Effectiveness of interventions to increase uptake and completion of treatment for diabetic retinopathy in low- and middle-income countries: a rapid review protocol.
Prescreen

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Subject Areas

Health Economics & Outcomes Research  Ophthalmology

Keywords

Low- and middle-income countries, diabetic retinopathy, treatment, uptake, completion, effectiveness
Abstract

Background

Vision loss due to diabetic retinopathy (DR) can largely be prevented or delayed through treatment. DR programmes focus on regular screening of people living with diabetes and referral to eye care services for further assessment. Patients with vision-threatening diabetic retinopathy (VTDR), including proliferative diabetic retinopathy (PDR) and/or diabetic macular oedema (DMO), are then offered laser treatment and/or intravitreal injections which often require more than one treatment visit. However, the effectiveness of DR treatment is dependent on the timely initiation and completion of the prescribed treatment course.

Different factors—both from the demand and the supply side - can affect treatment uptake and completion. Health systems in low- and middle-income country (LMIC) settings experience limitations in the delivery of high quality and timely DR treatment, including low numbers of ophthalmologists trained in DR management, inadequate referral systems, limited access to technology and equipment and the lack of health information systems and policies that address DR management. LMIC populations have competing health needs that determine their priorities and health seeking behaviours in relation to eye health. Barriers like fear, price of services, waiting times, or distance can lead to patients missing treatment, or initiating treatment but not completing it, resulting in poor visual outcomes. Low uptake of DR treatment compounds the challenge to

Discussion

This rapid review aims to identify and synthesise the peer-reviewed literature on the effectiveness of interventions to increase uptake and completion of treatment for DR and/or DMO in LMICs. The rapid review methodology was chosen in order to rapidly synthesise the available evidence to support program implementers and policy makers in designing evidence-based health programs, public health policy, and inform the allocation of resources.

Rapid review registration OSF: osf.io/h5wgr
prevent visual loss in people with diabetes and wastes resources in already limited health systems.\textsuperscript{6} Interventions aiming to improve uptake and completion of DR treatment need to target the relevant factors in the healthcare environment in which the patients are to receive treatment.\textsuperscript{6}

Access to DR services is a widespread problem in LMICs. Studies of DR services in Pakistan, Oman and China reported that 29.5\%, 22.8\% and 27.9\% of patients respectively did not initiate treatment.\textsuperscript{7-9} In the study in China, an additional 17.6 \% did not complete the treatment course, for reasons including being unaware of the importance of treatment and the need to complete the full course, and fear of treatment.\textsuperscript{9} In high-income countries the proportion of patients not completing treatment tends to be lower than in low-income countries but still significant. A review in the USA reported that approximately 15\% of patients didn’t initiate treatment and 15\% of those didn’t complete it.\textsuperscript{10}

Laser photocoagulation is a highly effective treatment for PDR and DMO.\textsuperscript{11-13} DMO and PDR can be treated with anti-vascular endothelial growth factor (VEGF) via intravitreal injections.\textsuperscript{14, 15} Intravitreal steroids, while not indicated as first-line therapy for most eyes with DMO, have been used by some clinicians for eyes that do not adequately respond to anti-VEGF therapy.\textsuperscript{16, 17} Anti-VEGF is also indicated in age related macular degeneration (ARMD).\textsuperscript{18} However, there is evidence that the uptake of anti-VEGF by patients with DMO is significantly lower compared to patients with ARMD.\textsuperscript{19-21} People with diabetes often have other co-morbidities that increase their need to attend hospital appointments, so completing an anti-VEGF treatment regime can be a significant additional burden. Patients receiving intravitreal injections report high levels of anxiety and significant psychological impact.\textsuperscript{22} The dependence on a caregiver to accompany the patient and the financial cost of treatment also pose a burden on the patient.\textsuperscript{23, 24}

This rapid review aims to identify and summarize the most recent information on the effectiveness of interventions to increase uptake and completion of treatment for DR and/or DMO in LMICs.

### Methods

#### Rapid review question

What interventions are effective in increasing uptake and completion of treatment for DR and/or DMO among people with diabetes in LMICs?

#### Protocol and registration

We used the STARR Decision Tool and the WHO practical guide to carefully consider the methods most appropriate for this rapid review and the possible limitations introduced by those methods.\textsuperscript{25, 26}

Additional file 1 provides the adapted preferred reporting items for systematic reviews and meta-analysis protocols (PRISMA-P) which is used to report this protocol.

