). This evaluation aims to determine the methodological quality of each study and to identify potential sources of bias that may influence conclusions regarding the effectiveness of AI. By systematically addressing these domains, the risk of overestimation or underestimation of AI's diagnostic performance can be better understood, providing a stronger basis for interpreting the overall evidence.

TABLE 3: Risk of Bias Assessment (QUADAS-2) of Included Studies.

No.	Author (Year)	Domain (QUADAS-2)	Risk of Bias	Notes
1	Nan-Nan Shi et al., 2024	Patient Selection	Low	Systematic, multiple databases, clear inclusion criteria
		Index Test	Low	AI model described with performance criteria
		Reference Standard	Low	SD-OCT + clinical evaluation
		Flow & Timing	Low	No significant delay between test and reference
2	Marco Zeppieri et al., 2024	Patient Selection	Unclear	Review, not primary data, possible selection bias
		Index Test	Low	AI model sufficiently explained
		Reference Standard	Unclear	Heterogeneity across reviewed studies
		Flow & Timing	Low	No specific delay data
3	Yuki Hagiwara et al., 2024	Patient Selection	Unclear	Review, no direct patient sample
		Index Test	Low	Deep learning AI model described generally
		Reference Standard	Unclear	Variation among studies
		Flow & Timing	Low	No reported delays
4	Emanuele Tonti et al., 2024	Patient Selection	Unclear	Systematic review, high population heterogeneity
		Index Test	Low	AI model described, applied to OCT & VF
		Reference Standard	Unclear	Heterogeneity in measurement protocols
		Flow & Timing	Low	No specific delays
5	Yan Zhu et al., 2024	Patient Selection	Unclear	Literature review, potential selection bias
		Index Test	Low	AI models described (DL, ML)
		Reference Standard	Unclear	Variation in study protocols
		Flow & Timing	Low	No delay information
6	Yu Jin et al., 2024	Patient Selection	Unclear	Literature review, no direct patient data
		Index Test	Low	AI described (ML & DL)
		Reference Standard	Unclear	Heterogeneity across studies
		Flow & Timing	Low	No delay reported
7	Patrick Xiang Ji et al., 2024	Patient Selection	Unclear	Literature review, population variation
		Index Test	Low	AI explained, focus on diagnosis & monitoring
		Reference Standard	Unclear	Heterogeneity in reference protocols
		Flow & Timing	Low	No specific delays
8	da Costa & Medeiros, 2024	Patient Selection	Unclear	Narrative review, high risk of selection bias
		Index Test	Low	AI & big data approaches described
		Reference Standard	Unclear	No single reference standard
		Flow & Timing	Low	No delay information

No.	Author (Year)	Domain (QUADAS-2)	Risk of Bias	Notes
9	Xiaoqin Huang et al., 2023	Patient Selection	Low	Systematic review, clear inclusion
		Index Test	Low	AI models & ML/DL techniques described
		Reference Standard	Low	OCT/fundus/VF used
		Flow & Timing	Low	No reported delays
10	Aidan Pucchio et al., 2022	Patient Selection	Low	Systematic review, 39 studies from >10,000 screened
		Index Test	Low	AI & bioinformatics explained
		Reference Standard	Low	Validated against controls & glaucoma patients
		Flow & Timing	Low	No significant delays
11	Delaram Mirzania et al., 2021	Patient Selection	Low	Systematic review, PRISMA, clear inclusion
		Index Test	Low	DL for fundus, OCT, SAP
		Reference Standard	Low	Standard clinical & VF tests
		Flow & Timing	Low	No significant delay
12	Jincy C. Mathew et al., 2023	Patient Selection	Low	Systematic review >100 articles, clear inclusion
		Index Test	Low	ML & DL explained
		Reference Standard	Low	Clinical data & imaging
		Flow & Timing	Low	No delays reported
13	Chaurasia et al., 2022	Patient Selection	Low	Meta-analysis of 79 studies, clear inclusion
		Index Test	Low	AI models (fundus & OCT) described
		Reference Standard	Low	Visual field & clinical combination
		Flow & Timing	Low	No reported delays
14	Devalla et al., 2019	Patient Selection	Unclear	Narrative review, no primary data
		Index Test	Low	AI applied to OCT/fundus
		Reference Standard	Unclear	Variation across reviewed studies
		Flow & Timing	Low	No specific delays
15	Yan Zhu et al., 2024	Patient Selection	Unclear	Literature review, selection bias possible
		Index Test	Low	AI models (DL & ML) explained
		Reference Standard	Unclear	Variability in reference protocols
		Flow & Timing	Low	No delays reported

