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Review

Artificial intelligence and deep learning in ophthalmology: Current status and future perspectives

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ABSTRACT

Background: The ophthalmology field was among the first to adopt artificial intelligence (AI) in medicine. The availability of digitized ocular images and substantial data have made deep learning (DL) a popular topic.
Main text: At the moment, AI in ophthalmology is mostly used to improve disease diagnosis and assist decision-making aiming at ophthalmic diseases like diabetic retinopathy (DR), glaucoma, age-related macular degeneration (AMD), cataract and other anterior segment diseases. However, most of the AI systems developed to date are still in the experimental stages, with only a few having achieved clinical applications. There are a number of reasons for this phenomenon, including security, privacy, poor pervasiveness, trust and explainability concerns.
Conclusions: This review summarizes AI applications in ophthalmology, highlighting significant clinical considerations for adopting AI techniques and discussing the potential challenges and future directions.

1. Introduction

As artificial intelligence (AI) technologies develop, ophthalmology has thrived partly due to its dependency on image-based clinical decision-making and investigations.[1] Deep learning (DL) played a key role in this progress, which has led to breakthroughs in information technology via the utilization of tools for feature extraction.[2] Recently, many AI researchers in ophthalmology used medical images to construct deep learning models to perform high-dimensional analyses. They have been used to automate screening and diagnosis of common vision-threatening diseases with expert-level accuracy, including diabetic retinopathy (DR),[3] glaucoma,[4] age-related macular degeneration (AMD),[5] cataract and other anterior segment disease,[6] with high accuracy. As deep learning technologies are maturing, researchers start trying to achieve disorder detection beyond the established scope of early--stage[7] and prognosis prediction.[8]

Due to the broadness of AI research in ophthalmology, experts are increasingly agreeing that consolidating data foundation and adopting standardized reporting and regulatory guidelines are needed to enhance explainability, repeatability, security and ethical compliance.[9–11] Even if the deployment of AI systems remains limited, this trend is expected to continue with the implementation of these frameworks to reduce inconsistencies among different studies. The development of high-performance DL systems alone is not sufficient to ensure eventual clinical translation of AI research, which poses a difficult conundrum to the clinical success of AI research. A wide range of factors must be aligned to achieve it, including algorithm development, clinical indication, security and public acceptance.[12] As such, to successfully implement AI in ophthalmology, clinicians need to develop a deep understanding of the interactions among these factors to formulate a clear lab-to-clinic strategy.

In this study, we aim to review the current status and future prospect of AI in ophthalmology by analyzing a variety of issues such as the development of AI in ophthalmology, the challenges for its application and potential future directions.

2. Development of AI in ophthalmology

Table 1 sums the performance of AI algorithms, data size and diversity, etc. for each ophthalmology diseases.

2.1. Diabetic retinopathy

It's a globally recognized strategy for preventing blindness to screening for DR and prompt referral for treatment. The screening process can be conducted by a variety of medical professionals, including ophthalmologists, optometrists, general practitioners, screening technicians, and ophthalmologic technologists. The use of AI-assisted screening

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Table 1
Summary of representative works of AI in ophthalmology.

