Interventions to increase attendance for diabetic retinopathy screening (Protocol)


This is a reprint of a Cochrane protocol, prepared and maintained by The Cochrane Collaboration and published in The Cochrane Library 2016, Issue 1

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Interventions to increase attendance for diabetic retinopathy screening

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Editorial group: Cochrane Eyes and Vision Group.


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ABSTRACT

This is the protocol for a review and there is no abstract. The objectives are as follows:

The primary objective of the review is to assess the effectiveness of intervention components that seek to increase attendance for diabetic retinopathy screening in people with type 1 and type 2 diabetes.

Secondary objectives:

- To use validated taxonomies of QI intervention strategies and behaviour change techniques (BCTs) to code the description of interventions in the included studies and determine whether interventions that include particular QI strategies or component BCTs are more effective in increasing screening attendance;
- To explore heterogeneity in effect size within and between studies to identify potential explanatory factors for variability in effect size;
- To explore differential effects in subgroups to provide information on how equity of screening attendance could be improved;
- To critically appraise and summarise current evidence on the resource use, costs and cost-effectiveness.
BACKGROUND

Description of the condition

Diabetic retinopathy is the most common microvascular complication of diabetes mellitus and a leading cause of blindness amongst the working-age adult population in the Western world (Sivaprasad 2012). The condition affects approximately a third of individuals with diabetes (Yau 2012) with a higher prevalence in people of South Asian, African and Latin American descent, compared to white populations (Sivaprasad 2012). Risk factors for the development and progression of diabetic retinopathy include: duration of diabetes, poor glycaemic control, hypertension and hyperlipidaemia (Yau 2012). It has been estimated that globally approximately 93 million individuals may have some form of diabetic retinopathy, with 28 million suffering from the sight-threatening end points of the disease (Yau 2012). There is limited evidence on the economic burden of diabetic retinopathy. One recent estimate for healthcare costs in Sweden was EUR 106,000 per 100,000 population per year based upon a prevalence of diabetes of 4.8% (95% confidence interval 4.7 to 4.9) (Heinzl 2010). These costs exclude cost impacts on those with diabetic retinopathy and their families. Although effective treatments are available for sight-threatening diabetic retinopathy in the form of laser photocoagulation (Evans 2014) and more recently the use of anti-vascular endothelial growth factor inhibitors (Virgili 2014), the success of these interventions is dependent on early detection and timely referral for treatment. Diabetic retinopathy screening fulfils the World Health Organization (WHO) criteria for a screening programme (Scanlon 2008); namely, diabetes-associated visual impairment is an important public health problem; potentially sight-threatening retinopathy has a recognisable latent stage; a universally accepted and effective treatment is available; and screening has been shown to be cost-effective in terms of sight years preserved compared with no screening (Jones 2010). Annual or biennial diabetic retinopathy screening is recommended in many countries using a variety of screening modalities including: ophthalmoscopy performed by a number of healthcare professionals (including ophthalmologists, optometrists, diabetic physicians) or using standard retinal photography or digital fundus imaging (American Diabetes Association 2015; Kristinsson 1995; Scanlon 2008). However, relatively few countries have introduced a national population-based diabetic retinopathy screening programme and in most parts of the world screening remains non-systematic. The reference standard for the detection of diabetic retinopathy consists of seven standard 35-degree colour photographic fields as described by the Early Treatment Diabetic Retinopathy Study (EDTRS) research group (EDTRS 1991). However this technique is impractical for widespread retinopathy screening. Although ophthalmoscopy through dilated pupils has traditionally been the method of choice for opportunistic screening, the procedure varies in diagnostic accuracy depending on the particular technique used (direct or indirect ophthalmoscopy) or the experience of the healthcare professional performing the test (Hutchinson 2000). Recent developments in digital retinal photography have facilitated rapid acquisition of high-quality fundus images that can be stored and subsequently graded. Digital imaging combined with trained graders has been shown to be an effective screening tool to identify sight-threatening retinopathy (Williams 2004) and is increasingly gaining acceptance for population screening (Kirkizlar 2013; Sharp 2003; Silva 2009; Taylor 2007).

Despite evidence supporting the effectiveness of retinopathy screening in reducing the risk of sight loss in people with diabetes, screening coverage is consistently below recommended levels (Millett 2006; Paz 2006; Saadine 2008). Several factors have been shown to affect access and attendance for retinopathy screening including ethnicity, younger age (less than 40 years), a longer duration of diabetes, and living in areas of high social deprivation (Byun 2013; Gulliford 2010; Hwang 2015; Kliner 2012).

Description of the intervention

Several interventions specifically aimed at improving retinopathy screening, including those targeting patients, health professionals or the healthcare system have been shown to be effective in improving attendance across a range of retinopathy screening models (Zhang 2007). Examples of patient-focused interventions include: (1) educational programmes to increase awareness of diabetic retinopathy and promote self management, and (2) the use of prompts/reminders. Provider-focused interventions include: (1) clinician education, and (2) audit and performance feedback. System interventions include: (1) team changes; (2) establishing electronic registration and recall, and (3) the use of telemedicine. In addition to strategies that specifically target retinopathy screening, general quality improvement (QI) implementation strategies for diabetes care may also be effective in improving screening coverage. A recent systematic review and meta-analysis of trials assessing a number of predefined QI strategies to improve diabetes care reported that these were associated with a significant increase in retinopathy screening compared to usual care (risk ratio 1.22 (95% confidence interval 1.13 to 1.32)) (Tricco 2012). However, this review did not include studies where interventions were solely targeted at patients, and the authors were unable to distinguish the effectiveness of individual QI components or identify potential effect modifiers. Furthermore, the review did not include an economic perspective.

