### UNIFIED INTELLIGENCE IN OPHTHALMOLOGY: A COMPREHENSIVE REVIEW OF A SINGLE FRAMEWORK FOR PREDICTING MULTIPLE EYE DISEASES

#### Anitha J

Department of Computer Science and Engineering Amrita School of Computing, Amrita Vishwa Vidyapeetham Chennai, Tamil Nadu, India – 601103 j\_anitha@ch.students.amrita.edu

Article history: Received 02.07.2025, Accepted 01.09.2025

#### **Abstract**

Diabetic ocular disorders are among the most important public health concerns, affecting millions of people with severe degrees of visual loss worldwide. Mild, nonblinding conditions and severe complications, such as diabetic retinopathy, diabetic macular edema, glaucoma, and cataracts, often appear due to uncontrolled diabetes. Presently, more than 145 million people worldwide are diagnosed with the raging global diabetes epidemic, and this number is estimated to increase further. Thus, early detection and prompt intervention play an important role in preventing vision damage. Earlier diagnostic systems faced a major drawback, as the framework was unable to handle different types of data. This restriction limited their capability in systematic multiple eye disease [MED] detection, particularly in clinical settings where diagnosis is a procedural task and where data is multisourced, such as clinical records, fundus-captured photos, and OCT exam information. This review discusses the development of a single AI framework that can handle structural and unstructured datasets to identify different stages of MED. It is termed as MED as it deals with multiple diseases such as diabetic retinopathy, diabetic macular edema, glaucoma, and cataracts. This survey also describes the developmental stages of segmentation techniques and also highlights the advanced techniques such as U-Net and SegFormer, which can be effectively used for anatomical segmentation, which is used in disease identification for both optical coherence tomography (OCT) and fundus datasets. Furthermore, it helps in understanding the workflow for developing an effective MED framework.

#### **Key words**

Multiple eye disease, Artificial Intelligence in Ophthalmology, U-Net, Data Privacy in Ophthalmology.

#### Sreenivasa Chakravarthi Sangapu\*

Department of Computer Science and Engineering Amrita School of Computing, Amrita Vishwa Vidyapeetham Chennai, Tamil Nadu, India – 601103 ss\_chakrayarthi@ch.amrita.edu

#### 1 Introduction

Artificial intelligence (AI) and machine learning have been an explosive impact in the field of ophthalmology and have resulted in significant advancements in the diagnosis and treatment of several ocular diseases such as diabetic retinopathy, age-related macular degeneration, glaucomatous optic neuropathy, and cataracts. Traditional diagnostic models are based on single diseases, are highly specific, and are often unworkable when information is scant or where large amounts of data are needed to exclude other potential conditions [He et al., 2021]. AI tools have shown great promise in aiding in these diagnostic roles using structured clinical data (eg., blood glucose, cholesterol, age) and unstructured image data (e.g. fundus photographs, OCT scans).

This review presents a conceptual single AI framework capable of diagnosing multiple eye diseases (MED) across their entire clinical spectrum without the necessity for direct integration of image and clinical data. Rather, the framework leverages modular branches enabling independent processing of structured and unstructured data under a common diagnostic workflow. This review aids in developing a unified framework capable of handling multiple modalities for effective forecasting of MED, from early detection to advanced stages. The article explores strategies for building a unified framework that leverages recent advances in artificial intelligence to address the challenges of diagnosing MED. The integration of many imaging modalities and clinical data presents a considerable obstacle in the development of MED models. The imaging modalities include Optical Coherence Tomography (OCT), fundus photography, and clinical datasets—each capable of serving as the ideal diagnostic tool for specific ocular conditions.

Effectively using multiple modalities within a singular AI framework can help build an efficient diagnostic tool capable of managing any stage of MED [Mateen et al., 2020]. This research examines the current state of MED platforms and their incorporation of various data sources to analyze contemporary MED models inside a centralized forecasting center, while evaluating the benefits and challenges of developing a fully integrated, data-driven framework.

Segmentation methods are used in various stages of the MED prediction process for anatomical analysis to find different parts in medical images. From simple methods like thresholding and region-growing, it has come a long way to more advanced deep-learning techniques including Convolutional Neural Networks (CNNs), Fully Convolutional Networks (FCNs), U-Net, to transformerbased approaches like SegFormer. Feature detection is now much more accurate, and tools can now process images to detect features that previously caused bottlenecks in diagnostic workflows. Segmentation techniques in medical image analysis have progressed significantly, transforming how MED can be predicted. Standard techniques, such as thresholding and region growing, provide the necessary tools for anatomical examination, but they often struggle with complex structures and variability in image quality [Piorkowski et al., 2017] Deep learning has provided an entirely new life to segmentation tasks by reducing error rates. CNNs introduced the automatic learning of hierarchical features, and FCNs enabled end-to-end training for pixel-wise predictions. The contracting and expanding paths of U-Net architecture have made it a staple in medical image segmentation, excelling in capturing both local and global contexts. The major hurdles in this field and proposes a systematic method has been listed below.