Year	Reference	Topic	Dataset	AUC	SE	SP
2016	Abramoff et al.[14]	DR	CFPs, 1748 images	0.980	96.8%	87.0%
2017	Gargeya et al.[15]	DR	CFPs, 75,137 images	0.97	94%	98%
2017	Ting et al.[16]	DR, glaucoma, and AMD	CFPs, 494,661 images	0.931–0.958	90.5%–100%	87.2%–91.6%
2020	Pan et al.[17]	DR lesions classification	FFAs, 4067 images	0.870–0.965	79.7%–98.0%	82.7%–99.5%
2022	Gao et al.[18]	DR grading	FFAs, 11,214 images	0.922–0.994	/	/
2020	Varadarajan et al.[20]	DME OCT-grading	CFPs, 7072 images	0.89	85%	80%
2019	Liu et al.[23]	Glaucoma	CFPs, 274,413 images	0.996	96.2%	97.7%
2021	Sun et al.[28]	Glaucoma	OCTs, 777 sets	0.957	89.6%	95.2%
2020	Thompson et al.[29]	Glaucoma	OCTs, 20,806 images	0.96	81%	95%
2019	Phene et al.[33]	Glaucoma	CFPs, 86,618 images	0.945	80.0%	90.2%
2019	Asaoka et al.[34]	Glaucoma	OCTs, 4316 images	0.937	82.5%	93.9%
2019	Wen et al.[37]	Forecast future Visual Fields	VFs, 32,443 VFs	/	/	/
2022	Huang et al.[38]	Glaucoma visual field grading	VFs, 16,356 VFs	0.93	/	/
2017	Burlina et al.[39]	AMD	CFPs, 213,997 iamges	0.96	88.4%	94.1%
2019	Peng et al.[40]	AMD grading	CFPs, 59,302 images	0.94	59.0%	93.0%
2020	Yan et al.[42]	AMD progression prediction	CFPs, 31,262 images	0.85	/	/
2018	Kermany et al.[43]	AMD	OCTs, 207,130 images	0.999	97.8%	97.4%
2020	Erfurth et al.[45]	Quantification of Fluid Volumes to AMD	OCTs, 24,362 images	/	/	/
2021	Yan et al.[47]	AMD	OCTs, 56,091 images	0.940–0.992	80.0%–96.5%	/
2021	Zhang et al.[48]	Detect and quantify geographic atrophy	OCTs, 5049 images	/	/	/
2021	Xu et al.[50]	AMD,PCV	CFPs and OCTs, 1099 CFPs, 821 OCTs	0.939	88.8%	95.6%
2022	Jin et al.[51]	Identification of choroidal neovascularization activity in AMD	OCTs and OCTAs, 462 image pairs	0.980	89.6%	95.6%
2011	Chueng et al.[52]	Cataract	Slit-lamp photographs, 5547 images	/	/	/
2021	Li et al.[54]	Keratitis	Slit-lamp photographs, 6567 images	0.998	97.7%	98.2%
2021	Ye et al.[55]	Myopic maculopathy	OCTs, 2342 images	0.927–0.974	73.9%–92.8%	84.8%–94.0%
2019	Yoo et al.[56]	Identify candidate patients for corneal refractive surgery	Multi-instrument data, 13,201 subjects	0.983	/	/
2020	WANG et al.[57]	Eyelid malignant melanoma	Pathological patches, 225,230 images	0.989	94.7%	95.3%

and staging of DR based on fundus images is currently among the most promising AI applications in clinical medicine. Recent studies have shown that such systems can reliably match experts' performance and, in some cases, perform better than them while being a more cost-effective[13] and broader-reaching way to the traditional screening programs.

Abramoff et al. implemented a DL model to screening DR, which achieved an area under the curve (AUC) of 0.980, a sensitivity of 96.8% and a specificity of 87.0%.[14] Gargeya et al. also used a DL system to detect DR[15] using a publicly available dataset including 75,137 color fundus photographs (CFP) of diabetic patients to train and test the model to distinguish between healthy fundus images and DR images. The model achieved a sensitivity of 94% and a specificity of 98%, indicating that the AI-based algorithm could reliably perform screening of fundus photographs. Ting et al. published a clinically acceptable DRZ diagnostic system developed and tested based on 10 external datasets from the Singapore Integrated Diabetic Retinopathy Program, which ran over a period of 5 years in 6 different countries or regions, including Singapore, China, Hong Kong, Mexico, the United States and Australia. Their model demonstrated an AUC, sensitivity, and specificity of 0.936, 90.5% and 91.6%, respectively, achieving reliable diagnosis in multiple ethnic groups.[16] Although most studies have developed robust DL models for DR screening and diagnosis based on CFP or optical coherence tomography (OCT) images, some studies focused on automatic DR lesion detection in fundus fluorescein angiography (FFA) images. Multi-label classification of non-perfusion areas, vascular leakages and microaneurysms were automatically classified based on DL models[17] to construct an end-to-end DL system for staging DR severity.[18] Further, DL technologies have also been used to determine the prevalence and related systemic cardiovascular risk factors for DR[19] and predict diabetic macular edema (DME) severity based on OCT (AUC of 0.89, sensitivity of 85% and specificity of 80%) from two-dimensional fundus images.[20] Furtherly, commercial products for DR screening have been developed, since American Food and Drug Administration (FDA) approved IDx-DR as the first automated AI diagnostic system[21] and then the EyRIS SELENA[22] received the permission for clinical use in the European Union.

