

Fight for Sight to maximise impact by funding solutions-focused research in priority eye conditions

BY ROD MCNEIL

Fight for Sight aims to stop sight loss by funding pioneering research. **Rod McNeil** takes a look at the Primer Fellowship Awards programme, which provides funding for up to £60,000 for individuals to undertake vision-related research for one year.

Among the global population who were blind in 2015 (36.0 million [80% uncertainty interval 12.9 million to 65.4 million]), the leading causes of blindness (crude prevalence) among all ages was cataract, followed by uncorrected refractive error, glaucoma, age-related macular degeneration (AMD), corneal opacity, trachoma and diabetic retinopathy [1]. Figure 1 summarises prevalence estimates for blindness in 2015 by cause in Western Europe for adults aged 50 years and older.

The main causes of blindness certifications in England and Wales in adults of working age (16-64 years) in 2009-2010 were inherited retinal diseases, diabetic retinopathy / maculopathy and optic atrophy [2]. These together accounted for almost half of all blindness certifications. Updated figures on causes of sight impairment in England and Wales for April 2012-March 2013 show that AMD remains the leading cause of certifications for sight impairment in England and Wales (both severe sight impairment or blindness, and partial sight impairment) [3]. The three leading causes of severe sight impairment were degeneration of the macula and posterior pole, glaucoma and hereditary retinal disorders.

Currently over two million people in the UK are affected by sight loss, a figure set to double by 2050. Fight for Sight's ambition is to stop sight loss by funding pioneering research and maximising the charity's impact by providing information, influencing opinion and shaping policy. To ensure it delivers, it says its approach will be patient-centric, solutions-focused and evidence-based.

Fight for Sight provides research funding

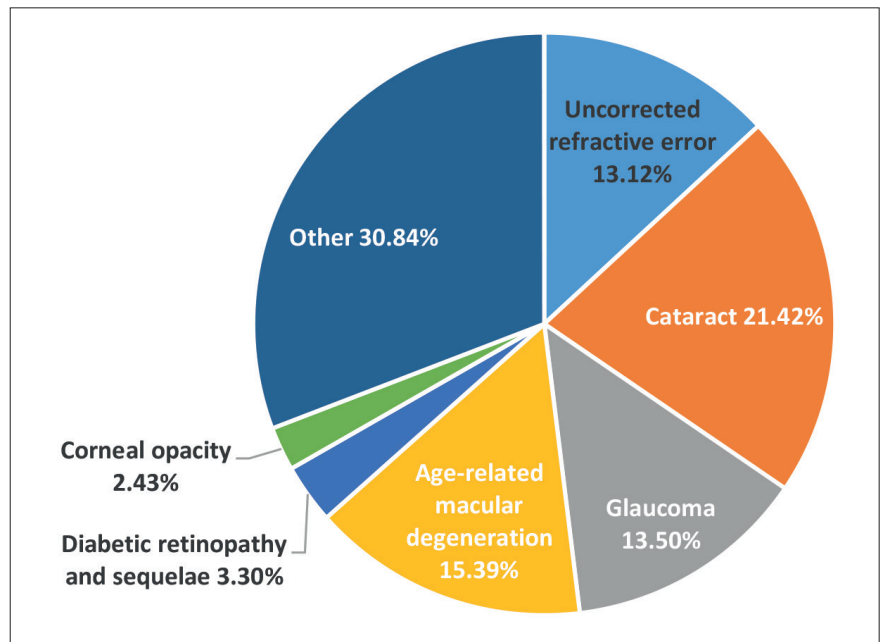


Figure 1: Western Europe: projected prevalence of blindness (VA <3/60 in the better eye) by cause among adults ≥50 years [1].

of around £3-4 million each year, with funding available through open competition and peer review. The eye charity spent £16.5 million on research over the five years to March 2017 and remains intensely ambitious to increase its charitable spending. As of 31 March 2017, the charity's overall research commitments amounted to £7.9m for 159 research projects at 44 different institutions across the UK.

