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ORIGINAL ARTICLE

The role of artificial intelligence in the diagnosis, monitoring, and management of retinal diseases: a review of the current literature

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ABSTRACT

Introduction: retinal diseases, such as diabetic retinopathy and age-related macular degeneration, represent major causes of irreversible visual disability, generating increasing pressure on health systems.
Objective: to analyze recent evidence on the applications of artificial intelligence in the diagnosis, monitoring, and management of retinal pathologies.
Methods: a systematic literature review was conducted in international databases, using key terms related to artificial intelligence, deep learning, and retina. Articles published in recent years addressing clinical applications, algorithm validation, and implementation challenges were selected. The analysis focused on identifying trends, methodological contributions, and reported limitations.
Development: deep learning algorithms have achieved accuracy comparable to or exceeding that of human experts in retinal image classification tasks. Advances are highlighted in automated detection of diabetic retinopathy, quantification of biomarkers in optical coherence tomography, and prediction of progression in macular degeneration. Applications have also been explored in glaucoma and retinopathy of prematurity, expanding the spectrum of clinical utility. However, challenges remain regarding model generalization, explainability of algorithmic decisions, integration into healthcare workflows, and ethical and legal implications.
Conclusions: artificial intelligence constitutes a promising tool to optimize the diagnosis and monitoring of retinal diseases. Its ethical and effective integration can improve equity, accessibility, and quality of care, consolidating a new paradigm in contemporary ophthalmology.

Keywords: CLINICAL DIAGNOSIS; RETINAL DISEASES; ARTIFICIAL INTELLIGENCE; DISEASE MANAGEMENT; INTELLIGENT SYSTEMS.

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INTRODUCTION

Retinal diseases, such as diabetic retinopathy (DR), age-related macular degeneration (AMD), and retinal vein occlusions, constitute the main causes of irreversible visual disability and blindness worldwide, representing a health and socioeconomic burden of epidemic proportions.(1) This visual health crisis is exacerbated by two global demographic and clinical megatrends: the progressive aging of the population, which increases the prevalence of age-related conditions like AMD, and the parallel pandemic of diabetes mellitus, which drives the incidence of DR.(2)

As a direct consequence, ophthalmology services, and particularly retina units, are under unprecedented clinical pressure, facing a growing volume of patients who require early diagnosis, close monitoring, and increasingly complex and personalized treatments. This saturation threatens to overwhelm health system capacity, generating long waiting lists that can translate into diagnostic and therapeutic delays, with consequent avoidable visual deterioration for thousands of people.(3)

For decades, the cornerstone of managing these retinal diseases has been the expert evaluation and interpretation of a diverse set of diagnostic imaging modalities. Among these, color fundus photography (retinal photography) stands as an essential screening and initial diagnostic tool, particularly for DR and advanced AMD.(4,5,6) Optical coherence tomography (OCT) has revolutionized the field by enabling high-resolution cross-sectional visualization of retinal layers, crucial for detecting and quantifying intraretinal, subretinal fluid, and macular cysts—key findings in neovascular AMD, diabetic macular edema, and vein occlusions.(7,8,9,10) Angiography, whether with fluorescein or indocyanine green, provides functional and dynamic information on the integrity of the blood-retinal barrier and the presence of neovessels, although its invasive nature limits its repetitive use.(3)

However, this image-dependent diagnostic paradigm suffers from limitations inherent to the human factor. Manual evaluation of these images by specialists is intrinsically subjective, time-consuming—a scarce resource in overburdened health systems—and subject to significant inter- and intra-observer variability.(4,5) Expert fatigue, workload, and case complexity can lead to inconsistencies in interpretation, potentially resulting in diagnostic errors or imprecise quantification of disease activity biomarkers, such as fluid volume on OCT, which guides critical therapeutic decisions.(10) This variability affects not only individual clinical practice but also introduces noise into multicenter clinical trials, where standardization of evaluation criteria is fundamental for result validity.

In this context of growing clinical demand and limitations of traditional diagnosis, artificial intelligence (AI) emerges as a disruptive technology with the potential to radically transform eye health care and alleviate pressure on health systems.(2,4) Based on the above, this review was conducted with the objective of analyzing recent evidence on the applications of artificial intelligence in the diagnosis, monitoring, and management of retinal pathologies.