2.2. Glaucoma

Glaucoma patients may lead to irreversible visual field (VF) loss unless the patients receive an early diagnosis and prompt intervention. This represents a well-defined clinical need that could benefit from AI use. Although AI research in glaucoma has faced several limitations, such as a lack of multimodal assessment and long-term natural progression, substantial progress has been made. Many researchers have successfully used AI for diagnosing glaucoma via structural changes, including retinal fundus photos[16,23–27] and OCT.[28–30] Zangwill et al. reported high accuracy in identifying glaucoma using an SVM classifier.[31] Burgansky et al. used five classifiers such as SVM and machine learning analysis of OCT image data to assist in diagnosing glaucoma.[32] Li et al. trained a machine-learning algorithm to detect glaucoma-like optic disc by defining the optic disc with a vertical cup-to-disc ratio of 0.7 on fundus photos, similar to glaucoma-like optic disc. The results showed that the algorithm could detect glaucoma optic neuropathy with considerable sensitivity (95.6%), specificity (92%) and AUC (0.986).[4] In another study, Phene et al. built a DL model trained on over 80,000 CFPs to screen referable glaucoma with an AUC of 0.945. Besides, its performance was proved when applied to two other independent datasets and the AUC performance declined slightly to 0.855 and 0.881, respectively.[33] Asaoka et al. reported a DL model trained for detecting early glaucoma with 4316 OCT images, which achieved an AUC of 93.7%, sensitivity of 82.5%, and specificity of 93.9%.[34] Using over 4000 Anterior segment OCT (AS-OCT) scans, Xu et al. detected gonioscopic angle closure and primary angle closure disease (PACD) based on fully automated analysis with the AUC of 0.928 and 0.964.[35]

VF assessment plays a significant role in the clinical diagnosis and management of glaucoma. VF provides multiple validated parameters that could be useful to develop a DL system. Elze et al. developed an unsupervised algorithm to classify glaucomatous vision loss with 17 prototypes.[36] They found that the unsupervised algorithm was useful in detecting VF loss in early glaucoma. DL models have been used to predict glaucomatous progression in the VF. Wen et al. trained a DL system that could generating a point-wise VF prediction for up to 5.5 years into the future, with a correlation of 0.92 between the MD of predicted and actual future HVF and an average difference of 0.41 dB[37]. The complexity of clinical situations requires fine-grained grading and comprehensive evaluation in order to provide an accurate diagnosis and management. Huang et al. proposed a DL system to grade VF of glaucoma with a high accuracy for data from two devices (Humphrey Field Analyzer and Octopus).[38] This tool could be used by glaucomatous patients for self-assessment as well as promote telemedicine.

