The Effectiveness, cost-effectiveness and acceptability of Community versus Hospital Eye Service follow-up for patients with neovascular age-related macular degeneration with quiescent disease (ECHoES): a virtual randomised balanced incomplete block trial

Barnaby C Reeves,[1] Lauren J Scott,[1] Jodi Taylor,[1] Ruth Hogg,[2] Chris A Rogers,[1] Sarah Wordsworth,[3] Daisy Townsend,[4] Alyson Muldrew,[2] Tunde Peto,[5] Mara Violato,[3,6] Helen Dakin,[3] Heike Cappel-Porter,[1] Nicola Mills,[4] Dermot O'Reilly,[7] Simon P Harding[8] and Usha Chakravarthy[2]*

[1]Clinical Trials and Evaluation Unit, School of Clinical Sciences, University of Bristol, Bristol, UK
[2]Institute of Clinical Science, Centre for Experimental Medicine, Queen's University Belfast, Belfast, UK
[3]Health Economics Research Centre, Nuffield Department of Population Health, University of Oxford, Oxford, UK
[4]School of Social and Community Medicine, University of Bristol, Bristol, UK
[5]National Institute for Health Research Biomedical Research Centre, Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, London, UK
[6]National Institute for Health Research Health Protection Research Unit in Gastrointestinal Infections, University of Oxford, Oxford, UK
[7]School of Medicine, Dentistry and Biomedical Sciences, Queen's University Belfast, Belfast, UK
[8]Department of Eye and Vision Science, Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK

*Corresponding author

Declared competing interests of authors: Barnaby C Reeves reports receiving grants from the National Institute for Health Research Health Technology Assessment programme during the conduct of the study; the National Institute for Health Research grants (paying for his time through his academic employer) for various ophthalmological studies, including ones investigating wet age-related macular degeneration; personal fees from Janssen-Cilag outside the submitted work; and membership of the Health Technology Assessment Commissioning Board and Systematic Reviews Programme Advisory Group. In particular, he is a coinvestigator on the National Institute for Health Research-funded IVAN trial (a randomised controlled trial to assess the effectiveness and cost-effectiveness of alternative treatments to Inhibit VEGF in Age-related choroidal Neovascularisation; ISRCTN92166560) and is continuing follow-up of the IVAN trial cohort. Ruth Hogg reports she received grants and personal fees from Novartis Pharmaceuticals UK, outside the submitted work. Chris A Rogers reports she received a fee from Novartis Pharmaceuticals UK for a lecture unrelated to this work. Simon P Harding reports grants from the National Institute for Health Research during the conduct of the study. Usha Chakravarthy reports membership of the Health Technology Assessment Interventional Procedures Panel.

Published October 2016
DOI: 10.3310/hta20800

Scientific summary

ECHoES

Health Technology Assessment 2016; Vol. 20: No. 80
DOI: 10.3310/hta20800

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Scientific summary

Introduction

Neovascular age-related macular degeneration (nAMD) causes severe sight loss and blindness. Anti-vascular endothelial growth factor (VEGF) drugs (drugs that inhibit VEGF) are used to treat nAMD until the lesion becomes quiescent; patients are subsequently monitored for lesion reactivation at regular (usually monthly) Hospital Eye Service (HES) appointments. Regular review, often without treatment, uses clinic space and other resources and is burdensome to patients and carers. If community-based optometrists were able to monitor lesion reactivation with similar accuracy to ophthalmologists in the HES, there would be a strong case for devolving monitoring of patients with quiescent disease to community optometrists. Community optometrists have the necessary training to recognise nAMD but would need training to acquire and interpret optical coherence tomography (OCT) images to decide whether or not lesions have reactivated. Advantages of devolving monitoring to community optometrists could include having clinic capacity freed up for the overstretched NHS and less travel time for patients.

Objectives

The study had five objectives:

1. to compare the proportion of ophthalmologists' and optometrists' lesion classifications scored as 'correct' with the reference standard
2. to estimate the agreement, and nature of disagreements, between lesion classifications and between lesion components identified by optometrists and ophthalmologists
3. to estimate the influence of vignette clinical and demographic information on lesion classifications
4. to estimate the cost-effectiveness of monitoring of patients with quiescent lesions in the community by optometrists compared with ophthalmologists in the HES
5. to ascertain the views of patients, their representatives, optometrists, ophthalmologists and clinical commissioners on the proposed shared care model.

