

Patient and public participation shapes biomedical research and access priorities in eye health

BY ROD MCNEIL

Patients, clinicians and clinician-scientists play a valuable role in shaping the future of vision research. Limited funding demands targeted research initiatives that ultimately will shape health policy and practice to secure progress in improving patient outcomes in eye health. This review outlines several initiatives designed to better identify and prioritise unanswered questions about the prevention, diagnosis and treatment of sight loss and eye conditions.

National priority setting partnership in action

Patients and health experts alike each add a valuable sense of reality and common sense based on direct experience in addressing treatment uncertainties. Top priorities for eye research were identified by the Sight Loss and Vision Priority Setting Partnership (SLV-PSP) last year, as part of a national collaborative initiative involving participation of patients, carers and eye health professionals [1]. In a rare initiative, those directly affected by eye conditions actively contributed to the research debate. Involving a prospective survey with support from the James Lind Alliance, a total of 2200 individuals took part, 65% of respondents having sight loss and / or an eye condition. Following final prioritisation workshops, the partnership identified a series of unanswered questions considered of greatest importance to patients, carers and eye health professionals (Table 1).

The aim is to better inform funders, researchers, clinicians and the public about the key areas identified by consumers as to where they believe the research money should be spent. Since then and up to September 2014, Fight for Sight, a UK charity dedicated

to funding eye research, has awarded grants totalling more than £3 million for 46 projects directly addressing research priorities in 10 of the 12 eye conditions considered by the priority setting partnership. The majority of funds support research focused on priorities in the top five of each ocular disease category. The research charity acknowledges that gaps remain and more funding is needed to address the priorities fully.

In the cataract category, priority research questions identified by the SLV-PSP include the potential for improvements in cataract surgery outcomes and the safety and efficacy of laser-assisted cataract surgery. The National Institute for Health Research (NIHR) has awarded a major grant of £1.37 million to fund a 42-month clinical trial designed to evaluate the safety and effectiveness of femtosecond laser-assisted cataract surgery versus manual phacoemulsification cataract surgery for adults with visually significant cataract (the FACT trial). The study will be conducted at two secondary care centres, a community hospital in North London and a second district general hospital. A total of 808 adults

with age-related cataract will be enrolled and randomly assigned to either standard cataract surgery using phacoemulsification or laser-assisted cataract surgery (404 per study group). Outcomes will be assessed at four and 12 months following surgery.

Supporting the research programme, investigators – led by Mark Wilkins, Moorfields Eye Hospital, London – note that following standard cataract surgery, 91% of subjects achieve a Snellen visual acuity (VA) of 6/12 and 46% achieve Snellen 6/6 (logMAR 20/20 equivalent, so-called normal vision). Complications such as posterior capsule rupture / vitreous loss, delayed healing and retinal detachment can, however, affect recovery and impair long-term outcomes. The overall complication rate for cataract surgery is put at 7.4%, with the surgical learning curve associated with a higher incidence of complications. The FACT trial research group say that the potential advantages of femtosecond laser-assisted surgery include better visual outcomes through greater precision and reproducibility and improved safety. The cost of femtosecond laser systems may be mitigated by fewer complications, less repeat surgery and better outcomes, but supporting evidence is still needed.

“Provision of effective and accessible eye care services is key for effectively controlling visual impairment including blindness.”

The big picture: global plan to cut prevalence of avoidable vision impairment
The World Health Organization (WHO) estimates that there were 285 million people visually impaired in 2010, of which 39 million were blind. Estimates from WHO further suggest that 80% of all causes of visual impairment are preventable or curable. Provision of effective and accessible eye care services is key for effectively

Table 1: Research priorities identified by Sight Loss and Vision Priority Setting Partnership.

