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Alison Brooks Date

Using Serology and GIS to Assess Risk Factors for Trachoma in Central Tanzania, A Novel Analysis

By

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An abstract of a thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Public Health in Global Environmental Health.

2014

Abstract

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By Alison Brooks

Abstract:
Background: Trachoma is the world's leading cause of preventable blindness affecting over 20 million people and costing over $5.3 billion USD in productivity loss. Efforts to eliminate this disease from its 57 endemic countries use the SAFE strategy to address the disease at its multiple stages.

Introduction: Efforts to eliminate trachoma have made great strides technologically and logistically. However, present sampling and clinical assessment tools lack the specificity and sensitivity necessary address areas winding down MDA and those with TF prevalence of below 9%.

Methods: Pre-MDA serological data in combination with GIS extracted data was used to build a logistical explanatory model for trachoma.

Results: The significant indicators in the model were age, village, entamoebiasis, and distance to water. Three models were built and validated; predicting 66.7% of trachoma cases in a validation set of 30 randomly selected observations.

Conclusions: Serological and GIS extracted variables were significant in the models. The successful combination of these technologies provides a frame work for other areas to follow.

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There were many people who supported me throughout this process; including Dr. Pat Lammie, Rebecca Mann, and my friends and family. I would like to give a special thanks to Dr. Diana Martin and Dr. Barry Ryan for their patience and guidance throughout this process.

Abbreviations:

MDA Mass Drug Administration

TS Trachomatous Scarring

TI Trachomatous Inflammation- Intense

TF Trachomatous Inflammation- Follicular

ROC receiver operating curve

GIS geographic information system

GPS Global Positioning System

WHO World Health Organization

NTD neglected tropical disease

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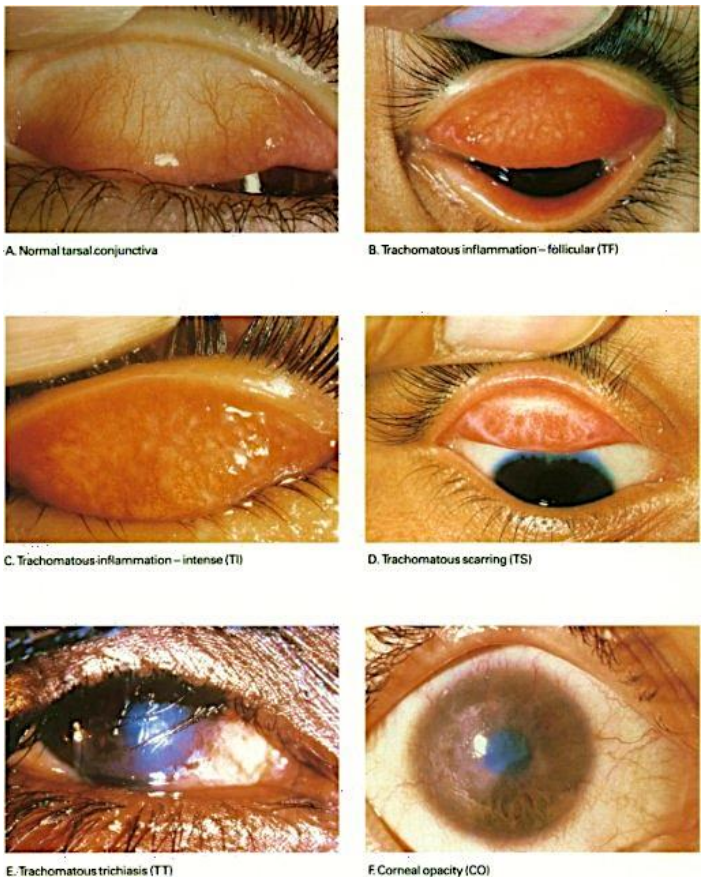
Background:

Trachoma is the third leading cause of blindness globally and the leading cause of preventable blindness in the world (Gambhir, Basáñez, Turner, Kumaresan, & Grassly, 2007). The blinding form of trachoma is a result of repeated infections of the bacteria *Chlamydia trachomatis* (Mariotti, Pascolini, & Rose-Nussbaumer, 2009). The progression of this blinding infection occurs in stages over multiple years. To identify the multiple stages of trachoma the World Health Organization (WHO) uses a simple clinical grading system (Solomon, Peeling, Foster, & Mabey, 2004). This grading system identifies the stages of trachoma infection, via a visually assessment guide (Figure 1). The grading categories are as follows:

- Trachomatous Inflammation- Follicular (TF)- the presence of 5 or more follicles in the upper tarsal conjunctiva.
- Trachomatous Inflammation-Intense (TI)- intense inflammation and thickening of the upper tarsal conjunctiva.
- Trachomatous Scarring (TS)- the presence of scarring of the upper tarsal conjunctiva.
- Trachomatous Trichiasis (TT)- one or more eyelashes rubbing against the globe of the eye.
- Corneal Opacity (CO)- the presence of a layer of opaque film over the eye limiting the amount of light able to reach the cornea.. (Solomon et al., 2004)

Figure 1: WHO Trachoma Grading Card shows a normal eyelid and the subsequent five grades of trachoma.



A. Normal tarsal conjunctiva

B. Trachomatous inflammation – follicular (TF)

C. Trachomatous inflammation – intense (TI)

D. Trachomatous scarring (TS)

E. Trachomatous trichiasis (TT)

F. Corneal opacity (CO)

It is estimated that approximately 21.4 million people globally have been affected by trachoma. This impact comes along with a predicted economic burden of $5.3 billion USD in productivity loss (Frick, Basilion, Hanson, & Colchero, 2003). Of those impacted by trachoma, about 3.8 million individuals suffer from blindness, 5.3 million have become visually impaired resulting in 39 million daily-adjusted life years (DALYs) lost. Confirmed endemic in 57 countries, trachoma is a part of a larger group of diseases coined “neglected tropical diseases” (NTDs). NTDs are a family of bacterial, parasitic, and protozoal infections that cause physical or cognitive impairment (Lavett, Lansingh, Carter, Eckert, & Silva, 2013). This subset of morbidity related diseases have been largely ignored as global health concerns in the wake of other diseases such as HIV/Aids and malaria (Mariotti et al., 2009). These wide-spread NTDs however help perpetuate

risk factors for the more well-known diseases of mortality (Feasey, Wansbrough-Jones, Mabey, & Solomon, 2010).

Trachoma specifically perpetuates cycles of poverty as it removes viable human productivity from communities. Blinding trachoma is typically an adult onset disease, impacting individual's vision at a time that they are most economically equipped to support communities (Frick, Melia, Buhrmann, & West, 2001). The effect radiates out to the larger community because of economic loss and an increased burden on caretakers (Gambhir et al., 2007). The development and perpetuation of trachoma is especially sinister as it is a preventable form of blindness that has been around since 1500 BC and requires multiple infections to progress to vision impairment.

Trachoma was identified as blinding illness as early as 1500 BC in ancient Egypt (Solomon et al., 2004). In the 19th/ early 20th centuries trachoma was a documented endemic disease in the US and Europe (Hu, Holland, & Burton, 2013). The eradication of trachoma from the present day western world is attributed to improved sanitation standards (Feibel, 2011). This eradication of trachoma by the natural evolution of hygiene practices undergirds the hypothesized links between hygiene and poverty to trachoma (Ramesh, Kovats, Haslam, Schmidt, & Gilbert, 2013).

Presently, trachoma primarily affects women and children living in arid, rural areas (McCauley, Lynch, Pounds, & West, 1990). In communities where trachoma is endemic, women are typically the primary caretakers of the infected children, putting these caretakers at greater risk of infection (King et al., 2013) (Figure 2).The ability for trachoma to persist in communities has been linked to the continued reinfection in young

populations (Solomon et al., 2004)(Solomon et al., 2004)(Solomon et al., 2004)(Solomon et al., 2004)(Solomon et al., 2004). High communicability of infectious disease among children is not unique to trachoma. Children function as community reservoirs for diarrheal diseases and the common cold, as they typically re-infect one another and share items that transmit disease (Pickering, Bartlett, & Woodward, 1986). In the case of trachoma the primary modes of transmission are fingers, flies and fomites (Figure 3). In addition to demographic factors, trachoma has been associated with dry regions lacking consistent access to water, socioeconomic factors, occupation, and facial cleanliness habits (Hsieh, Bobo, Quinn, & West, 2000).

Figure 2: Life Cycle of Trachoma.

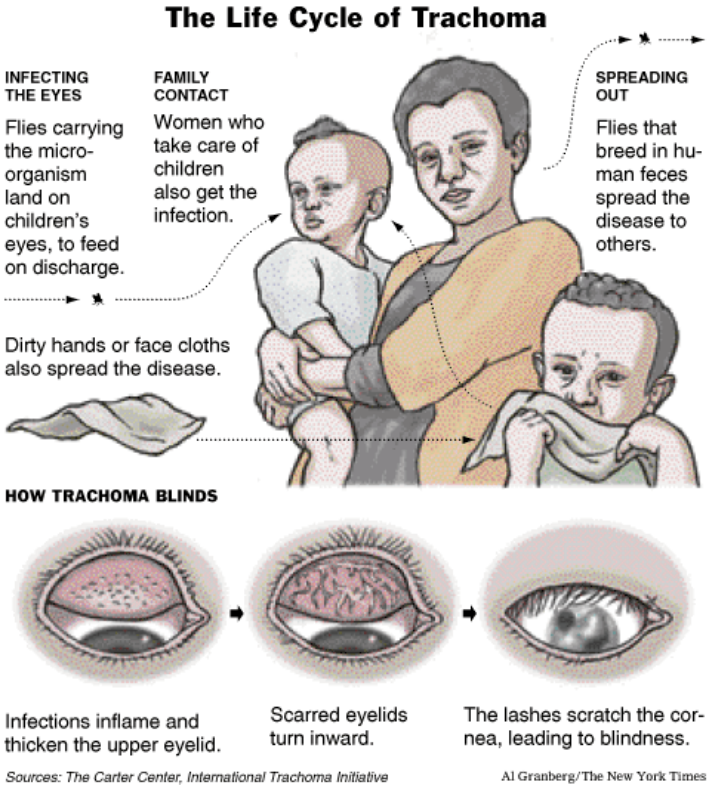
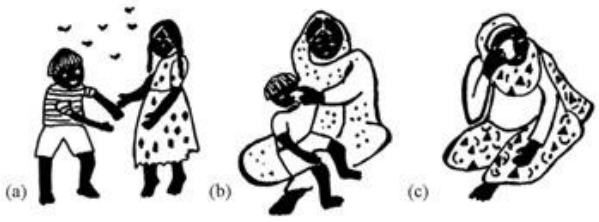


Figure 3: Fomite Transmission Diagram.



Trachoma transmission in many communities goes from children to adult. Children get infected (a); care taker wipes infected child's eyes with a cloth (b), the care taker then uses the cloth to wipe their own eyes, infecting themselves(c).

To combat trachoma in endemic areas, WHO, along with other global health organizations, partnered with the drug company Pfizer to implement a strategy for the elimination of trachoma by 2020 (Lavett, Lansingh, Carter, Eckert, & Silva, 2013). The Global Elimination of Trachoma (GET) 2020 goal endeavors to eliminate blinding trachoma as a public health problem through the mechanisms of the SAFE strategy. The approaches of the SAFE strategy address the various stages of trachoma:

- S –surgery
- A -administration of the antibiotic (azithromycin)
- F-promotion of facial cleanliness and other hygiene habits
- E -environmental improvement to increase access to water (Mariotti et al., 2009).

