PART 0: PREAMBLE

THESIS TITLE

Relationship between the prevalence of trachomatous inflammation in children (age 1-9years) and the prevalence of trichiasis in adults (age 15years and above) at a presumed steady state

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DECLARATION

I, Ellen K. Antwi-Adjei, hereby declare that this is my original work and has not been presented before for the award of a Masters' Degree in Public Health (Community Eye Health Track).

Signature: Signed by candidate Signature Removed

Date: 23/11/2016

DEDICATION

I would like to dedicate this thesis to my wonderful family and friends for all their support and encouragement to forge forward.

And also to all individuals with trachoma; “Elimination is possible!”

DISSERTATION ABSTRACT

Background: Trachoma is the leading cause of infectious eye disease that leads to blindness. Continuous re-infection by the bacteria, *Chlamydia trachomatis,* leads to scarring of the cornea and subsequently to blindness. It is commonly found in the poorest and remotest part of Africa, Asia, Latin America and Mid-east, where hygienic conditions are also poorer. The Alliance for the Global Elimination of Blinding Trachoma by the year 2020 (GET 2020) was launched by World Health Organization (WHO) with the main aim of eliminating trachoma as a public health problem globally by year 2020. The Alliance funded Sightsavers, as part of the strategy to meet this target, to set up the Global Trachoma Mapping Project (GTMP) which was to map all endemic places for intervention through a population-based prevalence survey. There are five main signs of the disease and the number of people affected by each sign explains the magnitude and the intervention needed in that population. WHO recommends the active trachoma survey in children age 1-9 years and the blinding signs in adults' age 15 years and above. More researches, that establish quicker means of intervention for the endemic trachoma areas, are needed using the GTMP data in order to meet the year 2020 target.

Methods: Baseline data from the Global Trachoma Mapping Project (GTMP) was used as a secondary dataset for this research. All eligible regions in Ethiopia were included. The GTMP teams conducted surveys in seven regions. All age groups were included, but for the purpose of planning, the study assessed TF in children age 1-9 years and TT in adults age 15 years and above. The prevalence of TF in children and TT in adults are indicators for programme decision making for intervention and establishing the relationship between them would aid in the intervention. The relationship if established could help in planning the extent of intervention needed in a given population. Data on sanitation and hygiene as well as altitude, which were

collected as part of GTMP, were assessed to determine if they contributed to relationship between TF and TT.

Results: The study included a total of 282,558 individuals living in 174 evaluation units from seven regions of Ethiopia, among whom 256,587 gave consent to be examined. This study found a significant relationship between the prevalence of TF in children and the prevalence of TT in adults when analysis is done at the evaluation unit level (correlation rho, 0.59; p-value <0.0001). Hence, 59% of the prevalence of TT in adults can be explained for by the presence of TF in children. Sub-group analysis showed that the correlation persisted at the regional level.

Conclusion: A better understanding of the relationship between the prevalence of TF and the prevalence of TT together with the factors influencing this association using this large dataset may aid in prioritization of districts for intervention and has implications for global activities for the elimination of trachoma.

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Last but not least, to my lovely husband, Mr James Antwi-Ajei, and the whole family for their love and support and bearing up with me during my stay in Cape Town, South Africa.

TABLE OF CONTENTS

PART A: PROTOCOL

NB: This protocol was written by the MPH candidate, Ellen K. Antwi-Adjei, and based on secondary data.

Study Protocol

Relationship between the prevalence of trachomatous inflammation in children (age 1-9 years) and the prevalence of trichiasis in adults (15 years and above) at a presumed steady state

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Purpose of Study

The purpose of this study is to establish the relationship between the children with active trachoma (TF) and adults with trichiasis (TT)- since blindness is a sequela to TT, in endemic areas of the world; and also find out factors that predict this relationship. This study intends to establish if a known prevalence of TF can be used to predict the prevalence of TT for priority setting. This study will inform on factors that lead to trichiasis (TT) in adults. Global Trachoma Mapping Project (GTMP) data for Ethiopia will be used for this study. The study's primary aim answers the question:

What is the relationship between the prevalence of Trachomatous inflammation: follicular (TF) in children (age 1-9years) and the prevalence of Trachomatous trichiasis (TT) in adults (age 15 years and above) at a presumed steady state in Trachoma endemic areas?

- Does the relationship exist at various sub- group?

Additionally, the study answers the question:

What are the factors that predict this association?

- Does the sanitation and hygienic factors predict the relationship?

Background

Trachoma is an eye infection by the bacteria, *Chlamydia trachomatis* that causes a chronic infection of the eyelid. Repeated re-infection cause scars, turning the eyelid inward and causing the eyelashes to scratch the surface of the eyeball. Continuous scratching over time leads to destruction of the corneal tissues and finally leads to blindness (Mabey, Solomon and Foster, 2003). Trachoma is a chronic conjunctivitis which is transmitted under poor hygienic conditions and is endemic in many of the poorest and remotest parts of Africa and Asia (Mariotti, Pascolini, Rose-Nussabaumer, 2009: Burton, 2007).

According to World Health Organization (WHO), currently 39 million people are estimated as being blind (visual acuity <3/60) globally with cataract responsible for nearly half of the global blindness (47.8%), followed by glaucoma (12.3%). Trachoma accounts for 3% of global burden of blindness and is the leading infectious cause of blindness (Pascolini and Mariotti, 2012). It is a blinding disease in communities where *Chlamydia trachomatis* exists and have favourable conditions to help in its transmission.

Transmission of trachoma occurs when *Chlamydia trachomatis* is spread through direct personal contact, clothing and shared sleeping materials and by *Musca sorbens*, which are eye-seeking flies that transmit infection by moving from one face to another. Exposed animal and human faeces support the breeding of these flies as well as environments that are dry and dusty. Rural and economically under-developed areas where good water supply and basic sanitation amenities are lacking are normally endemic with trachoma, (Berhane et al., 2007) and trachoma prevalence in the rural areas is much higher than in urban areas (42.5% in rural verses 10.7% in urban). Conditions in the rural communities enhance persistent and multiple re-infection with Chlamydia trachomatis.

In a given community, the burden of trachoma is established by the prevalence of clinical signs of the disease. Each of the signs is important for knowing the magnitude of the disease in that population and the control measures to take. The WHO grading scheme for assessing trachoma is based on 5 signs of trachoma: Trachomatous inflammation: follicular (TF), Trachomatous inflammation: Intense (TI), Trachomatous scarring (TS), Trachomatous trichiasis (TT) and Corneal opacity (CO). (Thylefors et al., 1987) The detailed description of the signs is shown in Table 1.

Table 1. WHO simplified trachoma grading classification system

SIGN	DESCRIPTION
TF	Trachomatous inflammation, follicular: the presence of five or more follicles of at least 0·5 mm diameter in the central part of the upper tarsal conjunctiva.
TI	Trachomatous inflammation, intense: pronounced inflammatory thickening of the upper tarsal conjunctiva obscuring more than half the normal deep tarsal vessels.
TS	Trachomatous conjunctival scarring: the presence of easily visible scars in the tarsal conjunctiva.
TT	Trachomatous trichiasis: at least one eyelash rubbing on the eyeball, or evidence of recent removal of in-turned eyelashes.
CO	Corneal opacity: easily visible corneal opacity over the pupil, so dense that at least part of the pupil margin is blurred when viewed through the opacity.

The active clinical manifestation of trachoma is TF; in some cases TI is also included in the definition. The prevalence of active trachoma is established by undertaking a population based survey of children age 1-9 years. The prevalence of TT is also assessed by a population based survey (using the same clusters) of adults of age 15 years and above. Active trachoma is a contagious chronic keratoconjunctivitis which occurs mainly in children (Johnson et al., 2003), with preschool children in highly endemic communities being the main carriers; the prevalence generally declines after the age of ten. The prevalence of TT increases with age and reflects the repeated episodes of re-infection.

According to WHO (2004), the Ultimate Intervention Goal (UIG) is achieved when TF prevalence in children age 1-9 in a district is less than 5% and TT prevalence in the whole

population is less than 0.1% (1 case per 1000 population in all ages). The strategy used to achieve this target consists of the combination of SAFE intervention. The aim globally is to achieve elimination of trachoma by 2020 and this can be achieved when the factors leading to increased transmission of the disease are interrupted.

WHO recommends the SAFE strategy for countries that have trachoma as a public health problem (WHO, 1998). SAFE is an acronym which means:

- S- Surgery for trichiasis cases
- A- Antibiotics to treat the infection
- F- Facial cleanliness to reduce transmission
- E- Environmental improvements to sustain reduction in transmission

Justification

Trichiasis, entropion and corneal opacities, which are the sequelae of active trachoma, are commonly found in adults, increasing with age (Munoz et al., 1997: Courtright et al., 1989). A study done in a rural Nile Delta hamlet of Egypt (Courtright et al., 1989) observed half of the children had conjunctival scaring by the age of 10 with 90% of residents 25 years with moderate or severe scarring, concluding that severe conjunctival scarring can sometimes appear in children in highly endemic areas but is generally found in adults, increasing prevalence with increasing age. It should be recognized that not all people with active trachoma (TF and/or TI) develop conjunctival scarring and not all people with conjunctival scarring develop trichiasis.

Generally, the severity of conjunctival scarring is related to the number of episodes of active trachoma in children but it is difficult to reliably assess who is at risk of developing trichiasis. There are many studies demonstrating a high prevalence (over 30%) of children with active trachoma yet the prevalence of trichiasis in adults is generally below 1%. Accordingly, in highly endemic areas in South Sudan and Ethiopia, studies done on risk factors have concluded

that the increased risk of trichiasis is associated with an increase in the prevalence of active trachoma in children in these communities (Ngondi et al., 2008; Ngondi et al., 2009). These associations have been established in individual countries. There has been limited prospective research to allow a prediction of TT based upon a TF prevalence on a global scale.

The lack of standardized, large scale data collection has limited previous efforts to assess the association between active trachoma and trichiasis. This study would make use of large data sets (GTMP) from Ethiopia, analyse them to establish if there is any relationship between trachomatous inflammation: follicular (TF) and trachomatous trichiasis (TT) in a presumed steady state and if the prevalence of TF can be used to predict the TT prevalence.

For the purpose of decision-making for intervention for active trachoma, WHO recommends TF (only) in children age 1-9 years. We would like to find out whether the prevalence of TI in children in these endemic areas contributes to this relationship and which might further indicate the need to consider TI when making intervention decisions. A cohort study done in Tanzania on preschool children indicated 29% of the children with constant severe trachoma with TI had scarring leading to trichiasis as compared to children with just TF but no TI, where only 9.6% of children with TF who had scarring (West et al., 2001). Their study established that severity of TI plays a role, but will this be the same on larger scale; the study was limited to one district in Tanzania. Factors which may contribute to the association according to studies done in different endemic areas include average age of children with TF, prevalence of TI in children, average age of adults with TT and sex-specific ratio of TT (West et al., 2001). The GTMP data for Ethiopia will be used to establish whether factors like water and sanitation can predict the association between TF and TT. It may help in establishing a predictive link, and help in early intervention so as to achieve total elimination as per the mission of WHO and Alliance for the Global Elimination of Trachoma by 2020 (GET 2020). A better understanding of the relationship between the prevalence of TF and the prevalence of TT together with the factors

influencing this association may aid in prioritization of districts for intervention. The main study questions are:

1. What is the relationship between the prevalence of TF (in children age 1-9 years) and the prevalence of TT in adults (15 years and above) at a presumed steady state?
2. What are the factors that predict this association?

If there is variation in the relationship according to the TF prevalence it may suggest that programmes need to prioritize additional groups for intervention. This study itself would not lead national programme managers to change programme decisions; it would likely lead to additional questions that need to be addressed through further research.

Methodology

Study Design

The proposed research is a cross-sectional observational study using secondary data from Global Trachoma Mapping Project (GTMP) in Ethiopia.

Sample size

All Ethiopia GTMP data (about 7 regions, 240,000 children, and similar number of adults) will be included. The sample will involve all households with TF and TT captured by the project.