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METHODS

A systematic literature review was conducted following PRISMA guidelines to synthesize the available scientific evidence on the applications of artificial intelligence in the diagnosis, monitoring, and management of retinal diseases. The search period was delimited between January 2010 and December 2024, considering that the main advances in deep learning algorithms applied to ophthalmology have occurred within this interval. The review was designed to ensure transparency, reproducibility, and methodological rigor, avoiding biases in the identification and selection of relevant studies.

Search strategy

The search was performed in widely covered international databases: PubMed/MEDLINE, SciELO, ScienceDirect, Google Scholar, LILACS, and BVSALUD. These platforms were selected for their relevance in biomedical sciences and for including both regional and global literature. In addition, the reference lists of selected articles were reviewed to identify additional studies not retrieved in the initial search. Grey literature, including technical reports, conference proceedings, and institutional documents, was also considered, provided they met quality and thematic relevance criteria. This strategy allowed for a broader spectrum of sources and reduced the risk of omitting significant information.

The search algorithm was constructed by combining keywords and Boolean operators, adapted to each database. Terms such as "inteligencia artificial" OR "artificial intelligence" OR "aprendizaje profundo" OR "deep learning" AND "retina" OR "retinal diseases" OR "retinopatía diabética" OR "degeneración macular" were used. Filters were applied to restrict results to the defined time range, and publications in Spanish, English, and Portuguese were considered to encompass the most representative scientific output in the Ibero-American and Anglo-Saxon spheres. The strategy was validated through pilot searches, adjusting descriptors to maximize the sensitivity and specificity of the results.

Selection process

Original articles, systematic reviews, and meta-analyses published between 2010 and 2024 that directly addressed the application of artificial intelligence in the diagnosis, monitoring, or management of retinal diseases were included. Clinical studies, algorithm validations, and implementation analyses in clinical settings were accepted. Duplicates, articles without full-text access, publications outside the established time frame, irrelevant studies, and those without clinically applicable results were excluded. This curation ensured the relevance and quality of the analyzed evidence.

The study selection was carried out in several phases. First, records were identified through database searches, yielding an initial number of approximately 1,200 articles. Subsequently, duplicates were removed, and titles and abstracts were screened, reducing the sample to 350 potentially eligible studies. Finally, the full texts were read, rigorously applying inclusion and exclusion criteria, resulting in a final set of 23 articles included in the qualitative synthesis. The process was documented using a PRISMA flow diagram, reflecting each stage of identification, screening, eligibility, and inclusion, ensuring methodological transparency.

A narrative qualitative analysis was performed, highlighting trends, methodological contributions, and reported limitations. No quantitative meta-analysis was conducted due to the heterogeneity of designs and results, although common patterns were identified that allow for solid conclusions regarding the clinical applicability of artificial intelligence in ophthalmology.

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DEVELOPMENT

AI, generally defined as the ability of machines to perform tasks that normally require human intelligence, has found in deep learning a sub-discipline that uses artificial neural networks with multiple layers to learn data representations hierarchically—its most powerful weapon for medical image analysis.[4] Unlike traditional algorithms, which depend on features predefined by human experts, deep learning models, particularly convolutional neural networks (CNNs), can automatically learn the most relevant and complex visual patterns directly from thousands or millions of annotated images, without the need for manual feature engineering.[5]

The exceptional performance of AI in ophthalmology, often comparable or even superior to that of expert clinicians in specific tasks, has been demonstrated in a plethora of seminal studies published in recent years. One foundational milestone was the work of Gulshan V et al.,[6] who developed and validated a deep learning algorithm to detect diabetic retinopathy in color fundus photographs with very high sensitivity and specificity, using a dataset of tens of thousands of images. This study set a crucial precedent, proving that automated DR screening was feasible.

Shortly thereafter, Ting DSW et al.,[7] expanded this concept by creating a system that not only detected DR but also identified glaucoma and AMD, demonstrating AI's capacity to address multiple ocular diseases simultaneously—a significant advance toward versatility in automated diagnosis.