The protocol was registered on the Open Science Framework (OSF): osf.io/h5wgr, more details are provided in Additional file 2. Any protocol amendments will be documented in the registration site.\textsuperscript{27}

#### Eligibility Criteria

Table 1: Eligibility Criteria
### Population
Adults (aged ≥18 years) with Type 1 or Type 2 diabetes in LMICs who have been identified as needing treatment for DR and/or DMO

### Intervention
Any intervention that seeks to increase uptake and/or completion of treatment for DR and/or DMO among adults with diabetes

### Comparator
Usual care or another intervention

### Outcomes
1. Proportion of patients initiating treatment for DR and/or DMO among those to whom it is recommended
2. Proportion of patients completing treatment for DR and/or DMO among those to whom it is recommended
3. Proportion of patients completing treatment for DR and/or DMO among those initiating treatment
4. Number and proportion of DR and/or DMO rounds from the recommended treatment protocol per patient
5. Cost-effectiveness of intervention to increase DR/DMO treatment uptake or completion

### Study design
Any interventional or observational comparative study.

We will limit the search to peer-reviewed publications of studies conducted in LMICs in any setting in the last 20 years, (i.e. community or facility-based), that examine the uptake and/or completion of treatment prescribed for DR or DMO. Studies will only be included if they report at least one of the first four outcomes. We will restrict to publications in the English language. We will only include studies where a full-text report is available.

### Information Sources
We will search MEDLINE, Embase, Global Health and the Cochrane Register of Studies. The search strategies will be developed by a Cochrane Eyes and Vision Information Specialist (IG). Grey literature will not be considered.

**Search strategy** (included in Additional file 3)

### Data management and selection process
Screening will be done using online review management software (Covidence, Veritas Health Innovation, Melbourne, Australia. Available at [www.covidence.org](http://www.covidence.org)). Each title and abstract will be screened independently by two reviewers. Disagreements will be resolved by discussion. Full text articles describing potentially relevant studies will be screened by two reviewers independently against the inclusion and exclusion criteria and any differences resolved by consensus. A PRISMA flow diagram will be completed to summarise the study selection process.

### Risk of bias assessment
Risk of bias will be assessed by a single reviewer using SIGN critical appraisal checklists for this purpose, available at [https://www.sign.ac.uk](https://www.sign.ac.uk). The overall risk of bias for included studies will be reported in narrative form and used to interpret the findings of the review.

### Data extraction
A custom designed Excel data extraction form will be piloted by two reviewers on 3 papers and adapted accordingly. Data will be extracted by one reviewer, and the accuracy of data extraction will be checked by a second reviewer for 10% of studies. If there are significant data extraction errors (for example important errors in more than 1% of records) then a further set of records will be checked. The following data items will be collected for each identified intervention.

Table 2. Data items
Data categories

Example data outcomes

Publication characteristics

Authors, title, publication date, journal citation

Study characteristics

Design

Dates of data collection

Population characteristics

Country

Population demographics (age, gender)

Sample size

Intervention characteristics

Setting (rural/urban, community/hospital)

Intervention target: patients, providers, policy makers

Treatment indication: pan retinal laser photocoagulation (PRP) for PDR, focal laser, in AntiVEGF or steroids for DMO

Treatment completion guideline: e.g.: number of laser sessions, number of burns, number injections.

Type of intervention: e.g.: guidelines, treatment regime, educational programmes, financial subsidies, follow up prompts and reminders, ongoing quality assurance and improvement processes, electronic patient management

Factors associated with uptake/completion of treatment: provider and patient

Outcomes

Proportion of patients initiating treatment for DR and/or DMO among those to whom it is recommended

Proportion of patients completing treatment for DR and/or DMO among those to whom it is recommended

Proportion of patients completing treatment for DR and/or DMO among those initiating treatment

Number and proportion of DR and/or DMO rounds from the recommended treatment protocol completed per patient

Cost-effectiveness of intervention to increase DR/DMO treatment uptake or completion

Data synthesis

We anticipate that there will be clinical and methodological diversity in the studies that we find, so we plan to summarize the data narratively, following SWiM reporting guidance: Synthesis Without Meta-analysis. We will report outcomes in terms of proportions in intervention and comparator groups and will calculate the risk ratio with 95% confidence intervals as the main measure of effect, but this will be dependent on how the data are reported by the included studies. In observational studies, for example, adjusted odds ratios may be the
most appropriate measure of effect. We will present key characteristics such as study design, sample size and risk of bias in tables and use visual displays for effect estimates when possible. We will consider heterogeneity by examining study design, geographical location, demographic characteristics such as age and sex as well as the nature of the interventions and the settings in which they have been applied. We will use the GRADE approach, as applied to narrative syntheses, to assess the certainty of the synthesis findings.29

Depending on the findings, we will group studies by setting, intervention target (patients, health providers, health system), type of intervention, study design and outcomes. For each comparison and outcome, we will provide a description of the findings alongside the certainty of the evidence, ensuring consistency with the review question and providing a judgement as to the extent to which the studies contribute to the synthesis.

Discussion

This rapid review aims to identify and synthesise the peer-reviewed literature on the effectiveness of interventions to increase uptake and completion of treatment for DR and/or DMO in LMICs. The rapid review methodology was chosen in order to rapidly synthesise the available evidence to support program implementers and policy makers in designing evidence-based health programs, public health policy, and inform the allocation of resources. This review may also identify gaps in the evidence that could inform further research priorities related to the management of diabetic retinopathy in LMICs.