Characteristics of the Study population

All children from the age of 1 to 9 years and adults from 15 years and above in districts in Ethiopia captured on the GTMP dataset from March 2012 to March 2015 will be included in this study. Ethiopia was selected as trachoma prevalence in these areas is likely to be at a steady state.

Data collection methods

The research will make use of secondary data from GTMP. An Expression of interest (EoI) (Appendix 1) has been approved by GTMP and the GTMP team will request release of data for analysis.

The GTMP dataset contains details of these stages, TF, TI, TS and TT, of trachoma in endemic districts that has been mapped by the GTMP team. The data was achieved through a population-based prevalence survey of households in more than 20 clusters (based on WHO guidelines) in each evaluation unit (100,000 – 250,000 people) by survey teams. All data are collected electronically on the field, using Android smartphones running the LINKS app, which is being maintained by the Task Force of Global Health, Atlanta, GA, USA.

Data Cleaning and Approval Process

A two-person team, consisting of a certified trachoma grader and a data recorder, is used for GTMP data collection. The certified grader examines individuals for trichiasis and active trachoma while the recorder asks and documents responses to a series of water, sanitation, and hygiene (WASH) questions. Data is recorded using Android smart phones and a web-based database application (LINKS). At the conclusion of data collection for each cluster, the GTMP data manager cleans the raw data by removing any noise generated by the data transmission process, checking for errors, and querying any inconsistencies with the field team. To ensure the validation of the data for each country, an epidemiologist appointed by the relevant Ministry of Health (MOH) evaluates the data, and then either approves the dataset or queries it with the GTMP Chief Scientist. This process is streamlined through the automation of analyses generating prevalence and summary data. Once the methodology is validated by the MOH epidemiologist, the MOH or designee signs off on the summary data. This allows the

categorical trachomatous inflammation-follicular (TF) and trachomatous trichiasis (TT) prevalence data to be displayed on the Trachoma Atlas (www.trachomaatlas.org).

Variables in this research include age (1-9years for children and 15years + for adults), gender and the presence and absence of the signs of trachoma at the individual level (TF, TI, and TT).

Data Safety and Monitoring

Computer-based records will only be available to those involved in this study through the use of access privileges and passwords.

Data management and analysis

Data will be exported into STATA 12 (STATA for Windows, version 12, Stata Corp; College Station, TX) for analysis. Data will be explored using univariate and bivariate descriptive statistics. Median and inter-quartile range (IQR), or means and confidence intervals (CI) will be used to describe the continuous covariates depending on their distribution. Binary and categorical covariates will be described using frequency distributions. Frequency tables will be used to describe the number of children and adults with TF and TT respectively and other factors associated with them. The frequency of TF and TT in the various endemic areas will be compared. The dependent variable will be the number of TT while number of TF, number of TI, age and sex will be evaluated as independent covariates. Regression models will be use to estimate and predict the relationship between the stages in trachoma and also to assess the contribution of other factors to this association.

Sub-group analyses will be done by a number of factors including average age of children TF, prevalence of TI in children, average age of adults with TT, level of TF endemicity (WHO implementation thresholds) and geographic location.

Informed Consent

All data is anonymous. Ethical approval was provided by the Ethiopian Federal Ministry of Health. There will be no direct contact with any research participant. As part of routine services in GTMP studies, all participants in the various districts complete a consent form before the study is carried out. Individuals aged 15 years and over give verbal consent for themselves if they are competent to do so. Verbal consent is used because of the low literacy rates in these study areas. Parent or guardian of individuals younger than 15 years give the consent on their behalf. For consent to be valid in GTMP survey, the person must understand what will happen as part of the survey; that they have the right to refuse consent; and that access to services will be the same regardless of whether or not the individual participates.

Risks

This study represents minimal risk research since there is no direct involvement of human subjects but rather collected data on GTMP.

Benefits

The proposed study holds direct benefit to all participating districts since knowledge gained may assist in identifying areas where effort should be focused to improve trachoma treatment (SAFE) in order to help prevent blindness in these areas. With GTMP survey, any person with TF and/or TI are given two tubes of tetracycline eye ointment with instructions to apply it to both eyes twice daily for six weeks. Persons with TT are referred to the nearest facility for trichiasis surgery using the standard referral form while persons with any other medical problem are referred to the nearest appropriate medical facility.

Privacy and Confidentiality

All personnel involved in the screening of trachoma patients and the data collection in the GTMP undergo specific training for the survey in confidentiality and related patient protection

issues. GTMP data does not have individual names but rather contains names of the various districts to maintain participants' privacy. All electronic records are kept in password-protected files and are released only per the decision of the GTMP partners including the MOH of the country involved.

Ethics approval

Ethics approval for this research would be sought from the University of Cape Town Human Research Ethics Committee. Additionally, permission to conduct the research with Ethiopia data would be obtained from the Ethiopian government through the GTMP team using Expression of Interest (EoI) form.

Budget

The study would be conducted as a Master's level mini-dissertation. The student would serve as the principal investigator and use her personal computer, hence no additional funds would be needed.

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PART B: STRUCTURED LITERATURE REVIEW

Literature Review

Introduction / Objectives

The structured literature review in this chapter is to create a review on the key researches on clinical knowledge on blinding trachoma disease as well as the public health implications. The review articles are on the definition, magnitude, aetiology, control, public health preventive intervention narrowing down on the blinding stage of the trachoma disease.

Trachoma is the leading infectious cause of blindness and is estimated to accounts for 3% of the global burden of blindness currently (Pascolini & Mariotti, 2012).

Literature Search Strategy

The search strategy for the literature review involved articles and documents that addresses topics related to trachoma in endemic areas. The following terms were included in the search: trachoma, trachoma initiatives, prevalence, age factors, prognosis, environmental factors and Africa (Ethiopia, etc.). Online databases such as EBSCO, PubMed and BioMed Central via MEDLINE were searched for these terms.

During the conduct of the literature search, there was no preference given to a particular study design. There were no exclusions based on publication date; however, for studies with multiple publications the most current articles were selected for inclusion.

Clinical Overview of Trachoma

<u>Definition</u>

Trachoma is a chronic conjunctivitis caused by Chlamydia trachomatis serotypes A, B and C. It is characterised in its late stages by conjunctival scarring and trichiasis that results in corneal opacification and blindness. It is due to repeated conjunctival infection with the bacterium Chlamydia trachomatis, and transmitted under conditions of poor hygiene.

Magnitude

In 2014, it was estimated that approximately 232 million people live in trachoma-endemic districts (Weekly Epidemiological Report, WHO). According to the current consensus, 51 countries are known to be endemic for blinding trachoma (WHO, 2014). However, about 24 percent of these countries, mostly in Africa, carry 80 percent of the global burden of trachoma. Trachoma accounts for approximately 2.2 million people with visual impairment, 1.2 million of whom are irreversibly blind (WHO, 2012). According to Weekly Epidemiological Report, WER, 2012, globally 7.3 million people suffer from trichiasis and are at risk of developing blindness while 84 million of children are estimated to have active trachoma.

In 2012, WHO received reports from some previously endemic countries namely: the Gambia, Ghana, Iran, Morocco, Myanmar, Oman and Viet Nam, on their achievement of the Ultimate Intervention Goals (UIGs). UIGs are the WHO intervention targets for the elimination of blinding trachoma as a public health problem. The targets are defined as <1 case of trichiasis per 1000 population as well as <5% prevalence of active trachoma (grade 4) in children aged 1-9years. These countries upon their achievement of the UIGs are in the post-endemic surveillance stage and are awaiting the results of the validation process (WHO, 2014).

Aetiology

The obligate intracellular organism, that has no observed animal reservoir, called *chlamydia trachomatis* is the causative agent of many diseases. These organisms are eubacteria in the order Chlamydiales. The other types of the serotypes of the *C. trachomatis* are responsible for different infections; example: the serovars D to K cause genital infections while L1 to L3 cause lymphogranuloma venereum. Trachoma is a chronic conjunctivitis caused by Chlamydia trachomatis serotypes A, B, Ba and C which develops under poor hygienic conditions.

Transmission of chlamydia trachomatis infection

The frequency of re-infection depends on the availability of the factors that promote transmission of the bacteria. These factors are:

a. Lack of water

Trachoma is easily spread in districts or households where there is consistent water shortage. The distance from the various houses to the source of water has been proved by several studies to be positively associated with the prevalence of trachoma in a community. The farther the source of water, the more the constraints put on the usage of water hence the use of water for hygienic purposes will be limited. Washing of faces, which is one of the hygienic ways to prevent trachoma infection, becomes difficult decision to make because of this scarcity of water (McCauley, Lynch, Pounds et al, 1990).

b. Poor personal hygiene

Some potential source of infection are through contact with ocular, nasal and other secretions. Poor personal hygiene contributes to the continuous exposure of these bodily secretions. Nasal discharge, dirty and dusty face due to lack of facial cleanliness all together favour the transmission of *C. trachomatis.* To buttress this point, a study done in Tanzania concluded that children that had nasal discharge as well as having flies on their on their faces had a significantly two-fold increased risk of active trachoma as compared to children that were without these signs (West, Congdon, Katala, et al., 1991). Transmission is highly favoured when there is poor hygienic conditions pertaining in crowded living environment. There is more exposure in a crowded place through close contact with infected people and fomites like clothes, skirts, beddings, towels, etc.

c. Presence of flies

Musca sorbens, which are eye-seeking flies, act as physical vectors for the transmission of *C. trachomatis* by carrying the organism from one infected person to another. In two clinical trials

done in Gambia and Tanzania to establish the value of fly control, there were different results reported (Emerson, Lindsay, Alexander, et al, 2004: West, Emerson, Mkocha, et al., 2006). The intervention arm of the randomized villages in both countries received intense space-spraying with permethrin to control flies while the villages in the control arm received nothing. In Gambia, the intervention villages experienced a significant reduction in trachoma from 7.18% to 3.69%, compared to the control villages. However, there were bias in the Gambia study since the trachoma graders were not masked to the status of the villages. On the contrary, the study in Tanzania found significant reduction in the number of flies but no significant reduction in the either trachoma or infection between the villages in the various arms of the study (Trachoma went from 63% to 43% in the intervention villages and from 68% to 44% in the control villages: Infection was 9% in intervention villages compared to 6% in the control villages). The Gambia study showed that flies play a significant role in *C.trachomatis* transmission while the Tanzania study buttress the point that flies are not the only source but fomites, etc. all play part in the transmission.

d. Presence and closeness to latrines

Exposed animal and human faeces support the breeding of the *Musca sorbens* flies. Many studies in several countries concluded that presence of useable latrine near households are associated with lower prevalence of trachoma these communities. The closeness of latrines to households prevent people from defecating in bushes and open spaces hence removing the favourable breeding sites for the eye-seeking flies. The interaction between the several risk factors can be demonstrated in Figure 2 below.

e. Age

Age is used in the predicting of the various signs of trachoma. Pre-school children are found with the infection and the active disease. Both males and females experience a significant

decrease in the prevalence of active trachoma after the age of nine. The prevalence of the sequelae of active trachoma: trichiasis and corneal opacities, increases as age increases and shows in the multiple numbers of re-infection. Percentage of the infection with respect to a person's age is illustrated in figure1 below (Cited by Courtright &West, 2004).