Surgery is performed on individuals with trichiasis (TT) to rotate eyelashes away from the globe of the eye. This alleviates the pain due to lashes rubbing against the eye and to halts the progression towards blindness. However, even after surgery re-infection and regression back to trichiasis is possible. This tertiary treatment alleviates symptoms but does not eliminate the bacteria from the eye.

To eliminate current trachoma infections, a single oral dose of the antibiotic azithromycin has been shown to be effective against the bacteria *C. trachomatis*

(Schachter et al., 1999). As part of trachoma elimination programs, yearly mass drug administration (MDA) of azithromycin (Zithromax™, donated by Pfizer) for all individuals over one year of age is advised. The MDA strategy was initially used to distribute anti-malarial drugs to entire communities as early as the 1930's(P. Hotez, 2009) (Cromwell, Ngondi, McFarland, King, & Emerson, 2012). The MDA of azithromycin works to reduce the community bacterial load and interrupt/slow transmission of *C. trachomatis*. For districts where TF prevalence in 1-9 year olds is above 10%, MDA is recommended for 3 years annually. For communities with an estimated TF prevalence of above 30%, 5 years of MDA is recommended. Districts with TF prevalence below 5% are not recommended for MDA and those with TF prevalence between 5% and 9% are recommended for re-assessment at a sub-district level. These re-assessments however are rarely conducted.

The facial cleanliness component of the SAFE strategy deals with the promotion of face washing and other hygienic behaviors. The promotion of hygiene activities is aimed at the primary prevention of trachoma. Consistent face washing has been indicated to be an effective method of trachoma prevention (Kerridge, Khan, Rehm, & Sapkota, 2013). The promotion of face washing is often coupled with the E component of SAFE, environmental modification. Programmatically, these two components work together to supply communities with the knowledge and the infrastructure to prevent the spread of the bacteria *C. trachomatis* (Kerridge et al., 2013). This occurs primarily through education and building of latrines (Gebre AJTMH 2011 and Ngondi PLoS NTDs 2008).

The antibiotic and surgery components (Cromwell et al., 2012) of SAFE have clear protocols for how to administer and when to take action. Facial cleansing and

environmental modification by their very nature differ based upon local needs and resources. Programmatically, this allows communities to develop locally appropriate strategies. From a research and evaluation perspective the lack of standard procedures make it difficult to study and quantify the impact of the F and E components of the SAFE strategy (Mariotti et al., 2009).

Introduction:

The elimination of trachoma has made great strides, particularly in the areas of logistic coordination. Trachoma has been a catalyst in the development of steering committees, annual meetings, funding streams, and partnerships with local and national ministries of health(P. J. Hotez & Pecoul, 2010). The elimination of this disease however faces major challenges including the locating and diagnosing of cases in areas that are between 5% and 9%. Within those districts and regions are often communities of varying risk to trachoma, some above the 10% threshold.

One of the key logistic considerations of eliminating trachoma is locating and estimation prevalence. To estimate the location and prevalence of trachoma three sampling strategies are primarily used: trachoma rapid assessment (TRA), acceptance sampling trachoma rapid assessment (ASTRA), and population-based prevalence survey's (PBPS) (Solomon et al., 2004)

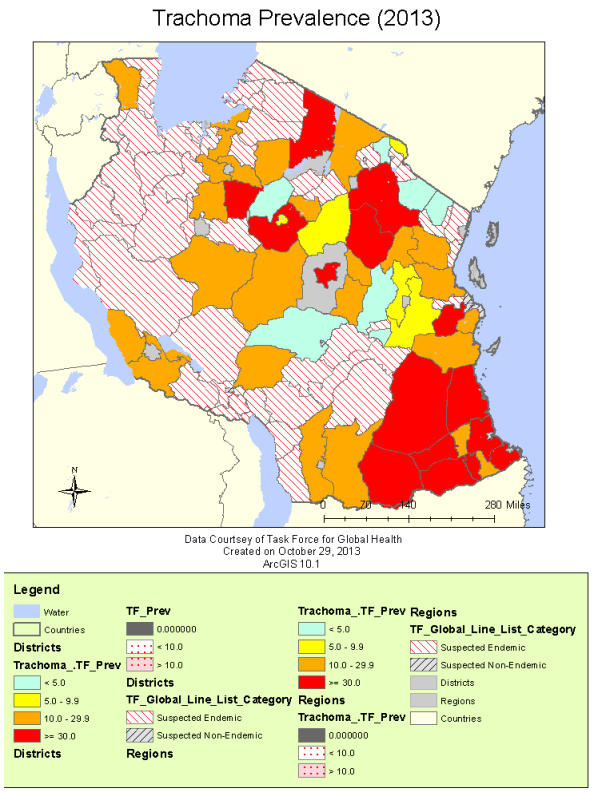
The TRA method of identifying areas that are likely to have trachoma involves a twofold approach. Communities are identified through the review of medical records, key informant interviews, and risk factor assessment. Once these communities are identified a field assessment is conducted. The field assessment includes an examination of at least 50

children per 15 houses and interviews with community members to assess their awareness of trichiasis. This method is criticized for having 'low constancy' that relies on subjective and often incomplete data. Furthermore, the quality of data produced from this sampling methodology does not rise to the standards necessary for monitoring or surveillance (Ngondi, 2009).

The ASTRA method is based upon a lot quality assurance-sampling frame, a sampling scheme based upon the size of the sampling lot. This methodology uses sound statistics but is not as viable in areas with small population size or low population density, characteristics of some trachoma endemic communities (Ngondi, 2009). PBPS is the gold standard for prevalence estimation and uses a sampling frame similar to cluster randomized trials. This method however can be costly in man power and in time. The areas where trachoma is now prevalent can be difficult to reach, making this type of sampling difficult to conduct (Ngondi, 2009). Some of the shortcomings of these sampling methodologies make it difficult to locate and assess levels of trachoma.

To address this one tool that is being implemented is the open source sharing of data through mapping technologies (Masum & Harris, 2011). Mapping of disease prevalence at a local level is a relatively new application of cartography but has been used to assess, and implement control programs for malaria, dengue, and the flu (Pascutto et al., 2000). Presently, trachoma prevalence is being mapped at the regional and district level but does not catch local variability in trachoma prevalence (Polack et al., 2005).

Figure 4: Map of District/Regional Level Trachoma Prevalence in Tanzania a tool used to estimate location of high levels of prevalence of trachoma. This map also indicates areas that are 'suspected', an indication that sampling has not yet been completed.



("Trachoma Atlas ", 2014)

In addition to some of the short comings with the sampling, the clinical grading scheme for trachoma leaves much to be desired. This system of assessment can be subjective and non-specific, producing inconsistent classifications of patients(Solomon et al., 2004). Inter-observer differences in grading are common, and follicles can be generated in response to other stimuli as well as *C. trachomatis*. Furthermore, ocular scarring has been associated with high bacterial infection rates (Burton 2007) and repeated infections of non-chlamydial bacteria (Hu 2011).

Serology:

Serology is currently being explored as a possible supplement to the clinical

grading system. It is more accurate than clinical grading and has the potential for long-term surveillance post-MDA. Clinical diagnostics are unlikely to be funded for surveillance, so the development of tests to measure trachoma transmission will be important in determining the sustainability of disease interruption. Recent work on serological assays to determine the presence of antibodies against trachoma antigens in children has shown promise for these tests in a programmatic setting. Serological data indicates if an individual has ever had trachoma and can act as a proxy for disease transmission. Antibody-based tests have the advantage over clinical exams of needing just a small volume of blood, producing consistent unbiased results.

Purpose of Analysis:

The purpose of this analysis was to develop an assessment model to look at the predictive influences serological disease prevalence and various calculations of distance to water bodies and roads. The interaction of diseases at the serology level in conjunction with environmental indicators may provide some insight on factors influencing trachoma at a village level. The information gained from this analysis may shed light on localized trachoma factors useful for surveillance and initial logistic considerations.

Methods:

Study Area:

The data used in this analysis was collected from eight communities in the Kongwa district in the Dodoma region of Tanzania (Figure 5). The Kongwa district was once hyper-endemic for trachoma and now is considered meso-endemic(Frick et al., 2001). Study villages were specifically selected because their predicted TF prevalence levels were between 5% and 9%. Data used in this analysis was collected as a base line for a larger study aimed at capturing the impact of integrated NTD programs in Tanzania.

From the eight study villages, 20 children aged 1-9 years were randomly selected from the 96 sub-village units included in the study. The sampling protocol used a Monte Carlo simulation to randomize the sample selection. From each household that a child's sample was taken an additional sample was taken from a person over the age of 9. For these analysis only participants under the age of 10, with serology and GPS point data were included, resulting in a subset of 929 observations. Data used for this analysis included seroprevalance data collected from multiplex analysis, survey results and GIS extracted data.

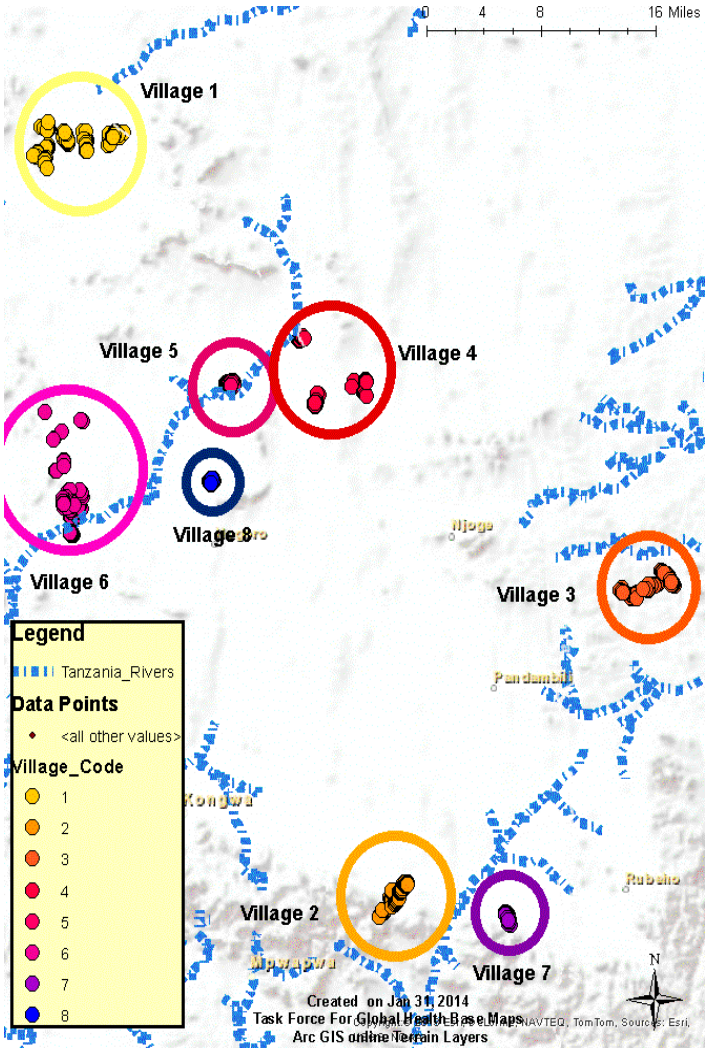
Statement of Ethics:

Institutional Review Board (IRB) approval was received from the National Institute for Medical Research (NIMR) Ethical Review Committee in Dar Es Salaam, Tanzania and the Centers for Disease Control and Prevention. Informed consent was collected from participants over the age of 18. Language appropriate written consent was provided by guardians of children ages 1-17. Children between ages 6-17 gave verbal assent for their participation.