Methods

Study design

Vignettes were created which summarised information about participants in a previous study with eyes affected by nAMD. Vignettes described eyes twice in the course of treatment: once when the disease was inactive (baseline) and subsequently (index) when the disease was inactive or active. Vignettes included patients' demographic details, a summary of their nAMD history, clinical information, colour fundus and OCT images. Ophthalmologists in the HES and optometrists in the community classified index lesions as 'reactivated', 'suspicious' or 'quiescent'. Their classifications were scored as correct or not against a reference standard. A total of 288 vignettes were created; each participant assessed 42 vignettes, each vignette being assessed seven times within each professional group in a randomised balanced incomplete block design. Participants had to attend two webinar training sessions (each lasting approximately 1 hour) and correctly classify the lesion status of at least 75% of 24 training vignettes before they could enter the main phase of the trial.

Settings and participants

We recruited ophthalmologists and optometrists working in the UK through information circulated to members of the UK and Welsh medical retina groups and through optometry journals and forums. Ophthalmologists had to have 3 years' post-registration experience in ophthalmology, have passed part 1 of the Royal College of Ophthalmologists examination or hold the Diploma in Ophthalmology or equivalent and have experience within the age-related macular degeneration (AMD) service. Optometrists had to be fully qualified, be registered with the General Optical Council for ≥ 3 years, and not be participating in any AMD shared care scheme.

Interventions

The trial sought to emulate a conventional trial, comparing optometrists' and ophthalmologists' decision-making, except that vignettes, not patients, were assessed; therefore, there were no interventions. Participants received training before assessing vignettes.

Reference standard

Three medical retina experts independently assessed all 288 vignettes, scoring lesion components and classifying the activity status of the index images in the same way as participants. Rules for classifying a lesion as reactivated or quiescent from the assessment of lesion components were pre-specified. The experts collectively reviewed the subset of vignettes for which their classifications disagreed and reached consensus. This consensus classification ('reactivated', 'suspicious' or 'quiescent' lesion) formed the reference standard for determining which of the participants' lesion classifications were 'correct.'

Outcomes

The primary outcome was correct classification of the lesion status in a vignette by a participant, based on assessing the index images in a vignette, compared with the reference standard. Activity status could be classified as 'reactivated', 'suspicious' or 'quiescent'. A lesion classification was scored as 'correct' if both participant and reference standard lesion classifications were 'reactivated' or if both participant and reference standard lesion classifications were 'suspicious'/'quiescent' (i.e. suspicious and quiescent classifications were grouped, making the primary outcome binary).

Secondary outcomes were the frequency of potentially sight-threatening errors (if the reference standard was 'reactivated' and participant classification was 'quiescent'); participants' judgements about the presence or absence, and increase from baseline, of lesion components [subretinal fluid (SRF), intraretinal cysts (IRCs), diffuse retinal thickening (DRT), pigment epithelial detachment (PED), blood and exudates]; participant-rated confidence in their decisions about the primary outcome on a five-point scale; and cost-effectiveness of monitoring patients with quiescent lesions by optometrists in the community compared with ophthalmologists in the HES.

Sample size

A sample of 288 vignettes was chosen to have at least 90% power to test the hypothesis that the proportion of lesions correctly classified by the optometrist group was no more than 10% lower than the proportion correctly classified by the ophthalmologist group, assuming that the proportion of lesions correctly classified by the ophthalmologist group was at least 95%. The trial, in fact, had 90% power to detect non-inferiority for lower proportions of vignettes correctly classified by the ophthalmologist group, since each vignette was assessed seven times by each group.

Statistical analyses

All primary and secondary outcomes were analysed using mixed-effects regression models, adjusting for the order in which vignettes were viewed as a fixed effect (tertiles: 1–14, 15–28, 29–42) and, for participant and vignette, as random effects. All outcomes were binary and analysed using logistic regression with group estimates presented as odds ratios (ORs) with 95% confidence intervals (CIs). Hypotheses were tested with likelihood ratio tests; two-tailed p-values < 0.05 were considered to be statistically significant.

Economic evaluation

A within-trial cost-effectiveness analysis compared optometrist-led with ophthalmologist-led reviews of the need for retreatment for patients with quiescent nAMD from the perspective of the UK NHS, Personal Social Services and private practice optometrists. The main outcome measure was a cost per 'correct' lesion classification. Costs of reviews by optometrists were collected using a bespoke resource-use questionnaire developed for trial participants; costs for ophthalmologists were taken from those calculated in the IVAN trial (a randomised controlled trial to assess the effectiveness and cost-effectiveness of alternative treatments to Inhibit VEGF in Age-related choroidal Neovascularisation). Decision trees were used to model alternative cost care pathways based on the optometrists' and ophthalmologists' lesion classifications for the trial vignettes. The optometrists were considered cost-effective if the incremental cost-effectiveness ratio fell below £20,000.