Fight for Sight research has so far resulted in breakthroughs including the identification of new genes responsible for glaucoma, the world's first clinical trial of a gene therapy for choroideremia and the design of a new test that can detect the early stages of sight loss in AMD.

When awarding grants, the potential

impact that the research may have for patients and the scientific quality of applications are the primary determinants.

In March 2017 the Board approved a new Five Year Plan 2017 to 2022 and the charity is now in the early stages of implementation. The key development is a heightened focus on outcomes, and a desire to enable a more flexible and proactive approach to the allocation of research funding. It has determined its key areas of focus and identified where it believes the real opportunities for maximising impact lie. This builds on the insights gathered from patients about focusing on outcomes that really matter to them. This, coupled with the development of an integrated on-going brand and fundraising campaign, will help

raise the profile of the charity with the aim of generating greater awareness and income over the next five years.

Priority eye conditions

Michele Acton, CEO of Fight for Sight, explained that the charity's new research strategy is to focus funding largely on four key strategic areas to maximise the impact of the work it supports: AMD, glaucoma, inherited eye diseases and sight loss related to other comorbidities, such as diabetes or stroke. Open call funding will still apply for all eye conditions. The top ten priority

research outcomes established by the James Lind Alliance Sight Loss and Vision Priority Setting Partnership for common eye conditions are summarised in Table 1 [4].

Michele Acton, said: "Fight for Sight's vision is simple – we want to stop sight loss. Our main way of achieving this is through funding medical research and finding innovative ways to treat eye conditions. We look forward to supporting more researchers who between them hold the answers to creating a future where everyone sees."

New vision research career route for young clinician scientists and ophthalmology trainees

The Primer Fellowship Awards programme has been established in partnership with The Royal College of Ophthalmologists and The Royal Society of Medicine and provides funding for up to £60,000 for individuals to undertake vision-related research for one year. The Fight for Sight / Royal College of Ophthalmologists Primer Fellowship Award is designed to fund trainee ophthalmologists at an early stage

Table 1: Top 10 research questions for AMD, glaucoma, inherited retinal diseases and retinal vascular diseases, from the Sight Loss and Vision Priority Setting Partnership^a.

| Priority | Age-related macular degeneration | Glaucoma | Inherited retinal diseases | Retinal vascular diseases |
|----------|--|---|---|---|
| 1. | Can a treatment to stop dry AMD progressing and / or developing into the wet form be devised? | What are the most effective treatments for glaucoma and how can treatment be improved? | Can a treatment to slow down progression or reverse sight loss in inherited retinal diseases be developed? | What are the best methods to prevent retinopathy of prematurity? |
| 2. | What is the cause of AMD? | How can loss of vision be restored for people with glaucoma? | How can sight loss be prevented in an individual with inherited retinal disease? | How can sight loss from diabetic retinal changes be prevented and reduced? |
| 3. | How can AMD be prevented? | How can glaucoma be stopped from progressing? | Is a genetic (molecular) diagnosis possible for all inherited retinal diseases? | What are the predictive factors for the progression to sight-threatening diabetic eye disease? |
| 4. | Are there ways of restoring sight loss for people with AMD? | What can be done to improve early diagnosis of sight-threatening glaucoma? | What factors affect the progression of sight loss in inherited retinal diseases? | Is there a way to improve screening of premature babies for retinopathy of prematurity? |
| 5. | Can the development of AMD be predicted? | What causes glaucoma? | What causes sight loss in inherited retinal diseases? | Can an effective long lasting treatment for diabetic macular oedema, both ischaemic and non-ischaemic, be developed? |
| 6. | What is the most effective way to detect and monitor the progression of early AMD? | What is the most effective way of monitoring the progression of glaucoma? | What is the most effective way to support patients with inherited retinal disease? | Can a retinal vein occlusion be predicted and prevented? |
| 7. | What factors influence the progression of AMD? | How can glaucoma patients with a higher risk to progress rapidly be detected? | Can the diagnosis of inherited retinal diseases be refined so that individuals can be given a clearer idea about their specific condition and how it is likely to progress? | Can new non-invasive treatments be developed to slow down the progression of diabetic retinopathy? |
| 8. | Can a non-invasive therapy be developed for wet AMD? | Why is glaucoma more aggressive in people of certain ethnic groups, such as those of West African origin? | What is the relationship between sight loss and mental health for people with inherited retinal diseases? | What are the barriers that prevent diabetic patients having regular eye checks? |
| 9. | Can dietary factors, nutritional supplements, complementary therapies or lifestyle changes prevent or slow the progression of AMD? | How can glaucoma be prevented? | Would having a treatment for an inherited retinal disease preclude a patient from having another treatment? | What rehabilitation programmes are best for the management of distorted vision from retinal diseases? |
| 10. | What are the best enablement strategies for people with AMD? | Is there a link between treatment adherence and glaucoma progression and how can adherence be improved? | With regard to inherited retinal diseases what is the role of prenatal and preimplantation diagnosis in helping parents make informed choices? | What is the efficacy and safety of anti-vascular endothelial growth factor (anti-VEGF) agents in the treatment of retinopathy of prematurity? |