- Multi-modality such of OCT, fundus images, and clinical data within can be used to improves the prognosis and diagnosis of MED.
- Efficient model to build MED also involves several techniques in each phase of its workflow therefore a clear understanding of these technique for image and clinical data is required.
- The accuracy of MED classification can be enhanced through the evolution of segmentation techniques from traditional methods to modern deep-learning models.
- Real-world clinical validation and generalisability of AI models for MED while balancing ethical compliance and effectiveness across heterogeneous datasets

The review helps in building a data-driven framework for MED detection which focuses on four key areas: Comparative and Comprehensive Study, detailed technical workflow for effective MED detection, History and Evolution of Segmentation Techniques, and understanding Performance Evaluation, and gives a unified idea in understanding the ethical considerations and approach for real-world testing. It details how clinical data and image data can be used in building a data-driven framework for MED that can help ophthalmologists to use it

as an aid to diagnose any stage of the disease.

#### 2 Literature Survey

Muthukannan et al. [Muthukannan2022] proposed CNN-MDD, which denotes Convolutional Neural Networks for Multi-Disease Diagnosis, as a high-performance, deep learning model specifically tailored for the ODIR data set. Their model was one among the high performances performed continuously outperforming various optimized models with significant margins along various criteria. The model realized very high precision at 98.30%, accuracy at 95.27%, specificity at 95.21%, and recall at 93.3%, therefore validating the CNN-MDD technique in the detection of various ocular illnesses. It represented a significant step toward automated diagnosis of ocular diseases and was expected to be clinically precise.

Shamsan et al. [Shamsan et al., 2023] proposed a model in which they classify a large number of eye diseases using feature extraction as well as fusion techniques. This technique utilises ANN along with PCA to reduce features produced from the classification model based on MobileNet and DenseNet121 models created for this dataset of eye disorders. The second approach combines feature from both MobileNet and DenseNet121 models. These are used either before or after dimensionality reduction to classify images of eye disorders. In the third approach, handcrafted features from the MobileNet and DenseNet121 models were combined with an ANN for the classification of the eye disease dataset. The images in the dataset were sourced from Ocular Recognition, the Indian Diabetic Retinopathy Image Collection (IDRiD), and High-Resolution Fundus.

Bowmik et al. [Bhowmik et al., 2019] designed a model for detecting age-related eye diseases based on pretrained VGG16 and Inception V3 models. The model was trained on 84,495 images from an OCT device in the Kaggle database, achieving accuracies of 94% for the test data and 99.94% for the training data.

Using eye movement analysis and a machine learning-based approach, Hammoud et al. [Hammoud et al.,2023] have developed a novel approach for the early diagnosis of Parkinson's disease (PD) and Progressive Supranuclear Palsy (PSP). The team used a deep learning system to extract features from pupil images, which they then visualized using a technique known as time-series imaging. These images were fed into the model of disease detection to determine whether the subject had PD, PSP, or neither. Interestingly, the maximum performance of the model occurred when the subject was undergoing optokinetic activity, an eye movement test.

Nazir et al. [Nazir et al.,2020] proposed a model which integrated Fuzzy K-means (FKM) clustering and the Fast Region-based Convolution Neural Network (FRCNN) approach. According to the authors, the model was designed for the automatic detection and diagnosis of

diabetes-related ocular pathologies such as DR, DME, and glaucoma. The methodology was divided into two major stages, which incorporated eye disease identification and the use of FKM clustering in localizing and segmenting the affected regions. The FRCNN approach significantly improves the segmentation performance and shows a stronger capability in extracting deep feature images for optimal representations of ocular problems. On average, the Intersection over Union (IoU) was 0.95, and the mean average.

Malik et al. [Malik et al.,2019] proposed a unified framework to record diagnostic data in an internationally standardized format to enable the disease diagnosis and prediction using machine learning algorithms, focusing on hierarchical data organization to enhance machine readability and precise analysis by machine learning models. Among these algorithms are decision trees, random forests, Naive Bayes, and even neural networks. With this, performance across these algorithms can be compared and the best method selected for each dataset. Additionally, the framework allows more emphasis on self-learning and its ability to come up with unique classifications of diagnoses and symptoms.

Table 1. Summary of MED with Limitation Inference

Ref No	Scope	Model Used	Moda- lity	Data Size	Dataset Used	Relevance	Limitation
[4]	Automatic detection of mul- tiple eye diseases	CNN- DNN	Fundus	3000 im- ages	ODIR	Classifi- cation mod- ule	Limited dataset size may affec generaliza- tion
[5]	Eye disease classi- fication from fundus images	Pre- trained CNN + Fea- ture fu- sion (PCA)	Fundus	11,897 im- ages	Multiple (e.g., OIH)	Feature- level fusion for DSS	Generaliz- ability is unclear due to no external validation
[6]	Predicting eye dis- eases from OCT	Transfe learn- ing	rOCT	4000 im- ages	Kaggle	Structural imag- ing input	Dataset imbalance may bias learning
[7]	Neurological disease diagnosis via eye move- ments	DL Frame- work	Eye move- ment (non- recti- nal)	30 sam- ples	Burna- zyan Cen- tre	Comple- mentary diag- nostic modal- ity	Needs integration for broader ap- plicability
[8]	Disease localiza- tion and segmen- tation	FRCNN + FKM	NFundus	1985 im- ages	DiaretDB MES- SI- DOR, ORIGA	IROI detec- tion for DSS	Not tested in real-time clinical workflow
[9]	Comparative study us- ing clinical parame- ters	ML Mod- els	Clinical	Not men- tioned	Internal hos- pital dataset	Clinical data mod- ule	Dataset size undis- closed; repro- ducibility concern

Figure 1 shows limitation of MED detection. It has various problems, including the inability to evaluate robustness on a large dataset, difficulties with cross-modality image integration, and a lack of real-time datasets and multi-disease model validation. Because of these constraints, developing and evaluating many eye disease prediction models that can perform reliably and quickly in real-world settings is complex.