2.3. Age-related macular degeneration

Age-related macular degeneration is a main cause of irreversible vision loss in the elderly population. CFP is the most widely used screening method, which can identify drusen, geographic atrophy, retinal hemorrhage, and other lesions. Due to its fast, noninvasive and low-cost advantages, CFP plays a very important role in screening AMD populations. A DL algorithm based on CFP was able to fully automatically diagnose and grade AMD with an accuracy comparable to ophthalmologists. In 2018, Burlina et al. developed a DL algorithm in which feature extraction and classification were automatically completed on more than 130,000 CFP datasets. When compared with previous methods on the binary classification task, their DL algorithm demonstrated greater prospects for application in clinical practice.[39] Meanwhile, Grassmann et al. defined a 13-category AMD fundus photography dataset, which included 12 AMD severity and one case that couldn't be graded because of poor image quality. They trained six advanced DL models and finally proposed an ensemble network on an untrained independent test set.[5] Peng et al. used a DL algorithm called DeepSeeNet integrated by 3 seed networks to identify AMD severity-related characteristic lesions at the single eye level and could provide a final score combined with binocular severity at the patient level.[40] In addition to diagnosing AMD based on CFP, some AI research has been focused on predicting the risk of disease progression. In 2019, Burlina et al. not only explored the diagnostic effect of the DL algorithm on the 4 and 9 classifications of AMD severity but also experimentally used a DL-based regression model to give patients a 5-year risk score for their estimated disease progression to advanced AMD, which further expands the application scope of the DL algorithm.[41] In 2020, Yan et al. performed a study that combined CFP and patients' corresponding AMD-related genotypes and could predict the risk of advanced AMD progression based on DL algorithms.[42]

OCT can display the status and lesions of the macular region of the retina. In 2018, Kermany et al. used a transfer learning method that only used a small part of the data of traditional DL methods for training and applied it to an OCT dataset for choroidal neovascularization (CNV) and other three classifications. Their model achieved an accuracy of 96.6%, sensitivity of 97.8% and specificity of 97.4%, reaching the level of senior ophthalmologists.[43] Recently, more and more studies are focusing on the quantitative analysis of OCT images using AI algorithms. Schlegl et al. developed a DL network which could automatically identify and quantify subretinal fluid (SRF) and intraretinal fluid (IRF) on OCT images and reported that their results were very close to expert annotations.[44] Erfurth et al. also used a DL algorithm to identify and quantify retinal effusions, including SRF, IRF and pigment epithelial detachment, and explore the relationship between the amount of effusion and visual function after intravitreal injection in AMD patients.[45] The quantitative study of OCT volume mode by Moraes et al. was not limited to retinal effusion but also used biomarkers such as hyperreflective foci and subretinal hyperreflective material on OCT images, which demonstrated results that were closely related to the treatment decision of AMD patients in follow-up reviews and demonstrated a high clinical application value.[46] Yan et al. used an attention-based DL algorithm to interpret the activity of CNV on OCT images to assist doctor to diagnose AMD.[47] In addition to wet AMD, Zhang et al. quantified geographic atrophy (GA) on OCT images using a DL model for determining retinal pigment epithelium loss, photoreceptor degeneration, and hyperprojection.[48] Liefers et al. also quantified multiple key features on OCT images of early and late AMD patients as biomarkers associated with disease progression.[49] The combined application of multiple modalities was shown to be closer to clinical practice implementation and is one of the hotspots in medical AI research. Xu et al. combined CFP and OCT images to diagnose AMD and polypoidal choroidal vasculopathy (PCV) and achieved an 87.4% accuracy, 88.8% sensitivity and 95.6% specificity.[50] Jin et al. determined the effectiveness of a multimodal DL model using OCT and optical coherence tomography angiography (OCTA) images to assess CNV in neovascular AMD.[51] The DL system reached an accuracy of 95.5% and an AUC of 0.9796 on multimodal data inputs, which was comparable to retinal specialists.