Risks to Participants:

Physical risks to participants were minimal, involving only momentary discomforts of a finger prick and an eye swab. All participants received information about protective behaviours against NTDs.

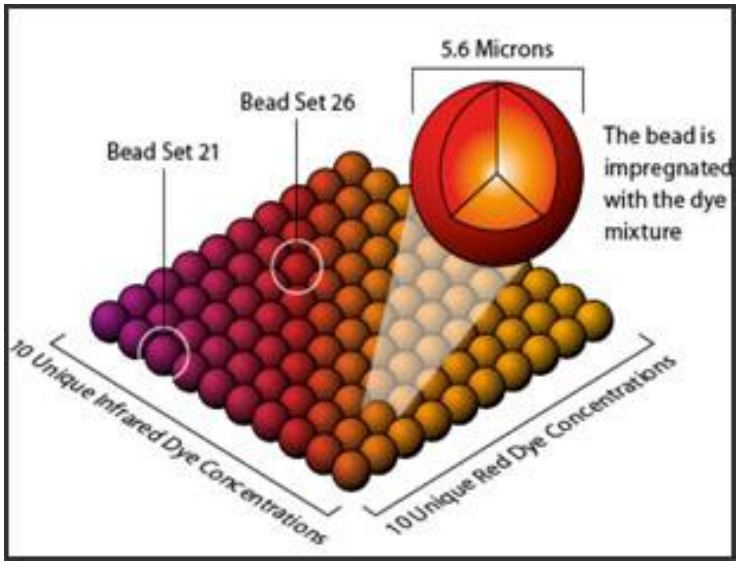
Figure 5: Map of study study area, each village is color coded and circled with the corresponding color.



Multiplex Disease/Seroprevalence:

From each participant approximately 300µl of whole blood was collected with EDTA-coated tubes by representatives of the Kongwa Trachoma Project (KTP), a local research organization. Whole blood was applied to filter paper to create dried blood spots (DBS). These DBS were transported from the field, stored and shipped to the Centers for Disease Control and Prevention (CDC) (Atlanta, GA). At the CDC, blood serum was analyzed with multiplex bead assay. The multiplex assay uses fluorescent polysterene beads coupled to antigens of interest to detect antibody responses in blood serum against 20 different pathogens. The fluorescence intensity of the signal corresponds to an antibody binding a particular antigen, and indicates an antibody response against the corresponding disease antigen and therefore a history of infection with that pathogen (Goodhew et al., 2012). The antigen florescent intensity served as to seroprevalence (i.e. percent of the population with an antibody response) for each of the disease antigens. For this analysis all disease pathogens were considered but filtered out by statistical testing of significance and biological relevance.

Figure 6: Multiplex bead array.

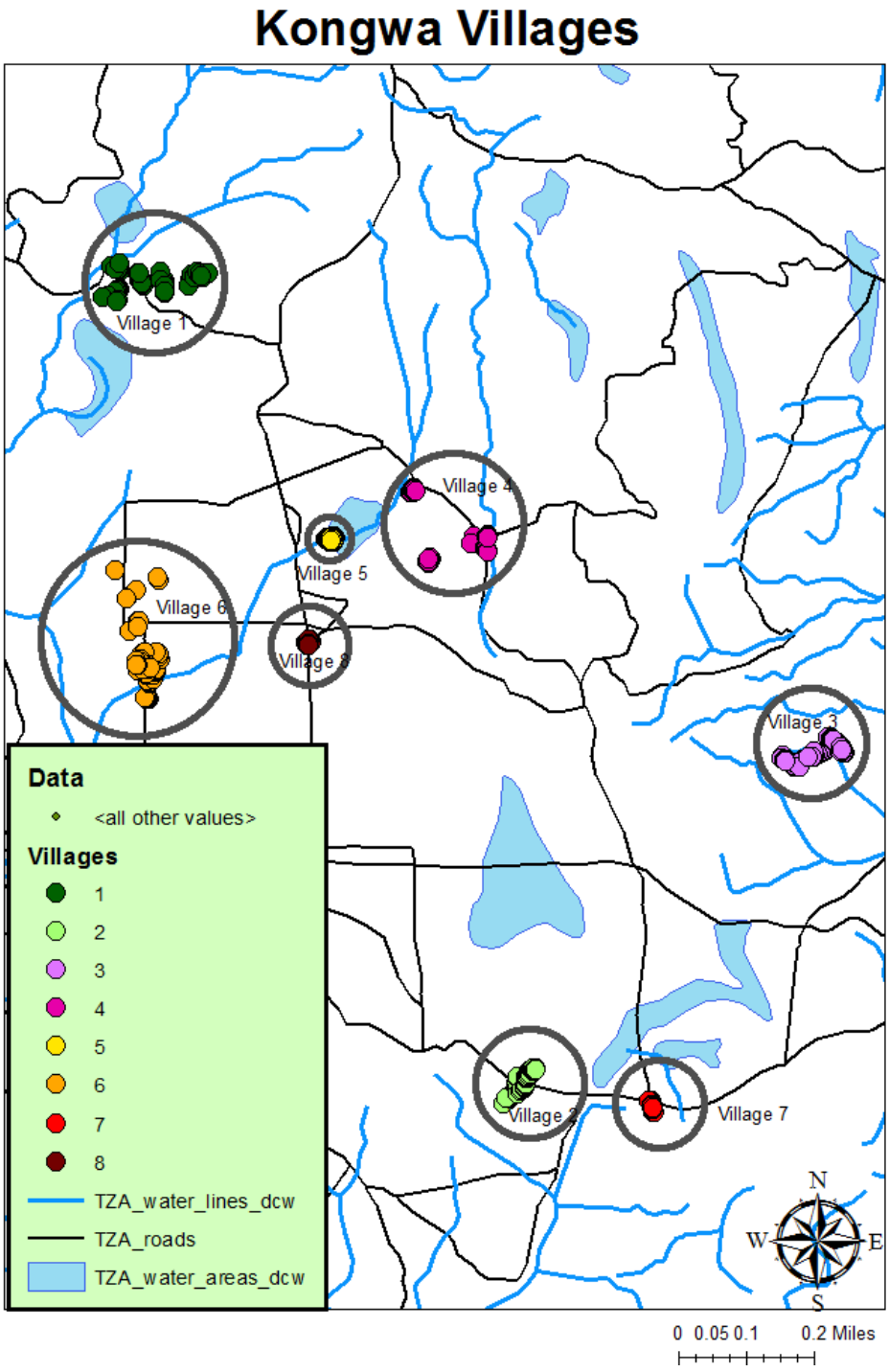


In addition to the supply of blood samples participants also completed a survey. This survey collected information on latrine access, perceived distance to water, age, gender, recent WASH interventions, and toilet type (Appendix4a).

Extracting Distance from Points:

Trachoma has been strongly correlated with water access. To try and account for village level water infrastructure with a non-subjective measure distances was calculated with Arc GIS. Map layers for roads, bodies of water, and flowing water lines were collected from DIVA GIS (Figure 7). Using Arc GIS distance calculations in meters were performed to measure the distance from each point to the respective layer of interest (water bodies, water lines, roads). These calculations were then assigned (extracted) to each point. Extracted distance calculations were exported as an Excel document and imported into SAS as continuous variables for logistic regression; see appendix for maps of individual villages.

Figure 7: Map of study area with additional water and road data.



Statistical Analysis:

In this analysis the software packages Arc GIS 10.1, Microsoft Excel 2010, SAS 9.2 were used for descriptive statistics, spatial analysis and logistic regression. The primary outcome of interest was trachoma, represented by a bivariate yes or no. For the purposes of this analysis trachoma was determined using a seroprevalence. Positive readings for both antigens pgp3 and CT694 corresponded to a yes (1) to trachoma, all other results were coded as a no (0) (Goodhew et al., 2012). A positive reading for fluorescence intensity of pgp3 was 818 and 150 for CT694. Only participants under the age of 9 with serological and location data were included as a part of this analysis. This resulted in a subset of 929 individuals who fit the necessary criteria.

Descriptive statistics were run on all 29 of the available variables using SAS 9.2 and Microsoft Excel. Univariate analysis was conducted on continuous variables: age, house distance to flowing water (calculated using GIS), house distance to water bodies (calculated using GIS), house distance to roads (calculated using GIS), *Campylobacter pylori* (Campy p 18 and p39), *Salmonella typimurium* B, *Salmonella enteriditis* D, *Streptococcus pyogenes*, leptospirosis, and measles. Frequency analysis was conducted on categorical variables: Village code, distance to water (survey), gender, toilet type, WASH Education (survey), cryptosporidiosis, giardia, lymphatic filariasis, onchocerciasis, tetanus, cysticercosis, Rift Valley fever, diphtheria, strongyloides, malaria (*Plasmodium vivax* and *P. falciparum*), entamoebiasis (*Entamoeba histolytica)*, toxoplasmosis, and dengue fever. Each variable was compared individually against the outcome of trachoma.

Dummy variables were created for distance to water and village codes. These dummy variables were created so that the numbers associated with the village and survey answer were not seen in SAS as meaningful. From the descriptive statistical analysis the disease variable entamoebiasis was identified as a potential interaction term. To adjust for this an interaction term was created for each village and the disease entamoebiasis (ENT*Village x).

Model Selection

The disease variables giardia, cryptosporidiosis, entamoebiasis, Rift Valley fever, and malaria (*P. vivax* and *P. falciparum*) were significant indicators at an alpha of 0.05. The variables giardia, diphtheria, and dengue were not significant when individually assessed but were still included as an option for model selection because of their high prevalence in this data set and their pathological association with water,(Appendix 2a-2h). Furthermore, one consistent risk factor for trachoma is distance to water. Two model selection procedures were run, one with the survey indicated distance to water and one with GIS calculated distance to water bodies and water lines. All participants in this analysis indicated that they had participated in a WASH program on the survey, so there was no variance in this parameter and no reason to consider it for model selection. In SAS 9.2 backward and forward regression procedure were used to determine the best variables for the model. The entrance criteria for the forward regression were 0.05 and for the backwards regression it was 0.10. For all model selection, village 4 was used as the reference group. This village was chosen because of its high seroprevalences of trachoma and large sample size (Figure 7, Table 1) (Appendix 1a-1c).

Figure 7: Graph of trachoma seroprevalence by village.