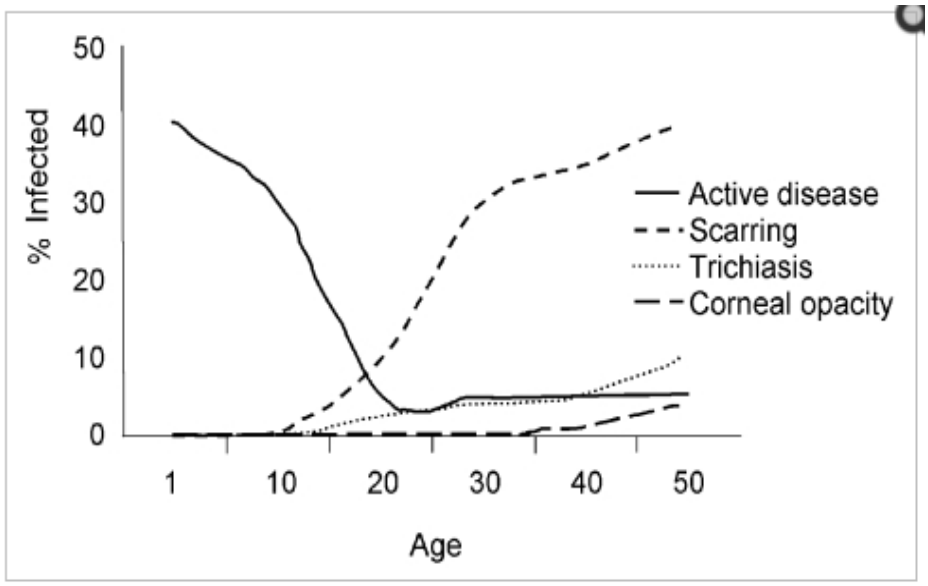


Figure 1. Trachoma infection and age of a person

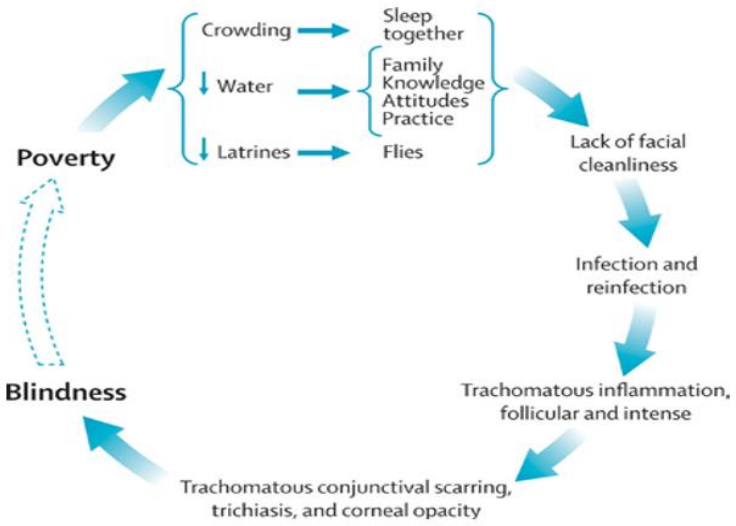


Figure 2. Interaction of trachoma environmental risk factors (Source Wright et al., 2008)

The Clinical Signs (Grading) of Trachoma

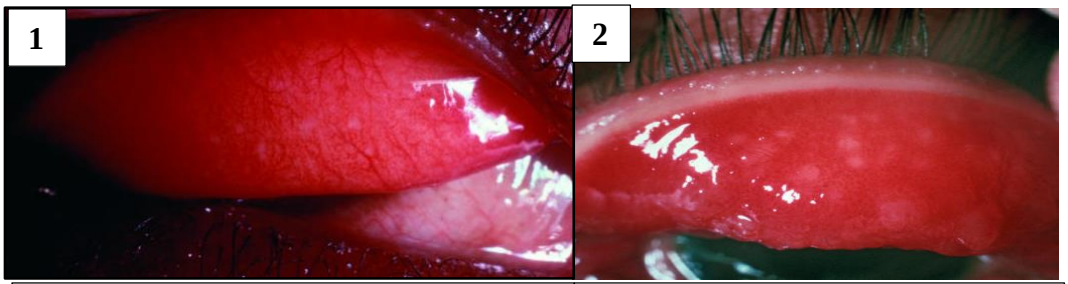
The burden of trachoma in any given community is concluded by the prevalence of the clinical signs of the disease. The WHO has developed a simplified classification grades for assessing the presence of trachoma based on the five clinical signs namely: Trachomatous inflammation: follicular (TF), Trachomatous inflammation: Intense (TI), Trachomatous scarring (TS), Trachomatous trichiasis (TT) and Corneal opacity (CO). (Thylefors et al., 1987).

Each of these signs explains the magnitude of the disease and the control measures to take in a population. The presence of active disease is known by the proportion of the population with Trachomatous inflammation: follicular (TF) and/ or Trachomatous inflammation: Intense (TI). Normally, people with TI are most infectious and are recommended for immediate treatment. WHO recommends the use of the prevalence of TF to assess the need for mass antibiotic drug distribution and other trachoma control measures (SAFE) in a district. Trachomatous scarring (TS) prevalence indicates long-term risk of trichiasis. The prevalence of Trachomatous trichiasis (TT) in a community indicates the need for surgical intervention while the prevalence of Corneal opacity (CO) gives indication of the public health burden of blindness that is due to trachoma in that community. The detailed description of the signs is shown in Table 1 and Figure 3.

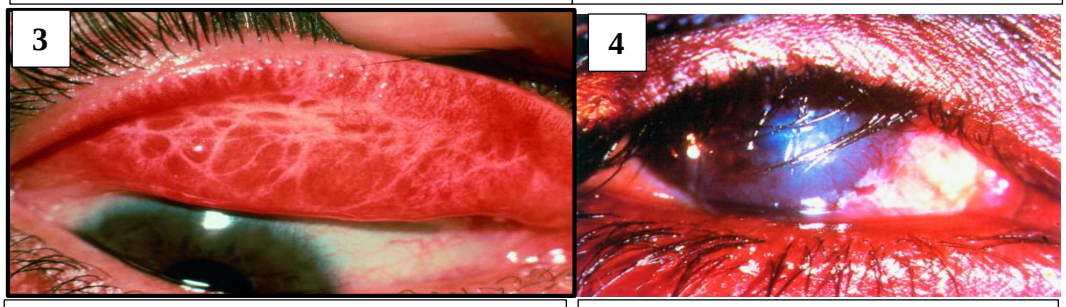
Table 1. WHO simplified trachoma grading classification system

SIGN	**DESCRIPTION**
TF	Trachomatous inflammation, follicular: the presence of five or more follicles of at least 0·5 mm diameter in the central part of the upper tarsal conjunctiva.

TI	Trachomatous inflammation, intense: pronounced inflammatory thickening of the upper tarsal conjunctiva obscuring more than half the normal deep tarsal vessels.
TS	Trachomatous conjunctival scarring: the presence of easily visible scars in the tarsal conjunctiva.
TT	Trachomatous trichiasis: at least one eyelash rubbing on the eyeball, or evidence of recent removal of in-turned eyelashes.
CO	Corneal opacity: easily visible corneal opacity over the pupil, so dense that at least part of the pupil margin is blurred when viewed through the opacity.



1. TF Trachomatous Inf – Follicular | 2. TF Trachomatous Inf – Intense



3. TS Trachomatous Scarring | 4. TT Trachomatous Trichiasis

5. CO Corneal Opacity

Figure 3. WHO Trachoma Grading (Articles from Community Eye Health are provided here courtesy of International Centre for Eye Health). Courtesy of the WHO.

Control of Trachoma

The WHO has recommended the SAFE strategy as control measures for countries battling with trachoma as a public health problem (WHO, 1998). This strategy is made up of four components which are inter-related in its implementation (Illustrated in figure 4 below). Surgery is performed for individuals with trachomatous trichiasis since if left untreated can lead to irreversible blindness from corneal opacity; Antibiotics given to individuals to treat the accumulated active infection and to reduce the chlamydia load in the community; Facial-washing to enhance facial cleanliness in order to reduce transmission; and Environmental

changes through the improvement of sanitation and water to reduce infection and sustain the reduction in transmission. Safe management of animal and human faeces are part of the environmental changes needed to sustain the reduction in transmission.

Figure 4. SAFE strategy Source; trachomcoalition.org

In 2012, 48.8 million people were reported as received treatment with antibiotics for active trachoma prevention and cure while 169,000 people underwent surgery for entropion or trichiasis (WHO, 2014).

Elimination of Trachoma

In 1997, the WHO launched the Alliance for the Global Elimination of Blinding Trachoma by the Year 2020 (GET 2020). This is open to members from all sectors; public, nongovernmental and commercial willing to work with governments to implement the SAFE strategy so as to help the various countries implement the SAFE strategy. Membership include: WHO, national governments, nongovernmental organizations, research institutions, foundations, and the pharmaceutical industries. Table 2 illustrates the TF and TT percentage in a community that will need intervention and the type of intervention needed.

Table 2. Endemicity classes for implementation of SAFE based on trachomatous inflammation–follicular (TF) and trichiasis (TT)

TF Prevalence band	***Classification***	***Implementation***
<5%	Non-endemic	No need for implementation of AFE
≥5% and <10%	Hypo-endemic	Mapping, F and E can be applied, focal A
≥10% and <30%	Meso-endemic	AFE at district level (≥3 years then review)
≥30%	Hyper-endemic	AFE at district level (≥5 years then review)
TT Prevalence band	**Classification**	
<0.1%	UIG achieved	
≥0.1%	UIG not yet achieved	

Courtesy of the WHO.

Global Trachoma Mapping Project (GTMP)

The WHO has year-marked the year 2020 as the year for the elimination of trachoma as a public health problem globally (WHO, 1998). The strategy outlined to meet this target includes knowing the depth of intervention needed which can be known through surveying the population-based prevalence of the disease (Solomon, Zondervan, Kuper, et al., 2006). The Global Trachoma Mapping Project (GTMP) was set up to help meet this target. "At minimum, trachoma mapping involves generation of prevalence data on the clinical signs follicular trachoma (TF) in children aged 1-9 years, and trachomatous trichiasis (TT) in adults aged 15+ years." (Solomon, Pavluck, Courtright, et al., 2015, pg 214-215). The GTMP started formal work on July 2012 with fieldwork starting on December 2012. The main aim was to finish mapping all the estimated 1238 suspected endemic districts in the 34 countries by the end of 2015. The GTMP has fieldworkers who collect the data on the prevalence based on the WHO simplified grading system (Table 1) using WHO recommended cluster random sample surveys of 20-30 clusters (Solomon et al., 2006). Each cluster has 100,000-250,000 people. Completion of this mapping phase implies immediate initiation of intervention with SAFE strategy at places that do not meet the WHO's UIGs in order to meet trachoma elimination by the year 2020.

Ethiopia

Studies on trachoma have been conducted in Ethiopia since the 1980's (Zerihun, 1997) but it is still the most affected country by trachoma worldwide (WHO, 2014). About 75 million people in Ethiopia are at risk of getting trachoma (WHO, 2014). Since the disease has been prevailing for long in Ethiopia, it is believed to have a presumed steady state hence this study looks for any relationship in the prevalence of TF and the prevalence in TT in Ethiopia as a good representative of countries globally that are already endemic.

Gaps / Need for Further Study

Blinding Trachoma (TT) and Active Trachoma (TF), any relationship?

Trichiasis, entropion and corneal opacities, which are the sequelae of active trachoma, are commonly found in adults, increasing with age (Munoz et al., 1997: Courtright et al., 1989). However, active trachoma, especially in hyper-endemic areas, are mostly seen in preschool children with the disease prevalence around 60% to 90% (West, Munoz, Turner, et al., 1991; Ngondi, Onsarigo, Adamu, et al., 2005) as a result of pre-school children having greatest infectious load (Solomon, Holland, Burton, et al.,2003). With the highest burden in children, it has been established by previous studies that only about 5% of adults show signs of active disease hence the prevalence of the active trachoma as well as the infectious load decreases with increasing age (West, Munoz, Turner, et al., 1991; Solomon, Holland, Burton, et al.,2003). In places of longer period of the disease, it is observed that scaring of the conjunctiva also increases as one ages and therefore increases the prevalence of trichiasis and corneal opacities in the adults. Since trichiasis and corneal opacities are evident only when there are several repeated episodes of the active trachoma (TF and/or TI), the prevalence the blinding stages are often too low and hence under-power statistically to make conclusion. Fortunately, it has been established by several studies that the prevalence of trichiasis and corneal opacities in adults in any given district most often demonstrates the past episodes of the active disease in this adults

when they were younger (Johnson et al., 2012). In addition, this study intends to find out if knowing the prevalence of active trachoma in children in any district can inform on the prevalence of trichiasis (TT) in that same district among adults. This knowledge hence would inform program planners on best and urgent intervention in that district. The blinding complications of trachoma will be reduced or eliminated when prompt surgical intervention is given to those at risk. Reports by many studies including that of (Roba et al., 2011) whose study was conducted in Ethiopia, have found that reduction of TF by antibiotics, facial and environmental cleanliness components (AFE of SAFE) were all statistically significant with the exception of surgery for TT (S of SAFE). These findings accentuate the need for more studies to fill the gap with respect to surgery part of the SAFE intervention. The severity of conjunctival scaring generally is enhanced by the number of times a child gets TF but it is often difficult to make inference from this on whether that child will develop TT as he/she ages. Studies have concluded that high prevalence (over 30%) of active trachoma are in children while that of adults with trichiasis is low (below 1%).

