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Comparing a comprehensive package of primary care to the standard of care to reduce blindness caused by severe corneal infections in Nepal

Submission date 26/10/2021	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 27/10/2021	**Overall study status** Completed	[X] Statistical analysis plan [_] Results
Last Edited 23/01/2026	**Condition category** Eye Diseases	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

The cornea is your eye's clear, protective outer layer. Infection of the cornea is an important cause of blindness. A scratch in the cornea allows infection to enter and an ulcer to begin. These infections can be very serious with some people losing the sight in the affected eye.

Different types of infectious organisms can cause corneal ulcers. These include bacteria and fungi. In tropical regions about half of all corneal ulcers are caused by fungi. Bacteria and fungi need to be treated with different types of eye drop medicines. Treatments for fungal eye infections are frequently not very effective, in addition access to these treatments in many countries is very limited and can be expensive.

Many people with corneal infection end up with poor vision or other eye problems because of delays in the infection being recognised and treatment being started. With this delay the condition becomes very severe, by which stage there is often nothing that can be done to save the vision or the eye itself.

This study is about testing out a new strategy in the primary health care setting to reduce the delay in diagnosis of cornea infection and the starting of an eye drop treatment, called chlorhexidine, that covers many different types of infections. They person with the infection would then be referred urgently to the regional eye hospital.

Chlorhexidine is an antiseptic. It is very effective at killing bacteria, fungi and other types of infectious organisms. It is used in medical care worldwide in several different ways. For example, it is used to clean skin before surgical operations, in antiseptic creams for skin cuts and as a mouth wash to prevent and treat mouth infections. It has been used in eye care for more than thirty years as an eye-drop preservative, for sterilizing contact lenses, for pre-operative topical antiseptic and for treating corneal infections.

If chlorohexidine eye drop were available at primary health care facilities, it would make this treatment much more easily accessible to many people with corneal infections and allow them to start appropriate treatment early in the course of the infection, as they proceed to an eye

hospital to have a change of getting a good outcome.
This study will test if using this approach of early intervention for people with corneal infection can reduce the risk of getting severe infections and blindness due to corneal infection.

Who can participate?
Patients with corneal infection attending the participating centers in Nepal.

What does the study involve?
In half of the health centres, a bottle of chlorhexidine eye drops will be provided to be taken one drop every hour. To be started straight away when you are in the health centre. To continue taking this until you are seen in the Eye Unit in Lahan. In addition, we will send you reminder phone messages on the phone number that you have given us, to remind you to attend the eye clinic for additional treatment.
In half of the health centres, the health workers are also going to give a bottle of chloramphenicol eye drops to be taken one drop every hour. To be started straight away when you are in the health centre. To continue taking this until you are seen in the Eye hospital at Lahan.
Once the initial results of the tests for infection are available, the eye doctor will prescribe eye drop treatment that is appropriate to the infection type that is identified. If you were already started on chlorhexidine eye drops in the primary health centre you may be advised to continue taking these if there is evidence that they are working well.
We will review the response to treatment and document the clinical findings at the following times after you start treatment: two days, 1 week, 2 weeks, 3 weeks, 2 months and 3 months.

What are the possible benefits and risks of participating?
Benefits:
The study will involve tests for the type of infection. This helps the doctor looking after you to choose the best type of treatment for your eyes. These tests are not usually available for patients in Nepal.
The costs for your clinical assessment, tests, treatment, and transport to the follow-up visit (after you initially come to Lahan) will be paid for by the study.
By participating in this study, you will be helping to answer the question about whether or not this early intervention programme can reduce the risk of sight loss in the affected eye.
Risks:
It is important to recognise that corneal infection is a serious, sight threatening condition. Many patients, whatever the treatment used, have reduced vision in the affected eye after it has resolved. In some people the affected eye will become blind. Sometimes the infection, despite lots of treatment, can progress to cause a hole to develop in the cornea (Perforation) and sometimes it is so severe it is necessary to perform an operation to remove the eye content.
Local Irritation: As with most eye drops, there is the risk of local irritation or stinging. This usually only lasts for a short time.
Allergic Response: Very rarely, eye drops can provoke a local allergic reaction on the surface of the eye or the eyelids.
Pregnancy and Breast Feeding: The risks to an unborn or breast-fed baby from these eye drops use are unknown. Therefore, pregnant and breastfeeding women are excluded from participating in this study.
Chlorhexidine 0.2% eye drops: Chlorhexidine eye drops are used on the surface of the eye as an antiseptic before procedures and also in the treatment of fungal and other eye infections. It has not been associated we any serious side effects. It may cause mild irritation and very rarely a local allergic response. This concentration of chlorhexidine is approved to be used in much larger volumes as a mouth wash. It is considered to be safe and is not associated with any systemic side effects.

Unknown Risks: The treatments in this study may have rare side effects that are currently not known. If during the course of the study new information becomes available, the researchers will share this with you.