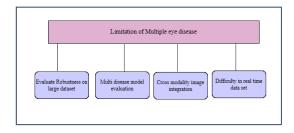


Figure 1. Exploring Limitations in MED Detection: A Diagrammatic Analysis

#### 2.1 Comparative and Comprehensive Study

The Comparative Study in this review elucidates the symptoms and clinical features that are conventionally utilized to diagnose various ophthalmic conditions. Traditionally, clinicians have relied on the identification of symptoms such as microaneurysms, hemorrhages, optic nerve damage, and lens opacity to diagnose conditions including diabetic retinopathy, glaucoma, and cataracts. However, manual identification of these symptoms can be subjective and time-intensive. By leveraging advanced image processing techniques, computer vision, and deep learning architectures, these manual processes can be supplanted with artificial intelligence (AI) models that offer enhanced accuracy and efficiency in diagnosis. AI systems offer the automatic identification and quantification of these features from multiple imaging modalities, enhancing resolution and minimizing potential human errors in disease detection [Goel et al.,2021].

It is important to study is to automate a manual diagnostic processes to build effective AI framework. For example, diagnosing diabetic retinopathy—understanding how clinicians detect microaneurysms and hemorrhages can help guide the development of AI models that can automatically spot these characteristic findings in optical coherence tomography (OCT) or fundus images. Likewise, knowing which regions are examined in glaucoma to determine damage to the optic nerve allows AI models to concentrate on these areas in Heidelberg Retina Tomograph (HRT) scans. This knowledge ensures that AI models not only replicate but exceed human diagnostic capabilities by providing faster, more reliable, and highly accurate predictions for various eye diseases [Bourne et al.,2013].

Table 3. MED Clinical Data and Symptoms Comparison

Type	Clinical Diagnosis	Symptoms	Primary Af- fected Area	Vision Loss
Diabetic Retinopa- thy	High blood sugar levels     High blood pressure     High cholesterol     Smoking     Long-term diabetes     Obesity	Eye floaters     Blurriness     Black spots in vision     Loss of central vision     Blindness	Retina	Gra- dual, periph- eral
Glaucoma	High blood sugar     Elevated Intraocular Pressure (IOP)     Optic nerve damage     Visual acuity reduction     Age-related risk	•Tunnel vision •Blindness	Optic nerve	Peri- pheral (tunnel)
Cataract	• Diabetes duration • Aging (senile) • Genetics • Smoking • UV exposure • Obesity	Cloudy/blurred vision     Glare/sensitivity to light     Difficulty with night driving     Yellowing of colors     Frequent lens prescription changes	Eye lens	Central
Diabetic Macular Edema	High blood sugar     High cholesterol     High blood pressure     Kidney disease     Smoking     Genetics     Caucasian ethnicity	Distorted central vision     Trouble reading or recognizing faces     Washed-out colors     Visual distortion     Central vision loss or blind spot	Macula (retina)	Central and pe- ripheral

Table 2. MED Image Modalities and Feature Comparison

		_		
Disease	Image Modal- ities	Ophthalmo- scope Infer- ence	Image Features	Level
Diabetic Retino- pathy	OCT, HRT, Fun- dus images	Microaneurysm, haemor- rhages, hard exudates, cotton wools, abnormal new vessels	Normal retinal appearance     Microaneurysms     Hemorrhages     Venous beading     Neovascularization, fibrous tissue	0: No DR 1: Mild NPDR 2: Moderate NPDR 3: Severe NPDR 4: Proliferative DR
Glau- coma	OCT, HRT, Fun- dus images	Cup-to-disc ratio, neural retinal rim, parapapillary atrophy	Slight visual field loss, slight cupping     Moderate visual field loss, moderate cupping     Severe visual field loss, large cupping	Mild Moderate Severe
Cataract	OCT, HRT, Fun- dus images	Mean in- tensity, uniformity, std. devia- tion, entropy	Slight to dense lens opacities     Reduced lens transparency     Advanced cataract characteristics	Mild Cataract Severe Cataract
Diabetic Macular Edema	OCT, HRT	Retinal thickness measurement	• Cysts on OCT • Retinal thickening in macula • Fluid accumulation	Presence / Absence Macular thickness

The above table 2 presents various features that are used to identify each eye disease, along with its imaging technology, which is used to examine its features. The basic modalities that have been used are OCT (Optical Coherence Tomography), which is an eye imaging technique that uses light for in-depth retina scans. The topography of the optic nerve head can be mapped using the HRT (Heidelberg Retinal Tomograph), a tool for glaucoma diagnosis and monitoring. A fundus image, which captures the retinal image as well as the optic nerve and blood vessels, is a helpful instrument for assessing different eye conditions [Goel et al.,2021], [Bourne et al.,2013], [Safi et al.,2018], [Mishra et al., 2022].

The above table 3 presents additional information like clinical diagnosis and symptoms, which are used to identify various eye diseases. These data can be combined to raise the accuracy level of the automatic diagnosis of any eye diseases [Alyoubi et al., 2020], [Medical-NewsToday], [Healthline], [Li et al., 2019], [Harangi et al., 2019].