Eye disease / condition	Illustrative priorities in treatment, prevention and diagnosis
Age-related macular degeneration	<ul style="list-style-type: none"> Preventing progression of dry AMD to wet AMD Causation and genetic factors responsible for development and progression of AMD Restoration of AMD-related sight loss Non-invasive treatment for wet AMD Detection, diagnosis and progression monitoring
Cataract	<ul style="list-style-type: none"> Preventive measures, improvements in cataract surgery outcomes, safety and efficacy of laser-assisted cataract surgery, prevention of posterior capsule opacity and secondary cataract
Childhood-onset eye disorders	<ul style="list-style-type: none"> How can cerebral visual impairment be identified, prevented and treated in children? Improved screening and surveillance from the antenatal period through to childhood to ensure early diagnosis of impaired vision and eye conditions Amblyopia treatment and better short- and long-term outcomes
Corneal and external	<ul style="list-style-type: none"> Can new therapies such as gene or stem cell treatments be developed for corneal disease? Optimal management of dry eye and potential new treatment strategies Can treatments to save sight from microbial keratitis be improved? Improved outcomes in corneal transplantation
Glaucoma	<ul style="list-style-type: none"> What are the most effective treatments for glaucoma and how can treatment be improved? Optic nerve regeneration Improved early diagnosis of sight-threatening glaucoma and progression monitoring
Inherited retinal	<ul style="list-style-type: none"> Can a treatment to slow down progression or reverse sight loss in inherited retinal diseases be developed? Prevention of sight loss in people with inherited retinal disease Possibility of genetic testing / diagnosis Risk factors for progression of sight loss in inherited retinal disease
Neuro-ophthalmology	<ul style="list-style-type: none"> What is the underlying cause of optic nerve damage in optic neuropathies? What are the most effective treatments for Leber's hereditary optic neuropathy and anterior ischaemic optic neuropathy Comparative effectiveness of hyperbaric oxygen therapy vs. Idebenone treatment for Leber's hereditary optic neuropathy
Ocular oncology	<ul style="list-style-type: none"> What can be done to help ocular cancer sufferers? Potential for gene-based targeted therapies Role of immunotherapy in metastatic ocular melanoma
Ocular inflammatory	<ul style="list-style-type: none"> What are the most effective treatments for ocular and orbital inflammatory disease? Causes of thyroid eye disease and birdshot retinopathy Prevention of further occurrences of retinal damage caused by toxoplasmosis
Refractive error & ocular motility	<ul style="list-style-type: none"> What factors influence the development of refractive error? Presbyopia prevention Prevention of both congenital and acquired nystagmus
Retinal vascular	<ul style="list-style-type: none"> What are the best methods to prevent retinopathy of prematurity? Predictive factors for the progression to sight-threatening diabetic eye disease Improved screening of premature babies for retinopathy of prematurity Effective long-lasting treatment for diabetic macular oedema (DMO), both ischaemic and non-ischaemic – potential for a fixed combination slow release monotherapy treatment for DMO
Vitreoretinal & ocular trauma	<ul style="list-style-type: none"> How can surgical techniques be improved to save sight for eyes damaged by injury? Improvements in the success rate of retinal detachment surgery Improved interventions for vitreous opacities / eye floaters

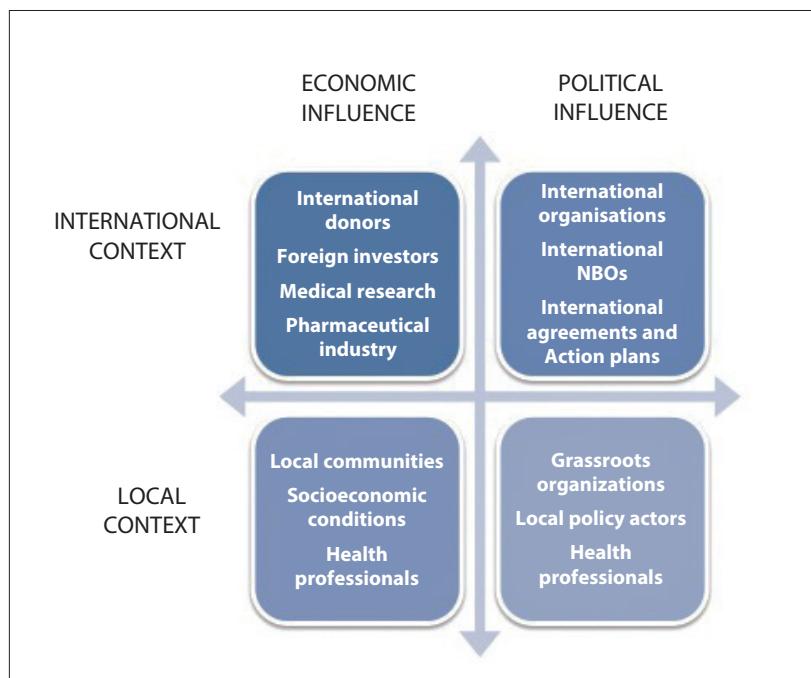


Figure 1: Investing in eye health – securing the support of decision-makers, WHO 2012.



Figure 2: WHO Eye Care Services Assessment Tool (2015).

controlling visual impairment including blindness. The WHO global eye health action plan for 2014-2019 targets universal eye health coverage through the provision of comprehensive eye care services integrated into the national health system at all levels (primary, secondary and tertiary) [2].