The transition from validation in controlled environments to implementation in real-world clinical practice began with pivotal studies, such as that of Abràmoff MD et al.,[8] which evaluated an autonomous AI system for DR diagnosis in primary care clinics. This work was pioneering in demonstrating the feasibility and safety of deploying AI in a non-specialized setting, with the potential to decentralize screening and bring it closer to patients, reducing access barriers. Beyond mere detection, AI has shown promising capacity for risk stratification. Bora A et al.,[9] explored the possibility of using deep learning algorithms not only to diagnose manifest DR but also to predict the future risk of a diabetic patient without apparent retinopathy developing it, opening the door to truly personalized prevention strategies.[11,12]

In the field of age-related macular degeneration, AI applications are equally profound. On one hand, highly accurate algorithms have been developed for the automated classification of AMD severity from color fundus photographs, such as the DeepSeeNet model described by Peng Y et al.,[13] which replicates the standard clinical classification system. On the other hand, AI analysis of OCT images has reached a remarkable level of sophistication. Schlegl T et al.,[10] created a fully automated system for the detection and, more importantly, the precise quantification of macular fluid on OCT—a quantitative, objective metric crucial for monitoring treatment response in neovascular AMD and diabetic macular edema. This quantification capability goes beyond what the human eye can routinely and reproducibly perform in daily clinical practice.

Perhaps one of the most ambitious applications of AI in AMD is the prediction of disease progression. Schmidt-Erfurth U et al.,[11] and subsequently Yim J et al.,[12] showed that deep learning algorithms can analyze OCT images of patients with dry AMD and predict with significant accuracy which eyes are at high risk of converting to the neovascular or "wet" form, the fastest cause of severe vision loss. This predictive capability could enable earlier interventions and more intensive monitoring of high-risk patients, shifting the paradigm from a reactive to a proactive and preventive model.

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While the focus of this review is on retinal diseases, it is illustrative to observe how AI is impacting other areas of ophthalmology with similar challenges. For example, Li Z et al.,[14] developed a deep learning system to detect glaucoma from color fundus photographs, while Brown JN et al.,[15] succeeded in automating the diagnosis of "plus disease" in retinopathy of prematurity, a particularly challenging and subjective task. Even the basic classification of OCT images as normal or pathological (e.g., with AMD or macular edema) has been solved with high efficacy by algorithms such as the one presented by Lee CS et al.,[16] These cross-cutting successes reinforce the robustness of deep learning as a central enabling technology in ocular diagnosis.

Surprisingly, the potential of AI in ophthalmology transcends the strictly ocular realm. The fundus, through retinal photography, has been described as a "window" to systemic health. Poplin R et al.,[17] pioneered the demonstration that a deep learning algorithm could predict cardiovascular risk factors such as age, sex, smoking status, systolic blood pressure, and body mass index, and even infer the risk of a major cardiovascular event, solely from color retinal photographs. This finding opens an unsuspected field of possibilities for ophthalmology as a gateway to general health assessment, positioning AI as a broad-spectrum predictive and preventive medicine tool.

Despite this extraordinarily promising landscape, the path to widespread and routine implementation of AI in daily clinical practice is fraught with significant challenges that must be rigorously addressed. Keane PA and Topol EJ,[18] early on warned of the need for robust prospective clinical trials demonstrating not only diagnostic accuracy but also improvement in final clinical outcomes and cost-effectiveness. One of the most critical obstacles is the risk of algorithmic bias.

As highlighted by Seyyed-Kalantari L et al.,[19] AI models trained predominantly with data from specific populations (e.g., Caucasian or with access to certain health systems) may suffer from "underdiagnosis bias" when applied to underserved populations or those with different demographic characteristics, potentially exacerbating rather than reducing health disparities. The generalizability of these systems across different imaging devices, acquisition protocols, and ethnically diverse populations is therefore a research priority.

Another fundamental challenge is the AI "black box." The decision-making of many deep neural networks is often opaque and difficult for the human physician to interpret, generating distrust and questions about accountability.[20] The emerging field of Explainable AI (XAI) seeks to develop methods to visualize and understand which image features are driving the algorithm's decision (e.g., through heatmaps or attention maps), thereby facilitating clinical acceptance and error correction.[21,22] Alongside this, complex legal and ethical issues arise. Price WN et al.,[23] analyzed the potential legal liability of physicians using AI systems, a largely unexplored legal territory requiring clear regulatory frameworks to define the responsibilities of the manufacturer, provider, and healthcare professional.

