Pre-validation survey for the elimination of trachoma and evaluation of the effectiveness of the trachoma surveillance strategy in Ghana V.2

Version 2

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ABSTRACT

Background: In order to achieve elimination of blinding trachoma, a country needs to demonstrate that the elimination prevalence thresholds have been surpassed and then sustained for a three year period. Ghana achieved the thresholds in 2008, and since 2011 have been implementing their trachoma surveillance strategy, which includes community and school screening for signs of follicular trachoma and trichiasis, in each trachoma-endemic district. In 2015, the country plans to conduct a number of district level population based survey to verify elimination of blinding trachoma. This decision is currently made based on prevalence of clinical evaluation of "trachomatous trichiasis" and "trachomatous inflammation – follicular" (TF), the second of which has been shown to be a problematic indicator in low prevalence settings. Further evidence is required to determine the optimal surveillance strategy and indicators for trachoma.

Objectives: This study will determine if Ghana has sustained the elimination prevalence thresholds. Additionally, the study will review the trachoma surveillance strategy employed in Ghana and if it was able to identify any potential resurgence of infection. It will also assess the relationships between the prevalence of the clinical sign TF, compared to prevalence of infection and antibody levels, after completion of what most observers believe to have been a successful programme. This will help to determine whether it may be appropriate to consider one or more alternative indicators for validating elimination of blinding trachoma. Surveillance for other infections (including yaws and other NTDs) will also be integrated into the pre-validation trachoma survey.

Methods: The standard World Health Organization (WHO)-recommended population-based prevalence survey will be conducted in areas already scheduled to conduct validation surveys in 2015, but with the addition of eye swabbing to test for infection and finger pricking to collect bloodspots for antibody testing. Villages identified with a TF prevalence ≥5%, either retrospectively, during the on-going surveillance or during the district level survey (index village), will result in focal screening of children in neighbouring villages (and the 'index' village), including a clinical assessment and tests for trachoma infection and antibody levels. Surveillance for additional infections will also be included through antibody testing using the same sera collected for trachoma. Finally, document analysis and qualitative methodologies will be employed to review the operationalization of the trachoma surveillance system in Ghana.

Impact: Results from this study will provide the Ghana Health Service with evidence, as to whether the country has sustained their elimination targets for trachoma. It will also inform the WHO-led Alliance for the Global Elimination of Trachoma by 2020 (GET2020) on the appropriateness of alternative indicators and surveillance methodologies for verification of blinding trachoma.

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Background and rationale

1 Trachoma, a result of infection with the bacterium *Chlamydia trachomatis*, remains the leading infectious cause of blindness worldwide [WHO, 2014a]. The intervention strategy for trachoma is the World Health Organization (WHO)-endorsed SAFE strategy (S: Surgery for in-turned eyelashes a result of trachomatous trichiasis; A: Antibiotics to clear *Chlamydia trachomatis* infection; F: Facial cleanliness and E: Environmental improvement to reduce transmission of C. trachomatis) [WHO, 2006]. Based on the implementation and scale up of this strategy, the World Health Assembly set the global goal to eliminate blinding trachoma by 2020 [WHA, 1998].
Countries or districts are eligible for acknowledgement of elimination of blinding trachoma when they provide evidence that they have reached the elimination prevalence thresholds[1] and sustained those achievements for at least three years [WHO, 2010]. A suitable surveillance strategy is therefore required to provide evidence that elimination prevalence targets have been sustained and to identify any potential resurgence of disease.

After initial baseline prevalence surveys in 2000, Ghana initiated a programme to eliminate blinding trachoma in the Northern and Upper West Regions. Full SAFE interventions started in 5 districts where trachoma was found to be a public health problem. An evaluation survey conducted in the first five districts after two years of implementing control activities showed between 41-79% reduction in the prevalence of active trachoma [Ghana Health Service Trachoma Control Programme 2003]. The SAFE strategy was extended to a sixth district in 2002 and after completing baseline surveys in all areas, by 2004 endemic communities in all districts in the two regions received full SAFE. With a full knowledge of trachoma endemic areas, the National Trachoma Control Program developed a five year strategic plan (2005-2009) to guide trachoma control activities [Ghana Health Service 2005]. The plan set various targets with the ultimate goal to eliminate blinding trachoma from Ghana by 2010. The plan also provided benchmarks to assess programme performance, such as evaluating the impact of at least three years of SAFE strategy on the prevalence of disease.