#### 2.2 MED Diagnosis Framework

The stages of MED framework with methods are given in Figure 2. The workflow is designed to explain the techniques involved in each stage of handling image and clinical dataset [Phan et al., 2019], [AlGhamdi et al., 2019], [Asaoka et al., 2019].

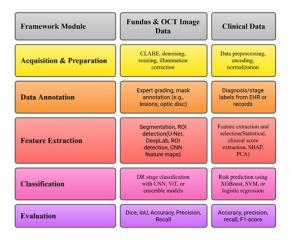


Figure 2. Unified MED Workflow

The workflow is divided into vertical modules, which are based on the specific type of dataset. Let us understand the workflow of unstructured datasets. It consists of image acquisition and preprocessing. The images are divided into different classes by identifying various ocular conditions such as normal, diabetic retinopathy, glaucoma and macular degeneration. The images are grouped according to the diseases to which they relate; therefore, the model is able to identify the distinguishing characteristics attached to each disease. In each stage of the module, many techniques are used for effective feature extraction and classification. Different preprocessing techniques, including contrast and noise adjustment, have been performed to clean the noise in the image dataset and to normalise the input for further downstream analysis. Depending on the model, the size of the images is normalised to obtain the same dimensions (if needed) and similar intensity values across various datasets. After normalisation, the images are sent to segmentation, which focuses on marking important anatomical structures such as the retina or optic disc. This step helps focus the algorithm on regions of clinical interest. After segmentation, Region of Interest (ROI) detection is carried out to identify specific characteristics, eg., lesions or other abnormalities related to the disease, for better analysis [Bajwa et al., 2019], [Lu et al., 2020], [Ramani et al., 2020].

Segmentation and ROI detection are performed as two completely distinct steps, as they serve different purposes. While segmentation is the general procedure of dividing the entire image into various regions to allow the algorithm to focus on corresponding anatomical

parts, it splits the foreground structures like the retina from the background and detects most of the important structural elements of the eye. On the other hand, ROI detection looks deeper into specific areas within these segmented regions—for instance, lesions or microaneurysms within the retina. This detailed approach allows the system to highlight what might be the most significant image features related to certain eye diseases. By separating each stage, the system ensures that the image undergoes systematic processing, which facilitates increased diagnostic precision [Zhang et al., 2019], [Torre et al., 2020].

Another vertical workflow involves structured data, which includes details such as patient-specific clinical information-age, blood pressure, HbA1c level, and medical history. These data then undergo a systematic iterative process beginning with data acquisition from clinical records, followed by multiple steps of data cleaning and normalisation that ensure consistency and comparability across variables [Bourne et al., 2013b], [Congdon et al., 2004]. After preprocessing, the important clinical features for identifying each MED condition are extracted using feature selection algorithms. Classification algorithms such as XGBoost, Random Forest, etc., have been used in identifying the type of MED based on the selected feature in the previous step. The developed MED framework is evaluated using metrics such as accuracy, precision, recall, and F1 score. This organised data pipeline provides a stable platform for MED identification within a data-driven decision-making system [Li et al., 2021], [Rekhi et al., 2017].

### 2.3 History of Segmentation Techniques in MED Prediction:

The segmentation techniques utilized in MED detection, is illustrated in Figure 3, It has been evolved from rudimentary methods such as thresholding, region growing, and edge detection in the 1990s to sophisticated deep learning hybrid models. During the 2000s, methodologies including K-means clustering, active contour models, graph cut, and watershed significantly enhanced anatomical localization of complex eye anatomy. Between 2015 and 2018, advancements in deep learning models such as Convolutional Neural Networks (CNNs), Fully Convolutional Networks (FCNs), U-Net, and DeepLab facilitated pixel-wise accuracy for segmentation of retinal layers and features [Nazir et al., 2021], [Zago et al., 2020], [Kunwar et al., 2015].

Convolutional Networks (FCNs), U-Net, and DeepLab enabled pixel-level precision in segmenting retinal layers and features. CNNs are characterized by the equation

$$y = f(W * x + b)$$

Where W represents the weights, x is the input, and b is the bias. U-Net's efficacy is attributed to its encoder-decoder structure with skip connections. Its segmentation accuracy is commonly quantified using Dice Loss:



Figure 3. Evolution of Segmentation Techniques in MED

$$DiceLoss = 1 - \frac{2|A \cap B|}{|A| + |B|}$$

DeepLab, employing atrous convolutions, is defined by:

$$y|i| = \sum_{K} x[i + r \cdot K]w[k]$$

where r is the dilation rate, extending the receptive field for better segmentation. From 2019 to 2020, hybrid models like Mask R-CNN, Residual U-Net, and Attention U-Net further enhanced segmentation. Mask R-CNN loss includes:

$$L = L_{cls} + L_{box} + L_{mask}$$

while Residual U-Net improves feature extraction with residual connections:

$$y = f(x) + x$$

Attention U-Net applies attention mechanisms to refine focus on relevant image regions:

$$\alpha = \sigma(W_{att} \cdot (x_{enc} \oplus x_{dec}))$$

Since 2020, the availability of methods (eg., Cycle-GAN, Pix2Pix) for synthesizing retinal images has given developers flexibility to combine simple procedure and benefit (ie., limited dataset and dataset label imbalance). This resulted in a remarkable increase of the robustness and generalizability of segmentation models in rare or less frequent disease stages. In 2021 and beyond, transformer-based models like SegFormer capture longrange dependencies using the attention mechanism:

$$Attention(Q,K,V) = softmax(\tfrac{QK^t}{\sqrt{d_k}})$$

For achieving high segmentation accuracy, these models use a combination of cross entropy and Dice loss. Although loss functions such as Dice Loss and cross entropy are important, U Net and DeepLab are built on strong architectures, access to large amounts of high-quality annotated data, and powerful optimization technique. Focusing on this interplay gives a view of segmentation performance that is more complete. Such has made MED predicting machines more accurate and more rapid and thus more life-enhancing by diagnosing other diseases such as diabetic retinopathy etc.[Quigley et al., 2006], [Bourne et al., 2017], [AlBander et al., 2018], [Chen et al., 2015], [Mary et al., 2016], [Ayub et al., 2016].