Qualitative research

Focus groups and interviews were conducted with HES users, eye specialists and other health professionals involved in caring for patients with eye conditions in the UK to explore their views on shared care for nAMD. Participants were recruited through various sources using maximum variation sampling. Discussions were audio-recorded, transcribed verbatim and analysed thematically until the point of data saturation.

Results

Trial cohort

Between 1 June 2013 and 6 March 2014, 155 participants registered their interest and, of these, 62 ophthalmologists and 67 optometrists consented to take part. Participants could withdraw or be withdrawn throughout the trial for various reasons: not completing webinar training; not attaining the required performance level in their training vignettes; no longer wanting to take part; no longer being required to reach the target sample size. Ninety-six participants, 48 from each profession, completed the main trial assessments and formed the analysis population.

Reference standard classifications

The reference standard classified 142 (49.3%) of the 288 vignettes as reactivated, five (1.7%) as suspicious and 141 (49.0%) as quiescent.

Participant characteristics

The average age and proportion of women among optometrists and ophthalmologists were similar {mean age 43.1 years [standard deviation (SD) 10.1 years] and 42.2 years (SD 8.0 years), respectively (50.0% vs. 43.8%)}. Optometrists had, on average, more years of qualified experience than ophthalmologists {median 17.4 years [interquartile range (IQR) 10.1–28.4 years] and 11.4 years (IQR 4.8–16.9 years), respectively}.

Primary outcome

Ophthalmologists and optometrists correctly classified 1722 out of 2016 (85.4%) and 1702 out of 2016 (84.4%) of vignettes. The difference was not statistically significant (OR 0.91, 95% CI 0.66 to 1.25; $p = 0.543$) and showed optometrists to be non-inferior to ophthalmologists with respect to lesion classification according to the pre-specified limit of 10% absolute difference (0.298 on the odds scale).

Secondary outcomes

Serious sight-threatening errors (which could occur only for the vignettes classified as 'reactivated' by the reference standard) occurred in 62 out of 994 (6.2%) of ophthalmologists' classifications and 57 out of 994 (5.7%) of optometrists' classifications. This difference was not statistically significant (OR, 0.93, 95% CI 0.55 to 1.57; $p = 0.789$). Ophthalmologists judged lesion components to be present less often than optometrists for all components except PED; the differences between groups were statistically significant for SRF (25.5% vs. 31.1%, OR 1.73, 95% CI 1.21 to 2.48), DRT (23.9% vs. 41.0%, OR 3.46, 95% CI 2.09 to 5.71), blood (7.4% vs. 9.6%, OR 1.56, 95% CI 1.00 to 2.44) and exudates (7.5% vs. 18.8%, OR 3.10,

95% CI 1.58 to 6.08), but not for IRC (39.6% vs. 40.1%, OR 1.00, 95% CI 0.61 to 1.65) or PED (41.9% vs. 41.8%, OR 0.91, 95% CI 0.47 to 1.79). Ophthalmologists were significantly more likely to be 'very confident' about their lesion classifications than optometrists (58.3% vs. 28.5%, OR 0.15, 95% CI 0.07 to 0.32).

Economic evaluation

The mean cost for an optometrist-led monitoring review in the community was £51.82 per review, compared with £75.60 for an ophthalmologist-led review in hospital. However, once information on retreatment decisions was considered (e.g. follow-up consultations and anti-VEGF injections), the average cost per care pathway was very similar between the two professional groups. The cost for optometrist-led monitoring was £410.78 compared with £397.33 for ophthalmologist-led monitoring (difference of £13.45).

Acceptability of the shared care model to patients and health professionals

Findings from the focus groups and interviews found consensus that optometrist-led monitoring of patients with quiescent nAMD in the community has the potential to reduce clinical workload and could represent a more patient-centred option for patients. However, potential barriers were identified which could limit the feasibility of a shared care scheme, including ophthalmologists' perceptions of optometrists' competence, the need for clinical training, whether or not optometry and ophthalmology could work more collaboratively and whether or not shared care was a financially efficient option for clinical commissioning groups.