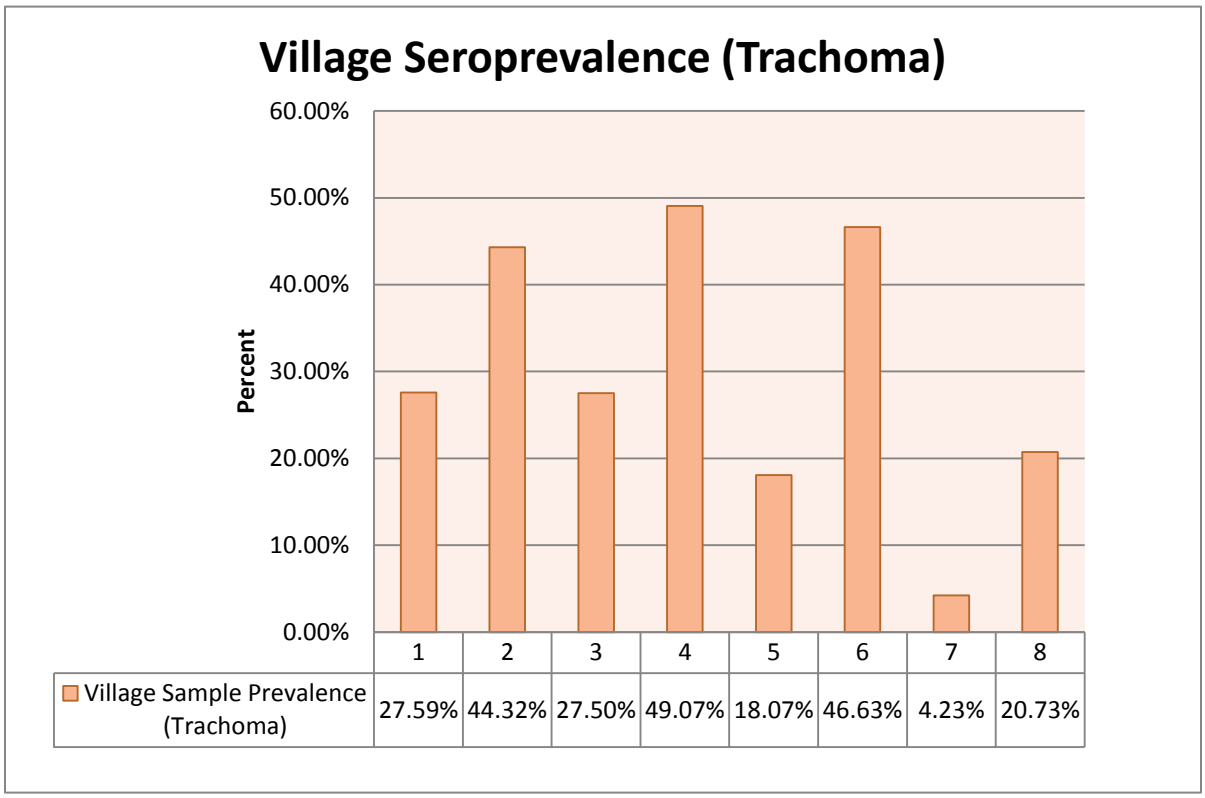


Table 1: Table of positive trachoma seroprevalence by village.

	Trachoma by Village Code							
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**
	N	**N**	**N**	**N**	**N**	**N**	**N**	**N**
Number of Samples	87	185	120	108	83	193	71	82
Number of Trachoma Cases	24	82	33	53	15	90	3	17

Validation Set:

Inclusion in the model was determined by Wald/χ2statistics and biological compatibility (Hsieh et al., 2000; Quicke et al., 2013; West et al., 1996). A validation set of 30 observations were randomly sorted and removed from the initial data set of 929. This data set was separated out before the models were created and used as a sample data set to validate the accuracy of the models. Final models were validated with the validation set and a Hosmer Lemeshow statistic.

Results:

Model Parameters:

For this analysis there were 929 observations available analysis. Of those 929, 317 displayed positive antigen response for both antigen pgp3 and CP694.

Model with quantitative distance to water, as calculated from GIS:

- Trachoma= -2.7934+ 0.01496(Age) + 0.1489 (*entamoebiasis*)+ -2.5302(Village 1) + -1.26700(Village 2) + -1.9009(Village 3) + -2.4035(Village 6) +-0.8175(Village 5)+ -2.8468(Village 7) + -3.1667(Village 8) + 2.2232 (*Entamoebiasis* *Village 1) + -0.0497(*Entamoebiasis* *Village 2)+ 0.3571(*Entamoebiasis* *Village 6) + -0.5806 (*Entamoebiasis* *Village 3) + 1.3654(*Entamoebiasis* *Village 5) + 0.4848(*Entamoebiasis* *Village 7) + 0.2770(*Entamoebiasis* *Village 8) + 0.000306 (Distance to Flowing Water) + 0.000151(Distance to Water Bodies)

In this model the significant indicators were age, villages 1, 2, 3, 6, and 8 (Appendix 3b) along with distance to flowing water and distance to water bodies. The ROC value under the curve is 0.7334.

Model with categorical water distance, as pulled from the survey:

- Trachoma= -1.9182+ 0.1526(Age) + 0.1896(*Entamoebiasis*) + -2.9757(Village 1)+ -0.2861(Village 2) + -2.4041(Village 3)+ 0.1623(Village 6) + -2.4041 (Village 5) + -2.5022(Village 7)+ -0.9987(Village 8) +2.5326 (*Entamoebiasis* *Village 1) + -0.0130(*Entamoebiasis* *Village 2)+ 0.2432(*Entamoebiasis* *Village 6) + -0.6850(*Entamoebiasis* *Village 3) + 1.3238(*Entamoebiasis* *Village 5) + 0.4713(*Entamoebiasis* *Village 7) + 0.2817(*Entamoebiasis* *Village 8)+0.000203 (Distance to Road)+ 0.4021(Distance to water is between 30mins and 1 hour) + 0.7206(Distance to Water is over 1 hour)

In this model the significant variables were age, villages 1, 3, 5, and 7 along with the category of distance to water over one hour. The ROC value under the curve for this model is 0.7300.

Validation of Results:

All of the models final had p values of above 0.05 for the Hosmer Lemoshow test indicating that the model is a better or just as good as the full model. To validate the accuracy of the models a subset of participants were set aside to further measure the goodness of fit. Both models produced the same predictive power with the validation set of 66.67%. Five out of the nine positive indicates for trachoma were predicted correctly (see appendix code, 5a). A positive trachoma value was considered to be a logit of above 0.50.

Interaction Term:

In the model the interaction term for village and entamoebiasis was only significant for villages 1 and 5. A regression analysis was run with both villages individually. Entamoebiasis was not significant in village 1 but was significat in village 5 producing an odds ratio of 4.729 with confidence interval between 1.360 and 16.441(appendix 3a). This is an indication that at the village level the disease entamoebiasis is interacting with the presence of trachoma. The overall logistic regression model had to include the interaction term entamoebiasis with all villages because of the interaction with village 5.

Discussion:

Many variables were considered in this analysis including demographic data, serological data and environmental indicators. The strongest predictors of trachoma seroprevalance were village, distance to water (GIS and Survey), age, and the serological indicator for entamoebiasis. For all of the models presented, the area under the ROC curve was over 0.700. This is an indication that the variables village, distance to water (survey and GIS), and entamoebiasis explain some of the variation regarding the presence of trachoma in the Kongwa communities in the children under 10. Furthermore, the consistent validation of results (66.7%) with both models suggests the consistent sensitivity of the indicators.

Demographic:

The demographic indicator of age is consistent in all models, and fits with risk factors indicated for the literature (Hsieh et al., 2000). As children get older their risk for

exposure to trachoma also increases. Gender was not significant in any of the models of this analysis. The analysis only included children under the age of 10. The lack of gender as a significant factor also fits with the evidence that exposure to *C. trachomatis* is linked to environmental and societal factors(King et al., 2013).

Water Distance:

The survey indicated and GIS extracted measures of distance to water were both significant when considered separately. In the model with only the calculated distance to water, every 1 meter increase resulted in a 0.000306 (Distance to Flowing Water) and 0.000151 (Distance to Water Bodies) increase in probability of a person having trachoma. In the model with survey data, those self-reporting living one hour or more away from drinking water had 2.056 increased odds of having a positive serological response to trachoma. The significance of both survey and calculated distances to water may indicate an additional use for GIS in determining risk factors for water related diseases like trachoma.

Entamoebiasis Interaction:

E. histolytica is a single-celled parasite that can cause a range of intestinal symptoms including: gastrointestinal distresses, dysentery, intestinal blockage, and abscess pain. Entamoebiasis is transmitted by fecal contamination, with food, water, hands, and fomites. A single cell of this parasite (*E. histolytica*) can be enough to cause symptoms in the body. The persistence of the disease entamoebiasis as an interaction term for village 5 may indicate a differential effect of *E. histolytica*, or that the entamoebiasis is interfering with true trachoma prevalence.

Limitations:

More information would be needed to determine if extrapolation to other areas is viable. Extrapolation of the exact model parameters to other areas may give false predictive information. There are country and village level nuances that caution against the extrapolation to other areas. The differential village interaction of the disease entamoebiasis, also indicates that there are village level differences that interfere with trachoma seroprevalence.

Strengths and Conclusions:

This analysis is the first attempt to combine serology data and GIS extracted information to better understand trachoma. The resulting significant indicators support the presently established risk factors for trachoma, and open the door for more analysis of this kind. The approach of using GIS layer to assess the impact of water infrastructure can be applied to other areas and other analysis forms. Also the presentation of the bacterium *E. histolytica* as an interaction term supports the connection between WASH diseases and may indicate that the correlation of WASH antigens and trachoma are unique to communities. This novel analysis opens the door to conducting more analysis using the best available diagnostic tools to assess disease burden in communities plagued with NTDs.

Appendix:

1a: Chart of descriptive statistics for disease seroprevalence.

Descriptive Statistics (Disease)			
Variable		Frequency	Percentage
Trachoma			
	Yes	317	34.1%
	No	612	65.9%
Giardia			
	Yes	446	48.0%
	No	483	52.0%
Crypto			
	Yes	522	56.2%
	No	407	43.8%
Tetanus			
	Yes	454	48.9%
	No	475	51.1%
Diptheria			
	Yes	146	15.7%
	No	783	84.3%
Entamoebiasis			
	Yes	547	58.9%
	No	382	41.1%
Rift Valley			0.0%
	Yes	17	1.8%
	No	912	98.2%
Malaria (P.F)			
	Yes	208	22.4%
	No	721	77.6%
Malaria (P.V)			
	Yes	13	1.4%
	No	916	98.6%

Chart 1b: Descriptive statistics of age distribution of study participants.