#### 2.4 MED Performance Evaluation

The deeper evaluation of these model results would lead to the acquisition of significant knowledge regarding model efficiency in identifying ocular diseases. Figure 4 represents five key metrics used in analyzing MED. This close examination of performance differences is helpful not only in selecting the most appropriate diagnostic model but also in evaluating its strengths and weaknesses. By assessing these metrics, researchers can identify areas where existing models perform well or poorly, encouraging targeted efforts to address weaknesses and develop more robust diagnostic systems for predicting MED. This iterative process of evaluation and improvement is crucial for advancing the field and ultimately improving patient care by providing more accurate and reliable diagnostic tools [Sarkar et al., 2017], [Nawaldgi et al., 2018], [Septiarini et al., 2018], [Zou et al., 2018], [Chudzik et al., 2018].

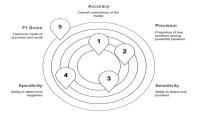


Figure 4. Performance Metrics used in MED

## 2.5 Data Privacy and Ethical Guidelines for AI in Ophthalmology

The following table 4 presents the Data Privacy and Ethical Guidelines by using WHO'S guideline for health that must be adhered to in order to ensure the safe and responsible development and implementation of AI models in ophthalmology. Compliance with these principles aids in safeguarding patient data, maintaining trust, and meeting regulatory standards while ensuring that AI tools support clinicians in enhancing patient care [Chen et al., 2020], [Faizal et al., 2023], [Liu et al., 2022], [Patankar et al., 2021], [Kuppusamy et al., 2022].

# 2.6 Real-World Testing and Performance Evaluation for AI in Ophthalmology

Real-world testing is crucial for AI and models to seamlessly integrate into high-impact workflows, managing diverse patient data and real-time demands. This testing evaluates the model's practicality, reliability, and scalability in routine healthcare operations. Figure 5 outlines critical aspects of real-world testing, such as clinical integration, system compatibility, and key performance indicators (eg., accuracy, efficiency, false positive/negative rates). It also assesses AI's impact on patient care, ensuring improvements in diagnosis and treatment outcomes. The system is then honed based on clinician feedback, with performance trends visually tracked.

Table 4. Key Data Privacy and Ethical Guidelines for AI in Ophthalmology

Category	WHO Guideline	Compliance	<b>Key Practice</b>	
Privacy Laws	Upholding Personal Data Protection	Secure, anonymized pa- tient data handling	Anonymization, encryption	
Data Secu- rity	Ensuring Data Integrity and Confidentiality	Protect from breaches, unautho- rized access	Encryption, access control	
Ethical Use	Promoting Equity and Inclusiveness	Prevent discrimina- tion, ensure trust	Diverse datasets, explainable AI	
Consent	Protecting Human Autonomy	Ensure patient awareness, agreement	Clear communica- tion, legal compli- ance	
Regu- lations	Promoting Human Well-Being and Safety	Adhere to medical device regulations	Regulatory ap- proval, safety checks	
Human Over- sight	Ensuring Transparency and Accountability	Support, not replace human judgment	Assist clinicians, retain accountability	

The solution undergoes testing across different clinical scenarios to validate its generalizability [ambyal et al., 2020], [Almazroa et al., 2015], [Ramzan et al., 2019], [Phan et al., 2016], [Samagaio et al., 2018]. Several studies have shown successful real-world applications of AI especially in the field of ophthalmology. Li et al. based on 47,269 individuals in China with sensitivity and specificity of the AI model being very high [Li et al., 2021]. Gulshan et al. analyzed performance variability of several different systems that are approved in the US by the FDA [Gulshan et al., 2019]. Kanagasingam et al. found a 100% sensitivity using THEIA system at new zealand clinics [Kanagasingam et al., 2022], [Plotnikov et al., 2019]. Standardization of real-world evaluation is enabled by many benchmark datasets such as Messidor, REFUGE and DRIONS-DB.



Figure 5. Real-World Testing and Performance Evaluation Framework

#### 3 Overall Summary

This review focuses on identifying the gaps in developing an AI-based, data-driven framework that could diagnose diabetic ocular complications in terms of MED. It highlights the drawbacks of previous diagnosis systems which could only detect one kind of disease and helps in understanding the AI-based cutting-edge segmentation methods for anatomical analysis from fundus imaging

and optical coherence tomography (OCT), such as U-Net, SegFormer, etc. A MED framework is presented in the review, including important steps and methods involved in each stage, such as preprocessing, segmentation, and classification. Therefore, AI offers promising solutions for predicting all stages of disease, starting from early detection till advanced stage. It also focuses on ensuring the reliability of models, addressing ethical considerations and safeguarding data privacy. Additionally, the review emphasizes the importance of improving diagnostic accuracy and achieving practical implementation of AI models in real-world ophthalmic practices. By emphasizing the crucial areas for advancement and further improvement, this study establishes the groundwork for future studies and advancements in AI-driven solutions in the field of ophthalmology.