Where is the study run from?
London School of Hygiene & Tropical Medicine (UK)

When is the study starting and how long is it expected to run for?
August 2018 to March 2025

Who is funding the study?
Wellcome Trust (UK)

Who is the main contact?
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
WT 207472/Z/17/Z

Study information

Scientific Title
Cluster randomised controlled trial of a complex intervention package to reduce blindness from severe microbial keratitis in Nepal

Study objectives
A complex intervention package (as described below) can reduce blindness from severe microbial keratitis (MK)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 26/04/2021, London School of Hygiene and Tropical Medicine Interventions Research Ethics Committee (Keppel Street, London, WC1E 7HT, UK; ethics@lshtm.ac.uk), ref: 25554

Study design
Prospective single-masked parallel-group two-arm cluster randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Microbial keratitis

Interventions
A total of 20 primary health centres will be enrolled; 10 clusters in each arm; each cluster serves a population of around 10,000 people (total ~100,000 per arm). The primary health centres will be the units of randomisation.

The primary health centres will be randomised to one of the following arms:
Arm I: Offer an early interventional package including smartphone-based triage system for MK, prompt treatment with g-chlorhexidine digluconate 0.2% eye drops, early facilitated referral to the eye hospital.
Arm II: Offer “standard of care” for MK.

If individuals present initially with a corneal abrasion but no evidence of a current infection they will be offered chloramphenicol eye ointment, in both arms, and then reviewed at three days.

Patients outcomes will be followed up at 3 months.

Intervention Type
Mixed

Primary outcome(s)
The proportion of people who are blind at 3 months in the affected eye (BSCVA vision less than 3 /60) measured by a trial-certified optometrist

Key secondary outcome(s))
Current key secondary outcome(s) as of 23/01/2026:

1. BSCVA at 3 months by a trial certified optometrist
2. Scar/infiltrate size at 3 months, slit lamp examination by ophthalmologists (trial certified).

3. Perforation and/or Conjunctival flaps and/or therapeutic corneal transplant (TPK) by three months, slit lamp examination by ophthalmologists.
4. Diagnostic accuracy in primary care
5. Time between symptom onset and presenting to primary care facility
6. Adherence to and time taken to attend referral at eye hospital
7. Quality of life questionnaires: EQ-5D, WHO/PBD-VF20, WHOQOL-BREF
8. Cost effectiveness analysis

Previous key secondary outcome(s):

1. Scar/infiltrate size at 3 months, slit-lamp examination by ophthalmologists (trial certified)
2. Perforation and/or therapeutic corneal transplant (TPK) by 3 months, slit-lamp examination by ophthalmologists.
3. Diagnostic accuracy in primary care measured compared to the final definitive diagnosis reached at the referral eye hospital using microbiology and in vivo confocal microscopy performed at the referral eye hospital at baseline.
4. Time between symptom onset and presenting to primary care facility measured using patient questionnaire at baseline
5. Adherence to and time taken to attend referral at eye hospital measured using the difference between patients' presentation date to primary care and the presentation to the referral eye hospital.
6. Quality of life questionnaires: EQ-5D, WHO/PBD-VF20, WHOQOL-BREF measured at baseline and at 3 months.
7. Cost effectiveness analysis measured using EQ5-D and direct cost questionnaire at baseline and at 3 months

Completion date
31/03/2025

Eligibility

Key inclusion criteria
1. Acute MK characterised by:
1.1. Corneal epithelial ulceration >1mm diameter
1.2. Corneal stromal infiltrate
1.3. Acute inflammation: e.g. conjunctival injection, anterior chamber inflammatory cells, hypopyon.
2. Informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit

18 years

Upper age limit
99 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Unwilling to participate in trial or attend follow-up
2. Aged less than 18 years
3. Pregnancy: self-reported
4. Breast feeding: self-reported
5. No light perception in the affected eye
6. Fellow eye visual acuity <6/60
7. Known allergy to study medication (including preservatives)
8. Previous penetrating keratoplasty in the affected eye
9. Bilateral corneal ulcers
10. Nationals of another country

Date of first enrolment
02/01/2023

Date of final enrolment
31/12/2024

Locations

Countries of recruitment
Nepal

Study participating centre
Sagarmatha Choudhary Eye Hospital
E-W Highway
Lahan
Nepal
56500

Sponsor information

Organisation
London School of Hygiene & Tropical Medicine

ROR
https://ror.org/00a0jsq62

Funder(s)

Funder type
Charity

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Prof Matthew Burton (matthew.burton@lshtm.ac.uk). The full data set will be available with all patient identifiable details removed. Data will be available after formal reporting of the study findings in a peer-reviewed scientific publication. Datasets will only be available to bona fide scientific investigators. Requests should be made to the Chief Investigator in writing detailing the scientific investigator's background and intended use for the data. Consideration will be given to all proposed analyses, with likely envisaged uses including investigators planning on conducting meta-analyses for example. Patient Information Sheets and consent forms specifically referenced making anonymised data available and this has been approved by the relevant ethics committees.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1	24/02/2021	26/10/2021	No	Yes
Statistical Analysis Plan	version 1.3	14/01/2026	23/01/2026	No	No