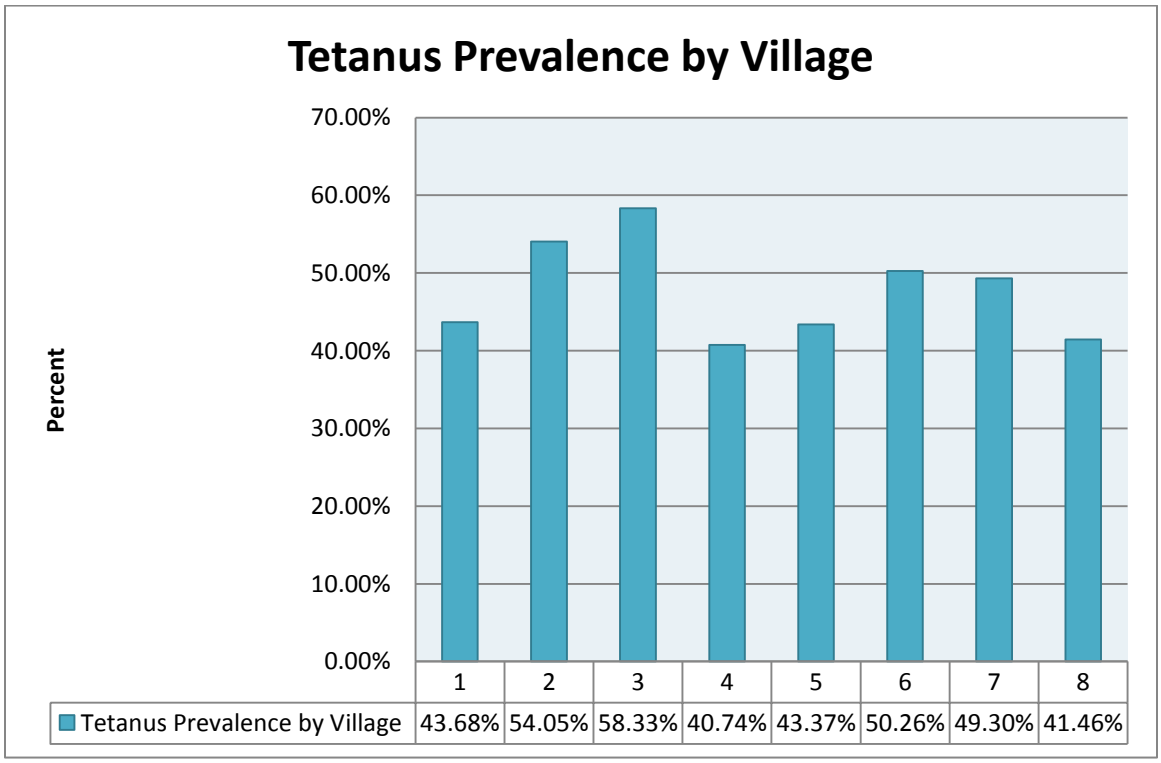
Descriptive Statistic (Age)		
Variable	Frequency	Percent
Age		
1	16	1.7%
2	35	3.8%
3	27	2.9%
4	26	2.8%
5	167	18.0%
6	177	19.1%
7	190	20.5%

8	133	14.3%
9	158	17.0%

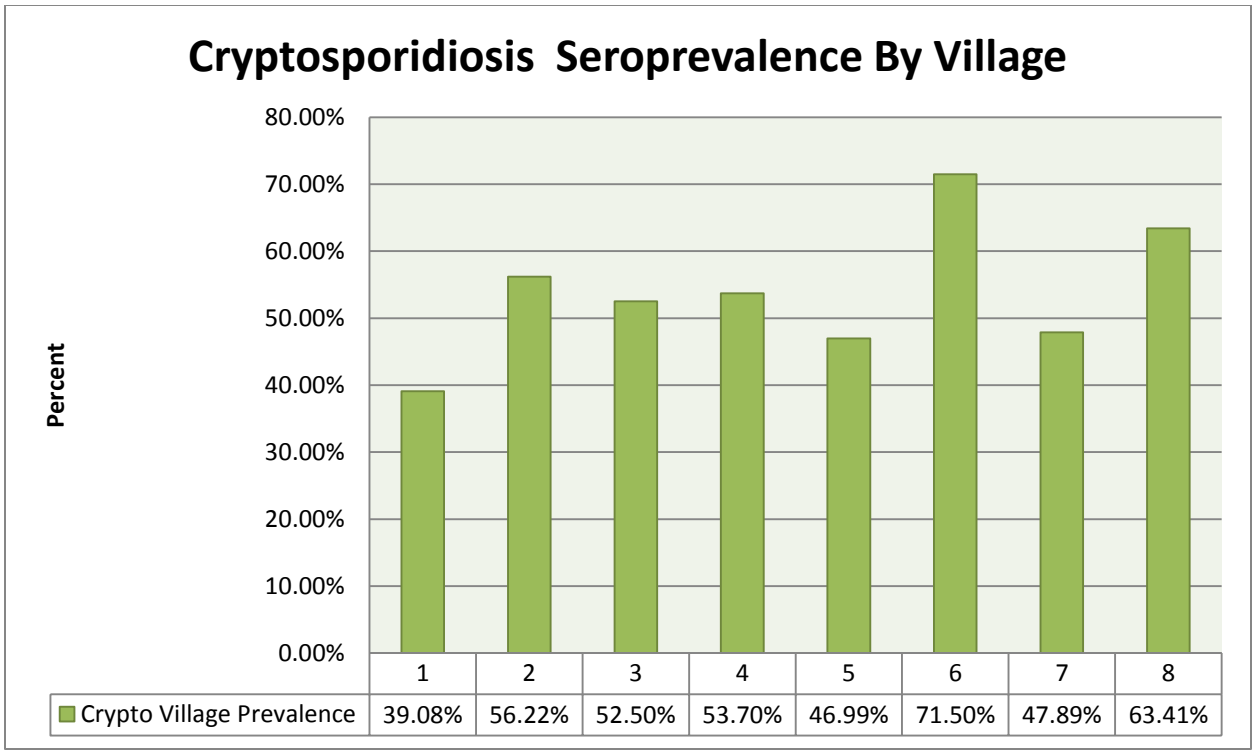
Chart 1c: Descriptive statistics of village distribution of study participants.

Descriptive Statistic (Village)		
Village		
1	**87**	**9.4%**
2	**185**	**19.9%**
3	**120**	**12.9%**
4	**108**	**11.6%**
5	**83**	**8.9%**
6	**193**	**20.8%**
7	**71**	**7.6%**
8	**82**	**8.8%**

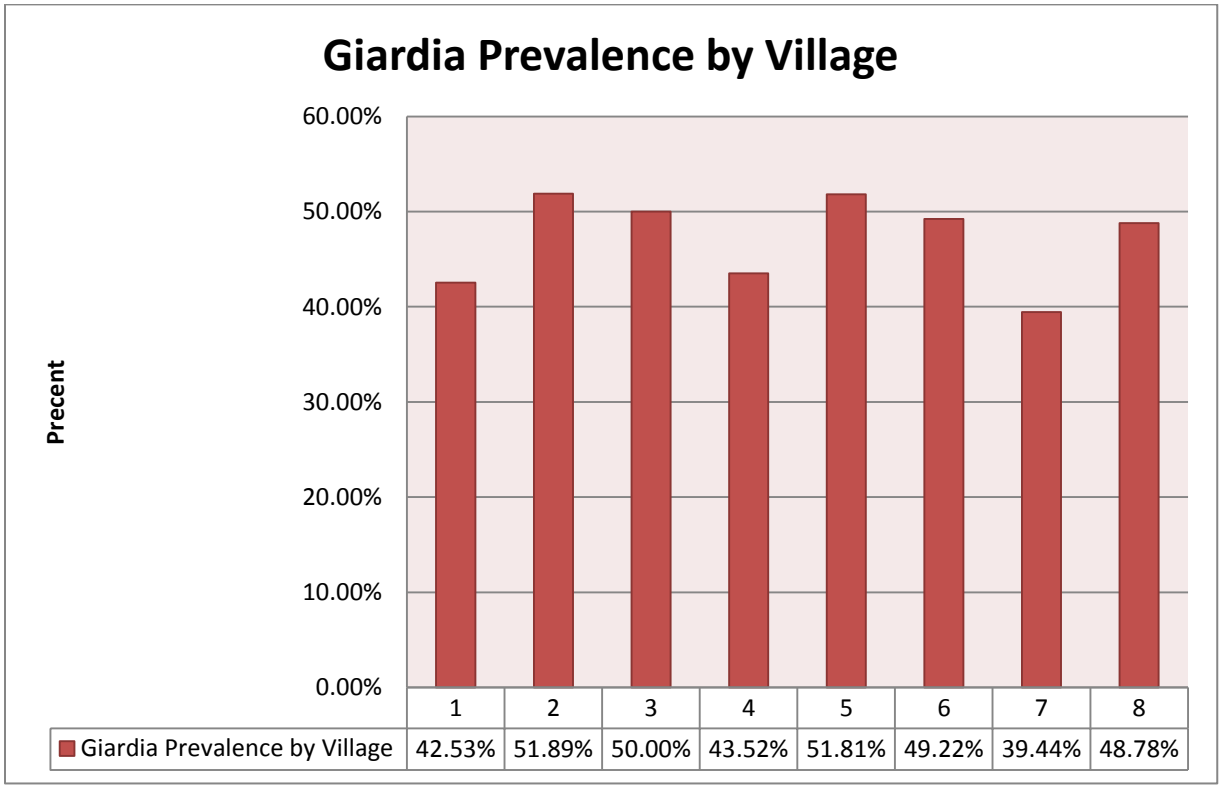
2a: Graph of trachoma prevalence by village.



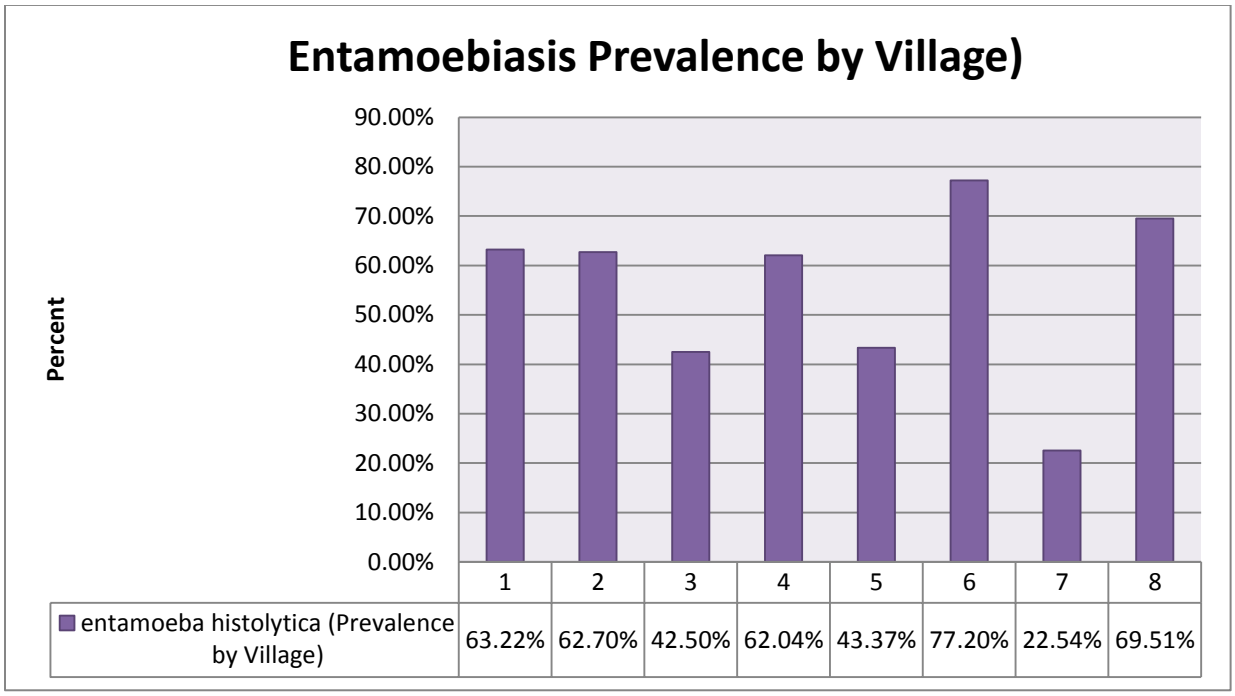
2b: Graph of cryptosporidiosis prevalence by village.