Accordingly, in highly endemic areas in South Sudan and Ethiopia, studies done on risk factors have concluded that the increased risk of trichiasis is associated with an increase in the prevalence of active trachoma in children in these communities (Ngondi et al., 2008; Ngondi et al., 2009). These associations have been established in individual countries. There has been limited prospective research to allow a prediction of TT based upon a TF prevalence on a global scale.

The lack of standardized, large scale data collection has limited previous efforts to assess the association between active trachoma and trichiasis. This study would make use of large data sets (GTMP) from Ethiopia, analyse them to establish if globally there is any relationship between trachomatous inflammation: follicular (TF) and trachomatous trichiasis (TT) in a presumed steady state and if the prevalence of TF can be used to predict the TT prevalence.

For the purpose of decision-making for intervention for active trachoma, WHO recommends TF (only) in children age 1-9 years. We would like to find out whether the prevalence of TI in children in these endemic areas contributes to this relationship and which might further indicate the need to consider TI when making intervention decisions, since other studies have established that in individual districts. A cohort study done in Tanzania on preschool children indicated 29% of the children with constant severe trachoma with TI had scarring leading to trichiasis as compared to children with just TF but no TI, where only 9.6% of children with TF who had scarring (West et al., 2001). Their study established that severity of TI plays a role, but will this be the same on larger scale; the study was limited to only district in Tanzania. Factors which may contribute to the association according to studies done in different endemic areas include average age of children with TF, prevalence of TI in children, average age of adults with TT and sex-specific ratio of TT (West et al., 2001). With regards to sex, a similar study done in 11 districts in southern Sudan which looked into trichiasis life expectancy established that women live longer and therefore spend greater part of their years with blinding trichiasis or low vision as compared to men (Ngondi, et al., 2009).

The GTMP data for Ethiopia, which is larger and standardised, will be used to establish whether these factors predict the association between TF and TT and the part TI plays in this association. Data for Ethiopia is used in this study to represent other endemic countries since Ethiopia has the longest standing history of Trachoma and presumed to have a steady state of the condition. The findings from this study may help in establishing a predictive link, and help in early intervention so as to achieve total elimination as per the mission of WHO and Alliance for the Global Elimination of Trachoma by 2020 (GET 2020). A better understanding of the relationship between the prevalence of TF and the prevalence of TT together with the factors influencing this association may aid in prioritization of districts for intervention. Any other

factors that influence this association would have to be looked into per district into to totally eliminate trachoma disease in that district.

If there is variation in the relationship according to the TF prevalence it may suggest that programmes need to prioritize additional groups such as TI prevalence, etc., for intervention. This study itself would not lead national programme managers to change programme decisions; it would likely lead to additional questions that need to be addressed through further research.

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PART C: JOURNAL "READY" MANUSCRIPT

TITTLE PAGE

Relationship between the prevalence of trachomatous inflammation in children (age 1-9 years) and the prevalence of trichiasis in adults (age 15 years and above) at a presumed steady state

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ABSTRACT

Purpose: To use the baseline trachoma mapping data from Ethiopia to establish the relationship between the prevalence of trachomatous inflammation: follicular (TF) in children (age 1-9 years) and the prevalence of trichiasis (TT) in adults (age 15 years and above) at a presumed steady state.

Methods: Baseline data from the Global Trachoma Mapping Project (GTMP) was used as a secondary dataset for this research. All eligible regions in Ethiopia were included. In a few situations, particularly in Somali Region, insecurity prevented mapping. The GTMP teams conducted surveys in seven regions. Although all age groups were included, for the purpose of planning, the study assessed TF in children age from 1-9 years and TT in adults aged 15 years and above as the prevalence of TF in children and TT in adults are indicators for programme decision making. Data on the prevalence of trachomatous intense inflammation (TI), sanitation and hygiene measures and altitude, which were collected as part of GTMP, were assessed to determine if they contributed to relationship between TF and TT.

Results: The study included a total of 282,558 individuals living in 174 evaluation units from seven regions of Ethiopia, among whom 256,587 gave consent to be examined. This study found a significant relationship between the prevalence of TF in children and the prevalence of TT in adults when analysis is done at the evaluation unit level (correlation rho, 0.59; p-value <0.0001). Hence, 59% of the prevalence of TT in adults can be accounted for by the presence of TF in children. Sub-group analysis showed that the correlation persisted at the regional level.

Conclusion: A better understanding of the relationship between the prevalence of TF and the prevalence of TT together with the factors influencing this association using this large dataset

may aid in prioritization of districts for intervention and has implications for global activities for the elimination of trachoma.

Keywords: Prevalence, risk factors, trachoma, Ethiopia, Global Trachoma Mapping Project (GTMP)

INTRODUCTION

Trachoma is an eye infection due to the bacteria, *Chlamydia trachomatis;* it causes a chronic infection of the eyelid. Repeated re-infection causes scarring of the upper tarsal conjunctiva, which can turn the eyelid inward and cause the eyelashes to scratch the surface of the cornea. Continuous scratching over time leads to destruction of the corneal tissues and can lead to blindness.[1] Trachoma is a chronic conjunctivitis which is transmitted under poor hygienic conditions and is endemic in many of the poorest and remotest parts of Africa and Asia. Trachoma is the leading cause of infectious blindness globally[2, 3]. It accounts for about 2.2 million people with visual impairment, among whom 1.2 million are irreversibly blind[4]. Only the European WHO Region, among the WHO regions, has no countries with known or suspected trachoma as a public health problem. Currently about 51 countries are either known or suspected to be endemic globally. The African Region is severely affected with 29 countries currently endemic or suspected, about 77% of the total population with trachoma in the world. [5] Certain factors in the environment are associated with increased risk for infection in individuals. These factors are lack of good water supply, lack of basic sanitation facilities, overcrowding and poverty as a whole. [5] Usually places with children with dirty faces and ocular and nasal discharge have high transmission potential[6]. The highest transmission is found in pre-school age children[7].

The burden of trachoma in a district is assessed by measuring the prevalence of the clinical signs of the disease. The WHO has developed a simplified classification system for grading the presence of trachoma based on the five clinical signs: trachomatous inflammation: follicular (TF), trachomatous inflammation: intense (TI), trachomatous scarring (TS), trachomatous trichiasis (TT) and corneal opacity (CO).[8]

Each of these signs helps determine the magnitude of the disease and the control measures to take in a population. The indicator for assessing the presence of active disease in the population

is the prevalence of TF in children age 1-9 years. WHO recommends the use of the prevalence of TF to determine the need for mass antibiotic drug distribution and other trachoma control measures (facial cleanliness and environmental improvements) in a district. TS prevalence indicates long-term risk of trichiasis while TT prevalence indicates the need for surgical intervention and CO prevalence gives indication of the public health burden of blindness that is due to trachoma.[9] TT is assessed in adults age 15 and over and it is the primary indicator for surgery or other management.[9]

This analysis was carried out using data from Ethiopia. Similar data from other countries was not used as it was unlikely that these settings were in a "steady state" of trachoma. A steady state was needed for the following reasons:

1. In settings where active trachoma was in decline due to improving socio-economic status (even without specific trachoma related interventions) the prevalence of TF might have been low while the prevalence of TT could be still be high.
2. In settings where eye care programmes are strong there are often programmes to provide surgical services to people with trichiasis; this could reduce the prevalence of trichiasis even when TF may be high.
3. In settings such as refugee camps active trachoma can resurge in populations that might have been relatively free of the disease; in these settings trichiasis would likely be rare.

Ethiopia was chosen because it has been trachoma endemic for many generations (likely hundreds of years) but there have been no intervention in the targeted EU either to address active trachoma or trichiasis. In Ethiopia, trachoma is one of the major causes of low vision and blindness.[10]There have been many studies on trachoma in Ethiopia which have helped the global understanding of the mechanisms of the disease as well as means of prevention and treatment. [10-13] Generally, areas in which research has been undertaken have had interventions;

any area with interventions was not included in the baseline mapping. That said, most of the country has not had any trachoma control activities.

Elimination of trachoma can be achieved by initiating a group of interventions, namely the SAFE strategy. SAFE is an acronym for:

 Surgery for trachomatous trichiasis

 Antibiotic treatment to treat ocular *Chlamydia trachomatis* infection

 Facial cleanliness to reduce transmission of ocular infection

 Environmental improvement, particularly improved access to water and sanitation, to reduce transmission of ocular infection.

One of the main sanitary interventions is promotion of appropriate hygienic methods of disposing of human faeces. The *Musca sorbens* flies are commonly found where human and animal faeces are present because that is where they lay their eggs, hence an increased risk for trachoma at places where open defecation is common.

The WHO Alliance for the Global Elimination of Blinding Trachoma by the year 2020 (GET 2020) was formed by WHO in 1997 and endorsed in 1998 by the World Health Assembly [5.] The main aim of the GET 2020 Alliance is to eliminate trachoma globally as a public health problem by soliciting resources and enabling cooperation among a worldwide partnership of Member States, non-governmental organizations and private institutions. The WHO has used the term Ultimate Intervention Goal (UIG) to define the desired outcome for the elimination effort. There are two UIGs for trachoma: (1) TF prevalence of <5% in children aged 1-9 years and (2) TT prevalence in the population <0.1% (1 case per 1000 population) or <0.2% in the population group age 15 years and above.

Defining the need for intervention is the first step; this is best done through surveying the population-based prevalence of the disease in a district [14]. The Global Trachoma Mapping Project (GTMP) was set up to accomplish this. The GTMP (2012-2015) worked with Ministries of Health of the various countries to estimate trachoma prevalence in potentially endemic districts through population-based surveys.[14] Besides mapping potentially endemic districts for TF and TT, GTMP collected WASH data (water, sanitation and hygiene) to provide information for planning F & E activities. Based upon GTMP findings, districts and countries were encouraged to develop Trachoma Action Plans focused on the steps needed to reach elimination of trachoma as a public health problem by year 2020.

Trichiasis, entropion and corneal opacities can lead to blindness and are the sequelae of active trachoma. It is estimated that over 100 repeated infections will cause scarring which can lead to blindness[15]. From this, inference can be made that when active trachoma is reduced conjunctival scarring, trichiasis and blindness can be reduced or avoided. Generally, the severity of conjunctival scarring is related to the number of episodes of active trachoma in children but it is difficult to reliably assess who is at risk of developing trichiasis. In high endemic areas in South Sudan and Ethiopia a few small studies have concluded that the increased risk of trichiasis is associated with an increase in the prevalence of active trachoma in children in these communities however the sample size has been quite small. [11, 12] A cohort study done in Tanzania on preschool children indicated 29% of the children with TI had conjunctival scarring that could lead to trichiasis as compared to 9.6% of children with TF but no TI. [16]

There has been limited prospective research to predict TT based upon a TF prevalence; the long duration between TF in children and development of TT in adults makes prospective research extremely difficult. A limitation of previous data collection comparing TF to TT has

been the lack of standardization of grading of trachoma; GTMP employed rigorous intra-observer testing techniques for TF to ensure the quality of data over large study populations.

