AI IN DME: FROM PROMISE TO CLINICAL PRACTICE

New data show the growing utility of AI-assisted screening, referrals, and treatment response prediction.

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As AI continues to creep into nearly every aspect of our daily lives, many of us wonder whether AI in diabetic macular edema (DME) is an emerging clinical tool or simply another wave of promising algorithms unlikely to translate into practice. AI has been applied to detect DME from color fundus photographs (CFPs) and OCT, estimate visual acuity, quantify OCT biomarkers, and predict response to anti-VEGF therapy. Thus, the central question is not whether AI can perform these tasks, but which applications will ultimately change clinical practice. Three recent studies illustrate how AI may address practical problems along the DME care pathway by expanding screening, improving referral efficiency, and personalizing treatment.

EXPANDING ACCESS: AUTONOMOUS DME SCREENING

One of the clearest opportunities to improve outcomes in diabetic eye disease remains expanding access to DME screening (Figure). Bressler et al evaluated whether deep learning could identify DME using CFPs, which are already widely used for diabetic retinopathy (DR) screening.[1] Unlike many earlier CFP-based DME studies, this work emphasized extensive external validation across independent datasets, representing an important step toward real-world deployment rather than another proof-of-concept algorithm. The model was trained on a large, diverse dataset of more than 32,000 CFPs from nearly 16,000 patients. Performance was then evaluated at the image, eye, and patient levels.

Internal validation demonstrated strong performance, with a patient-level area under the curve of 0.962 and sensitivity and specificity of approximately 90%. Results also remained favorable across several external datasets. On Messidor-2, for example, the patient-level area under the curve was 0.964, with sensitivity of 0.897 and specificity of 0.932. External validation is particularly important for screening tools, which must perform across different populations, cameras, and image-acquisition conditions.[1]

Because CFPs do not directly visualize retinal fluid, the

KEY TAKEAWAYS

- Color fundus photography-based AI models may extend diabetic macular edema (DME) screening to patients who lack access to OCT.
- AI-assisted OCT screening may reduce unnecessary referrals while preserving access to specialist care for patients with DME most likely to benefit.
- Multimodal prediction models of anti-VEGF treatment response may eventually support more personalized treatment decisions.

Image courtesy of Retina Rocks (retinarocks.org, @retina.rocks)

Figure. AI-assisted screening may be able to identify patients such as this one with severe nonproliferative DR with DME.

model instead identifies DME likely based on the presence of hard exudates in the fundus photographs. Its role is therefore not to replace OCT-based diagnosis but to identify patients who warrant further evaluation. A scalable CFP-based system could extend DME screening into primary care and teleophthalmology settings where OCT is unavailable, potentially reaching patients who might otherwise never see a retina specialist. Prospective studies are needed to determine how such systems perform in real-world screening workflows and whether they improve access to care and patient outcomes.

IMPROVING CLINICAL WORKFLOW: AI-ASSISTED OCT REFERRAL

Once patients enter a screening program, the challenge shifts from identifying possible disease to determining who truly requires specialist evaluation. CFP-based programs frequently rely on surrogate signs of DME and consequently generate many false-positive referrals. Zhang et al addressed this problem by evaluating an AI-based OCT system within a territory-wide DR screening pathway in Hong Kong.[2]

The investigators conducted a multicenter randomized clinical trial involving 276 patients whose CFP-based screening reports suggested possible DME. In the conventional pathway, all patients meeting the existing screening criteria were automatically referred for specialist DME evaluation based on their CFP screening reports, reflecting standard practice. In the AI-assisted pathway, patients also underwent OCT imaging, and ophthalmologists reviewed both the CFP screening report and the AI-generated OCT analysis report, which included DME probability scores to determine whether referral for specialist evaluation was warranted.

For ethical reasons, all participants ultimately underwent specialist evaluation, so the referral decisions in the AI-assisted pathway were effectively hypothetical. The false-positive referral rate decreased from 69.1% in the conventional pathway to 24.1% with the AI-assisted pathway, while referral sensitivity remained 100% in both groups. Importantly, there were no false negatives in the AI-assisted pathway.