The action plan aims to reduce avoidable visual impairment as a global public health problem and to secure access to rehabilitation services for the visually impaired. It incorporates a global target of a 25% reduction in the prevalence of

avoidable visual impairment by 2019, from a baseline global prevalence estimated at 3.18% in 2010. This translates into a target prevalence of 2.37% by 2019. The two principal causes of avoidable visual impairment are cataract and uncorrected refractive errors, accounting for 75% of all visual impairment. By 2019, WHO estimates that 84% of all visual impairment will be among people aged 50 years or more.

All 194 WHO member states and international partners are encouraged to focus on the development of

innovative approaches to the prevention and treatment of eye diseases to help secure this goal. In the area of health research, WHO highlights two principal activities:

- 1) biomedical research for the development of new and more cost-effective interventions for major causes of visual impairment; and
- 2) operational research for overcoming barriers in service provision and uptake, and improvement of public health approaches and strategies.

Guidance for public eye health research from WHO includes eye health research priorities, information on causes and magnitude of visual impairment, guidance on stakeholder analysis for the development of national eye health plans, as well as data collection and monitoring (Figure 1). An Eye Care Service Assessment Tool is currently being developed to assist the introduction of structured national eye health action plans (Figure 2).

International partners include the International Council of Ophthalmology and International Agency for the Prevention of Blindness (IAPB). The latter represents an alliance of civic organisations, corporations and professional bodies promoting eye health through advocacy, knowledge and partnerships. It defines avoidable blindness as blindness which could be either treated or prevented by known, cost-effective means. In 2010 the IAPB developed via a VISION 2020 workshop a research plan and identified research areas and priorities for improved control of avoidable visual impairment and blindness over the next 10 years [3].

For the Western Pacific Region, the proposed top ten research priorities embrace diabetic retinopathy (to optimise management, quality of treatment), glaucoma (to determine optimal treatments for different disease stages and to improve health workforce capacity), cataract (to optimise utilisation and quality of cataract surgeries) and refractive error (to increase service delivery coverage). Table 2 lists the proposed top ten global research priorities (no order of precedence is implied).

WHO and its partners provide a good resource of supporting documentation to help prepare persuasive arguments to win support for grant applications, get research funded, and engage with policy decision-makers. The latter want to know the size and underlying cause of the problem, the proposed possible

Table 2: Proposed top ten global research priorities (IAPB).

Diabetic retinopathy	Research to develop and test new paradigms for earlier treatment of DR relevant to resource-poor settings
Diabetic retinopathy	Research to develop and test interventions and systems effective in promoting and monitoring life-long adherence to treatment of diabetes and diabetic eye disease within the non-communicable disease framework
Open-angle and angle closure glaucoma	Research to develop low cost and effective modalities and systems for identifying, treating and monitoring glaucoma as well as promoting adherence with care in resource-poor settings
Childhood blindness	Research to demonstrate and evaluate a model for populations of up to 10 million at all levels of care which is comprehensive and integrated into child health programs (includes evaluation of interventions to improve referral, uptake, coverage and follow-up)
Low vision	Research to evaluate models and content for low vision care across the life spectrum as part of comprehensive health services in resource-poor settings
Advocacy / Impact	Research to demonstrate and disseminate the economic, social and quality of life benefits of eye care to individuals and societies
Health systems	Research on the governance and structures within strengthened national healthcare and education systems necessary to optimise the delivery of, and demand for, cataract, trachoma and refractive error services, leading to elimination of blindness and visual impairment from these conditions
Health systems	Research on the governance and structures within strengthened national healthcare and education systems necessary to optimise the delivery of, and demand for, comprehensive eye care services across the life spectrum
Primary health	Research on how to create and strengthen the systems for, and determine the benefits of, integrating Primary Eye Health into Primary Health Care and community development approaches
Planning and monitoring progress	Research to develop and test indicators and information systems to monitor eye care service outcomes at the program, local, national and regional levels, as part of integrated health management information systems

Table 3. The age-standardised prevalence rates of blindness for population aged 50 years or more for the world and for regions 1990-2010.

	World	East & South East Asia	High Income Countries	Latin America	North Africa + Middle East	South & Central Asia	Sub Saharan Africa
1990	2.95%	3.10%	0.92%	3.10%	6.96%	5.23%	6.11%
1995	2.73%	2.79%	0.82%	2.72%	6.30%	4.87%	5.64%
2000	2.46%	2.40%	0.71%	2.40%	5.52%	4.50%	5.20%
2005	2.17%	1.97%	0.63%	2.10%	4.67%	3.97%	4.73%
2010	1.93%	1.70%	0.57%	1.86%	3.97%	3.46%	4.25%

solution and supporting information on cost-effectiveness and value.