How the intervention might work

The majority of studies assessing the effectiveness of interventions to improve diabetes care (including those delivered specifically to improve retinopathy screening) often involve multicomponent...
interventions (i.e. consisting of more than one quality improvement strategy) that attempt to change the behaviour of healthcare professionals (e.g. advising patients to attend diabetic retinopathy screening) or patients (e.g. actually attending), or both. As there is no consistent association between the number of intervention components and their effectiveness (Grimshaw 2004), the ‘ideal’ number of components in such programmes is unknown. Furthermore, given the complexity of interventions tested to date, it is not always clear which specific components are the effective elements of these interventions (i.e. the ‘active ingredients’). Hence, the content of complex behaviour change interventions has been referred to as 'black box' (Grimshaw 2014). There is evidence that the more clearly the ‘active’ components of a complex intervention are described, the more readily the intervention may be delivered in an effective, consistent and cost-effective manner (Michie 2009). Therefore, identification of the effective interventions for increasing attendance for diabetic retinopathy screening first requires clarity about intervention content and the functional relationship between components of interventions and the intended outcome. The Cochrane Effective Practice and Organisation of Care (EPOC) Group have developed a taxonomy that can be used to classify intervention content in systematic reviews (EPOC 2002). Although the EPOC taxonomy provides a common language and a useful summary description of the intervention, the taxonomy may not be sufficiently detailed to specify the components of the intervention clearly (Presseau 2015). A complementary approach is to provide a comprehensive categorisation of the ingredients of the intervention in terms of the behaviour change techniques (BCTs) used. BCTs are defined as the ‘observable, replicable and irreducible components of an intervention that are designed to alter or redirect causal processes regulating behaviour’ (Michie 2013). Recently, a reliable taxonomy of 93 BCTs has been published (co-developed by team member JF) to provide a common, consistent terminology (BCT Taxonomy version 1 (BCTTv1)), by which the component BCTs in complex interventions may be identified and described. Examples of BCT labels include: ‘goal setting,’ ‘self-monitoring,’ ‘providing feedback on behaviour’ and ‘problem solving’. Review team members (JP, NI and JG) have successfully demonstrated the feasibility of using the BCTTv1 within trials of QI interventions for diabetes care (Presseau 2015).

By identifying the active components of interventions that increase attendance for screening, this review will contribute to the identification of implementation strategies for early detection of sight-threatening retinopathy. Furthermore, by exploring the differential effects of interventions in particular subgroups the results may provide clues to help to reduce inequalities in screening attendance and determine the impact of inequity on intervention effectiveness and efficiency. Although there have been a number of systematic reviews on interventions to optimise adult screening programmes (Everett 2011; Holden 2010), it is likely that this evidence is not directly transferable to retinopathy screening. Screening for diabetic retinopathy differs from other forms of screening in that the target group already has significant contact with the healthcare system due to their underlying diabetes, and screening has to be life-long (i.e. annual surveillance is necessary).

**OBJECTIVES**

The primary objective of the review is to assess the effectiveness of intervention components that seek to increase attendance for diabetic retinopathy screening in people with type 1 and type 2 diabetes.

Secondary objectives:

- To use validated taxonomies of QI intervention strategies and behaviour change techniques (BCTs) to code the description of interventions in the included studies and determine whether interventions that include particular QI strategies or component BCTs are more effective in increasing screening attendance;
- To explore heterogeneity in effect size within and between studies to identify potential explanatory factors for variability in effect size;
- To explore differential effects in subgroups to provide information on how equity of screening attendance could be improved;
- To critically appraise and summarise current evidence on the resource use, costs and cost-effectiveness.

**METHODS**

**Criteria for considering studies for this review**

**Types of studies**

We will include randomised controlled trials (RCTs), both individually randomised and cluster-RCTs, conducted in a primary or
secondary care setting, that were either specifically designed to improve attendance for diabetic retinopathy screening or were evaluating general strategies to improve diabetes care, and where the impact of the intervention on retinopathy screening attendance was measured. For economic data we will include full economic evaluations (cost-effectiveness analyses, cost-utility analyses and cost-benefit analyses), cost analyses and comparative resource utilisation studies conducted alongside a RCT.

**Types of participants**

Participants with type 1 and type 2 diabetes mellitus who are eligible for screening. Controls/comparators will be those persons with diabetes who were eligible for screening and who did not receive the trial intervention or received standard care.

**Types of interventions**

Interventions will comprise any planned strategy or combination of strategies to improve attendance for diabetic retinopathy screening targeted at individuals with diabetes (e.g. reminders, promotion of self-management), healthcare professionals (e.g. education, audit and feedback) or the healthcare system (e.g. electronic registries, team changes). Interventions will include those specifically targeting diabetic retinopathy screening or that were part of a general strategy to improve diabetes care.