Abbreviations: age-related macular degeneration, AMD; anti-vascular endothelial growth factor, anti-VEGF.

^a Adapted from: Rowe F, Wormald R, Cable R, et al. [4]

in their career in order to aid the successful applicant to produce a strong application for Clinical Research Training Fellowships in the future. The Fight for Sight / Royal Society of Medicine Primer Fellowship Award supports trainee ophthalmologists, ophthalmic nursing or allied health professional graduates (including optometrists and orthoptists) to undertake vision research.

The aim is to attract the brightest minds amongst eye health professionals to ophthalmic and vision research. This will better equip those who wish to embark on research fellowships in the future, leading to better and more impactful research, said Ms Acton. Applicants are required to make a written application followed by an interview. The science has to be of good quality, the research project should fit the aims and scope of the fellowship award, and be structured with the right level of ambition for a 12-month project, added Ms Acton.

The first two 2017 recipients of the Primer Fellowship Awards will undertake research into corneal infections and vision loss in people living with dementia, respectively:

Dr Darren Shu Jeng Ting, an Ophthalmologist Specialist Registrar from Sunderland Eye Infirmary, for research into new treatments for corneal infections. This research will focus on the development of novel human-derived hybrid antimicrobial peptides (AMPs) which have shown promise as potential therapeutic agents.

Dr Marianne Coleman, a Research Orthoptist at the University of Surrey, to undertake research to help determine whether binocular vision and pupil response testing should be included in dementia-friendly eye-testing guidelines. More accurate diagnosis of visual problems could significantly improve the quality of life for people with dementia.

Further details about these research projects are provided in an accompanying box panel. Applications for the 2018-19 Primer Fellowship Awards will be open from August 2018.

Advancing development of novel therapeutic approaches and improved diagnostics

Dr Neil Ebenezer was appointed in May 2018 as Fight for Sight's Director of Research, Policy and Innovation. He will lead the charity's programme of developing future solutions for those who are or may be affected by sight loss, taking forward a revised research strategy, providing direction on policy and influencing initiatives while working towards delivering innovative solutions.

Primer Fellowship Awards 2017-2018*

Human hybrid antimicrobial peptides for ocular surface infection: from conceptualisation to translation

Damage to the cornea can lead to permanent scarring with subsequent visual impairment or blindness. Corneal blindness represents the fourth leading cause of blindness (5.1%) globally. Dr Darren Shu Jeng Ting aims to create and develop novel human-derived hybrid AMPs for a range of ocular surface infections. Different combinations of human-derived hybrid peptides will be designed and tested for antimicrobial efficacy and toxicity to host tissue. Developing a new class of efficacious and broad-spectrum antimicrobial agent could potentially improve the management and outcome of various types of ocular surface infection, including bacterial, fungal, viral and acanthamoeba infection.