Discussion

Main findings: study conduct

The virtual trial design required each participant to assess a specific set of vignettes, which made recruitment and conduct of the trial challenging in a short time frame. Fewer suitable images were available to create vignettes than anticipated, requiring changes to the methods. Some images used to create vignettes were suboptimal and paired viewing of baseline and index images was not possible. The reference standard was not available to assess performance after training but this did not disadvantage any participant.

Main findings: study results

Optometrists were non-inferior to ophthalmologists with respect to the overall proportion of lesions correctly classified, but they made different kinds of error. Compared with ophthalmologists, they were less likely to classify a reactivated lesion as quiescent or suspicious and more likely to classify a quiescent or suspicious lesion as reactivated. These findings suggested optometrists adopted a more cautious decision criterion. Such caution may be desirable, although it limits the potential for community monitoring to reduce the HES workload and be cost-effective. No harms could arise in the trial because decisions were being made on the basis of vignettes.

The economic evaluation showed that monitoring by optometrists had slightly higher costs and resulted in slightly fewer correct retreatment decisions compared with ophthalmologists. However, the differences were very small (an incremental cost of £13 per consultation and one additional incorrect decision per 101 reviews conducted).

Focus group participants and interviewees agreed that monitoring by community-based optometrists may reduce HES workload and could represent a more patient-centred option for patients. However, potential barriers to implementation include ophthalmologists' perceptions of optometrists' competence and the need for training and for optometrists and ophthalmologists to work more collaboratively.

Strengths and limitations

The Effectiveness, cost-effectiveness and acceptability of Community versus Hospital Eye Service follow-up for patients with neovascular age-related macular degeneration with quiescent disease (ECHoES) study was done rapidly at low cost and was feasible when a conventional trial may not have been. The virtual nature of the trial and the adequacy of training are important potential limitations. However, 'two-stop clinics' in the HES are common and often depend on 'virtual' lesion assessment in the absence of the patient; the trial results suggest training was satisfactory. The absence of an existing shared care pathway required optometrists to identify hypothetical resources and costs. It also contributed to uncertainty about the cost-effectiveness estimates, highlighted by a sensitivity analysis which excluded rereview in the HES of a patient rapidly referred by an optometrist.

Lessons for the future (if applicable)

We applied methods planned at the time of trial conception with few modifications and recommend further trials of this nature to address research questions when appropriate data repositories are available.

The study required participating optometrists and service users interviewed about the proposed shared model to consider a hypothetical scenario. This is not intrinsic to a virtual trial but is a probable feature, as the design has most to offer when a particular service is not yet established. This constraint imposes some limitations and uncertainties. Conversely, the qualitative research highlighted the importance of exploring views of relevant stakeholders alongside a virtual trial; key concerns were identified that would need to be addressed in formulating a concrete shared care model.

Conclusion

Optometrists were as good as ophthalmologists at classifying the activity status of a lesion in vignettes, but made different types of error. Optometrists adopted a more cautious decision criterion, making them less likely to misclassify reactivated lesions, which is potentially a desirable attribute. The economic evaluation showed small differences in the costs and effects of monitoring by optometrists and ophthalmologists for patients with quiescent nAMD. Patients and professionals were enthusiastic about the possibilities of a shared care model for nAMD but had concerns about implementation.

Future research

The ECHoES study web application was robust and could be used for future training or research. Improvements in technology, and increasing expertise of OCT technicians in capturing OCT images, may make the vignettes based on the IVAN trial image repository irrelevant. Creating new vignettes based on up-to-date images for patients managed in the HES would be easy to do but would require investment.

The web application could be modified to allow automatic image importation from imaging equipment and viewing by multiple users across a local area network. Wider integration with the HES could allow for telemedicine-style shared care, including interaction with HES ophthalmologists in scheduled virtual clinics, providing training and potentially improving trust between professions.

The benefit of reducing HES workload was not considered in the economic evaluation. A framework of programme budgeting and marginal analysis could explicitly explore the resource implications of shifting resources within a given health service area.

Future qualitative research could investigate professional differences of opinion that were identified in multidisciplinary focus groups.

Trial registration

This trial is registered as ISRCTN07479761.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.058

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the ISI Science Citation Index.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: nihredit@southampton.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the *Health Technology Assessment* journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

The HTA programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

For more information about the HTA programme please visit the website: http://www.nets.nihr.ac.uk/programmes/hta

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 11/129/195. The contractual start date was in March 2013. The draft report began editorial review in February 2015 and was accepted for publication in April 2015. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).