While absolute numbers of worldwide blindness (<3/60 in the better eye) remain unchanged at around 32 million, there has been a marked and steady decline in age-standardised prevalence rates of blindness over the two decades to 2010, both globally (from 0.6% in 1990 to 0.47% in 2010) and in each major geographic region (Table 3) [4]. Improved public health and development of improved eye health services may explain some of this

decline. A systematic analysis of causes of vision loss worldwide found that leading causes of blindness and visual impairment were cataract, uncorrected refractive error and macular degeneration [5]. The authors estimated that, for 2010, 65% of 32.4 million blind people and 76% of 191 million people with moderate to severe visual impairment worldwide had a preventable or treatable cause. In high-income countries, the Vision Loss Expert Group notes that macular degeneration has become the most important cause of blindness, while

glaucoma and diabetic retinopathy were the fourth and fifth most common causes of blindness in both high-income regions and central / eastern Europe, in 1990 and in 2010 [6].

Turning research priorities into relevant studies and rigorous evaluation requires funding. Levels of research activity have been climbing since a landmark 10/90 report more than two decades ago showed that less than 10% of global research spending was targeted at those diseases and conditions responsible for more than 90% of the global ill-health burden

[7]. But, as WHO cautions, high quality research doesn't necessarily translate into improved health if the subsequent findings are not properly implemented. The results need also to be clinically relevant and appropriately valued over existing technologies or standards of care.

NHS Call to Action for improved eye health and prevention of sight loss – seven key themes identified

NHS England this year launched a Call to Action campaign encouraging patients, professionals and the general public to get involved via consultation in a debate about the provision of eye health services. It focuses on prevention, early accurate detection by primary care services and effective management in the community.

Consultation closed in September 2014.

In its response, the Royal College of Ophthalmologists emphasises that, to improve capacity and reduce the risk of sight loss, patients must be seen by the appropriate medically qualified professional in the right location and at the right time. Its recommendations call for evidence-based financial decisions by Clinical Commissioning Groups and NHS England to optimise eye care services for the entire population and to improve access for disadvantaged and hard to reach groups.

Core recommendations include: identify need (gather accurate and timely data), ensure adequate quality standards, train the workforce for extended roles, utilise consultant-led pathways, develop relationships across teams inside and outside of hospital settings, and provide adequate communication systems and IT that help monitor and assess patient follow-up care. The College calls for NHS England "to remove arbitrary tariffs that 'reward' new referrals but put at risk the safety of existing patients with known eye diseases who require follow-up appointments".

The Lay Advisory Group of the Royal College of Ophthalmologists highlights the need for more ophthalmologists and allied healthcare professionals to ensure effective clinical provision with a focus on patient outcomes. The Lay Group further supports wider initiatives designed to extend ophthalmic knowledge about eye disorders amongst general practitioners. Effective screening for

diabetic retinopathy, cataracts and age-related macular degeneration (AMD) may also help address avoidable sight loss through timely detection and intervention.

An NHS England spokesperson told Eye News: "NHS England had over 400 responses from the call to action; alongside this we held a national workshop event for eye health for about 150 people. Local eye health network chairs held local call to action meetings with eye health professionals, patients and Clinical Commissioning Groups in their areas.

"From an initial review we have identified seven key themes including: improving IT and communications in the sector; developing clinical leadership and changing organisational cultures; developing pathways; making better use of professionals' skills; exploring new contractual opportunities; improving case management and improving accessibility to eye sight tests. Following the publication of the five-year forward view, we are taking stock, to ensure that our vision and action plans are consistent with the overall ambitions for the health system. We will want to understand the implications of new care models on eye health services as part of a more integrated primary care package for patients and hope to publish our vision in the coming months."