#### 4 Conclusion

This review provides a thorough analysis of the challenges and solutions involved in developing a MED framework. This also highlights the importance of clinical data using image datasets to improve the framework from early detection to other stages of diagnosis. It also goes beyond simply highlighting the gap in developing the MED framework by critically investigating the technical workflow in each stage of building the data-driven MED model. The review also examines the evolution of segmentation techniques, with a focus on modern approaches like GAN, U-Net and SegFormer, and evaluates the steps in constructing an efficient, adaptable AIbased MED framework. Considering the sensitivity of medical data and the possible consequences for decisions on patient care by AI, this emphasis on ethical considerations is highly relevant. Future work should endeavour to overcome these limitations with better integration of datasets, improved segmentation techniques, and ensuring ethical use, leading to more effective and robust AI healthcare solutions. This review helps in improving the accuracy and scalability of diagnosis and also helps in building a complete decision support system that can handle structural and unstructured data.

#### References

He, J., Li, C., Ye, J., Qiao, Y., & Gu, L. (2021). Multilabel ocular disease classification with a dense correlation deep neural network. *Biomedical Signal Processing and Control*, 63, 102167.

Mateen, M., Wen, J., Hassan, M., Nasrullah, N., Sun, S., & Hayat, S. (2020). Automatic detection of diabetic retinopathy: A review on datasets, methods, and evaluation metrics. *IEEE Access*, 8, 48784–48811.

Piorkowski, A., Nurzynska, K., Gronkowska-Serafin, J., Selig, B., Boldak, C., & Reska, D. (2017). Influence of applied corneal endothelium image segmentation techniques on the clinical parameters. *Computerized Medical Imaging and Graphics*, 55, 13–27.

- Muthukannan, P. (2022). Optimized convolution neural network-based multiple eye disease detection. Computers in Biology and Medicine, 146, 105648.
- Shamsan, A., Senan, E. M., & Shatnawi, H. S. A. (2023). Automatic classification of colour fundus images for prediction of eye disease types based on hybrid features. Diagnostics, 13(10), 1706.
- Bhowmik, A., Kumar, S., & Bhat, N. (2019). Eye disease prediction from optical coherence tomography images with transfer learning. In Engineering Applications of Neural Networks: 20th International Conference, EANN 2019, Heraklion, Crete, Greece, May 24–26, 2019, Proceedings (Vol. 20, pp. 104–114). Springer.
- Hammoud, M., Kovalenko, E., Somov, A., Bril, E., & Baldycheva, A. (2023). Deep learning framework for neurological disease diagnosis through near-infrared eye video and time series imaging algorithms. Internet of Things, 24, 100914.
- Nazir, T., Irtaza, A., Javed, A., Malik, H., Hussain, D., & Naqvi, R. A. (2020). Retinal image analysis for diabetes-based eye disease detection using deep learning. *Applied Sciences*, 10(18), 6185.
- Malik, S., Kanwal, N., Asghar, M. N., Sadiq, M. A. A., Karamat, I., & Fleury, M. (2019). Data-driven approach for eye disease classification with machine learning. Applied Sciences, 9(14), 2789.
- Goel, N., Takkar, B., & Shah, P. (2021). Clinical trials in diabetic retinopathy-III. In Handbook of Clinical Trials in Ophthalmology (p. 103).
- Bourne, R. R., Stevens, G. A., White, R. A., Smith, J. L., Flaxman, S. R., Price, H., & Taylor, H. R. (2013). Causes of vision loss worldwide, 1990-2010: A systematic analysis. The Lancet Global Health, 1(6). e339-e349.
- Safi, H., Safi, S., Hafezi-Moghadam, A., & Ahmadieh, H. (2018). Early detection of diabetic retinopathy. Survey of Ophthalmology, 63(5), 601–608.
- Mishra, A., Singh, L., Pandey, M., & Lakra, S. (2022). Image-based early detection of diabetic retinopathy: A systematic review on artificial intelligence (AI) based recent trends and approaches. Journal of Intelligent & Fuzzy Systems, 43(5), 6709–6741.
- Alyoubi, W. L., Shalash, W. M., & Abulkhair, M. F. (2020). Diabetic retinopathy detection through deep learning techniques: A review. Informatics in Medicine Unlocked, 20, 100377.
- Today. Medical News (n.d.) Retrieved from https://www.medicalnewstoday.com/ articles/183417
- Healthline. (n.d.). Diabetic macular edema symptoms and treatment. Retrieved from https://www. healthline.com/health/eye-health/
  - symptoms
- Li, X., Hu, X., Yu, L., Zhu, L., Fu, C. W., & Heng, P. A. (2019). CANet: Cross-disease attention network for joint diabetic retinopathy and diabetic mac-