**Types of outcome measures**

**Primary outcomes**

The primary outcome will be one or more visits for diabetic retinopathy screening within a two-year period following implementation of the intervention. This could be based on self reports or health-record audit (hospital, primary care physician or screening administration system record).

**Secondary outcomes**

- Ongoing adherence to screening based on attendance for screening following the initial screening post-intervention;
- Economic outcomes:
  - i) resources (staff time, equipment, consumables) required to deliver interventions to increase attendance for screening
  - ii) costs of staff used to provide interventions; costs of treatment and care; cost of primary care; lost wages and lost productivity (work output)
  - iii) cost-effectiveness (incremental cost-effectiveness ratios (ICERs); incremental cost per quality-adjusted life year (QALY); incremental cost per disability-adjusted life year (DALY); incremental cost-benefit ratios; net benefits)

**Search methods for identification of studies**

**Electronic searches**

We will search the Cochrane Central Register of Controlled Trials (CENTRAL) (which contains the Cochrane Eyes and Vision group Trials Register) and the NHS Economic Evaluation Database (NHS EED) on the Cochrane Library (latest issues), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE Daily, Ovid OLDMEDLINE (January 1946 to present), EMBASE (January 1980 to present), PsycINFO (1967 to present), the Web of Science Conference Proceedings Citation Index-Science (CPCI-S) (January 1990 to present) and Emerging Sources Citation Index (ESCI) (January 2015 to present), ProQuest Family Health (January 1987 to present), OpenGrey (January 1980 to present), the ISRCTN registry (www.isrctn.com/editAdvancedSearch), ClinicalTrials.gov (www.clinicaltrials.gov) and the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). We will not use any date or language restrictions in the electronic search for trials. See: Appendices for details of search strategies for CENTRAL and NHS EED (Appendix 1), MEDLINE (Appendix 2), EMBASE (Appendix 3), PsychINFO (Appendix 4), CPCI-S and ESCI (Appendix 5), ProQuest (Appendix 6), OpenGrey (Appendix 7), ISRCTN (Appendix 8), ClinicalTrials.gov (Appendix 9) and the ICTRP (Appendix 10).

**Searching other resources**

We will handsearch the Diabetes UK and World Diabetes Congress from 1990 onwards, and will search the reference lists of included studies to identify any additional relevant studies. In particular we will search the reference lists of included and excluded studies in Tricco 2012 to identify further potentially relevant studies. Tricco 2012 has identified studies which have multiple interventions to improve the quality of care in diabetes. Some studies in this review include screening for diabetic retinopathy, one of the outcomes being assessed. However, the information on screening for diabetic retinopathy is not reported in the abstract or coded in the MeSH or thesaurus headings, so it is unlikely that the electronic searches will retrieve these studies. In addition to searching the reference list of Tricco 2012, we will also identify further new studies as this review is currently being updated. The protocol for this review has been republished (Ivers 2014), as whilst the scope of the review remains the same, the update will explore the role of innovative meta-analysis in systematic reviews of complex interventions. We will also contact experts in the field to request information on any ongoing or unpublished studies that would be relevant for this review.
Data collection and analysis

Selection of studies
Two review authors will independently screen the titles and abstracts of studies identified in the electronic searches. We will seek full copies of research papers in the case of uncertainty, and will resolve any differences of opinion between review authors by discussion. We will document reasons for exclusion at this stage.

Data extraction and management
Two review authors working independently will extract data from the included studies by using a modified version of the Cochrane Effective Practice and Organisation of Care (EPOC) group data collection form. This template incorporates information on study design, type and duration of interventions, participants, setting, methods, outcomes, and results. For the extraction of data on the sociodemographic characteristics of participants that are known to be important from an equity perspective, we will use the PROGRESS (place, race, occupation, gender, religion, education, socioeconomic status, social status) framework (O’Neill 2014), and will also record whether any interventions were aimed at disadvantaged or low- and middle-income country populations.

We will adapt the data extraction form for economic evaluations from the format used to produce structured abstracts of full economic evaluations for inclusion in the NHS Economic Evaluation Database.

Two review authors will conduct data extraction, and will resolve discrepancies between them by discussion.

Coding QI intervention components
We will code extracted intervention descriptions using the taxonomy of knowledge translation/quality improvement intervention strategies used by Triceo 2012, which incorporates 12 QI components targeting healthcare systems, clinicians or patients. Two review authors will independently code QI components as ‘present’ or ‘absent’ for both intervention and control arms. We will resolve discrepancies in QI intervention coding by discussion and if necessary by the involvement of a third review author.

BCT coding of intervention content
We will also code extracted intervention descriptions into component BCTs using an established taxonomy of 93 BCTs (Michie 2013) as a coding framework. We will code BCTs for each intended recipient. We will code each intervention separately, including control arms. We will code system-level interventions as targeting either healthcare provider or patient behaviour, or both, unless an alternative intervention recipient and their behaviour are reported (e.g. administrative staff sending reminder letters).