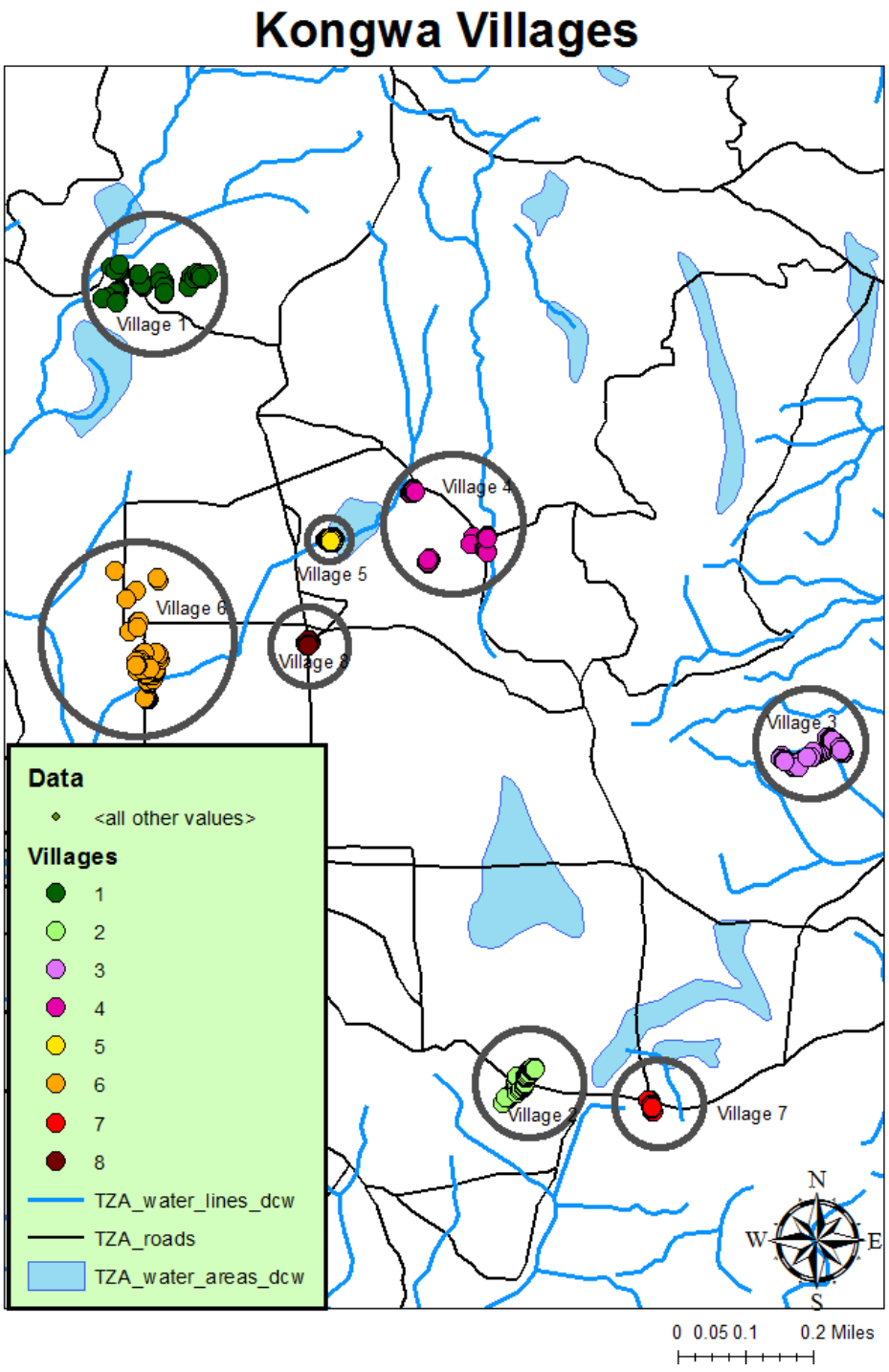
2c: Graph of giardia prevalence by village.



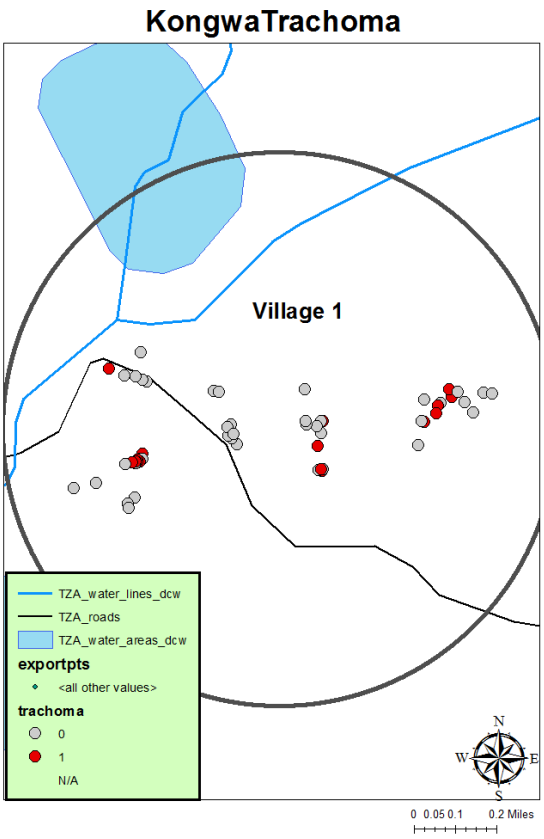
2d: Graph of entamoebiasis prevalence by village.



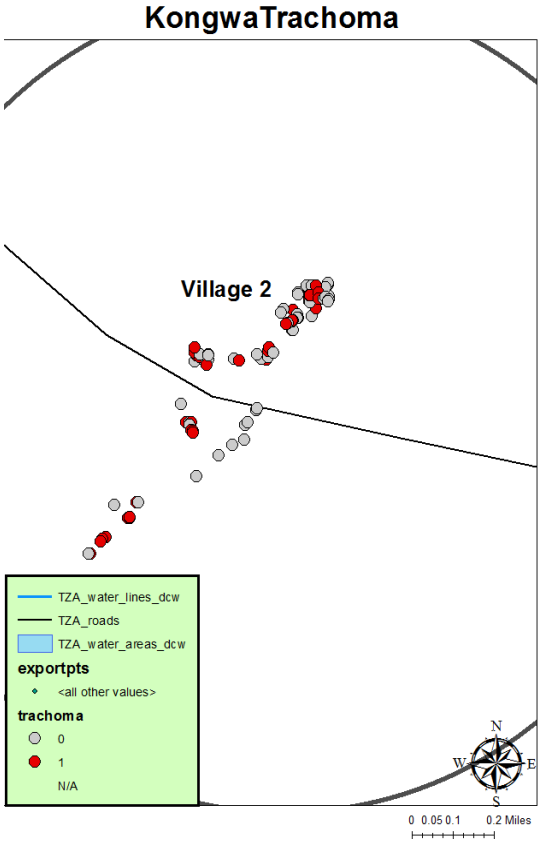
2e: Map of all study villages.



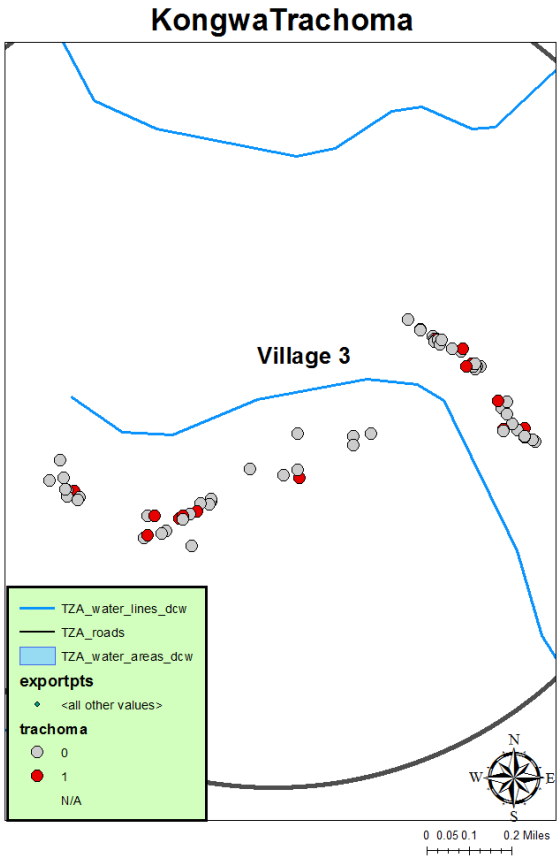
2f: Map of Village 1 homes, red dots indicate positive seroprevalence of trachoma.



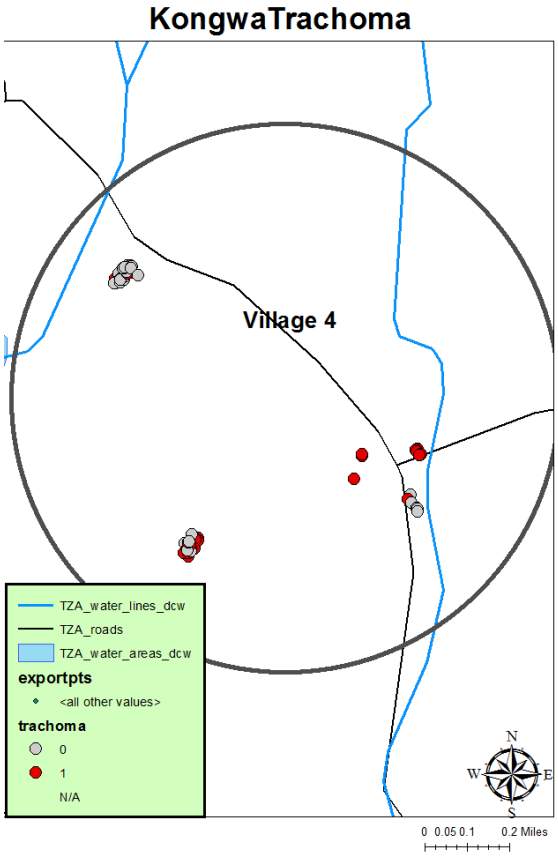
2g: Map of Village 2 homes, red dots indicate positive seroprevalence of trachoma.



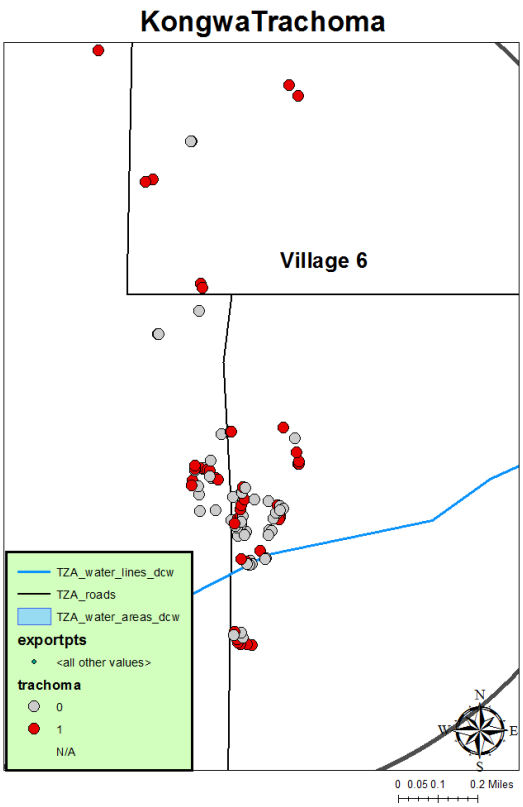
2h: Map of Village 3 homes, red dots indicate positive seroprevalence of trachoma.