Currently, Ghana is one of the countries in the post-endemic surveillance stage [WHO 2012]. Following a post-intervention impact assessment in 2008 after all endemic communities had received at least three years of SAFE interventions, the prevalence of TF fell to 0.14-2.87% from a baseline of 2.8-16.1% in 2003 [Yayemain et al. 2009]. These results revealed that Ghana has reached the ultimate intervention goal of reducing TF in children aged 1-9 years to <5.0% in all endemic districts. However, in order to achieve elimination of blinding trachoma, it is required that TF in children aged 1-9 years remains at <5% after interventions to control trachoma have ceased [Resnikoff et al. 2007, WHO 2013]. Further, the target threshold for elimination of trichiasis is a prevalence of TT <0.1% in 15 years and older. TT prevalence fell from 0.4-8.4% in 2003 to 0.05-1.07% in 2008 [Yayemain et al. 2009], but is still above the recommended threshold for validation of elimination in some districts (Table 1).

Following the post-intervention impact assessment, a post MDA surveillance strategy was put in place between 2011 and 2014, conducting both active and passive surveillance for Trachomatous Inflammation- Follicular (TF) and Trachomatous Trichiasis (TT) cases [GHS, 2010]. The surveillance strategy included the following:

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- Passive surveillance for TT cases in all health facilities, integrated into the Integrated Disease Surveillance Report (IDSR) reporting
- A convenience sample of children (aged 1-9 years) in two communities per year assessed for signs of TF. If the TF prevalence was ≥5%, then second line or neighbouring communities were also assessed for signs of clinical trachoma [WHO, 2008]
- School screening was conducted at the beginning of the school year in pre-school children, up to class three
- Sentinel sites selected for assessment of trichiasis cases in the community
- Prevalence based survey to validate if elimination targets have been sustained, at least three years after stopping MDA

There is therefore the need to evaluate the current prevalence of active trachoma as a first step towards the validation of Ghana as a trachoma free country. Further re-emergence of infection after MDA is a possibility (West et al. 2011), and as such the prevalence of disease must be regularly monitored to ensure that the gains made during 10 years of control activities are maintained. This protocol seeks to guide the surveillance assessment after 2014.
In addition, the latest guidance from WHO (which still needs to be ratified by WHO Strategic and Technical Advisory Group (STAG) on NTDs) recommends that sentinel site data are no longer recommended but the verification is to be primarily based upon a single cross-sectional epidemiologically rigorous prevalence survey, to be conducted at the district level, at least 2.5 years after the last round of antibiotic distribution. A review of the Ghana surveillance system provides a potential opportunity to provide evidence as to the relative effectiveness of these different approaches, the on-going surveillance strategy and the one-off cross-sectional population based survey.
Currently, the recommendations are based on the diagnosis of trachoma using clinical signs, as outlined in the WHO simplified grading system [Thylefors, 1987]. However, the use of TF as an indicator for trachoma in low prevalence settings can be suboptimal:

- The correlation between follicular trachoma and C. trachomatis infection is poor in low prevalence settings, often with much higher levels of TF compared to infection [Burr et al, 2013; Burton et al, 2011; Munoz et al, 2011].
- Post infection, it is uncertain how long TF lasts in an individual
- Follicles can be caused by infection with pathogens other than C. trachomatis
- Concerns over the low inter-grader reliability and precision of grading TF [Miller et al, 2004]

Therefore, diagnosis of TF as an indication of programme success can have low specificity in areas of low infection prevalence. Relying on an indicator that has low specificity and may over-estimate the prevalence of infection in the community can result in a waste of valuable resources, especially if potential 'hotspots' of infection are wrongfully identified and antibiotics are unnecessarily distributed.