We will code BCTs as ‘present’ or ‘absent’ for each intervention description. There is substantial evidence that the content of complex behaviour change interventions is often poorly described in published reports, rendering it more difficult to clearly specify the content of interventions on this basis alone and increasing the risk of misclassification (Lorencatto 2013). Therefore, in the case of insufficient information being available to adequately specify the content of the included interventions, we will supplement this analysis by contacting the authors of included studies with a request for additional materials or information that provides further detail on the content of the intervention (e.g. a trial protocol, letters sent to patients, written or audiovisual materials used for QI strategy). Initial examinations of papers identified via the scoping searches indicate this step is likely to be necessary. We will code received materials using the taxonomy in the same manner as for the corresponding published reports.

Two review authors will independently conduct BCT coding, resolving discrepancies by discussion and if necessary by the involvement of a third review author.

Coding of resource requirement needed to deliver interventions
The various behaviour change interventions may differ in terms of the quantity of resources needed to deliver them. However, the quantity of resources required to deliver the intervention may also be a determinant of the effectiveness of the intervention. We will explore whether we can review the description of the interventions (treatment and control) in the included studies and classify the intensity of resource use on a five-point Likert scale. These data might be used in a meta-regression, with sensitivity analysis conducted on alternative methods of including such data in a meta-analysis (e.g. as binary covariates, as continuous variables, dichotomised).

Two members of the review team will independently review a sample of 10 included studies, and will grade the intervention between 1 (least resource-intensive) to 5 (most resource-intensive), or 0 (unable to determine), and will record how they graded each study. We will compare the scores from each review author, and will resolve disagreements by discussion or if necessary by arbitration from a third review author. We will judge this initial pilot to be a success if the scores from nine out of 10 studies are within one mark of each other following discussion between the review authors. If we consider that we can make a feasible and reproducible approach to grading, we will use the notes about how each study is graded to produce a reproducible description of the resource input associated with each grade on the Likert scale. We will then use the scale to extract the resource use required to deliver the interventions in the other included studies within this review.

Assessment of risk of bias in included studies
Two review authors will independently assess study quality by using the Cochrane Effective Practice and Organisation of Care (EPOC) ‘Risk of bias’ tool (EPOC 2012). The EPOC criteria for assessing risk of bias uses nine standard criteria:

- was the allocation sequence adequately generated?
- was the allocation adequately concealed?
- were baseline outcome measurements similar?
- were baseline characteristics similar?
were incomplete outcome data adequately addressed?
• was knowledge of the allocated interventions adequately prevented during the study?
• was the study adequately protected against contamination?
• was the study free from selective outcome reporting?
• was the study free from other risks of bias?

For cluster-RCTs, we will consider particular biases, including: (i) recruitment bias; (ii) baseline imbalance; (iii) loss of clusters, and (iv) incorrect analysis; as described in Chapter 16 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). For each domain, two review authors will perform the 'Risk of bias' assessment independently and will assign a judgement of 'low risk' 'high risk' or 'unclear risk' of bias. The review authors will resolve any discrepancies between them by discussion.

Assessment of the overall methodological quality of included economic evaluations based on single, empirical studies will be informed by application of guidelines for authors and peer reviewers of economic submissions to the BMJ (Drummond 1996) and ISPOR guidelines for good practice in economic evaluations conducted alongside trials (Ramsey 2015).

Measures of treatment effect

Attendance at screening post-intervention is a dichotomous outcome. Our measure of intervention effect will be the risk difference, the actual difference in the observed events between experimental and control interventions.

Unit of analysis issues

To avoid unit-of-analysis errors, we will perform analyses at the same level as the intervention or control group allocation. For individual randomised trials the unit of analysis will be the individual participant. For cluster-randomised trials, we will analyse data adjusted for clustering. If in cluster-RCTs, outcomes are presented at patient level (i.e. a unit-of-analysis error) we will use established methods to adjust for clustering, e.g. by dividing the original sample size by the design effect, which can be calculated from the average cluster size and the intra-cluster correlation coefficient (ICC). Where the ICC is unknown, we will estimate it from similar trials.

Dealing with missing data

We will contact authors of included studies if important data are not available. If we are not able to obtain these data we will report the available results and will not impute missing data.

Assessment of heterogeneity

We will assess heterogeneity between trials by visual inspection of forest plots, and by formal statistical tests of heterogeneity (Chi² test and the I² statistic). If there is evidence of substantial heterogeneity (defined as I² > 50%) and sufficient numbers of trials are available, we will explore the possible reasons for heterogeneity using subgroup and random-effects meta-regression analyses.

Assessment of reporting biases

Provided there are sufficient studies (at least 10 for a meta-analysis), we will examine funnel plots to assess the potential for publication bias.

Data synthesis

We will conduct meta-analyses in Review Manager 5 (RevMan 2014), using a random-effects model to estimate the pooled risk difference across studies. We anticipate that a large number of included studies will use a cluster-RCT design. We will include data from RCTs randomised by individual and from cluster-adjusted RCTs in the same meta-analysis.

In the case of multiple intervention groups, we will combine groups to create a single pair-wise comparison as recommended in Chapter 16 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We will summarise characteristics and results of included economic evaluations using additional tables, supplemented by a narrative summary that will compare and evaluate methods used and principal results between studies. We will also tabulate unit cost data, when available. We will report the currency and price year applicable to measures of costs in each original study alongside measures of costs, incremental costs and incremental cost-effectiveness, by study. Where details of currency and price year are available in original studies, we will convert measures of costs, incremental costs and cost-effectiveness to 2016 International Dollars using implicit price deflators for gross domestic product (GDP) and GDP Purchasing Power Parities (CCEMG - EPPI-Centre Cost Converter).