The main objective of this study was to establish if there is a relationship between the prevalence of TF (measured in children) and the prevalence of TT (measured in adults) in a "steady state" situation. We also sought to determine if the relationship persisted in sub-group analyses and if hygiene, water, and sanitation factors contributed to the association.

METHOD

The GTMP was the largest disease mapping project in history; in all, the GTMP covered 29 countries and surveyed 2.6 million people. In Ethiopia all previously unmapped districts (referred to as "woredas") were included in the GTMP project. That included all of the regions except for Amhara Region and the capital city, Addis Ababa (Fig 1). In Oromia and SNNPR a few isolated districts that had been surveyed previously and were undergoing intervention and were not re-surveyed. As all (non-urban) districts were considered potentially trachoma endemic, all un-surveyed districts were included. In a few situations, particularly in Somali Region, insecurity prevented mapping.

Fig 1, Map of Ethiopia showing the regions.

Throughout Ethiopia the GTMP teams conducted surveys in the seven regions among all age groups. Although all age groups were included, for the purpose of planning, the study assessed TF in children age 1-9 years and TT in adults aged 15 years and above.

Study sampling and sample size

The GTMP used a 2-stage cluster random sample method within each evaluation unit (EU) .[14] In places where the evaluation units were larger than districts, the team selected first-stage clusters considering the district population size. A minimum number of clusters per EU was 20.[14]

An expected TF prevalence of 10% in children aged 1-9 years was used to calculate the sample size in each EU because it is the WHO threshold for initiating interventions to reduce active trachoma. If TF in children age 1-9 years is 10% or more, it warrants annual single-dose distribution of antibiotic (Azithromycin) and facial cleanliness and environmental

improvement strategies for the entire population for three years or more. EUs that have a TF prevalence of 5-9.9% require one year of intervention while EUs with a TF prevalence of less than 5% do not need an intervention.

Additional assumptions for the sample size included 95% confidence level and absolute precision of true prevalence estimated as 3%. Based upon this and a design effect of 2.65 it was calculated that at least 1019 children were needed per EU. As non-response can happen, the sample was increased by 1.2 times; this led to a target sample of 1222 children aged 1-9 years per EU. The number of clusters within an evaluation unit was derived by dividing 1222 by the mean number of children aged 1-9 years in each household to obtain the number of households. . Based upon the practical number of children to be examined per day (around 50) the number of clusters (villages) varied but generally was between 20 and 30.

GTMP also sought to determine the prevalence of TT in persons aged 15 years and above. No sample size calculation was made for TT; instead, all residents age 15 years and above in selected households in each cluster were included. Since TT prevalence is often low it was anticipated that the sample size for TT would be under-powered.

Active trachoma is linked to hygiene and the environmental conditions and the team also collected data on water sources, place of defecation and other variables. Household – level water, sanitation and hygiene variables were included in GTMP data collection. The variables included: the main source of drinking water for members of the household during dry season; how long it takes to go get water and come back home; the main source of water the household use to wash their faces: how long to fetch that water home; where adults in the house hold usually defecate. The GTMP team also did observation of the kind of toilet facility used, the handwashing facility located from the toilet, availability of water at the handwashing facility, and availability of soap at the facilities.

Field work

The GTMP field team comprised one trachoma grader and one data recorder; both were trained using standardized training materials including a trainers' manual, a series of slide sets and Microsoft Excel-based kappa score calculators to achieve high agreement on grading of trachoma.

In Ethiopia, all residents from 1 year of age in the selected households were invited for examination. The heads of households were asked for consent and, if approved, the team took global positioning system (GPS) points at the outside front gate of the house and afterwards asked the household head the water and sanitation questions. The team also asked permission to inspect the place of defecation as well as the hand-washing facility if it existed. Individuals who had given consent are examined for signs of TF, TI, and TT by the team using 2.5 x magnifying loupes and a touch light for illumination.[17] All of the data were captured and stored in electronic form using a purpose-built Open Data Kit-based Android smartphone application (LINKS).

Data Analysis

The unit of analysis for this study is the evaluation unit (EU) which generally corresponds with the district (woreda). All EU data was age and sex adjusted for the purpose of standardization. Regional prevalence are self-weighted without adjustment while the overall is the sum of the cases and population examined in all the EUs.

The dataset provided by the GTMP team was in Microsoft Excel but analysis was done with Stata 12. All data had been cleaned in advance. Univariate analysis (chi square test) was used to assess the association of TF and categorical variables (water and sanitation, altitude, and TI). Frequencies tested were used to generate prevalence and linear regression was used to

determine the regression coefficient and the significance of the environmental and hygienic risk factors. Pearson or Spearman's correlation was used to assess associations at the EU level among continuous variables (e.g., TF, TT, TI). To conduct sub-group analyses, data were grouped by region and by WHO-defined TF prevalence (for decision making).

Ethical Consideration

Secondary data from Ethiopia was used through the permission granted by GTMP team, as trachoma mapping is mandatory for ministries of health. There was no direct contact with any research participant. As part of routine services in GTMP studies, all participants in the various districts complete a consent form before the study is carried out. Individuals aged 15 years and over give verbal consent for themselves if they are competent to do so. Verbal consent is used because of the low literacy rates in these study areas. Parent or guardian of individuals younger than 15 years give the consent on their behalf. For consent to be valid in GTMP survey, the person must understand what will happen as part of the survey; that they have the right to refuse consent; and that access to services will be the same regardless of whether or not the individual participates.

This project was approved by the University of Cape Town Human Research Ethics Committee. Additionally, permission to conduct the research with Ethiopia data was obtained from the Ethiopian government through the GTMP team using Expression of Interest (EoI) form. The study conforms to the tenets of the Declaration of Helsinki.

RESULTS

Survey population

A total of 282,558 individuals were enumerated in seven regions of Ethiopia by the GTMP team, among whom 256,587 gave consent and were examined (90.8% response rate). Those who could not be examined were either absent when the team visited their EU or refused to be examined. Of the examined, 115,730 (45.1%) were males and 140,857 (54.9%) were females. Their age ranged from 1 year to 100 years with a mean age of 21.9 years (SD 18.2). There were 94,830 individuals age 1-9 years. There were 131,922 individuals age 15 years and above; their mean age was 34.8 years (SD 15.5). Table 1 lists the surveyed seven regions and sex distribution of the study population.

Table1. *Regions and sex distribution of population examined in Ethiopia by GTMP*

Regions (reference)	**Male, n**	**Female, n**	**Total**	**%**	**EU**
Afar	9,653	12,127	21,780	8.5	11
Benishangul-Gumuz [18]	8,467	11,063	19,530	7.6	7
Gambela [19]	3,334	4,684	8,018	3.1	3
Oromia [20]	28,792	33,517	62,309	24.3	79
SNNP [21]	27,411	32,924	60,335	23.5	41
Somali	25,655	30,379	56,034	21.8	18
Tigray [22]	12,418	16,163	28,581	11.2	15
Total	**115,730**	**140,857**	**256,587**	**100**	**174**

The number of EUs in a region depended on the population of the region. There were seven regions with 174 EUs (Table 1).

Prevalence of active trachoma

Among the 94,830 examined children 47,225 (49.8%) were males and 47,605 (50.2%) were females. The prevalence of TF was not significantly different in males and females (Table 2).

TF in children aged 1-9 years in the 174 EU ranged from a high of 48.5% to a low of 1.1%, the mean being 20.6% and the median being 19.0%. (Table 3) The prevalence of TI was quite low, ranging from 0.0% to 10.0% with a mean of 2.4% and a median prevalence of 1.7%.

Table 2. *Differences between the prevalence of TF and TT between the sexes.*

Prevalence	**Male**	**Female**	**OR**	**95%CI**	**P-Value**
TF	10.6%	10.7%	1.01	0.95-1.07	0.79
TT	0.6%	1.7%	2.6	2.23-3.07	0.00

Table 3: *The prevalence of TF, TI and TT in all the districts mapped.*

Region	**District**	**EU**	**TF**	**TI**	**TT**
Afar	KilbetRasu	177	6.52%	0.43%	0.38%
Afar	KilbetRasu	178	2.04%	0.03%	0.35%
Afar	Awssii Rasu	179	2.95%	1.32%	0.22%
Afar	Zone 3	180	5.63%	0.29%	0.68%
Afar	KilbetRasu	181	3.84%	0.68%	0.06%
Afar	Fanti Rasu	182	6.10%	0.73%	0.22%
Afar	Awssii Rasu	183	5.59%	0.15%	0.09%
Afar	Awssii Rasu	184	6.20%	0.60%	0.19%
Afar	Zone 3	185	6.01%	0.60%	1.04%
Afar	KilbetRasu	186	5.09%	0.13%	0.23%
Afar	Hari Rasu	212	16.33%	0.83%	1.16%
Bgumuz	Metekel	215	5.82%	0.06%	0.34%
Bgumuz	Metekel	216	17.58%	1.02%	2.53%
Bgumuz	Metekel	217	15.18%	1.66%	1.11%
Bgumuz	Kamashi	218	1.73%	0.13%	0.74%

Bgumuz	Asosa	219	5.07%	0.48%	1.78%
Bgumuz	Asosa	220	2.78%	0.29%	0.93%
Bgumuz	Asosa	221	3.28%	0.06%	1.72%
Gambella	Agnua II	235	11.48%	1.82%	0.84%
Gambella	Agnua II	236	19.29%	2.88%	2.39%
Gambella	Agnua II	237	12.55%	3.07%	1.31%
Oromia	E. Shewa	57	30.90%	1.18%	0.98%
Oromia	Kelem Wellega	503	2.80%	0.22%	0.13%
Oromia	Kelem Wellega	504	4.18%	0.40%	0.19%
Oromia	Kelem Wellega	505	9.86%	0.74%	0.96%
Oromia	Kelem Wellega	506	6.43%	0.08%	0.67%
Oromia	West Wellega	507	14.26%	0.66%	1.28%
Oromia	West Wellega	508	9.40%	0.09%	0.96%
Oromia	West Wellega	509	2.54%	0.11%	0.36%
Oromia	West Wellega	510	2.90%	0.00%	0.44%
Oromia	West Wellega	511	2.95%	0.41%	0.19%
Oromia	West Wellega	512	1.25%	0.00%	0.60%
Oromia	West Wellega	513	4.31%	0.00%	0.04%
Oromia	West Wellega	514	1.71%	0.00%	0.54%
Oromia	West Wellega	515	2.95%	0.00%	0.36%
Oromia	Illu Aba bora	516	14.03%	0.22%	0.17%
Oromia	Illu Aba bora	517	7.28%	0.31%	0.34%
Oromia	Illu Aba bora	518	1.24%	0.00%	0.26%
Oromia	Illu Aba bora	534	10.01%	0.32%	0.05%
Oromia	West Wellega	535	1.08%	0.00%	0.10%
Oromia	West Wellega	536	1.96%	0.08%	0.18%
Oromia	E. Harerge	538	37.56%	2.95%	1.00%
Oromia	Illu Aba bora	55016	4.88%	0.53%	0.27%
Oromia	E. Shewa	1	36.35%	8.57%	1.50%
Oromia	Arsi	2	30.13%	5.20%	0.73%
Oromia	Arsi	3	24.32%	3.09%	0.89%
Oromia	Arsi	4	29.59%	4.70%	0.34%
Oromia	Arsi	5	23.56%	4.10%	1.30%
Oromia	Arsi	6	20.92%	2.20%	0.82%
Oromia	West Arsi	7	45.78%	9.89%	1.65%
Oromia	West Arsi	8	21.94%	1.88%	0.14%
Oromia	West Arsi	9	13.16%	0.72%	0.28%
Oromia	Arsi	10	27.35%	3.34%	0.67%
Oromia	S.W. Shewa	11	32.11%	6.83%	1.71%
Oromia	S.W. Shewa	12	30.34%	5.58%	0.81%
Oromia	North Shoa Zone	13	48.39%	7.02%	1.99%
Oromia	North Shoa Zone	14	47.10%	6.36%	0.61%
Oromia	North Shoa Zone	15	25.52%	2.42%	0.48%
Oromia	W. Shewa	16	17.01%	2.05%	0.44%
Oromia	W. Shewa	17	39.79%	7.26%	1.23%
Oromia	W. Shewa	18	29.12%	4.83%	0.44%