Glaucoma is an eye disorder characterized by optic disc cupping and visual field defects resulting from damage to retinal ganglion cells [8]. These findings highlight the importance of evaluating methodological quality in AI-based glaucoma research, as variations in study design and patient selection may influence the reliability and generalizability of diagnostic outcomes. The results indicate that most studies showed a low risk of bias in the *Index Test* and *Flow & Timing* domains, suggesting that AI models were clearly described and that there were no significant delays between testing and reference standards. However, the level of bias in *Patient Selection* and *Reference Standard* varied across studies. Systematic reviews and meta-analyses tended to demonstrate low risk of bias, largely due to explicit inclusion criteria and consistent diagnostic benchmarks. In contrast, narrative and literature reviews relying on secondary data frequently present unclear risk, mainly driven by heterogeneity in patient populations, variations in reference protocols, and potential study selection bias. Overall, while several domains reflect robust methodology, the methodological diversity across studies highlights the need for cautious interpretation of AI's reported effectiveness in glaucoma.

The emergence of artificial intelligence (AI) represents a promising advancement in ophthalmology, particularly in glaucoma detection and management. Because glaucoma often remains asymptomatic until late stages, timely diagnosis is essential to preserve vision. Recent evidence shows that AI, especially deep learning (DL) systems, can accurately identify glaucomatous changes on OCT images, and diagnostic performance improves further when paired with clinician expertise [9].

Beyond OCT, AI can analyze fundus photography and visual field tests to detect glaucomatous changes, predict disease progression, and enable automated large-scale screening [10]. Despite these advantages, challenges remain. Model interpretability, generalizability across diverse populations, and the need for large, high-quality datasets are critical issues before AI can be fully adopted into routine practice [10, 11]. Importantly, AI also facilitates more personalized patient management by guiding therapy selection, predicting prognosis, and monitoring progression through longitudinal data analysis [11–13]. The integration of AI with teleophthalmology further extends access, enabling timely interventions for patients in remote or underserved areas [11].

AI systems have already demonstrated the ability to detect subtle, early-stage glaucomatous changes by leveraging big data analytics, while transparent and explainable algorithms strengthen clinical trust [14, 15]. Combined with big data, AI not only accelerates early detection but also deepens our understanding of disease mechanisms [16]. Emerging strategies even combine AI with biofluid marker analysis (e.g., metabolomics, proteomics) to distinguish glaucoma patients from controls with high accuracy, though these remain experimental in clinical application [17]. Notably, DL-based models have matched or even outperformed clinical experts in interpreting OCT, fundus, and visual field results, reinforcing AI's potential as a powerful diagnostic tool [18, 19, 20].

A wide range of machine learning (ML) and DL methods, including SVM and fuzzy c-means clustering, have also proven effective for automated glaucoma diagnosis and prediction [21, 22]. These methods promise to reduce clinician workload, accelerate diagnostic processes, and support more reliable clinical decision-making [23, 24].

Taken together, the evidence from the literature review, PICO analysis, and bias assessment underscores the transformational potential of AI in glaucoma care. AI demonstrates high sensitivity, specificity, and diagnostic accuracy, with the ability to detect early disease, predict progression, and support precision therapy. The QUADAS-2 risk of bias evaluation confirms that while many studies show strong methodological rigor, others, particularly narrative and secondary reviews, carry limitations related to population heterogeneity and reference variability.

Ultimately, AI is not merely a diagnostic adjunct but a strategic partner for clinicians in glaucoma management. For safe and effective clinical integration, AI tools must undergo broader validation, adhere to standardized protocols, ensure algorithmic transparency, and account for patient diversity, ethical considerations, and regulatory frameworks. Continued systematic development and rigorous testing will enhance AI's reliability and enable its seamless incorporation into everyday clinical practice.

CONCLUSION

Artificial intelligence, particularly machine learning and deep learning, has been shown to significantly enhance screening, diagnosis, progression monitoring, and personalized management of glaucoma with high accuracy. The PICO analysis reinforces the effectiveness of AI compared to conventional methods, while the risk of bias assessment indicates that most studies exhibit low bias in test performance and flow domains, although some reviews demonstrate unclear risk in patient selection and reference standards. AI holds transformational potential; however, its clinical implementation requires broader validation, standardized protocols, algorithmic transparency, and careful consideration of ethical aspects and patient diversity.