Subgroup analysis and investigation of heterogeneity

If sufficient studies are available, we will perform the following subgroup analyses to investigate whether the presence or absence of particular covariates explain the variability in effect size:
• population subgroups: type 1, type 2 diabetes mellitus, participant characteristics across PROGRESS categories (race, gender, education, socioeconomic status)
• component QI strategies/BCTs
• resource requirements to deliver an intervention

We will further investigate associations between screening attendance, Q1 strategy used and type and number of BCTs and the impact of baseline screening uptake on effect size by meta-regression. We will perform meta-regression using the ‘metareg’ macro available for the Stata statistical package.
Sensitivity analysis
If data are sufficient, we will conduct a sensitivity analysis to compare studies of high versus low risk of bias (we define ‘high risk’ as a study showing a high risk of bias in one or more domains).

ACKNOWLEDGEMENTS
This review is being carried out as part of an evidence synthesis project funded by NIHR-HTA (Project reference Number 13/137/05). We wish to acknowledge the ‘What Works to Increase Attendance for Diabetic Retinopathy Screening? An Evidence sYNthESI (WIDeR-EyeS)’ Project Stakeholder Advisory Group for their input to the development of this protocol.

We acknowledge Cochrane Eyes and Vision Group (CEV) for assisting with the preparation of this protocol. We thank Iris Gordon, Trials Search Co-ordinator for CEVG for developing the electronic search strategy. We thank the peer reviewers and editors for comments to the draft of this protocol.

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Byun 2013

CCEMG - EPPI-Centre Cost Converter
CCEMG - EPPI-Centre Cost Converter v1.4. eppi.ioe.ac.uk/costconversion/default.aspx (accessed 1 September 2015).

Drummond 1996

EDTRS 1991

EPOC 2002

EPOC 2012

Evans 2014

Everett 2011

Glanville 2006

Grimshaw 2004

Grimshaw 2014

Gulliford 2010

Heintz 2010
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Higgins 2011

Holden 2010

Hutchinson 2000

Hwang 2015

Ivers 2014

Jones 2010

Kirkizlar 2013

Kliner 2012

Kristinsson 1995

Lorencatto 2013

Michie 2009

Michie 2013

Millett 2006

O’Neill 2014

Paz 2006

Presseau 2015

Ramsey 2015

RevMan 2014 [Computer program]