Alternative indicators to provide evidence for elimination have been suggested and tested in a number of settings. Nucleic Acid Amplification Tests (NAAT), including Polymerase Chain Reaction (PCR) have been shown to be highly sensitive and specific tests [Keenan et al, 2012; Mabey and Solomon, 2003] however it is not yet clear how to use the results in program decision making. In addition, the NAAT tests for C. trachomatis infection are still quite expensive and must be conducted by specialised technicians in a laboratory where a NAAT platform is available, which may or may not be readily available in-country.

The use of serological tests (detecting antibody responses to chlamydial antigens e.g pgp3 and CT694) [Goodhew et al, 2012; Goodhew et al, 2014] provides an opportunity to determine prevalence of exposure to infection and if combined with age can potentially give a useful indicator of transmission intensity over time (especially after antibiotic distribution was stopped). The use of multiplex assays also provides the opportunity to integrate tests for a number of other pathogens using the same sera, saving costs across public health programmes. Further research is required in order to determine the interpretation and potential utility of using the prevalence of antibodies to C. trachomatis in decision-making around the elimination of blinding trachoma.

Further evidence is also required in order to better understand the thresholds for potential resurgence of infection and the implications. It is believed that repeated exposure to C. trachomatis bacteria is necessary for an immunopathologic response in an individual. If infection levels remain low this progression in sequelae and potential blindness, may not be a concern [Grayston et al, 1991; Bobo et al, 1985; Detels et al, 1966]. It is currently difficult to predict and determine the significance of potential re-emergence of infection.

[1] Less than 5% prevalence Trachomatous Inflammation, Follicular (TF) in children aged 1-9 years and less than 0.1% prevalence of Trachomatous Trichiasis (TT) in adults aged 15 and over.

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Expected Outcomes

2 Results from this pre-validation trachoma surveillance strategy will provide the Ghana Health Service (GHS) with evidence as to whether the country has sustained their elimination targets for trachoma. It will also inform the WHO-led Alliance for the Global Elimination of Trachoma by 2020 (GET2020) on the appropriateness of alternative indicators and surveillance methodologies for validation of blinding trachoma.

Aims and Objectives

3 **Aim:** To determine the prevalence of TF and TT, review the effectiveness of the trachoma surveillance strategy in Ghana and provide evidence as to whether Ghana has sustained the elimination prevalence thresholds, achieving validation for the elimination of blinding trachoma.
Objective 1: To determine the prevalence of TT "unknown to the health system" in adults aged 15 and over and to determine the prevalence of TF in children aged 1-9 years old
Objective 2: To determine the proportion of clean faces in endemic communities by observing the presence and absence of ocular and nasal discharge among children 1-9 years
Objective 3: To determine environmental improvements in previously endemic communities, through measuring the proportion of households that have access to (potable) water and household latrines
Objective 4: To compare the different indicators (TF, infection and antibody levels) for trachoma surveillance and their use in decision making to validate elimination
Objective 5: To assess the potential of the "on-going" trachoma surveillance strategy used in Ghana, to identify hotspots of infection and potential areas of on-going transmission, detecting recurrence and/or recrudescence of TT cases and management of new TT cases
Objective 6: To review the operationalization, processes and performance of the on-going trachoma surveillance strategy in Ghana and provide recommendations to improve implementation
Objective 7: To inform the understanding of the transmission of other key infections, including yaws, through the integration of tests for other infections into the single cross-sectional trachoma surveillance survey

Methodology

4 The study will use a mixed methods design, including cross-sectional surveys, qualitative interviews and documentary analysis.
A) District population based survey, to validate if elimination targets have been sustained. This will include an assessment of clinical signs, infection and antibody levels for trachoma. Additional serological tests for antibodies to other key pathogens, including other Neglected Tropical Diseases (NTDs) will also be included.
B) Focal screening of villages neighbouring potential 'index' villages to determine any potential hotspots of infection or areas of on-going transmission. An 'index' village is defined as a community with a TF prevalence ≥5% (in children aged 1-9 years). These 'index' villages are either identified retrospectively from data collected during the on-going surveillance strategy, employed by Ghana or will be identified as part of the new, single cross-sectional district level population based survey.
C) Documentary analysis, in-depth interviews and costing analysis (Annex F) with key stakeholders aimed at reviewing the performance and operationalization of the Ghana trachoma surveillance strategy. Key criteria to be covered (not exhaustive) includes key barriers and constraints to implementation of the surveillance system, reporting, data management, cost-effectiveness and funding gaps, co-ordination, management and review structures, sustainability and acceptability of approach and recommendations to improve surveillance system methodology.