Oromia	W. Shewa	19	35.36%	3.35%	0.96%
Oromia	Finfine Zuriya	20	29.78%	4.25%	0.70%
Oromia	W. Harerge	21	32.95%	1.34%	1.18%
Oromia	W. Harerge	22	21.28%	0.69%	0.97%
Oromia	W. Harerge	23	27.72%	1.79%	1.76%
Oromia	W. Harerge	24	35.81%	3.49%	1.65%
Oromia	E. Harerge	25	34.39%	2.49%	1.41%
Oromia	E. Harerge	26	30.36%	1.80%	1.06%
Oromia	E. Harerge	27	46.17%	2.92%	1.70%
Oromia	E. Harerge	28	24.59%	1.30%	1.38%
Oromia	E. Harerge	29	41.80%	3.61%	1.07%
Oromia	Bale	30	41.84%	4.57%	0.32%
Oromia	Bale	31	38.47%	4.53%	0.68%
Oromia	Bale	32	39.44%	3.54%	1.46%
Oromia	Guji	33	35.39%	2.41%	0.93%
Oromia	Guji	34	29.49%	3.55%	0.34%
Oromia	Guji	35	24.64%	1.09%	0.04%
Oromia	Borena	36	28.93%	2.54%	0.95%
Oromia	Borena	37	36.49%	2.32%	0.71%
Oromia	Borena	38	42.64%	2.16%	0.62%
Oromia	Kelem Wellega	39	3.09%	0.00%	0.44%
Oromia	Kelem Wellega	40	8.41%	0.17%	0.57%
Oromia	West Wellega	41	7.88%	0.07%	1.08%
Oromia	West Wellega	42	3.32%	0.19%	0.38%
Oromia	West Wellega	43	5.49%	0.14%	0.22%
Oromia	E. Wellega	44	48.20%	4.99%	1.48%
Oromia	E. Wellega	45	18.42%	0.91%	0.53%
Oromia	E. Wellega	46	19.55%	0.93%	0.73%
Oromia	E. Wellega	47	42.65%	3.90%	1.06%
Oromia	Jimma	48	35.32%	3.63%	2.51%
Oromia	Jimma	49	45.34%	5.43%	2.30%
Oromia	Jimma	50	20.17%	1.25%	0.98%
Oromia	Jimma	51	40.99%	6.40%	0.95%
Oromia	Jimma	52	46.52%	4.39%	1.56%
Oromia	Illu Aba bora	53	5.27%	0.44%	0.49%
Oromia	Illu Aba bora	54	16.27%	2.64%	1.11%
Oromia	Illu Aba bora	55	21.12%	2.61%	1.09%
Oromia	Illu Aba bora	56	8.84%	0.22%	0.28%
Oromia	E. Shewa	58	29.09%	1.33%	1.07%
SNNPR	Sidama	283	6.33%	0.84%	0.07%
SNNPR	Sidama	284	10.26%	0.97%	0.04%
SNNPR	Sidama	285	-	1.27%	-
SNNPR	Sidama	286	13.63%	1.42%	0.30%
SNNPR	Hadiya	126	44.99%	8.64%	2.13%
SNNPR	Hadiya	127	35.99%	4.13%	2.58%
SNNPR	Hadiya	128	37.83%	6.10%	3.01%

SNNPR	Sidama	129	30.57%	4.54%	1.57%
SNNPR	Sidama	130	39.46%	5.51%	1.12%
SNNPR	Sidama	131	17.42%	1.03%	0.06%
SNNPR	Sidama	132	22.65%	2.47%	0.50%
SNNPR	Sidama	133	8.42%	1.35%	0.34%
SNNPR	Sidama	134	27.72%	2.60%	0.37%
SNNPR	Gedio	135	18.32%	1.52%	0.82%
SNNPR	Gedio	136	14.45%	1.95%	0.69%
SNNPR	South Omo	137	25.53%	3.01%	0.57%
SNNPR	South Omo	138	20.15%	1.67%	1.09%
SNNPR	Sheka	139	11.96%	1.13%	0.68%
SNNPR	Kafa	140	40.80%	7.30%	1.12%
SNNPR	Kafa	141	36.88%	5.94%	0.90%
SNNPR	Bench Maji	142	30.77%	4.07%	0.57%
SNNPR	Bench Maji	143	28.52%	3.32%	0.78%
SNNPR	Segen	144	46.63%	8.19%	2.53%
SNNPR	Dawro	145	34.24%	5.81%	2.24%
SNNPR	Dawro	146	28.11%	5.76%	1.20%
SNNPR	Silti	147	26.43%	4.84%	0.79%
SNNPR	Silti	148	27.02%	4.61%	1.98%
SNNPR	Gamo Gofa	149	26.42%	2.35%	1.07%
SNNPR	Gamo Gofa	150	15.78%	1.76%	1.22%
SNNPR	Gamo Gofa	151	18.97%	2.44%	0.85%
SNNPR	Special	152	35.55%	3.43%	1.04%
SNNPR	Kembata Tembaro	153	41.05%	5.97%	1.97%
SNNPR	KAT	154	29.11%	5.12%	3.10%
SNNPR	Gurage	155	29.13%	2.79%	6.11%
SNNPR	Gurage	156	14.95%	0.36%	2.39%
SNNPR	Gurage	157	27.59%	3.19%	4.30%
SNNPR	Gurage	158	28.41%	3.38%	4.20%
SNNPR	Gurage	159	5.93%	1.75%	0.61%
SNNPR	Gurage	160	14.14%	0.76%	3.17%
SNNPR	Gurage	174	2.26%	0.15%	0.34%
SNNPR	Gurage	175	33.51%	5.24%	1.42%
Somali	Shinile	685	10.03%	1.49%	0.48%
Somali	Shinile	686	9.01%	0.51%	0.70%
Somali	Afder	90	11.29%	0.27%	0.14%
Somali	Afder	91	10.33%	0.17%	0.76%
Somali	Jigjiga	94	18.71%	1.29%	1.25%
Somali	Jigjiga	95	37.69%	6.98%	0.35%
Somali	Shinile	96	8.98%	0.78%	0.99%
Somali	Shinile	97	9.06%	5.26%	0.20%
Somali	Degehabur	98	5.69%	1.86%	0.51%
Somali	Degehabur	99	5.27%	0.00%	0.03%
Somali	Degehabur	100	4.60%	1.58%	0.19%
Somali	Warder	102	2.43%	0.16%	0.22%

Somali	Gode	103	7.68%	0.66%	0.15%
Somali	Afder	105	8.07%	0.68%	0.17%
Somali	Liban	106	11.88%	1.98%	0.81%
Somali	Afder	107	16.81%	1.14%	0.96%
Somali	Liban	108	4.35%	0.42%	0.18%
Somali	Jigjiga	109	31.98%	5.35%	1.24%
Tigray	Mekele	72	48.48%	6.63%	1.44%
Tigray	W Tigray	287	8.71%	0.13%	1.99%
Tigray	W Tigray	288	5.25%	0.23%	1.05%
Tigray	W Tigray	289	8.58%	0.33%	0.13%
Tigray	C. Tigray	61	32.58%	4.78%	1.88%
Tigray	C. Tigray	62	23.69%	3.57%	2.28%
Tigray	C. Tigray	63	29.50%	3.84%	1.41%
Tigray	S. Tigray	64	39.09%	3.68%	2.56%
Tigray	Eastern Tigray	65	20.79%	1.02%	0.75%
Tigray	Eastern Tigray	66	20.02%	1.01%	1.97%
Tigray	S. Tigray	67	41.44%	5.00%	2.29%
Tigray	S. Tigray	68	40.98%	4.12%	1.87%
Tigray	W Tigray	69	9.32%	0.42%	0.58%
Tigray	NW Tigray	70	18.25%	1.43%	1.27%
Tigray	NW Tigray	71	10.24%	0.69%	1.29%

The highest age and sex standardized prevalence of TF was found in Mekele district (EU= 0072) in Tigray with prevalence of 48.5% (Table 3 & 4) followed by North Shoa district (EU=0013) in Oromia (48.4%). West Wellega district in Oromia had the lowest prevalence of TF of 1.1%. Consequently all the regions had one or more districts whose prevalence of TF was above the WHO threshold for intervention of 10% or more (Table 4).

Table 4. *Lowest and highest age and sex adjusted prevalence of TF in children in each region depending on EU.*

Region	**Lowest TF prevalence in the region (%)**	**Highest TF prevalence in the region (%)**
Afar	2.0	16.3
Benishangul-Gumuz	21.7	17.6
Gambela	11.5	19.3
Oromia	1.1	48.4
SNNPR	2.3	46.6
Somali	2.4	37.7
Tigray	5.3	48.5

Water and sanitation findings

The main variables considered in the Ethiopian data used were the main source of drinking water for members of the household during dry season; how long it takes to go get water and come back home; the main source of water the household use to wash their faces: how long to

fetch that water home; where adults in the house hold usually defecate and the distance of the hand washing facility.

The main sources of water for drinking and for washing faces during the dry season in these regions were: piped water into dwelling (0.01%), piped water into yard/pot (1.5%), public tap/standpipe (10.8%), tube well/borehole (16.3), protected dug well (3.8%), unprotected dug well (4.3%), protected spring (27.0%), unprotected spring (15.8%), rainwater collection (1.1%), water vendor (0.8%), surface water –e.g. river, dam, lake, canal (18.5%), and other (0.1%). Improved water source (Table 5) was used to represent water from treated sources which were: piped water into dwelling, piped water into yard/pot, public tap/standpipe, tube well/borehole, protected dug well and protected spring.

Members of households in the district defecate using a shared or public latrine (7.2%), private latrine (36.8%), outside near the house (no structure) (9.6%), in the bush or field (46.3%) or other (0.1%). Any place for defecation that is not neat and well-kept has tendency to harbour most of the eyes-seeking flies hence classified as unimproved place for defecation. Improved latrine (Table 5) involved shared or public latrine and private latrine.

There was no correlation between TF and the various water and sanitation factors. (Table 5). There was a slight inverse correlation between altitudes at TF; the majority of individuals lived in houses below the altitude of 2000m above sea level.

The correlation analysis performed was also to measure the extent of multicollinearity among variables. The logic behind the assumption of no multicollinearity is simply that if two or more independent variables are linearly dependent on each other, one of them should be included instead of both. If the correlation coefficient was greater than 0.70 or less than -0.70, it can be interpreted that variables are not independent. The solution to the multicollinearity problem is to drop one of the collinear variables from further analyses. According to the correlation done, some of the independent variables (e.g., drinking water source and source of water for washing

face as well as duration for collecting drinking water and facial washing water) were highly correlated and Households with improved facial wash water source together with households with facial wash water source within 1 km, which were highly correlated variables, were removed from the regression analysis.

Table 5. *Regression Coefficients: Factors on TF at household level*

	Correlation coefficient **(standard error)**	p-value
Constant	0.258 (0.04)	0.000
Households with improved drinking water source.	-0.039 (0.062)	0.523
households with wash water source within 1 km.	-0.064 (0.068)	0.348
Households with improved latrine facility.	-0.091 (0.176)	0.607
Households with hand wash station within 15m of latrine.	0.131 (0.226)	0.563
Altitude	-0.0002 (0.00003)	0.000

The R-square (coefficient of determination) which measures the total contribution of TF accounted for by the independent variables is 1.2%. This means that the water and sanitation variables are not associated with TF.