2.4. Cataract and other ophthalmologic diseases

AI research in ophthalmology used to pay more attention to the screening and diagnosing fundus diseases. The fact shows that AI has the potential for the diagnosis and management of various diseases, such as automated diagnosis and severity grading of cataracts based on slit-lamp or fundus photographs. AI agents have demonstrated good-to-excellent overall diagnostic performance in classifying different types of cataracts, with high AUC (0.86–1.0), accuracy (69.0%–99.5%), sensitivity (60.1%–99.5%), and specificity (63.2%–99.6%).[52] Long et al. used a DL model to develop an artificial intelligence management application for congenital cataracts involving 3 functions: a congenital cataract screening network in the population, a risk stratification network for congenital cataract patients, and assisting a network of strategies for ophthalmologists to make treatment decisions.[53] Li et al. improved the performance of a DL algorithm for diagnosing anterior segment diseases in slit-lamp images such as cataracts, keratitis and pterygium through segmenting the anatomical structures and annotating pathological lesions.[6] Another DL system exhibited considerable performance automatically classifying keratitis, other cornea abnormalities, and normal cornea in slit-lamp images captured by the different devices and a smartphone with the super macro mode (all AUCs$>$0.96).[54] The sensitivity and specificity of AI in keratitis detection were found to be comparable with experienced cornea specialists. Ye et al. developed a DL system for detecting and classifying myopic maculopathy in patients with high myopia. Their model achieved sensitivities equal to or even better than junior ophthalmologists.[55] Yoo et al. combined preoperative data and compiled a machine learning model from 10,561 eye images and showed that their model could predict suitability for refractive surgery achieving an accuracy of 93.4% and an AUC of 0.97 in external validation.[56] For ocular tumors, a large-scale statistical analysis of epidemiological and clinicopathological characteristics was performed in combination with public medical databases and multicenter clinical data to develop a set of convolutional neural networks for identifying malignant tumors. The DL diagnosis system for melanoma visualization could distinguish between benign and malignant tumors with an accuracy of 94.9% and a sensitivity of 94.7%.[57]

3. Challenges in the application of AI

3.1. Consolidate the data foundation

A major challenge of current DL models is that their training requires a large amount of data because insufficient data may decrease the performance of DL models.[58] Thus, for some rare eye diseases, their low incidence makes it difficult for researchers to collect enough data for AI research.[59] Some multimodal and longitudinal cohort studies have high requirements for patient data, and researchers need to collect data prospectively, which is very time- and energy-consuming. Hence, dealing with the limited amount or even no data in certain conditions still requires further attempts and efforts. Currently, most of the AI algorithms successfully applied in the field of ophthalmology use a fully supervised learning model which requires doctors to perform high-standard data annotation on the original data according to specific tasks. Medical data labeling is difficult to obtain because it's time-consuming and labor-intensive. Further, the gaps in labeling standards and levels among labelers should also be considered.

With the advancement of computer science, weakly supervised learning models that require only a small amount of annotation, semi-supervised learning models or even unsupervised learning models that do not require annotation have been proposed and applied in ophthalmology.[60–62] It could reduce dependence on data labeling in a way, however the fact can't be ignored that various image-related factors have been shown to play more predominant parts than technical factors in determining the performance of AI models, suggesting DL training and application in real-world scenarios require robust training and testing datasets.[63,64]

3.2. Reporting guidelines

A computational perspective on AI often overlooks clinically relevant details that clinicians believe are essential to determining effectiveness. For example, the criteria for participant recruitment, demographics, risk control and other abilities to administer the trail. Therefore, to better reflect the specific requirements for AI implementation, it is necessary to update some of the widely accepted international reporting protocols using extant evidence-based clinical trial workflows.[65] In recent decades, many standardized reporting protocols have arisen, of which CONSORT-AI,[66] STARD-AI,[11] SPIRIT-AI[67] and TRIPOD[68] are among the most extensively applied. These protocols aremainly differentiated by the type of research and setting in which they are applicable and offer a list of items grouped according to different article sections. CONSORT[69] was one of the first protocols and was introduced in 1996. It was updated in 2001 and 2010 to specify reporting guidelines for parallel-group randomized controlled trials. STARD[70] was developed in 2000 to standardize studies comparing new or alternative diagnostic tests with defined reference standards. SPIRIT,[71] which arose in 2007, covers general clinical intervention trials and incorporates some of the features of CONSORT by farther emphasizing the significance of pre-registration trials to reduce reporting selectivity and encourage transparency.[72] In spite of the propagation of reported protocol expansions addressing AI in medicine, it should be acknowledged that AI is a fast developing technique, and the range of potential application would multiply in the not-too-distant future.[73] Therefore, it is expectable that these protocol extensions would be updated while AI-specific protocols for clinical decision-making may be formalized in the future.

