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An overview of artificial intelligence use in diabetic retinopathy treatment: a narrative review

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Abstract

Background: Artificial intelligence (AI), usually called machine intelligence, is a scientific field that allows robots thinking like people. The most common diseases that cause visual impairment and blindness, such as age-related macular degeneration (ARMD), cataract, glaucoma, and diabetic retinopathy (DR), have recently been subject to deep learning-based on AI screening and prediction models.

Aim: to discuss the core ideas of AI and its apply to DR, as well as to evaluate the currently faced issues and the future of ophthalmology.

Methods: In this review, English studies from common databases such as Pubmed/MEDLINE, Google Scholar, Web of Science, Scopus, and the Cochrane Library with the keywords "Machine Learning," "Artificial Intelligence," "Deep Learning," combined with keywords, involving "diabetic retinopathy" were involved. The end date for this review is April 2022.

Scientific novelty: This paper illustrates the core AI concepts and their application in diabetic retinopathy. The current ophthalmology issues and future opportunities, offering undiscovered knowledge in this field are also analysed. It will raise community knowledge of employing AI and reveal new capabilities in the analysis of ocular disorders to present the fundamental idea of AI regarding its therapeutic applications.

Conclusion: Medical professionals can make quick and precise decisions using AI technologies in orded to analyse massive volumes of data, such as physiological imaging and clinical presentations. It is believed that over time, AI systems will become more precise and successful at predicting the onset and course of DR.

Keywords: diabetic retinopathy, artificial intelligence, diabetes Mellitus, machine learning.

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Introduction

A large field of computer science called artificial intelligence (AI) explores theories, techniques, tools, and software to replicate, enhance, and grow machine intelligence [1]. Machine learning (ML) [2] is an AI branch that creates intelligent systems using statistical methods. Without being specifically designed, the intelligent system can automatically learn and improve its performance, such as precision, using either an unsupervised or supervised approach. Deep learning (DL) [3], a method for ML that takes advantage of cutting-edge approaches, has been very successful in computer vision and NLP tasks. Thus, the input is associated with a diagnostic output. As a result of this extraordinary accomplishment, numerous researchers have used DL for healthcare-related and medical tasks and DL has lately developed into a potent tool for intelligent diagnosis, treatment, and screening of different diseases. Thyroid classification from ultrasound imaging, COVID-19 identification from chest X-rays, thyroid classification from computed tomography (CT) images, lung nodule staging, and detection from CT images have all been accomplished with the use of DL [4,5]. The foundation of evidence-based medicine is the development of relationships and patterns from the already-existing collection of data in order to produce clinical correlations and insights. In the past, one has relied on statistical techniques to identify these patterns and relationships. Using flowcharts and database approaches, computers can learn how to diagnose patients. The history-taking process, in which a doctor asks a series of questions and then combines the reported symptom complex to get a probable diagnosis, is translated using the flowchart-based technique.

By learning from examination images, AI assures the diagnostic of medical images at a radiologist's level, greatly enhancing clinical workflows. AI for medical image analysis is widely used to maximise productivity and improve doctors' treatment and diagnosis precision. The application of AI also significantly contributes to solving current logistical and financial problems. Four essential eye diseases that cause blindness have been treated using DL in the field of ophthalmology: diabetic retinopathy (DR), glaucoma, cataracts, and age-related macular degeneration (ARMD) [6–12]. Optic coherence tomography (OCT) and fundus photographs are the foundation for DL [13]. The potential for using AI for the auxiliary diagnosis of retinopathy of prematurity (14), refractive error (15), ocular cancers [16], choroidal disease [17], and retinal detachment [18] has been quite promising [19]. Current research focuses on image-based AI-assisted medical diagnosis and screening. Currently, the use of this technology in ophthalmology is primarily concentrated on conditions with a high incidence, such as DR, age-related macular degeneration (ARMD), age-related or congenital cataract, glaucoma, retinal vein occlusion (RVO), and retinopathy of prematurity (ROP).