REFFERENCE

[1] Nitiyoso N. Diagnosis and management of glaucoma. Cermin Dunia Kedokteran. 2024; 51(7):384-6. doi:10.55175/cdk.v51i7.1017

[2] Thompson A., Jammal A., Berchuck S., Mariottoni E., & Medeiros F. Assessment of a segmentation-free deep learning algorithm for diagnosing glaucoma from optical coherence tomography scans. Jama Ophthalmology 2020;138(4):333. https://doi.org/10.1001/jamaophthalmol.2019.5983

[3] Cellini F., Caamaño D., Carrasco B., Juberías J., Ossa C., Bringas R.et al.. Deep learning application to detect glaucoma with a mixed training approach: public database and expert-labeled glaucoma population. Ophthalmic Research 2023;66(1):1278-1285. https://doi.org/10.1159/000534251

[4] Kresnia GM, Parikesit AA. Use of artificial intelligence in the diagnostics of autism spectrum disorder. Cermin Dunia Kedokteran. 2022;49(6):341-4. doi:10.55175/cdk.v49i6.246

[5] Gu B., Sidhu S., Weinreb R., Christopher M., Zangwill L., & Baxter S. Review of visualization approaches in deep learning models of glaucoma. Asia-Pacific Journal of Ophthalmology 2023;12(4):392-401. https://doi.org/10.1097/apo.0000000000000619

[6] Medeiros F., Tatham A., & Weinreb R. Strategies for improving early detection of glaucoma: the combined structure& ndash;function index. Clinical Ophthalmology 2014:611. https://doi.org/10.2147/opth.s44586

[7] Yousefi S. Clinical applications of artificial intelligence in glaucoma. Journal of Ophthalmic and Vision Research 2023;18(1):97-112. https://doi.org/10.18502/jovr.v18i1.12730

[8] Dewi M, Soetedjo AV. Efektivitas tetes mata citicoline terhadap perbaikan lapang pandang dan ketebalan lapisan serabut saraf retina pada glaukoma primer sudut terbuka. Cermin Dunia Kedokteran. 2024;51(2):104-9. doi:10.55175/cdk.v51i2.1046

[9] Chaurasia A., Greatbatch C., & Hewitt A. Diagnostic accuracy of artificial intelligence in glaucoma screening and clinical practice. Journal of Glaucoma 2022;31(5):285-299. https://doi.org/10.1097/ijg.0000000000002015

[10] Vemulapalli K. Artificial intelligence for glaucoma. Cochrane Database of Systematic Reviews 2025;2025(6). https://doi.org/10.1002/14651858.cd016114

[11] Shi NN, Li J, Liu GH, Cao MF. Artificial intelligence for the detection of glaucoma with SD-OCT images: a systematic review and meta-analysis. 2024.

[12] Zeppieri M, Gardini L, Culiersi C, Fontana L, Musa M, D'Esposito F, Surico PL, Gagliano C, Sorrentino FS. Novel approaches for the early detection of glaucoma using artificial intelligence. 2024.

[13] Hagiwara Y, Ciora OA, Monnet M, Lancho G, Lorenz JM. AI-driven approaches for glaucoma detection — A comprehensive review. 2024.

[14] Tonti E, Tonti S, Mancini F, Bonini C, Spadea L, D'Esposito F, Gagliano C, Musa M, Zeppieri M. Artificial intelligence and advanced technology in glaucoma: A review. 2024.

[15] Zhu Y, Salowe R, Chow C, Li S, Bastani O, O'Brien JM. Advancing glaucoma care: Integrating artificial intelligence in diagnosis, management, and progression detection. 2024.

[16] Zhu Y, Salowe R, Chow C, Li S, Bastani O, O'Brien JM. Advancing glaucoma care: Integrating artificial intelligence in diagnosis, management, and progression detection. 2024.

[17] Jin Y, Liang L, Li J, Xu K, Zhou W, Li Y. Artificial intelligence and glaucoma: a lucid and comprehensive review. 2024.

[18] Ji PX, Ramalingam V, Balas M, Pickel L, Mathew DJ. Artificial intelligence in glaucoma: A new landscape of diagnosis and management. 2024.

[19] da Costa DR, Medeiros FA. Big data for imaging assessment in glaucoma. 2024.

[20] Huang X, Islam MR, Akter S, Ahmed F, Kazami E, Abu Serhan H, Abd-alrazaq A, Yousefi S. Artificial intelligence in glaucoma: Opportunities, challenges, and future directions. 2023.

[21] Pucchio A, Krance S, Felfeli T, et al. The role of artificial intelligence in analysis of biofluid markers for diagnosis and management of glaucoma: A systematic review. 2022.

[22] Mirzania D, Thompson AC, Muir KW. Applications of deep learning in detection of glaucoma: A systematic review. 2021.

[23] Mathew JC, Ilango V, Asha V. Machine learning techniques, detection and prediction of glaucoma – A systematic review. 2023.

[24] Chaurasia AK, Greatbatch CJ, Hewitt AW. Diagnostic accuracy of artificial intelligence in glaucoma screening and clinical practice. 2022.

[25] Devalla SK, Liang Z, Pham TH, Boote C, Strouthidis NG, Thiery AH, Girard MJA. Glaucoma management in the era of artificial intelligence. 2019.