Study sites

5 The study will be conducted in the two trachoma endemic regions of Northern and Upper West regions of Ghana. There is a single rainy season, from May to October, when humidity generally reaches 70-90%. During the long dry season (November to April), the humidity drops significantly and the colder, dusty and dry harmattan winds blow northeast. Many farmers migrate south during this period. A number of rivers run through the regions, including the tributaries of the Volta (Black Volta, White Volta), Kulpawn and Sissili. However, many communities in these regions rely on underground water, especially during the dry season.
The ethnic groups of the regions are diverse and distinct, each having their own beliefs and traditional practices. However the predominant ethnic groups in the study areas are Sissala and Dagaaba in the Upper West and Dagomba, Konkomba and Gonja in the Northern region. The literacy rate among adults in this part of the country is among the lowest in Ghana.

These two regions were identified as trachoma endemic regions between 2001-2004, see table 1 below. In 2008, all 37

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districts (split from 18 parent districts) were declared to have achieved the elimination prevalence thresholds and mass distribution of antibiotics was stopped. Surveillance activities began in 2011 and a validation survey is to be conducted in 2015.
For the purposes of this study, districts will be combined back to their original parent districts (same as those used for the baseline study) to create 18 evaluation units with a population of between 100,000 to 250,000 population, see Annex A.

Table 1: Trachoma prevalence in Northern and Upper West region districts at baseline and at follow-up

Mother District	%TF	%TFTI	%TT	Survey year	%TF	%TFTI	%TT	Survey year
Category 1								
Tolon Kumbungu	-	12.4	8.4	2000	0.19	-	0.33	2008
West Gonja	-	11.7	3.7	2002	0.14	-	0.76	2008
Sissala	-	11.5	1.6	2000	0.83	0.88	1.07	2008
Wa	-	16.1	2.6	2000	1.34	-	0.57	2008
Savelugu Nanton		9.7	4.5	2000	1.15	-	0.52	2008
Bole	8.2	-	1.8	-	2.81	0.07	0.31	2008
West Mamprusi	6.8	-	0.8	2003	0.88	-	0.47	2008
Zabzugu/ Tatale	6.7	-	0.4	2003	1.66	-	-	2008
Tamale Municipal		4.7	4.9	2000	0.53	-	0.41	2008
Jirapa/ Lambussie	5.0	-	0.8	2003	0.57	-	0.34	2008
Gushiegu/ Karaga	4.4	-	0.8	2003	0.97	-	0.19	2008
Nanumba	3.8	-	0.5	2003	1.88	0.12	0.05	2008
Gonja	3.7	-	0.9	2003	0.38	-	0.09	2008
Nadowli	3.6	-	1.3	2003	0.15	-	0.19	2008
Yendi	3.5	-	1	2003	0.31	-	0.23	2008
Saboba/ Chereponi	3.2	-	0.5	2003	0.38	-	-	2008
Lawra	2.8	-	0.7	2003	0.18	0.26	0.15	2008
East Mamprusi	2.8	-	0.6	2003	0.36	-	0.13	2008

Study population

6 **Inclusion criteria**

Districts or evaluation units will be eligible for inclusion if they achieved the elimination prevalence thresholds at least three years ago. All evaluation units will be assessed for clinical criteria and a selection (based on baseline trachoma prevalence) will also be eligible for infection and serological indicators and focal screening activities. Within eligible districts and selected households, everyone aged ≥1 year is eligible for some portion of the study.

Exclusion criteria

Districts or evaluation units that have not reached the elimination prevalence thresholds or did so less than three years ago. Children less than 1 year old will not be eligible for participation in the study.

