PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The Village-Integrated Eye Worker trial (VIEW): rationale and design of a cluster-randomized trial to prevent corneal ulcers in resource-limited settings
AUTHORS	O'Brien, Kieran; Byanju, Raghunandan; Kandel, Ram; Poudyal, Bimal; Gautam, Mariya; Gonzales, John; Porco, Travis; Whitcher, John; Srinivasan, Muthiah; Upadhyay, Madan; Lietman, Thomas; Keenan, Jeremy; Group, The Village-Integrated Eye Worker Trial

VERSION 1 – REVIEW

REVIEWER	GVS Murthy International Centre for Eye Health, London School of Hygiene & Tropical Medicine, UK
REVIEW RETURNED	06-Feb-2018

GENERAL COMMENTS	The study will add great value to the current literature on prevention and early detection and management of corneal opacities. The authors should address the following points in the manuscript: 1. There should be a mention of how comparable the intervention and study clusters were at baseline, including socio-developmental parameters. This is important as corneal opacities are affected by the level of social development and the access to eye care services. The authors should mention whether the two arms are comparable in this respect. 2. Is it planned to report the findings from the annual surveys separately from the findings on photographic evidence from persons reporting symptoms in the intervening period? This is important because the annual surveys may fail to pick up cases which resolved since the last round and underestimate incidence. 3. How much is the geographical separation between the intervention and control clusters? This should be mentioned in the manuscript. 4. Authors mention that they included 24 villages from 100+ villages based on eligibility criteria. These criteria have not been mentioned and should be mentioned. 5. The BMJ Open is categorical about the protocol papers being published well before the completion of the study. The trial was registered in 2013 and no dates have been mentioned for the start and end of the study in the manuscript. This should be clearly mentioned.

REVIEWER	Dr Wani Mena Juba Teaching Hospital Eye Department, Unity Avenue, Juba, South Sudan
REVIEW RETURNED	12-Feb-2018

GENERAL COMMENTS	This is generally a good study relevant to eye care in developing countries where corneal ulceration is common and an important and preventable cause of visual impairment and blindness. Described in more details how contamination of randomization if any by the indicators will be measured during the conduct of the study

REVIEWER	Walter Lehmacher Uni Cologne
REVIEW RETURNED	20-Mar-2018

GENERAL COMMENTS	Statistical Aspects are well done.

VERSION 1 – AUTHOR RESPONSE

Manuscript ID bmjopen-2018-021556: The Village-Integrated Eye Worker trial (VIEW): rationale and design of a cluster-randomized trial to prevent corneal ulcers in resource-limited settings – Response to reviewers

- Reviewer comments in bold
- Author response in italics
- Revisions highlighted

Editors comments:

- Along with your revised manuscript, please include a copy of the SPIRIT checklist indicating the page/line numbers of your manuscript where the relevant information can be found (http://www.spirit-statement.org/)

We have included a copy of the SPIRIT checklist with page numbers indicated.

Reviewer(s)' Comments to Author:

Reviewer: 1
Reviewer Name: GVS Murthy

Institution and Country: International Centre for Eye Health, London School of Hygiene & Tropical Medicine, UK

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below The study will add great value to the current literature on prevention and early detection and management of corneal opacities. The authors should address the following points in the manuscript:

1. There should be a mention of how comparable the intervention and study clusters were at baseline, including socio-developmental parameters. This is important as corneal opacities are affected by the level of social development and the access to eye care services. The authors should mention whether the two arms are comparable in this respect.

   We would like to thank the reviewer for taking the time to comment thoughtfully on our manuscript. We agree with the reviewer that baseline balance will be essential to review, particularly across socio-developmental factors. As the study is ongoing and we are currently cleaning the baseline data, we are unable to provide data in this manuscript. Any census information we provide here is very likely to change during the data cleaning process, and we are concerned about differences between numbers reported in this manuscript compared to the primary outcome manuscript.

2. Is it planned to report the findings from the annual surveys separately from the findings on photographic evidence from persons reporting symptoms in the intervening period? This is important because the annual surveys may fail to pick up cases which resolved since the last round and underestimate incidence.

   Yes, the responses to the screening questions asked during the annual census data collection will be reported separately from the photographic evidence of corneal ulcer incidence. The primary outcome analysis will compare the incidence of corneal ulcers between the study arms over the entire study period, and will be estimated from photographic evidence only.

3. How much is the geographical separation between the intervention and control clusters? This should be mentioned in the manuscript.
   Thank you for catching this accidental omission in the manuscript, we agree this is important to describe for a cluster-randomized trial. In this setting, we did not include any geographic separation between randomization units, opting instead to include the entirety of the area that fit within our eligibility criteria.

   We have clarified this on page 5 as follows (revisions highlighted):

We are conducting this study in all communities from 24 Village Development Committees (VDCs; government-defined administrative units) in the Chitwan and Nawalparasi districts of Nepal. VDCs are eligible for the study if they lie within the catchment area of the Bharatpur Eye Hospital and have a population of less than 15,000 per the 2001 government census. Of 112 VDCs in these districts, 24 meet the eligibility criteria and are included in the trial. Geographic separation was not considered in selection of eligible VDCs. All residents in study communities are offered enrollment in each annual census. A census worker visits each household in each village included in the study. At the baseline visit, verbal consent from each head of household is obtained for participation of all household members in the census visits.