3.3. Security

Medical AI research should be performed on multicenter datasets; otherwise, the generalization of the proposed AI models might not be difficult. Data from a single-center database could be biased by factors such as patients' race and image equipment. Data transfers between research collaborators, especially for international collaborations, are often limited because of patient privacy and data security.[74] Thus, the management of data from multicenter research centers in different countries is also a major challenge. One of the key shortcomings of the DL algorithm is its inexplicability.[75] From the perspective of medical personnel, it is impossible to understand how DL models make decisions and predictions for specific tasks because existing methods such as heatmaps are inadequate to fully explain them. Therefore, the AI models should provide a certain degree of transparency to justify their medical diagnosis, treatment decisions and risk predictions so that medical personnel can fully trust them to further generate new clinical insights. Xu et al. proposed a possible approach to enhance the interpretability by comprehensively simulating the diagnostic thinking of human experts that they establish a hierarchical deep learning system that includes pre-diagnosis module, image segmentation module, and final diagnosis module and makes the AI diagnosis of glaucoma a visualized interactive process.[27] Although DL models have achieved performance close to or even surpassed ophthalmologists in specific medical tasks, the real practical application of AI systems in complex ophthalmology clinics is still far from being achieved.[12,76] Its problems include a relatively narrow range of disease spectrum applications, doctors' interpretation of DL model results, integration of software systems and hardware devices, resistance to malicious attacks, and approval by relevant policies.

3.4. Ethics

As AI is gradually being integrated in clinical practice and medical professionals are getting used to it, there is also a growing trend for an ethical framework to guide the real application of DL systems. The concern roots in the possibility that AI could lead to discrimination against patients or worsen health inequalities. For example, vulnerable groups with complicated health problems may lose their priority if an AI health system is purely focused on maximizing efficiency.[77] Psychosocial factors may also influence the acceptance and trust in AI-involved healthcare.[78] Once AI systems turn into the gateway to healthcare, this could be disadvantageous for patients who don't trust this technique or can't operate it. Beyond access, we must also recognize the fundamental biases in AI systems.[79] For instance, if an AI algorithm is trained or tested on a dataset in which only certain groups in the population are represented, the algorithm may perform poorly on other groups. Health inequalities can be exacerbated if AI system performance metrics are too strictly defined to ignore its impacts on ethnic minorities. As such risks seem difficult to mitigate, potential ethical frameworks for guiding consent and incorporation into DL datasets must be carefully considered. Models for informed consent for AI research in medicine have been proposed,[80] and when balanced with the actual problem of managing large AI data, dropout models seem to be preferred.

4. Future directions

Recent achievements using ophthalmology-based AI will facilitate more research and clinical translation efforts. To increase the chance of success for DL systems in the future, several elements should be simultaneously considered. In terms of development, the systems should be guided to consider unmet clinical demands. Issues like ill-considered indications, doubtful methods, and unsuitable AI platforms should be addressed before full development. Additional focus directions include multiclass and multimodal AI networks for disease diagnosis, progression prediction, or treatment decision-making. The sensitivity and specificity of DL are both very important in ophthalmology and medical diagnosis. In disease screening and early diagnosis, the sensitivity of AI systems would be deemed more important sometimes. There is a definite unmet clinical need to improve diagnostic capabilities of these procedures, including improving test sensitivity and specificity. These may involve evaluating the optic nerve head using optic discs or fundus photographs to screening a variety of optic neuropathy in mydriatic or non-mydriatic conditions,[81] prediction of myopia progression in kids, and the use of combined automatical detection and management of glaucoma VF. Advanced segmentation networks would also improve the localization of anatomical structures and identification of pathological features, enhancing the robustness of the AI systems.