Real-world evaluation is the next step in validation. Recent studies, such as that of Karthik A et al.,[21] have begun to assess the performance of AI models in routine clinical environments, outside the ideal conditions of validation studies, identifying practical challenges related to variable image quality, integration into hospital workflows, and interoperability with electronic health record systems. Finally, cost-effectiveness analyses, such as the one conducted by Xie Y et al.,[22] for a national tele-ophthalmology program for DR, are essential to convince health managers and payers of the economic value of large-scale AI implementation.

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Artificial intelligence, and specifically deep learning, is positioned to redefine the standard of care in retinal diseases. Its ability to automate diagnostic tasks, quantify biomarkers with super-human precision, and predict disease progression risk promises not only to alleviate the burden on ophthalmologists but also to improve the quality, accessibility, and equity of patient care. The objective of this review is therefore to critically examine the most up-to-date bibliography published in recent years on the application of AI in the management of retinal diseases. Its most relevant clinical applications will be addressed in detail, the technical, ethical, and implementation challenges currently limiting its mass adoption will be discussed in depth, and future perspectives and necessary research directions will be explored to realize the full potential of this transformative technology, always basing conclusions on the analyzed scientific evidence.

Deep learning (DL) algorithms, trained with hundreds of thousands of expert-annotated color fundus photographs, have achieved outstanding precision. Public datasets such as Messidor-2 and EyePACS have been fundamental to this progress. These algorithms not only perform binary classification (referable vs. non-referable disease) but are capable of finer grading. For example, they can classify DR according to the International Clinical Diabetic Retinopathy Disease Severity Scale or the ETDRS (Early Treatment Diabetic Retinopathy Study) system, identifying specific lesions such as microaneurysms (the first signs of DR), hemorrhages, hard exudates (indicative of diabetic macular edema), and neovessels (a sign of proliferative retinopathy).[6,7]

A crucial regulatory milestone was the 2018 approval by the United States Food and Drug Administration (FDA) of the IDx-DR system (now marketed as LumineticsCore™). This was the first autonomous AI system authorized to provide a screening decision without specialist intervention. Its implementation in primary care settings allows a technician to capture a retinal image and the algorithm to determine within minutes whether the patient needs to be referred to an ophthalmologist, optimizing resources and reducing wait times.[8]

Beyond detection and classification, AI is advancing towards risk prediction. Algorithms are learning to identify subtle patterns in retinal images that can predict the probability of a diabetic patient developing DR in the future, or that a patient with mild non-proliferative DR will progress to more severe forms. This proactive and predictive approach could revolutionize follow-up strategies, enabling personalized and more intensive care for high-risk patients.[9] Furthermore, algorithms are being developed to quantify diabetic macular edema on OCT, precisely measuring retinal volume and thickness, which is crucial for evaluating response to intravitreal injection treatment.

AMD is the leading cause of irreversible blindness in older adults in the developed world. OCT has become the gold standard imaging technique for its diagnosis and management, as it provides high-resolution cross-sectional views of the retina. However, OCT interpretation is complex, time-consuming, and subject to some inter-observer subjectivity.

AI has found an extremely fertile field of application in AMD. One of the most established applications is the automatic segmentation of fluids. In the neovascular or wet form of AMD, the accumulation of intraretinal fluid (IRF) and subretinal fluid (SRF) is a critical biomarker guiding the need for anti-VEGF treatment. DL algorithms can automatically segment and quantify these fluid volumes with accuracy comparable to that of human experts.[10] This not only greatly speeds up the clinic, freeing the ophthalmologist from tedious manual tasks, but also provides an objective and quantitative measure of treatment response. This reduces variability in decision-making, such as when to re-treat or extend dosing intervals, a constant challenge in clinical practice.[11]