In order to prevent treatment delays and visual loss, it is especially crucial to get an early diagnosis. Patients with prostate, lung, and other malignancies can benefit from the diagnostic and therapeutic approaches offered by the IBM Watson System, a question-and-answer platform. This system's development was effective because it incorporated lessons from empirically supported publications, medical articles, treatment regimens, experiment reports, and clinical data. All people with diabetes, regardless of the type, require routine annual retinal screenings for the prompt detection and appropriate management of DR. Traditionally, ophthalmologists accomplish fundus examinations to check for retinopathy, or trained eye technicians or optometrists use conventional fundus cameras (mydriatic or non-mydriatic) to take color fundus images. The main problem is the lack of retina specialists—ophthalmologists—to grade the retinal scans, as there are far fewer of them than people who need to be screened. AI is expanding into the public health field and will significantly impact all areas of primary care. Primary care providers will be better able to recognise patients who need extra attention and deliver individualised regimens for each individual with the aid of AI-enabled computer programs. Primary care doctors can use AI to take notes, evaluate patient conversations, and upload necessary data into EHR systems. These programs will gather and examine patient information and give primary care doctors knowledge of the patients' medical requirements. Ophthalmologists can expect new automated tools from the back to the front of the eye, thanks to AI that can help identify and cure ocular illnesses. Big players in the digital world, including Google and IBM, have recently shown a lot of interest in the use of AI in medicine. As a result, it is anticipated that research and development for identifying and managing diseases will increase. Compared to current methods of eye care, researchers in the field of AI ophthalmology consider that computerised analytics will lead to more effective and objective image interpretation methods.

Research focus

This paper illustrates the core AI concepts and their application in diabetic retinopathy. The current ophthalmology issues and future opportunities, offering undiscovered knowledge in this field were analysed. It will raise community knowledge of employing AI and reveal new capabilities in the analysis of ocular disorders to present the fundamental idea of AI regarding its therapeutic applications.

Research problem

Late detection and DR diagnosis will lead to many complications, up to the visual loss. Many challenges prevent the early DR diagnosis. AI utilisation for the management of DR is still under development and needs more research to help this development.

Research questions

1. What are the causes of DR?
2. What is the role of AI in the management of DR?
3. What are the challenges of utilising AI for DR?
4. How to develop AI in order to make it more effective in the management of DR?

Research aim

In this study, the core ideas of AI and its apply to DR are discussed, the currently faced issues and the future of ophthalmology are discussed.

Research Methodology

General background

Smart home technology and future wearables will be able to dynamically monitor personal health data, providing a plethora of information for medical diagnosis. Using this personal health data in modeling will make it possible to accurately and consistently predict the illness risk. AI provides the general public with comprehensive, full-cycle health services daily in a high-quality manner, and the artificial intelligence makes the proper recommendations for controlling blood glucose and blood pressure levels as well as serves as a monitor for various aspects of health and a medication reminder system.

Unprecedented chances to solve some of the most pressing issues in DR and other ocular illnesses are made possible by the recent advancements in AI algorithms. For example, after being trained with labeled fundus images, the Inceptionv3 system can attain diagnosis performance comparable to human experts. Although the community has published several evaluations on connected topics, the technical basis has sadly not received sufficient attention.

In this review, English studies from common databases such as Pubmed/MEDLINE, Google Scholar, Web of Science, Scopus, and the Cochrane Library with the keywords "Machine Learning," "Artificial Intelligence," "Deep Learning," combined with keywords, involving "diabetic retinopathy" were involved. The end date for this review is April 2022. The studies using each set of keyword combinations were then pooled to create an impartial collection of publications. Studies and/or articles that weren't subjected to peer review, as well as proposals, procedures, letters, and opinions, were eliminated. The references include publications that were chosen as they are related to our topic. In this paper, one concentrated on providing an overview of AI's use in DR. As a result, we try to choose appropriate AI methods for DR.

Research Results | Literature review

The result of the search using the chosen search strategy was 2825 articles. These papers were screened in order to choose the articles related to the topic. A full-text screening of 237 articles after excluding the remaining article by title and abstract screening was evaluated. Finally, 50 articles to gather information about our topic and write this review were used (Figure 1).

