



# Is early diagnosis always better?

AI-powered retinal scans can predict a patient's risk of developing a particular disease, writes **Kim Thomas**. But they raise ethical questions that are not easy to solve.

**I** imagine a routine patient consultation. You carry out the standard eye examination, then use your optical coherence tomography (OCT) device to scan the patient's retina. A few minutes later, you provide a printout that tells the patient that they have a raised risk of developing heart disease in the next five years, and you recommend they consult their GP. You haven't seen visible cardiovascular structural change; rather real-time OCT analysis has utilised an artificial intelligence (AI) review of the vessels to predict a clinically significant increased risk profile.

This scenario is – potentially – just a few years away, thanks to the new discipline of ophthalmics. The term was coined as recently as 2019 by Professor Alastair Denniston, Consultant Ophthalmologist at University Hospitals Birmingham NHS Foundation Trust, and a pioneer in the field.

Ophthalmics combines a number of technologies, including high-resolution imaging such as OCT and fundus photography, AI and large-scale datasets such as INSIGHT and UK Biobank. By training algorithms on databases of millions of eye images and comparing them with images of other organs, as well as data from patient records, it is possible to observe a correlation between changes in the eye and particular health conditions.

As Alastair says: "The power of ophthalmics is that we can look into your eye and see signals of your present and future health. We've been able to do this to some extent for more than 100 years, seeing changes in blood pressure and diabetes, but technology is enabling us to see things that were previously invisible." These include early signs of diseases such as stroke and Alzheimer's.

### GENETIC PROFILES

We know there is an appetite among the public for information about how their genetic profile affects their health risk. Consumer genetic testing products such as 23andMe, which provide an easy-

to-understand risk profile based on an individual's genome, have proved popular (see *The growth of health-based genetic testing in the UK*). Ophthalmics offers the prospect of a very simple, non-invasive test that could be carried out as part of a regular sight test and provides the patient with their individual risk profile – alerting them to the likelihood, for example, that in the next five years they will have a stroke.

Research by Rudnicka et al (2022) and Poplin et al (2018) has shown that retinal imagery can be used to predict the risk of cardiovascular disease (CVD). The biggest ophthalmics study to date, however, has demonstrated a correlation between changes in the retina and the likelihood of developing dementia or Parkinson's (see *The AlzEye project overleaf*).

Ophthalmics also has uses beyond indicating risk, including monitoring degenerative diseases such as multiple sclerosis (MS) and Alzheimer's. "We now know that Alzheimer's is associated with optic nerve and retinal changes, and these could be a really helpful signal for us to know early on whether a drug is working or not," Alastair says. "This could be used in early-phase clinical trials to help screen which drugs should be taken through to a full clinical trial."

It may not be long before commercial products based on ophthalmics arrive in the UK. Siegfried Wagner, Senior Research Fellow at the Institute of Ophthalmology, University College London, says that the first medical device algorithms to predict a five- or 10-year risk of developing CVD are now being approved by regulators in Asia.



The justification for CVD models is straightforward

There is discussion about the regulatory framework relating to AI in the UK opening up – if an AI medical device has been approved for use in Canada or Japan, for example, the regulatory status would automatically be recognised in the UK. "If you are registered in one of those countries you could then enter the UK market," says Daniel Hardiman-McCartney MBE FCOptom, Clinical Adviser to the College.

### COMMUNICATING RISK

The first products are likely to be those that offer patients a prediction of their likelihood of developing CVD, followed by those that predict the risk of developing diseases such as dementia or MS. They are emphatically not diagnostic, says Siegfried. "Instead, you're someone who is flagged as being at high risk, so you should have further tests. And then those further tests give you a better idea of your risk."

This raises difficult ethical questions, however. There are clear benefits to screening for CVD, as Siegfried points out: "The justification for CVD models is relatively straightforward. It's the number one cause of mortality and morbidity in the world, and there is treatment that can reduce mortality, whether it's statins or blood pressure tablets."

For other diseases, where there are few preventive actions a patient can take, the benefits are less obvious. A patient told that they have an elevated risk of Alzheimer's is simply likely to become more anxious. "There's an argument you should only screen for something if there's an intervention you can apply to reduce the risk of someone having that problem," Daniel says.