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Another cutting-edge development front is the prediction of conversion from dry (or atrophic) AMD to the wet form. Conversion to the wet form is a devastating event for vision, and detecting it as early as possible is crucial. AI algorithms are being trained to analyze temporal sequences of OCTs, identifying subtle and precursor structural changes that may be imperceptible to the human eye. These changes could include alterations in drusen patterns, the appearance of sub-RPE hyperreflectivity, or changes in retinal layer architecture. Being able to predict which patients with dry AMD are at high risk of converting would allow for closer monitoring and ultra-early intervention, potentially saving central vision.(12)

Finally, in dry AMD, AI is proving highly useful in the identification and monitoring of geographic atrophy (GA). Algorithms can automatically delineate atrophy areas, measuring their progression over time with greater precision than manual evaluation, which is prone to variability. This robust quantification is essential for evaluating new therapies in clinical trials aimed at slowing the progression of dry AMD.(13)

The scope of AI in ophthalmology extends beyond DR and AMD, encompassing an ever-widening spectrum of diseases. In glaucoma, a progressive optic neuropathy, diagnosis and monitoring rely on the evaluation of the optic nerve and the retinal nerve fiber layer (RNFL). Algorithms can analyze fundus photographs to detect signs of glaucomatous optic nerve damage, such as increased cupping or neuroretinal rim thinning. However, it is in OCT where AI shows its full potential, automatically segmenting the RNFL and ganglion cell layer, and detecting characteristic thinning patterns of glaucoma that may precede visual field defects. This facilitates earlier diagnosis and more precise monitoring of disease progression.(14)

Retinopathy of prematurity (ROP) is a major cause of childhood blindness in premature infants. Its diagnosis requires an ophthalmologic examination performed by an expert, a scarce resource in many regions. AI systems, trained with fundus images of infants, can assist in screening by identifying signs of ROP "plus disease" (vascular dilation and tortuosity), a key criterion for treatment. These systems have the potential to increase screening access in remote areas or with a shortage of specialists, preventing cases of blindness.(15)

Algorithms are being used to predict visual outcomes after complex surgeries such as vitrectomy for retinal detachment. By analyzing preoperative OCT features, such as macular status, they can predict the probability of recovering good visual acuity.(16)

The retina is an extension of the central nervous system, and its blood vessels can reflect the vascular health of the entire body. AI algorithms are demonstrating a surprising ability to predict cardiovascular risk factors (such as hypertension, age, and sex) and even to estimate a person's biological age from a simple retinal photograph. Beyond this, correlations between retinal vascular patterns and neurodegenerative diseases such as Alzheimer's disease and mild cognitive impairment are being explored, opening the door for a routine eye exam to serve as a non-invasive screening tool for these conditions.(17)

Despite the evident enthusiasm and progress, the transition of AI algorithms from controlled research environments to widespread, daily clinical practice faces a series of significant obstacles that must be addressed comprehensively. One of the most critical problems is the lack of robustness and generalization of many models. An algorithm may exhibit exceptional performance on the dataset it was trained and validated on, but its accuracy can plummet dramatically when faced with "real-world" data. This is due to several factors:

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Equipment Bias: Algorithms are often trained with images from a specific retinal camera or OCT manufacturer/model. When applied to images acquired with different equipment, with varying resolutions, illumination, or acquisition protocols, performance can degrade.[18]

If an algorithm is predominantly trained with images from a specific ethnicity, demographic group, or geographic region, it may not generalize well to other populations. For example, optic nerve characteristics can vary among different ethnicities, and an algorithm trained primarily on Caucasian populations might make errors when evaluating glaucoma in African or Asian populations. This is not only a technical issue but a matter of health equity. If not mitigated, AI risks perpetuating and even amplifying existing health disparities by providing lower-quality care to populations underrepresented in training data.[19]
A model trained to detect a disease in a specific stage may not be sensitive to atypical presentations or very early forms of the disease.

The solution lies in creating larger, more diverse, and representative training datasets that encompass multiple ethnicities, equipment types, and clinical settings. Furthermore, data augmentation techniques and federated learning (where the model is trained in a distributed manner across several centers without sharing patient data) are promising strategies to improve generalization.