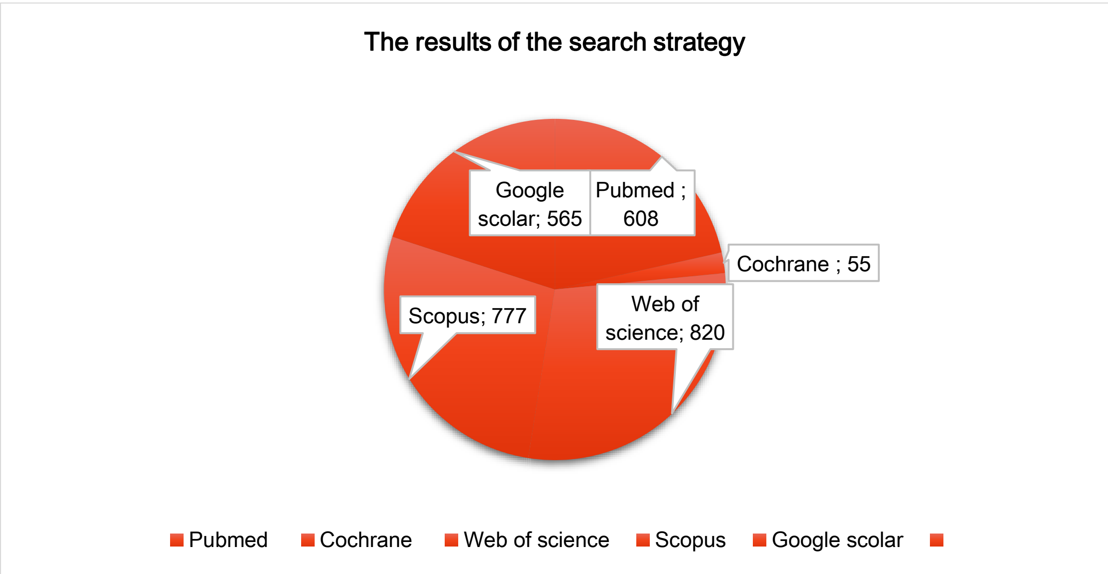

Figure 1. Research results

Artificial intelligence (AI), usually called machine intelligence, is a scientific field that allows robots to think like people. AI is a term used to describe a system that simulates human intelligence using computer programs. AI is quickly advancing in many interdisciplinary domains, including ophthalmology, healthcare, and diagnosing, managing, and preventing illnesses [20,21]. The most common diseases that cause visual impairment and blindness, such as age-related macular degeneration (ARMD), cataract, glaucoma, and diabetic retinopathy (DR), have recently been subject to deep learning-based AI screening and prediction models. Smart home technology and future wearable will dynamically monitor personal health data, providing a plethora of information for medical diagnosis [22,23]. Using this personal health data in modeling will make it possible to accurately and consistently predict the illness risk [24]. The used dataset should be split into validation, training, and test sets, with no overlap, while creating AI-based diagnostic systems for DR. The algorithm is trained using the training set. For parameter tuning and selection, the validation set is utilised. The testing set is used to assess the AI system's actual performance in clinical settings. The testing set must be separate from the validation and training sets and cannot be reused since otherwise it may cause errors when the algorithm is being evaluated for performance. Both the validation and training sets are used to create and optimise the algorithm. AI provides the general public with comprehensive, full-cycle health services on a daily basis in a high-quality manner, and intelligence makes the proper recommendations for controlling blood glucose and blood pressure levels as well as serving as a monitor for various aspects of health and a medication reminder system.

Diabetic retinopathy

The primary factor in working-age persons becoming blind in both developing and developed nations is diabetic retinopathy (DR), which is the most severe diabetes mellitus (DM) ocular complication. The International Diabetes Federation projects that there will be 600 million diabetics worldwide by 2040, of whom 30% will eventually suffer kidney illness associated with diabetes. Based on a meta-analysis of 35 cohort articles involving 22,869 patients, the DR prevalence worldwide is 34.6%, and vision-threatening DR accounts for 10.2% of instances of blindness globally or 51% of all occurrences of blindness [19]. One of the main neurovascular consequences of diabetes is diabetic retinopathy, which is also the main factor in adulthood-related blindness. The main pathogenic factor in DR is regarded to be chronic hyperglycemia. The polyol pathway and other alternative glucose metabolism routes are activated by hyperglycemia. Advanced glycation end products are produced as a result of oxidative stress, non-enzymatic protein glycation (AGEs), and protein kinase C activation. The activation of cytokines, growth factors, and vascular endothelial dysfunction that results from these alternate pathways finally causes an increase in microvascular occlusion and vascular permeability. Microvascular blockage causes retinal ischemia, which results in the development of neovascularisation and IRMA (intraretinal microvascular abnormalities). The timely prevention and treatment of vision loss depend on routine DR screening [25]. For both endocrinologists and ophthalmologists, time and cost restrictions are significant problems. The insufficient number of registered ophthalmologists, especially retinal specialists, has a considerable negative impact on the efficacy of fundus photograph-based screening. The most typical fundus features of DR include microaneurysms, hemorrhages, exudates, and neovascularization. DR is the most prevalent retinal vascular illness. These lesions should be manually tagged on fundus pictures for automatic disease screening before establishing a tentative diagnosis using ML Figure 2 [26, 27].

