Review Article

A Review of the Management of Eye Diseases Using Artificial Intelligence, Machine Learning, and Deep Learning in Conjunction with Recent Research on Eye Health Problems

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Abstract

In the field of computer science, Artificial Intelligence can be considered one of the branches that study the development of algorithms that mimic certain aspects of human intelligence. Over the past few years, there has been a rapid advancement in the technology of computer-aided diagnosis (CAD). This in turn has led to an increase in the use of deep learning methods in a variety of applications. For us to be able to understand how AI can be used in order to recognize eye diseases, it is crucial that we have a deep understanding of how AI works in its core concepts. This paper aims to describe the most recent and applicable uses of artificial intelligence in the various fields of ophthalmology disease.
Keywords: Artificial Intelligence; Machine Learning; Deep Learning; Eye Diseases; Glaucoma; Age-related Macular Degeneration.

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Introduction

Eye problems will become more prevalent as the population ages. Maintaining eyesight and improving quality of life requires early detection and proper treatment of eye diseases. In ophthalmology, artificial intelligence (AI) may be useful for achieving this goal. AI is a branch of computer science where algorithms are created using computers in order to replicate human intelligence [1]. This field has made significant progress since 1956 [2], and is now called it has been referred to as the fourth industrial revolution in human history [3].

Deep learning (DL) is sometimes used interchangeably with artificial intelligence (AI) and machine learning (ML). It is necessary to separate the three terms [4] (figure 1).

A computer that mimics human intelligence by performing visual perception, decision-making, and speech recognition tasks is called an artificial intelligence system [5]. Since the 1980s, artificial intelligence has advanced in several ways, particularly in the area of machine learning, where computers are able to become more proficient at completing tasks through practice or It is not necessary to program them explicitly; they learn on their own [6]. There are a number of algorithms within machine learning that use multilayered neural networks [7,8]. In deep learning, neural networks have several hidden deep layers [9], which enable them to explore more complex inputs, such as whole images, by analyzing them at multiple levels [10] (figure 2).

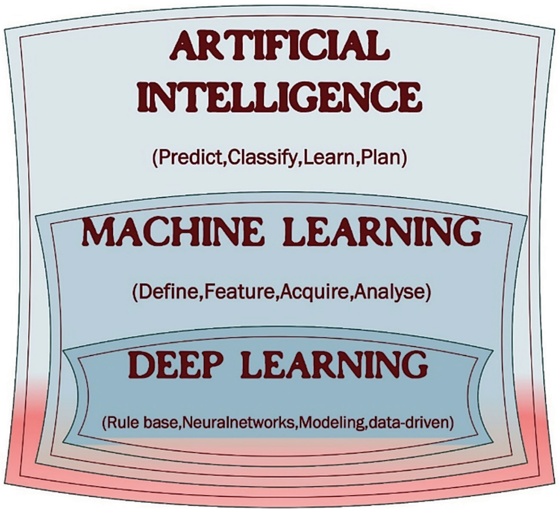

Figure 1: A detailed explanation of artificial intelligence (AI) and related topics

Artificial intelligence (AI) has been applied to many areas of clinical workflow in recent years, including detecting lung cancer [11], detecting skin cancer [12], predicting cardiovascular risks [13], and analyzing breast histopathology specimens [14]. This has led to various research studies investigating how artificial intelligence can be used in ophthalmology, resulting in the creation of cutting-edge algorithms and extensive datasets such as EyePACS, Messidor [15], and Kaggle [16], which are all publicly accessible [17].

Many eye disorders like as diabetic retinopathy (DR), and retinopathy of prematurity, including glaucoma, and age-related macular degeneration (AMD) are being screened and diagnosed using deep learning [18]. In this paper, the authors aim to describe the most recent and applicable uses of artificial intelligence in the various diagnosis fields of ophthalmic disease. Materials and Methods

Independently searched the literature were the two databases used; PubMed and Scopus [19]. The words searched were Ophthalmology, Age-Related Macular Degeneration, Pediatric Ophthalmology, Glaucoma, Cataract, Diabetic Retinopathy, Retinopathy of Prem, Retinal Detachment, Keratoconus, Retinal Vein Occlusion, Retinal Vein Occlusion, and Artificial Intelligence. Keyword searches were not restricted. Based on the evaluation of search results, chose papers with the most clinical impact [20].