Saadine 2008

Scanlon 2008

Sharp 2003
Silva 2009

Sivaprasad 2012

Taylor 2007

Tricco 2012

Virgili 2014

Williams 2004

Yau 2012

Zhang 2007

* Indicates the major publication for the study

### APPENDICES

#### Appendix 1. CENTRAL and NHS EED search strategy

#1 MeSH descriptor: [Diabetes Mellitus] explode all trees
#2 MeSH descriptor: [Diabetes Complications] explode all trees
#3 MeSH descriptor: [Diabetic Retinopathy] explode all trees
#4 (diabet* or proliferative or non-proliferative) near/4 retinopath*
#5 diabet* near/3 (eye* or vision or visual* or sight*)
#6 retinopath* near/3 (eye* or vision or visual* or sight*)
#7 DR near/3 (eye* or vision or visual* or sight*)
#8 #1 or #2 or #3 or #4 or #5 or #6 or #7
#9 MeSH descriptor: [Mass Screening] explode all trees
#10 MeSH descriptor: [Vision Tests] explode all trees
#11 MeSH descriptor: [Telemedicine] explode all trees
#12 MeSH descriptor: [Photography] explode all trees
#13 MeSH descriptor: [Ophthalmoscopes] explode all trees
#14 MeSH descriptor: [Ophthalmoscopy] explode all trees
#15 ophthalmoscop* or fundoscop* or funduscop*:ti
#16 (exam* or photo* or imag*) near/3 fundus
#17 photography or retinography
#18 (mydriatic or digital or retina* or fundus or steroscopic) near/3 camera*
#19 (mydriatic or digital or retina* or fundus or steroscopic) near/3 imag*
#20 screen$.tw.
#21 (eye* or retina* or ophthalm*) near/4 exam*
#22 (eye* or vision or retinopathy or ophthalmic) near/4 test*
#23 (eye* or retina* or ophthalm*) near/4 visit*
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#126 MeSH descriptor: [Drug Costs] this term only
#127 MeSH descriptor: [Employer Health Costs] this term only
#128 MeSH descriptor: [Hospital Costs] this term only
#129 MeSH descriptor: [Health Expenditures] this term only
#130 MeSH descriptor: [Capital Expenditures] this term only
#131 MeSH descriptor: [Economics, Hospital] explode all trees
#132 MeSH descriptor: [Economics, Medical] explode all trees
#133 MeSH descriptor: [Economics, Nursing] this term only
#134 MeSH descriptor: [Economics, Pharmaceutical] this term only
#135 MeSH descriptor: [Fees and Charges] explode all trees
#136 MeSH descriptor: [Budgets] explode all trees
#137 low* near/2 cost*
#138 high* near/2 cost*
#139 (health care or healthcare) near/2 cost*
#140 fiscal or funding or financial or finance
#141 cost near/2 estimate*
#142 cost near/2 variable*
#143 unit near/2 cost*
#144 economic* or pharmacoeconomic* or price* or pricing
#145 MeSH descriptor: [Uncompensated Care] this term only
#146 MeSH descriptor: [Reimbursement Mechanisms] this term only
#147 MeSH descriptor: [Reimbursement, Incentive] this term only
#148 insurance near/3 (health or scheme*)
#149 financial or economic or pay or payment or copayment or paid or fee or fees or monetary or money or cash or incentiv* or disincentiv*
#150 #114 or #115 or #116 or #117 or #118 or #119 or #120 or #121 or #122 or #123 or #124 or #125 or #126 or #127 or #128 or #129 or #130 or #131 or #132 or #133 or #134 or #135 or #136 or #137 or #138 or #139 or #140 or #141 or #142 or #143 or #144 or #145 or #146 or #147 or #148 or #149
#151 #59 or #79 or #113 or #150
#152 MeSH descriptor: [Patient Acceptance of Health Care] explode all trees
#153 MeSH descriptor: [Attitude to Health] explode all trees
#154 MeSH descriptor: [Health Behavior] explode all trees
#155 barrier* or obstacle* or facilitat* or enable*
#156 uptake or takeup or attend* or accept* or adhere* or attitude* or participat* or facilitat* or utiliat* or utiliat*
#157 compile* or comply or compliance* or noncompliance* or non compliance*
#158 encourag* or discourage* or reluctan* or nonrespon* or non respon* or refuse* or refusal
#159 non-attend* or non attend* or dropout or drop out or apath *
#160 MeSH descriptor: [Health Education] this term only
#161 MeSH descriptor: [Patient Education as Topic] explode all trees
#162 MeSH descriptor: [Health Promotion] explode all trees
#163 health near/2 (promotion* or knowledge or belief*)
#164 educat* near/2 (intervention* or information or material or leaflet)
#165 MeSH descriptor: [Socioeconomic Factors] this term only
#166 MeSH descriptor: [Poverty] explode all trees
#167 MeSH descriptor: [Social Class] this term only
#168 MeSH descriptor: [Educational Status] this term only
#169 (school or education*) near/3 (status or level* or attain* or achieve*)
#170 MeSH descriptor: [Employment] this term only
#171 MeSH descriptor: [Healthcare Disparities] this term only
#172 MeSH descriptor: [Health Status Disparities] this term only
#173 MeSH descriptor: [Medically Underserved Area] explode all trees
#174 MeSH descriptor: [Rural Population] this term only
#175 MeSH descriptor: [Urban Population] this term only
Appendix 2. MEDLINE (Ovid) search strategy

1. randomized controlled trial.pt.
2. random$.ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. trial.ab,ti.
6. (group or groups).ab,ti.
7. or/1-6
8. exp animals/
9. exp humans/
10. 8 not (8 and 9)
11. 7 not 10
12. exp Randomized Controlled Trials as Topic/
13. 11 or 12
14. exp Diabetes Mellitus/
15. exp Diabetes Complications/
16. exp Diabetic Retinopathy/
17. ((diabet$ or proliferative or non-proliferative) adj4 retinopath$).tw.
18. diabetic retinopathy.kw.
19. (diabet$ adj3 (eye$ or vision or visual$ or sight$)).tw.
20. (retinopath$ adj3 (eye$ or vision or visual$ or sight$)).tw.
21. (DR adj3 (eye$ or vision or visual$ or sight$)).tw.
22. or/14-21
23. exp Mass Screening/
24. exp Vision Tests/
25. exp Telemedicine/
26. exp Photography/
27. exp Ophthalmoscopes/
28. exp Ophthalmoscopy/
29. (ophthalmoscop$ or funduscop$ or funduscop$).ti.
30. ((exam$ or photo$ or imag$) adj3 fundus).tw.
31. (photography or retinography).tw.
32. ((mydriatic or digital or retina$ or fundus or steroscopic) adj3 camera).tw.
33. ((mydriatic or digital or retina$ or fundus or steroscopic) adj3 imag$).tw.
34. screen$.tw.
35. ((eye$ or retina$ or ophthalm$) adj4 exam$).tw.
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88. Social Networking/
89. (email$ or text$ or message$).tw.
90. (letter or mail or mailed or print$ or brochure$ or newsletter$).tw.
91. Primary Health Care/
92. General Practitioners/ or Physicians, Family/ or Physicians, Primary Care/
93. Primary Prevention/
94. Preventive Health Services/
95. Community Health Services/
96. Community Health Nursing/
97. Health Services, Indigenous/
98. Rural Health Services/
99. Mobile Health Units/
100. (Ophthalmologist$ or Optometrist$ or Optician$ or Orthopist$ or Refractionist$).tw.
101. ((Ophthalmic or eye) adj3 (surgeon$ or nurse$ or technician$ or officer$ or assistant$ or staff$)).tw.
102. Physician’s Practice Patterns/
103. Professional Practice/
104. (professional adj3 (practice or develop$ or educat)).tw.
105. Education, Medical, Continuing/
106. exp nurses/
107. Specialties, Nursing/
108. Nurse’s Role/
109. Education, Nursing, Continuing/
110. (nurse or nurses).tw.
111. Pharmacists/
112. pharmacist$.tw.
113. ((role or roles) adj3 expand$).tw.
114. (task$ adj3 shift$).tw.
115. exp Medical Records Systems, Computerized/
116. Management Information Systems/
117. Database Management Systems/
118. Computer Systems/
119. Point-of-Care Systems/
120. Hospital Information Systems/
121. ((health or healthcare) adj4 (record or management system$)).tw.
122. (decision adj5 support).ti.
123. Economics/
124. “costs and cost analysis”/
125. Cost allocation/
126. Cost-benefit analysis/
127. Cost control/
128. Cost savings/
129. Cost of illness/
130. Cost sharing/
131. “deductibles and coinsurance”/
132. Medical savings accounts/
133. Health care costs/
134. Direct service costs/
135. Drug costs/
136. Employer health costs/
137. Hospital costs/
138. Health expenditures/
139. Capital expenditures/
140. Value of life/
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Appendix 3. EMBASE (Ovid) search strategy