Sampling

7 **A) Population based survey**

i) Sample selection

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A population based survey, following a two-stage cluster sampling methodology, will be conducted. The primary sampling unit, the village (or enumeration area), will be selected probability proportional to size. A list of all villages with respective populations will be compiled for each mother district. All communities with population greater than 5000 and less than 200 will be excluded. Twenty-four clusters will be selected in each district. The total cumulative population of the district will be divided by 24, to obtain the sampling interval. A random number between 1 and the sampling interval will be generated to select the first cluster. The sampling interval will then be successively added to select the remaining 23 clusters.

The secondary sampling unit, the household, will be randomly selected using the household listing approach, or if household lists at the village level is not easily attainable, compact segment sampling. All eligible individuals in the household will be sampled.

All 18 evaluation units (EU) will conduct the clinical assessment for diagnosis of trachoma. In addition, 9 evaluation units (3 from EUs with a baseline TF of ≥10%, 3 from EUs with a baseline TF 5-9.9% and 3 from EUs with a baseline <5% in children aged 1-9 years, see Annex A) will also be included for the additional aspects of the study i.e. collection of ocular swabs, dried blood spots and focal screening activities. Only children aged 1-9 years old will have samples taken for analysis.

Outline of compact segment sampling: When the team gets to the village, they will meet the highest-ranking village leader and seek consent. Once permission is granted, the village leader will be asked to provide information on the number of households in the village. If the number of households is greater than the required number (for this study we require 40 households per village, see sample size calculations below), a sketch map and household listing of the village will be required. If the number of households is 40 or less, all households in the village would be examined. Several people can help with the listing on the sketch map: the village chief, elders, community health worker and trachoma volunteer. The village boundaries will be drawn orienting the North, South, East and West, along with key landmarks or easily identifiable points in the village e.g internal paths, churches, schools, water points. All households will be marked per their location within the village.

All households will be grouped into segments of 20 households and each segment numbered. A corresponding number for each segment will be written on a piece of paper that will be placed in a container such as a cup or hat. After all the pieces of paper have been mixed together, two segments will be selected at random (by someone from the village) and these will represent the two segments to be surveyed. All households in the segment selected will be surveyed.

Selected households will not be replaced when residents are absent or refuse examination. To minimize the number of residents missed in selected households, survey teams will re-visit the household before leaving the village on the day of the survey.

ii) Sample size calculations for district level survey

The sample size was calculated for the required precision of TF in children aged 1-9 years old, based on the following parameters:
Prevalence of TF (p): 4%
Precision (d): +/- 2%
Z value (z): 1.96 or 95% confidence level
Design Effect: 3.3
Expected non-response: 10%

Using the following formula:

Sample Size= z2(p(1-p))/d2

Taking into account the design effect and non-response, this gives a total sample size of 1,338 children aged 1-9 years old, per evaluation unit (District). The above sample size is per evaluation unit. Therefore a total of 24,084 children will be sampled across 18 evaluation units (parent districts).

iii) Data collection tools and methods

- Questionnaire

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The survey team will ask the head of each selected household for basic demographic information as well as other standard trachoma survey questions about access to water, sanitation and hygiene. GPS data will be collected.

- Clinical assessment

All individuals aged ≥1 year in every selected household will be examined for signs of trachoma (TF, TI, TS, TT) based on the WHO Simplified Grading Scale.

Digital photographs will be taken of all cases, clinically assessed to be TF, TT, for evaluation by a second experienced grader.

- Ocular Swabs

Children aged 1 to 9 years in every selected household will have ocular swabs collected for NAAT testing by swabbing the upper tarsal conjunctiva of the left eye (see Annex E for more detailed outline of procedures). Negative control swabs will also be taken by passing a clean swab in the air within 2 inches of a child's eyes, once in every 50 swabs, determined at random, using the random number generator in Microsoft Excel.

- Dried Blood Spots

Children aged 1 to 9 years in every selected household will have a finger pricked and their blood (60µl) will be collected on filter paper. Filter papers are labelled with a bar code, dried, and stored in individual Ziploc bags at -20° until tested. See Annex C and D for more detailed outline of procedures.