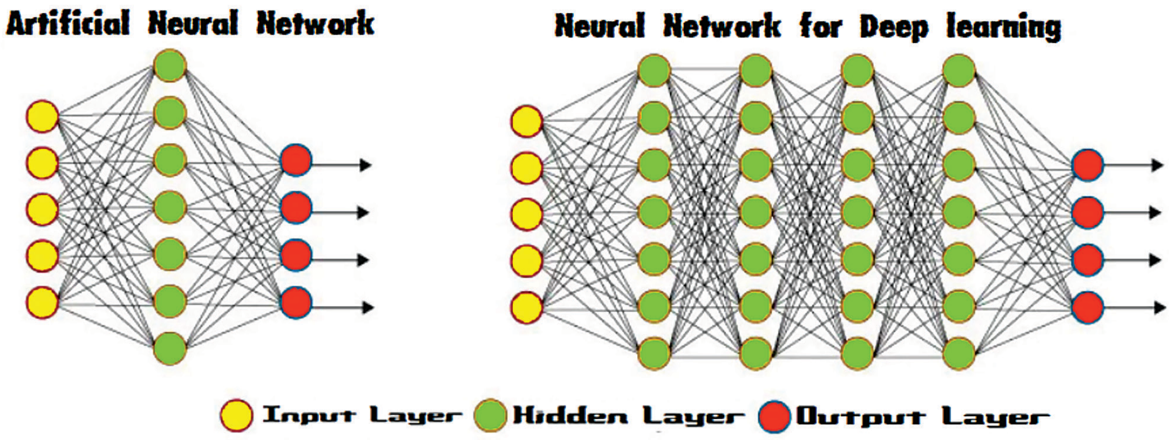

Figure 2: A neural network model of artificial intelligence processes the signals of the system by routing them through a system of nodes that resemble the neurons found in the brain. Signals are sent from one node to another via links, analogous to the synaptic connections between neurons. Depending on the settings, a different weight can be assigned to each connection that amplifies or dampens the signals so that the "learning" enhances the result. As with the various cortical processing units, the nodes are generally arranged in layers that are roughly comparable in structure. Today's computers can handle complex "deep-learning" networks composed of several layers of connections

It was essential to consider several factors in different studies: location, the time of year, the study's design, the length of follow-up, the number of eyes recruited, demographics (age, gender, and ethnicity), any type of imaging, general diagnosis of the disease, and even the level of accuracy, specificity, and sensitivity [21]. This study considered several criteria: a transparent methodology for developing algorithms (DL or ML), a large amount of imagery or data to train, and predicting and detecting diseases with high accuracy and specificity.

Study selection

In total, 37 studies were reviewed. One dealt with exophthalmos, three with strabismus, two with eyelid tumors, three with keratoconus, seven with cataracts, three with keratoconus, seven with cataracts pediatric cataracts, and one with myopia, glaucoma, and DR, each one of nine studies. Glaucoma

There is minimal agreement among professionals about identifying ONH injuries based on a study of optic nerve head (ONH) injuries. Asymptomatic glaucoma makes it difficult for doctors to diagnose and treat it in its early stages [22]. A glaucomatous ONH might be hard to detect early due to its different structure from an optic disc. Visual field test results and clinical trials related to glaucoma discs can be interpreted using artificial intelligence [23,24].

Fundus photos and OCT scans show the visual pathway, but a visual field shows how it works. Current algorithms cannot distinguish between mild regional loss, glaucoma-related abnormalities and aberrations, and non-glaucoma-related abnormalities and aberrations, despite evaluating the visual field [23]. Furthermore, the present automated programs do not break down the visual field data into loss patterns. RNFs that are impaired project to specific areas of the optic disc, causing patterns of loss of visual field. Elze et al [25]. identified geographic patterns of loss using archetypal analysis, a method known as corner learning.

In addition to stratifying the visual fields geographically, an archetypal analysis is used to determine what factors contribute to each pattern loss. Additionally, AI algorithms may help physicians to better understand how the visual field evolves [26]. Finally, some AI-based glaucoma prediction models have been developed using Kalman filtering to forecast glaucoma development. By using multiple data sources, physicians can make medical decisions based on tailored illness predictions [27, 28].