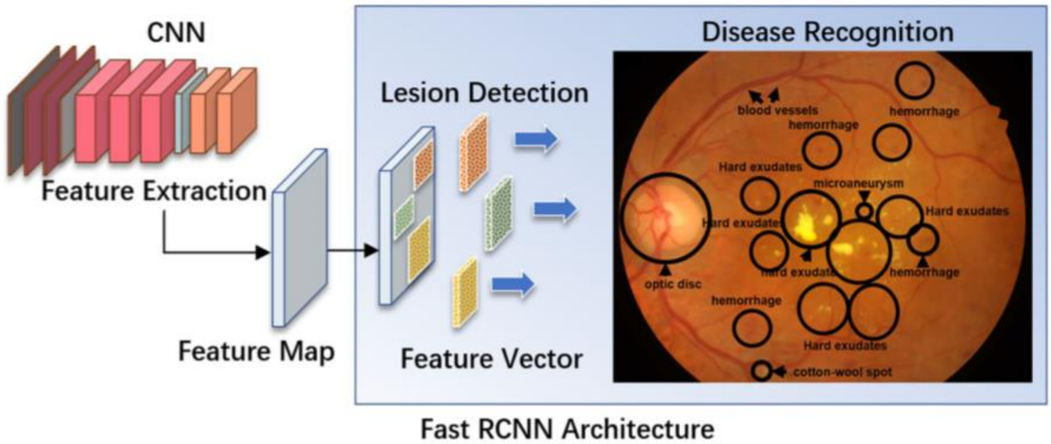

Figure 1 **A diagram demonstrating a fast R-CNN algorithm for automatic lesion detection and disease detection from fundus images (28)**

Artificial intelligence and diabetic retinopathy

ML detects quicker and more accurately DR than humans [29]. Deep neural networks also provide better DR screening utilising retinal image prediction capabilities [30,31]. Patients in endocrinology outpatient clinics can use and accept the AI-based DR screening tool [32]. Enough training datasets are crucial for DL models to function well. However, getting enough data in the actual world is difficult due to convoluted data-collecting processes and ethical limitations. Researchers have used migration learning to create a neural network with minimal data and incorporated features from conventional approaches to get over this restriction. In categorising diabetic macular edema (DME) and ARMD, this technique performs as well as human specialists [33,34].

Diabetic choroidal vasculopathy (DCV) has recently gained popularity as a study topic. Patients with DR may receive information regarding their risk of developing DR through early DCV detection. Due to the weak contrast, variable intensity, irregular texture, and unclear borders between the choroid and sclera in the OCT images, automatic segmentation of the choroidal layer are still difficult. Regions of interest are still segmented either semi-automatically or manually in current methodologies. Researchers proposed DL segmentation of the choroidal layer and morphological segmentation of Bruch's membrane (BM) in OCT images [26,27]. Additionally, a segmentation technique was created to divide the retinal layers based on the prior shape and adaptive appearance information [35].

With various potential future directions, AI has huge potential for DR diagnosis and screening. More AI systems based on portable devices like smartphones will be developed, allowing patients to complete DR screening on their own devices at home without the assistance of medical staff. This greatly reduces the need for trained medical staff and medical equipment and increases the accessibility of DR screening. Such telemedicine is becoming increasingly important during the coronavirus disease pandemic of 2019 (COVID-19) and would benefit patients and medical professionals in many ways. Presently, classical fundus imaging is the foundation of the majority of AI-assisted DR screening methods. As innovative examination procedures are developed, AI-based systems may be able to do more types of assessments, such as multispectral fundus imaging and OCT. The accuracy may also be increased by combining several examinations. This technology will play a crucial role in diagnosing DR in addition to the current AI-assisted screening tools. In recent studies, AI-based systems outperform ophthalmologists in sensitivity and have the potential to outperform ophthalmologists in accuracy. As a result, the AI-assisted diagnosis tools can help ophthalmologists diagnose patients more effectively and accurately.