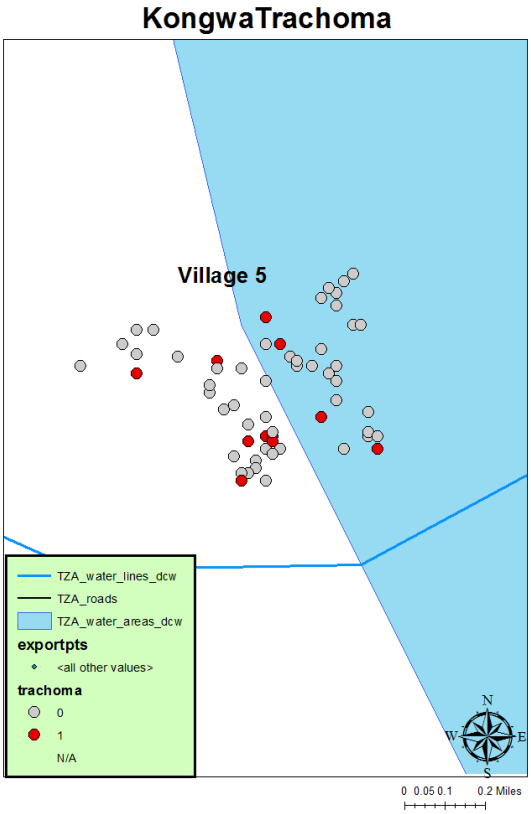
2i: Map of Village 4 homes, red dots indicate positive seroprevalence of trachoma.



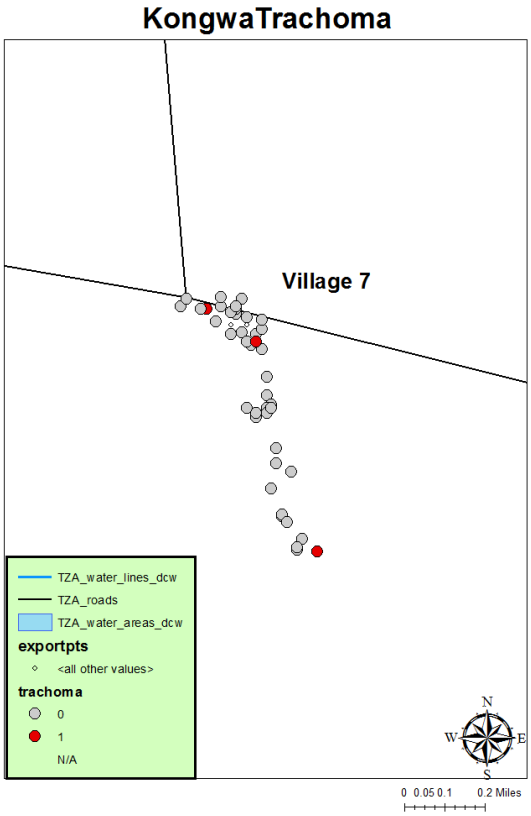
2j: Map of Village 6 homes, red dots indicate positive seroprevalence of trachoma.



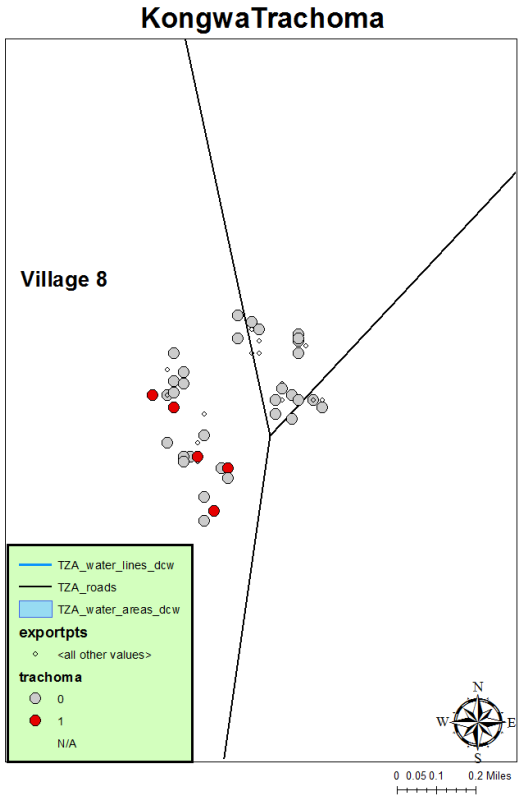
2k: Map of Village 5 homes, red dots indicate positive seroprevalence of trachoma.



2l: Map of Village 7 homes, red dots indicate positive seroprevalence of trachoma.



2m: Map of Village 8 homes, red dots indicate positive seroprevalence of trachoma.



3a:Model parameters variables *Entamoebiasis* age, village, *Entamoebiasis* *village, Calculated distance to water, and calculated distance to water bodies.

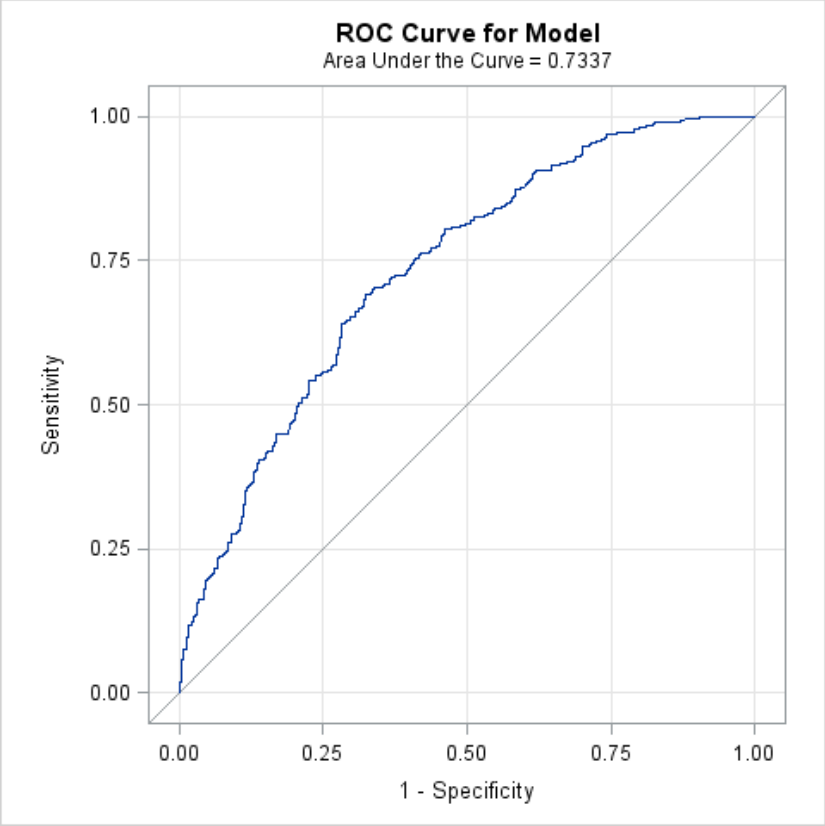
Analysis of Maximum Likelihood Estimates					
Parameter	**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
Intercept	1	-2.7934	0.6040	21.3911	<.0001
Age	1	0.1496	0.0409	13.3706	0.0003
Entamoebiasis	1	0.1489	0.4353	0.1170	0.7323
V1	1	-2.5302	1.0905	5.3836	0.0203
V2	1	-1.2670	0.4733	7.1667	0.0074
V3	1	-1.9009	0.7100	7.1680	0.0074
V6	1	-2.4035	0.8895	7.3009	0.0069
V5	1	-0.8175	0.7389	1.2238	0.2686
V7	1	-2.8468	0.8082	12.4078	0.0004
V8	1	-3.1667	0.7187	19.4121	<.0001
Ent1	1	2.2232	1.1793	3.5537	0.0594
Ent2	1	-0.0497	0.5349	0.0086	0.9259
Ent6	1	0.3571	0.5671	0.3966	0.5289
Ent3	1	-0.5806	0.6089	0.9093	0.3403
Ent5	1	1.3654	0.7718	3.1293	0.0769
Ent7	1	0.4848	1.3336	0.1322	0.7162
Ent8	1	0.2770	0.7685	0.1299	0.7185
Water_Dis_lines	1	0.000306	0.000064	22.9352	<.0001
Water_Body_distance	1	0.000151	0.000051	8.7096	0.0032

3b: Odds Ratio estimates and confidence intervals for model with variables *Entamoebiasis* age, village, *Entamoebiasis* *village, calculated distance to water, and calculated distance to water bodies.

Odds Ratio Estimates			
Effect	**Point Estimate**	**95% Wald Confidence Limits**	
Age	1.161	1.072	1.258
Entamoebiasis	1.161	0.494	2.724
V1	0.080	0.009	0.675
V2	0.282	0.111	0.712
V3	0.149	0.037	0.601

V6	0.090	0.016	0.517
V5	0.442	0.104	1.879
V7	0.058	0.012	0.283
V8	0.042	0.010	0.172
Ent1	9.236	0.916	93.183
Ent2	0.951	0.333	2.715
Ent6	1.429	0.470	4.343
Ent3	0.560	0.170	1.846
Ent5	3.917	0.863	17.782
Ent7	1.624	0.119	22.169
Ent8	1.319	0.293	5.949
Water_Dis_lines	1.000	1.000	1.000
Water_Body_distance	1.000	1.000	1.000

3c: ROC curve for model with variables *Entamoebiasis* **age, village,** *Entamoebiasis* ***village, Calculated distance to water, and calculated distance to water bodies.**



3d:Model parmeters variables *Entamoebiasis* age, village, *Entamoebiasis* *village, survey indicated distance to water and calculated distance to roads.

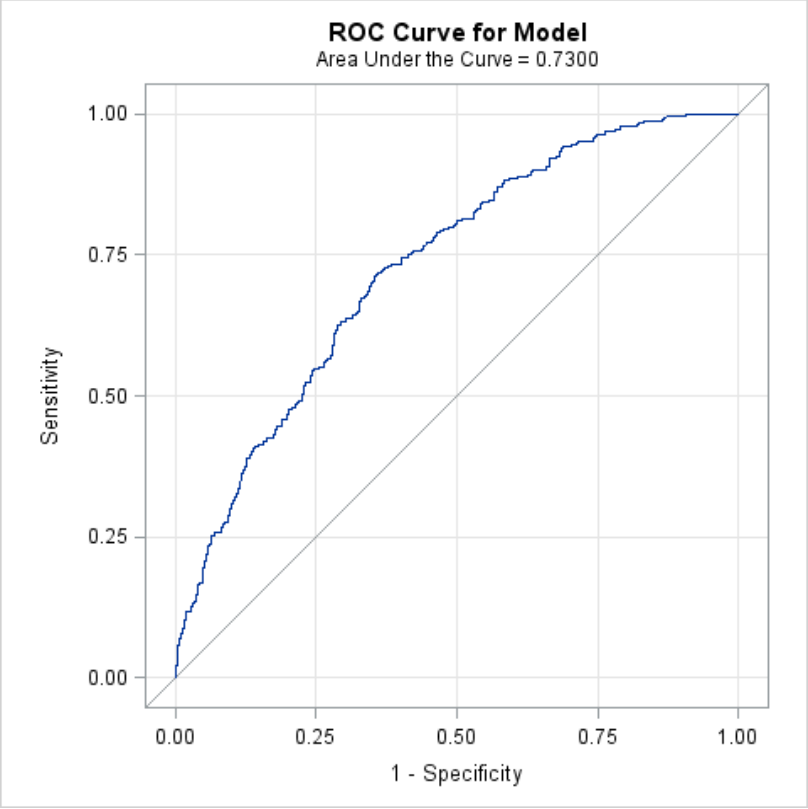
Analysis of Maximum Likelihood Estimates					
Parameter	**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
Intercept	1	-1.9182	0.4842	15.6949	<.0001
Age	1	0.1526	0.0409	13.9104	0.0002
Entamoebiasis	1	0.1896	0.4324	0.1922	0.6611
V1	1	-2.9757	1.0877	7.4848	0.0062
V2	1	-0.2861	0.5003	0.3270	0.5674
V3	1	-2.4820	0.8915	7.7508	0.0054
V6	1	0.1623	0.4911	0.1091	0.7411
V5	1	-2.4041	0.6443	13.9235	0.0002
V7	1	-2.5022	0.8196	9.3202	0.0023
V8	1	-0.9987	0.6743	2.1937	0.1386
Ent1	1	2.5326	1.1708	4.6790	0.0305
Ent2	1	-0.0130	0.5312	0.0006	0.9804
Ent6	1	0.2432	0.5637	0.1861	0.6662
Ent3	1	-0.6859	0.6070	1.2770	0.2585
Ent5	1	1.3238	0.7717	2.9429	0.0863
Ent7	1	0.4713	1.3329	0.1250	0.7236
Ent8	1	0.2817	0.7691	0.1342	0.7142
Road_distance_meters	1	0.000203	0.000093	4.7289	0.0297
30 mins distance to water	1	0.4021	0.2214	3.2995	0.0693
1 hour distance to water	1	0.7206	0.3366	4.5840	0.0323

3e: Odds radios and confidence intervals for model with variables *Entamoebiasis* age, village, *Entamoebiasis* *village, survey indicated distance to water and calculated distance to roads.