Eyelid Tumors

A method was developed by Wang et al [29]. that can detect eyelid cancers utilizing Philips intelligible pathology slides that show small patches of malignant or benign melanoma. ImageNet2014 parameters were used to compose a DL (VGG16). A comparison between 18 and 55 histopathology slides from 24 patients showed malignant melanoma patches and non-malignant melanoma patches, respectively. In total, 141,104 patches from 79 slides were assessed for validation, of which 61,031 were benign, and 81,073 were malignant. 0.989 was a very good AUC for the algorithm in this case. An assessment of surgical difficulty preoperatively, surgery delay, and tumor size indicated surgical problems. Tan et al. [24] developed a model predicting reconstructive surgery will be challenging when periocular basal cell carcinomas are removed. Strabismus

Lu et al. [30] used convolutional neural networks (CNNs) and photographs of the face to identify aberrant eye positions. This technology could ease telemedical screening and assessment [31]. CNNs are useful for in-office assessments that use eye tracking [32, 21] or retinal birefringence scans [33].

Keratoconus

To diagnose keratoconus, AS-OCT, Placido disc-based imaging, three-dimensional tomography, and AS-OCT are required. Placido disc corneal topography is also an important diagnostic method. Based on 3,156 AS-OCT pictures of keratoconus grades 0 to 4, Yousefi et al. A machine learning algorithm was developed on top of this foundation for grading keratoconus. This resulted in 97.7 % sensitivity and 94.1 % specificity [34 , 35]. Kamiya et al. 304 keratoconus AS-OCT pictures were used, ranging from grade 0 to grade 4, the researchers reported 98.4 % specificity and 99.1 % sensitivity for the classification of keratoconus(36). Last but not least, a CNN based on 150 validation eyes, 1,350 features of healthy eyes, and 1,350 topographies of keratoconus eyes, demonstrated 99.3 % accuracy [37].

Exophthalmos

Thyroid-induced ophthalmopathy can cause exophthalmos (TAO), or ocular exophthalmos. Salvi et al. [38] developed a model to categorize diseases and predict their progression. TAO was found to be improving or active in 152 patients, and absent, mild, or inactive in 246 patients. This study collected 13 clinical ocular indicators. In terms of concordance with the clinical evaluation, their neural network has a 67 % correlation with that [39].

Cataract

Using artificial intelligence (AI) in cataract care encompasses both clinical and surgical aspects, such as cataract diagnosis and biometric optimization for intraocular lens power (IOL). Cortical, subcapsular, and nuclear sclerotic cataracts are included in the clinical categorization of cataracts. A slit lamp microscope or a light source can be used to diagnose these conditions. The Lens Opacities Classification System III is used to grade cataracts [40, 41]. Study by Li et al. Using 2009-published artificial intelligence applications, nuclear cataracts are evaluated. Their method achieved a 95 % success rate [42]. Xu et al. In 2013, a mean absolute error was examined for an automated nuclear cataract grading method based on group sparsity regression using slit lamp lens images. This error was 0.333 [43]. Using 5380 slit lamp images from 2015, Gao et al. [44] graded nuclear cataracts with 70.7 % accuracy. Meanwhile, Wu et al. [45], from China, have developed a three-step sequential AI method to detect cataracts using residual neural networks (ResNets). [37, 638] slit lamp images were analyzed in order to train the algorithm to distinguish between cataracts (AUC > 0.99) and intraocular lenses (AUC > 0.91).

There have been other studies that used color fundus pictures to develop an automated cataract assessment system for the effects of retinal imaging on cataracts. The artificial intelligence method was developed using deep learning and machine learning by Dong et al. [46] Fundus pictures need to be categorized according to the severity of the cataract (normal, mild, moderate, severe) to report four grades. 94.07 percent was achieved due to precision. According to Zhang et al. Cataract categorization method had a 93.52 % accuracy rate [47]. A 2018 publication by Li et al. reported accuracy ratings of 87.7 % and 97.2 for grading tasks. A deep convolutional neural network (DCNN) was used to produce two-dimensional feature datasets for a six-level classification system for cataracts [48]. The ability of Xu et al. [49,50] to diagnose and grade cataracts was 86.2 % accurate using 8,030 fundus images, AlexNet and VisualDN algorithms. When tested in 2019, Pratap and Kokil's CNN was able to categorize cataracts autonomously with 92.91 % accuracy [46]. Zhang et al. [51] demonstrated that 1,352 fundus pictures improved the diagnosis and grading of cataracts.

Pediatric Cataract

The development of pediatric cataracts is more varied than that of adult cataracts. Additionally, slit lamp examinations and cataract visualization may be challenging due to the child's cooperation. The cloud-based CC-Cruiser system automatically recognizes cataracts from slit lamp images, assesses them, and suggests appropriate treatment options [52,53]. This method may be advantageous for patients since it allows them to see a physician more quickly. When it comes to diagnosing cataracts and prescribing treatment, it does not perform as well as specialists.