B) Focal screening around 'index' villages

i) Sample selection

During the surveillance, a number of villages were identified to have a TF prevalence ≥5% in children aged 1-9 years old. These 'index' villages will be re-visited and all consenting children aged 1-9 years in the village will be assessed for clinical signs, ocular C. trachomatis infection and antibody levels, using procedures outlined above.

Any villages identified to have a TF prevalence ≥ 5% during the district survey, will also lead to the neighbouring villages (immediate villages in any direction from the point of reference) being selected for additional sampling. As above, all children aged 1-9 years in the village (or a minimum of 329 children) will be each assessed for clinical signs, ocular C. trachomatis infection and antibody levels. It should be noted that although ocular swabs will be taken from all villages included in the focal screening activity, analysis of ocular C. trachomatis infection (using PCR) will be prioritised to the 'index' villages and only extended to neighbouring villages if the index village has any positive samples. This is because the PCR process is time consuming and expensive and there is a necessity to prioritise samples for analysis. Antibody levels will be tested in all villages.

Basic information about the social dynamics of the villages e.g ethnicity, points of interaction of children under five e,g pre-schools or nursery, place of worship, water points, trade centres, will also be collected. This will help review the focal screening strategy and help explain any potential differences in prevalence estimates obtained from the index village in comparison to neighbouring villages.

Where school entrance screening identified TF prevalence ≥5%, the communities linked to the school will also be re-examined for potential infection and antibody response.

C) Assessment of operationalization of trachoma surveillance system

i) Documentation analysis

This will include a desk review of available information regarding the roll out and review of the trachoma surveillance system in Ghana (Annex E). This will include available reports, protocols, publications and meeting notes.

ii) Qualitative interviews

Additional information on the process, performance and operationalization of the trachoma surveillance system will also be collected through in-depth interviews with key stakeholders (Annex E and F). This will include the national co-ordinator for trachoma and other NTDs, regional and district trachoma co-ordinators and health facility workers responsible for trachoma surveillance activities.

iii) Cost-effectiveness analysis

We intend to look at the incremental cost-effectiveness ratio (or ICER) of the various components of the surveillance system/strategy. The objective is to compare the incremental cost and benefits of different options for active

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surveillance (i.e. school screening, community screening for TF, and sentinel sites for TT) versus passive surveillance (used as a comparator). Costing data will be based on actual expenditures collected from project and GHS records. The effect of each surveillance component will be calculated using the number of TF and TT cases detected.

Team composition for the survey

8 Each team will consist of the following:
- Trachoma grader (to also take ocular swabs)
- Recorder
- Technician/nursing assistant (to take blood spots)
- Driver
- Community guide

Data handling and analysis

9

Data collection and storage

Questionnaires and clinical examination results will be collected on a smart phone data collection system. Trainings will be held on the use of the system in advance of field work to ensure correct and uniform usage of the tool.

Interviews will be conducted by experienced qualitative researchers and will be audio-recorded.
The GHS will have primary ownership over all data collected. Information collected using the electronic data collection system will be uploaded to a cloud server with password-protected access to the database only granted to the GHS and collaborative study investigators for analysis.

Specimen processing

Ocular swabs will be analysed at Noguchi Memorial Institute, using a commercially available NAAT platform (GeneXpert). International certification and quality assurances will be put in place before the ocular swabs are processed.
The bloodspot specimens (from the 9 districts and the focal screening activities) will be processed at Noguchi Memorial Institute, using an enzyme-linked immunosorbent assay (ELISA) to test for the presence of C. trachomatis antibodies. The bloodspot specimens will also be tested at the Centers for Disease Control and Prevention (CDC), Atlanta, USA. , using the Luminex multiplex assay, which allows to test with multiple antigens from sera eluted from a single dried blood spot. Assays will be conducted to detect antibodies against two C. trachomatis antigens: pgp3 and CT694, with other antigens to be explored if these two provide insufficient resolution for program needs. We will also include antibody tests to detect evidence of exposure to the following pathogens: yaws (T. pallidum), onchocerciasis (O. volvulus), Lymphatic Filariasis (W. bancrofti), schistosomiasis (S. mansoni), Strongyloides, Ascaris. The results of the tests for C. trachomatis antigens from CDC will be compared to the results from the ELISA testing at Noguchi, this will provide evidence to validate the use of ELISA in trachoma-endemic countries.