1. exp randomized controlled trial/
2. exp randomization/
3. exp double blind procedure/
4. exp single blind procedure/
5. or/1-4
6. (animal or animal experiment).sh.
7. human.sh.
8. 6 and 7
9. 6 not 8
10. 5 not 9
11. exp clinical trial/
12. (clin$ adj3 trial$).tw.
13. random$.tw.
14. exp placebo/
15. placebo$.tw.
16. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
17. exp experimental design/
18. exp crossover procedure/
19. exp control group/
20. exp latin square design/
21. or/11-20
22. 21 not 9
23. 22 not 10
24. exp comparative study/
25. exp evaluation/
26. exp prospective study/
27. (control$ or prospectiv$ or volunteer$).tw.
28. or/24-27
29. 28 not 9
30. 29 not (10 or 22)
31. 10 or 23 or 30
32. "randomized controlled trial (topic)"/
33. 31 or 32
34. exp diabetes mellitus/
35. exp diabetic retinopathy/
36. ((diabet$ or proliferative or non-proliferative) adj4 retinopath$).tw.
37. diabetic retinopathy.kw.
38. (diabet$ adj3 (eye$ or vision or visual$. or sight$)).tw.
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91. (increas$ adj3 (attend$ or visit$ or intervention$ or adhere$)).tw.
92. (appointment$ adj3 (miss$ or fail$ or remind$ or follow up)).tw.
93. telephone/
94. telephone.tw.
95. Mobile Phone/
96. Mobile Application/
97. Teleconsultation/
98. (m-health or e-health or g-health or u-health).tw.
99. (phone$ adj1 (smart or cell)).tw.
100. (smartphone$ or cellphone$).tw.
101. (hand adj1 held device$).tw.
102. (mobile adj2 (health or healthcare or phone$ or device$ or monitor$ or comput$ or app or apps or application)).tw.
103. Internet/
104. Social Network/
105. (email$ or text$ or message$).tw.
106. (letter or mail or mailed or print$ or brochure$ or newsletter$).tw.
107. Primary Health Care/
108. General Practitioner/
109. Primary Prevention/
110. Preventive Health Service/
111. Community Care/
112. Community Health Nursing/
113. exp Transcultural Care/
114. Rural Health Care/
115. Ophthalmologist/
116. (Ophthalmologist$ or Optometrist$ or Optician$ or Orthopist$ or Refractionist$).tw.
117. ((Ophthalmic or eye) adj3 (surgeon$ or nurse$ or technician$ or officer$ or assistant$ or staff$)).tw.
118. Clinical Practice/
119. Professional Practice/
120. Continuing Education/
121. (professional adj3 (practice or develop$ or educat)).tw.
122. Nurse/
123. Nursing Discipline/
124. Nurse Attitude/
125. Nursing Education/
126. (nurse or nurses).tw.
127. pharmacist/
128. Pharmacist$.tw.
129. ((role or roles) adj3 expan$).tw.
130. (task$ adj3 shift$).tw.
131. Electronic Medical Record/
132. Information System/
133. Database/
134. Computer System/
135. Hospital Information System/
136. ((health or healthcare) adj4 (record or management system$)).tw.
137. (decision adj5 support).ti.
138. cost benefit analysis/
139. cost effectiveness analysis/
140. cost of illness/
141. cost control/
142. economic aspect/
143. financial management/
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Appendix 4. PsychINFO search strategy