High Myopia

Low doses of atropine may delay or prevent the development of high-risk myopia in children [54]; however, it is difficult to determine which children should receive this treatment [55]. Lin et al. [56] used a clinical measure to predict high-grade myopia in children for up to 8 years in the future. Some have suggested that this strategy could be used to prevent disease more effectively.

Diabetic Retinopathy

For Diabetic Retinopathy patients with microaneurysms, hemorrhages, hard exudates, and cotton wool patches, deep learning algorithms have been utilized to make the diagnosis. Recent studies have demonstrated that DL algorithms can detect DR more accurately than manual detection by ophthalmologists [57]. It is still necessary to conduct further research in order to support this claim [58].

A quality dataset is essential for AI training to be accurate. A study by Gulshan et al. [15] compared photographs from 5,997 patients with images from 1,748 individuals in the MESSIDOR-2 dataset to identify DR from fundus photographs. Based on these two datasets, this two-dataset method effectively determines DR from fundus photographs. One of the first studies to report automated identification of DR was published by Abramoff et al. in 2008 [59]. Using retrospective analysis, non-mydriatic pictures were identified as referable DR 84 % of the time. According to a study conducted in 2013 [60], the Iowa Detection Program scored 96.8 % sensitivity and 59.4 % specificity. When operated with the MESSIDOR-2 dataset, EyeArt AI's program detected DR in a study carried out in 2015 with 93.3 % sensitivity and 72.2 % specificity [61]. Using retinal pictures taken from EyePACS and MESSIDOR-2, which had been trained on 128,175 retinal images, Gulshan et al. developed a method for simulating the macula in 2016. There was 97.5 and 96.1 % sensitivity and 93.4 and 93.3 % specificity across the two experiments [15]. According to Gargeya and Leng's [62] study, EyePACS was found to have 94 % sensitivity and 98 % specificity for the detection of referable DR in mild, non-proliferative patients.

Retinopathy of Prematurity

Artificial intelligence has made significant advances in pediatric ROP. In addition to improving the efficiency and objectivity of the screening process, AI applications may also reduce the stress experienced by newborns undergoing the examination [63]. Through the development of tools such as Vessel Finder [64], Vessel Map [65], ROP tool [66], Computer-Assisted Image Analysis of the Retina (CAIAR), and Retinal Image Multiscale Analysis (RISA), it has been extensively studied how fundus images can be used to estimate vessel tortuosity and width. [67-72]

Age-Related Macular Degeneration

The visual field has been used in several studies to diagnose AMD. Among the main topics of Burlina et al's study was automating the grading of AMD. On the basis of color fundus photographs, their findings showed an accuracy of 0.94-0.96 in categorizing absence/early AMD from intermediate/advanced AMD. For the detection and classification of spatial atrophy, Treder et al. [73] used autofluorescence fundus images to train a DCNN classifier. They achieved a 91–96 % accuracy rate. An undefined deep CNN was found to be 100 % sensitive, 97.31 % specific, and 99.76 % accurate in distinguishing between images of wet AMD and normal AMD [74]. Two hundred and fifty-seven fundus photographs were used for training and one hundred and eleven for validation. DL algorithm developed by Keel et al. [75], for the diagnosis of neovascular AMD using color fundus pictures showed 96.7 % sensitivity, 96.4 % specificity, and 99.5 % accuracy. Ting et al. [76] demonstrated that their algorithm had an AUC of 0.931, a sensitivity of 93.2 %, and a specificity of 88.4 %.

Teleophthalmology and Screening

In telemedicine, medical information improves a patient's health status through electronic connections from one location to another [77, 78]. Healthcare services can be expanded, wait times reduced, and acute conditions treated more effectively using telemedicine in rural areas with a shortage of medical personnel. This hub and spoke model consist of an optometrist, a pharmacist, a pediatrician, a general practitioner, an ophthalmologist, a health worker, screening facilities, and a hospital. Eye University Clinics act as spokes of the wheel in addition to national and international glaucoma institutions. The figure 3 shows how to treat glaucoma with telemedicine [79]. The model enhances the availability of clinical services to rural areas by facilitating interaction between patients and experts in referral centers (sometimes referred to as hubs) and the spread of clinical services (sometimes referred to as spokes) [80].