For optometrists, whose expertise lies in eyes rather than in general health, there are other issues to consider, such as how likely a product is to provide false positives or false negatives. The consequences of wrongly telling someone either that they don't have an increased risk of dementia, or that they do, can be "profound," says Daniel. "What if they completely turn their lives upside down?"



## The AlzEye project

The AlzEye project, led by Dr Pearse Keane of Moorfields Eye Hospital and Dr Siegfried Wagner of University College London, is the most ambitious ophthalmology study to date. The project studied 350,000 people over the age of 40 who attended Moorfields between 2008 and 2018. Of these, about 186,000 also had hospital admission records. The researchers linked the six million retinal scans of this group with their hospital admissions data.

So far, the research has found that it is possible to detect early signs of CVD, Alzheimer's and MS in retinal scans, as well as signs of neurodegeneration in the scans of people with schizophrenia. Most recently, the study has identified markers in eye scans that indicate the presence of Parkinson's in patients on average seven years before clinical presentation.

The team repeated the analysis using the Biobank database of healthy volunteers, which confirmed the findings.

to embrace a new role as a provider of general health information. Yet the alternative, in which unlicensed providers offer these tests, is decidedly unappealing.

"Surely it would be much better for a healthcare professional to be delivering this information and analysis than a non-healthcare professional," says Daniel. "If it's an optometrist doing the scan and analysis, helped by ophthalmology and AI, they are a registered healthcare professional, they have an obligation to follow the evidence and they have a duty of care to ensure that they give sufficient information about the tests."

In short, our understanding of the future potential of ophthalmology is continuing to evolve, and the impact of how, if and when the optometrist should communicate any risk to the patient needs full consideration. 🤖

What if they commit suicide? What if they spend their life savings on a cruise and it turns out that they don't have that risk?"

Patients' concerns may range from seeing their insurance premiums go up in response to a raised risk of heart disease, for example, to the distress of an unexpected result, such as finding that the eye scan has picked up very early signs of Parkinson's. This is new territory for optometrists, who will need training in how to explain test results in a clear and empathic way. It is also a good opportunity to participate in more varied CPD around general health conditions and systemic issues.

As Daniel says: "It's very difficult to communicate risk and probability in a meaningful way to the general population." There are options, however, such as the use of Cates plots ("smiley face plots"), which are a "nice clear way of understanding probability of positive outcomes and bad outcomes". The job of a clinician, he adds, is that of an educator rather than a decision-maker.

The other significant question is how the information is used. GPs and hospital specialists may not welcome an influx of worried patients who have been told they have a raised risk of either heart disease or neurological disease, particularly considering the strain the

NHS is under. "It may be that the NHS says that it's not cost-effective, it can't be done," says Daniel.

## EVOLVING OPHTHALMOLOGY

Ophthalmology technology doesn't necessarily have to be a burden on the NHS. Danish company Retinalyze ([retinalyze.com](https://retinalyze.com)) is trialling a product in the UK that detects signs of eye disease from a fundus photographs and OCT scans. Retinalyze scans and returns images within 30 to 45 seconds, and uses traffic-light colour coding to highlight areas of potential disease, with images being available for the optometrist to review before the patient goes into the consultation.

"We like to think we're the optometrist's best friend, as Retinalyze will support decision-making and, in many cases, identify early signs of eye disease before the human eye can," says Chris Flynn, Retinalyze's UK Lead.

Once the optometrist has assessed the risk, Retinalyze provides the option to refer the image directly to an ophthalmologist for a second opinion, returned within 24 hours, which reduces the rate of false referral by about 50%, according to internal Retinalyze data.

It may be a few years before there is an AI product in every optometrist's premises, and some may feel reluctant

## The growth of health-based genetic testing in the UK

The popularity of consumer genetic tests is growing. By June 2020, one of the most popular companies, 23andMe, had sold more than 250,000 genomic testing kits in the UK (UK Parliament, 2021).

As well as alerting people to specific health risks (for example, of developing heart disease or cancer), the tests claim to be able to diagnose rare genetic conditions that might otherwise take significant effort to identify.

There are concerns, however, both that the tests sometimes offer inaccurate findings, and that they offer no follow-up advice or counselling. One study found that the tests fail to identify 89% of those at risk of developing cancer or heart disease, and wrongly tell 5% of people that they will develop a major illness (Hingorani et al, 2023).