The diagnostic performance of middle- and late-stage PDR and non-proliferative DR (NPDR) has recently improved thanks to the rapid development of DL methods for detecting DR significantly [8,9,27,36]. Researchers have also looked into how to grade and predict DR based on the presence of lesions. DR is classified as moderate, PDR, severe NPDR, or/and macular edema (ME) by the International Clinical Classification of Referable DR (rDR). According to Abràmoff et al., VGG and AlexNet each achieved 98% area under the curve (AUC), 96.8% sensitivity, and 87% specificity [6]. This AI system's sensitivity, specificity, and imageability were each 87.2%, 90.7%, and 96.1% [36]. Gulshan et al. identified the referable DR using CNN and achieved 93.4% specificity, 97.05% sensitivity, and 99.1% AUC. They also classified the referable DR as referable DME, moderate or worse DR, or both [8,9].

Researchers from Aalto University discovered that DL could precisely distinguish macular edema and DR in a different investigation by training a model based on Inception-v3 [37]. By combining a multiple-improvement depth to refine the Inception-v4 algorithm, Feng Li et al. could detect DMO and DR with an AUC, specificity, and sensitivity of 99.2%, 96.1%, and 92.5%, respectively [38]. For DR categorisation, Inception-v3, Xception, recognising deep residual learning (ResNet) 50, and InceptionresNet50 all achieved accuracy levels of 89–95% with corresponding specificities, AUCs, and sensitivity 93–97%, 95–98%, and 74–86%, respectively. Reguant et al. evaluated image features and illustrated the neural network decision process [39]. Based on optical coherence tomography angiography (OCTA) pictures, Ryu et al. suggested a convolutional neural network (CNN) model for DR diagnosis that has 91-98% accuracy, 91.9-97.6% AUC, 94-99% specificity, and 86-97% sensitivity [40].

Discussion

The deep neural network-based artificial intelligence (AI) a system developed by researchers at Shanghai Jiao Tong University has significantly increased the accuracy of the automatic identification of early STDR and DR, especially proliferative DME and DR [41]. The captured fundus images can be sent to a server for diagnostic analysis, such as the localisation of the optic disc and macular, the segmentation of the vascular network, the identification of lesions, and the classification of lesions. When this system's diagnostic outcomes were compared to those of ophthalmologists, it had an 85% accuracy rate [12]. The researchers also suggested a kernel least squares classifier-based technique for detecting the optic disc and macular area. The field of deep learning DR diagnostic software is currently undergoing rapid development. The ideas underlying automatic DR screening have changed over the past ten years, going from a few expert-designed algorithms with various degrees of accuracy to a wide variety of methods utilising the most recent advancements in deep learning and other areas. As studies have become more thorough, they have demonstrated the accuracy and dependability of diagnostic or decision-support algorithms. Some studies used millions of images, while others rigorously set their gold standard. Many software systems have received approval from regulatory agencies during the past two years and are almost ready to be incorporated into widespread screening in the different nations. Following the overall global trend, mobile solutions are receiving more attention, which may make them a better fit for areas with limited resources.

This approach establishes an accurate mapping from the image to the region by using numerous images of the macular and optic discs that have already been tagged. Using a kernel least-squares classifier to determine the optic disc area, the researchers developed a method to identify the optic disc region and pinpoint its location for retinal color pictures [42].

The approach then uses multimodal data to locate the vascular aggregation and pinpoint the optic disc's center more precisely. This method detected 332 out of 340 test images concerning optic disc localization, yielding a detection success percentage of 97.65%. On 112 out of the 340 test photos, the approach correctly located the borders of the optic disc, yielding a detection of 94.54% success rate for the optic disc boundary and 97.06% for the macular region [43,44].