Odds Ratio Estimates			
Effect	**Point Estimate**	**95% Wald Confidence Limits**	
Age	1.165	1.075	1.262
Entamoebiasis	1.209	0.518	2.821
V1	0.051	0.006	0.430
V2	0.751	0.282	2.003
V3	0.084	0.015	0.480
V6	1.176	0.449	3.080

V5	0.090	0.026	0.319
V7	0.082	0.016	0.408
V8	0.368	0.098	1.381
Ent1	12.587	1.268	124.889
Ent2	0.987	0.349	2.795
Ent6	1.275	0.422	3.850
Ent3	0.504	0.153	1.655
Ent5	3.758	0.828	17.051
Ent7	1.602	0.118	21.841
Ent8	1.325	0.294	5.984
Road_distance_meters	1.000	1.000	1.000
30 mins distance to water	1.495	0.969	2.307
1 hour distance to water	2.056	1.063	3.976

3f: ROC curve for model with variables *Entamoebiasis* age, village, *Entamoebiasis* *village, survey indicated distance to water and calculated distance to roads.



3g:Model parameters variables *Entamoebiasis* age, village, *Entamoebiasis* *village, calculated distance to water, calculated distance to water bodies, calculated distance to roads, and survey responses to water distance.

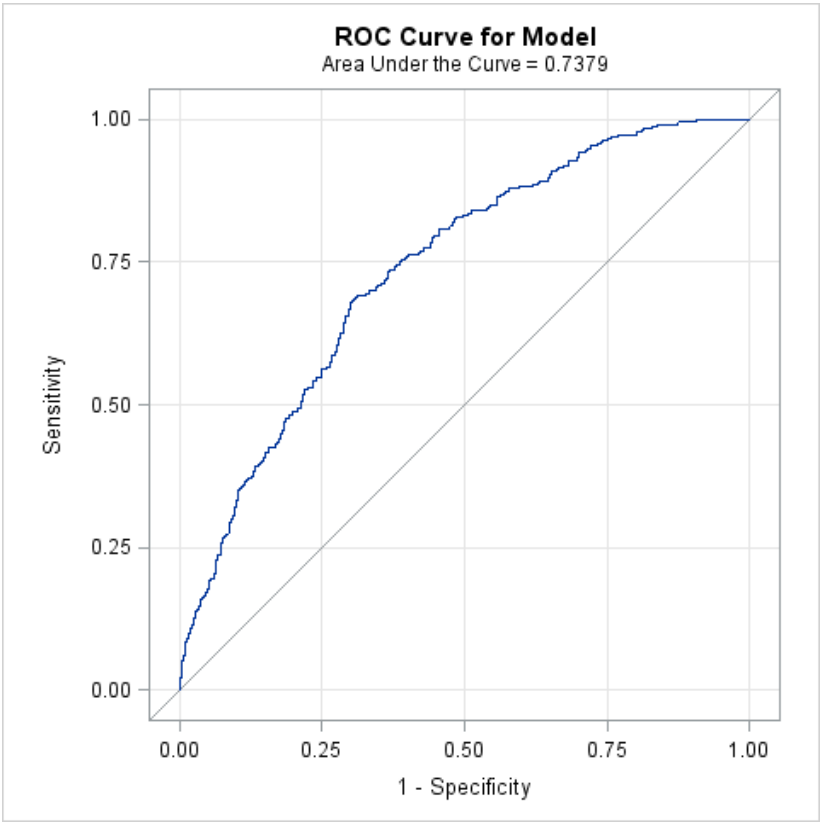
Analysis of Maximum Likelihood Estimates					
Parameter	**DF**	**Estimate**	**Standard Error**	**Wald Chi-Square**	**Pr > ChiSq**
Intercept	1	-2.8424	0.6189	21.0903	<.0001
Age	1	0.1514	0.0410	13.5985	0.0002
Entamaeba	1	0.1787	0.4469	0.1600	0.6892
V1	1	-2.6288	1.0995	5.7167	0.0168
V2	1	-1.0045	0.5828	2.9707	0.0848
V3	1	-2.6387	1.1338	5.4166	0.0199
V6	1	-1.9032	0.9610	3.9225	0.0476
V5	1	-1.1445	0.7972	2.0612	0.1511
V7	1	-2.5564	0.8398	9.2654	0.0023
V8	1	-2.5130	0.9068	7.6809	0.0056
Ent1	1	2.2506	1.1846	3.6093	0.0575
Ent2	1	-0.0500	0.5428	0.0085	0.9266
Ent6	1	0.3033	0.5760	0.2773	0.5985
Ent3	1	-0.6280	0.6178	1.0333	0.3094
Ent5	1	1.3283	0.7789	2.9080	0.0881
Ent7	1	0.4694	1.3377	0.1231	0.7257
Ent8	1	0.2732	0.7763	0.1239	0.7249
30 mins distance to water	1	0.2577	0.2288	1.2685	0.2600
1 hour distance to water	1	0.3386	0.3871	0.7652	0.3817
Distance to roads	1	0.000090	0.000109	0.6943	0.4047
Calculated Distance to flowing water	1	0.000218	0.000097	5.0987	0.0239
Calculated Distance to Water Bodies	1	0.000130	0.000053	5.8999	0.0151

3h:Odds ratios and confidence intervals for model with variables *Entamoebiasis* age, village, *Entamoebiasis* *village, calculated distance to water, calculated distance to water bodies, calculated distance to roads, and survey responses to water distance.

Odds Ratio Estimates			
Effect	**Point Estimate**	**95% Wald Confidence Limits**	
Age	1.163	1.073	1.261
Entamaeba	1.196	0.498	2.871

V1	0.072	0.008	0.623
V2	0.366	0.117	1.148
V3	0.071	0.008	0.659
V6	0.149	0.023	0.980
V5	0.318	0.067	1.519
V7	0.078	0.015	0.402
V8	0.081	0.014	0.479
Ent1	9.493	0.931	96.773
Ent2	0.951	0.328	2.756
Ent6	1.354	0.438	4.188
Ent3	0.534	0.159	1.791
Ent5	3.774	0.820	17.372
Ent7	1.599	0.116	22.004
Ent8	1.314	0.287	6.017
far2	1.294	0.826	2.026
far3	1.403	0.657	2.996
Road_distance_meters	1.000	1.000	1.000
Water_Dis_lines	1.000	1.000	1.000
Water_Body_distance	1.000	1.000	1.000

3h:ROC curve for model with variables *Entamoebiasis* age, village, *Entamoebiasis* *village, calculated distance to water, calculated distance to water bodies, calculated distance to roads, and survey responses to water distance.



4a: Survey Questions from Census

Gates T1B Demographic Survey

1. How far away is your primary water source during the dry season?

   Less than 30 minutes (1)
   30 minutes to one hour (2)
   More than one hour away (3)

2. What type of toilet facility do you have?

   Own flush toilet (1)
   Shared flush toilet (2)
   Pit latrine (3)
   Bush/field (4)
   Other (5)

3. Has there been a health education program in this village in the last year to promote face washing?

   Yes (1)
   No (0)
   Don't know (4)

4. Age:

5.. Gender:

   Male (1)
   Female (0)
   Male (1)

5a: Subset of SAS code, validation set.

```
data work.test;

   set work.valid;

   logit =  -2.7934+ 0.01496*(Age) + 0.1489*(Entamaeba)+ (V1)* -2.5302
+ (V2)* -1.26700 + (V3)* -1.9009 + (V6)* -2.4035 + (V5)*-0.8175+ (V7)*
-2.8468
+ (V8)*-3.1667 + 2.2232*(Ent1) + -0.0497*(Ent2)+
0.3571*(Ent6) + (Ent3)*-0.5806 + 1.3654*(Ent5) + 0.4848*(Ent7) +
0.2770*(Ent8) + 0.000306*(Water_Dis_Lines) +
0.000151*(Water_Body_distance);

phat = exp(logit) / (1 + exp(logit));

 if phat ge 0.5 then pred_trachoma = 1;
else pred_trachoma= 0;
 if pred_trachoma= trachoma then Match= 'yes';
 else Match='no';
```

```
      run;

data work.test2;

   set work.valid;
  logit = -1.9182+ 0.1526*(Age) + 0.1896*(Entamaeba) + (V1)*-2.9757+
(V2)*-0.2861 + (V3)*-2.4041+ 0.1623*(V6) + (V5)*-2.4041 + (V7)*-2.5022+
(V8)*-0.9987 +2.5326*(Ent1) + (Ent2)*-0.0130+ 0.2432*(Ent6) + (Ent3)*-
0.6850 + 1.3238*(Ent5) +
0.4713*(Ent7) + 0.2817*(Ent8)+ 0.000203*(Road_distance_meters)+
0.4021*(Far2) + 0.7206*(Far3);

phat = exp(logit) / (1 + exp(logit));

 if phat ge 0.5 then pred_trachoma = 1;
else pred_trachoma= 0;
if pred_trachoma= trachoma then Match= 'yes';
 else Match='no';
      run;

data work.test3;

   set work.valid;

 logit = -2.8424+ 0.1514*(Age) + 0.1787*(Entamaeba) + -2.6288*(V1)+ -
1.0045*(V2) + -2.6387*(V3)+
-1.9032*(V6) + -1.1445*(V5) + -2.5564*(V7)+ -2.5130*(V8) +2.2506*(Ent1)
+
-0.0500*(Ent2)+ 0.3033*(Ent6) + -0.6280*(Ent3) +
1.3283*(Ent5) + 0.4694*(Ent7) + 0.2732*(Ent8)+
0.00009*(Road_distance_meters)+  0.2577*(Far2) + 0.3386*(Far3)+
0.000218*(Water_Dis_Lines) + 0.000130*(Water_Body_distance);
phat = exp(logit) / (1 + exp(logit));

 if phat ge 0.5 then pred_trachoma = 1;
else pred_trachoma= 0;
if pred_trachoma= trachoma then Match= 'yes';
else Match='no';
run;
```

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