Dr Ting notes: "Our work aims to create and develop novel antimicrobial peptides for treating bacterial corneal infection. Antimicrobial peptides are important components of our immune system and they have recently shown promise as a potential antimicrobial treatment due to their unique antimicrobial ability against a wide range of organisms with low risk of resistance. Therefore the successful development of these drugs will open up an exciting therapeutic avenue for infection because they could be potentially be used in other types of infection, such as fungal and acanthamoeba infection, for which the treatments are currently limited."

Binocular vision, visual function and pupil dynamics in people living with dementia

People with dementia experience difficulties coping with visual issues. Problems with binocular vision can lead to double vision, headaches and sore eyes and coupled with a loss of depth perception can increase the risk of falls and make hand-eye coordination tasks harder. Such problems are remedied with simple treatments, yet testing for this is not included in current dementia-friendly eye test guidelines.

Dr Marianne Coleman aims to determine how common binocular vision problems and pupil changes are in people with recently-diagnosed dementia. The relationship between changes in binocular vision, pupils, level of letter chart vision, and memory test scores over time will be examined to determine whether changes are related to changes in brain structure, or activation of brain areas used in vision for people with Alzheimer's disease.

Two hundred and forty people recently diagnosed with dementia (within the last 12 months) will be invited to have an eye check-up.

This project will show how often people with dementia experience binocular vision problems. If they are frequent, diagnosing / treating them could improve the quality of life for those affected. This research will show whether changes in depth perception, pupil responses and quality of vision relate to changes in memory, and brain structure / function. If they are related, these quick and non-invasive eye-tests will help to monitor dementia. This would justify whether binocular vision and pupil response testing should be included in dementia-friendly eye-testing guidelines.

"It's fairly common knowledge that dementia affects depth perception but there's hardly any research on it. It's great that Fight for Sight aren't afraid to fund something a bit different."

*Extracts drawn from Fight for Sight blog reports by winning applicants

Commenting on the Primer Fellowship Awards, Dr Ebenezer said: "We need to nurture the development of the future generation of clinicians committed to eye research and treatment or prevention of sight loss. The Primer Fellowship Award programme is about helping create clinician scientists of the future and is particularly suited to those who are at an early stage in their career and are looking to develop a career path in ophthalmic and vision research.

"The charity aims to advance its impact on reducing the huge burden of sight loss, both in terms of the development of novel therapeutic approaches but also with improved diagnostics. We are at an exciting time in the evolution of eye research, with advances progressing with small molecules, gene therapy and promising work with stem cells. Future developments include clinical applications of artificial intelligence and machine learning, the latter for example being used in retinal pattern recognition

for improved detection, prognosis and possible therapeutic insights.”

Enhancing impact via partnerships and collaborative funding

In addition to this research funding initiative, Ms Acton said that the charity is forging different partnerships and collaborative funding approaches in newer areas.

By 2020, it is predicted almost 700,000 people in the UK will have late-stage AMD and this number is predicted to double by 2050. Fight for Sight, Blind Veterans UK, the Macular Society and Scottish War Blinded have formed Action Against AMD to increase the funding for research into the condition and specifically to help develop an intervention that stops people losing their sight from AMD.

BenevolentAI, the largest private artificial intelligence company in Europe and one of the world’s top five private AI companies, is collaborating with Action Against AMD in a partnership to find a potential cure for AMD.

BenevolentAI is a global leader in the development and application of artificial intelligence (AI) for scientific innovation, including accelerating drug discovery and development. The company’s deep learning linguistic models, knowledge graph and algorithms will be applied to create a better understanding of AMD, generate new insights and identify promising new research areas for treating AMD. The company uses AI technology to perform sophisticated reasoning on over 50 billion ingested and contextualised facts to extract knowledge and generate complex insights into the cause of disease and then quickly generate drug candidates at scale. The technology is also able to decipher the molecular process of disease and link these disease signatures within patients to ensure that the best drug candidate is given to the best patient responders.

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