With telemedicine and artificial intelligence, physicians can remotely visit their patients and receive their health data which is automatically collected and screened in situations such as this. The use of remote triaging before admission to hospitals can reduce the risk of infection in healthcare settings, particularly during the pandemic of Coronavirus illness 2019 (COVID-19) [81]. Many clinics have followed his method of therapy for a very long time. Numerous methods [82] have been used to demonstrate how DL algorithms can help with visual impairment screening, including retinal fundus images acquired by them et al. By putting this technique into practice, eye care facilities that treat eye diseases might be referred to more quickly. The use of artificial intelligence to monitor metrics such as visual acuity and intraocular pressure at home might improve the effectiveness of conventional clinic visits [83,84]. In the near future, teleophthalmology from home will probably become a reality with the advent of these gadgets, although more research will be necessary.

A summary of the results of the studies and

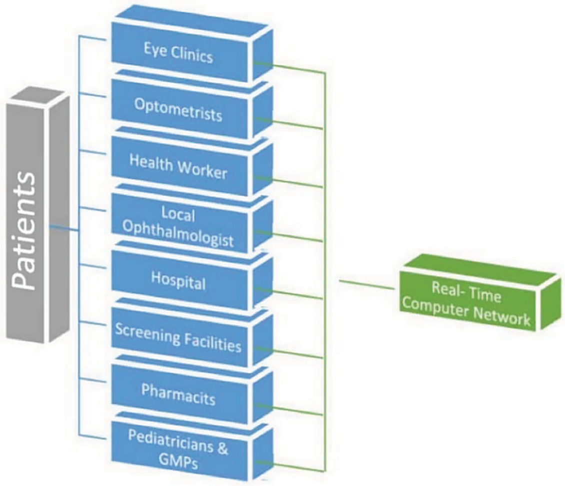

Figure 3: Glaucoma is modeled as a hub and spoke system

reviews included in this article is presented in table 1.

Discussion

In this review, we have discussed some of the most relevant advancements and future directions in artificial intelligence in ophthalmology, as well as the primary applications of AI in the field.

A few other evaluations of artificial intelligence in ophthalmology have been published [85], however, they focus on conditions like DR and AMD [73, 86, 87]. We aimed to provide physicians with a concise summary of AI evidence for use in ophthalmology, regardless of the degree of detail of these publications.

The DL algorithms are highly accurate, sensitive, and specific for DR, AMD, and glaucoma, which are three of the most prevalent visual disorders. Some of these algorithms also performed well for common disorders. Numerous AI initiatives have also been concentrated on pediatric ophthalmology in order to help doctors get over the usual practical constraints brought on by children's resistance to receiving treatment. In spite of the hopefulness with which this new technology

Table 1: Here is a brief summary of the research on AI and glaucoma, diabetic retinopathy, and age-related macular degeneration (AMD) that has been conducted. Not Specified (ns), *Drusen, **Normal, ***DME,****CNV

Imaging	No. of Pics	Specificity	AUC	Accuracy	Sensitivity	Disease term
Fundus images	48116	0.920	0.988		0.956	CRD, 0.7+
Fundus images	125189	0.872	0.942		0.964	CRD, 0.8+
Fundus images	1399	0.802	0.872		0.813	Glaucoma
Fundus images	3620	Not Specified	0.965		Not Specified	Glaucoma
Fundus images and OCT scans	9282	Not Specified	0.933		Not Specified	Glaucomatous visual loss
Fundus images and OCT scans	32820	Not Specified	0.944		Not Specified	Glaucomatous visual loss
OCT	2132	0.939	0.937		825	Early glaucoma
Fundus images	315	1.0	ns	95.71 %	0.7692	Grade of DR
Fundus images	755	0.722	0.933	ns	0.933	Detection of DR
Fundus images	1748	0.594	0.937	ns	0.968	Detection of DR
Fundus images	9936	ns	ns	64 %-82 %	ns	Grade of DR
Fundus images	76370	0.916	0.939	ns	0.905	Detection of DR
Fundus images	76885	0.98	0.94-0.97	ns	0.94	Evaluation of DR
Fundus images	136886	0.934 & 0.939	0.991	ns	0.975 & 0.961	Evaluation of DR
Smartphone-base fundus image	2048	0.668	ns	ns	0.958	Detection of DR
Fundus Images	253	0.9731	0.9976	ns	1	AMD (Normal vs Wet)
OCT images	317	ns	0.7-0.8	ns	ns	Treatment with anti-VEGF
Autofluorescence	600	0.92	ns	91 %-96 %	1	Classification of region atrophy
OCT Images	*8617	974	ns	ns	0.978	Differentiate DME & AMD
	**51140					Differentiate DME & AMD
	***11349					Differentiate DME & AMD
	****37206					Differentiate DME & AMD
Fundus images	27397	0.964	0.995	ns	0.967	Neovascular AMD
Fundus Images	35948	0.884	0.931	ns	0.932	Detection AMD
Color fundus Images	More than 130000	0.941	0.94-0.96	ns	0.884	Grading AMD
OCT images	153912	0.962	0.968	ns	0.901	Treatment with anti-VEGF

has been adopted, its adoption is not without difficulties or even controversy.