Additionally, to diagnose related illnesses, it is crucial to locate and inspect blood vessels in fundus images [45]. Researchers have suggested a method for automatically extracting blood vessels from fundus images. It provides an orientation-aware detector based on direction-aware detectors capable of successfully extracting blood vessels from fundus images. This technique teaches the detector the orientation and distribution characteristics of blood vessels using the Fourier transform's energy distribution [46]. On the global public dataset DRIVE and the STARE dataset, the algorithm attained an accuracy of 80.82% and 68.94%, respectively, as measured by the reliable connectivity, length (CAL), and area provided by Gegndez-Arias. According to experimental findings, the suggested method outperforms the already-used segmentation techniques and has high accuracy and robustness [47]. To overcome the localisation difficulty, researchers created a CNN-WSSH model by fusing a weakly supervised localisation technique with automatic DR category identification. In addition, they incorporated a weakly supervised sensitive heat map (WSSH) into the CNN [48]. Small retinal arteries in DR exhibit morphological changes such as early pericyte loss, basement membrane thickening, increased vascular permeability, loss of endothelial cells, leukostasis, platelet aggregation, and capillary dropout. The major glial cells of the retina, the Müller cells, are also impacted by diabetic retinopathy in addition to the microvessels. The maintenance of the retina's structural integrity, control over the retinal blood flow and blood-retinal barrier, retinoic acid compounds, uptake and recycling of various neurotransmitters, and ions (such as potassium), control over metabolism, and provision of nutrients to the retina are all responsibilities of Müller cells.

DL methods enable routine screening, especially in rural areas, which allows the earlier detection of common chronic illnesses [49]. Self-filming fundus imaging (SFI) allows patients to take fundus images similar to those of skilled professionals [50]. The researchers came to the conclusion that DL models are helpful in predicting disease development in a longitudinal population through a prospective investigation of fundus photos captured with mobile phones and chronic kidney disease and type 2 diabetes [51]. Modern machine learning (ML) techniques like deep learning have demonstrated promising diagnostic results in the areas of speech recognition, picture recognition, and natural language processing. It has been broadly accepted in various fields, such as social media, telephones, cybersecurity, and health. DL continues the long tradition of autonomous and helped analyse retinal images, which has appeared in ophthalmology since the 1990s and before. Medical imaging analysis, in general, has achieved robust results in various medical specialties such as dermatology and radiology.

Although the use of AI technology in the healthcare profession, especially in ophthalmology, is growing, numerous issues still need to be handled before they can be effectively integrated into clinical practice. OCT is a crucial part of ophthalmology care and is crucial for diagnosing, grading, and evaluating treatment outcomes in DR. The success of the model is directly determined by the labels and data quality because the usage of AI technology is based on a substantial amount of treatment data. The following issues with data quality are possible:

1. Poor quality of the data itself includes blurry images and other artifacts
2. Poor quality of the data labels, including inaccurate labels.
3. Only a tiny percentage of the data has been labeled, indicating inadequate data.

The development of DL, which carried the robustness findings on diagnostic accuracy from in silico evaluation to offline validation on multiple datasets from different populations, led to the breakthrough in AI for DR screening on color retinal images. Even though many prospective validation studies were conducted in the evaluation's latter stages to support the diagnostic accuracy, the overall results were still appropriate for use in clinical settings. Several practical concerns must be considered seriously in deciding to use AI for screening in the real world. These concerns are at least as significant as diagnostic accuracy. They include mydriasis, integration with existing camera systems, integration into electronic health record systems, and patient and provider acceptability. To promote fairness, transparency, trustworthiness, and responsibility for all stakeholders, including policymakers, healthcare providers, AI developers, and patients, AI for DR screening should adhere to the governance of AI in healthcare.

Conclusion

1. Medical professionals can make quick and precise decisions using AI technologies to analyse massive volumes of data, such as physiological imaging and clinical presentations.

2. The desire to increase the effectiveness and efficiency of health care continues to inspire a wide range of innovations, including AI.

3. Computer-assisted diagnosis will aid in detecting early lesions and improving patients' prognoses. Although much work remains to be done, the use of AI in DR has a promising future due to a lack of common databases, standardised guidelines created by various institutes, and relevant national policies and regulations. More precise and sensitive algorithms or machines are required to reach the goal of individual treatment.

4. One believes that over time, AI systems will become more precise and successful at predicting the onset and course of DR.

5. All people with diabetes, regardless of the type, require routine annual retinal screenings for the prompt

detection and appropriate management of DR.

6. AI mimics medical professionals' diagnostic and thinking abilities by absorbing their knowledge and medical information to quickly and accurately diagnose patients and provide individualised treatment plans utilising medical imaging and other pertinent data.

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