Abbreviations

DR: diabetic retinopathy; DMO: diabetic macular oedema; LMIC: low and middle income country; VTDR: vision-threatening diabetic retinopathy; OSF: Open Science Framework; PDR: proliferative diabetic retinopathy; VEGF: vascular endothelial growth factor; ARMD: age related macular degeneration; PRISMA-P: preferred reporting items for systematic reviews and meta-analysis protocols; SING: Scottish Intercollegiate Guidelines Network; PRP: pan retinal laser photocoagulation; SWiM: Synthesis Without Meta-analysis; GRADE: Grading of Recommendations Assessment, Development and Evaluation

Declarations

Authors’ Contributions

FD conceived the idea for the review. CB, NM, drafted and revised the protocol with suggestions from, JE, JR, FD, MJB, CC, RM, SM, JALU, who reviewed the protocol and provided feedback on the draft. IG constructed the search.

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Availability of data and materials

Not applicable - no data sets currently available.

Ethics approval and consent to participate

Not applicable.

Consent for publication
Not applicable.

**Competing Interests**

None declared.

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Not applicable.

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**References**

1. Wong TY, Sun J, Kawasaki R, Ruamviboonsuk P, Gupta N, Lansingh VC, et al. Guidelines on Diabetic Eye Care: The International Council of Ophthalmology Recommendations for Screening, Follow-up, Referral, and Treatment Based on Resource Settings. Ophthalmology. 2018 Oct;125(10):1608-22
2. Mwangi N ea. Clinical guidelines for diabetic retinopathy in Kenya: An executive summary of the recommendations. JOECSA. 2017;21(2):33-9
3. Jacobs B, Ir P, Bigdeli M, Annear PL, Van Damme W. Addressing access barriers to health services: an analytical framework for selecting appropriate interventions in low-income Asian countries. Health policy and planning. 2012 Jul;27(4):288-300
4. Poore S, Foster A, Zondervan M, Blanchet K. Planning and developing services for diabetic retinopathy in Sub-Saharan Africa. International journal of health policy and management. 2015 Jan;4(1):19-28
5. Burgess PI, Msukwa G, Beare NA. Diabetic retinopathy in sub-Saharan Africa: meeting the challenges of an emerging epidemic. BMC medicine. 2013 Jul 2;11:157
6. Sabaté E. Adherence to long-term therapies: evidence for action. In: Organization WH, editor. Geneva, Switzerland2003.
7. Memon S, Ahsan S, Alvi R, Fawwad A, Basit A, Shera S, et al. Retinal Screening Acceptance, Laser Treatment Uptake and Follow-up Response in Diabetics Requiring Laser Therapy in an Urban Diabetes Care Centre. Journal of the College of Physicians and Surgeons--Pakistan : JCPSP. 2015 Oct;25(10):743-6
8. Khandekar R, Al Lawati J, Barakat N. A Retrieval System for Patients with Avoidable Blindness Due to Diabetic Retinopathy who do not Present for Ophthalmic Assessment in Oman. Middle East African journal of ophthalmology. 2011 Apr;18(2):93-7
9. Hua W, Cao S, Cui J, Maberley D, Matsubara J. Analysis of reasons for noncompliance with laser treatment in patients of diabetic retinopathy. Canadian journal of ophthalmology journal canadien d'ophtalmologie. 2017 Nov;52 Suppl 1:S34-s8
10. Will JC, German RR, Schuman E, Michael S, Kurth DM, Deeb L. Patient adherence to guidelines for diabetes eye care: results from the diabetic eye disease follow-up study. American journal of public health. 1994 Oct;84(10):1669-71
11. Group TDRSR. Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. Early Treatment Diabetic Retinopathy Study research group. Archives of ophthalmology (Chicago, Ill : 1960). 1985 Dec;103(12):1796-806
12. Jorge EC, Jorge EN, Botelho M, Farat JG, Virgili G, El Dib R. Monotherapy laser photoagulation for diabetic macular oedema. The Cochrane database of systematic reviews. 2018 Oct 15;10:Cd010859
13. Mouatay T, Evans JR, Lois N, Armstrong DJ, Peto T, Aza activity A. Different lasers and techniques for proliferative diabetic retinopathy. The Cochrane database of systematic reviews. 2018 Mar 15;3:Cd012314
14. Martinez-Zapata MJ, Marti-Carvajal AJ, Sola I, Pijoan JL, Buil-Calvo JA, Cordero JA, et al. Anti-vascular endothelial growth factor for proliferative diabetic retinopathy. The Cochrane database of systematic reviews. 2014 Nov 24(11):Cd008721
Additional Files

Additional file 1. Reporting standards - PRISMA-P Checklist.

Additional file 2. Registration OSF: https://osf.io/h5wgr/

Additional file 3. Search strategy.
Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile1.docx
- Additionalfile2.docx