North America: improving quality through national ocular disease database

The Intelligent Research In Sight (IRIS) registry is a comprehensive database of eye diseases and conditions in the United States (US) that is currently used by more than 5,000 ophthalmologists. Aggregate data from the IRIS database, disclosed by the American Academy of Ophthalmology in October 2014 and covering 10.14 million patient visits and 3.94 million unique patients, reveal:

- 80% of patients without comorbidities have a vision of 20/30 or better within 90 days after cataract surgery
- 2% of patients without comorbidities require an additional procedure for complications within 30 days after cataract surgery (not including YAG laser)
- 28% of all patients seen by an ophthalmologist had at least one of the following conditions: AMD,

diabetic retinopathy (DR), primary open-angle glaucoma (POAG) or cataract surgery

- 16% of all patients had two or more of the following: AMD, DR, POAG or cataract surgery
- 10% of patients have AMD
- 46% of patients with AMD receive counselling about antioxidants when seen by an ophthalmologist
- 11% of all patients have primary open-angle glaucoma
- 6% of all patients have diabetic retinopathy.

The ophthalmology database is designed to provide the ability for clinical benchmarking at practice, regional and national levels, monitor patient care and evaluate outcomes across different populations for AMD, cataract surgery, diabetic retinopathy and retinal surgery, and help advance ongoing research initiatives.

Patients' participation for better quality of opinions on new medicines

Greater patient and public involvement in the assessment and appraisal of new medicines is also being encouraged by regulatory drug agencies. The European Medicines Agency (EMA) started in September 2014 a pilot project to involve patients in the assessment of the benefits and risks of medicines in the EMA's Committee for Medicinal Products for Human Use (CHMP). The project, which will run for an initial 12 months, reflects the work programme of the CHMP which recommends further integrating patients' views in the assessment process. Patients or carers with personal experience and knowledge of the particular disease / condition under evaluation will be invited to participate, adding to the quality of opinions given by the Agency's scientific committees. Patients will be involved upon request from scientific committees or on request from patients' organisations.

According to the EMA, the contribution from patients in benefit-risk discussions is expected to provide a unique and critical input based on their real-life experience of being affected by a disease and its current therapeutic environment. Patient involvement is also expected, says the EMA, to increase confidence and trust in the regulatory process and lead to greater transparency.

The UK's National Institute for Health and Care Excellence (NICE) recently completed consultation

on proposals regarding value based assessment, principally around proportional vs. absolute QALY shortfall, burden of illness impact and societal benefit metrics. NICE received responses from 121 organisations and individuals, including the life science industry, patient groups, academics and clinical and professional organisations.

There was no consistent response to any of the questions posed, notes NICE in its Board meeting report, while the majority of respondents in the industry and patient categories argued for keeping 'end of life' as a stand-alone modifier. There was broad support for the incorporation of burden of illness as one of the criteria to consider, but how it should be measured and valued is far from clear. It was recommended to the Board of NICE that no changes to the technology appraisal methodology should be made in the short-term. Further consideration is to be given to the use of QALY shortfall as a means of quantifying burden of illness and to the inclusion of wider societal benefit when evaluating new treatments or technologies.

References

- Rowe F, Wormald R, Cable R, et al. The Sight Loss and Vision Priority Setting Partnership (SLV-PSP): overview and results of the research prioritisation survey process. *BMJ Open* 2014;4(7):e004905.
- World Health Organization. Universal eye health: a global action plan 2014-2019. WHO 2013.
- Workshop Report: A VISION 2020 Workshop on Research for Global Blindness Prevention. http://www.iapb.org/sites/iapb.org/files/Research%20Workshop%20Report_1.pdf Last accessed November 2014.
- Bourne R, Ackland P. The Global Burden of Disease (GBD) 2010 Study. IAPB Briefing Paper, December 2013.
- Bourne RR, Stevens GA, White RA, et al; Vision Loss Expert Group. Causes of vision loss worldwide, 1990-2010: a systematic analysis. *Lancet Glob Health* 2013;1(6):e339-49.
- Bourne RR, Jonas JB, Flaxman SR, et al; Vision Loss Expert Group of the Global Burden of Disease Study. Prevalence and causes of vision loss in high-income countries and in Eastern and Central Europe: 1990-2010. *Br J Ophthalmol* 2014;98(5):629-38.
- The 10/90 report on health research 2000. Geneva, Global Forum for Health Research, 2000.



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- The WHO global eye health action plan aims to reduce avoidable visual impairment as a global public health problem.
- Health policy and practice are shaped by biomedical research into improved interventions and by operational research, the latter addressing barriers in service provision and uptake, and improvement of public health approaches and strategies.
- To improve capacity and reduce the risk of sight loss, patients must be seen by the appropriate medically qualified professional in the right location and at the right time.
- Greater involvement of patients and consumers of eye research in identifying research priorities can help add a valuable sense of reality and common sense based on direct experience.
- More ophthalmologists and allied healthcare professionals are needed in the UK to ensure effective clinical provision with a focus on patient outcomes.