Prevalence of trichiasis in adults

A total of 131,922 individuals (51.4% of the population examined) were aged 15 years and above. There were 54,220 (41.1%) males and 77,702 (58.9%) females. The prevalence of

trichiasis in the age group 15 years and over in the 174 EU ranged from 0.0% to 6.1% with a mean of 1.0% and a median prevalence of 0.8%. Women were 2.6 times (95% CI 2.2-3.1) more likely to have TT compared to men (Table 2). The district of Gurage (EU=00030) in SNNPR had the highest prevalence of TT of 6.1% while Degehabur district (EU=00099) in Somali Region had the lowest prevalence of TT of 0.0% (Table 3 & 6).

Table 6. *Lowest and highest standardized prevalence of TT in adults in each region depending on EU.*

Region	**Lowest Prevalence (%)**	**Highest Prevalence (%)**
Afar	0.1	1.2
Benishangul Gumuz	0.3	2.5
Gambela	0.8	2.4
Oromia	0.0	2.5
SNNPR	0.0	6.1
Somali	0.0	1.3
Tigray	0.1	2.6

All of the regions had districts in which the prevalence of TT was above the WHO threshold of 0.1% (equivalent to 0.2% in adults age 15 years and over). There were 25 EU in which active trachoma was not a public health problem (TF prevalence <5%), 32 EU in which one year of antibiotic distribution and WASH efforts were needed (TF prevalence 5-9.9%), and 116 EU in which three or more years of antibiotic distribution and water and sanitation efforts were needed (TF prevalence 10% or more). The prevalence of trichiasis was above the WHO threshold (0.2% in the age group 15 years and over) in 150 EU; these EUs require a community based approach to address trichiasis. In the remaining 24 EU the prevalence of trichiasis was <0.2% and no specific interventions are required. Table 7 shows the population requiring

interventions in each region. The regions with the highest burden (highest proportion of EU with TF 10% and over) were SNNPR (90.2%), Tigray (73.3%), and Oromia (69.6%) while the lowest were Benishangul Gumuz (28.6%) and Afar (9.1%).

Table 7: *Population requiring trachoma interventions*

Region	TF prevalence (age 1-9 y)	# EU (%)	TT prevalence (age 15+ y)	# EU
Afar	<5%	3	<0.2%	3
	5-9.9%	7	0.2+%	8
	10+%	1 (9.1)		
Benishangul Gumuz	<5%	3	<0.2%	0
	5-9.9%	2	0.2%+	7
	10+%	2 (28.6)		
Gambela	<5%	0	<0.2%	0
	5-9.9%	0	0.2%+	3
	10+%	3 (100)		
Oromia	<5%	15	<0.2%	10
	5-9.9%	9	0.2%+	69
	10+%	55 (69.6)		
SNNPR	<5%	1	<0.2%	4
	5-9.9%	3	0.2%+	37
	10+%	37 (90.2)		

Somali	<5%	3	<0.2%	6
	5-9.9%	7	0.2%+	12
	10+%	8 (44.4)		
Tigray	<5%	0	<0.2%	1
	5-9.9%	4	0.2%+	14
	10+%	11 (73.3)		

Correlation of TF prevalence with TT prevalence

There was a significant positive association (r = 0.593) between the prevalence of TF and TT when all regions were combined. (Table 8) This indicates that 59% of the prevalence of TT in adults can be predicted by the presence of TF in children in these districts. TI was also associated with TF (r=0.873) and with TT (r=0.525).

Table 8. *Relationship between TF, TI and TT at the EU level*

	TF in children age 1-9 years Correlation coefficient (Significance (2 tailed)	TI in children age 1-9 years Correlation coefficient (Significance (2 tailed)	TT in adults age 15 years and older Correlation coefficient (Significance (2 tailed)
TF	1.000	0.873 (0.000)	0.593 (0.000)
TI	0.873 (0.000)	1.000	0.525 (0.000)
TT	0.593 (0.000)	0.525 (0.000)	1.000

At the regional level the correlation persisted among all the regions. Statistical significance was achieved for all regions except for Afar, Benishangul -Gumuz, and Gambela. (Table 9).

Table 9: *Correlation between TF and TT for individual regions*

Region	# EU	Correlation coefficient	Significance (2 tailed)
Afar	11	0.44	0.18
Benishangul-Gumuz	7	0.46	0.29
Gambela	3	1.00	_
Oromia	79	0.65	0.00
SNNPR	41	0.56	0.00
Somali	18	0.57	0.01
Tigray	15	0.58	0.03
All Regions	174	0.59	0.00

The correlation between TF and TT varied slightly at different levels of TF with a positive relation increasing as the prevalence of TF (using WHO intervention categories) shifted to higher groupings. (Table 10). A scatterplot of the correlation between TT and TF in all the EUs is shown in Figure 2.

Table 10. *Correlation between TF and TT at different levels of TF*

TF%	N of EU	Correlation coefficient	Significance (2 tailed)
TF<5%	25	-0.26	0.21
TF 5-9.9%	32	0.14	0.46
TF 10-29.9%	67	0.18	0.15
TF 30%+	50	0.19	0.18
All TF	174	0.59	0.00

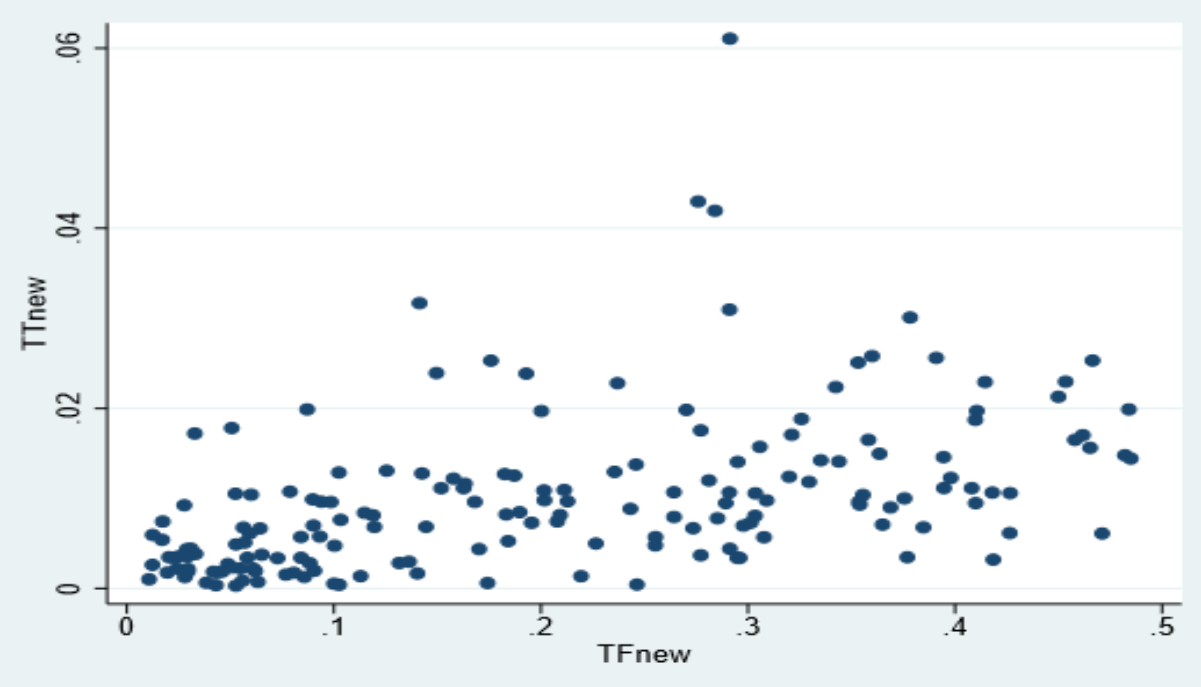

Fig 2. A scatter plot of TF and TT prevalence in all EUs

DISCUSSION

The lack of standardized, large scale data collection has limited previous efforts to assess the association between active trachoma and trichiasis. This study makes use of large data sets (GTMP) from Ethiopia, analyse them to establish if there is a relationship between trachomatous inflammations: follicular (TF) and trachomatous trichiasis (TT) in a presumed steady state and to assess if the association persists among sub-groups. A better understanding of the relationship between the prevalence of TF and the prevalence of TT together with the factors influencing this association may aid in prioritization of districts for intervention.

For the purpose of decision-making for intervention for active trachoma, WHO recommends TF (only) in children age 1-9 years since children normally are the reservoirs of *Chlamydia trachomatis* in households and communities.[23] Children in this age group are constantly and closely in contact with each other through play, facilitating transmission.[9, 23]

While the prevalence of TF was slightly higher in females than in males, the difference was not statistically significant, in line with findings of other studies.[12, 24] Pre-school boys and girls do not have gender specific roles and are at equal risk of infection. Trichiasis has a particular gender component; a previous meta-analysis has shown that women have a 1.8 fold excess risk of trichiasis compared to men[25] likely due to re-infection as an adult.

Decision making regarding trichiasis interventions is based upon assessment of the age group 15 years and above. It is recognized however that trichiasis is extremely rare in people under the age of 40 years. Nevertheless, the use of age and sex standardized data gives a true depiction of the burden of trichiasis in these EU. Pathophysiologically, trichiasis is the result of multiple episodes of active trachoma, usually in childhood, that lead to scarring of the upper tarsal conjunctiva.[1, 9] That said, not all people with multiple episodes of active trachoma continue to conjunctival scarring and trichiasis. In Gambia researchers showed that only 6.4% of people with conjunctival scarring progressed to trichiasis.[26] Thus, while it would be expected that there would be a correlation between TF prevalence and TT prevalence it was unclear how strong the relationship would be and whether the relationship was consistent across all sub-groups. Furthermore, the strength of the relationship between TF and TT may be affected by the excess prevalence of TT in women compared to men; it is likely the excess prevalence of TT in women is due to factors in adulthood, which cannot be captured in this analysis.

This study found a significant relationship between the prevalence of TF in children and the prevalence of TT in adults when analysis is done at the evaluation unit level (correlation rho, 0.59; p-value <0.0001); the rho suggests that 59% of the prevalence of TT in adults can be accounted for by the presence of TF in children. A positive correlation means that, at the EU level, when TF increases, TT will also increase.

As all surveys in this data set used the same age group for analyses of active trachoma it is reasonable to compare findings from different settings. The correlation between TF and TT was consistent across all regions in Ethiopia. The lowest correlation was found in Afar and Benishangul Gumuz; these two regions had the lowest proportion of EU with active trachoma 10% or more. The lack of a positive relationship between TF and TT when TF is <5% is interesting. TF 5% or less indicates that active trachoma is a not a public health problem; this means that it is unlikely that TF identified will be contributing to the development of conjunctival scarring and trichiasis later in life. It must be remembered that some of the trichiasis being detected in these EUs is not due to trachoma; the survey tool did not include the detection of trachomatous conjunctival scarring (TS); trichiasis can be due to other causes. It is also true that TF identified in some children may not be due to trachoma; this is particularly true in settings in which trachoma is not a public health problem, that is, where TF <5%.

Ideally, we would like to determine if the prevalence of TI in children in these endemic areas contributes to the relationship between TF and TT. There is a strong association between TF and TI (r = 0.873), both assessed in children, which is to be expected.[16] There is an association between TI and TT (r = 0.525) but this association is less than the association between TF and TT (r = 0.593) which suggests that the relationship between TF and TI is likely contributing to the relationship between TI and TT.

Environmental factors like access to water source, use of latrine, flies, socioeconomic status, nasal and ocular discharge have been found to predict the prevalence of TF [11, 12, 16] however, our study found no significant association between the prevalence of TF and a variety of water and sanitation variables. This agrees with the report done in Amhara, Ethiopia[12]which did not find any associations between trachoma and time for collecting water or between it and the availability of pit latrines. There may be many reasons we did not detect an association between TF and the water and sanitation variables. These include the variables themselves; they may

not have been robust enough for detecting differences within these communities. It may also be that there are other factors, not measured during the survey, which account for differences in TF in the EU. Data on water and sanitation variables were collected at the household level while TF data was collected at the individual level; there may be variables, not accounted for within households that may contribute to the prevalence of TF.