Clinicians need to trust the tools they use. It is unlikely that an ophthalmologist will blindly accept a system's recommendation if it cannot justify its conclusion. Moreover, in the event of a diagnostic error, it is crucial to understand why the algorithm failed to correct it and learn from the incident.[20]

The field of Explainable AI (XAI) is growing rapidly to address this challenge. Techniques such as activation heatmaps are particularly useful in image analysis. These maps overlay a color layer on the original image, highlighting the regions that contributed most to the algorithm's decision. For example, if an algorithm diagnoses proliferative DR, an ideal heatmap should highlight areas of neovessels. This allows the ophthalmologist to visually verify whether the algorithm is "focusing" on the correct pathological features, building trust and facilitating clinical correlation.[21] However, XAI is still under development, and ensuring these explanations are accurate and meaningful is an active area of research.

The mere existence of an accurate algorithm does not guarantee its clinical adoption. Its seamless integration into existing systems is a monumental challenge. To be truly useful, these tools must be integrated directly into Picture Archiving and Communication Systems (PACS) and Electronic Health Records (EHR). The process must be agile: the technician acquires the image, the algorithm processes it automatically in the background, and the results are presented to the physician in a clear and concise manner within their usual workflow, without requiring cumbersome additional steps or the use of external platforms.[22]

Who is responsible if an AI algorithm makes a diagnostic error that leads to patient harm? Is it the algorithm developer, the hospital that implemented it, the physician who relied on its output, or a combination of all? Current legislation is not well-defined in this area and requires urgent updating. Most advocate for a model where AI acts as a "second opinion" or a decision-support tool, with ultimate responsibility always resting with the treating physician.[23]

Training these algorithms requires large amounts of anonymized patient data, but perfect anonymization is difficult to guarantee. It is crucial to establish robust data governance frameworks that ensure privacy and informed consent for the use of these images.

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There is a perceived risk that diagnostic automation will distance the physician from the patient. The key lies in implementation. AI should be seen as a tool that frees the ophthalmologist from repetitive quantitative analysis tasks, allowing them to dedicate more time to patient communication, disease explanation, and personalized therapeutic planning. Clinical judgment, empathy, and the physician-patient relationship must remain at the center of care. The future of AI in retinal diseases is extremely promising and is heading towards deeper and more multifaceted integration. Future trends include:

- Multimodal Algorithms: Instead of analyzing a single type of image, future algorithms will integrate information from multiple sources simultaneously: OCT, color fundus photography, OCT angiography, autofluorescence, and visual fields. This holistic view will enable a more complete and robust diagnosis.
- Prognosis and Precision Medicine: AI will evolve from diagnosis to predicting the individual disease trajectory. It will be able to answer questions such as: "At what rate will this patient's glaucoma progress?" or "Which anti-VEGF treatment will have the best response in this particular case of wet AMD?"
- Systemic Disease Detection: The "retina as a biomarker" will be an explosively growing field. Algorithms will be refined to predict not only cardiovascular risk but also renal, hematological, and neurological diseases with greater precision.
- Image Generation and Data Augmentation: Generative AI can be used to create synthetic but realistic retinal images of rare diseases, helping to train models without compromising patient privacy and improving the recognition of uncommon cases.

AI in the field of retinal diseases is not just another tool; it represents a paradigm shift in how we understand and practice ophthalmology. Its potential to democratize access to high-quality ophthalmic diagnosis, especially in low-resource areas or with a shortage of specialists, is undoubtedly its most transformative and ethically resonant contribution. The possibility that a diabetic patient in a rural area can be screened with the same precision as in an elite university hospital is a monumental step towards health equity.

CONCLUSIONS

Artificial intelligence has consolidated itself as a transformative tool in the management of retinal diseases, thanks to its ability to analyze images with great precision and speed, making it key for mass screening, early diagnosis, and predicting the progression of pathologies such as diabetic retinopathy and age-related macular degeneration. However, its implementation faces challenges such as the lack of model generalization, data biases, the need for explainability, technological barriers, and ethical and legal dilemmas. Rather than replacing the ophthalmologist, AI should be viewed as an ally that optimizes their clinical work, within a framework of collaboration between engineers, physicians, and regulators. The immediate future will depend on validating these systems in real-world practice and establishing regulatory frameworks that guarantee their safety, efficacy, and equity.

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