Together, these findings suggest incorporation of AI-assisted OCT analysis has the potential to substantially reduce unnecessary referrals without compromising patient safety. The AI-assisted pathway also incorporated image-quality assessment, uncertainty flagging, and clinician

THE MOST USEFUL AI APPLICATIONS WILL BE THOSE THAT SOLVE PRACTICAL PROBLEMS FOR PATIENTS, CLINICIANS, AND HEALTH CARE SYSTEMS.

oversight, illustrating that the most effective implementation of AI may not be full autonomy, but a carefully designed human-AI workflow in which the algorithm supports routine triage while clinicians retain responsibility for uncertain or complex cases.

Because all participants ultimately underwent specialist evaluation, the study did not directly assess the effect of this workflow on real-world clinic use. Future implementation studies must determine whether these improvements translate into meaningful reductions in specialist workload and improvements in health care delivery.

TOWARD PRECISION MEDICINE: PREDICTING ANTI-VEGF RESPONSE

The next frontier extends beyond diagnosis and triage. Ideally, AI should not only identify patients with DME but also help predict how they will respond to treatment. Unlike prior AI models that relied primarily on OCT images alone, Yoon et al developed a multimodal deep-learning model that combined baseline OCT images, quantified lesion features, and clinical variables. Including age, diabetes history, prior ocular treatments, and systemic comorbidities helped the model predict anatomic response after three monthly anti-VEGF injections, reflecting a shift toward more individualized prediction of treatment response.[3]

The retrospective study included 107 patients, of whom 65 were classified as good responders and 42 as poor responders. During internal validation, the model achieved an area under the receiver operating characteristic of 0.962, accuracy of 0.953, sensitivity of 0.969, and specificity of 0.928. It also outperformed retina specialists and fellows in an experimental comparison, in which clinician accuracies ranged from 0.571 to 0.857.[3]

However, performance declined when the model was tested on two independent validation cohorts: a temporally separate holdout cohort from the same internal institution and an external cohort from a different hospital, with area under the receiver operating characteristics of 0.764 and 0.728, respectively. This drop illustrates the gap between promising internal results and reliable real-world generalization. Before such a model could influence treatment selection, it would require larger prospective multicenter validation and evidence that acting on its predictions improves outcomes.

Even so, the clinical use case is compelling. Earlier identification of patients unlikely to respond adequately to initial anti-VEGF therapy could support closer monitoring, earlier consideration of alternative treatment, and more realistic counseling, while potentially reducing prolonged exposure to an ineffective initial treatment strategy.

AI ACROSS THE DME CARE CONTINUUM

Together, these studies illustrate how AI in DME is beginning to mature across the continuum of care: from identifying patients who need evaluation and improving referral efficiency to personalizing treatment decisions. The most useful AI applications will be those that solve practical problems for patients, clinicians, and health care systems. Future progress depends on prospective validation, performance across diverse populations and devices, thoughtful workflow integration, cost-effectiveness, and sustainable reimbursement. Ultimately, success will be measured not by how well an algorithm performs in isolation, but by whether its use meaningfully improves access, efficiency, treatment decisions, and visual outcomes for patients with DME. ■

1. Bressler I, Aviv R, Margalit D, et al. Autonomous screening for diabetic macular edema using deep learning processing of retinal images. *Ophthalmology Science.* 2025;5(4). doi.org/10.1016/j.xops.2025.100722
2. Zhang S, Ran A, Zhou J, et al. An AI-based OCT system to detect diabetic macular edema: a prospective validation and noninferiority randomized clinical trial. *JAMA.* 2026;336;(3):215-223. doi.org/10.1001/jama.2026.7025
3. Yoon JM, Jung SH, Chung MJ, et al. Multimodal deep learning prediction of treatment response to anti-vascular endothelial growth factor in diabetic macular oedema. *Eye.* 2026;40:1454-1460. doi.org/10.1038/s41433-026-04505-1

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