1. exp Treatment Effectiveness Evaluation/
2. exp Clinical Trials/
3. exp Placebo/
4. placebo$.tw.
5. randomly.tw.
6. randomised.tw.
7. trial$.tw.
8. (((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$ or dummy))).tw.
9. (factorial$ or allocat$ or assign$ or volunteer$).tw.
10. (crossover$ or cross over$).tw.
11. (quasi adj (experimental or random$)).tw.
12. (control$ adj3 (trial$ or study or studies or group$)).tw.
13. or/1-12
14. diabetes/
15. ((diabet$ or proliferative or non-proliferative) adj4 retinopath$).tw.
16. (diabet$ adj3 (eye$ or vision or visual$ or sight$)).tw.
17. (retinopath$ adj3 (eye$ or vision or visual$ or sight$)).tw.
18. (DR adj3 (eye$ or vision or visual$ or sight$)).tw.
19. or/14-18
20. exp Screening/
21. ophthalmologic examination/
22. telemedicine/
23. (ophthalmoscopy$ or fundoscopy$ or funduscopy$).ti.
24. ((exam$ or photo$ or imag$) adj3 fundus).tw.
25. (photography or retinography).tw.
26. (mydriatic or digital or retina$ or fundus or stereoscopic) adj3 camera).tw.
27. (mydriatic or digital or retina$ or fundus or stereoscopic) adj3 imag$).tw.
28. screen$.tw.
29. (eye$ or retina$ or ophthalm$) adj4 exam$).tw.
30. (eye or vision or retinopathy or ophthalmic) adj4 test$.tw.
31. (eye$ or retina$ or ophthalm$) adj4 visit$.tw.
32. (telemedicine$ or telemonitor$ or telescreen$ or telehealth or teleophthalmology).tw.
33. or/20-32
34. 13 and 19 and 33
Appendix 5. CPCI-S and ESCI search strategy
#11 #10 AND #2 AND #1
#10 #9 OR #8 OR #7 OR #6 OR #5 OR #4 OR #3
#9 TS = (photography OR retinography OR telemedicine* OR telemonitor* OR telescreen* OR telehealth OR teleophthalmology)
#8 TS = (fundus NEAR/3 exam* OR fundus NEAR/3 photo* OR fundus NEAR/3 imag*)
#7 TS = (imag* NEAR/3 mydriatic OR imag* NEAR/3 digital OR imag* NEAR/3 retina* OR imag* NEAR/3 fundus OR imag* NEAR/3 stereoscopic OR camera NEAR/3 mydriatic OR camera NEAR/3 digital OR camera NEAR/3 retina* OR camera NEAR/3 fundus OR camera NEAR/3 stereoscopic)
#6 TI = (ophthalmoscop* OR fundoscop* OR funduscop*)
#5 TS = (visit NEAR/4 eye* OR visit NEAR/4 retina* OR visit NEAR/4 ophthalmic)
#4 TS = (exam* NEAR/4 eye* OR exam* NEAR/4 retina* OR exam* NEAR/4 ophthalmic)
#3 TS = (screen* OR test* NEAR/4 eye OR test* NEAR/4 vision OR test* NEAR/4 ophthalmic)
#2 TS = (diabetic NEAR/3 retinopath* OR diabetic NEAR/3 eye* OR diabetic NEAR/3 vision OR diabetic NEAR/3 visual* OR diabetic NEAR/3 sight* OR diabetic NEAR/3 proliferative OR diabetic NEAR/3 non proliferative)
#1 TS =(clinical trial* OR research design OR comparative stud* OR evaluation stud* OR controlled trial* OR follow-up stud* OR prospective stud* OR random* OR placebo* OR single blind* OR double blind*)

Appendix 6. ProQuest Family Health search strategy
ab(diabetic AND (retinopathy OR eye OR vision OR visual OR sight)) AND ab(screen OR screening OR test OR exam OR examination OR telemedicine ) AND ab(random OR randomly OR randomised OR randomized )

Appendix 7. OpenGrey search strategy
(screen OR test OR exam OR Ophthalmoscopy OR digital OR imaging OR fundus OR telemedicine OR telemonitor OR telescreen OR telehealth) AND diabetic retinopathy

Appendix 8. ISRCTN search strategy
(screen OR test OR exam OR ophthalmoscopy OR digital OR imaging OR fundus OR telemedicine OR telemonitor OR telescreen OR telehealth) within Condition: diabetic retinopathy

Appendix 9. ClinicalTrials.gov search strategy
(screen OR test OR exam OR Ophthalmoscopy OR digital OR imaging OR fundus OR telemedicine OR telemonitor OR telescreen OR telehealth) | Interventional Studies | diabetic retinopathy

Appendix 10. ICTRP search strategy
Condition = diabetic retinopathy AND Intervention = screen OR test OR exam OR Ophthalmoscopy OR digital OR imaging OR fundus OR telemedicine OR telemonitor OR telescreen OR telehealth
CONTRIBUTIONS OF AUTHORS

JL produced the first draft of the protocol
EG-R, FL, JP, JB, NI, AQ, CB, JF, JG, TP, SR, LV reviewed and commented on the draft

DECLARATIONS OF INTEREST

JL: None known
EG-R: None known
FL: None known
JP: None known
JB: None known
NI: None known
AQ: None known
CB: None known
JF: None known
JG: None known
TP: None known
SR: None known
LV: None known

SOURCES OF SUPPORT

Internal sources
- No sources of support supplied

External sources
- National Institute for Health Research (NIHR), UK.
- This review is funded by the NIHR health technology assessment programme.
- Richard Wormald, Co-ordinating Editor for the Cochrane Eyes and Vision (CEV) acknowledges financial support for his CEV research sessions from the Department of Health through the award made by the National Institute for Health Research to Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology for a Specialist Biomedical Research Centre for Ophthalmology.
- The NIHR also funds the CEV Editorial Base in London.

The views expressed in this publication are those of the authors and not necessarily those of the NIHR, NHS, or the Department of Health.