4. Authors mention that they included 24 villages from 100+ villages based on eligibility criteria. These criteria have not been mentioned and should be mentioned.

   We have clarified this on page 6 as follows (revisions highlighted):

We are conducting this study in all communities from 24 Village Development Committees (VDCs; government-defined administrative units) in the Chitwan and Nawalparasi districts of Nepal. VDC-level eligibility criteria include location within the catchment area of the Bharatpur Eye Hospital and population of less than 15,000 per the 2001 government census. Of 112 VDCs in these districts, 24 meet the eligibility criteria and are included in the trial. Geographic separation was not considered in selection of eligible VDCs. All residents in study communities are offered enrollment in each annual census. A census worker visits each household in each village included in the study. At the baseline visit, verbal consent from each head of household is obtained for participation of all household members in the census visits.

5. The BMJ Open is categorical about the protocol papers being published well before the completion of the study. The trial was registered in 2013 and no dates have been mentioned for the start and end of the study in the manuscript. This should be clearly mentioned.

   The grant was awarded in September 2013, and the study commenced in January 2014. The study is currently ongoing and we are actively collecting data. We have added study start date on page 5:

We are conducting this study in all communities from 24 Village Development Committees (VDCs; government-defined administrative units) in the Chitwan and Nawalparasi districts of Nepal. VDC-level eligibility criteria include location within the catchment area of the Bharatpur Eye Hospital and population of less than 15,000 per the 2001 government census. Of 112 VDCs in these districts, 24 meet the eligibility criteria and are included in the trial. Geographic separation was not considered in selection of eligible VDCs. All residents in study communities are offered enrollment in each annual census. A census worker visits each household in each village included in the study. At the baseline visit, verbal consent from each head of household is obtained for participation of all household members in the census visits. Data collection for the baseline visit began in January 2014.

Reviewer: 2
Reviewer Name: Dr Wani Mena

Institution and Country: Juba Teaching Hospital Eye Department, Unity Avenue, Juba, South Sudan

Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
> This is generally a good study relevant to eye care in developing countries where corneal ulceration is common and an important and preventable cause of visual impairment and blindness.
Described in more details how contamination of randomization if any by the indicators will be measured during the conduct of the study

Thank you for your review and comments. We have clarified our use of process indicators to assess contamination in two places:

1) Page 7 (revisions highlighted)

FCHVs will not refuse diagnosis or prophylaxis to anyone based on their residence, even if people present from control VDCs. FCHVs will record the VDC of all people who present, which will allow us to assess the level of contamination.

<u>Publicity</u>
Study staff at Bharatpur Eye Hospital hold orientation meetings with teachers, traditional healers, and local political leaders to introduce the program and to encourage community leaders to advertise the programs. FCHVs in study communities advertise their services for ocular trauma through door-to-door visits with households in their wards and monthly meetings with their ward-level Mother's Groups. The FCHV describes her role as a community health worker and encourages the community to present to her within 24 hours of experiencing ocular trauma. FCHVs also post advertisements describing ulcer prevention throughout the community and distribute pamphlets, greeting cards, and calendars describing the program. All public publicity materials such as posters are removed prior to the annual census to maintain masking of the census workers. Publicity activities will be limited to the confines of the VDC boundaries in order to prevent contamination.

2) Page 10

<u>Intervention awareness surveys</u>

An intervention awareness survey is conducted annually in all VDCs, with survey workers not informed about the trial intervention, and masked to whether the community has been randomized to intervention or control. A random sample of households from the most recent census is selected to

participate in the survey. Census data, including name, phone number, and household GPS coordinates, are uploaded to the mobile software platform GIS Cloud (GIS Cloud Ltd., London, United Kingdom, http://www.giscloud.com) for the survey. The trained survey workers use handheld mobile devices to identify households from a map generated by the software, and ask an adult in the household a series of questions designed to determine their level of awareness of the intervention. Survey workers are required to complete the survey on at least 10 of the 15 selected households in each ward.

Conducting the intervention awareness surveys in control VDCs will provide a measure of contamination. Publicity is limited to intervention VDCs to reduce the likelihood of contamination, but it is possible that residents of control VDCs will learn of the intervention through exposure to publicity materials or word of mouth. Any awareness of the intervention found in control VDCs will be indicative of contamination.

Reviewer: 3
Reviewer Name: Walter Lehmacher

Institution and Country: Uni Cologne

Please state any competing interests or state 'None declared': none declared

Please leave your comments for the authors below

Statistical Aspects are well done.

Thank you for your review.

VERSION 2 – REVIEW

REVIEWER	GVS Murthy International Centre for Eye Health, London School for Hygiene & Tropical Medicine, London, UK.
REVIEW RETURNED	02-May-2018

GENERAL COMMENTS	Points raised in the review have been addressed satisfactorily by the authors.