- ular edema grading. IEEE Transactions on Medical Imaging, 39(5), 1483–1493.
- Harangi, B., Toth, J., Baran, A., & Hajdu, A. (2019, Automatic screening of fundus images using a combination of convolutional neural network and hand-crafted features. In 2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) (pp. 2699-2702). IEEE.
- Phan, S., Satoh, S. I., Yoda, Y., Kashiwagi, K., & Oshika, T. (2019). Evaluation of deep convolutional neural networks for glaucoma detection. Japanese Journal of Ophthalmology, 63(3), 276-283.
- Al Ghamdi, M., Li, M., Abdel-Mottaleb, M., & Abou Shousha, M. (2019, May). Semi-supervised transfer learning for convolutional neural networks for glaucoma detection. In ICASSP 2019 - 2019 IEEE International Conference on Acoustics, Speech and Signal Processing (ICASSP) (pp. 3812–3816). IEEE.
- Asaoka, R., Tanito, M., Shibata, N., Mitsuhashi, K., Nakahara, K., Fujino, Y., & Kiuchi, Y. (2019). Validation of a deep learning model to screen for glaucoma using images from different fundus cameras and data augmentation. Ophthalmology Glaucoma, 2(4), 224-231.
- Bajwa, M. N., Malik, M. I., Siddiqui, S. A., Dengel, A., Shafait, F., Neumeier, W., & Ahmed, S. (2019). Two-stage framework for optic disc localization and glaucoma classification in retinal fundus images using deep learning. BMC Medical Informatics and Decision Making, 19(1), 1–16.
- Lu, Z., & Chen, D. (2020). Weakly supervised and semisupervised semantic segmentation for optic disc of fundus image. Symmetry, 12(1), 145.
- Ramani, R. G., & Shanthamalar, J. J. (2020). Improved image processing techniques for optic disc segmentation in retinal fundus images. Biomedical Signal Processing and Control, 58, 101832.
- Zhang, W., Zhong, J., Yang, S., Gao, Z., Hu, J., Chen, Y., & Yi, Z. (2019). Automated identification and grading system of diabetic retinopathy using deep neural networks. Knowledge-Based Systems, 175, 12-25.
- de La Torre, J., Valls, A., & Puig, D. (2020). A deep learning interpretable classifier for diabetic retinopathy disease grading. *Neurocomputing*, 396, 465–476.
- Ayzenberg, V., Kamps, F. S., Dilks, D. D., & Lourenco, S. F. (2022). Skeletal representations of shape in the human visual cortex. *Neuropsychologia*, 164, 108092.
- Bourne, R. R., Stevens, G. A., White, R. A., Smith, J. L., Flaxman, S. R., Price, H., & Taylor, H. R. (2013). Causes of vision loss worldwide, 1990-2010: A systematic analysis. The Lancet Global Health, 1(6), e339-e349.
- diabetic-macular-edema-symptoms-treatme@or#gdon, N., O'Colmain, B., Klaver, C. C., Klein, R., Munoz, B., Friedman, D. S., & Mitchell, P. (2004). Causes and prevalence of visual impairment among adults in the United States. Archives of Ophthalmol-

- ogy (Chicago, Ill.: 1960), 122(4), 477-485.
- Li, T., Bo, W., Hu, C., Kang, H., Liu, H., Wang, K., & Fu, H. (2021). Applications of deep learning in fundus images: A review. *Medical Image Analysis*, 69, 101971.
- Rekhi, R. S., Issac, A., & Dutta, M. K. (2017, October). Automated detection and grading of diabetic macular edema from digital colour fundus images. In 2017 4th IEEE Uttar Pradesh Section International Conference on Electrical, Computer and Electronics (UP-CON) (pp. 482–486). IEEE.
- Nazir, T., Irtaza, A., & Starovoitov, V. (2021). Optic disc and optic cup segmentation for glaucoma detection from blur retinal images using improved mask-RCNN. *International Journal of Optics*, 2021, 1–12.
- Zago, G. T., Andreão, R. V., Dorizzi, B., & Salles, E. O. T. (2020). Diabetic retinopathy detection using red lesion localization and convolutional neural networks. *Computers in Biology and Medicine*, 116, 103537.
- Kunwar, A., Magotra, S., & Sarathi, M. P. (2015, August). Detection of high-risk macular edema using texture features and classification using SVM classifier. In 2015 International Conference on Advances in Computing, Communications and Informatics (ICACCI) (pp. 2285–2289). IEEE.
- Quigley, H. A., & Broman, A. T. (2006). The number of people with glaucoma worldwide in 2010 and 2020. *The British Journal of Ophthalmology*, 90(3), 262.
- Bourne, R. R., Flaxman, S. R., Braithwaite, T., Cicinelli, M. V., Das, A., Jonas, J. B., ... & Zheng, Y. (2017). Magnitude, temporal trends, and projections of the global prevalence of blindness and distance and near vision impairment: A systematic review and meta-analysis. *The Lancet Global Health*, 5(9), e888–e897.
- Al-Bander, B., Williams, B. M., Al-Nuaimy, W., Al-Taee, M. A., Pratt, H., & Zheng, Y. (2018). Dense fully convolutional segmentation of the optic disc and cup in colour fundus for glaucoma diagnosis. *Symmetry*, 10(4), 87.
- Chen, X., Xu, Y., Wong, D. W. K., Wong, T. Y., & Liu, J. (2015, August). Glaucoma detection based on deep convolutional neural network. In 2015 37th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC) (pp. 715–718). IEEE.
- Mary, V. S., Rajsingh, E. B., & Naik, G. R. (2016). Retinal fundus image analysis for diagnosis of glaucoma: A comprehensive survey. *IEEE Access*.
- Ayub, J., Ahmad, J., Muhammad, J., Aziz, L., Ayub, S., Akram, U., & Basit, I. (2016, April). Glaucoma detection through optic disc and cup segmentation using K-mean clustering. In 2016 International Conference on Computing, Electronic and Electrical Engineering (ICE Cube) (pp. 143–147). IEEE.
- Sarkar, D., & Das, S. (2017). Automated glaucoma detection of medical image using biogeography based optimization. In *Advances in Optical Science and*