First of all, it is difficult to describe DL algorithms within the context of ophthalmology. There is a phenomenon known as the "black box phenomenon," which may ultimately make physicians less inclined to embrace this new technology [88,89]. There is something called a "black box," which is a term used to describe the lack of understanding of the algorithm's decision-making process that results in a particular result. Several techniques have been employed to restrict this phenomenon, such as the "occlusion test, in which a blank area is systematically moved throughout the entire image, and the area with the greatest drop in predictive probability is considered to be the area with the highest probability for the algorithm to operate" [90], or "saliency maps (heat maps) generation techniques, such as activation mapping, which, again, highlight areas that are relevant to classification decisions within an image" [91]. The visualization technique, despite its advancements, revealed non-traditional diagnostic interest areas in certain cases [92], and it is unclear as to whether or not the saliency analysis of the attributes of these regions should be factored into the analysis [93].

Secondly, there is a problem with external validation of algorithms. While many DL algorithms have been developed using publicly accessible datasets, the performance of some of these algorithms in "real-world" clinical practice environments has been questioned, despite the fact that many algorithms have been developed based on public datasets [94]. Because of the variations in several factors affecting the performance of these algorithms in clinical settings, including the quality of the imaging of the patient, the illumination, and the various methods of dilation, these algorithms may perform worse in clinical settings.

Another topic of debate in the field of algorithm training is the existence of bias in the datasets used to train the algorithms. As well, bias in the training data used to build AI systems may contribute to a strengthening of the biases already present, while reducing the external applicability [93]. In order to identify possible biases and prevent undesirable results, it is necessary to rebalance the training dataset if a given minority is underrepresented. In addition, it is required to collect a training dataset with varied patient groups in order to identify possible biases. Among a number of ethnic groups, the training dataset used by Ting et al. [76], who confirmed their algorithm for detecting diabetic retinopathy in a variety of ethnic groups, provides a good example of a training dataset that can be utilized in a variety of situations.

It is also important to consider the legal implications of applying Deep Learning (DL) algorithms to clinical practice [95]. There is a question that needs to be answered as to who will suffer the legal repercussions of an adverse event caused by an erroneous forecast provided by an artificial intelligence algorithm in the event of an adverse event? There are still many complicated medical legal issues that remain unresolved, even though it may appear that a machine is thinking like a human ophthalmologist, and might make errors [96].

Conclusions

As we concluded, we discussed the primary areas in which artificial intelligence is likely to be utilized in the practice of ophthalmology in the near future. The use of artificial intelligence algorithms should be seen as an extra tool to support physicians, rather than as a substitute for them. With artificial intelligence, there are significant opportunities for streamlining certain procedures, easing the burden on medical professionals, and eliminating diagnostic errors that can occur thanks to a lack of data integration. It is possible for artificial intelligence to extract characteristics from complicated and varied imaging modalities. This will enable us to find novel biomarkers and increase our understanding of illnesses in this way. We might be able to develop new innovative treatments for eye diseases as a result of this research. In addition, we could introduce new, automatically recognized diagnostic factors into clinical practice as a result of this research. As a result, the application of these technologies continues to face a variety of challenges including the validation of algorithms, patient acceptance of these technologies, as well as the education and training of healthcare professionals. The doctors must continue to work closely with data scientists, engineers, and technology experts in order to achieve high standards in terms of research and interdisciplinary clinical practice in order to keep up with the rapidly advancing models of care delivery.

Abbreviations

AI: Artificial intelligence
ML: Machine Learning
DL: Deep Learning
IOL: Intraocular Lens
CAD: Computer-Aided Diagnosis
NN: Neural Network
CNN: Convolutional Neural Network
GMPs: General Practitioners
CAIAR: Computer-Aided Image Analysis of the Retina
DME: Diabetic Macular Edema
CNV: Choroidal neovascularization
OCT: Optical Coherence Tomography
AMD: Age-related Macular Degeneration
DR: Diabetic Retinopathy
ROP: Retinopathy of Prematurity
AS-OCT: Anterior Segment Optical Coherence Tomography

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Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.