Data analysis

Results from clinical examination of all participating children aged 1 to 9 years within an evaluation unit will be aggregated to determine an evaluation unit-level prevalence of TF.
Results from clinical examination, infection, and antibody testing will be compared by age to understand the correlation of the three indicators. The antibody response to the additional infections (i.e. not trachoma) will also be analysed by age group.
Qualitative data will be transcribed verbatim. It is expected the interviews will be conducted in English although if the interviewee is not comfortable in this language, an appropriate language will be used and the interview transcribed into English. Analysis will be conducted using a relevant methodology e.g. grounded theory approach.

Dissemination and reporting of results

All data will be made available to the GHS in real time as it is received from the field. The GHS can then choose with whom they will share the data (e.g. implementing non-governmental organization partners, WHO, etc.). Investigators will have access to de-identified data for the purpose of analysis. Aggregated analysis may be presented at local and international meetings to inform recommendations around trachoma surveillance policies. Results will also be written up for publication and as a contribution towards the attainment of a PhD, with express prior permission and involvement of the GHS.

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Quality assurance and trainings

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Trainings

The teams will be trained over a one week period and will include both theory and practical sessions. The training will cover issues of data collection (including how to safely conduct clinical examinations, collect blood spots and take ocular and ulcer swabs), recording, sampling procedures and ethical considerations.

All trachoma clinical graders will be assessed for their accuracy in diagnosis of actual TF cases as compared to a gold standard grader trainer, who has extensive experience of training graders and has been certified by the Global Trachoma Mapping Project. All graders must achieve a kappa score of at least 0.7 for inclusion in the team. Due to the low prevalence of TF cases in Ghana, the graders assessment may need to be conducted in a country with a higher trachoma prevalence e.g., Nigeria.

Supervision

The Principal Investigators will have overall responsibility and oversight of the quality and implementation of the study. During data collection, each research team will be directly supervised by a supervisor, who has extensive experience in conducting similar studies.

Ethical considerations

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Confidentiality

All information collected will be confidential. Individuals will be assigned a personal identification number, which will link the results of clinical examination, infection, and antibody testing, removing any personal identifiers in the database. However, personal identifiers will be retained at the country level for the purpose of following up with patients in need of trichiasis surgery or other medical attention. All electronic databases will be password protected with logged, individual-level access only available to staff designated by the GHS and the study data manager.

Risks of participation

The risks to participants of this study are extremely low and will be minimized by using standard precautions for all procedures. Participants may experience minor discomfort and bleeding resulting from the finger prick, and minor discomfort from the eye or ulcer swab and clinical examination.
Field teams will receive thorough, standardised training on clinical examination, eye swabs, and blood collection. A sterile lancet will be used to prick the finger, the finger will be cleaned with an alcohol swab prior to pricking, and a sterile dressing will be applied afterwards. Examiners will change gloves after each examination.

Benefits of Participation

Any individuals identified as having active trachoma or other infection during the survey process, will receive appropriate treatment. If the individual has a medical condition that can not be handled by the team or in the community, the person will be referred to the nearest health facility that can manage them.
More widely, the results will help to determine if blinding trachoma has been eliminated in the district or there has been potential resurgence of disease that may require intervention. It will also provide information to help inform decisions over the implementation of interventions for other infections tested for through serology.

Informed consent

Information about the study and the use of data (see Annex G) will be read out to the invited participants before they consent to taking part. The informed consent form and information sheets will be translated into the local language. Where they are unable to sign their name, a thumbprint will be taken. The written informed consent of the household head and each study participant (see Annex H) will be obtained before data collection and specimen collection. Parental consent and assent from older children will also be sought in the case of minors (see Annex I).

Written informed consent will also be obtained from all requested for interview.

Ethical review and authorisation of the study

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The study will be reviewed by the Ghana Health Service, Ethical Review Committee in Ghana. The study will also have been reviewed and authorisation received from relevant persons within the GHS e.g. Trachoma and NTD Programme Managers and regional administration.

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