- Engineering: Proceedings of the Third International Conference, OPTRONIX 2016 (pp. 381–388). Springer Singapore.
- Nawaldgi, S., Lalitha, Y. S., & Reddy, M. (2018). A novel adaptive threshold and ISNT rule based automatic glaucoma detection from color fundus images. In *Data Engineering and Intelligent Computing: Pro*ceedings of IC3T 2016 (pp. 139–147). Springer Singapore.
- Septiarini, A., Khairina, D. M., Kridalaksana, A. H., & Hamdani, H. (2018). Automatic glaucoma detection method applying a statistical approach to fundus images. *Healthcare Informatics Research*, 24(1), 53–60.
- Zou, B., Chen, Q., Zhao, R., Ouyang, P., Zhu, C., & Duan, X. (2018). An approach for glaucoma detection based on the features representation in radon domain. In *Intelligent Computing Theories and Application: 14th International Conference, ICIC 2018, Wuhan, China, August 15–18, 2018, Proceedings, Part II* (pp. 259–264). Springer International Publishing.
- Chudzik, P., Majumdar, S., Calivá, F., Al-Diri, B., & Hunter, A. (2018). Microaneurysm detection using fully convolutional neural networks. *Computer Methods and Programs in Biomedicine*, 158, 185–192.
- Chen, J., Qi, X., Wang, W., Li, B., & Liu, Y. (2020). Real-time location of surgical incisions in cataract phacoemulsification. *Multimedia Tools and Applications*, 79, 30311–30327.
- Faizal, S., Rajput, C. A., Tripathi, R., Verma, B., Prusty, M. R., & Korade, S. S. (2023). Automated cataract disease detection on anterior segment eye images using adaptive thresholding and fine tuned inception-v3 model. *Biomedical Signal Processing and Control*, 82, 104550.
- Liu, R., Gao, S., Zhang, H., Wang, S., Zhou, L., & Liu, J. (2022). MTNet: A combined diagnosis algorithm of vessel segmentation and diabetic retinopathy for retinal images. *PLOS ONE*, 17(11), e0278126.
- Patankar, A. M., & Thorat, S. S. (2021, July). Diagnosis of ophthalmic diseases in fundus image using various machine learning techniques. In 2021 6th International Conference on Communication and Electronics Systems (ICCES) (pp. 1114–1118). IEEE.
- Kuppusamy, P., Basha, M. M., & Hung, C. L. (2022, March). Retinal blood vessel segmentation using random forest with Gabor and Canny edge features. In 2022 International Conference on Smart Technologies and Systems for Next Generation Computing (ICSTSN) (pp. 1–4). IEEE.
- Sambyal, N., Saini, P., Syal, R., & Gupta, V. (2020). Modified U-Net architecture for semantic segmentation of diabetic retinopathy images. *Biocybernetics and Biomedical Engineering*, 40(3), 1094–1109.
- Almazroa, A., Burman, R., Raahemifar, K., & Lakshminarayanan, V. (2015). Optic disc and optic cup segmentation methodologies for glaucoma image detection: A survey. *Journal of Ophthalmology*, 2015, 1–

12.

- Ramzan, A., Usman Akram, M., Shaukat, A., Gul Khawaja, S., Ullah Yasin, U., & Haider Butt, W. (2019). Automated glaucoma detection using retinal layers segmentation and optic cup-to-disc ratio in optical coherence tomography images. *IET Image Processing*, 13(3), 409–420.
- Phan, T. V., Seoud, L., Chakor, H., & Cheriet, F. (2016). Automatic screening and grading of age-related macular degeneration from texture analysis of fundus images. *Journal of Ophthalmology*, 2016, 1–15.
- Samagaio, G., de Moura, J., Novo, J., & Ortega, M. (2018). Automatic segmentation of diffuse retinal thickening edemas using Optical Coherence Tomography images. *Procedia Computer Science*, 126, 472–481.
- Li, Z., Keel, S., Liu, C., He, Y., Meng, W., Scheetz, J., ... & He, M. (2021). Real-world performance of an AI-

- based diabetic retinopathy screening system in China: A multicenter study. *The Lancet Digital Health*, 3(10), e603–e611.
- Gulshan, V., Rajan, R. P., Widner, K., Wu, D., Wubbels, P., Rhodes, T., ... & Whalen, J. (2019). Performance of a deep learning algorithm vs manual grading for detecting diabetic retinopathy in the Veterans Affairs Eye Screening Program. *JAMA*, 322(16), 1669–1677.
- Kanagasingam, Y., Soyer, H. P., Williamson, T. H., & Kumar, D. K. (2022). Prospective evaluation of the THEIA<sup>TM</sup> automated diabetic retinopathy screening system in real-world settings. *npj Digital Medicine*, 5(1), 1–9.
- Plotnikov, S. A., Lipkovich, M., Semenov, D. M., and Fradkov, A. L. (2019). Artificial intelligence based neurofeedback. *Cybernetics and Physics*, 8(4), 287–291.