While many diagnostic AI algorithms proposed before shows promising performances, it's worth noting that most of them were trained on small samples, and few algorithms have been tested in real clinical settings. Patient heterogeneity can lead to less accurate AI algorithms when tested in real-world settings. Additionally, considering the effects of reporting bias, algorithms with unsatisfactory performance are more likely to be rejected to be reported. These issues should be adequately handled before AI technologies can be translated into real-world applications. As eye diseases become more prevalent, such as cataracts and glaucoma, there is a wealth of patient data available for training, testing, and validating AI models, which were ideally derived from multi-ethnic patient cohorts to enhance algorithms. In addition to diagnostic accuracy, the effectiveness of AI tools should also be assessed whether it can improve patient outcomes by prospective clinical trials. The challenge is to democratize this technology for stakeholders when clinically proven and implement robust AI algorithms. As AI technologies may pave the way for a "smart" healthcare model before long, it has been recently highlighted that agreed-on international reporting guidelines for AI-related interventions are needed.[63] Thanks to these guidelines, Reporting will become more consistent and transparent, while regulators and relevant stakeholders will also be able to assess the cost and effectiveness of the AI-related interventions more confidently. Other potential challenges, such as the "AI black box", the explainability of AI by medical professionals, and forensic and regulatory challenges, should be carefully addressed prior to applying AI techniques to clinical settings.

5. Conclusions

Although medical AI research has attained many milestones and achieved breakthroughs in the field of ophthalmology, it also faces many difficulties and challenges. The emergence of the period of big data, the development of medical electronics, and people's demand for high-quality medical services are all driving AI systems to maximize their potential in improving clinical medical workflows, patient care and assessing patient prognosis. Ophthalmic medical workers and AI researchers should work closely with computer scientists to apply cutting-edge AI concepts and technologies to solve ophthalmic clinical problems, and should also pay more attention to the translation of the research results. Developments in digital ophthalmology could solve issues such as unbalanced medical resource allocation in countries like China, heavy workload of professional ophthalmologists and challenges in popularizing high-quality medical services. The future of AI interventions in ophthalmology seems promising, but there is still a long way to go prior to their wide clinical application.

Method of literature search

The literature search for this review was conducted in PubMed and Google Scholar from January 2016 to June 2022. The search terms combined a set of keywords from the medical field (ophthalmology, retina, diabetic retinopathy, glaucoma, age-related macular degeneration, cataract, anterior segment disease) and the machine learning field (artificial intelligence, deep learning, machine learning, and convolutional neural network). Term from each set was independently combined with term from the other set. A total of 800 studies assessed as eligible by inspecting the titles and abstracts were reviewed. The main inclusion criterion is that the researches must focus on artificial intelligence in ophthalmology with perceived quality. Several selected typical articles before 2016 and some researches with closely related topics were included as well. Most of the papers were in English. For non-English articles, only their abstract was considered.

Study approval

This study was approved by the Medical Ethics Committee of the Second Affiliated Hospital, Zhejiang University, and complied with the Declaration of Helsinki.

Author contributions

All the authors were involved in conceptualizing, researching and writing of the manuscript, and edited all versions.

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Declaration of completing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

AI	artificial intelligence
DL	deep learning
DR	diabetic retinopathy
AMD	age-related macular degeneration
AUC	area under the curve
CFP	color fundus images
OCT	optical coherence tomography
FFA	fundus fluorescein angiography
VF	visual field
CNV	choroidal neovascularization
SRF	subretinal fluid
IRF	intraretinal fluid
GA	geographic atrophy
OCTA	optical coherence tomography angiography

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