Our finding of no association between TF and latrine is in contrast with two studies on risk factors of trachoma in Ethiopia which found a lower odds of active trachoma in children who had pit latrines at home compared to children without pit latrines at home[27, 28]. Other studies in addition to these, have reported that improved latrines are associated with reduction in the prevalence of active trachoma.[29, 30] Previous research has demonstrated that improved latrines play an important role in reducing Musca sorbens breeding (due to less access to open human faeces) [31] but GTMP did not collect information on flies making it difficult to establish a direct relationship between flies, latrines and TF in these communities. There was a significant association between trachoma and altitude, which agreed with the result of study done in central Ethiopia. [32]

A previous study in Ethiopia suggested that adults living in household with children with active trachoma were three times as likely to have trichiasis compared to adults living in households without children having active trachoma.[12] The wide confidence interval in this study may suggest that other factors, including environmental conditions and genetics may have contributed.

There are a number of limitations to the interpretation of the findings from this study. First, this study is cross-sectional in nature, a snapshot in time; we do not know the situation prior to examination. We assume a "steady state" of trachoma in Ethiopia but we cannot state

equivocally that all EUs have been in a steady state for the last few generations because of the fast growing economy in Ethiopia.

We are measuring clinical trachoma, not infection and there is sufficient evidence to suggest that clinical active trachoma may not be a good measure of infection [9;] this is likely the case at low levels of active trachoma.

There is the loss of precision in the estimation of TT prevalence since the sampling approach used is for recruiting children aged 1-9 years. The adults enrolled in the survey for assessment of trichiasis are from the households sampled for assessment of children. Thus, the confidence intervals for the estimates of trichiasis can be quite wide. Finally, as noted earlier, the surveys measured all trichiasis rather than just trichiasis due to trachoma. It is likely that some of the trichiasis noted in these surveys were unrelated to trachoma but it is impossible to estimate the proportion. In other settings in which trachoma was endemic, non-trachomatous trichiasis was generally in the range of 5-25% of all trichiasis.

The findings from this study reveals that TF is positively associated with TT. The association between TF and TT in districts with a high prevalence of TF is of particular concern and attention given to these area may want to be a priority to other areas.

ACKNOWLEDGEMENTS

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PART D: APPENDICES TO THE DISSERTATION

Appendix 1: Request for Permission to Use GTMP Data; Expression of Interest Form

EXPRESSION OF INTEREST (EOI) TO TENDER
Part A: Organisation and contact details

1. ORGANISATION DETAILS	
1a Enter the full name of the organisation submitting EoI.	
1b Registered office address	
1c If this is a consortium submission, please enter the names of the other organisations here.	

2. CONTACT PERSON	
Contact details for enquiries (one contact point only)	
2a Name	
2b Address	
2c Daytime phone number	
2d Mobile number	
2e Email	

You may expand the boxes for Parts B and C so that they occupy no more than 2 A4 pages).
PART B – Project description

3a Research question	Research questions and possible hypotheses must: • be clearly stated; • be driven by the current knowledge gaps identified in the literature.
3b Methodology	Please provide a brief outline of the proposed methodology, explaining: • specific methods to address the research questions; • a rationale for the selection of country or countries. If the project will include an element of research capacity building in endemic countries, please describe it here.

3c Expected outcomes	Please list the expected main results of the project and their relationship to current trachoma elimination programme needs.
3d Timeline	Outline the timeline of the proposed project, including • proposed start date; and • proposed report submission date.

PART C – Experience and financial standing

4a Experience	Please describe briefly the experience that your organisation or consortium has that would enable it to complete the proposed project.
4b Resources available to undertake the work	Briefly describe resources which will be made available to this project including personnel time, space, travel costs, equipment and other materials.
4c Resources requested (please note that only limited resources for publication and dissemination of project results can be requested)	Please detail additional resources requested for publication and/or dissemination of project results.

Appendix 2: Survey Form of Primary Data Used For GTMP

Survey form

Annex 8 Survey form

[GTMP] Trachoma baseline prevalence survey

Date

(A) Household questionnaire

Recorder

Section 1: Identifying information		
1	Country	
2	Evaluation Unit [put 5-digit code in boxes]	
3	Cluster [put 2-digit, 3-digit, or 4-digit code in boxes]	
4	Household [write name of household head]	
Section 2: Household GPS		
G1	Latitude (N)	
G2	Longitude (E)	
G3	Elevation (metres)	
G4	Accuracy (metres)	
Section 3: Water, sanitation and hygiene questions		
W1	In the dry season, what is the main source of drinking-water for members of your household?	01 = Piped water into dwelling 02 = Piped water to yard/plot 03 = Public tap/standpipe 04 = Tubewell/borehole 05 = Protected dug well 06 = Unprotected dug well 07 = Protected spring 08 = Unprotected spring 09 = Rainwater collection 10 = Water vendor 11 = Surface water (e.g. river, dam, lake, canal) 99 = Other (specify)
W2	How long does it take to go there, get water, and come back?	1 = Water source in the yard 2 = Less than 30 minutes 3 = Between 30 minutes and 1 hour 4 = More than 1 hour

W3	In the dry season, what is the main source of water used by your household for washing faces?	01 = Piped water into dwelling 02 = Piped water to yard/plot 03 = Public tap/standpipe 04 = Tubewell/borehole 05 = Protected dug well 06 = Unprotected dug well 07 = Protected spring 08 = Unprotected spring 09 = Rainwater collection 10 = Water vendor 11 = Surface water (e.g. river, dam, lake, canal) 99 = Other (specify)
W4	If you collected water there to bring back to the house, how long would it take to go there, get water, and come back?	0 = All face washing done at water source 1 = Water source in the yard 2 = Less than 30 minutes 3 = Between 30 minutes and 1 hour 4 = More than 1 hour
S1	Where do you and other adults in the household usually defecate?	1 = Shared or public latrine 2 = Private latrine 3 = No structure, outside near the house 4 = No structure, in the bush or field 9 = Other
S2	Ask to see the latrine/toilet. *Observation*: What kind of toilet facility do the adults in the household use?	01 = Flush/pour flush to piped sewer system 02 = Flush/pour flush to septic tank 03 = Flush/pour flush to pit latrine 04 = Flush/pour flush to open drains 05 = Flush/pour flush to unknown place 06 = Ventilated improved pit latrine (VIP) 07 = Pit latrine with slab 08 = Pit latrine without slab/open pit 09 = Composting toilet 10 = Bucket 11 = Hanging toilet/hanging latrine 12 = No facilities or bush or field 99 = Other (specify)
H1	*Observation*: Is there a handwashing facility within 15 metres of the latrine/toilet?	0 = No 1 = Yes 5 = Not applicable (no latrine/toilet)
H2	*Observation*: At the time of the visit, is water available at the handwashing facility?	0 = No 1 = Yes 5 = Not applicable (no handwashing facility)
H3	*Observation*: At the time of the visit, is soap or ash available at the handwashing facility?	0 = No 1 = Yes 5 = Not applicable (no handwashing facility)

Annex continues over page

Annex 8

(B) Census and examination findings

Country ☐☐☐ EU ☐☐☐ Cluster ☐☐ Household ☐☐ Recorder ☐☐

List all household residents. Ask for consent to examine all residents aged 1 year and above.

ID number	Name	Sex 1 = M 2 = F	Age (years)	Examined? 1 = Yes (with consent) 2 = Absent 3 = Refused 4 = Other	Right Eye 0 = Sign absent 1 = Sign present			Left Eye 0 = Sign absent 1 = Sign present			Notes
					TT	TF	TI	TT	TF	TI	

Appendix 3: UCT Ethics Committee Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
Email: sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

11 December 2015

HREC REF: 906/2015

Prof P Courtright
Division of Ophthalmology
Room 45 H53
OMB

Dear Prof Courtright

PROJECT TITLE: RELATIONSHIP BETWEEN THE PREVALENCE OF TRACHOMATOUS INFLAMMATION IN CHILDREN (AGE 1-9 YEARS) AND THE PREVALENCE OF TRICHIASIS IN ADULTS (15 YEARS AND ABOVE) GLOBALLY AT A PRESUMED STEADY STATE (Masters-candidate-Dr E Antwi-Adjei)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30th January 2017.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the following student:- Dr E Antwi-Adjei is also involved in this project.

Please quote the HREC reference no in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Yours sincerely

pp T.Burgess

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

Hrec/ref:906/2015

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Hrec/ref:906/2015

Appendix 4: Instructions for Authors of Journal Whose Format Has Been Used

OPHTHALMIC EPIDEMIOLOGY

Accessed at:
http://www.tandfonline.com/action/authorSubmission?show=instructions&journalCode=iope20

Instructions for Authors

All submissions should be submitted at http://mc.manuscriptcentral.com/nope

All submissions should be double spaced, with consecutively numbered pages.

All abbreviations/acronyms must be defined at first use in the abstract, again at first use in the text and in each and every table or figure, regardless of seeming redundancy.

The following are the files need to make your online submission complete:

I. MANUSCRIPT FILE

1. Cover page –

a) list the title of your submission – no abbreviations or acronyms (acronyms may be considered if important for recognition of a prominent study, and in that case they should be used only after defining the acronym in the title)

b) supply a running head - a shortened version of title, not to exceed 50 characters. If the full title is 50 characters or less, they can be the same.

c) list all authors in publication order and their related affiliations,

d) indicate who is the corresponding author and the corresponding contact information (especially email),

e) financial support – list all financial support

f) list any proprietary interests or conflicts of interest for any and all authors related to this submission. "If none, please state: None of the following authors have any proprietary interests or conflicts of interest related to this submission:"; then list all the authors with no such interests. "None of the authors" suffices if no one has any such interests. Please err on the side of disclosure if it is unclear whether something is an interest or not, and please include relationships that may be perceived by others as a conflict of interest.

g) statement that this submission has not been published anywhere previously and that it is not simultaneously being considered for any other publication. Note: if the paper previously has been reviewed and rejected by another journal, please indicate so, and please indicate what criticisms were given and what changes have been made in response (as if you were revising and resubmitting to the original journal). We are open to accepting such papers if they have merit, and there is no need to hide this information.

2. Abstract – start on new page – not to exceed 250 words, define all abbreviations or acronyms used at first use, formatted into the following four sections:

a) Purpose

b) Methods

c) Results

d) Conclusion

3. Manuscript text – start on a new page. The text should not exceed 4,000 words. Define all abbreviations and acronyms at first use (even if previously defined in abstract). The text

should be divided into the following 5 sections:

a) Introduction—give the rationale for why this manuscript is important

b) Materials and Methods – should include a statement regarding adherence to the guidelines of the Declaration of Helsinki as well as giving the name of the Institutional Review Board which granted approval or which indicated approval was not needed. Any waivers granted, such as HIPAA waivers or waiver of consent, should be mentioned. Whether patients consented to participate in the study should be mentioned; if not, the reason why not should be mentioned (e.g., Institutional Review Board waiver of consent)

c) Results—summarize the key and supportive results in a clear, crisp, straightforward manner.

d) Discussion—discuss what the key findings are, how it fits in with existing knowledge on the subject, and if there alternative explanations of the observations such as bias or random error. Please include a strengths and limitations paragraph, as well as a concluding paragraph summarizing the main items of knowledge that the paper has provided and relevant applications.

e) References – Please follow the directions in Section 4 below.

4. References - cite in the text as superscript by reference number, consecutively as they appear in the text, starting with 1. Prepare a numbered reference list. Only published and accepted (in press) articles can be cited. Abstracts should be cited parenthetically within the text as should any personal communication or unpublished data. Submitted articles are not citable, and should be referenced as unpublished data. Examples:

Journal:

Mohney BG, Robertson DM, Schomberg PJ. Second nonocular tumors in survivors of heritable retinoblastoma and prior radiation therapy. *Am J Ophthalmol*. 1998;126(2):269-277.

Book:

Raven JC, Court JH, Raven J. *Manual for Raven' Progressive Matrices and Vocabulary Scales*. London: H.K. Lewis & Co. Ltd., 1986.

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